Copper Catalysis in Organic Synthesis and the Functionalization of Heteroarenes

Von der Fakultät für Mathematik, Informatik und Naturwissenschaften

der RWTH Aachen University

zur Erlangung des akademischen Grades

eines Doktors der Naturwissenschaften

genehmigte Dissertation

vorgelegt von

Master of Science

Lianghua Zou

aus Loudi, China

Berichter:

Universitätsprofessor Dr. C. Bolm

Universitätsprofessor Dr. D. Enders

Tag der mündlichen Prüfung: 23. Oktober 2013

This work was carried out from September 2009 to April 2013 under the supervision of Prof. Dr. Carsten Bolm at the Institute of Organic Chemistry, RWTH Aachen University.

I would like to thank my supervisor Prof. Dr. Carsten Bolm for giving me the opportunity to work in his group and his great guidance within my research that is presented here.

I am indebted to Prof. Dr. Dieter Enders for agreeing to be my "zweitgutachter".

Parts of this work have already been published:

1) **L.-H. Zou**, Z.-B. Dong, C. Bolm*, *Synlett* **2012**, *23*, 1613. Metal-free phosphorylations of 1,3,4-oxadiazoles and related heteroarenes.
2) **L.-H. Zou**, J. Reball, J. Mottweiler, C. Bolm*, *Chem. Commun.* **2012**, *48*, 11307. Transition metal-free direct C–H bond thiolation of 1,3,4-oxadiazoles and related heteroarenes.
3) **L.-H. Zou**, J. Mottweiler, D. L. Priebbenow, J. Wang, J. A. Stubenrauch, C. Bolm*, *Chem. Eur. J.* **2013**, *19*, 3302. Mild copper-mediated direct oxidative cross-couplings of 1,3,4-oxadiazoles with polyfluoroarenes using dioxygen as oxidant.
4) **L.-H. Zou**, A. J. Johansson, E. Zuidema, C. Bolm*, *Chem. Eur. J.* **2013**, *19*, 8144. Mechanistic insights into the copper-catalyzed Sonogashira-Hagihara-type cross-coupling reactions: sub-mol% catalyst loadings and ligand effects.
5) **L.-H. Zou**, D. L. Priebbenow, L. Wang, J. Mottweiler, C. Bolm*, *Adv. Synth. Catal.* **2013,** *355*, 2558. Copper-catalyzed synthesis of α-thiophenyl carbonyl compounds through S–S bond cleavage and C–C bond activation.

Acknowledgements

First of all, I would like to show my appreciation to my supervisor Prof. Dr. Carsten Bolm for giving me the opportunity to study and finish my doctoral thesis within his group. I am very grateful to Prof. Dr. Carsten Bolm for leading me into the wonderful world of transition metal catalysis chemistry and training me to become a researcher in this scientific field.

I am very thankful to Chinese Scholarship Council (CSC) for a predoctoral stipend. I would like to thank Jenna, Daniel, Jakob, Jens and Zhanhu for their careful correction of the manuscript. Furthermore, I would especially like to thank Ingo, Erik, Bernhard, Ankur, Julien, Astrid, Anne, Petra, Isabelle, Zhenjiang, Meg, Jiang, Zhibing, Jun, Timon, Seong Jun, Long, Wanrong, Jan and everyone else for their kind and invaluable help. I thank Susi and Pierre very much for their help in the preparation of starting materials. I also would like to give my thanks to the technical and administrative personnel in this institute, such as Dr. Wolfgang Bettray, Björn Dreindl, Dr. Gunter Geibel, Annette Müller, Christian Muschiol, Jürgen Purwin, Birgit Renardy, Dr. Christoph Räuber, Heinz Wollgarten and Rolf Winkels for their kind help. Particular appreciation is due to Dr. Adam Johannes Johansson for his kind help and great contribution with DFT calculation and mechanistic studies in my first research topic. I would like to thank Mrs. Ingrid Voss very much for all her kind help.

Finally, I am grateful to my parents, my sister Xianghua, my wife Pinggui and my daughter Sisi for their love, encouragement and understanding over the years. It is difficult for me to recall all the names here but I really appreciate all of my friends very much who have supported me during this journey.

ABSTRACT

In the research projects presented in this thesis, copper-catalyzed reactions and their application in the synthesis of a variety of useful organic compounds were investigated. Specifically, new methods were developed for the construction of C–C, C–S, C–P bonds involving the direct functionalization of heteroarenes, two of which were performed under transition metal-free reaction conditions.

The first work "The copper-catalyzed Sonogashira-Hagihara-type cross-coupling reactions" described a sub-mol% copper-catalyzed system for the cross-coupling reactions of aryl halides and terminal alkynes. In the process, all the tested copper salts were effective and it was determined that the structure of the ligand was crucial for the success of reactions. In addition, the reaction scope and mechanistic details by kinetic measurements and DFT (density functional theory) were investigated.

The second work "Copper-mediated direct oxidative cross-couplings of 1,3,4-oxadiazoles with polyfluoroarenes" showed the significant effect of copper catalysts in direct Csp^2–H/Csp^2–H coupling reactions under mild conditions. Previously, polyfluoroarene-containing 1,3,4-oxadiazoles were obtained by cyclization of 1-benzoyl-2-pentafluorobenzoylhydrazine. It was envisaged that it would be feasible to couple two C–H bonds to form this kind of biaryl compounds catalyzed by a copper catalyst. Acetonitrile as a solvent and an atmosphere of dioxygen played a key role in the reaction. A series of biaryl substrates were prepared in moderate to good yields.

The third and fourth work "Transition metal-free direct C–H bond thiolation or phosphorylation of 1,3,4-oxadiazoles and related heteroarenes" exhibited the charm of transition metal-free reactions and provided new bond forming reactions for the

functionalization of 1,3,4-oxadiazoles. In these two cases, the construction of C–S and C–P bonds was realized by the direct functionalization of a series of heteroarenes, respectively. In the former work, aside from 1,3,4-oxadiazoles, indoles, benzothiazole, *N*-phenylbenzimidazole and caffeine were also thiolated to produce the corresponding products in excellent yields. In the latter work, a variety of 2-substituted 1,3,4-oxadiazoles and related heterocycles were phosphorylated in good to excellent yields.

Furthermore, another reaction process was discovered involving copper-catalyzed reactions "Copper-catalyzed synthesis of α-thiophenyl carbonyl compounds through S–S bond cleavage and C–C bond activation", in which a new procedure for the synthesis of α-thiophenyl carbonyl compounds through copper-catalyzed dual C–C/S–S bond cleavages was reported. Despite a variety of carbon-carbon bond formations by selective C–C cleavages, however, it was the first time to form C–S bonds through selective C–C cleavage of β-diketones. Acetonitrile was crucial for the success of the reaction. Under the optimized reaction conditions, a series of α-arylthioketones and α-arylthioesters were synthesized from diaryl disulfides and β-diketones or β-ketoesters. Both alkyl and aryl functionalized β-diketones/β-ketoesters, as well as a variety of diaryl disulfides were well applied in the reaction.

Table of Contents

Introduction

1. Overview to Transition Metal Catalysis

The transition metal-catalyzed reaction has become a powerful tool in organic synthesis in the past decades, which has played an important role in developing chemical science and technology by the discovery and development of new types of chemical compounds and powerful new synthetic methodologies.[1] Commonly, transition metal catalysts are based on metals such as palladium,[2] nickel,[3] copper,[4] cobalt,[5] iron,[6] gold,[7] manganese,[8] rhodium[9] and ruthenium.[10] The importance of transition metal chemistry was recently further underlined by the three Nobel Prizes in Chemistry to Richard F. Heck, Ei-ichi Negishi and Akira Suzuki for their pioneering work on the palladium-catalyzed cross couplings (in 2010). Before seven other individuals had won Nobel Prizes in Chemistry for their seminal contributions in the field of catalysis (in 2001, 2005 and 2007).

Until now, the application of transition metal catalysts for various bond-breaking/forming reactions is well established, however, many important and often unexpected achievements continue unabated. Apart from the continuous development and application of traditional noble metals, such as palladium,[11] rhodium[12] and ruthenium,[13] other cheap metal catalysts have also attracted increasing attention recently due to their easy-handling in use and absolute competitiveness in price. Herein, some recent advances on cheap metal-catalyzed reactions including iron, nickel and cobalt will be highlighted. Copper catalyst chemistry, as the major theme of this thesis, will be introduced in detail in following subsections.

1.1 Iron, Nickel and Cobalt Chemistry-Selected Examples

1.1.1 Iron-Catalyzed Reactions

In view of the relatively high price and significant shortage of noble metal catalysts, Bolm and co-workers started to investigate the effect of iron salts as catalysts for chemical transformations several years ago. After the first publication about iron-catalyzed enantioselective oxidation of sulfides,[14] the Bolm group developed a variety of reactions using iron salts as catalysts. For example, they employed iron salts for the synthesis of optically active Sulindac,[15] oxidation/aldol coupling,[16] oxidation of C–H bonds,[17] imination of sulfoxides and sulfides,[18] *N*-arylation of sulfoximines,[19] *N*/*O*/*S*-arylation of N–H/O–H/S–H bonds,[20] and others.[21] Other groups such as Jiao,[22] Li,[23] and Singh[24] have recently also achieved significant progress in this field.

1.1.2 Nickel-Catalyzed Reactions

Recently, there has been increasing interest in nickel-catalyzed reactions.[3] In 2011, Yoshikai and co-workers developed a nickel-catalyzed and directing group-assisted [2+2+2]-cycloaddition of imine and alkynes to access a polysubstituted nitrogen-containing six-membered ring.[25] In the same year, Chatani[26] and Itami[27] reported a cycloaddition of aromatic amides to alkynes and an arylation of azoles with haloarenes using a nickel catalyst, respectively. Subsequently, Itami and co-workers disclosed coupling reactions of azoles and aryl esters[28] or phenol derivatives.[29] Later, Martin and co-workers reported another decarbonylative C–H coupling reaction for the synthesis of bis(heteroaryl) backbones.[30] In addition, a nickel-catalyzed coupling of thiomethyl-substituted 1,3-benzothiazoles with secondary alkyl Grignard reagents was developed by Ghaderi *et al.*in 2013.[31]

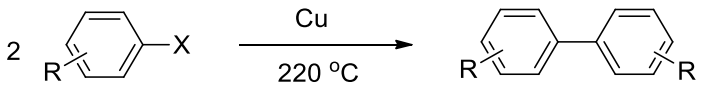
1.1.3 Cobalt-Catalyzed Reactions

Significant progress has been achieved in cobalt-catalyzed reactions in the past half century.[5] Differing from the procedures of Pd- and Ni-mediated reactions, cobalt-catalyzed cross-coupling reactions are efficient for the formation of Csp^2–Csp^2 bonds and especially interesting for couplings involving alkyl halides.[5b] Recently, the Yoshikai group has contributed pioneering work on cobalt-catalyzed C–H bond functionalization. They first developed a cobalt-catalyzed addition of (hetero)aromatic C–H bonds to alkynes.[32] Subsequently, a similar system was introduced to enable the addition of aromatic C–H bonds to styrenes.[33] In addition, they also demonstrated a cobalt-catalyzed *ortho*-arylation of aromatic imines with aryl chlorides.[34] Apart from the work by Yoshikai, other groups such as Nishimura[35] and Ackermann[36] have also impressively contributed to this field. Very recently, Guo and co-workers discovered a cobalt-porphyrin-catalyzed aerobic oxidative homocouplings of phenols.[37]

1.2 Copper Catalysis Chemistry

Since the findings of the Ullmann reaction (**Scheme 1**), copper salts as catalysts have been known for more than one century and served well for C–N, C–S, C–O and other bond formation reactions.[38] After the discovery of palladium-catalyzed cross-coupling reactions, however, copper chemistry was somewhat neglected for an extended period of time. To date, aside from being capable of catalyzing the reactions for the synthesis of arylamines, palladium catalysts have been also employed in many other bond formations.[2], [11] Despite many advantages of its use in organic synthesis, palladium chemistry itself has some drawbacks, including its cost, high toxicity and restrictions in scope. Therefore, chemists have started to reconsider other metal catalysts as an alternative for palladium. In the past years, copper has again received

increasing attention for the construction of various bonds in organic synthesis.



Scheme 1. Ulmann reaction.

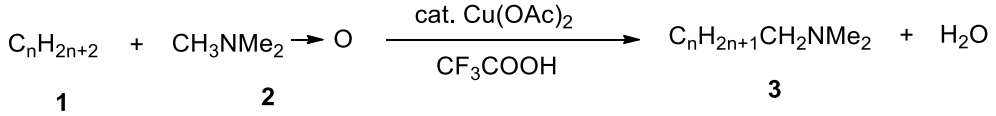
Copper catalysts fascinate chemists for several reasons. First of all, copper is very cheap compared to palladium and the total amount of copper on earth is vast. Furthermore, copper salts generally present a low toxicity. More importantly, copper can take part in cross-coupling chemistry in a way strikingly similar to palladium and possesses unique chemoselectivity and reactivity.

Although a number of reviews on copper-catalyzed reactions already exist, no specific summary on the type of reactions has been published yet.[4] In order to make it easier for the reader to find the respective synthetic applications, a detailed introduction to copper chemistry will be organized with respect to the type of reactions here.

1.2.1 Copper-Catalyzed Direct Functionalization of C–H Bonds

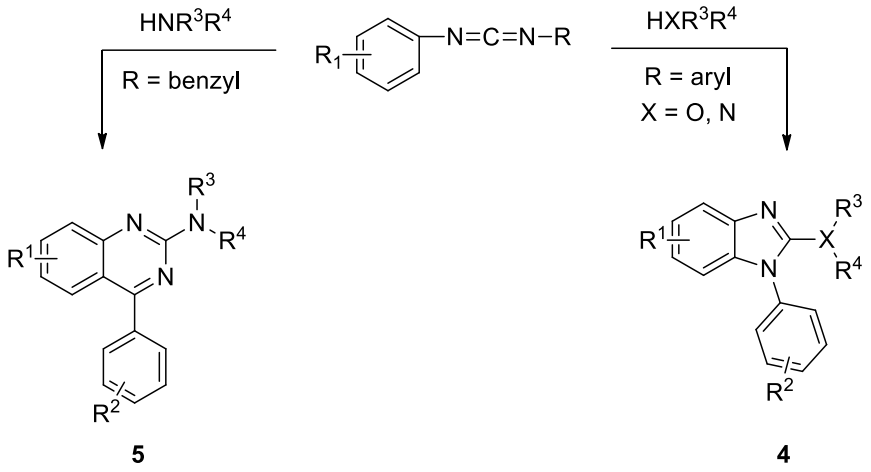
The activation of C–H bonds by transition metal complexes represents one of the most important and challenging problems in modern chemistry.[39] Transition metal-catalyzed reactions by C–H bond activation normally offer straightforward pathways for the synthesis of target molecules because the preactivation by halogenation and/or metalation is not needed. In the past years, copper salts have been broadly employed as catalysts in C–H bond activation reactions.[4] As early as 1995, Fujiwara and co-workers reported an aminomethylation of gaseous alkanes **1** with trimethylamine *N*-oxides **2** through C–H bond activation (**Scheme 2**).[40] *N*,*N*-dimethylisobutylamines or *N*,*N*-dimethylpropylamines **3** were synthesized from

propane and ethane using a $Cu(OAc)_2/CF_3COOH$ system in good yields, respectively.



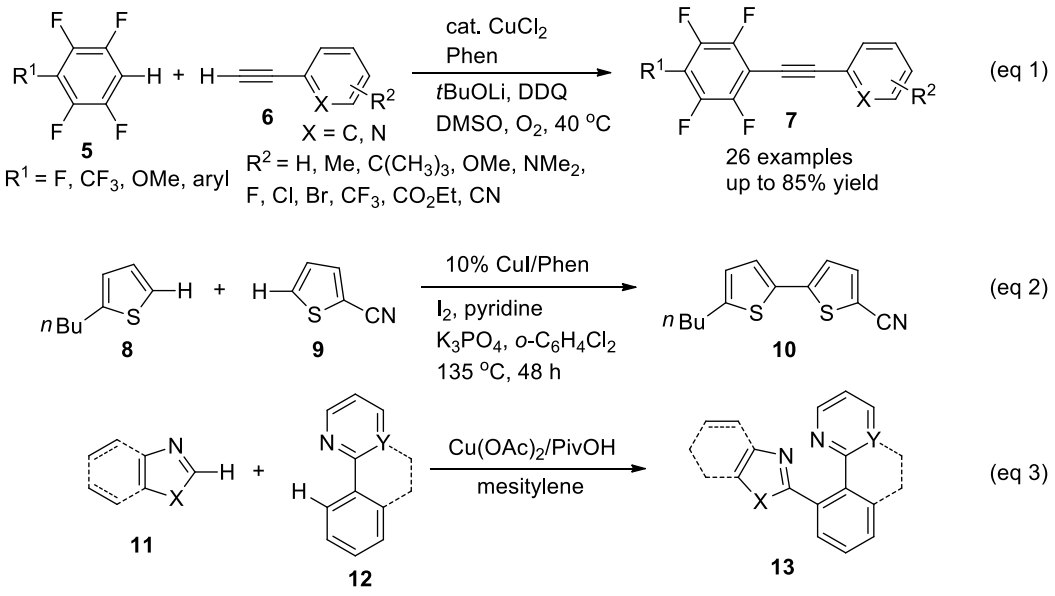
Scheme 2. Copper-catalyzed aminomethylation of gaseous alkanes through C–H bond activation.[40]

In 2010, the Bao group showed that 1,2-disubstituted benzimidazoles **4** and 1,2-disustituted quinazolines **5** could be prepared from diarylcarbodiimides and benzylphenylcarbodiimides through addition/intramolecular C–H bond activation (**Scheme 3**).[41] The reactions were performed using $Cu(OAc)_2/O_2$ as oxidants at 100 ^oC in one-pot cascade procedure.



Scheme 3. Copper(II) acetate/oxygen-mediated nucleophilic addition and intramolecular C–H activation.[41]

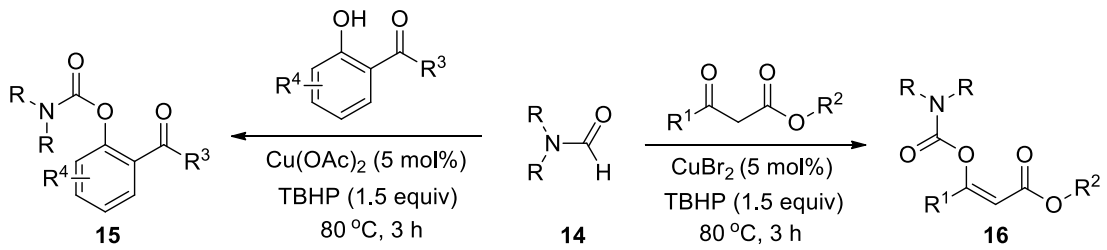
A copper-catalyzed Sonogashira-type reaction was developed by Su and co-workers in 2010. They used $CuCl_2$ as a catalyst for the direct alkynylation of electron-deficient polyfluoroarenes **5** with terminal alkynes **6** under mild conditions (**Scheme 4**, eq 1).[42] The procedure tolerated a number of functional groups using dioxygen as an oxidant.



Scheme 4. Copper-catalyzed cross-coupling reactions through dual C–H cleavages.[42], [43], [44]

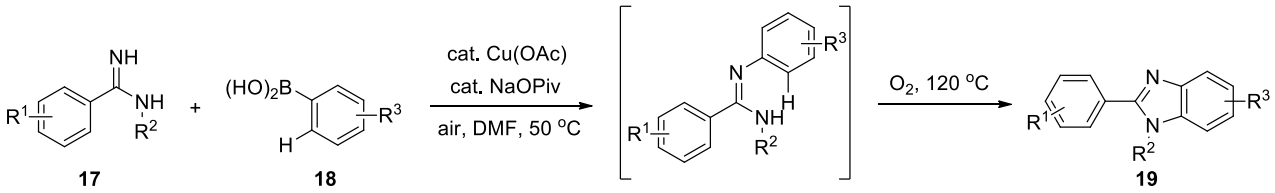
Do and Daugulis reported a general method for copper-catalyzed arene cross-dimerization, which provided a highly regioselective cross-coupling of two aromatic compounds using iodine as an oxidant (**Scheme 4**, eq 2).[43] This procedure involved the initial iodination of one arene **8** followed by arylation of the most acidic C–H bond of the other coupling component **9**. Electron-rich/poor arenes and five/six-membered heterocycles were employed in the reactions and various substitutes like esters, ketones, aldehydes, nitro- and amine-groups were well tolerated. Later, Miura and co-workers reported a copper-mediated intermolecular direct biaryl coupling between **11** and **12** (**Scheme 4**, eq 3).[44] This work showed the high potential of copper salts in direct C–H arylation chemistry and offered a new approach to biaryl compounds **13**.

Reddy and co-workers demonstrated a formamide C–H bond activation under oxidative conditions (**Scheme 5**).[45] They synthesized *Z*-enol carbamates **15** and 2-carbonyl-substituted phenol carbamates **16** using a copper catalyst and TBHP as the external oxidant in high yields.



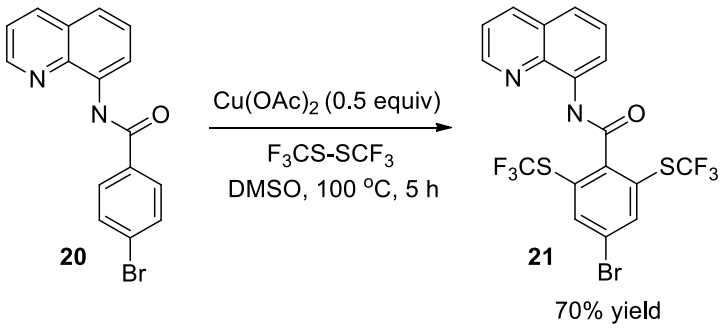
Scheme 5. Copper-catalyzed C–O coupling by direct C–H bond activation of formamides.[45]

In 2012, Neuville and co-workers showed that mono-*N*-arylation of benzamidines **17** with aryl boronic acids **18** could be effectively performed in the presence of a catalytic amount of $Cu(OAc)_2$ and NaOPiv under mild aerobic conditions. Combining this step with an intramolecular direct C–H bond functionalization, benzimidazoles **19** were synthesized using the same catalytic system but under dioxygen at 120 °C in good to excellent yields (**Scheme 6**).[46]



Scheme 6. One-pot synthesis of benzimidazoles through a copper catalyzed C–H activation/C–N bond forming process.[46]

Recently, the transition metal-catalyzed direct C–H bond functionalization through bidentate-chelation assistance such as a quinolinamide bidentate system has attracted much attention. These include arylation,[47] alkylation,[26], [47b], [48] ethynylation,[49] sulfenylation,[50] and alkoxylation.[51] Among them, a copper-promoted sulfenylation of Csp^2–H bonds was developed by Daugulis and co-workers in 2012 (**Scheme 7**).[50] The reaction was performed using disulfide reagents and $Cu(OAc)_2$ in DMSO with the assistance of an auxiliary at 90–130 °C.



Scheme 7. Copper-promoted sulfenylation of Csp^2–H bonds.[50]

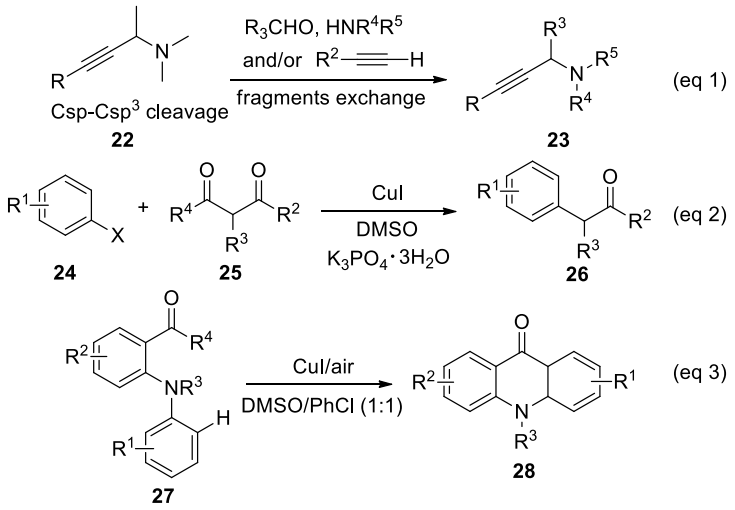
1.2.2 Copper-Catalyzed Reactions Through C–C Bond Cleavage

Typically, C–C σ-bonds are considered to be relatively inert bonds. Doubtlessly, transition metal-catalyzed reactions through C–C bond cleavage fascinate chemists due to their high selectivity and diversity. In the past years, a variety of selective C–C cleavages have been reported.[52]

Recently, Nakamura and co-workers discovered that substitution reactions of propargylic amines **22** could proceed in the presence of copper(I) catalysts (**Scheme 8**, eq 1).[53] Mechanistic studies showed that Csp–Csp^3 bond cleavage assisted by nitrogen lone-pair electrons was essential for the reaction and the resulting iminium intermediates underwent amine exchange, aldehyde exchange and alkyne addition reactions. Furthermore, aside from reconstructing propargylic amines, this transformation was also effective for asymmetric induction of racemic compounds in the presence of chiral catalysts.

In 2010, He *et al.* discovered an efficient arylation/C–C bond activation process, in which the reaction of β-diketones **25** with aryl iodides or aryl bromides **24** reacted readily in the presence of Cu(I) or Cu(II) salts in DMSO (**Scheme 8**, eq 2).[54] Trace amounts of H_2O were critical for the activation of the C–C bond. Under the optimized reaction conditions, various α-aryl ketones **26** could be efficiently synthesized.

A copper-catalyzed approach for the synthesis of acridones **28** through C–C bond cleavage and intramolecular cyclization of **27** was very recently reported by Zhou and co-workers using air as the oxidant under neutral conditions (**Scheme 8**, eq 3).[55]



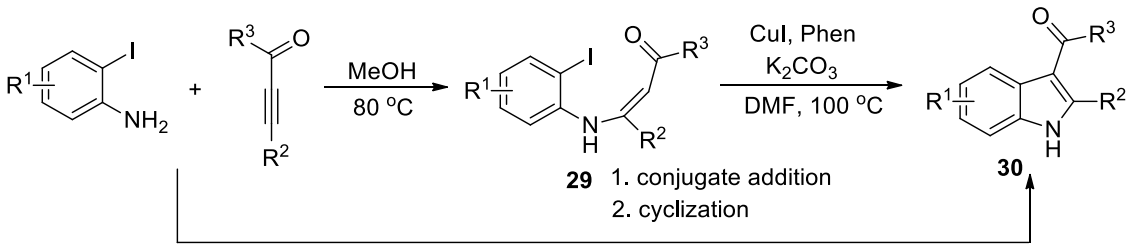
Scheme 8. Copper-catalyzed reactions through C–C bond cleavage.[53], [54], [55]

1.2.3 Copper-Catalyzed Cyclization Reactions

Transition metal-catalyzed cyclization reactions are very attractive to organic chemists due to their applications for the preparation of heteroatom-containing products. Heteroatom-containing ring cores are known for their biological activity in a number of compounds such as the potent vasodilator amauromine.[56] Here a short review on recent copper-catalyzed cyclization reactions is presented.

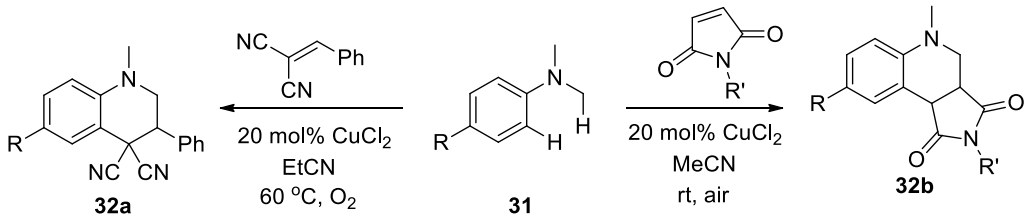
1.2.3.1 Through C–C Bond Formation

In 2009, Cacchi and co-workers[57] reported a copper-catalyzed cyclization of *N*-(2-iodoaryl)enamiones **29** for the synthesis of 3-aroylindoles **30** (**Scheme 9**). A variety of useful functionalities including ether-, keto-, cyano-, bromo-, and chloro-substituents were well tolerated.



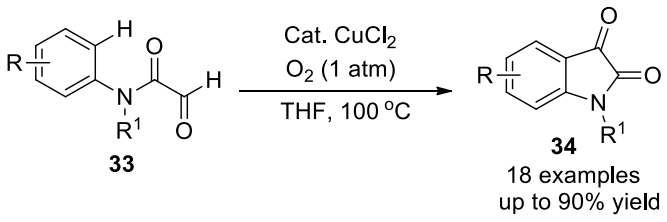
Scheme 9. Copper-catalyzed cyclization of *N*-(2-iodoaryl)enamiones.[57]

Later, Hirano, Miura and co-workers[58] developed a copper-catalyzed oxidative direct cyclization of *N*-methylanilines **31** with electron-deficient alkenes for the synthesis of corresponding tetrahydroquinolines **32a** and **32b** in good yields (**Scheme 10**). The procedure involved maleimides and benzylidene malononitriles through sp^3 and sp^2 C–H bond cleavage.



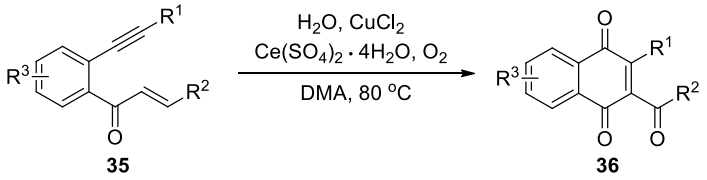
Scheme 10. Copper-catalyzed oxidative direct cyclization of *N*-methylanilines.[58]

A copper-catalyzed intramolecular C–H oxidation/acylation of starting material **33** was presented by Li and co-workers[59] for the synthesis of indoline-2,3-diones **34** (**Scheme 11**). A variety of functional groups were well tolerated under the optimized reaction conditions.



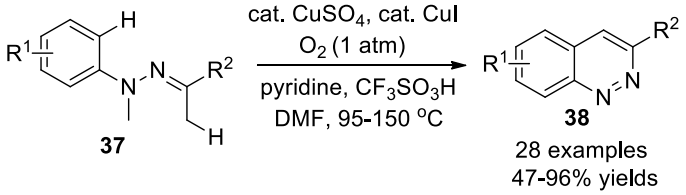
Scheme 11. Copper-catalyzed intramolecular C–H oxidation/acylation.[59]

In 2011, the Li group[60] demonstrated a copper-catalyzed intramolecular oxidative 6-*exo*-trig cyclization of 1,6-enynes **35** in the presence of H_2O and O_2 (**Scheme 12**). This was the first example of a copper-catalyzed enyne oxidative cyclization for constructing 1,4-naphthoquinones **36** by the incorporation of two oxygen atoms into the organic framework from molecular oxygen and water.



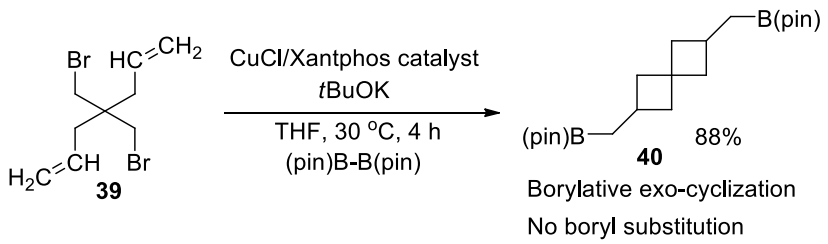
Scheme 12. Copper-catalyzed intramolecular oxidative 6-*exo*-trig cyclization of 1,6-enynes.[60]

Recently, Zhang *et al.*[61] presented a copper-catalyzed aerobic dehydrogenative cyclization of **37** for the synthesis of cinnolines **38** (**Scheme 13**). This transformation was the first example on copper-catalyzed coupling reactions of hydrazones through a Csp^3–H bond functionalization pathway.



Scheme 13. Copper-catalyzed aerobic dehydrogenative cyclization leading to cinnolines.[61]

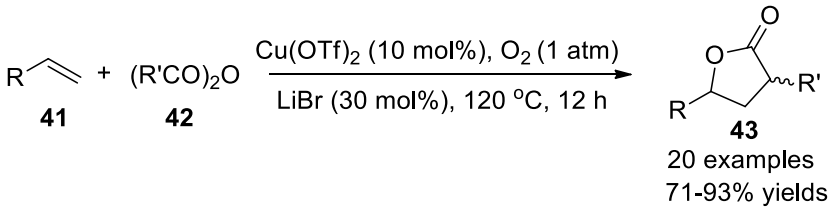
Ito and co-workers[62] reported a copper(I)-catalyzed borylative *exo*-cyclization of alkenyl halides **39** very recently (**Scheme 14**). The reaction involved the regioselective addition of a borylcopper(I) intermediate to unactivated terminal alkenes, followed by the intramolecular substitution of the resulting alkylcopper(I) moiety for the halide leaving groups. Various alkylboronates **40** containing strained cycloalkyl structures were synthesized from simple starting materials.



Scheme 14. Copper(I)-catalyzed borylative exo-cyclization of alkenyl halides.[62]

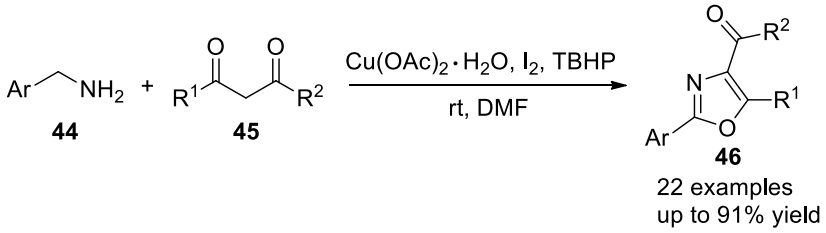
1.2.3.2 Through C–O Bond Formation

In 2010, Jiang and co-workers[63] discovered a copper-catalyzed intermolecular oxidative [3+2] cycloaddition between alkenes **41** and anhydrides **42** using oxygen as the sole oxidant (**Scheme 15**). The reaction provided a new synthetic approach to γ-lactones **43** in good to excellent yields.



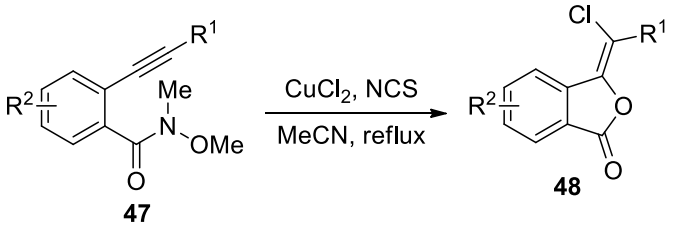
Scheme 15. Copper-catalyzed intermolecular oxidative [3+2] cycloaddition between alkenes and anhydrides.[63]

In the same year, a facile synthesis of polysubstituted oxazoles **44** through copper-catalyzed tandem oxidative cyclization between **44** and **45** was developed by Wang and co-workers[64] (**Scheme 16**). From readily available starting materials, various oxazole derivatives **46** were synthesized under mild conditions.



Scheme 16. Synthesis of polysubstituted oxazoles through copper-catalyzed tandem oxidative cyclization.[64]

In 2011, Miyata and co-workers[65] reported a $CuCl_2$-mediated cyclization reaction of *N*-alkoxy-*ortho*-alkynylbenzamides **47** (**Scheme 17**). Under the optimized reaction conditions, 3-(chloromethylene)isobenzofuran-1-ones **48** were exclusively obtained through *5-exo-dig* cyclization in moderate to excellent yields. This approach was further employed to synthesize a biaryl compound by Suzuki-Miyaura reaction.

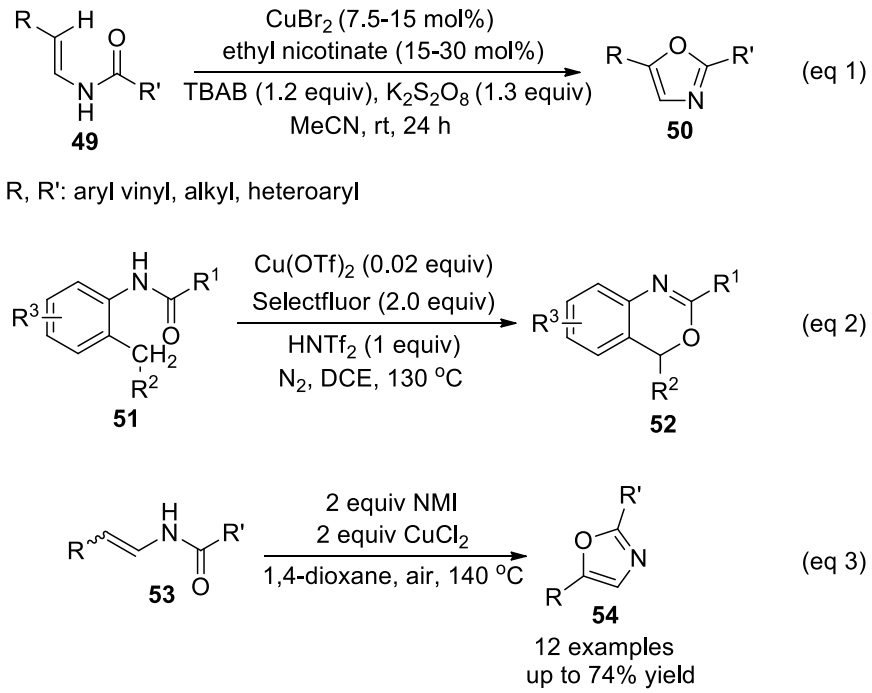


Scheme 17. $CuCl_2$-mediated cyclization reaction of *N*-alkoxy-*ortho*-alkynylbenzamides.[65]

Later, the Buchwald group[66] developed a copper(II)-catalyzed oxidative cyclization of enamides **49** leading to 2,5-disubstituted oxazoles **50** through vinylic C–H functionalization (**Scheme 18**, eq 1). Various 2,5-disubstituted oxazoles **50** bearing aryl, vinyl, alkyl, and heteroaryl substituents were synthesized in moderate to high yields.

A Selectfluor-mediated copper-catalyzed selective benzylic C–O cyclization of *N*-*o*-tolylbenzamides **51** was presented by Li *et al*.[67] for the synthesis of 4*H*-3,1-benzoxazines **52** (**Scheme 18**, eq 2). A little later, a copper-mediated oxidative

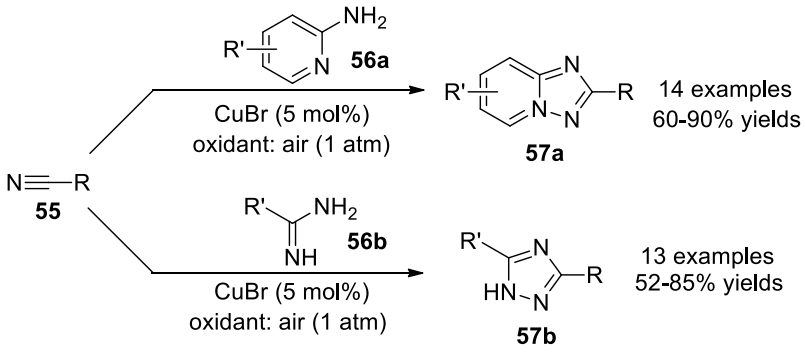
cyclization of (*E*)- or (*Z*)-enamides **53** for the synthesis of 2,5-disubstituted oxazoles **54** was discovered by the Stahl group (**Scheme 18**, eq 3).[68] Various 2,5-disubstituted oxazoles were prepared in moderate to good yields from simple amide and alkyne precursors.



Scheme 18. Copper-catalyzed cyclization through C–O bond formation.[66], [67], [68]

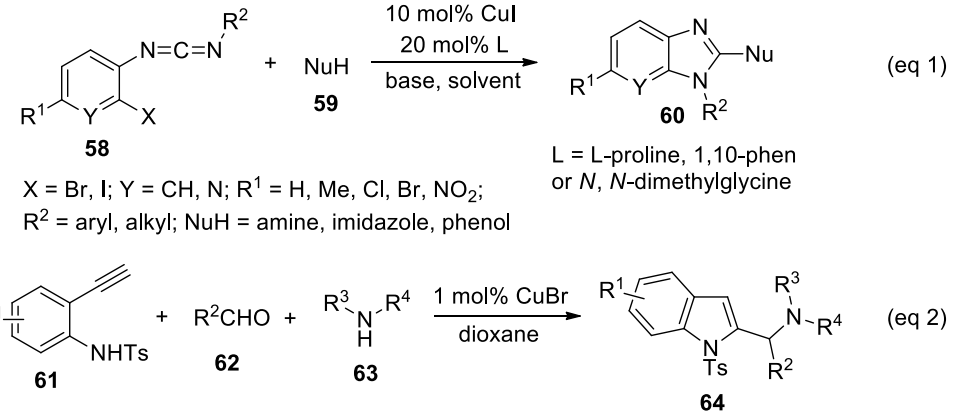
1.2.3.3 Through C–N Bond Formation

In 2009, Nagasawa and co-workers[69] reported a facile synthesis of 1,2,4-triazoles **57a** and **57b** through a copper-catalyzed tandem addition-oxidative cyclization between **55** and **56a** or **56b** under an atmosphere of air (**Scheme 19**). The process is presumed to consist of sequential C–N and N–N bond-forming copper-catalyzed oxidative coupling reactions. Under the optimized reaction conditions, a wide range of functional groups were well tolerated.



Scheme 19. Copper-catalyzed synthesis of 1,2,4-triazoles through tandem addition-oxidative cyclization.[69]

In the same year, Lv and Bao developed a novel and efficient method for a one-pot synthesis of *N*-substituted 2-heterobenzimidazoles **60** (**Scheme 20**, eq 1).[70] Through a copper-catalyzed cascade intermolecular addition/intramolecular C–N coupling process, a wide variety of 2-heterobenzimidazoles **60** were synthesized from *o*-haloarylcarbodiimides **58** and *N*- or *O*-nucleophiles **59**.



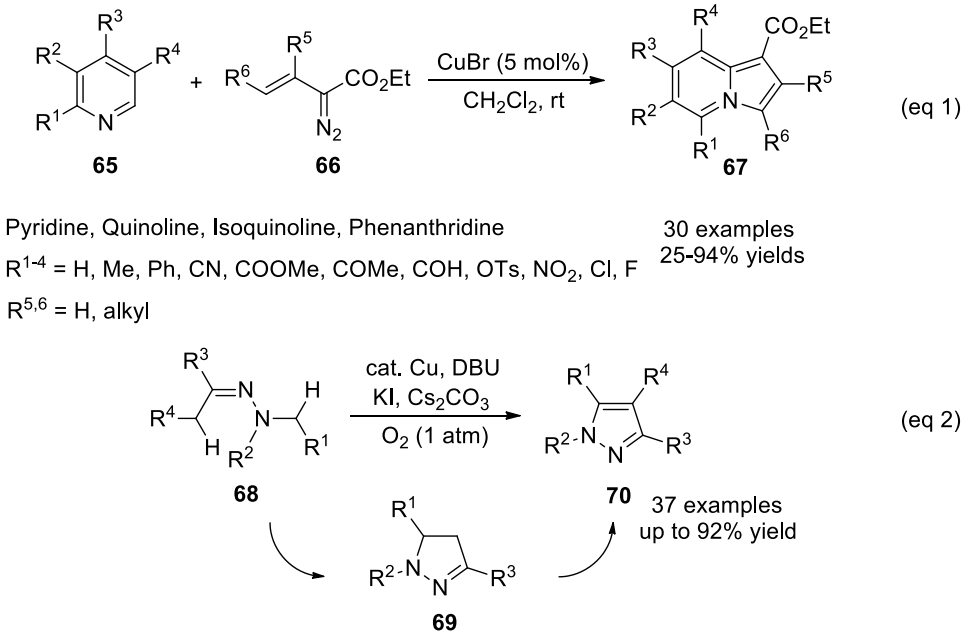
Scheme 20. Copper-catalyzed synthesis of 1,2,4-triazoles and domino three-component coupling-cyclization.[70], [71]

Later, Fujii and co-workers[71] reported the construction of nitrogen-containing heterocycles through copper-catalyzed domino three-component coupling−cyclization (**Scheme 20**, eq 2). A cyclic or acyclic secondary amine **63** and aldehyde **62**

(paraformaldehyde, aliphatic or aromatic aldehydes) in the presence of 1 mol% of CuBr were used to transform 2-ethynylanilines **61** into a variety of substituted 2-(aminomethyl)indoles **64** in good to excellent yields.

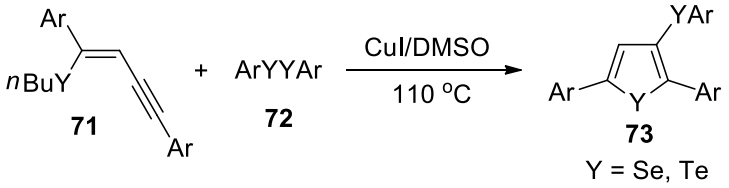
In 2010, pyridine activation through copper(I)-catalyzed annulation was presented by Barluenga, Tomás and co-workers[72] for the synthesis of indolizines **67** (**Scheme 21**, eq 1). The reaction tolerated a broad range of pyridine derivatives **65** (including quinoline and isoquinoline).

Very recently, Zhang *et al.*[73] developed a copper-catalyzed aerobic intramolecular dehydrogenative cyclization of *N*,*N*-disubstituted hydrazones **68** (**Scheme 21**, eq 2). This reaction proceeded through an iminium intermediate **69** for the Csp^3–H bond functionalization and provided an environmentally friendly and atom-efficient access to substituted pyrazoles **70**.



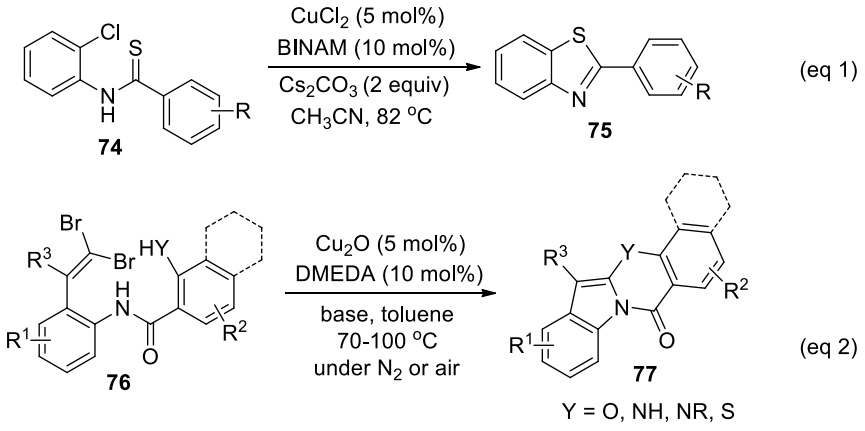
Scheme 21. Copper-catalyzed annulation for the synthesis of indolizines and aerobic intramolecular dehydrogenative cyclization of *N*,*N*-disubstituted hydrazones.[72], [73]

1.2.3.4 Through Other Bond Formations



Scheme 22. CuI-catalyzed cyclization of (*Z*)-chalcogenoenynes.[74]

In 2008, Alves, Zeni and co-workers[74] reported a CuI-catalyzed cyclization of (*Z*)-chalcogenoenynes **71** with **72** for the synthesis of 3-substituted chalcogenophenes **73** in good to excellent yields (**Scheme 22**). In addition, they transformed the obtained chalcogenophenes to more complex products using the palladium-catalyzed cross-coupling reactions with boronic acids to get Suzuki-type products in good yields.



Scheme 23. Copper(II)-catalyzed synthesis of benzothiazoles and polycylic indole derivatives through intramolecular cyclization.[75], [76]

Later, an efficient copper(II)-catalyzed synthesis of benzothiazoles **75** through intramolecular coupling-cyclization of *N*-(2-chlorophenyl)benzothioamides **74** was reported by Jaseer *et al.* using 1,1'-binaphthyl-2,2'-diamine (BINAM) as a ligand (**Scheme 23**, eq 1).[75] They synthesized a wide range of 2-aryl or 2-alkyl-substituted

benzothiazoles **75** through intramolecular C(aryl)–S bond forming-cyclization. In 2012, Wang and co-workers[76] reported a copper-catalyzed domino intramolecular cyclization of **76** for the synthesis of polycyclic indole derivatives **77** (**Scheme 23**, eq 2).

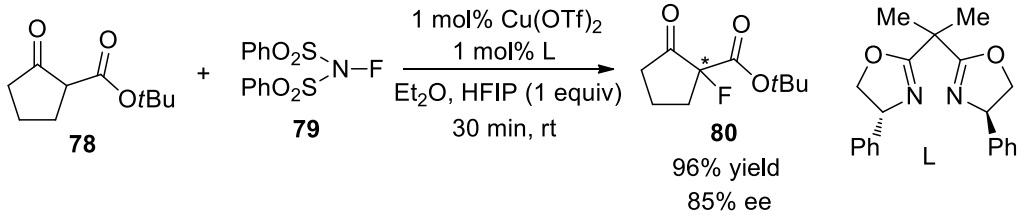
1.2.4 Copper-Catalyzed Fluorination/Trifluoromethylation Reactions

C–F bonds play an important role in medicinal chemistry[77] and material sciences.[78] Despite a long history of organofluorine chemistry (more than 100 years) and its importance, it still remains challenging to construct C–F bonds.[79] Recently, the CF_3 group has also attracted much attention in the realm of medicinal chemistry because it normally enhances efficacy by promoting electrostatic interactions with targets, improving cellular membrane permeability, and increasing robustness towards oxidative metabolism of the drug after its incorporation into small molecules.[77a], [77b], [80] Differing from conventional fluorination reactions that were developed in the early twentieth century and generally suffered from limited substrate scope,[81] chemists have developed many novel methods for transition metal-catalyzed fluorination/trifluoromethylation reactions to incorporate fluorine into organic molecules in the past several years.[82] Furthermore, significant progress has also been made in trifluoromethylation of arenes and heteroarenes by means of photoredox catalysis.[83] Here a short summary on the recent advances regarding copper-catalyzed fluorination and trifluoromethylation reactions is presented.

1.2.4.1 Copper-Catalyzed Fluorination Reactions

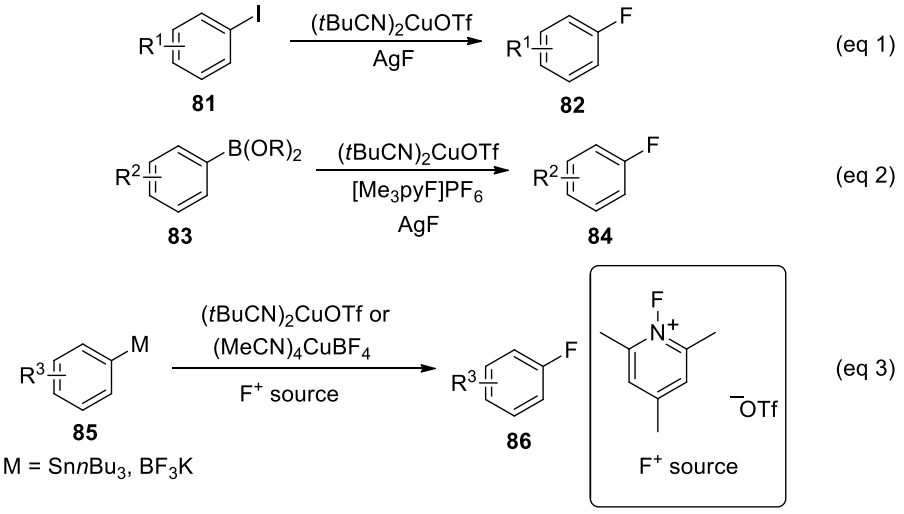
In 2004, Cahard and co-workers[84] reported a copper(II) triflate-bis(oxazoline)-catalyzed enantioselective electrophilic fluorination of β-ketoesters **78** with **79** (**Scheme 24**). The catalyst loading was as low as 1 mol% and the use of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) was crucial for achieving high

enantioselectivity.



Scheme 24. Copper(II)-catalyzed enantioselective electrophilic fluorination of β-ketoesters.[84]

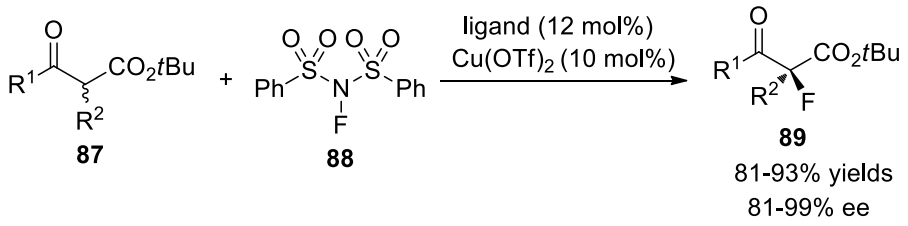
Recently, the Hartwig group[85] demonstrated a copper-mediated fluorination of aryl iodides **81** (**Scheme 25**, eq 1). The reaction was performed in the presence of a cationic copper reagent and silver fluoride and tolerated the functional groups of ethers, amides, esters, ketones, and aldehydes as well as some heterocyclic systems. This reaction was presumed to occur through oxidative addition to form a Cu(III) intermediate and C−F reductive elimination from an aryl copper(III) fluoride. One year later, the same group[86] reported a copper-mediated fluorination of arylboronate esters **83** (**Scheme 25**, eq 2). Tandem reactions were developed for the fluorination of arenes and aryl bromides through arylboronate ester intermediates. Mechanistic studies suggested that this fluorination reaction occured through facile oxidation of Cu(I) to Cu(III), followed by rate-limiting transmetalation of a bound arylboronate to Cu(III). Fast C–F reductive elimination was proposed to occur from an aryl-copper(III)-fluoride complex. Cu(III) intermediates were generated independently and identified by NMR spectroscopy and ESI-MS.



Scheme 25. Copper-mediated procedures for the synthesis of fluorinated arenes.[85], [86], [87]

In 2013, Sanford and Ye developed a copper-mediated fluorination of aryl stannanes and aryl trifluoroborates **85** (**Scheme 25**, eq 3).[87] This method had a broad substrate scope and tolerated various functional groups. The reaction did not require the use of any noble metal additives and was proposed to proceed through an aryl copper(III) fluoride intermediate.

Very recently, a copper(II)-catalyzed enantioselective fluorination of esters **87** with **88** was presented by Shibatomi and co-workers[88] in the presence of chiral spiro-oxazoline ligands (**Scheme 26**). The reaction was performed using a chiral Lewis acid catalyst prepared from $Cu(OTf)_2$ and enantiopure spiro-oxazoline ligands. The fluorination proceeded in a highly enantioselective manner both when cyclic and acyclic substrates were applied to the reaction. Fluorination of α-alkylmalonates was also performed to afford the corresponding products in good enantioselectivity.



Scheme 26. Copper(II)-catalyzed enantioselective fluorination of esters.[88]

1.2.4.2 Copper-Catalyzed Trifluoromethylation Reactions

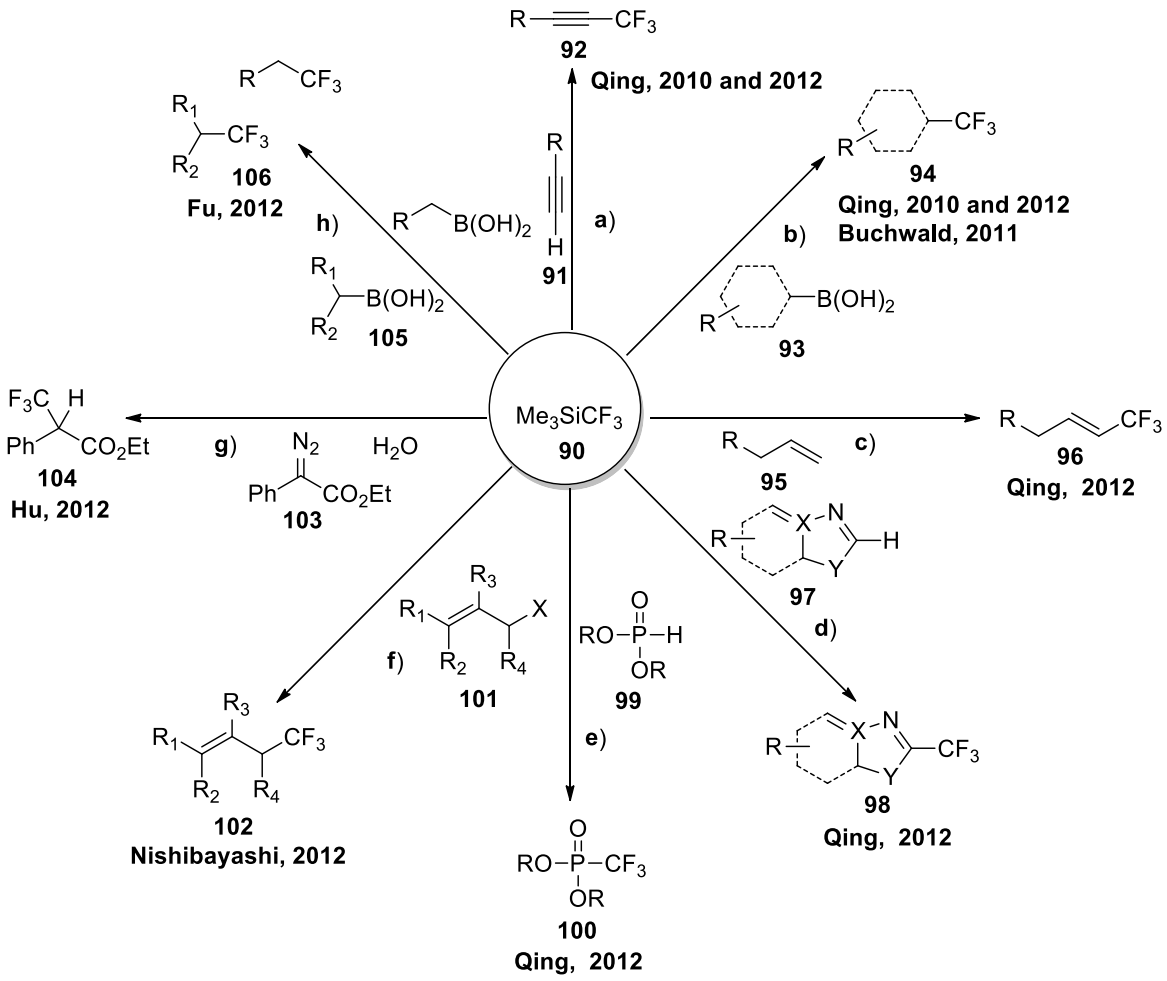
1.2.4.2.1 Using Ruppert's Reagent as a Trifluoromethylation Reagent

Trifluoromethyltrimethylsilane (**90**) is a reagent used in organic chemistry for the introduction of the trifluoromethyl group, which is often called Ruppert's reagent or Ruppert-Prakash reagent. The compound was first prepared by the Ruppert group in 1984.[89] Among recent reports on copper-catalyzed trifluoromethylation reactions, Me_3SiCF_3 was widely used as a very powerful trifluoromethylation reagent (**Scheme 27**).

In 2010, Qing and co-workers[90] pioneered a copper-mediated aerobic oxidative trifluoromethylation of terminal alkynes **91** for the synthesis of trifluoromethylated acetylenes **92** using **90** as a trifluoromethylation reagent (**Scheme 27**, **a**). Both aromatic alkynes and aliphatic alkynes were employed in the process and a variety of functionalities such as $–NH_2$, -OMe, $-CO_2Et$, -Br, and $-NO_2$ were tolerated under the reaction conditions. This procedure was further improved by the Qing group later by decreasing the amount of a copper catalyst and Me_3SiCF_3 or using a lower reaction temperature.[91]

Subsequently, the Qing group[92] also published another copper-mediated oxidative trifluoromethylation reaction but using boronic acids **93** and Ag_2CO_3 as coupling partners and an oxidant, respectively (**Scheme 27**, **b**). The procedure tolerated a wide

range of functional groups for the synthesis of trifluoromethylated arenes and alkenes **94**. They improved this method in a recent publication using catalytic amounts of a copper catalyst.[91a] This work was also further developed by the Buchwald group one year later (**Scheme 27**, **b**).[93] In this work, O_2 was used as an oxidant instead of Ag_2CO_3 at room temperature. Under mild conditions, the reaction tolerated a range of functional groups, allowing access to a variety of trifluoromethylarenes **94**.



Scheme 27. Copper-catalyzed trifluoromethylation reactions using Me_3SiCF_3 as a trifluoromethylation reagent.

Replacing terminal alkynes with terminal alkenes **95**, Qing and co-workers showed an efficient Csp^3–CF_3 bond formation in 2012 (**Scheme 27**, **c**).[94] This reaction proceeded

well under mild conditions to provide a variety of trifluoromethylated allylic compounds **96** in good yields. In the same year, the Qing group developed a copper-catalyzed oxidative trifluoromethylation of heteroarenes and highly electron-deficient arenes **97** through direct C–H activation (**Scheme 27**, **d**).[95] The combination of $Cu(OAc)_2$, 1,10-phenanthroline, *t*BuONa/NaOAc as cobases, as well as air or di-*tert*-butyl peroxide as an oxidant proceeded to give the corresponding trifluoromethylated 1,3,4-oxadiazoles **98** in high yields. In addition, a copper-catalyzed aerobic oxidative trifluoromethylation of H-phosphonates **99** was presented by the same group (**Scheme 27**, **e**).[96] As the first example on the construction of a P–CF_3 bond through transition metal catalysis, this work provided an alternative method for the facile synthesis of a series of biologically important CF_3-phosphonates **100**.

In 2012, Nishibayashi and co-workers reported a copper-catalyzed nucleophilic trifluoromethylation of allylic halides **101** (**Scheme 27**, **f**).[97] The reaction provided the corresponding allylic trifluoromethylation products **102** with complete regioselectivity in good to high yields. The use of THF as a solvent is crucial for obtaining good yields. A little later, Hu *et al.* reported a copper-mediated trifluoromethylation of α-diazo esters **103** (**Scheme 27**, **g**).[98] H_2O acted as a promoter in the reaction to activate the "$CuCF_3$" species prepared from CuI/$TMSCF_3$/CsF (1.0:1.1:1.1). This reaction had a broad substrate scope and was efficient for the synthesis of a variety of aryl-, benzyl-, and alkyl-substituted 3,3,3-trifluoropropanoates **104**. In addition, a copper-promoted trifluoromethylation of primary and secondary alkylboronic acids **105** was recently developed by Xu *et al*. (**Scheme 27**, **h**).[99]

1.2.4.2.2 Using Togni's Reagent as a Trifluoromethylation Reagent

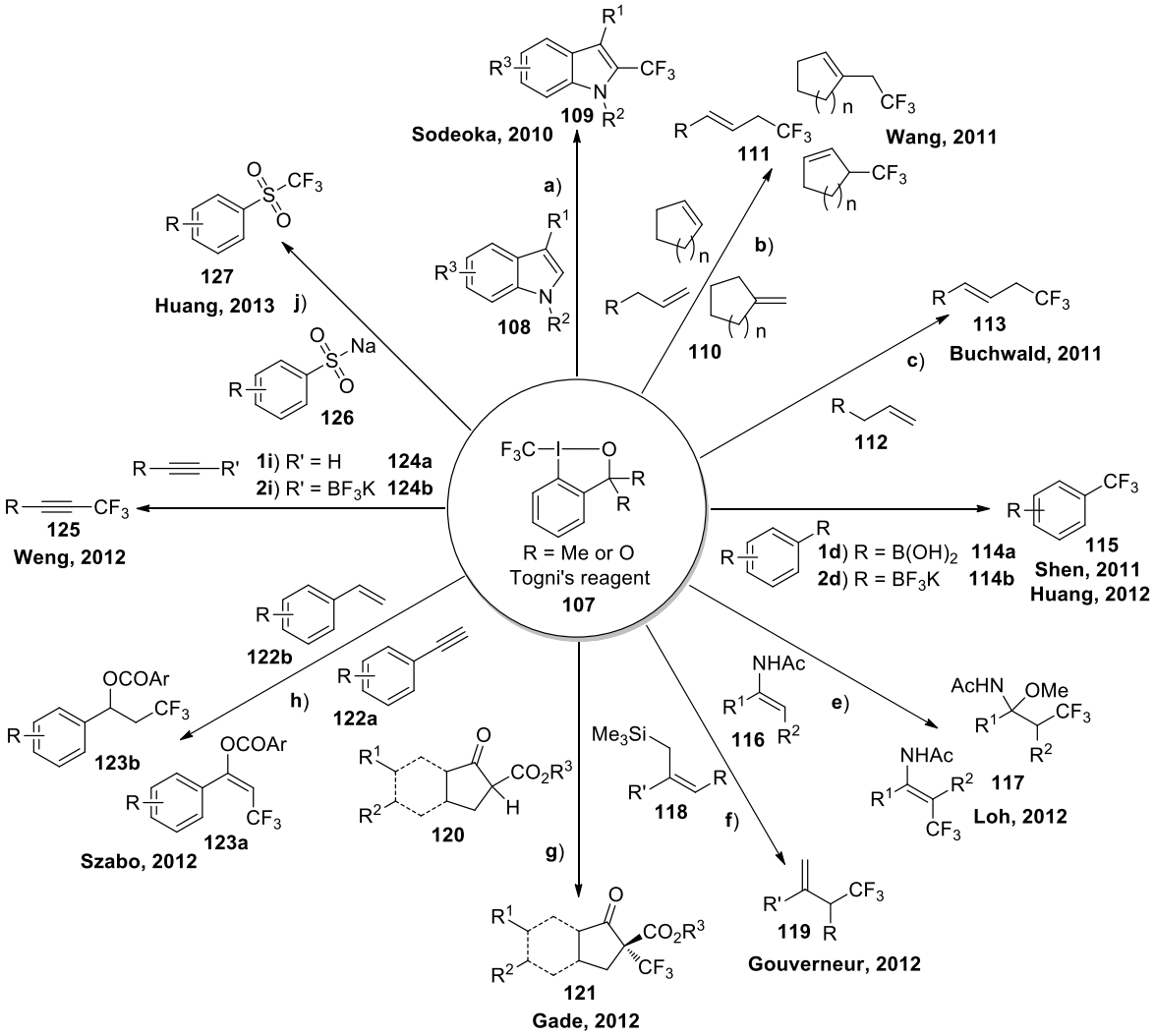
Nucleophilic trifluoromethylation is the most common method due in large part to the broad application of the Ruppert-Prakash reagent **90** (Me_3SiCF_3). However, electrophilic trifluoromethylation reagents are considerably less developed. A new electrophilic reagent has recently been reported by Togni and co-workers based on hypervalent iodine, 3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole (**107**), which significantly complements the nucleophilic Ruppert-Prakash reagent. Togni's reagent is characterized with its easy-handling and stability that can be exposed to moist air for short period of time without any apparent alteration.

In 2010, Sodeoka and co-workers reported a copper-catalyzed direct C2-selective trifluoromethylation of indole derivatives **108** (**Scheme 28**, **a**).[100] The reaction proceeded under mild conditions with only a small excess of Togni's reagent and 10 mol% of copper(I) acetate to provide C2-trifluoromethylated **109** indoles in good yields.

One year later, another example on the use of Togni's reagent was reported by Wang *et al.* (**Scheme 28**, **b**).[101] They performed the copper-catalyzed trifluoromethylation of allylic compounds **110** under mild conditions and obtained corresponding allylic trifluoromethylated products **111** in good yields. In the reaction, simple alkenes could be used as substrates and a wide range of functional groups were well tolerated.

In the same year, Parsons and Buchwald discovered a copper-catalyzed trifluoromethylation of unactivated olefins **112** under mild conditions (**Scheme 28**, **c**).[102] This procedure provided linear allylic trifluoromethylated products **113** with high *E*/*Z* selectivity and could be applied to a range of substrates bearing various functional groups. A little later, Shen and co-workers introduced Togni's reagent to the trifluoromethylation of aryl and vinyl boronic acids **114a** catalyzed by CuI under

mild reaction conditions (**Scheme 28**, **1d**).[103] The reaction had a broad substrate scope including heteroarylboronic acids and tolerated a variety of functional groups. Another work on copper-catalyzed trifluoromethylation of organotrifluoroborates **114b** was presented by the Huang group in 2012 (**Scheme 28**, **2d**).[104] They performed the reaction at room temperature to provide the corresponding trifluoromethylarenes **115** in good to excellent yields.



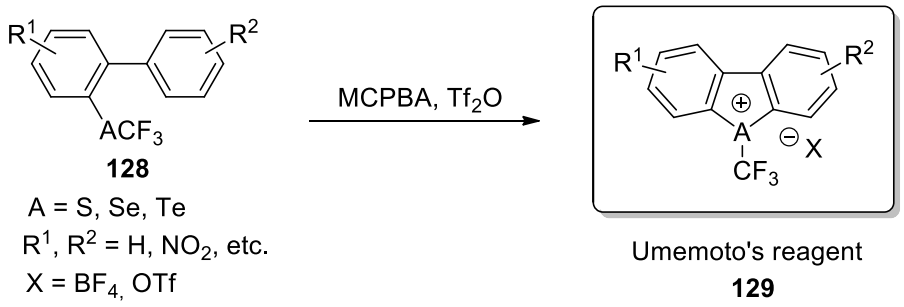
Scheme 28. Copper-catalyzed trifluoromethylation reactions using Togni's reagent as a trifluoromethylation reagent.

In 2012, Loh and co-workers reported a copper-catalyzed olefinic trifluoromethylation of enamides **116** at room temperature (**Scheme 28**, **e**).[105] This work provided an efficient method for the stereoselective synthesis of β-trifluoromethyl subsitituted enamids **117**. Later, Gouverneur and co-workers developed a copper-catalyzed trifluoromethylation of allylsilanes **118** using Togni's reagent (**Scheme 28**, **f**).[106] The silyl group was crucial to control the yield of this reaction. An example on highly enantioselective copper-catalyzed trifluoromethylation of β-ketoesters was shown by Gade and co-workers later (**Scheme 28**, **g**).[107] Using Togni's reagent as a trifluoromethylation reagent, five-membered ring β-ketoesters **120** were converted to the corresponding products **121** in high yields with up to 99% ee under mild conditions. Interestingly, Janson *et al*. showed that Togni's reagent could be incorporated into alkynes **122a** or alkenes **122b** through addition reactions (**Scheme 28**, **h**).[108] In the reaction, electron-donating substituents accelerated the process and alkenes reacted faster than alkynes emphasizing the electrophilic character of the addition reaction.

Recently, using terminal alkynes **124a** or alkynyltrifluoroborates **124b** as coupling partners, Weng and co-workers reported two independent works on mild copper-catalyzed trifluoromethylation in the presence of Togni's reagent (**Scheme 28**, **1i and 2i**).[109] The two procedures both proceeded the reaction at room temperature to provide trifluoromethylated acetylenes **125** in good to excellent yields. Very recently, Huang and co-workers reported a copper-catalyzed trifluoromethylation of arylsulfinate salts **126** (**Scheme 28**, **j**).[110] The reaction provided aryltrifluoromethylsulfones **127** in moderate to good yields with a broad substrate scope.

1.2.4.2.3 Using Umemoto's Reagent as a Trifluoromethylation Reagent

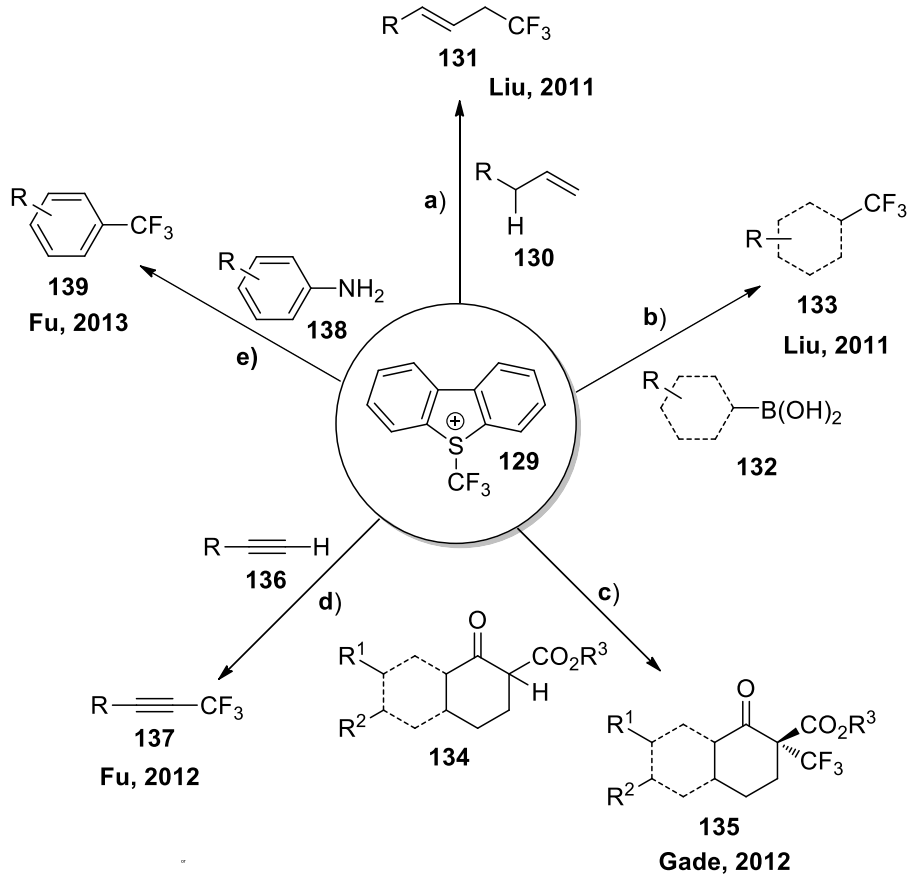
In 1990, Umemoto's reagent **129** was prepared by Umemoto and co-workers through an oxidation of the starting materials **128** (sulfides, selenides or telluride) followed by a cyclization or a direct fluorination (**Scheme 29**).[111] Umemoto's reagent is featured by its superior performance in stability, ease of use, and being commercially available. To date, it has been efficiently applied in the trifluoromethylation of various nucleophiles such as carbanions, silyl enol ethers, enamides, phenols, anilines, phosphines and thiolates.[112]



Scheme 29. Umemoto's reagent.

In 2011, Liu and co-workers reported a copper-catalyzed trifluoromethylation of terminal alkenes **130** through allylic Csp^3–H bond activation (**Scheme 30**, **a**).[113] In this reaction, Umemoto's reagent was used as a trifluoromethylation reagent to provide a mechanistically unique example of copper-catalyzed allylic C–H activation/functionalization. The trifluoromethylation is supposed to occur through a Heck-like four-membered-ring transition state according to both experimental and theoretical analyses. Later, the Liu group employed Umemoto's reagent in trifluoromethylation of aryl boronic acids **132** catalyzed by copper(II) acetate (**Scheme 30**, **b**).[114] The reaction was accelerated by a pyridine-derived ligand under mild conditions and showed tolerance to moisture and a variety of functional groups.

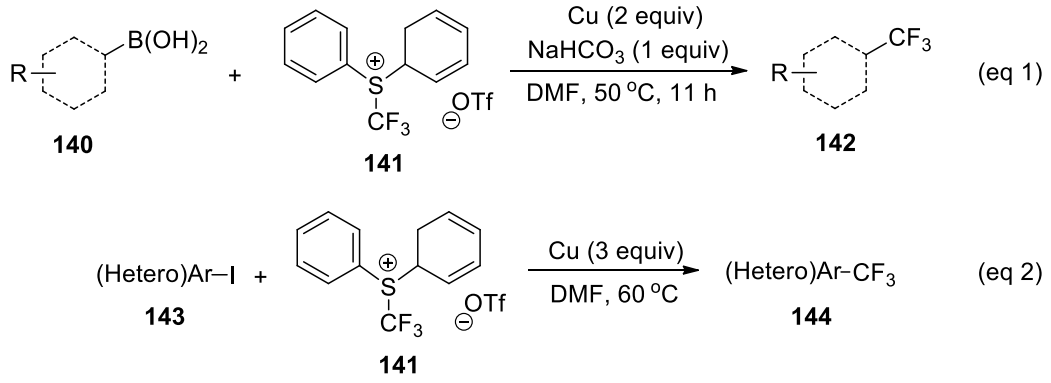
In 2012, Deng *et al.* developed a highly enantioselective copper-catalyzed trifluoromethylation of β-ketoesters (**Scheme 30**, **c**).[107] Differing from the aforementioned examples,[107] six-membered ring β-ketoesters **134** were converted to the corresponding products **135** in high yields with up to 99% ee in the presence of Togni's reagent as a trifluoromethylation reagent. In addition, a recent example on copper-catalyzed trifluoromethylation of terminal alkynes **136** was shown by Fu and co-workers (**Scheme 30**, **d**).[115] The reaction was conducted at room temperature and showed good tolerance to a variety of functional groups.



Scheme 30. Copper-catalyzed trifluoromethylation reactions using Umemoto's reagent as a trifluoromethylation reagent.

Very recently, another example of the use of this reagent was demonstrated by the Fu

group (**Scheme 30**, e).[116] This trifluoromethylation reaction proceeded smoothly in the presence of 3 equivalents of copper powder and tolerated a wide range of functional groups. A variety of trifluoromethylated arenes and heteroarenes **139** were synthesized from the corresponding amines **138** in moderate to good yields. This reaction provided a new example to the family of Sandmeyer reaction.



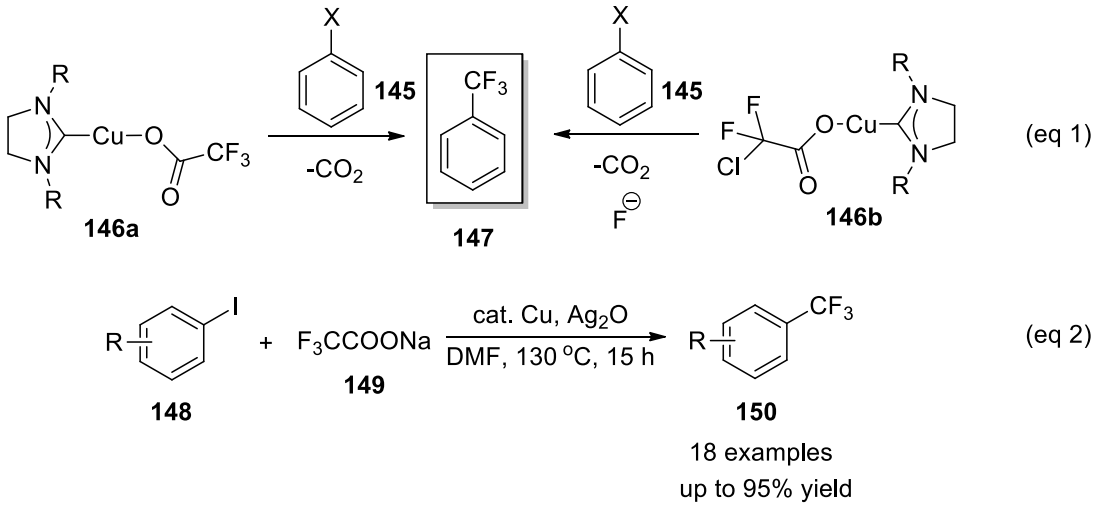
Scheme 31. Copper-mediated trifluoromethylation reactions using the precusor of Umemoto's reagent as a trifluoromethylation reagent.[117], [118]

Furthermore, using the precusor of Umemoto's reagent **141** and replacing $Cu(OAc)_2$ with copper power (2 equiv), another trifluoromethylation of arylboronic acids was developed by Zhang *et al.* in the absence of a ligand (**Scheme 31**, eq 1).[117] A $CuCF_3$ species was formed from copper powder and compound **141**. The choice of base had an important influence on the trifluoromethylation process. Aryl-, alkenyl- and heteroarylboronic acids **140** with a variety of functional groups were all suitable substrates for this reaction. A little later, the Xiao group reported a copper-mediated trifluoromethylation of heteroaromatic compounds **143** using a similar system (**Scheme 31**, eq 2).[118]

1.2.4.2.4 Using Other Trifluoromethylation Reagents

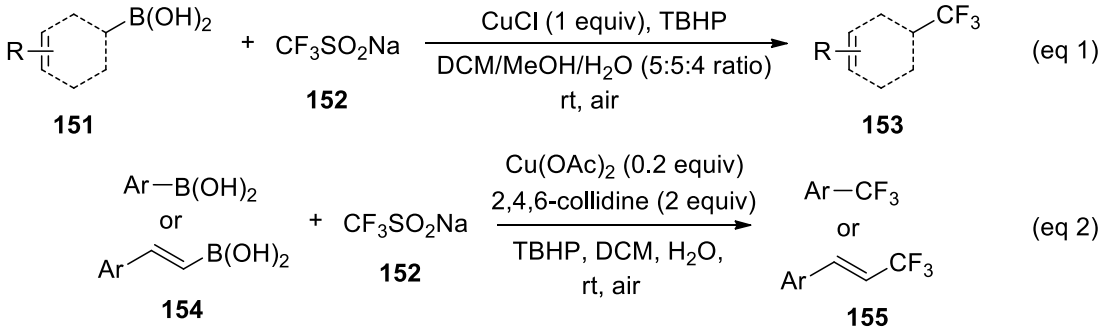
In 2010, a decarboxylative trifluoromethylation of aryl halides **145** was reported by

McReynolds and co-workers using well-defined copper-trifluoroacetate and -chlorodifluoroacetate precursors **146a** and **146b**, respectively (**Scheme 32**, eq 1).[119] In the process, the formation of aryl-CF_3 was realized by the loss of CO_2 from these precursors at 160 ^oC. One year later, another decarboxylative trifluoromethylation of aryl halides **148** with **149** was discovered by Li *et al.* (**Scheme 32**, eq 2).[120] Sodium trifluoroacetate was used as a trifluoromethylation reagent in the reaction, which occurred under a ligand-free copper-catalyzed decarboxylative system using Ag_2O as a promoter. The method was used to synthesize a variety of trifluoromethylated aromatics **150** under relatively mild reaction conditions in moderate to excellent yields.



Scheme 32. Copper-mediated/catalyzed decarboxylative trifluoromethylation reactions.[119], [120]

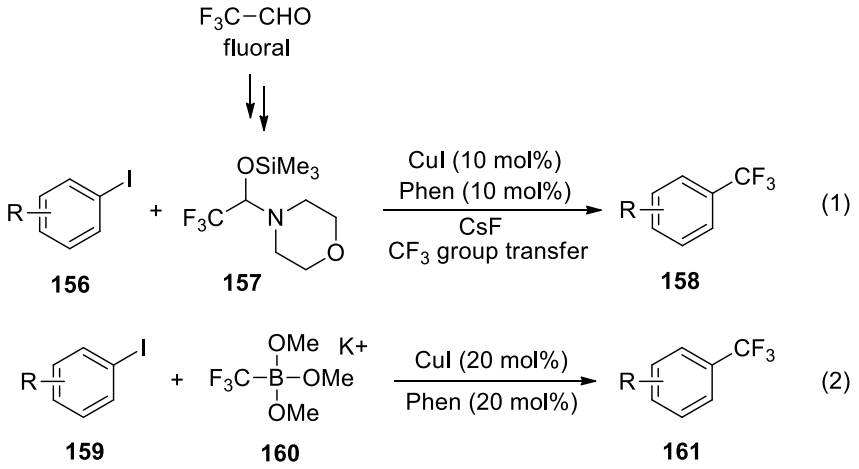
Sodium trifluoromethanesulfinate (Langlois reagent, **152**) is a useful trifluoromethylating reagent for introducing the CF_3 group into electron-rich aromatic compounds. The process is supposed to proceed through a free radical mechanism.[121] This reagent can be also used to trifluoromethylate electron-deficient aromatic compounds under biphasic conditions.[122]



Scheme 33. Copper-mediated/catalyzed trifluoromethylation reactions using Langlois reagent as a trifluoromethylation reagent.[123], [124]

In 2012, Sanford and co-workers developed a copper-mediated trifluoromethylation of (hetero)arylboronic acids **151** using the Langlois reagent **152** that reacted with TBHP to generate a CF_3 radical (**Scheme 33**, eq 1).[123] The reaction proceeded under ambient conditions to provide a variety of trifluoromethylated (hetero)aryl products **153**. Very recently, this system was further improved by the Beller group using catalytic amount of a copper catalyst $Cu(OAc)_2$ with the aid of a suitable ligand 2,4,6-collidine (**Scheme 33**, eq 2).[124] A variety of aryl- and vinylboronic acids were trifluoromethylated using CF_3SO_2Na as the CF_3 source in the presence of a large excess of TBHP (16.1 equiv).

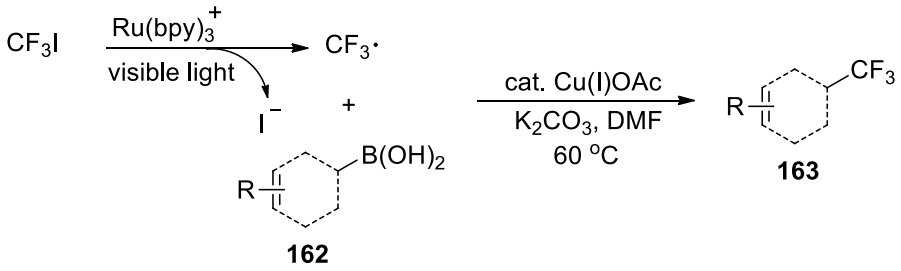
Using fluoral (trifluoroacetaldehyde) derivatives as CF_3 source, a copper-catalyzed aromatic trifluoromethylation was developed by Amii and co-workers in 2011 (**Scheme 34**, eq 1).[125] A small amount of copper(I) iodide-phenanthroline complex catalyzed the cross-coupling reactions of aryl/heteroaryl iodides **156** with the *O*-silylated hemiaminal of fluoral **157** to provide trifluoromethylated arenes **158** in moderate to high yields.



Scheme 34. Copper-catalyzed trifluoromethylation of aryl/heteroaryl iodides.[125], [126]

In the same year, another trifluoromethylation reagent potassium (trifluoromethyl)trimethoxyborate **160** was employed in a copper-catalyzed trifluoromethylation of aryl iodides **159** by Knauber *et al.* (**Scheme 34**, eq 2).[126] This trifluoromethylation reagent allowed the conversion of various aryl iodides into the corresponding benzotrifluorides **161** in high yields under mild, base-free conditions in the presence of catalytic amounts of a CuI/1,10-phenanthroline complex.

One example based on dual catalysis for the trifluoromethylation of boronic acids **162** with CF_3I was reported by Ye and Sanford in 2012 (**Scheme 35**).[127] They used both a visible-light photocatalyst and a transition metal catalyst in the reaction. In the process, reduction of CF_3I resulted in the formation of $CF_3\cdot$, which could then react with Cu(II) to generate a Cu(III)CF_3 intermediate. Subsequent transmetalation between the intermediate and arylboronic acids **162** afforded the Cu(III)(aryl)(CF_3) complex, which underwent reductive elimination to provide the desired products **163**.



Scheme 35. Trifluoromethylation of arylboronic acids catalyzed by dual catalysts.[127]

2. Objectives

Inspired by the recent progress on the applications of copper catalysts in organic synthesis and the attractive properties of copper itself, my research interests focused on copper-catalyzed reactions during my whole doctoral studies, including the Sonogashira reaction, oxidative cross-coupling reactions, C–H/C–C bond activation and C–H bond functionalization of (hetero)aryl compounds.

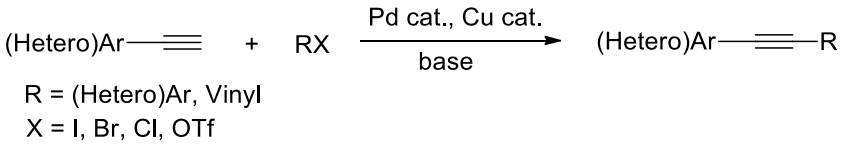
The aim of this thesis is the investigation of various copper-catalyzed reactions mentioned above, as well as their applications for the synthesis of a broad range of useful organic compounds. Specifically, the construction of various bonds such as C–C, C–S and C–P bonds would become a key point through the whole work.

Results and Discussion

1. Sonogashira-Hagihara-Type Cross-Coupling Reactions Catalyzed by a Sub-Mol% Copper Catalyst

1.1 Introduction

The Sonogashira-Hagihara reaction is a very well known cross-coupling reaction for the formation of carbon–carbon bonds (**Scheme 36**). It was first reported by Kenkichi Sonogashira, Yasuo Tohda, and Nobue Hagihara in 1975.[128] Before this reaction, other reactions such as the Heck reaction also provided similar products, but required harsh reaction conditions such as high temperature. In fact, the Sonogashira reaction is normally considered to be an extension to the latter. All of these reactions have a common feature that they all require a palladium catalyst. However, the Sonogashira reaction is much more efficient for these coupling reactions with the aid of a copper co-catalyst, allowing the reaction to occur even at room temperature.[129] This reaction has played an important role for the construction of Csp^2–Csp bonds in organic synthesis,[1d], [130] which is particularly powerful in the alkynylation of aryl and alkenyl halides.



Scheme 36. Sonogashira reaction.

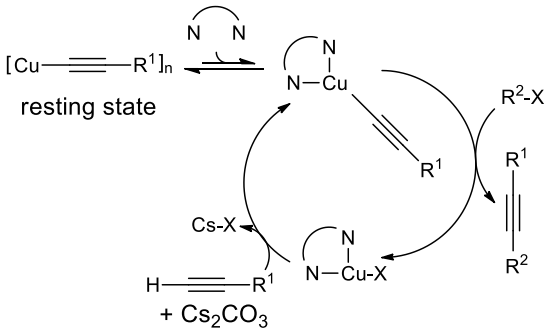
Typically, two catalysts, i.e., a zerovalent palladium complex and a halide salt of Cu(I), are required in the reaction process. This catalytic system has some shortcomings such as the use of high loadings of a palladium catalyst and large amounts of a copper

co-catalyst.[1d] Due to its higher stability than Pd^0, Pd^{II} is often applied as a pre-catalyst in the reaction.[129c] Pd^0 can be generated through the reduction of Pd^{II} by a ligand (such as an amine or a phosphine ligand) or a reactant in the reaction process.[131] In addition, in some cases, Pd^0 can be also formed *in situ* by the oxidation of triphenylphosphine to triphenylphosphine oxide. The role of Cu(I) salts, such as copper iodide, is to generate an activated species through reacting with the terminal alkyne and producing a Cu(I) acetylide, which is often used to accelerate the reaction.[130d]

1.2 Background

For many years, the research on understanding and optimizing the synthetic capabilities of the Sonogashira-Hagihara reaction remains unabated, which emphasizes the remarkable utility of this reaction. To date, significant progress has been made for the development of this well-known reaction. For example, in 2009, Hu and co-workers reported a nickel-catalyzed Sonogashira coupling reaction of unactivated alkyl halides with acetylene in the presence of a copper co-catalyst but without the use of a palladium catalyst.[132] In addition, gold catalysts were also used to catalyze the coupling of phenylacetylene and iodobenzene.[133]

Nowadays all the reactions that use only a palladium catalyst[134] or other cheap metal catalysts such as iron,[135] copper,[136] and cobalt[137] to couple a halide or triflate with a terminal alkynes are often called “Sonogashira reactions”, despite of the use of non-typical Sonogashira reaction conditions. Recently, Bolm and co-workers showed the effect of low copper concentrations in Sonogashira-Hagihara-type coupling reaction between aryl halides and terminal alkynes.[138] They proposed a mechanism for this ligand accelerated cross-coupling reaction (**Scheme 37**).[138], [139]



Scheme 37. Proposed reaction mechanism.[138]

1.3 Research Objective

In this work, a sub-mol% copper-catalyzed Sonogashira-Hagihara-type cross-coupling reaction was investigated in detail. Furthermore, the mechanistic aspects of the reaction were discussed based on kinetic measurements and DFT (density functional theory) calculations.

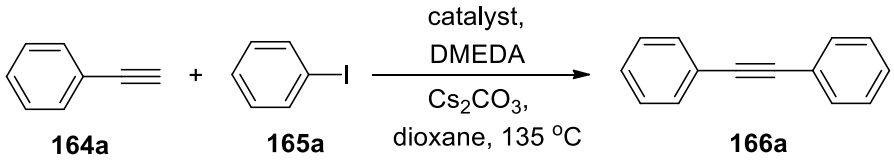
1.4 Optimization of Reaction Conditions

1.4.1 The Effect of Copper Sources on the Cross-Coupling Reaction

At first, the catalytic efficacies of various copper sources in the coupling reaction of phenylacetylene **164a** and iodobenzene **165a** were investigated using DMEDA as a ligand (**Table 1**).

From Table 1, it was determined that all tested copper sources were effective for this reaction, affording the desired product **166a** in good to excellent yields, whereas only trace amounts of product were observed in the absence of a copper catalyst (**Table 1**).

Table 1. The effect of the copper source.[a, [140]]



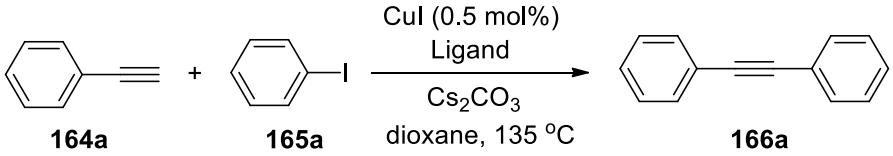
Entry	Catalyst	Yield[b] (%)	
		3 h	22 h
1	CuI	36	98
2	$CuCl_2$	36	90
3	Cu_2O	22	99
4	$Cu(OAc)_2$	35	97
5	$Cu(CF_3SO_3)_2$	33	98
6	CuCl	30	88
7	CuO	33	85
8	$Cu(DMEDA)_2Cl_2 \cdot H_2O$	30	90
9	no catalyst	0	8

[a] Reaction conditions: Iodobenzene **165a** (1.5 mmol), phenylacetylene **164a** (1 mmol), catalyst (0.5 mol%), Cs_2CO_3 (2 mmol), DMEDA (0.3 mmol), and dioxane (1 mL) under argon atmosphere at 135 °C. [b] Determined by GC using tetradecane as internal standard.

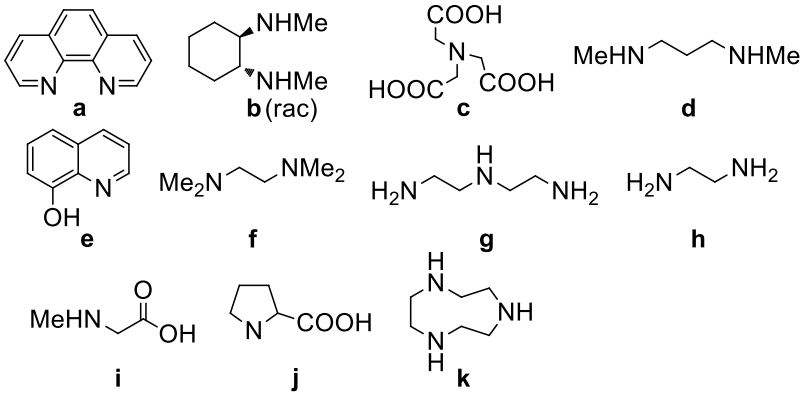
1.4.2 The Effect of Ligands on the Cross-Coupling Reaction

Subsequently, the effect of the ligand on the reaction was investigated. The reactions were performed using 1 mol% and 30 mol% of ligand, successively (**Table 2**). The results showed that the ligand structure had a profound influence on the catalytic activity. Ligands **a**, **b** and **g** (**Table 2**, entries 1, 2 and 7), which featured two or three nitrogen donor groups, had an excellent effect on the reaction with 30 mol% loadings. Furthermore, it was worthy to note that these ligands could form stable 5-membered chelates when coordinated to a metal center.

Table 2. Ligand screening.[a, 140]



Entry	Ligand	Yield[b] (%)			
		1 mol%		30 mol%	
		3 h	22 h	3 h	22 h
1	**a**	11	80	47	97
2	**b**	3	19	46	98
3	**c**	1	9	nd[c]	1
4	**d**	1	10	9	53
5	**e**	12	37	7	41
6	**f**	1	10	3	22
7	**g**	2	28	38	95
8	**h**	1	12	6	25
9	**i**	0	13	2	15
10	**j**	1	18	0.6	12
11	**k**	0	14	nd[c]	nd[c]



[a] Reaction conditions: Iodobenzene **165a** (1.5 mmol), phenylacetylene **164a** (1 mmol), CuI (0.5 mol%), Cs_2CO_3 (2 mmol), ligand (0.01 or 0.3 mmol), and dioxane (1 mL) under argon at 135 °C. [b] Determined by GC using tetradecane as an internal standard. [c] Not done.

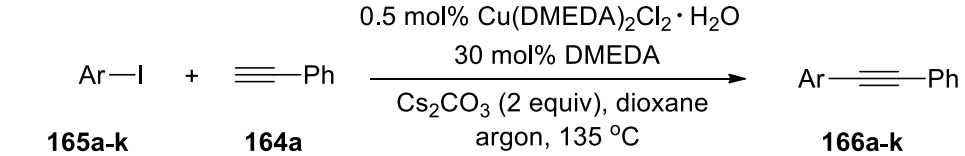
Using 1 mol% of ligand, only phenanthroline (ligand **a**) was effective for the reaction (80%, Table 2, entry 1). From the results after 3 h, it was shown that the catalytic activity with 1 mol% of ligand was generally much lower than that when 30 mol% of ligand was used.

1.5 The Reaction Scope

With the optimized reaction conditions in hand, the scope of the methodology was extended for the coupling of aryl iodides and terminal alkynes. At first, a variety of aryl iodides were set to react with phenylacetylene **164a** (**Table 3**). Electron-poor and electron-rich groups were well tolerated in this reaction. Haloheteroarenes such as iodopyridines and iodothiophenes were also good coupling partners (**Table 3**, entries 9-11). However, aryl bromides or chlorides did not react under these conditions.

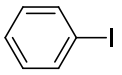
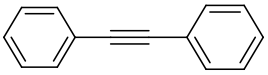
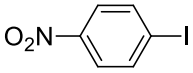
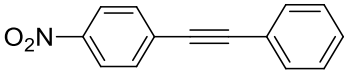
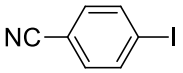
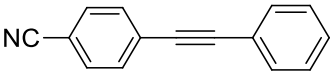
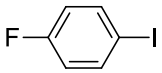
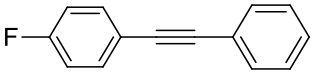
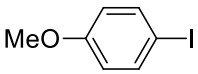
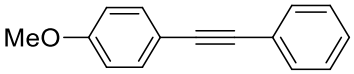
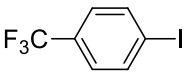
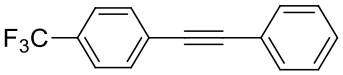
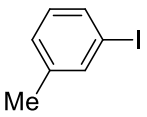
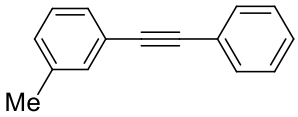
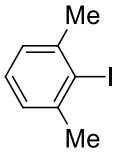
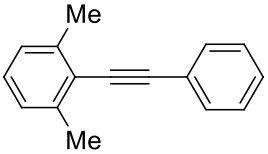
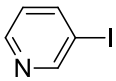
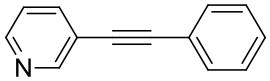
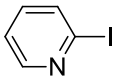
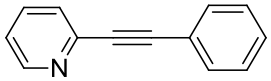
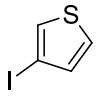
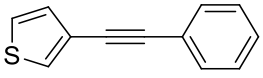
Furthermore, this procedure was extended to various aryl alkynes to react with iodobenzene **165a** under the optimized reaction conditions (**Table 4**). The electronic properties of the arene group significantly influenced the outcome of this reaction. Alkynes with electron-withdrawing groups gave the corresponding products in lower yields. However, raising the amount of DMEDA led to a significant increase in yield (entry 6). Heteroaryl alkynes **164h** and **164i** also reacted with iodobenzene **165a**, providing **166j** and **166i** in moderate yields (entries 7 and 8). Substrates with a strongly electron-deficient nitro-group did not work under the reaction conditions.

Table 3. Couplings of various aryl iodides with phenylacetylene.[a, [140]]



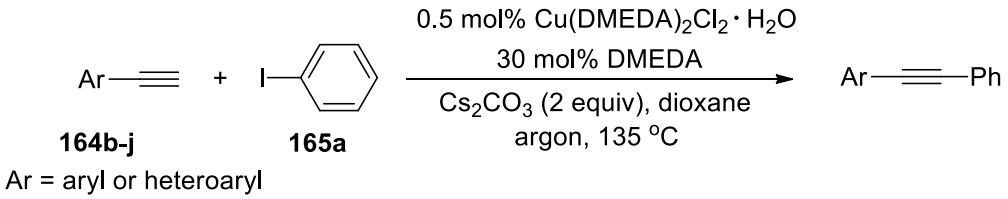
165a-k **164a** **166a-k**

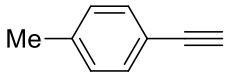
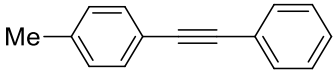
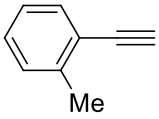
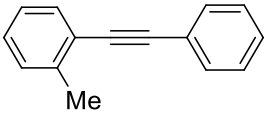
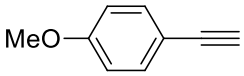
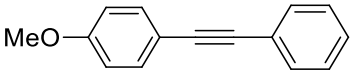
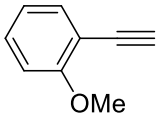
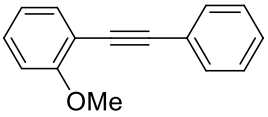
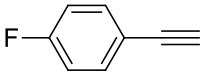
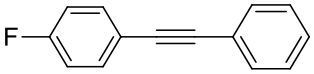
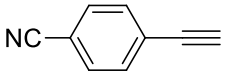
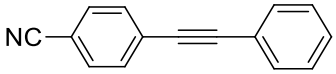
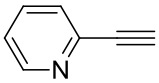
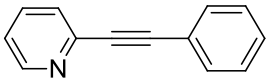
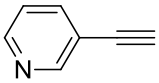
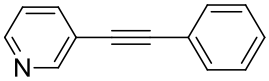
Ar = aryl or heteroaryl

Entry	Aryl iodide		Product		Yield[b] (%)
1		**165a**		**166a**	94
2		**165b**		**166b**	75
3		**165c**		**166c**	88
4		**165d**		**166d**	85
5		**165e**		**166e**	86
6		**165f**		**166f**	93
7		**165g**		**166g**	86
8		**165h**		**166h**	80
9		**165i**		**166i**	84
10		**165j**		**166j**	86
11		**165k**		**166k**	54

[a] Reaction conditions: Aryl iodide (1.5 mmol), phenylacetylene **164a** (1 mmol), $Cu(DMEDA)_2Cl_2 \cdot H_2O$ (0.5 mol%), Cs_2CO_3 (2 mmol), DMEDA (0.3 mmol), and dioxane (1 mL) under argon atmosphere at 135 °C. [b] After column chromatography.

Table 4. Couplings of various aryl alkynes with iodobenzene.[a, [140]]



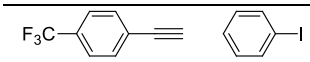
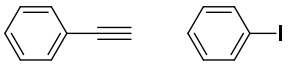
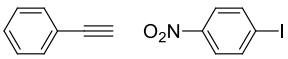
Entry	Aryl alkyne		Product		Yield[b] (%)
1		**164b**		**166l**	83
2		**164c**		**166m**	85
3		**164d**		**166e**	70
4		**164e**		**166n**	63
5		**164f**		**166d**	67
6		**164g**		**166c**	24 (50)[c]
7		**164h**		**166j**	44
8		**164i**		**166i**	35

[a] Reaction conditions: Iodobenzene **165a** (1.5 mmol), aryl alkynes (1 mmol), $Cu(DMEDA)_2Cl_2 \cdot H_2O$ (0.5 mol%), Cs_2CO_3 (2 mmol), DMEDA (0.3 mmol), and dioxane (1 mL) under argon atmosphere at 135 °C. [b] After column chromatography. [c] Use of 50 mol% of DMEDA.

1.6 The Mechanism of the Reaction

The detailed mechnism based on density functional theory (DFT) calculations was then investigated. In this work, the study on DFT was performed by Dr. Adam Johannes Johansson. In order to gain a deeper insight into the reaction mechanism, several electronically different aryl halides were chosen for the investigation. It was determined that the reaction was accelerated by the presence of electron-withdrawing substituents on the aryl iodide just as in C–N bond-forming reactions catalyzed by similar catalysts.[141] Furthermore, the rate limiting step was the C–C bond formation, but not the dissolution of the resting state or the transmetallation step.

Table 5. Computational results.[a, 140]

Alkyne/Aryl iodide	E_{HOMO}-E_{LUMO}(eV)	$G^{‡}/G^{o}$ (kJ mol^{-1})
	4.00	90.7/–194.8
	3.63	88.3/–204.8
	3.55	85.3/–205.7
	1.47	75.2/–211.5

[a] E_{HOMO}-E_{LUMO} is the energy difference between the interacting orbitals. $G^{‡}$ is the activation free energy, while G° is the reaction free energy.

TS^1 and TS^2 were successively found when we searched the potential energy surface (PES) for transition states (TS) (**Figure 1**). In addition, it was determined that the Cu(III)-intermediate in Figure 1 was the only configuration to be a local energy minimum on the potential energy surface. Transition states of TS^3-type were located for a selection of the substrates of the experimental scope in previous work by the Bolm group (**Table 5**).[138] The computed activation energies correlated well with the HOMO-LUMO gap, and the kinetics of the reaction were significantly influenced by

the strongly electron withdrawing NO_2-group. Therefore, the rate limiting step of this reaction is most likely the concerted C–I bond dissociation and C–C bond formation.

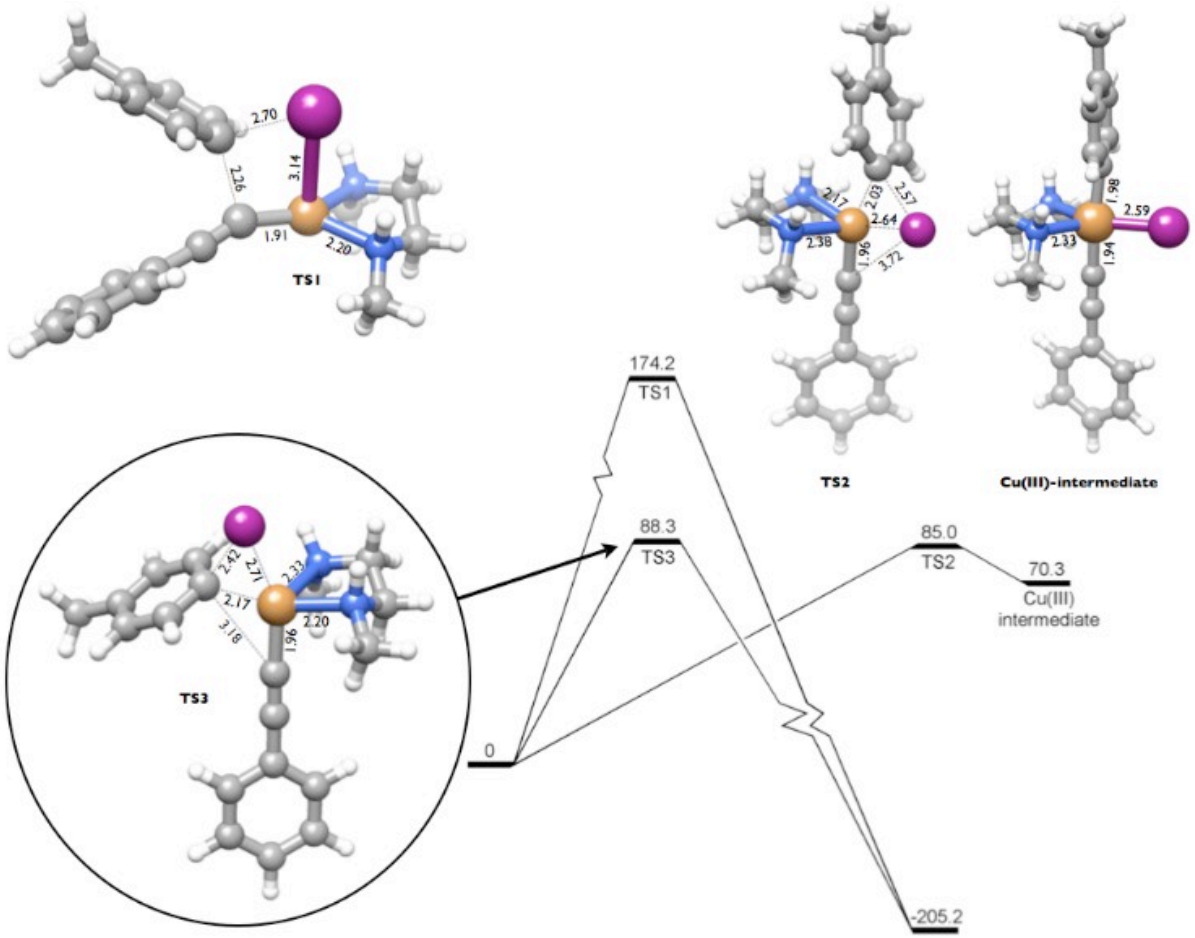


Figure 1. Free energy (kJ mol^{-1}) profile and optimized transition states for the copper-catalyzed coupling of phenylacetylene with 4-iodotoluene.[140]

1.7 Conclusion

A sub-mol% copper-catalyzed Sonogashira-Hagihara-type reaction has been developed for the construction of Csp^2–Csp bonds, which is accelerated by diamine ligands. A number of copper catalysts are efficient for this reaction. The structure of

the ligand has a major impact on the coupling efficiency. The catalytic system tolerates various electron-poor and electron-rich (hetero)aryl iodides and (hetero)aryl alkynes, providing the desired products in good yields. Mechanistic details have been elucidated by kinetic measurements and DFT calculations, showing that the reaction proceeds through a concerted breaking of the phenyl iodide bond and formation of the new C–C bond.

2. Copper-Mediated Oxidative Cross-Couplings of 1,3,4-Oxadiazoles with Polyfluoroarenes

2.1 Introduction

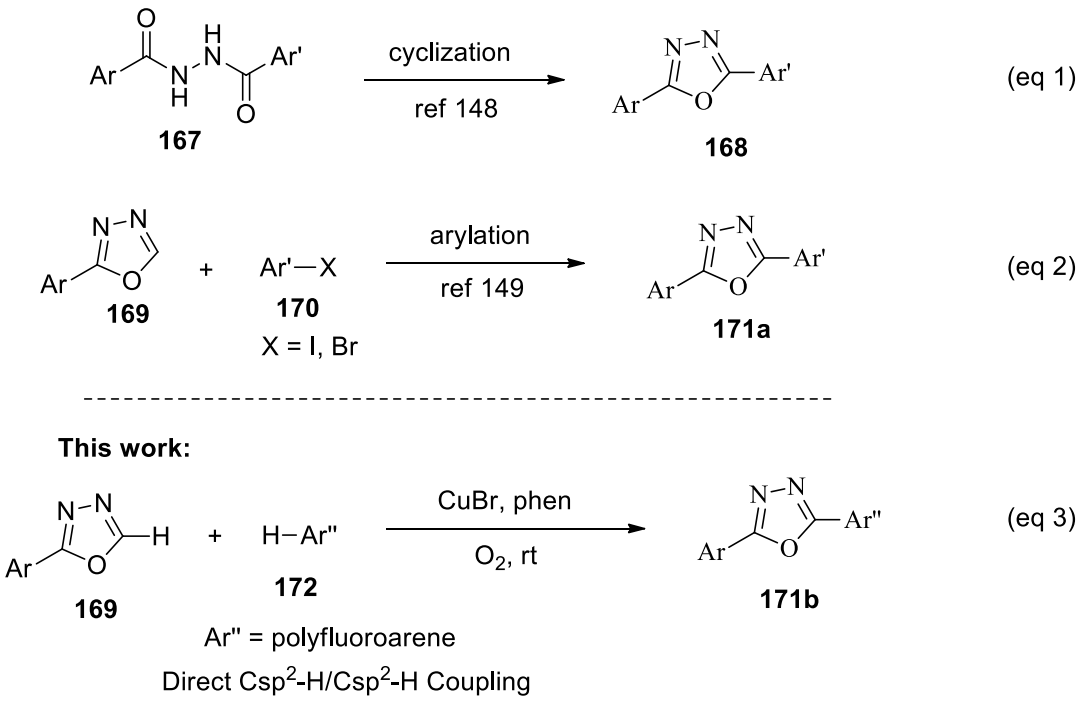
Transition metal-catalyzed C–H activation is a reaction that involves a cleavage of C–H bond and the term is normally restricted to reactions in which organometallic complexes are involved.[2f] The process of these reactions proceeds through coordination of a hydrocarbon to the inner-sphere of a metal, either through an intermediate "alkane or arene complex" or as a transition state leading to a "M–C" intermediate.[142]

Nowadays, both theoretical studies and experimental investigations exhibit that it is feasible to cleave C–H bonds by coordination, despite the fact that they are unreactive.[143] As we know, the research on C–H activation brings the prospect of enabling transformations with cheap and abundant alkanes into a variety of functionalized organic compounds.

2.2 Background

Since the first example on C–H activation reactions by Chatt *et al.* in 1965,[144] significant work has been reported in this field in the following years.[145] Over the past decades, considerable attention has been focused on the design and synthesis of new reagents and catalysts that can facilitate C–H activation.[146] The direct formation of C–C bonds though dual C–H bond cleavage has also been widely explored.[147] However, most of these cases require noble metal catalysts for example palladium under harsh reaction conditions. Moreover, in some cases, stoichiometric amounts of an expensive metal salt are also required as an oxidant.[148] Although recently some

groups have reported copper-catalyzed direct oxidative C–H/C–H cross-couplings,[42], [149] examples based on dual Csp^2–H/Csp^2–H cleavages are still rare.[43], [44], [150]



Scheme 38. Synthetic approaches towards 2-aryl-1,3,4-oxadiazoles.[151]

Nearly half a century ago, 2-(pentafluorophenyl)-5-phenyl-1,3,4-oxadiazole **168** was first prepared by Prudchenko *et al.* through the cyclization of **167** (**Scheme 38**, eq 1).[152] In 2009, the Miura group synthesized 2-aryl-5-phenyl-1,3,4-oxadiazoles **171a** from 1,3,4-oxadiazoles **169** and aryl halides **170** (**Scheme 38**, eq 2).[153]

2.3 Research Objective

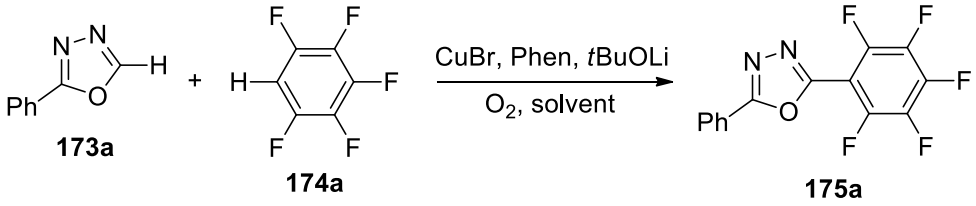
Inspired by the pioneering work on copper-catalyzed oxidative cross-couplings,[42], [149], [150b], [154] the direct oxidative cross-couplings of 1,3,4-oxadiazoles with polyfluorobenzenes was investigated. Finally, a copper-mediated procedure was developed for the direct synthesis of

2-aryl-5-phenyl-1,3,4-oxadiazoles **171b** from 1,3,4-oxadiazoles **169** and polyfluoroarenes **172** (**Scheme 38**, eq 3).[151]

2.4 Optimization of Reaction Conditions

2-Phenyl-1,3,4-oxadiazole (**173a**) and pentafluorobenzene (**174a**) were chosen for the model reaction to screen the reaction conditions.

Table 6. The effect of various solvents.[a, 151]



Entry	Solvent	Yield (%)
1	DMSO	0
2	Toluene	0
3	MeCN	34
4	Dioxane	0
5	PhCN	trace
6	THF	0
7	NMP	0
8	DMF	0
9	EtCN	25
10	Neat	trace

[a] Reaction conditions: **173a** (0.2 mmol), **174a** (1 mmol), CuBr (0.2 mmol), 1,10-phenanthroline (0.2 mmol), *t*BuOLi (0.6 mmol), O_2 (1 atm), solvent (1.5 mL), rt, 14 h.

From Table 6, it can be deduced that acetonitrile proved to be the best solvent for this reaction. Benzonitrile or propionitrile gave lower yields of the product. Other solvents such as toluene, DMF, DMSO, NMP, and THF were not effective for this reaction. A

yield of 34% was obtained when the reaction of **173a** with **174a** (0.2 mmol scale, 1:5 ratio) was performed using 1 equivalent of CuBr, 3 equivalents of *t*BuOLi and 1 equivalent of 1,10-phenanthroline in acetonitrile under an atmosphere of dioxygen.

Table 7. The effect of metal sources.[a, [151]]

Entry	Catalyst	Yield (%)
1	CuF_2	0
2	$CuCl_2$	6
3	$Cu(OAc)_2$	trace
4	$CuBr_2$	12
5	$CuBr_2$·Phen	13
6	CuCl	mixture
7	CuI	24
8	CuO	0
9	Cu_2O	0
10[b]	$PdCl_2(PPh_3)_2$	0
11[b]	$Pd(OAc)_2$	0
12	$FeCl_3$	0
13[c]	CuBr	65
14	no catalyst	0
15[c,d]	CuBr	64

[a] Reaction conditions: **173a** (0.2 mmol), **174a** (1 mmol), catalyst (0.2 mmol), 1,10-phenanthroline (0.2 mmol), *t*BuOLi (0.6 mmol), O_2 (1 atm), MeCN (1.5 mL), rt, 14 h. [b] Use of 5 mol% of catalyst. [c] Use of 30 equivalents of **173a**. [d] The purity of CuBr was 99.999%.

Following optimization of the copper salts (**Table 7**), it was determined that CuBr was the best catalyst for this reaction. Palladium catalysts such as $PdCl_2(PPh_3)_2$ and $Pd(OAc)_2$ were not effective in this reaction process (entries 10 and 11). The reaction did not work in the absence of a catalyst (entry 14). Product **175a** was formed in 65% yield when the homocoupling of **173a** was reduced by increasing the loading of **174a**

to 30 equivalents (entry 13).[149a] A control reaction was carried out using CuBr with a purity of 99.999%, providing product **175a** in a similarly good yield (entry 15), which could exclude the possibility of contamination by other catalytically active transition metals.[155]

Table 8. The effect of various ligands.[a, 151]

Entry	Ligand	Yield (%)
1	2,2'-bipyridine	28
2	DMEDA	27
3	bathophenanthroline	60
4	bathocuproine	37
5	2,2',6',2''-terpyridine	41
6	*N*,*N*'-dimethyl-1,2-cyclohexanediamine	15
7	no ligand	24

[a] Reaction conditions: **173a** (0.2 mmol), **174a** (6 mmol), CuBr (0.2 mmol), ligand (0.2 mmol), *t*BuOLi (0.6 mmol), O_2 (1 atm), MeCN (1.5 mL), rt, 14 h.

Next, the effect of various ligands, oxidants, and bases was investigated and the results were summarized in Table 8, Table 9, and Table 10, respectively. The reaction proceeded well when bathophenanthroline was used instead of 1,10-phenanthroline (entry 6). The yield was much lower in the absence of a ligand (entry 7). Other oxidants such as $PhI(OAc)_2$, Selectfluor, and AgOAc were ineffective for this reaction (entries 8-10). The reaction did not work in the absence of dioxygen (entry 11). Other bases such as *t*BuONa, *t*BuOK, Na_2CO_3, and Cs_2CO_3 gave lower yields or only trace amounts of product.

Table 9. The effect of various oxidants.[a, 151]

Entry	Oxidant	Yield (%)
1	$PhI(OAc)_2$	0
2	Selectfluor	0
3	AgOAc	0
4	no oxidant	0

[a] Reaction conditions: **173a** (0.2 mmol), **174a** (6 mmol), CuBr (0.2 mmol), 1,10-phenanthroline (0.2 mmol), *t*BuOLi (0.6 mmol), oxidant (0.4 mmol), MeCN (1.5 mL), rt, 14 h.

Table 10. The effect of various bases.[a, 151]

Entry	Base	Yield (%)
1	Na_2CO_3	trace
2	Cs_2CO_3	trace
3	K_2CO_3	trace
4	KOH	trace
5[b]	KOH	trace
6	K_3PO_4	trace
7	*t*BuONa	16
8	*t*BuOK	12

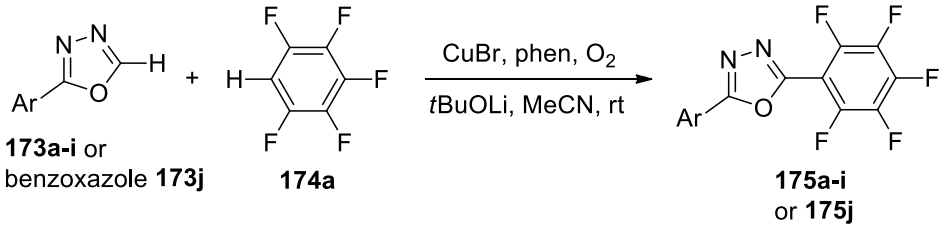
[a] Reaction conditions: **173a** (0.2 mmol), **174a** (1 mmol), CuBr (0.2 mmol), 1,10-phenanthroline (0.2 mmol), base (0.6 mmol), O_2 (1 atm), MeCN (1.5 mL), rt, 14 h. [b] Using DMSO as solvent.

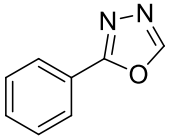
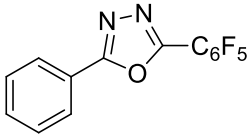
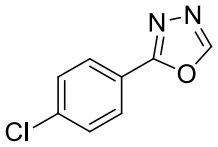
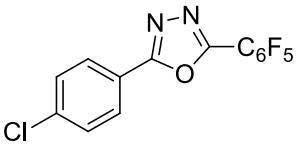
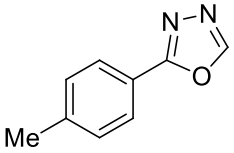
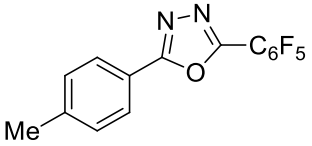
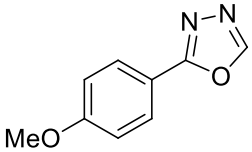
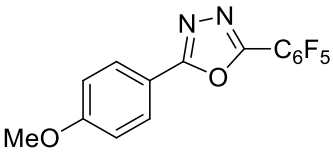
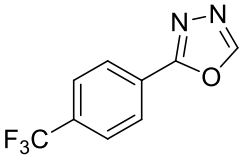
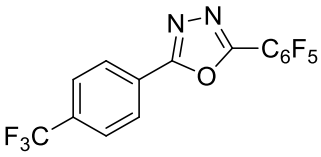
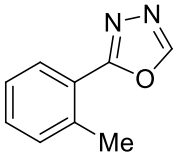
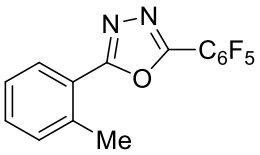
2.5 The Reaction Scope

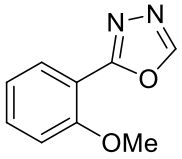
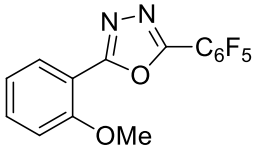
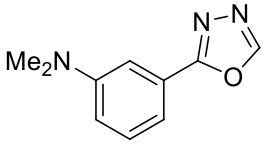
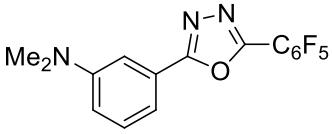
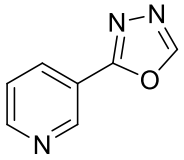
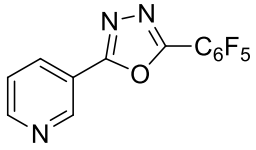
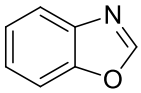
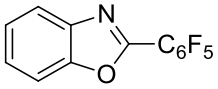
With the optimized conditions in hand (**Table 7**, entry 13), the reaction scope was investigated (**Table 11**). A broad range of substrates with electron-rich or electron-deficient aromatic substituents were reacted with pentafluorobenzene **174a** (entries 1-8). Product **175i** was obtained from 2-(3-pyridyl)-1,3,4-oxadiazole **173i** in 45% yield using only 10 equivalents of **174a** (1 mmol scale) (entry 9). Only 20% of product **175j** was provided for the coupling of benzoxazole **173j** with 5 equivalents of

174a (Entry 10).

Table 11. Copper-mediated direct arylations of 2-aryl-1,3,4-oxadiazoles (**173a-i**) and benzoxazole (**173j**) with pentafluorobenzene (**174a**).[a, 151]



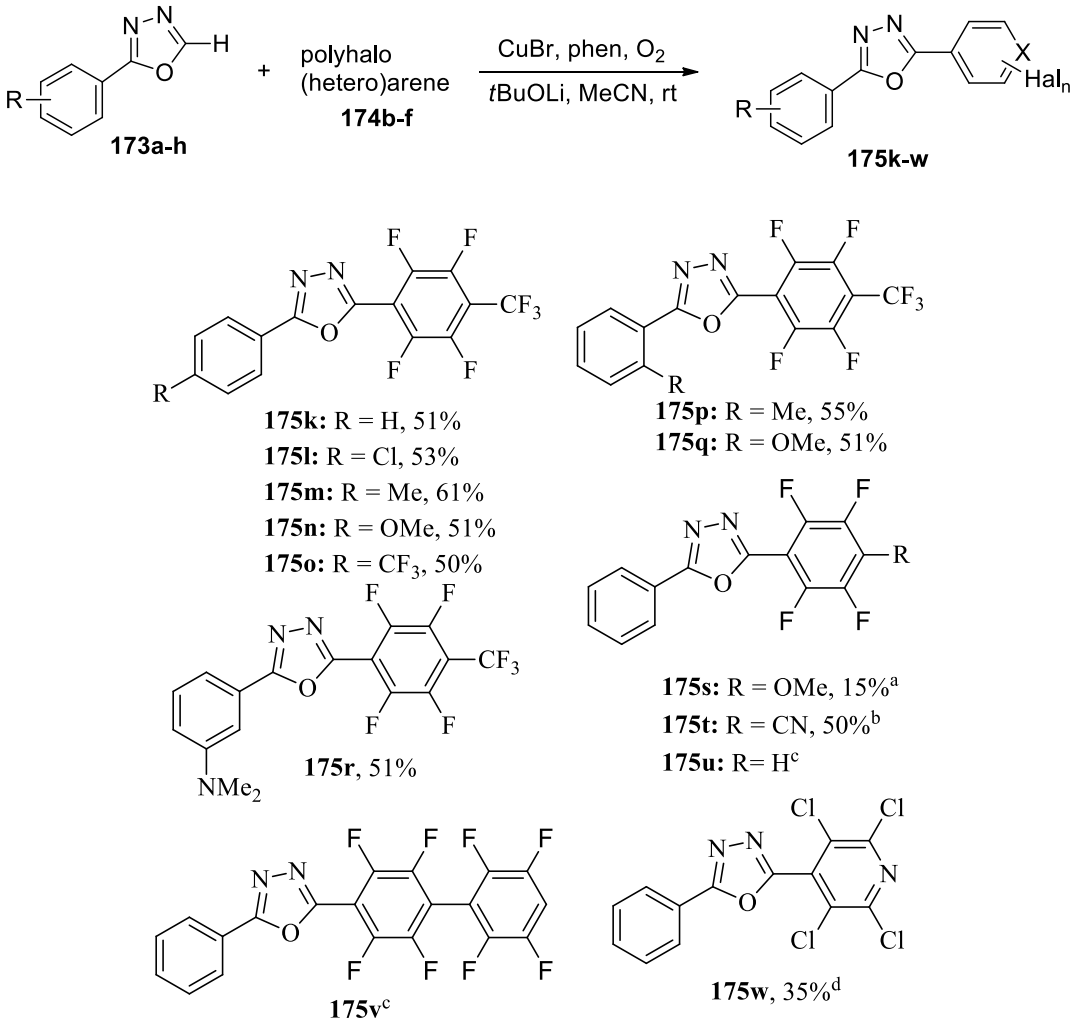
Entry	Heterocycle		Product		Yield (%)
1		**173a**		**175a**	65
2		**173b**		**175b**	68
3		**173c**		**175c**	67
4		**173d**		**175d**	65
5		**173e**		**175e**	61
6		**173f**		**175f**	63

7		**173g**		**175g**	64
8		**173h**		**175h**	62
9		**173i**		**175i**	45[b]
10		**173j**		**175j**	20[c]

[a] Reaction conditions: Heterocycle (0.2 mmol), **174a** (6 mmol), CuBr (0.2 mmol), phen (0.2 mmol), *t*BuOLi (0.6 mmol), O_2 (balloon), CH_3CN (1.5 mL), rt, 14 h. [b] Scale: 1 mmol; use of 10 equivalents of **174a**. [c] Scale: 1 mmol; use of 5 equivalents of **174a**.

Subsequently, the procedure was extended to a range of tetrahalo(het)arenes containing additional substituents (**Scheme 39**). The amount of polyfluoroarenes was reduced to 10 equivalents. Tetrafluoroarenes bearing electron-withdrawing substituents reacted well with a variety of 2-aryl-substituted 1,3,4-oxadiazoles. 1-Trifluoromethyl-2,3,5,6-tetrafluorobenzene (**174b**) coupled with oxadiazoles **173a**-**h** leading to products **175k**-**r** in 50-61% yields. 1-Cyano-2,3,5,6-tetrafluorobenzene **174c** (5 equiv) gave product **175t** in 50% yield.

The reaction of electron-rich 1-methoxy-2,3,5,6-tetrafluorobenzene (**174d**) with **173a** provided **175s** in a yield of only 15%. 2,3,5,6-Tetrafluorobenzene (**174e**) (10 equiv) reacted with **173a**, affording products **175u** and **175v** in 8% and 9% yields, respectively. 2,3,5,6-tetrachloropyridine (**174f**) (3 equiv) gave **175w** in 35% yield.

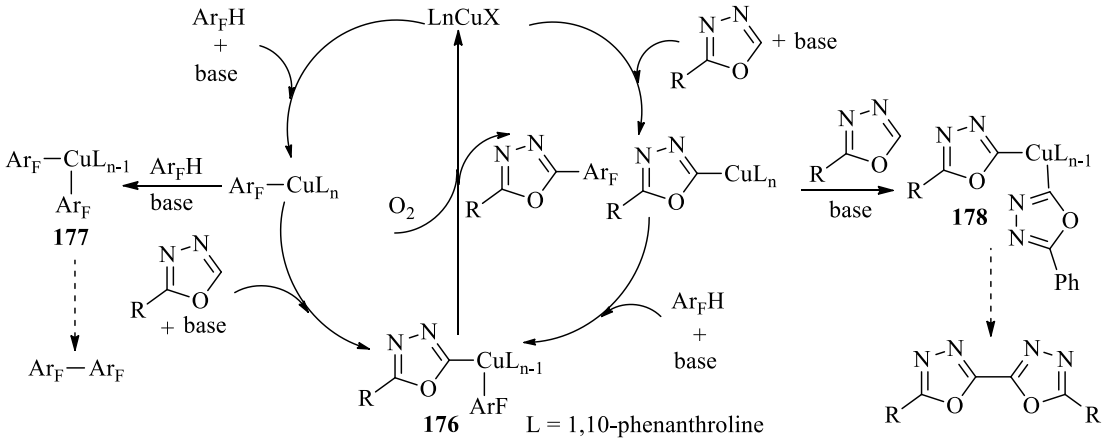


Scheme 39. Copper-mediated direct arylation of polyhalo(het)arenes with 2-substituted 1,3,4-oxadiazoles.[151] Reaction conditions: 1,3,4-Oxadiazole (0.2 mmol), polyhalo(het)arene (2 mmol), CuBr (0.2 mmol), phen (0.2 mmol), *t*BuOLi (0.6 mmol), O_2 (balloon), CH_3CN (1.5 mL), rt, 14 h. [a] 1 mmol scale. [b] Use of 5 equivalents of polyfluoroarene. [c] Scale: 1 mmol; Products **175u** and **175v** were obtained in 8% and 9%, respectively. [d] 0.5 mmol scale; use of 3 equivalents of 2,3,5,6-tetrachloropyridine and 4 equivalents of *t*BuOLi, 0.4 M.

2.6 The Mechanism of the Reaction

On the basis of the pioneering work,[42] a possible reaction mechanism was proposed (**Scheme 40**). The formation of the homo-coupling by-products can also be observed in the reaction process.[149] The reductive elimination of Cu(azole)(fluoroaryl)L_{n-1} complex **176** releases the desired product. The homo-coupling products of the

polyhaloarene and the azole are formed based on Cu(fluoroaryl)$_2$L$_{n-1}$ complex **177** and Cu(azole)$_2$L$_{n-1}$ complex **178**, respectively. In the process, formation of the azole-derived by-product is suppressed by an excess of polyhaloarene.



Scheme 40. Proposed reaction mechanism.[151]

2.7 Conclusion

In conclusion, a copper-mediated procedure for the direct oxidative cross-coupling of 2-(het)aryl-1,3,4-oxadiazoles with polyhaloarenes has been developed through dual Csp^2–H activation. The reaction proceeds under mild reaction conditions at room temperature, which provides concise access to polyhaloarenes-containing biaryl compounds. Molecular oxygen and acetonitrile are crucial for the success of this reaction.

3. Transition Metal-Free Direct C–H Bond Thiolation of 1,3,4-Oxadiazoles and Related Heteroarenes

3.1 Introduction

Sulfur shares the chalcogen group with oxygen, selenium and tellurium. It widely exists in nature and is essential for life. Not only two of the 20 common amino acids, i.e. cysteine and methionine, but also some important drugs such as the antibiotics contain sulfur. Furthermore, organosulfur compounds are normally important components of natural resources such as fossil fuels, coal, and natural gas. As we know, sulfur-containing antibiotics can save many lives, but sulfur mustard is a deadly chemical warfare agent with the ability to form large blisters on the exposed skin and in the lungs.[156]

Furthermore, organosulfur compounds (thioethers, thioesters, sulfonates) can also be employed as electrophiles for cross-coupling reactions.[157] Recently, considerable attention has been focused on transition metal-catalyzed C–C bond formations through bond cleavage reactions, particularly C–S bond cleavage due to their relative stability and readily availability.[158]

The formation of C–S bonds represents a key step in the synthesis of a broad range of biologically active molecules and functional materials.[4h], [38], [159] Over the past years, the cross-coupling of aryl halides with thiols has become one of the dominant methods for the synthesis of C–S bond compounds in the presence of a transition metal catalyst, based on metals such as palladium,[160] nickel,[161] copper,[162] and so on. In addition, sometimes aryl triflates[163] and boronic acids[164] can be used as an alternative instead of aryl halides for such transformations. The formation of C–S bonds has also been realized by couplings of aryl halides with diaryl disulfides.[165]

3.2 Background

Recently, the C–H bond functionalization of 1,3,4-oxadiazoles has attracted considerable attention,[166] due to their interesting properties in medicinal chemistry[167] and material sciences.[168] Previously, a copper-mediated oxidative cross-couplings of 1,3,4-oxadiazoles with polyfluoroarenes under mild conditions was reported by our group.[151] Despite of a few examples on the synthesis of heterocyclic thioethers containing 1,3,4-oxadiazole units and derivatives,[169] pre-functionalized 1,3,4-oxadiazoles and/or metal catalysts are normally required for most of these cases.

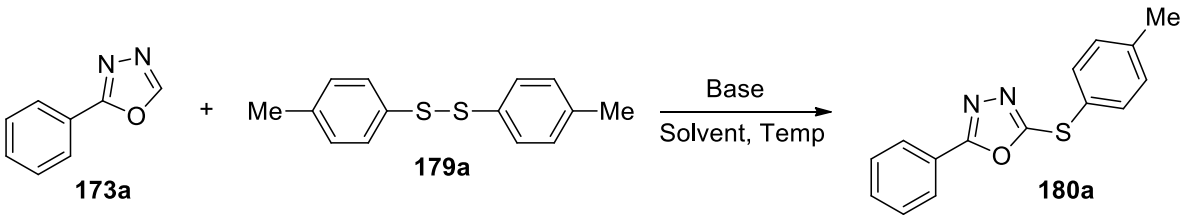
3.3 Research Objective

Considering the importance of organosulfur compounds and 1,3,4-oxadiazoles themselves, the direct thiolation of 1,3,4-oxadiazoles and other related heteroarenes such as indole, benzothiazole, *N*-phenylbenzimidazole, and caffeine was investigated.

3.4 Opitimization of Reaction Conditions

The inital screening and optimization of the reaction conditions was conducted with 2-phenyl-1,3,4-oxadiazole (**173a**) and di-*p*-tolyl disulfide (**179a**) as substrates (**Table 12**). Using **173a** and **179a** in a 1:2.5 ratio (on a 0.5 mmol scale), Cs_2CO_3 (2 equiv) in 2 mL toluene, product **180a** was obtained in the first reaction in the presence of CuI (20 mol%) in 47% yield after 18 h at 130 °C under argon atmosphere (entry 1). To our surprise, however, an increase in yield (54%) was observed in the absence of the copper salt (entry 2). With 5 equivalents of disulfide **179a** the yield of **180a** increased to 77% (entry 3). A yield of 77% was also obtained when 7 equivalents of **179a** was used (entry 4). It was worth noting that the excess of di-*p*-tolyl disulfide (**179a**) could be recovered quantitively upon work-up.

Table 12. Thiolation of 2-phenyl-1,3,4-oxadiazole with di-*p*-tolyl disulfide.[a, 170]



173a + **179a** → **180a**

Entry	Base	Solvent	Temp (°C)	Yield (%)
1[b]	Cs_2CO_3	toluene	130	47
2	Cs_2CO_3	toluene	130	54
3[c]	Cs_2CO_3	toluene	130	77
4[d]	Cs_2CO_3	toluene	130	77
5	Cs_2CO_3	CH_3CN	130	30
6	Cs_2CO_3	DMSO	130	0
7	Cs_2CO_3	DMF	130	0
8	Cs_2CO_3	1,4-dioxane	130	87
9	NEt_3	1,4-dioxane	130	0
10	*t*BuOLi	1,4-dioxane	130	0
11[e,f]	Cs_2CO_3	1,4-dioxane	130	85
12[e]	Cs_2CO_3	1,4-dioxane	110	83
13[g]	Cs_2CO_3	1,4-dioxane	130	58
14[h]	Cs_2CO_3	1,4-dioxane	130	86

[a] Reaction conditions: **173a** (0.5 mmol), **179a** (1.25 mmol), base (1 mmol), solvent (2 mL), 130 °C, argon atmosphere, 18 h. [b] Addition of 20 mol% of CuI. [c] Use of 5 equivalents of **179a**. [d] Use of 7 equivalents of **179a**. [e] 24 h. [f] Use of 1.3 equivalents of Cs_2CO_3. [g] Performed in air. [h] The purity of Cs_2CO_3 was 99.994%.

Next, various solvents were tested for their influence on the reaction behaviour (entries 5-8). The reaction in acetonitrile gave a lower yield of **180a**. DMSO and DMF were ineffective for this reaction. 1,4-dioxane proved to be the best solvent, providing **180a** in 87% yield (entry 8). Further studies showed that the use of other bases such as triethylamine and *t*BuOLi were ineffective (entries 9 and 10). Using less base or performing the reaction at lower temperature decreased the yield of **180a**

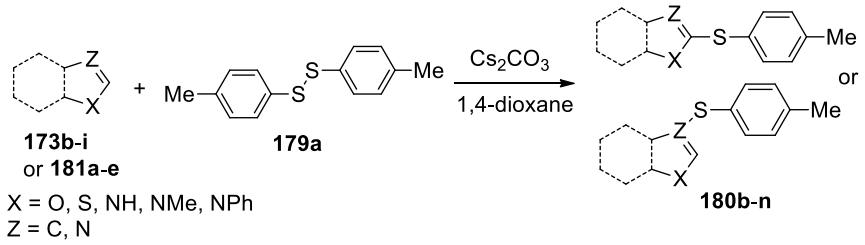
(entries 11 and 12). Under an atmosphere of air instead of argon the yield of **180a** dropped to 58% (entry 13). A control experiment was performed using Cs_2CO_3 with a purity of 99.994% and freshly distilled 1,4-dioxane, in which the yield of 86% made it unlikely that a trace metal was involved in these reactions (entry 14).[155]

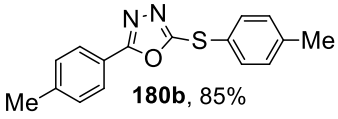
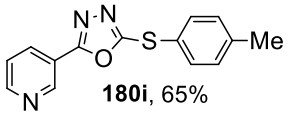
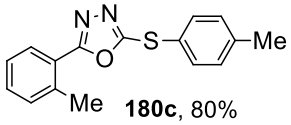
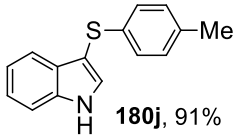
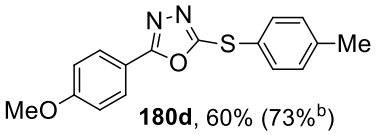
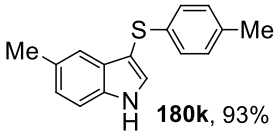
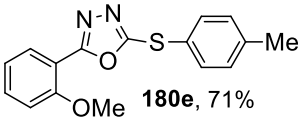
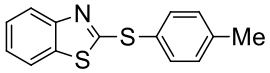
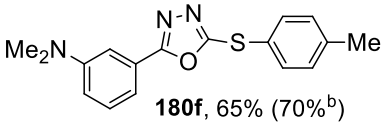
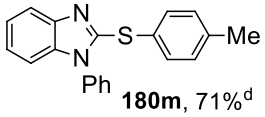
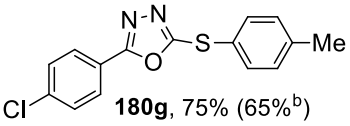
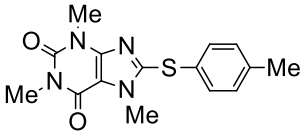
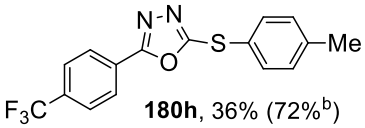
3.5 The Reaction Scope

With the optimized reaction conditions in hand, the scope of the substrates was investigated (**Table 13**). Various 2-aryl substituted 1,3,4-oxadiazoles and related heterocycles were employed to react with disulfide **179a**. Good yields of the corresponding thiolated products were obtained for most of the substrates. 2-Aryl 1,3,4-oxadiazoles with electron-donating substituents on the arene gave higher yields than those with electron-withdrawing groups. In addition, the preparation of 2-(3-pyridyl)-substituted product **173i** was also realized in this manner with a yield of 65%, which suggested that such heteroaryl groups in the 2-position of the substrate were tolerated well (entry 8).

To extend the substrate scope, related heterocycles were applied to these reaction conditions (enties 9-13). The reactions of indole **181a** and its 5-methylated derivative **181b** with **179a** provided 3-thiolated products **180j** and **180k** in excellent yields (entries 9 and 10). Those results compare well to the known metal-catalyzed procedure for the synthesis of 3-sulfenyl indoles.[171] The reaction of benzothiazole **181c** with **179a** was sluggish, providing **180l** in only 55% yield after 10 days. By replacing the base with *t*BuOLi, the reaction time was shortened to 32 h and the yield was enhanced to 86% (entry 11). Similarly, with *t*BuOLi as a base, the reaction of *N*-phenylbenzimidazole **181d** and caffeine **181e** with **179a** provided the corresponding products **180m** and **180n** in 71% and 55% yields, respectively (entries 12 and 13).

Table 13. Thiolation of 1,3,4-oxadiazoles and related heteroarenes with di-*p*-tolyl disulfide.[a, 170]

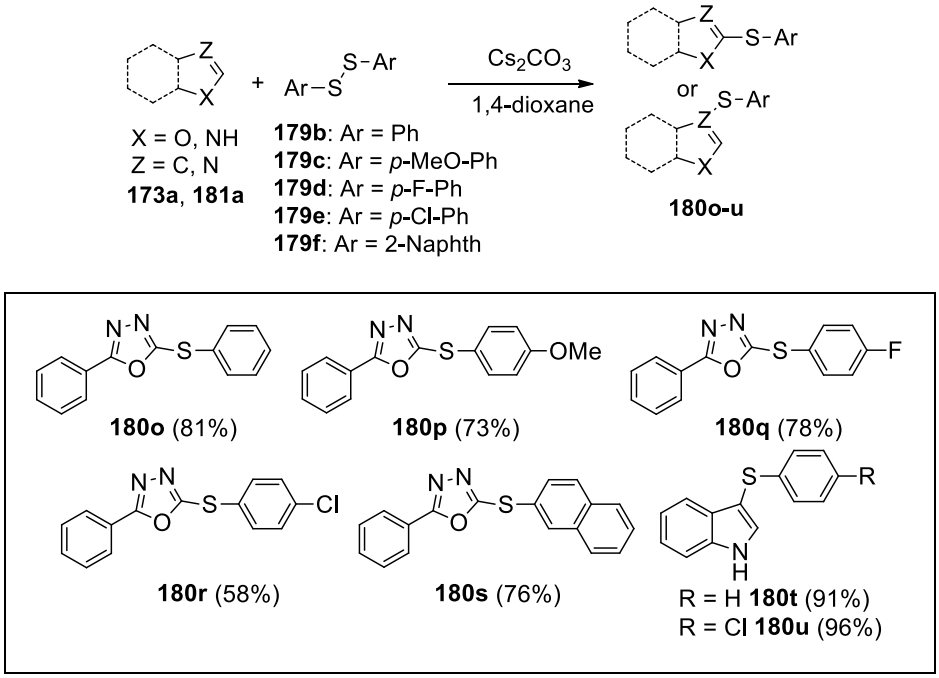


Entry	Product, Yield (%)	Entry	Product, Yield (%)
1	 **180b**, 85%	8	 **180i**, 65%
2	 **180c**, 80%	9	 **180j**, 91%
3	 **180d**, 60% (73%[b])	10	 **180k**, 93%
4	 **180e**, 71%	11	 **180l**, 55%[c] (86%[d])
5	 **180f**, 65% (70%[b])	12	 **180m**, 71%[d]
6	 **180g**, 75% (65%[b])	13	 **180n**, 55%[d]
7	 **180h**, 36% (72%[b])		

[a] Reaction conditions: Heteroarene (0.5 mmol), **179a** (1.25 mmol), Cs_2CO_3 (1 mmol), 1,4-dioxane (2 mL), 130 °C, argon atmosphere, 18 h. [b] Performed at 110 °C for 24 h. [c] Reaction time of 10 days. [d] Use of 3 equivalents of *t*BuOLi as base instead of Cs_2CO_3; reaction time of 32 h.

The diaryl disulfide component was varied to react with 2-phenyl 1,3,4-oxadiazole **173a** and indole **181a** (**Table 14**). Accordingly, products **180o-s** were obtained in yields ranging from 58% to 81%. Indole **179a** reacted well with diaryl disulfides **179b** and **179e**, providing the corresponding products **180t** and **180u** in 91% and 96% yields, respectively. Unfortunately, dibenzyl disulfide and bis(4-nitrophenyl) disulfide did not react with compound **173a** under the given reaction conditions.

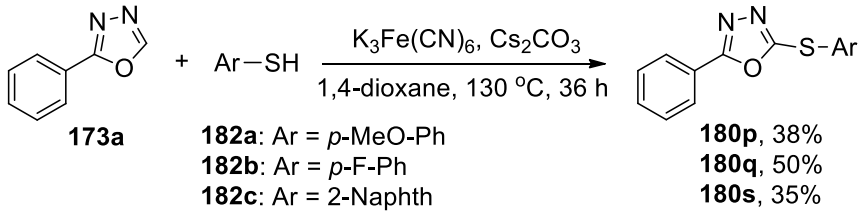
Table 14. Scope of diaryl disulfide coupling partners.[a, [170]]



[a] For the reaction conditions, see **Table 12**, entry 8.

Furthermore, the direct thiolation of **173a** with aryl thiols instead of diaryl disulfides was also investigated. In a first attempt, 2-phenyl 1,3,4-oxadiazole (**173a**, 0.5 mmol) was combined with aryl thiol **182a** (1.25 mmol, 2.5 equiv), $K_3Fe(CN)_6$ (1.25 mmol, 2.5 equiv) and Cs_2CO_3 (1 mmol, 2 equiv) in 1,4-dioxane (2 mL), and the mixture was kept at 130 ^oC under argon atmosphere (**Scheme 41**). Analysis by thin layer chromatography (TLC) showed that the corresponding diaryl disulfide **179c** was formed quickly, but even after 2 days no product **180p** was observed. After 4 days,

product **180p** was obtained in 35% yield. Increasing the amount of base to 4 equivalents, gave **180p** in 38% yield after a shorter reaction time (36 h). Under the same reaction conditions, thioethers **180q** and **180s** were obtained in 50% and 35% yields, respectively (**Scheme 41**).



Scheme 41. Direct thiolation of 1,3,4-oxadiazoles with aryl thiols.[170]

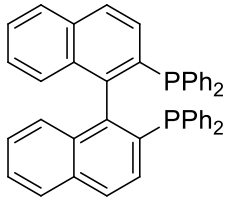
3.6 Conclusion

In conclusion, a facile procedure has been developed for the synthesis of heterocyclic thioethers under transition metal-free conditions. Various 2-aryl 1,3,4-oxadiazoles were thiolated at C5 in good to high yields using diaryl disulfides as an aryl sulfide source. Aryl thiols could also be applied, albeit only in moderate yields. Finally, the method proved applicable to other heterocycles including indole, benzothiazole, *N*-phenylbenzimidazole, and caffeine, providing the corresponding thioethers in good yields.

4. Metal-Free Phosphorylations of 1,3,4-Oxadiazoles and Related Heterocycles

4.1 Introduction

Organophosphorus compounds widely exist in nature. Organophosphines such as BINAP (**Scheme 42**) are known as useful ligands in catalysis where they form complexes in combination with various metal ions.[172] Reactions catalyzed by complexes that derived from chiral phosphines can provide enantiomerically enriched products.[173]



Scheme 42. (R-,S-)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP).

Typically, azole-derived phosphines are prepared through deprotonation-phosphorylation sequences in the presence of a strong base like *n*BuLi.[174] Alternatively, Zarudnitskii *et al.* reported silylation of 1,3,4-oxadiazoles with a weak base to prepare silylated derivatives.[175]

4.2 Background

Stimulated by the importance of their relevant core structures in medicinal chemistry[167a] and material sciences,[168] functionalizations of 1,3,4-oxadiazoles through C–C[151] and C–S[170] bond formation were investigated by our group. Inspired by these findings, it was envisioned that phosphorylations of such heterocycles could also be performed under those comparably mild reaction conditions. Tolmachev and

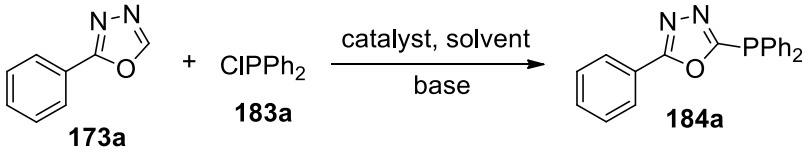
co-workers reported two examples in a similar work before, in which 1,3,4-oxadiazoles were phosphorylated with chlorodiphenylphosphine using triethylamine as base, but the details about yields and full product characterization were not given.[176]

4.3 Research Objective

Based on our previous work on the functionalization of 1,3,4-oxadiazoles and in view of the relatively rare reports of phosphorylations of 1,3,4-oxadiazoles, the phosphorylation of these oxadiazoles and related heterocycles was investigated.

4.4 Optimization of Reaction Conditions

2-Phenyl-1,3,4-oxadiazole (**173a**) and chlorodiphenylphosphine (**183a**) were chosen for the inital screening and optimization of the reaction (**Scheme 43**).



Scheme 43. Phosphorylation of 1,3,4-oxadiazole (**1a**).[177]

Using a 1:1 ratio of starting materials **173a** and **183a** (1 mmol scale), 1 equivalent of triethylamine and pyridine as solvent, **184a** was obtained in a yield of 40% after stirring the reaction mixtue at 25 °C for 24 h. Raising the temperature to 40 °C increased the yield of **184a** to 51%. Inorganic bases such as Cs_2CO_3 and K_3PO_4 instead of triethylamine were not effective in this reaction. The yield was enhanced significantly for the reaction by replacing pyridine with DCM and varying the reagent ratios. The initial conditions provided product **184a** in 75% yield when the reaction

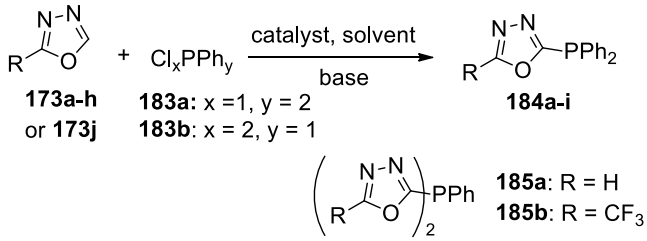
was performed in DCM. Later the yield was raised to 82% when 1.2 equivalents of **173a** and 2 equivalents of base were used. Finally, **184a** was obtained in 90% yield (after 48 h at 40 °C in DCM) when 2 equivalents of chlorophosphine **183a** and NEt_3 were used, respectively (**Table 15**, entry 1).

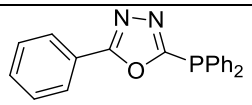
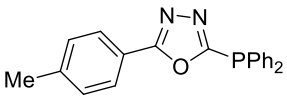
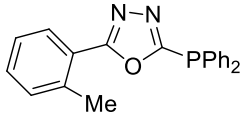
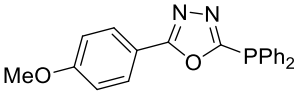
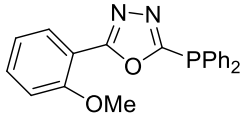
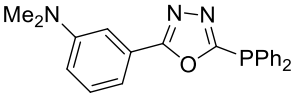
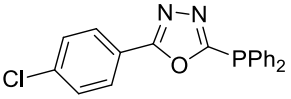
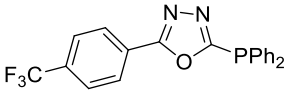
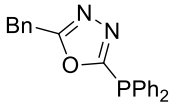
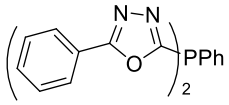
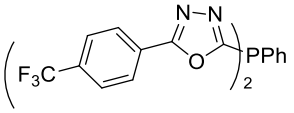
4.5 The Reaction Scope

With the optimized reaction conditions in hand, the substrate scope of the reaction was investigated (**Table 15**). The reactions of a series of functionalized 2-aryl-1,3,4-oxadiazoles **173a-h** with chlorophosphine **183a** provided the corresponding products in good to excellent yields (enties 1-8). It seemed that steric and electronic effects on the arene group of the azole played a minor role in the reaction. In addition, 2-benzyl-substituted 1,3,4-oxadiazole **173j** also reacted well with **183a**, affording product **184i** in good yield (entry 9).

With dichlorophenylphosphine (**183b**) as electrophile and 3 equivalents of azole, double arylated phosphine reactions were performed (**Table 15**). As the first example, the reaction of 2-phenyl-1,3,4-oxadiazole (**173a**) with **183b** provided **185a** in 68% yield. Increasing the reaction scale to 10 mmol, a similarly good yield of 70% was obtained (entry 10). Using trifluoromethyl-substituted **173e** as starting material, product **185b** was formed in 46% yield (entry 11).

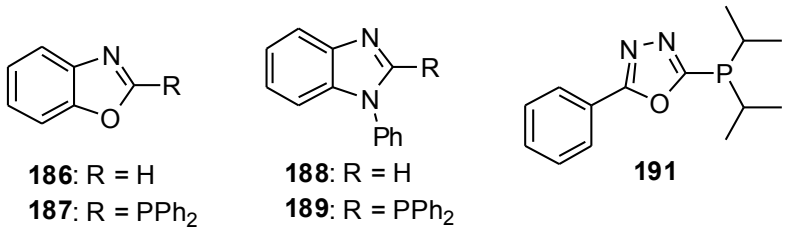
Table 15. Substrate scope of the transition metal-free phosphorylation of azole derivatives.[a, 177]



Entry	Substrate	R	Product		Yield (%)
1	**173a**	Ph		**184a**	90
2	**173c**	*p*-Tol		**184b**	86
3	**173f**	*o*-Tol		**184c**	89
4	**173d**	*p*-MeO-Ph		**184d**	75
5	**173g**	*o*-MeO-Ph		**184e**	74
6	**173h**	*m*-NMe_2-Ph		**184f**	68
7	**173b**	*p*-Cl-Ph		**184g**	91
8	**173e**	*p*-CF_3-Ph		**184h**	83
9	**173j**	Bn		**184i**	80
10[b]	**173a**	ph		**185a**	68 (70[c])
11[b]	**173e**	*p*-CF_3-Ph		**185b**	46

[a] Conditions: azole (1.0 mmol), $ClPPh_2$ (2.0 mmol), NEt_3 (2 mmol), DCM (1.5 mL), 40 °C, 48 h. [b] Use of 3.0 mmol of azole and Cl_2PPh instead of $ClPPh_2$. [c] In parentheses: result of a 10 mmol scale reaction.

Other heterocycles such as benzoxazole (**186**) and *N*-phenyl benzimidazole (**188**) could also be employed under this reaction conditions, though showing some challenges in such transformations. The yields of the corresponding phosphorylated products **187** and **189** were only 30% and 20%, respectively. In order to investigate the general applicability of this procedure to aliphatic phosphine chlorides, 2-phenyl-1,3,4-oxadiazole (**173a**) was set to react with chlorodiisopropyl phosphine (**190**) under the standard reaction conditions, providing product **191** in 59% yield (**Scheme 44**).



Scheme 44. Benzoxazole- and *N*-phenyl benzimidazole based starting materials and products; diisopropylphosphino-substituted 1,3,4-oxadiazole **191**.[177]

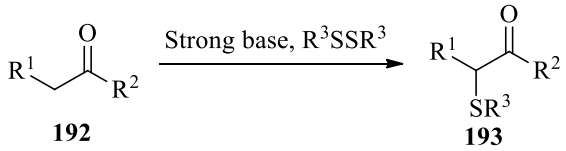
4.6 Conclusion

In conclusion, various phosphine arylated reactions of 2-substituted 1,3,4-oxadiazoles and related heterocycles with chlorodiphenylphosphine (**184a**) or dichlorophenylphosphine (**183b**) were investigated under metal-free reaction conditions, providing the corresponding phosphorylated products in good to excellent yields. Triethylamine and DCM were crucial for the success of the reaction as a base and a solvent, respectively.

5. Copper-Catalyzed S–S Bond Cleavage and C–C Bond Activation: Synthesis of α-Thiophenyl Carbonyl Compounds

5.1 Introduction

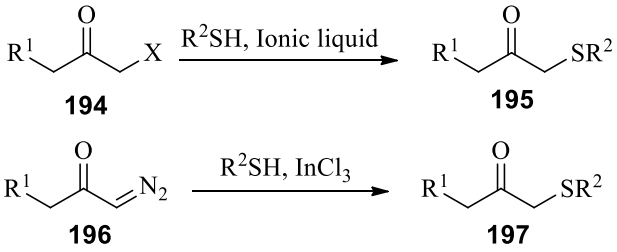
α-Thiophenyl carbonyl compounds are very useful synthetic intermediates in organic synthesis.[178] Normally, they can be prepared by sulfenylation of enolates with various sulfenylating agents, such as disulfides (**Scheme 45**)[179] and so on.[180]



192 **193**

Scheme 45. Sulfenylation of enolates with disulfides.[179b]

Alternatively, they can also be synthesized by either S_N2 substitution reaction of α-halogenated carbonyl derivatives with benzenethiols[181] (or disulfides[182]) or metal-catalyzed intermolecular insertion of an S–H bond into α-diazoketones (**Scheme 46**).[183]



194 **195**

196 **197**

Scheme 46. Sulfenylation of enolates with disulfides.[181], [183b]

In addition, Nishiyama and co-workers recently reported a direct phenylthiolation of carbonyl compounds in the presence of catalytic amounts of cesium carbonate and

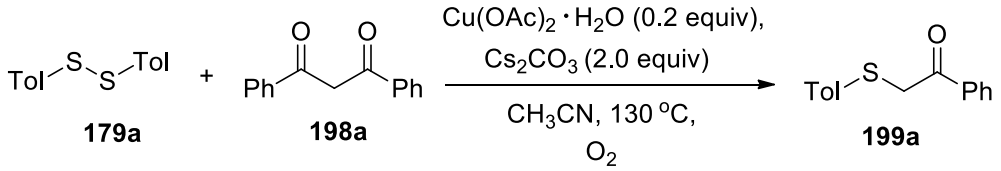
diphenyl diselenide.[184]

5.2 Background

In the past decades, transition-metal-catalyzed selective C–C bond cleavage reactions have attracted considerable attention due to their potential for broad applications in organic synthesis.[39b], [185] They fascinated us especially for their potential use of copper catalysts in such reactions. To date, various carbon–carbon bond formations have been reported by selective C–C cleavages of alcohols,[52a], [52d] diketones,[54] and others.[52c] However, no examples have been reported on the formation of C–S bonds by selective C–C cleavage of β-diketones so far.

5.3 Research Objective

Previously, a direct thiolation of 1,3,4-dioxazoles and related heterocycles was reported by our group.[170] In the course of studying copper-catalyzed reactions, the effect of copper catalysts on C–C cleavage was investigated. Finally, a copper-catalyzed procedure was developed for the synthesis of α-thiophenyl carbonyl compounds through selective C–C cleavage of β-diketones,[186] in combination with S–S cleavage of disulfides in an atmosphere of dioxygen (**Scheme 47**).

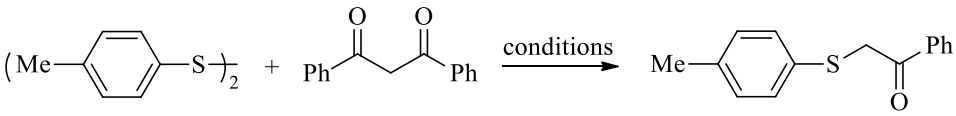


Scheme 47. Copper-catalyzed synthesis of α-thiophenyl carbonyl compounds.

5.4 Optimization of the Reaction

Di-*p*-tolyl disulfide (**179a**) (0.5 mmol scale) and dibenzoylmethane (**198a**) (in a 1:3 ratio) were chosen for the model reaction to screen the reaction conditions under an atmosphere of dioxygen (**Table 16**).

Table 16. Screened reaction conditions.[a, 187]



179a **198a** **199a**

Entry	Catalyst	Base	Solvent	Yield[b] (%)
1	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	dioxane	trace
2	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	DMF	trace
3	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	DMSO	0
4	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	CH_3NO_2	0
5	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	toluene	0
6	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	CH_3CN	85
7	CuBr	Cs_2CO_3	CH_3CN	43
8	$CuBr_2$	Cs_2CO_3	CH_3CN	57
9	$CuCl_2$	Cs_2CO_3	CH_3CN	48
10	none	Cs_2CO_3	CH_3CN	20
11[c]	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	CH_3CN	9
12[d]	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	CH_3CN	13
13[e]	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	CH_3CN	35
14[f]	$Cu(OAc)_2 \cdot H_2O$	Cs_2CO_3	CH_3CN	90 (87)
15[f]	$Cu(OAc)_2$	Cs_2CO_3	CH_3CN	(77)

[a] Reaction conditions: **179a** (0.5 mmol), **198a** (1.5 mmol), catalyst (0.2 equiv), base (2 equiv), solvent (1 mL), 130 °C, under an atmosphere of dioxygen, 24 h. [b] GC yields, using tetradecane as an internal standard. Yields after column chromatography are in parentheses. [c] Under an atmosphere of argon. [d] Under an atmosphere of air. [e] 110 °C. [f] Using 4 equiv of **198a**.

At first, the effect of various solvents on the reaction behaviour was investigated

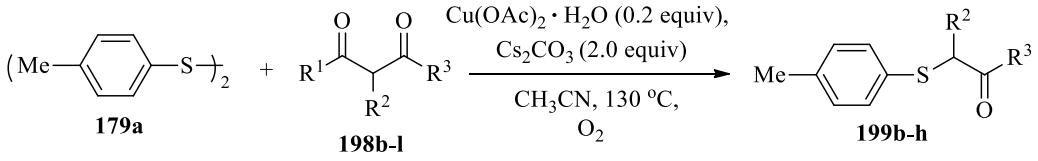
(Entries 1-6). Dioxane, DMF, DMSO, CH_3NO_2 or toluene proved ineffective for the reaction. The desired product was formed in 85% yield when the reaction was performed in acetonitrile at 130 ^oC after 24 h.

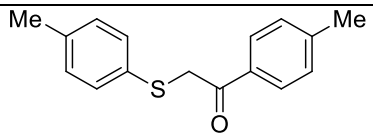
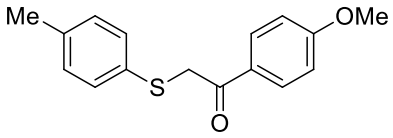
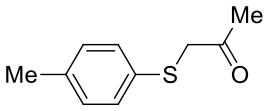
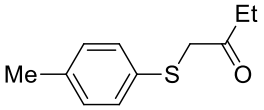
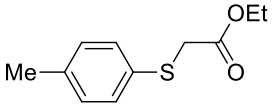
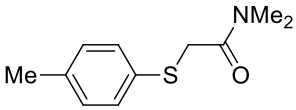
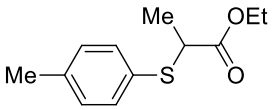
Other copper catalysts such as CuBr, $CuBr_2$ and $CuCl_2$ provided **199a** in lower yields (entries 7-9). Product **199a** was obtained only in 20% yield in the absence of a catalyst (entry 10). It was shown that an atmosphere of dioxygen was crucial for the success of the reaction. A much lower yield was obtained when the reaction was performed under an atmosphere of argon or air instead of dioxygen (entries 11 and 12). Lower reaction temperature (110 ^oC) gave a low yield of 35% (entry 13). Product **199a** was obtained in 90% yield when the loading of **198a** was increased to 4 equivalents (entry 14, yield after column chromatography: 87%). Interestingly, the yield decreased slightly when anhydrous $Cu(OAc)_2$ was employed as a catalyst (entry 15).

5.5 The Reaction Scope

Under the optimized reaction conditions [see footnote (a) of **Table 16**], the scope of the reaction of β-diketones with **179a** was investigated. Both aryl and alkyl β-diketones reacted well with **179a**, providing the corresponding products in good to excellent yields (**Table 17**). Interestingly, it was necessary for β-diketones **198b** and **198c** to use more amounts of solvent (3 mL) to obtain high yields, affording products **199b** and **199c** (**Table 17**, entries 1 and 2, 87% and 74%, respectively).

Table 17. Reactions of various of β-diketones with di-*p*-tolyl disulfide.[a, [187]]



Entry	R^1	R^2	R^3	Substrate	Product		Yield (%)
1	*p*-Tol	H	*p*-Tol	**198b**		**199b**	87[b]
2	*p*-MeO-Ph	H	*p*-MeO-Ph	**198c**		**199c**	74[b]
3	Me	H	Me	**198d**		**199d**	99[c]
4	Et	H	Et	**198e**		**199e**	95[c,d,e]
5	EtO	H	EtO	**198f**		**199f**	96[c]
6	*p*-CF_3-Ph	H	*p*-MeO-Ph	**198g**		**199c**	75[b]
7	CF_3	H	Me	**198h**		**199d**	85[c]
8	Me	H	NMe_2	**198i**		**199g**	88[c]
9	Me	H	Ph	**198j**		**199a/199d**	30/61
10	Me	H	EtO	**198k**		**199f**	99[c,d,e]
11	Me	Me	EtO	**198l**		**199h**	45[e,f]

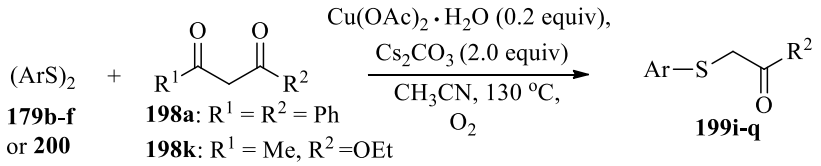
[a] Reaction conditions: Di-*p*-tolyl disulfide **179a** (0.5 mmol), β-diketone (4 equiv), $Cu(OAc)_2 \cdot H_2O$ (0.2 equiv), Cs_2CO_3 (2 equiv), CH_3CN (1 mL), 130 °C, under an atmosphere of dioxygen, 24 h. [b] Using 3 ml CH_3CN. [c] Using 10 equiv of β-diketone, 16 h. [d] 0.1 equiv of $Cu(OAc)_2 \cdot H_2O$. [e] Without acetonitrile as solvent. [f] Using 0.25 mmol scale, 10 equiv of β-diketone, under an atmosphere of air.

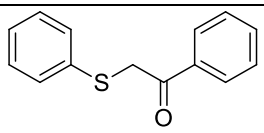
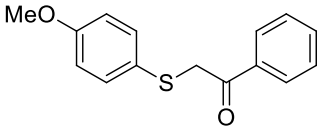
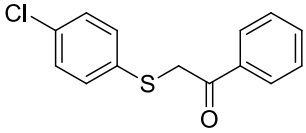
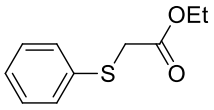
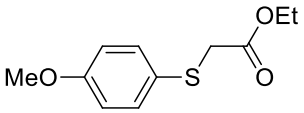
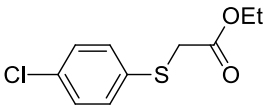
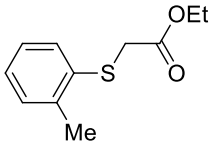
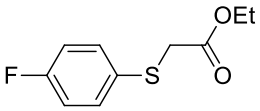
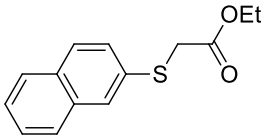
To determine which C–C bond was being cleaved preferentially, the reactions of unsymmetric β-diketones **198g**, **198h** and **198i** with **179a** were performed under the corresponding conditions. The results indicated that the C–C bond closest to the electron-withdrawing substituent was easier to be cleaved.

With both aryl and alkyl substituents, substrate **198j** was employed and reacted with **179a**, affording a mixture of two products **199a** and **199d** (**Table 17**, entry 9, 30% and 61% yield, respectively). In the absence of acetonitrile, unsymmetric alkyl β-diketone **198k** (10 equiv) gave product **199f** in an excellent yield (99%) using 0.1 equivalent of catalyst (**Table 17**, entry 10). It was noteworthy that the reaction of substrate **198l**, which had one methyl group in the α-position of the carbonyl, still proceeded smoothly to provide **199h** in 45% yield (**Table 17**, entry 11).

To further extend the substrate scope, using aryl or alkyl β-diketones **198a** and **198k** as coupling partners, various diaryl disulfides were employed in the reaction (**Table 18**). The reaction of **198k** with the corresponding disulfides proceeded well under neat reaction conditions with only 10 mol% of catalyst. Consequently, products **199i-q** were provided in good to excellent yields.

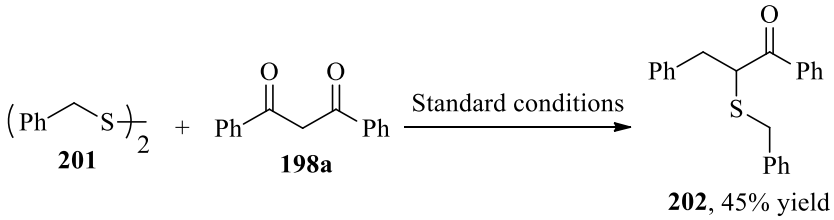
Table 18. The scope of thiolation of β-diketones with diaryl disulfides.[a, 187]



Entry	Ar	β-diketone	Product		Yield (%)
1	Ph (**179b**)	**198a**		**199i**	99
2	*p*-MeO-Ph (**179c**)	**198a**		**199j**	81
3	*p*-Cl-Ph (**179e**)	**198a**		**199k**	93
4	Ph (**179b**)	**198k**		**199l**	88[b]
5	*p*-MeO-Ph (**179c**)	**198k**		**199m**	85[b]
6	*p*-Cl-Ph (**179e**)	**198k**		**199n**	75[b]
7	*o*-Tol (**200**)	**198k**		**199o**	98[b]
8	*p*-F-Ph (**179d**)	**198k**		**199p**	80[b]
9	2-naphthyl (**179f**)	**198k**		**199q**	92[b]

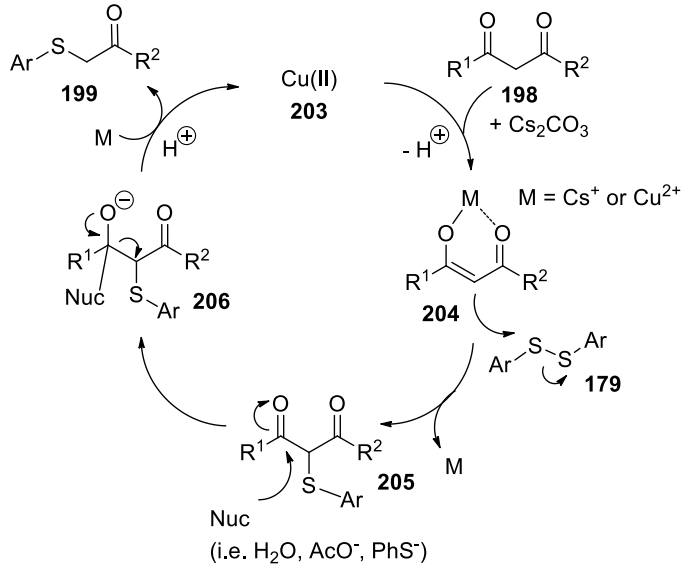
[a] Reaction conditions: Diaryl disulfide (0.5 mmol), β-diketone (4 equiv), $Cu(OAc)_2 \cdot H_2O$ (0.2 equiv), Cs_2CO_3 (2 equiv), 130 °C, dioxygen atmosphere, 24 h. [b] Using 10 equiv of **198k**, without acetonitrile as solvent, 0.1 equiv of $Cu(OAc)_2 \cdot H_2O$, 16 h.

Besides, dibenzyl disulfide (**201**) was also applied and reacted with aryl β-diketone **198a** under the optimized reaction conditions. To our surprise, the C–C bond cleavage did not proceed and in this case the *in situ* reduction of one carbonyl group was observed, affording **202** in 45% yield (**Scheme 44**). More details on the reaction process remain to be illucidated, but the structure of compound **202** is clear, which has been verified by ^{1}H NMR, ^{13}C NMR, elemental anylysis, MS and HRMS.



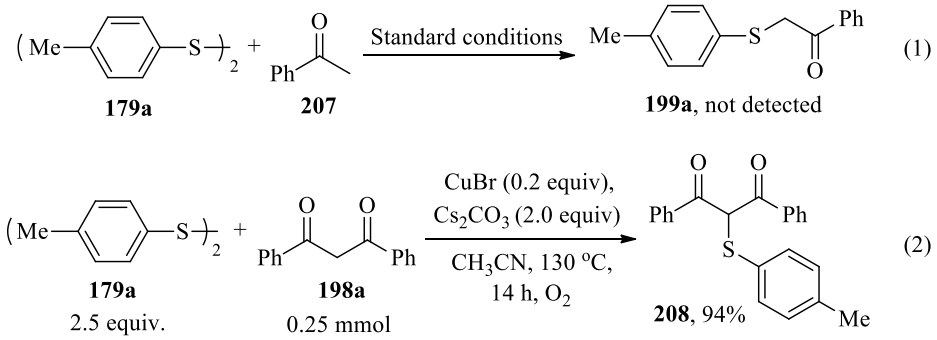
Scheme 48. Reaction of dibenzyl disulfide (**201**) with **198a**.[187]

5.6 The Mechanism of the Reaction



Scheme 49. Proposed reaction mechanism.[187]

Based on the observations, a possible reaction mechanism was proposed (**Scheme 49**). At first, a metal enolate species **204** is formed by deprotonation of β-diketone **198** in the presence of copper(II) acetate (**203**) and a base (here Cs_2CO_3). Then **204** attacks diaryl disulfide **179** to provide intermediate **205**. The attack of a nucleophlic species to the carbonyl group results in intermediate **206**. The C–C bond cleavage occurs to lead to the desired product **199**. The role of dioxygen remains unclear at this stage. Most probably, the nucleophile might be residual water, acetate ions (from the catalyst or hydrolysis of acetonitrile at elevated temperatures) or a sulfur derivative. It was found that the yield decreased slightly when anhydrous copper(II) acetate was employed as a catalyst (**Table 16**, entry 15) and the yield increased significantly to 98% when HPLC grade acetonitrile, which contained small amounts of water, was used as a solvent instead of extra dry acetonitrile.



Scheme 50. Control reactions.[187]

In order to get more details about the mechanism, additional control reactions were performed (**Scheme 50**). According to the analysis of the crude reaction mixture by GC-MS, acetopheneone (**207**) was formed as a by-product in this reaction.[188] Control reactions were carried out in the absence of diaryl disulfide **179a**, in which the formation of **207** was still observed. From the result of a control reaction, however, acetophenone (**207**) did not act as an intermediate in the reaction process (**Scheme 50**,

eq 1).[184] Interestingly, using 2.5 equivalents of **198a** and 0.2 equivalent of CuBr instead of $Cu(OAc)_2$ in 2 mL acetonitrile, the C–C bond cleavage did not occur and **208** was obtained in 94% yield (**Scheme 50**, eq 2).

5.7 Conclusion

In conclusion, a copper-catalyzed procedure has been developed for the synthesis of various α-arylthioketones and α-arylthioesters starting from diaryl disulfides and β-diketones or β-ketoesters. The cleavage of both C–C and S–S bonds occurs efficiently in the presence of a copper catalyst under dioxygen atmosphere. The reaction tolerates a broad range of functional groups. Alkyl or aryl functionalized β-diketones/β-ketoesters, as well as a variety of diaryl disulfides can be employed in this reaction. The existence of small amounts of water is good for this reaction.

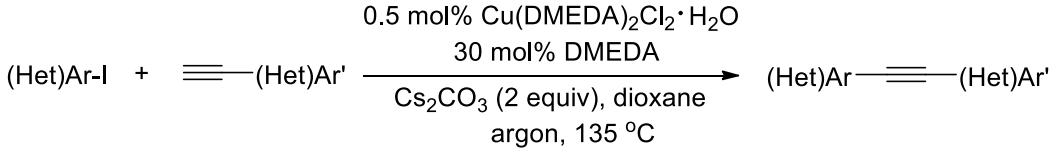
6. Conclusions and Perspectives

6.1 Conclusions

My research interests/expertise lie in transition metal-catalyzed C–H/C–C bond activation, the C–H bond functionalization of (hetero)aryl compounds and oxidative cross-coupling reactions and their applications for the synthesis of interesting target molecules. The aim of this thesis is to develop new synthetic methods and design highly efficient, mild, and selective organic reactions, as well as to investigate the mechanism to gain deeper understanding of the corresponding reactions.

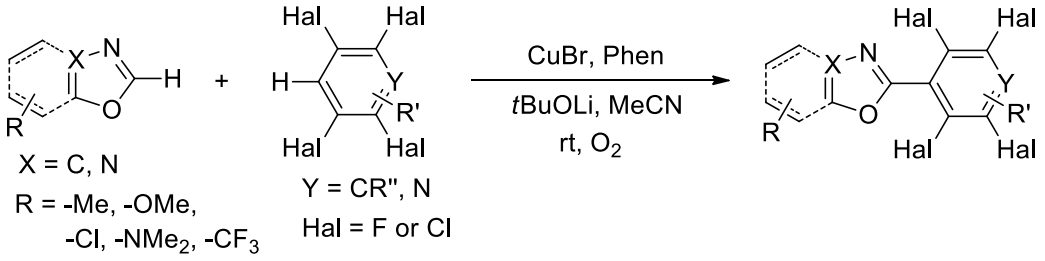
During my doctoral studies, my work focused on strategies that enable reactions to proceed directly through C–H/C–C bond activation in the presence of cheap and easily available transition metal catalysts. In particular, copper salts as catalysts in many reactions were investigated, because they are not only cheap and readily available, but also versatile in their applications and proven to be effective for numerous transformations.

1) Copper-catalyzed Sonogashira-Hagihara-type cross-coupling reactions[140]



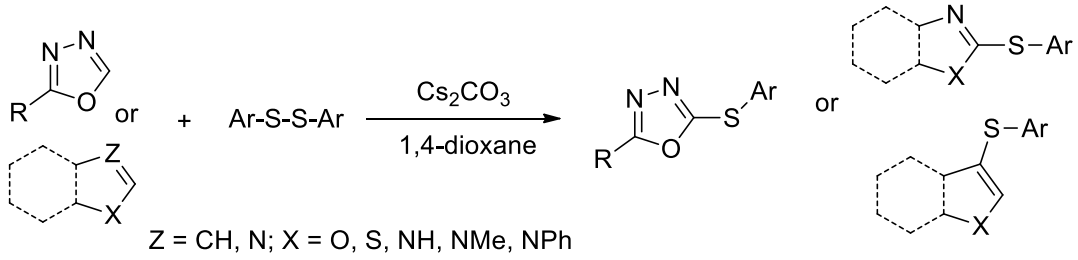
In this work, the effect of the copper sources and various ligands on the reaction was investigated. All the tested copper salts were effective for the reaction. It was determined that the structure of the ligand played a significant role in the process. The reaction scope was extended and mechanistic details were revealed following kinetic measurements and DFT (density functional theory) calculations.

2) Copper-catalyzed direct oxidative cross-couplings of 1,3,4-oxadiazoles with polyfluoroarenes[151]



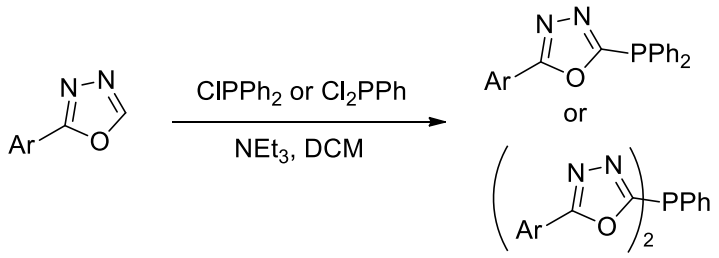
Inspired by recent reports in copper-catalyzed direct functionalization of C–H bond, Csp^2–H/Csp^2–H coupling reactions were investigated. In this work, various copper salts, ligands, solvents and oxidants were tested in the reaction. Acetonitrile and dioxygen were crucial for the success of this reaction. A series of biaryl substrates were prepared in moderate to good yields. The reactions were performed under mild reaction conditions at room temperature using an inexpensive copper source.

3) Transition metal-free direct C–H bond thiolation of 1,3,4-oxadiazoles and related heteroarenes[170]



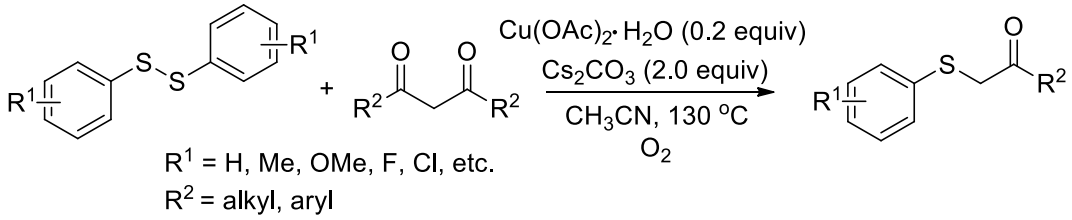
C–S bond formation between 1,3,4-oxadiazoles and diaryl disulfides was investigated. The reaction proceeded well under transition metal-free reaction conditions. Other related heterocycles including indoles, benzothiazole, *N*-phenylbenzimidazole and caffeine were thiolated, providing the corresponding products in excellent yields.

4) Metal-free phosphorylations of 1,3,4-oxadiazoles and related heterocycles[177]



The phosphorylation of 1,3,4-oxadiazoles was investigated. DCM and NEt_3 were the best solvent and base, respectively. Under the optimized reaction conditions, a variety of phosphorylated 2-substituted 1,3,4-oxadiazoles were obtained in good to excellent yields.

5) Copper-catalyzed synthesis of α-thiophenyl carbonyl compounds[187]



A copper-catalyzed procedure was developed for C–S bond formation through dual C–C/S–S bond cleavages under an atmosphere of dioxygen. In this work, acetonitrile is crucial for the success of the reaction. The reaction has a wide tolerance of funcitional groups.

6.2 Perspectives

As catalysts employed in reactions, the use of copper can date back to more than one century ago when the copper-catalyzed homocoupling of aryl halides was discovered by Ullmann. Since the discovery of the Ulmman reaction, copper-catalyzed reactions

have been developed for a long time in the past century. Particularly over the past couple decades, chemists have employed copper catalysts in various chemical transformations, which in some cases provide complementary methods to the well-established palladium-based procedures. The catalytic ability of copper to succeed in some reactions when palladium has failed was observed by our group and others. Actually, more and more groups have transfered their attention to the field of copper catalysts, endeavouring to contribute to the booming world of copper catalyst chemsitry.

Currently the state-of-the-art copper-based methods primarily allow the formations of various C–C bonds through direct oxidative/dehydrogenative cross-couplings and C–H/C–C bond activation reactions, and so on. However, there is still a lot to do to improve copper-catalyzed methods. For example, the copper-catalyzed direct Sonogashira-type cross-couplings of aromatic compounds with terminal alkynes still suffer from a limited substrate scope.[42] It can be envisioned that this cross coupling would proceed through halogenation-Sonogashira-Hagihara-type-cross-coupling sequences. If this assumption should be verified, then the reaction would surely have a broad substrate scope.

The work presented here will provide alternative methods in the synthesis of interesting and important target molecules, which contain various bonds such as C–C, C–S and C-P bonds, under mild reaction conditions. The future of copper chemistry is supposed to be even more promising in the near future.

Experimental Part

1. General Techniques

All the synthetic operations described in the present experimental part including reactions, work-ups and chromatographic separations were carried out in a well ventilated hood according to the current safety dispositions.

Air and moisture sensitive reactions were conducted under an inert atmosphere of argon using Schlenk techniques. For water-free and oxygen-free reactions, all glasswares were oven dried prior to use, and then filled with argon.

2. Solvents

Solvents for anhydrous reactions were dried and purified according to standard techniques.[189]

CH_2Cl_2: Distillation from calcium hydride.

Toluene: Distillation from sodium-benzophenone ketyl radical.

THF: Pre-drying on KOH/Al_2O_3, followed by distillation from sodiumbenzophenone ketyl radical.

Ethyl acetate (EtOAc) and *n*-pentane for flash column chromatography were distilled before use. DMF, MeOH, 1,4-dioxane, DMSO and acetonitrile were HPLC- or reagent grade and were used as received.

3. Determination of the Physical Properties of the Synthesized Compounds

3.1 NMR Spectroscopy

^{1}H NMR spectra were recorded on a *Varian* Mercury 300 spectrometer (300 MHz), a *Varian* Inova 400 spectrometer (400 MHz), or a Varian VNMRS 600 spectrometer (600 MHz). Chemical shifts are given in ppm relative to tetramethylsilane (TMS, 0.00 ppm). Solvent residual peaks ($CDCl_3$: 7.26 ppm; DMSO-d_6: 2.50 ppm) were used as internal standard. Coupling patterns are described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Coupling costants (*J*) are given in Hertz (Hz).

^{13}C NMR spectra were recorded on a *Varian* Mercury 300 spectrometer (75 MHz), a *Varian* Inova 400 spectrometer (100 MHz), or a Varian VNMRS 600 spectrometer (150 MHz).

^{19}F NMR spectra were recorded either on a *Varian* Mercury 300 spectrometer (282 MHz), a *Varian* Inova 400 spectrometer (376 MHz), or a Varian VNMRS 600 spectrometer (564 MHz).

^{31}P NMR spectra were recorded either on a *Varian* Mercury 300 spectrometer (122.0 MHz) or on a *Varian* VNMRS 600 spectrometer (243.9 MHz).

3.2 Mass Spectroscopy

Mass spectra were recorded on a *Varian* MAT 212 or on a *Finnigan* MAT 95 spectrometer with EI (electronic impact) ionization, at a 70 eV ionization potential. Peaks are listed according to their *m/z* value. High resolution mass spectra (HRMS) were recorded on a *Finnigan* MAT 95 spectrometer.

3.3 Infrared Spectroscopy

IR Spectra were recorded with a Perkin Elmer 100 FT/IR spectrometer and are reported in frequency of absorption (cm^{-1}).

3.4 GC-MS Measurements

GC-MS measurements were conducted with the following instrument: GC (HP 6890 Series), MSD 5973, column: HP-5 MS (30 m × 0.25 mm × 0.25 μm); carrier gas: He, constant flow, 200 °C.

3.5 Elemental Analysis

Elemental analyses were performed using a *Heraeus* CHN-O-Rapid instrument.

3.6 Melting Point

Melting points were measured in open glass capillaries with a *Büchi* B-540 apparatus and were uncorrected.

4. Chromatographic Methods

Column chromatography was carried out in glass columns (10-50 mm diameter) using *Merck* silica gel 60, particle size 0.035-0.070 mm. Analytical thin layer chromatography (TLC) was performed using precoated aluminium-backed plates (silica gel 60 F254) and visualized with UV radiation at 254 nm.

5. Typical Synthetic Procedures

5.1 Procedure for Sub-Mol% Copper-Catalyzed Sonogashira-Hagihara-Type Cross-Coupling Reaction of Terminal Alkynes with Aryl Iodides

A representative procedure for the copper-catalyzed coupling (synthesis of **166a**): A magnetic stirring bar and 651.6 mg Cs_2CO_3 (2.0 mmol) were added to a 10 mL sealed tube. Then the aperture of the tube was covered with a rubber septum and purged using argon for 10 min. After that, 109.6 μL phenylacetylene (**164a**) (1.0 mmol), 168.1 μL iodobenzene (**165a**) (1.5 mmol), 32.2 μL DMEDA (0.30 mmol), a solution (0.1 mL) of $Cu(DMEDA)_2Cl_2 \cdot H_2O$ in MeOH [prepared by dissolving 16 mg (0.05 mmol) of the copper complex in 1 mL of HPLC-grade MeOH], and 1 mL dioxane were sequentially added via a syringe. The septum was then quickly replaced by a teflon-coated screw cap. After stirring in a pre-heated oil bath at 135 ^oC for 22 h, the mixture was cooled to room temperature and 5 mL ethyl acetate were added. The resulting solution was filtered through a pad of silica gel and concentrated under reduced pressure. Column chromatography was performed on silica gel (eluent: hexane), affording **166a** as a white solid in 94% yield (0.94 mmol, 167.5 mg).

5.2 Procedure for Mild Copper-Mediated Direct Oxidative Cross-Coupling of 1,3,4-Oxadiazoles with Polyfluoroarenes

Representative procedure for the copper-mediated direct oxidative cross-coupling of 1,3,4-oxadiazoles with polyfluoroarenes (synthesis of **175a**): 28.8 mg CuBr (0.2 mmol), 36 mg 1,10-phenanthroline (0.2 mmol), and 48 mg *t*BuOLi (0.6 mmol) were added in a 10 mL oven-dried Schlenk tube, which was equipped with a magnetic stirring bar. Then the tube was sealed with a rubber septum and filled with O_2 by using standard Schlenk techniques for three times. After adding CH_3CN (1.5 mL) via a

syringe, the reaction mixture was stirred at room temperature (25 °C) for 5 min. Then, **174a** (6 mmol, 664.1 mL) and **173a** (0.2 mmol, 29.2 mg) were sequentially added under an atmosphere of dioxygen. A balloon filled with dioxygen was connected to the Schlenk tube by a needle. After stirring at room temperature for 14 h, the reaction mixture was diluted with ethyl acetate. The resulting solution was directly filtered through a pad of silica gel and concentrated under reduced pressure. Purification by column chromatography (silica gel, eluent: pentane/ethyl acetate 15:1) afforded product **175a** as a white solid in 65% yield (0.13 mmol, 40.6 mg).

5.3 Procedure for Transition Metal-Free Direct C–H Bond Thiolation of 1,3,4-Oxadiazoles and Related Heteroarenes

5.3.1 Syntheses of Azoles 173a-i, Compound 181 and Disulfides 179c-f

For the procedure for the synthesis of azoles **173a-i**, compound **181** and disulfides **179c-f**, see literature[170].

5.3.2 General Procedure for the Thiolation of Azoles with Disulfides

The preparation of 2-phenyl-5-(4-methylphenylthio)-1,3,4-oxadiazole (**180a**) is representative for the syntheses of the thiolated products: A 10 mL sealed tube equipped with a magnetic stirring bar was charged with 2-phenyl-1,3,4-oxadiazole (**173a,** 0.073 g**,** 0.5 mmol), bis(4-methylphenyl) disulfide (**179a**, 0.308 g**,** 1.25 mmol), Cs_2CO_3 (0.325 g**,** 1.0 mmol). Then the aperture of the tube was covered with a rubber septum, and purged using an argon flow for 10 minutes. 1,4-Dioxane (2 mL) was added via a syringe and the septum was quickly replaced by a teflon-coated screw cap. After stirring at 130 °C for 18 h, the reaction mixture was cooled to room temperature and diluted with ethyl acetate. The resulting solution was directly filtered through a filter paper and concentrated under reduced pressure. Flash chromatography was

performed on silica gel (at first pentane, then pentane/ethyl acetate = 8:1), providing product **180a** in 87% yield (0.435 mmol, 116.6 mg).

5.4 Procedure for the Phosphorylation of 1,3,4-Oxadiazoles and Related Heterocycles

A representative procedure for the phosphorylation of 1,3,4-oxadiazoles and related heterocycles (synthesis of **184a**): 2-Phenyl-1,3,4-oxadiazole (**173a**, 1 mmol), NEt_3 (277 μL, 2 mmol), $ClPPh_2$ (180 μL, 2 mmol), and CH_2Cl_2 (1.5 mL) were successively added to a Schlenk tube, which was equipped with a magnetic stirring bar and filled with argon. The mixture was stirred at 40 °C for 48 h. After full conversion of **173a** (as confirmed by TLC), the reaction mixture was cooled to room temperature and diluted with ethyl acetate. The resulting solution was concentrated under reduced pressure and purified by silica gel column chromatography (using pentane/ethyl acetate = 8:1 as eluent), providing **184a** as a white solid in 90% yield (0.9 mmol, 297.5 mg).

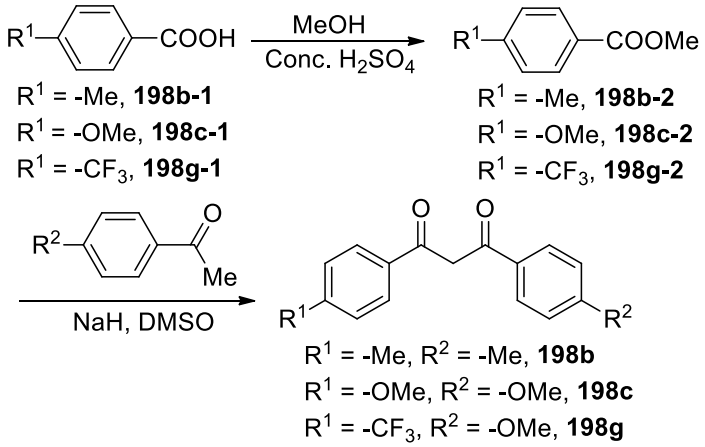
5.5 Procedure for Copper-Catalyzed Synthesis of α-Thiophenyl Carbonyl Compounds Through S–S Bond Cleavage and C–C Bond Activation

5.5.1 Synthesis of β-Diketones 198b, 198c and 198g[190]

The preparation of 1,3-bis(4-methylphenyl)propan-1,3-dione **198b** is representative for the syntheses of β-diketones **198b**, **198c** and **198g**.

Step 1: 4-Methylbenzoic acid **198b-1** (13.6 g, 100.0 mmol), MeOH (100 mL) and conc. H_2SO_4 (10 mL) were added in a 250 mL three-necked flask, which was equipped with a reflux condenser. After stirring under reflux for 10 hours, the reaction mixture was cooled to room temperature and diluted with ethyl acetate. The resulting solution

was extracted with EtOAc (3 x 50 mL) and washed with a saturated $NaHCO_3$ aqueous solution and brine. The combined organic layers were dried over $MgSO_4$, filtrated and concentrated under reduced pressure to afford 4-methoxymethylbenzoate **198b-2** as a white solid in 90% yield (90 mmol, 13.5 g).



Scheme 51. Synthesis of β-diketones **198b**, **198c** and **198g**.

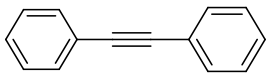
Step 2: A 250 mL three-necked flask, covered with a rubber septum, and purged using an argon flow for 10 minutes, was placed in an ice-water bath. 3.8 g (100 mol) NaH solution 60% and 10 mL dry DMSO were added in the flask. Then, 8.3 g (55 mol) 4-methoxymethylbenzoate **198b-2** was dissolved in 10 mL dry DMSO and added dropwise via a syringe. After the addition of **198b-2**, 4-methylacetophenone (11 g, 82.5 mmol), dissolved in 10 mL dry DMSO, was added dropwise via a syringe. After that, the ice bath was removed and the reaction mixture was stirred at room temperature for an additional 1 h. It was moved to a pre-heated oil bath at 30 ^{o}C and stirred for another 1 h. The reaction mixture was poured into a mixture of 150 g ice water and 5.0 mL H_3PO_4. The precipitate was filtered off and washed with cold water. Recrystallization from ethanol afforded the desired product **198b** as yellow needles in 85% yield (46.8 mmol, 11.8 g).

5.5.2 General Procedure for the Synthesis of α-Thiophenyl Carbonyl Compounds

A representative procedure for the synthesis of α-thiophenyl carbonyl compounds: (synthesis of **199a**): A 10 mL sealed tube equipped with a magnetic stirring bar was charged with **179a** (123 mg, 0.5 mmol), **198a** (448.5 mg, 2 mmol), Cs_2CO_3 (325.8 mg, 1.0 mmol), and $Cu(OAc)_2 \cdot H_2O$ (20.0 mg, 0.1 mmol). The aperture of the tube was then covered with a rubber septum, and purged using a dioxygen flow for 5 minutes. After the addition of acetonitrile (1 mL) via a syringe, the septum was quickly replaced by a teflon-coated screw cap. The reaction mixture was stirred at 130 °C for 24 h, then cooled to room temperature and diluted with ethyl acetate. The resulting solution was directly filtered through a filter paper and concentrated under reduced pressure. Purification by column chromatography on silica gel (using pentane/ethyl acetate = 20:1 as eluent) provided **199a** as a colorless oil in 87% yield (0.435 mmol, 105.4 mg) (Recrystallization from ethanol afforded yellow solid, m.p. 38–39 °C).

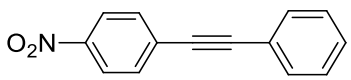
6. Product Characterization

Diphenylacetylene (166a)[191]



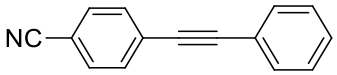
White solid, m.p. 60 °C (lit.[191] 60–61 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56–7.53 (m, 4H), 7.36–7.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 131.6, 128.3, 128.2, 123.2, 89.4; Anal. Calcd for $C_{14}H_{10}$ (178.08): C, 94.34; H, 5.66; Found: C, 94.35; H, 5.72; MS *m/z* (EI) (relative intensity, %): 178 (100, M^+), 176 (16), 85 (18), 83 (26), 57 (7).

Nitro-(4-phenylethynyl)benzene (166b)[191]



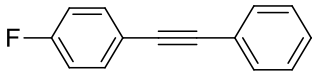
Yellow solid, m.p. 117–118 °C (lit.[191] 120–122 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, J = 8.8 Hz, 2H), 7.67 (d, J = 9.1 Hz, 2H), 7.58–7.55 (m, 2H), 7.40–7.39 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.9, 132.2, 131.8, 130.2, 129.2, 128.5, 123.6, 122.1, 94.6, 87.6; Anal. Calcd for $C_{14}H_9NO_2$ (223.06): C, 75.33; H, 4.06; N, 6.27; Found: C, 75.42; H, 4.13; N, 6.35; MS *m/z* (EI) (relative intensity, %): 223 (100, M^+), 193 (24), 177 (19), 176 (60), 165 (21), 151 (23).

Cyano-(4-phenylethynyl)benzene (166c)[191]



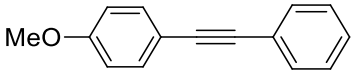
Light yellow solid, m.p. 107–108 °C (lit.[191] 109–110 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65–7.59 (m, 4H), 7.56–7.54 (m, 2H), 7.40–7.37 (m, 3H); ^{13}CNMR (100 MHz, $CDCl_3$,) δ = 132.0, 131.9, 131.7, 129.1, 128.5, 128.2, 122.2, 118.5, 111.4, 93.8, 87.8; Anal. Calcd for $C_{15}H_9N$ (203.24): C, 88.64; H, 4.46; N, 6.89; Found: C, 88.64; H, 4.46; N, 6.79; MS *m/z* (EI) (relative intensity, %): 203 (100, M^+), 202 (12), 101 (11), 88 (9).

Fluoro-(4-phenylethynyl)benzene (166d)[191]



White solid, m.p. 109–110 °C (lit.[191] 108–110 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54–7.50 (m, 4H), 7.39–7.33 (m, 3H), 7.08–7.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.4 ($J_{C\text{-}F}$ = 249.1 Hz), 133.4 ($J_{C\text{-}F}$ = 8.3 Hz), 131.5, 128.3 (2C), 123.0, 119.3 ($J_{C\text{-}F}$ = 3.5 Hz), 115.6 ($J_{C\text{-}F}$ = 22.0 Hz), 89.0, 88.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ = –111.03; Anal. Calcd for $C_{14}H_9F$ (196.22): C, 85.69; H, 4.62; Found: C, 85.78; H, 4.56; MS *m/z* (EI) (relative intensity, %): 196 (100, M^+), 194 (6), 170 (4).

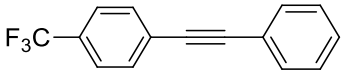
Methoxy-(4-phenylethynyl)benzene (166e)[191]



White solid, m.p. 57–59 °C (lit.[191] 58–60 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53–7.46 (m, 4H), 7.37–7.32 (m, 3H), 6.90–6.87 (m, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ = 159.5, 133.0,

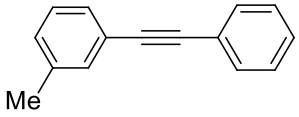
131.4, 128.2, 127.9, 123.5, 115.3, 114.0, 89.4, 88.1, 55.4; Anal. Calcd for $C_{15}H_{12}O$ (208.26): C, 86.51; H, 5.81: Found: C, 86.52; H, 5.90; MS *m/z* (EI) (relative intensity, %): 208 (100, M^+), 202 (5), 193 (44), 165 (34), 104 (8).

Trifluoromethyl-(4-phenylethynyl)benzene (166f)[191]



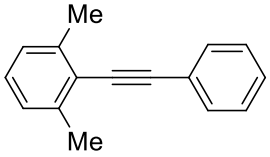
White solid, m.p. 103–104 °C (lit.[191] 108–110 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65–7.60 (m, 4H), 7.57–7.54 (m, 2H), 7.39–7.36 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 131.7 (2C), 129.8 (J = 32.8 Hz), 128.8, 128.4, 127.1, 125.2 (J = 3.7 Hz), 122.7 (q, $J_{C\text{-}F}$ = 253.2 Hz), 122.5, 91.7, 88.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ = –62.82; Anal. Calcd for $C_{15}H_9F_3$ (246.23): C, 73.17; H, 3.68; Found: C, 73.19; H, 3.79; MS *m/z* (EI) (relative intensity, %): 246 (100, M^+), 227 (9), 196 (8), 176 (10), 98 (8).

1-Methyl-(3-phenylethynyl)benzene (166g)[129d]



Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57–7.53 (m, 2H), 7.39–7.33 (m, 5H), 7.24 (t, J = 7.6 Hz, 1H), 7.15 (d, J = 7.6 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.0, 132.2, 131.6, 129.1, 128.7, 128.4, 128.3, 128.2, 128.1, 123.0, 89.6, 89.1, 21.4; Anal. Calcd for $C_{15}H_{12}$ (192.26): C, 93.71; H, 6.29; Found: C, 93.75; H, 6.29; MS *m/z* (EI) (relative intensity, %): 192 (100, M^+), 191 (31), 189 (24), 165 (12).

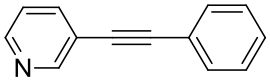
1,3-Dimethyl-(2-phenylethynyl)benzene (166h)[192]



Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.58–7.56 (m, 2H), 7.40–7.35 (m, 3H), 7.17–7.08

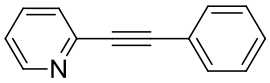
(m, 3H), 2.54 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.2, 131.3, 128.3, 128.0, 127.7, 126.7, 123.8, 122.9, 97.8, 87.1, 21.3; Anal. Calcd for $C_{16}H_{14}$ (206.28): C, 93.16; H, 6.84; Found: C, 93.18; H, 6.89; MS *m/z* (EI) (relative intensity, %): 206 (100, M^+), 204 (25), 202 (29), 192 (14), 189 (27), 165 (16), 89 (10).

3-(Phenylacetylene)pyridine (166i)[193]



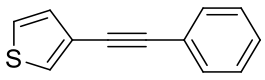
White solid, m.p. 49–50 °C (lit.[193] 50 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.77 (dd, *J* = 2.1 Hz, *J* = 0.8 Hz, 1H), 8.54 (dd, *J* = 4.9 Hz, *J* = 1.7 Hz, 1H), 7.82–7.79 (m, 1H), 7.56–7.53 (m, 2H), 7.38–7.35 (m, 3H), 7.30–7.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.2, 148.5, 138.3, 131.6, 128.7, 128.4, 123.0, 122.5, 120.4, 92.6, 86.0; Anal. Calcd for $C_{13}H_9N$ (179.22): C, 87.12; H, 5.06; N, 7.82; Found: C, 87.15; H, 5.21; N, 7.86; MS *m/z* (EI) (relative intensity, %): 179 (100, M^+), 178 (22), 152 (8), 151 (10), 126 (11), 76 (8).

2-(Phenylacetylene)pyridine (166j)[194]



Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.61 (d, *J* = 5.0 Hz, 1H), 7.69–7.64 (m, 1H), 7.61–7.59 (m, 2H), 7.52 (dd, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H), 7.36–7.34 (m, 3H), 7.24–7.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.0, 143.4, 136.1, 132.0, 128.9, 128.3, 127.1, 122.7, 122.2, 89.2, 88.6; Anal. Calcd for $C_{13}H_9N$ (179.22): C, 87.12; H, 5.06; N, 7.82; Found: C, 87.02; H, 5.04; N, 8.12; MS *m/z* (EI) (relative intensity, %): 179 (100, M^+), 178 (38), 151 (12), 76 (9).

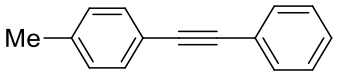
3-(Phenylethynyl)thiophene (166k)[195]



White solid, m.p. 43–44 °C (lit.[195] 44–45 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54–7.51 (m, 3H), 7.37–7.34 (m, 3H), 7.32–7.30 (m, 1H), 7.21 (dd, *J* = 5.0 Hz, *J* = 1.4 Hz, 1H); ^{13}C NMR (100MHz,

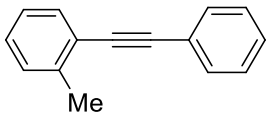
$CDCl_3$) δ = 131.5, 129.8, 128.5, 128.3, 128.2, 125.3, 123.2, 122.3, 88.9, 84.5; Anal. Calcd for $C_{12}H_8S$ (184.26): C, 78.22; H, 4.38; Found: C, 78.24; H, 4.45; MS *m/z* (EI) (relative intensity, %): 184 (100, M^+), 152 (14), 139 (25), 121 (4).

Methyl-(4-phenylethynyl)benzene (166l)[191]



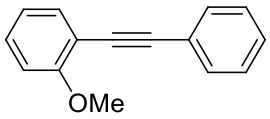
White solid, m.p. 71–72 °C (lit.[191] 72–73 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.55–7.52 (m, 2H), 7.44 (dd, *J* = 6.6 Hz, *J* = 1.8 Hz, 2H), 7.37–7.33 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.4, 131.5 (2C), 129.1, 128.3, 128.1, 123.5, 120.2, 89.5, 88.7, 21.5; Anal. Calcd for $C_{15}H_{12}$ (192.26): C, 93.71; H, 6.29; Found: C, 93.71; H, 6.32; MS *m/z* (EI) (relative intensity, %): 192 (100, M^+), 191 (41), 189 (22), 165 (14), 95 (8).

1-Methyl-(2-phenylethynyl)benzene (166m)[196]



Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47–7.45 (m, 2H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.29–7.24 (m, 3H), 7.15 (dd, *J* = 6.2 Hz, *J* = 1.5 Hz, 2H), 7.10–7.06 (m, 1H), 2.44 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.1, 131.8, 131.5, 129.4, 128.3, 128.2, 128.1, 125.5, 123.5, 123.0, 93.3, 88.4, 20.9; Anal. Calcd for $C_{15}H_{12}$ (192.26): C, 93.71; H, 6.29; Found: C, 93.70; H, 6.41; MS *m/z* (EI) (relative intensity, %): 192 (100, M^+), 191 (41), 189 (23), 165 (12), 95 (6).

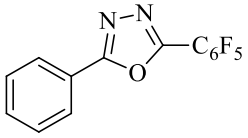
1-Methoxy-(2-phenylethynyl)benzene (166n)[129d]



Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57–7.54 (m, 2H), 7.51–7.48 (dd, *J* = 7.1 Hz, *J* = 1.4 Hz, 1H), 7.35–7.27 (m, 4H), 6.95–6.86 (m, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.8, 133.5, 131.6, 129.7, 128.2, 128.0, 123.5, 120.4, 112.4, 110.7, 93.4, 85.8, 55.9; Anal. Calcd

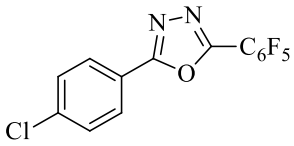
for $C_{15}H_{12}$ (208.26): C, 86.51; H, 5.81; Found: C, 86.57; H, 6.10; MS *m/z* (EI) (relative intensity, %): 208 (100, M^+), 207 (67), 179 (12), 178 (22), 165 (32), 164 (14).

2-Phenyl-5-(pentafluorophenyl)-1,3,4-oxadiazole (175a)[152]



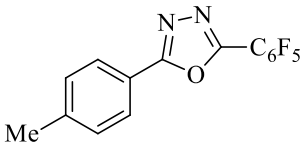
White solid, m.p. 146–147 °C (lit.[152] 148–149 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.11 (d, J = 8.0 Hz, 2H), 7.58–7.51 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.7, 154.6 (m), 145.1 (dm, J = 260.7 Hz), 143.2 (dm, J = 265.7 Hz), 138.1 (dm, J = 252.8 Hz), 132.4, 129.2, 127.1, 122.9, 100.9 (td, J = 14.5, 4.2 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.5 (m, 2F), –147.5 (m, 1F), –159.7 (m, 2F); Anal. Calcd for $C_{14}H_5F_5N_2O$ (312.03): C, 53.86; H, 1.61; N, 8.97; Found: C, 53.77; H, 1.58; N, 9.07; MS *m/z* (EI) (relative intensity, %): 312 (82, M^+), 313 (17), 237 (25), 195 (32), 105 (100), 77 (34); IR: 3275, 3162, 3060, 2128, 1658, 1556, 1490, 1447, 1103, 1014, 987, 895, 827, 744, 690.

2-(4-Chlorophenyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175b)



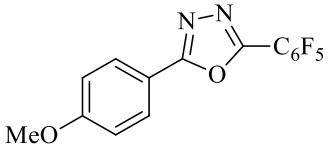
White solid, m.p. 178–180 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.09–8.06 (m, 2H), 7.55–7.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 164.9, 154.9 (m), 145.2 (dm, J = 273.1 Hz), 143.3 (dm, J = 266.5 Hz), 138.8, 138.2 (dm, J = 252.9 Hz), 129.6, 128.5, 121.4, 100.3; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.4 (m, 2F), –146.9 (tt, J = 21.0, 4.6 Hz, 1F), –159.4 (m, 2F); Anal. Calcd for $C_{14}H_4ClF_5N_2O$ (345.99): C, 48.51; H, 1.16; N, 8.08; Found: C, 48.73; H, 1.32; N, 8.09; MS *m/z* (EI) (relative intensity, %): 346 (51, M^+), 255 (28), 195 (38), 167 (16), 139 (100), 111 (29), 75 (19); IR: 3090, 2324, 2084, 1602, 1489, 1231, 1178, 1095, 985, 829, 746, 695.

2-(4-Methylphenyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175c)



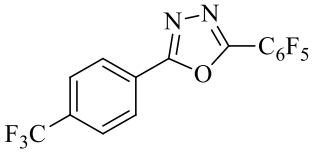
White solid, m.p. 171–173 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.00–7.98 (m, 2H), 7.00 (d, J = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.9, 154.4 (m), 145.1 (dm, J = 264.0 Hz), 143.2 (dm, J = 256.7 Hz), 143.1, 138.0 (dm, J = 243.7 Hz), 129.9, 127.2, 120.2, 101.0 (m), 21.7; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.5 (m, 2F), –147.8 (tt, J = 5.6, 1.2 Hz, 1F), –159.8 (m, 2F); Anal. Calcd for $C_{15}H_7F_5N_2O$ (326.05): C, 55.23; H, 2.16; N, 8.59; Found: C, 55.60; H, 2.42; N, 8.67; MS *m/z* (EI) (relative intensity, %): 326 (54, M^+), 327 (9), 255 (12), 195 (14), 119 (100), 91 (29), 77 (13), 65 (13); IR: 3077, 2108, 1654, 1558, 1493, 1414, 1318, 1169, 1109, 985, 856, 831, 754, 708.

2-(4-Methoxyphenyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175d)



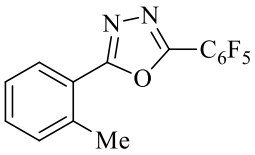
White solid, m.p. 145–146 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.02 (dd, J = 8.8, 2.0 Hz, 2H), 7.00 (dd, J = 8.8, 2.0 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.6, 162.9, 154.1 (m), 145.0 (dm, J = 259.2 Hz), 143.1 (dm, J = 260.8 Hz), 138.1 (dm, J = 251.9 Hz), 129.0, 115.3, 114.6, 101.0 (td, J = 14.7, 3.3 Hz), 55.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.6 (m, 2F), –147.8 (tt, J = 5.6, 1.2 Hz, 1F), –159.8 (m, 2F); Anal. Calcd for $C_{15}H_7F_5N_2O_2$ (342.04): C, 52.64; H, 2.06; N, 8.19; Found: C, 53.03; H, 2.43; N, 8.36; MS *m/z* (EI) (relative intensity, %): 342 (56, M^+), 343 (9), 195 (6), 135 (100), 92 (7), 77 (11); IR: 3112, 2109, 1657, 1608, 1559, 1491, 1422, 1305, 1254, 1171, 1098, 1020, 985, 827, 748, 705.

2-(4-Trifluoromethylphenyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175e)



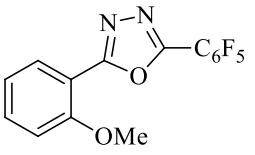
White solid, m.p. 161–163 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.27 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 164.6 (m), 155.3 (m), 145.3 (dm, J = 261.8 Hz), 143.5 (dm, J = 266.9 Hz), 138.2 (dm, J = 253.6 Hz), 134.0 (q, J = 34.1 Hz), 127.6, 127.4 (d, J = 5.8 Hz), 126.4 (q, J = 3.7 Hz), 123.4 (q, J = 272.7 Hz), 100.5 (tt, J = 14.5, 4.2 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –63.3 (s, 3F), –135.2 (m, 2F), –146.5 (tt, J = 5.5, 1.3 Hz, 1F), –159.2 (m, 2F); MS *m/z* (EI) (relative intensity, %): 380 (58, M^+), 381 (10), 305 (12), 255 (25), 195 (52), 173 (100), 167 (17), 145 (41); HRMS *m/z* (M^+) calcd for $C_{15}H_5F_8N_2O$: 381.0269, found: 381.0268; IR: 2323, 1654, 1558, 1493, 1415, 1319, 1171, 1105, 1062, 986, 830, 754, 708.

2-(2-Methylphenyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175f)



White solid, m.p. 141–142 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.04–8.02 (m, 1H), 7.47–7.45 (m, 1H), 7.39–7.34 (m, 2H), 2.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 166.0, 154.3 (m), 145.2 (dm, J = 264.7 Hz), 143.2 (dm, J = 261.2 Hz), 138.8, 138.1 (dm, J = 251.9 Hz), 131.9 (2C), 129.2, 126.3, 122.0, 100.9 (td, J = 14.6, 4.8 Hz), 22.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.5 (m, 2F), –147.5 (tt, J = 21.0, 4.5 Hz, 1F), –159.6 (m, 2F); MS *m/z* (EI) (relative intensity, %): 326 (100, M^+), 327 (18), 297 (13), 195 (12), 119 (22), 118 (26), 91 (16), 90 (21), 89 (12), 77 (12); HRMS *m/z* (M^+) calcd for $C_{15}H_8F_5N_2O$: 327.0551, found: 327.0552; IR: 2325, 2107, 1737, 1656, 1519, 1489, 1453, 1227, 1098, 988, 827, 780, 730, 666.

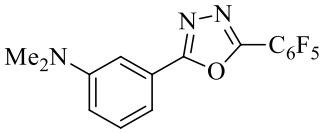
2-(2-Methoxyphenyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175g)



White solid, m.p. 143–144 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.02 (dd, J = 8.0, 2.0 Hz, 1H), 7.58–7.53 (m, 1H), 7.13–7.08 (m, 2H), 3.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 164.6, 158.1, 154.4 (m), 145.2 (dm, J = 265.3 Hz), 143.1 (dm, J = 263.3 Hz), 138.1 (dm, J = 251.3 Hz), 133.8,

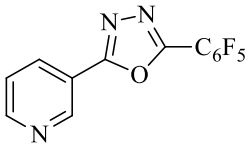
130.6, 120.8, 112.1, 101.1, 56.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.5 (m, 2F), –147.8 (tt, J = 5.6, 1.2 Hz, 1F), –159.8 (m, 2F); Anal. Calcd for $C_{15}H_7F_5N_2O_2$ (342.04): C, 52.64; H, 2.06; N, 8.19; Found: C, 52.46; H, 1.97; N, 8.10; MS *m/z* (EI) (relative intensity, %): 342 (100, M^+), 343 (18), 195 (37), 167 (14), 147 (26), 135 (52), 105 (39), 92 (16), 91 (17), 77 (29); IR: 3072, 2115, 1654, 1600, 1496, 1284, 1261, 1175, 1095, 990, 828, 776, 751, 709, 670.

2-(3-*N,N*-Dimethylaminophenyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175h)



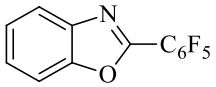
Yellow solid, m.p. 168–169 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.45 (bs, 1H), 7.42–7.40 (m, 1H), 7.39–7.35 (m, 1H), 6.92–6.89 (m, 1H), 3.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 150.7, 145.1 (dm, J = 260.5 Hz), 143.2 (dm, J = 259.3 Hz), 138.1 (dm, J = 255.9 Hz), 129.8, 123.5, 116.1, 114.9, 101.0 (td, J = 14.6, 3.8 Hz), 40.3 (2C); ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.5 (d, J = 18.2 Hz, 2F), –147.6 (tt, J = 21.0, 4.4 Hz, 1F), –159.7 (m, 2F); MS *m/z* (EI) (relative intensity, %): 355 (100, M^+), 356 (17), 354 (38), 161 (14), 120 (15); HRMS *m/z* (M^+) calcd for $C_{16}H_{10}F_5N_3O$: 356.0817, found: 356.0812; IR: 2925, 1657, 1608, 1550, 1494, 1371, 1228, 1102, 991, 948, 831, 792, 744, 686.

2-(3-Pyridinyl)-5-(pentafluorophenyl)-1,3,4-oxadiazole (175i)



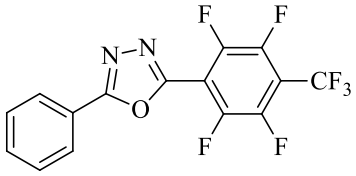
White solid, m.p. 112–113 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 9.31 (s, 1H), 8.80 (s, 1H), 8.42–8.39 (m, 1H), 7.52–7.48 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 163.6, 155.2, 153.0, 148.1, 145.2 (dm, J = 266.4 Hz), 143.5 (dm, J = 261.9 Hz), 138.1 (dm, J = 252.1 Hz), 134.4, 123.9, 119.5, 100.5 (td, J = 14.5, 4.3 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.3 (m, 2F), –146.6 (m, 1F), –159.4 (m, 2F); MS *m/z* (EI) (relative intensity, %): 313 (34, M^+), 314 (4), 257 (10), 195 (30), 167 (17), 117 (11), 106 (100), 78 (76), 63 (26), 62 (11), 51 (43), 50 (19); HRMS *m/z* (M^+) calcd for $C_{13}H_5F_5N_3O$: 314.0347, found: 314.0344; IR: 1658, 1603, 1496, 1408, 1235, 1107, 1015, 989, 827, 748, 703.

2-(Pentafluorophenyl)-benzoxazole (175j)



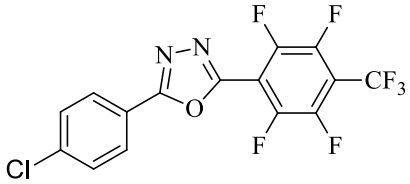
White solid, m.p. 114–115 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.90–7.88 (m, 1H), 7.67–7.65 (m, 1H), 7.49–7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 153.8 (m), 152.3 (m), 150.5, 145.6 (dm, J = 260.7 Hz), 141.0, 140.5 (dm, J = 233.3 Hz), 135.4 (dm, J = 274.7 Hz), 126.5, 125.2, 120.9, 111.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –136.8 (m, 2F), –148.5 (tt, J = 21.0, 4.3 Hz, 1F), –160.2 (m, 2F); MS *m/z* (EI) (relative intensity, %): 285 (100, M^+), 286 (14), 92 (13), 64 (32), 63 (43); HRMS *m/z* (M^+) calcd for $C_{13}H_5F_5NO$: 286.0286, found: 286.0282; IR: 2925, 1745, 1652, 1605, 1553, 1515, 1492, 1341, 1241, 1178, 1080, 992, 943, 857, 753.

2-Phenyl-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175k)



White solid, m.p. 167–168 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.17–8.15 (m, 2H), 7.62–7.55 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 166.1, 159.6, 154.4, 146.0 (m), 143.4 (m), 132.7, 129.3, 127.4, 122.7, 115.0, 108.2, 103.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –55.6 (t, J = 21.9 Hz, 3F), –133.8 (m, 2F), –138.2 (m, 2F); Anal. Calcd for $C_{15}H_5F_7N_2O$ (362.03): C, 49.74; H, 1.39; N, 7.73; Found: C, 49.76; H, 1.43; N, 7.74; MS *m/z* (EI) (relative intensity, %): 362 (42, M^+), 245 (14), 237 (10), 217 (11), 105 (100), 77 (42); IR: 2114, 1664, 1547, 1503, 1329, 1141, 989, 965, 810, 708.

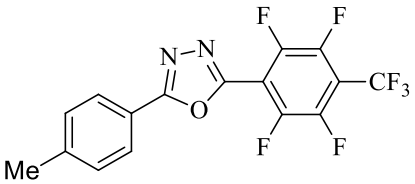
2-(4-Chlorophenyl)-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175l)



White solid, m.p. 145–147 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.11–8.07 (m, 2H), 7.57–7.53 (m,

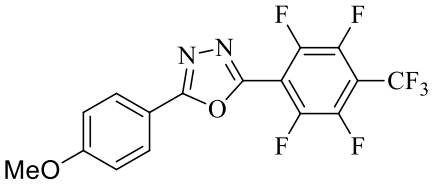
2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.2, 154.6, 146.0 (m), 143.3 (m), 139.1, 129.7, 128.5, 121.2, 118.9, 112.3, 108.6; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –56.6 (t, J = 21.9 Hz, 3F), –133.7 (m, 2F), –138.1 (m, 2F); MS *m/z* (EI) (relative intensity, %): 396 (30, M^+), 397 (6), 398 (10), 305 (9), 245 (19), 217 (13), 141 (41), 139 (100), 123 (11), 111 (24), 75 (12); HRMS *m/z* (M^+) calcd for $C_{15}H_4ClF_7N_2ONa$: 418.9793, found: 418.9789; IR: 3479, 2978, 2804, 1715, 1504, 1408, 1322, 1260, 1208, 1151, 1086, 991, 845, 776, 714.

2-(4-Methylphenyl)-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175m)



White solid, m.p. 142–143 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.02 (dd, J = 8.3, 1.9 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 166.2 154.2 (m), 145.9 (m), 143.5, 130.0, 127.3, 121.7, 119.9, 118.9, 112.2, 108.8, 21.7; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –56.6 (t, J = 21.9 Hz, 3F), –133.7 (m, 2F), –138.1 (m, 2F); Anal. Calcd for $C_{16}H_7F_7N_2O$ (376.04): C, 51.08; H, 1.88; N, 7.45; Found: C, 51.35; H, 2.01; N, 7.55; MS *m/z* (EI) (relative intensity, %): 376 (34, M^+), 305 (4), 245 (9), 119 (100), 91 (24), 77 (14); IR: 2926, 2112, 1664, 1498, 1463, 1327, 1147, 988, 815, 733, 711.

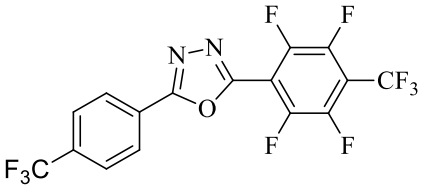
2-(4-Methoxyphenyl)-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175n)



White solid, m.p. 134–135 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.09–8.06 (m, 2H), 7.06–7.03 (m, 2H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 166.0, 163.1, 153.9, 145.9 (m), 143.3 (m), 129.2, 115.1, 114.8, 108.9, 96.6, 55.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –56.6 (t, J = 21.8 Hz, 3F), –133.9 (m, 2F), –138.4 (m, 2F); Anal. Calcd for $C_{16}H_7F_7N_2O_2$ (392.04): C, 48.99; H, 1.80; N, 7.14; Found: C, 49.24; H, 2.03; N, 7.29; MS *m/z* (EI) (relative intensity, %): 392 (37, M^+), 393 (7), 245 (7), 135

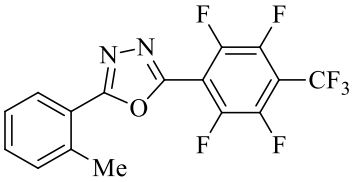
(100); IR: 2848, 1662, 1607, 1495, 1327, 1252, 1156, 1024, 985, 959, 813, 742, 709.

2-(4-Trifluoromethylphenyl)-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175o)



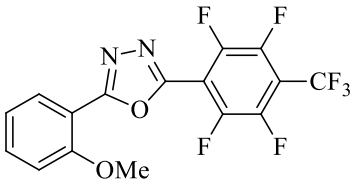
White solid, m.p. 126–127 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.29 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 164.8, 155.0 (m), 146.0 (m), 143.4 (m), 134.3 (q, J = 33.1 Hz), 127.7, 126.3 (q, J = 3.8 Hz), 126.0, 123.3 (q, J = 272.8 Hz), 118.9, 115.0, 112.9, 108.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –56.6 (t, J = 21.9 Hz, 3F), –63.4 (s, 3F), –133.6 (m, 2F), –137.9 (m, 2F); Anal. Calcd for $C_{16}H_4F_{10}N_2O$ (430.02): C, 44.67; H, 0.94; N, 6.51; Found: C, 44,74; H, 1.09; N, 6.52; MS *m/z* (EI) (relative intensity, %): 430 (33, M^+), 305 (17), 245 (29), 217 (14), 173 (100), 145 (38); IR: 2114, 1549, 1491, 1318, 1261, 1165, 1131, 985, 852, 811, 712.

2-(2-Methylphenyl)-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175p)



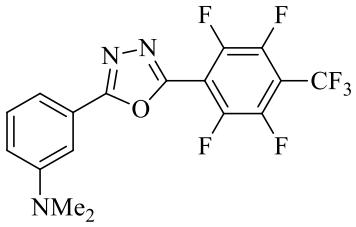
White solid, m.p. 122–123 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.05 (d, J = 7.7 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.40–7.35 (m, 2H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 171.1, 166.4, 154.1 (m), 146.0 (m), 143.4 (m), 139.0, 132.1, 132.0, 129.3, 126.4, 121.8, 118.9, 108.8 (m), 22.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –56.6 (t, J = 21.8 Hz, 3F), –133.8 (m, 2F), –138.3 (m, 2F); Anal. Calcd for $C_{16}H_7F_7N_2O$ (376.04): C, 51.08; H, 1.88; N, 7.45; Found: C, 51.48; H, 2.01; N, 7.71; MS *m/z* (EI) (relative intensity, %): 376 (100, M^+), 377 (18), 357 (6), 119 (17), 118 (41), 91 (14), 90 (24); IR: 2929, 2325, 1661, 1542, 1497, 1357, 1321, 1143, 989, 813, 779, 711, 667.

2-(2-Methoxyphenyl)-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175q)



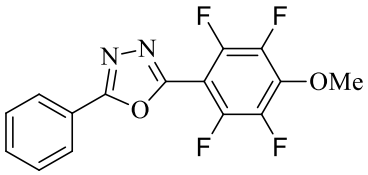
White solid, m.p. 127–128 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.05 (dd, J = 7.7, 1.7 Hz, 1H), 7.59–7.55 (m, 1H), 7.13–7.09 (m, 2H), 3.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.0, 158.2, 154.3, 146.0 (m), 143.3 (m), 134.0, 130.7, 121.7, 120.9, 119.0, 112.1, 111.8, 109.0, 105.7, 56.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –56.6 (t, J = 21.8 Hz, 3F), –133.8 (m, 2F), –138.5 (m, 2F); Anal. Calcd for $C_{16}H_7F_7N_2O_2$ (392.04): C, 48.99; H, 1.80; N, 7.14; Found: C, 48.83; H, 2.14; N, 6.84; MS *m/z* (EI) (relative intensity, %): 392 (87, M^+), 393 (20), 373 (13), 245 (40), 217 (23), 179 (11), 148 (15), 147 (42), 135 (100), 132 (36), 105 (95), 92 (26), 91 (37), 77 (47), 65 (28); IR: 2923, 1587, 1492, 1326, 1262, 1147, 987, 813, 779, 754, 712, 668.

2-(3-*N,N*-Dimethylaminophenyl)-5-(1-trifluoromethyl-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175r)



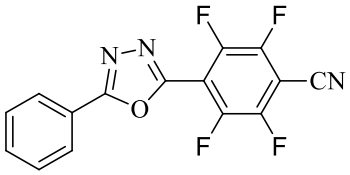
Yellow solid, m.p. 162–163 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.45–7.35 (m, 3H), 6.92 (d, J = 8.1 Hz, 1H), 3.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 166.8, 154.3, 150.7, 146.0 (m), 143.5 (m), 129.9, 123.2, 121.7, 119.0, 116.3, 115.0, 110.2, 108.9, 40.3 (2C); ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –56.5 (t, J = 21.8 Hz, 3F), –133.8 (m, 2F), –138.4 (m, 2F); Anal. Calcd for $C_{17}H_{10}F_7N_3O$ (405.07): C, 50.38; H, 2.49; N, 10.37; Found: C, 50.68; H, 2.77; N, 10.44; MS *m/z* (EI) (relative intensity, %): 405 (100, M^+), 406 (21), 161 (27), 148 (23), 145 (17), 120 (25), 77 (9); IR: 2924, 1661, 1602, 1544, 1495, 1462, 1355, 1317, 1151, 989, 854, 815, 712.

2-Phenyl-5-(1-methoxy-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175s)



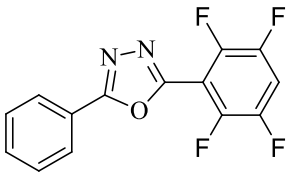
White solid, m.p. 119–120 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.14–8.12 (m, 2H), 7.58–7.52 (m, 3H), 4.22 (t, J = 1.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.3, 155.5 (m), 146.6 (m), 145.3 (dm, J = 260.7 Hz), 141.1 (m), 140.7 (dm, J = 253.2 Hz), 132.2, 129.1, 127.1, 123.2, 115.0, 98.0, 62.1; ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –137.7 (m, 2F), –156.8 (m, 2F); MS *m/z* (EI) (relative intensity, %): 324 (60, M^+), 268 (12), 253 (23), 237 (10), 225 (8), 207 (30), 105 (100), 77 (51), 63 (10), 51 (11); HRMS *m/z* (M^+) calcd for $C_{15}H_9F_4N_2O_2$: 325.0595, found: 325.0590; IR: 2963, 2923, 2116, 1648, 1551, 1489, 1230, 1120, 1023, 986, 819, 781, 694.

2-Phenyl-5-(1-cyano-2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175t)



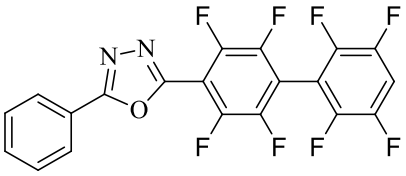
White solid, m.p. 217–220 °C. ^{1}H NMR (DMSO-d_6, 600 MHz) δ = 8.12–8.10 (m, 2H), 7.74–7.66 (m, 3H); ^{13}C NMR (DMSO-d_6, 150 MHz) δ = 170.3, 165.1, 154.9 (m), 148.2 (m), 146.4 (m), 144.7 (m), 143.0 (m), 132.9, 129.7, 127.0, 122.4, 107.8; ^{19}F NMR (DMSO-d_6, 376 MHz) δ = –127.9 (m, 2F), –130.0 (m, 2F); Anal. Calcd for $C_{15}H_5F_4N_3O$ (319.04): C, 56.44; H, 1.58; N, 13.16; Found: C, 55.76; H, 1.66; N, 12.77; MS *m/z* (EI) (relative intensity, %): 319 (68, M^+), 320 (10), 318 (5), 262 (10), 202 (21), 174 (13), 105 (100), 89 (23), 77(47), 63 (25), 51 (16); HRMS *m/z* (M^+) calcd for $C_{15}H_6F_4N_3O$: 320.0441, found: 320.0440; IR: 2248, 1604, 1548, 1497, 1319, 1273, 1101, 989, 816, 714, 691.

2-Phenyl-5-(2,3,5,6-tetrafluorophenyl)-1,3,4-oxadiazole (175u)



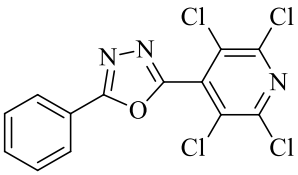
White solid, m.p. 113–114 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.17–8.15 (m, 2H), 7.62–7.53 (m, 3H), 737–7.26 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.6 (m), 159.6, 155.4 (m), 146.3 (dm, J = 242.2 Hz), 144.5 (dm, J = 259.1 Hz), 132.4, 129.2, 127.2, 123.1, 109.2 (t, J = 22.4 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –136.4 (m, 2F), –133.7 (m, 2F); MS *m/z* (EI) (relative intensity, %): 294 (89, M^+), 295 (14), 237 (32), 105 (100), 77 (63); HRMS *m/z* (M^+) calcd for $C_{14}H_7F_4N_2O$: 295.0489, found: 295.0489; IR: 3064, 1771, 1609, 1551, 1500, 1445, 1390, 1279, 1178, 1020, 932, 888, 851, 778, 746, 708, 685.

2-Phenyl-5-[1-(2,3,5,6-tetrafluorophenyl)-2,3,5,6-tetrafluorophenyl]-1,3,4-oxadiazole (175v)



White solid, m.p. 198–201 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.19–8.16 (m, 2H), 7.64–7.55 (m, 3H), 736–7.28 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 165.9 (m), 159.5, 155.1 (m), 147.3 (m), 145.9 (m), 145.2 (m), 144.8 (m), 143.4 (m), 142.7 (m), 132.5, 129.2, 127.3, 123.0, 108.5 (t, J = 22.2 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ = –135.4 (m, 2F), –136.1 (m, 2F), –137.1 (m, 2F), –137.7 (m, 2F); MS *m/z* (EI) (relative intensity, %): 442 (79, M^+), 443 (13), 385 (27), 325 (29), 278 (21), 105 (100), 77 (33), 63 (10); HRMS *m/z* (M^+) calcd for $C_{20}H_7F_8N_2O$: 443.0425, found: 443.0422; IR: 3081, 2325, 1604, 1550, 1476, 1264, 1179, 989, 930, 856, 783, 704.

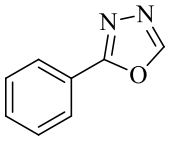
2-Phenyl-5-(2,3,5,6-tetrachloropyridinyl)-1,3,4-oxadiazole (175w)



White solid, m.p. 173–174 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.10 (d, J = 7.9 Hz, 2H), 7.60–7.52 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 166.2, 157.1, 147.1, 136.0, 132.6, 130.7, 129.3, 127.3, 122.8; Anal. Calcd for $C_{13}H_5Cl_4N_3O$ (361.01): C, 43.25; H, 1.40; N, 11.64; Found: C, 43.30; H, 1.64; N, 11.70; MS *m/z* (EI) (relative intensity, %): 361 (56, M^+), 362 (9), 363 (26), 360 (7), 359 (47), 272

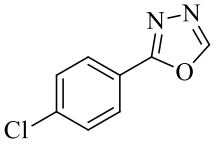
(8), 271 (3), 270 (22), 269 (4), 268 (24), 244 (14), 106 (8), 105 (100), 89 (9), 77 (28); IR: 3060, 2325, 1250, 1204, 1096, 779, 740, 708, 664.

2-Phenyl-1,3,4-oxadiazole (173a)[197]



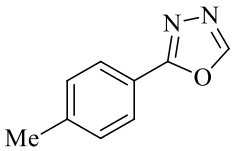
White solid, m.p. <30 °C (lit.[197] m.p. <30 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.46 (s, 1H), 8.00 (bm, 2H), 7.47–7.41 (bm, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.6, 152.7, 131.9, 129.0, 127.0, 123.4; MS *m/z* (EI) (relative intensity, %): 146 (100, M^+), 105 (53), 91 (27), 90 (61), 77 (54).

2-(4-Chlorophenyl)-1,3,4-oxadiazole (173b)[197]



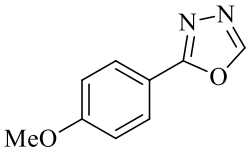
White solid, m.p. 132–133 °C (lit.[197] 133–135 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.42 (s, 1H), 7.33 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 7.41 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.9, 152.7, 138.3, 129.5, 128.3, 121.9; MS *m/z* (EI) (relative intensity, %): 180 (100, M^+), 182 (35), 181 (27), 141 (23), 140 (6), 139 (73), 125 (10), 124 (17), 111 (11), 90 (8), 89 (31), 75 (12), 63 (9).

2-(4-Methylphenyl)-1,3,4-oxadiazole (173c)[197]



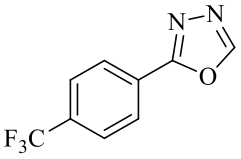
White solid, m.p. 89–90 °C (lit.[197] 84.3–86.0 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.41 (s, 1H), 8.01 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 7.01 (dd, *J* = 6.8 Hz, 2.0 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.7, 162.5, 152.2, 128.9, 116.0, 114.6, 55.5; MS *m/z* (EI) (relative intensity, %): 160 (100, M^+), 161 (40), 120 (6), 119 (68), 104 (19), 103 (13), 91 (19), 78 (12), 77(9), 65 (8).

2-(4-Methoxyphenyl)-1,3,4-oxadiazole (173d)[166a]



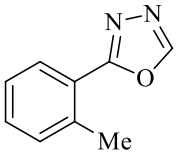
White solid, m.p. 60–61 °C (lit.[166a] 62.5–63.5 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.40 (s, 1H), 7.96 (dd, J = 7.2 Hz, 2.4 Hz, 2H), 6.97 (dd, J = 6.8 Hz, 2.0 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.6, 162.4, 152.2, 128.8, 115.9, 114.5, 55.4; MS *m/z* (EI) (relative intensity, %): 176 (100, M^+), 177 (37), 135 (64), 105 (3), 92 (4), 91 (5), 90 (2).

2-(4-Trifluoromethylphenyl)-1,3,4-oxadiazole (173e)[197]



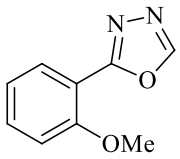
White solid, m.p. 111–113 °C (lit.[197] 112–114 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.47 (s, 1H), 8.14 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.9, 153.1, 133.6 (d, $J_{F\text{-}C}$ = 32.7 Hz), 127.4, 126.7, 126.2 (q, $J_{F\text{-}C}$ = 3.8 Hz), 123.5 (d, $J_{F\text{-}C}$ = 272.5 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ = –63.1; MS *m/z* (EI): 214 (M^+).

2-(2-Methylphenyl)-1,3,4-oxadiazole (173f)



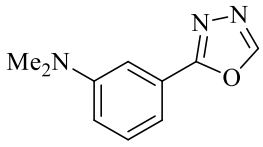
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.49 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.35–7.30 (m, 2H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.9, 152.2, 138.6, 131.7, 131.4, 129.1, 126.2, 122.6, 22.0; MS *m/z* (EI) (relative intensity, %): 160 (100, M^+), 161 (89), 159 (4), 132 (9), 131 (11), 119 (16), 118 (52), 105 (31), 104 (12), 99 (13), 90 (23), 89 (12), 77 (11), 51 (11).

2-(2-Methoxyphenyl)-1,3,4-oxadiazole (173g)[198]



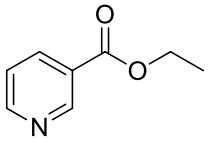
White solid, m.p. 55–56 °C (lit.[198] 47–49 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.47 (d, 1H), 7.93–7.91 (bm, 1H), 7.49–7.48 (bm, 1H), 7.07–7.03 (bm, 2H), 3.93 (t, J = 4.1 Hz, 8.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 163.5, 157.9, 152.5, 133.3, 130.6, 120.7, 112.6, 112.0, 56.0; MS *m/z* (EI) (relative intensity, %): 176 (99, M^+), 178 (10), 177 (100), 175 (7), 147 (29), 135 (30), 132 (33), 118 (11), 105 (33), 92 (15), 91 (25), 90 (15), 89 (12), 77 (18), 63 (12), 51 (16), 50 (12).

2-[3-*N*,*N*-Dimethylphenyl]-1,3,4-oxadiazole (173h)[199]



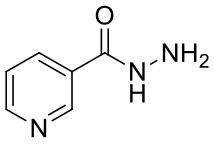
White solid, m.p. 60–61 °C (lit.[199] 61–62 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.44 (s, 1H), 7.43–7.42 (bm, 1H), 7.37–7.33 (m, 2H), 6.90–7.87 (m, 1H), 3.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.5, 152.4, 150.6, 129.7, 124.0, 115.7, 114.8, 110.3, 40.4; MS *m/z* (EI) (relative intensity, %): 189 (100, M^+), 190 (26), 188 (54), 161 (10), 146 (3), 145 (9), 119 (4).

3-(Ethoxycarbonyl)-pyridine (173i-1)[200]



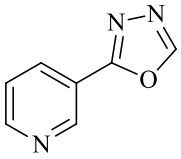
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.20–9.19 (m, 1H), 9.74 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 8.28–8.26 (m, 1H), 7.38–7.34 (m, 1H), 4.39 (q, J = 7.2 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.2, 153.2, 150.8, 136.9, 126.3, 123.2, 61.4, 14.2.

3-Pyridinecarbohydrazide (173i-2)[201]



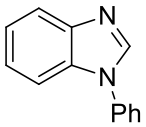
Solid, m.p. 160–162 °C (lit.[201] 161–163 °C). ^{1}H NMR (600 MHz, d_6-DMSO) δ = 8.96 (s, 1H), 8.68 (d, J = 4.8 Hz, 1H), 8.15–8.14 (m, 1H), 7.50–7.47 (m, 1H), 3.43 (bq, 3H); ^{13}C NMR (150 MHz, d_6-DMSO) δ = 164.8, 152.2, 148.5, 135.1, 129.3, 123.9.

2-(3-Pyridinyl)-1,3,4-oxadiazole (173i)[198]



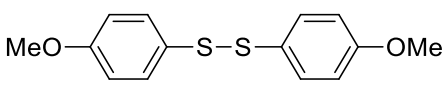
Pale yellow solid, m.p. 72–74 °C (lit.[198] 75–76 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.25 (bd, J = 0.8 Hz, 1H), 8.75–8.74 (bm, 1H), 8.55 (s, 1H), 8.36–8.33 (bm, 1H), 7.47–7.43 (bm, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.7, 153.1, 152.6, 147.9, 134.3, 123.8, 120.0; MS *m/z* (EI) (relative intensity, %): 147 (100, M^+), 149 (6), 148 (69), 106 (35), 91 (21), 78 (20), 77 (3), 64 (10), 63 (14), 51 (17).

***N*-Phenylbenzimidazole (181d)[202]**



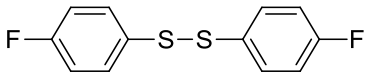
Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 (s, 1H), 7.87–7.84 (m, 1H), 7.52–7.44 (m, 3H), 7.44–7.37 (m, 3H), 7.31–7.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.0, 142.2, 136.3, 133.6, 130.0, 128.0, 123.9, 123.6, 122.7, 120.6, 110.4; MS *m/z* (EI) (relative intensity, %): 194 (100, M^+), 196 (7), 195 (54), 193 (10), 168 (3), 167 (4), 139 (3), 77 (3), 51 (4).

4,4'-Dimethoxydiphenyl disulfide (179c)[203]



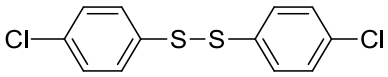
White solid, m.p. 35–36 °C (lit.[203] 34–35 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 (dd, J = 9.2 Hz, 3.2 Hz, 4H), 6.83 (dd, J = 8.8 Hz, 2.8 Hz, 4H), 3.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.9, 132.7, 128.4, 114.6, 55.4; MS *m/z* (EI) (relative intensity, %): 278 (20, M^+), 279 (3), 140 (8), 139 (100), 124 (15), 96 (28), 95 (24), 78 (2), 77 (6), 70 (13), 69 (10).

4,4'-Difluorodiphenyl disulfide (179d)[204]



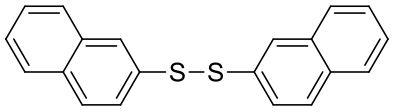
White solid, m.p. 49–51 °C (lit.[204] 50–52 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40–7.37 (m, 4H), 7.28–7.24 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.6 ($J_{F\text{-}C}$ = 246.7 Hz), 132.2 ($J_{F\text{-}C}$ = 3.3 Hz), 131.3 ($J_{F\text{-}C}$ = 8.0 Hz), 116.2 ($J_{F\text{-}C}$ = 22.1 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ = –113.4 (s, 2F); MS *m/z* (EI) (relative intensity, %): 254 (95, M^+), 255 (15), 127 (100), 83 (38).

4,4'-Dichlorodiphenyl disulfide (179e)[205]



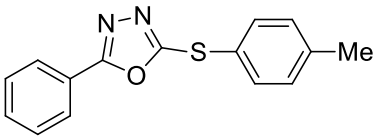
Pale yellow solid, m.p. 71–73 °C (lit.[205] 70–72 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47–7.43 (m, 4H), 7.04–6.99 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 135.1, 133.6, 129.3, 129.2 MS *m/z* (EI) (relative intensity, %): 286 (100, M^+), 288 (80), 287 (16), 224 (3), 145 (22), 144 (5), 143 (65), 108 (35), 82 (3), 69 (5), 63 (6).

2,2'-Dinaphthyl disulfide (179f)[206]



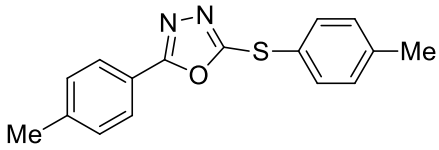
White solid, m.p. 139–141 °C (lit.[206] 138–140 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 (J = 1.6 Hz, 2H), 7.81–7.78 (m, 4H); 7.75–7.73 (m, 2H); 7.63 (dd, J = 8.8 Hz, 2.0 Hz, 2H); 7.49–7.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 134.2, 133.5, 132.5, 128.9, 127.7, 127.4, 126.7, 126.5, 126.2, 125.6; MS *m/z* (EI) (relative intensity, %): 318 (70, M^+), 319 (14), 254 (31), 159 (66), 115 (100).

2-Phenyl-5-(4-methylphenylthio)-1,3,4-oxadiazole (180a)[169c]



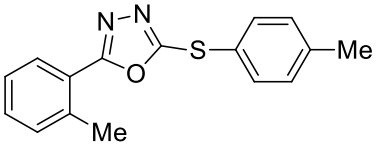
White solid, m.p. 71–72 °C (lit.[169c] 68–69 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.97–7.94 (m, 2H), 7.57 (dd, J = 6.3 Hz, 1.8 Hz, 2H); 7.51–7.44 (m, 3H), 7.24 (d, J = 8.1 Hz 2H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.2, 163.4, 140.4, 134.0, 131.7, 130.5, 129.0, 126.7, 123.6, 123.2, 21.3; Anal. Calcd for $C_{15}H_{12}N_2OS$ (268.33): C, 67.14; H, 4.51; N, 10.44; found: C, 67.23; H, 4.53; N, 10.50; MS *m/z* (EI) (relative intensity, %): 268 (100, M^+), 270 (11), 269 (40), 226 (3), 179 (5), 165 (4), 146 (4), 145 (39), 123 (9), 121 (15), 105 (9), 77 (18).

2-(4-Methylphenyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180b)



White solid, m.p. 71–73 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.85–7.83 (m, 2H), 7.58–7.55 (m, 2H), 7.28–7.22 (m, 4H), 2.40 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.4, 163.0, 142.3, 140.3, 133.9, 130.5, 129.7, 126.7, 123.4, 120.8, 21.6, 21.3; Anal. Calcd for $C_{16}H_{14}N_2OS$ (282.36): C, 68.06; H, 5.00; N, 9.92; Found: C, 67.99; H, 4.76; N, 9.88; MS *m/z* (EI) (relative intensity, %): 282 (80, M^+), 283 (18), 159 (100), 135 (27), 91 (48).

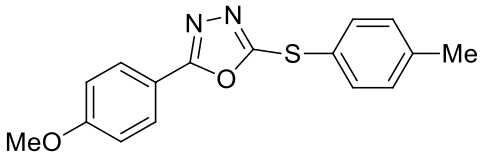
2-(2-Methylphenyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180c)



White solid, m.p. 51–52 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82–7.79 (m, 1H), 7.59–7.55 (m, 2H), 7.39–7.34 (m, 1H), 7.29–7.21 (m, 4H), 2.59 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.3, 163.2, 140.4, 138.3, 134.2, 131.7, 131.2, 130.5, 128.8, 126.1, 123.1, 122.6, 22.0, 21.3; Anal.

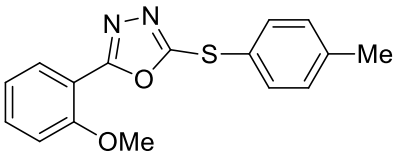
Calcd for $C_{16}H_{14}N_2OS$ (282.36): C, 68.06; H, 5.00; N, 9.92; Found: C, 68.00; H, 4.77; N, 9.90; MS *m/z* (EI) (relative intensity, %): 282 (51, M^+), 283 (11), 159 (100), 117 (27), 116 (29), 91 (31).

2-(4-Methoxyphenyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180d)



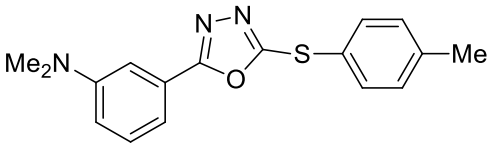
White solid, m.p. 73–74 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.88 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 3.85 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.3, 162.5, 162.3, 140.2, 133.8, 130.5, 128.5, 123.6, 116.1, 114.4, 55.4, 21.3; Anal. Calcd for $C_{16}H_{14}N_2O_2S$ (298.08): C, 64.41; H, 4.73; N, 9.39; Found: C, 64.53; H, 4.69; N, 9.40; IR: 3075, 2938, 2103, 1898, 1610, 1478, 1304, 1254, 1163, 1067, 1022, 955, 835, 803, 733, 697; MS *m/z* (EI) (relative intensity, %): 298 (86, M^+), 299 (18), 175 (76), 135 (27), 133 (100).

2-(2-Methoxyphenyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180e)



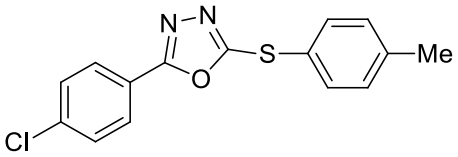
White solid, m.p. 91–93 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83–7.80 (bdd, *J* = 8.1 Hz, 1.5 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.50–7.44 (m, 1H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.02 (t, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.0, 157.8, 140.1, 133.9, 133.1, 130.4, 130.3, 129.6, 123.6, 120.7, 112.8, 111.9, 55.9, 21.3; Anal. Calcd for $C_{16}H_{14}N_2O_2S$ (298.36): C, 64.41; H, 4.73; N, 9.39; Found: C, 64.28; H, 4.36; N, 9.29; MS *m/z* (EI) (relative intensity, %): 298 (53, M^+), 299 (12), 175 (100), 151 (21), 133 (67), 77 (21).

2-(3-N,N-Dimethylaminophenyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180f)



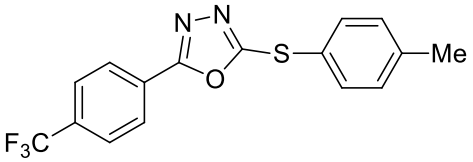
Yelllow solid, m.p. 103–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57–7.55 (m, 2H), 7.32–7.28 (bm, 2H), 7.24–7.22 (bm, 3H), 6.85 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 3.00 (s, 6H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.0, 163.0, 150.5, 140.2, 133.8, 130.4, 129.6, 124.1, 123.5, 115.6, 114.7, 110.0, 40.4, 21.3; Anal. Calcd for $C_{17}H_{17}N_3OS$ (311.40): C, 65.57; H, 5.50; N, 13.49; Found: C, 65.30; H, 5.43; N, 13.20; MS *m/z* (EI) (relative intensity, %): 311 (35, M^+), 164 (17), 148 (32), 146 (100), 145 (43.3).

2-(4-Chlorophenyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180g)



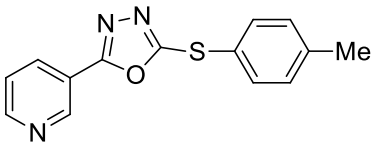
White solid, m.p. 121–122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.90–7.88 (m, 2H), 7.58–7.56 (m, 2H), 7.46–7.43 (m, 2H), 7.24 (d, J = 8.0 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.3, 163.8, 140.5, 138.0, 134.1, 130.6, 129.4, 128.0, 122.9, 122.0, 21.3; Anal. Calcd for $C_{15}H_{11}ClN_2OS$ (302.78): C, 59.50; H, 3.66; N, 9.25; Found: C, 59.12; H, 3.33; N, 9.11; MS *m/z* (EI) (relative intensity, %): 302 (90, M^+), 303 (17), 304 (36), 181 (31), 179 (100), 155 (31), 137 (30), 123 (36), 111 (30).

2-(4-Trifluoromethylphenyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180h)



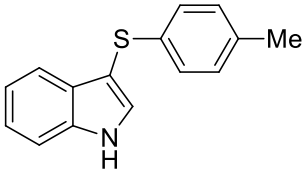
White solid, m.p. 116–118 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.07 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 7.8 Hz , 2H), 7.58 (d, J = 7.8 Hz, 2H), 7.25 (d, J = 7.8 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 164.9, 164.6, 140.7, 134.2, 133.3 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.6, 130.4, 127.0, 126.8, 126.3 (q, $J_{C\text{-}F}$ = 3.7 Hz), 123.5 (q, $J_{C\text{-}F}$ = 272.6 Hz), 21.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ = –63.2 (s, 3F); Anal. Calcd for $C_{16}H_{11}F_3N_2OS$ (336.33): C, 57.14; H, 3.30; N, 8.33; Found: C, 57.57; H, 3.39; N, 8.18; MS *m/z* (EI) (relative intensity, %): 336 (97, M^+), 337 (17), 213 (100), 189 (47), 145 (99), 123 (52), 91 (20).

2-(3-Pyridinyl)-5-(4-methylphenylthio)-1,3,4-oxadiazole (180i)



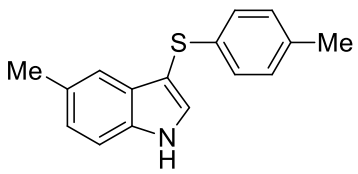
White solid, m.p. 78–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.13 (s, 1H), 8.72 (d, J = 4.4 Hz , 1H), 8.23 (d, J = 8.0 Hz , 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.42–7.39 (m, 1H), 7.23 (d, J = 7.2 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.9, 164.6, 140.7, 134.3, 130.6, 127.0, 126.1 (2C), 126.0 (2C), 122.6, 21.3; Anal. Calcd for $C_{14}H_{11}N_3OS$ (269.32): C, 62.43; H, 4.12; N, 15.60; Found: C, 62.48; H, 3.90; N, 15.87; MS *m/z* (EI) (relative intensity, %): 269 (30, M^+), 180 (23), 146 (100), 123 (47), 122 (50).

3-(4-Methylphenylthio)-indole (180j)[207]



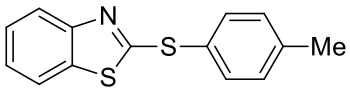
White solid, m.p. 127–129 °C (lit.[207] 125.0–126.0). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.30 (bs, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.44–7.43 (m, 1H), 7.42–7.40 (m, 1H), 7.28–7.24 (m, 1H), 7.18–7.14 (m, 1H), 7.04 (dd, J = 8.8 Hz, 2.0 Hz, 2H), 6.98 (d, J = 8.0 Hz, 2H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.4, 135.5, 134.7, 130.4, 129.5, 129.1, 126.2, 123.0, 120.8, 119.7, 111.5, 103.4, 20.9; Anal. Calcd for $C_{15}H_{13}NS$ (239.34): C, 75.28; H, 5.47; N, 5.85; Found: C, 75.16; H, 5.19; N, 5.72; MS *m/z* (EI) (relative intensity, %): 239 (100, M^+), 240 (22), 238 (18), 224 (13), 223 (13), 207 (15), 206 (13).

3-(4-Methylphenylthio)-6-methylindole (180k)



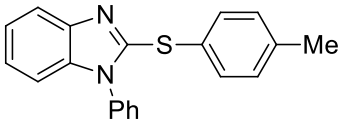
White solid, m.p. 137–138 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.23 (bs, 1H), 7.44 (s, 1H), 7.41 (s, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.10 (d, J = 8.4 Hz, 1H), 7.05 (d, J = 8.4 Hz, 2H), 7.00 (t, J = 7.8 Hz, 2H), 2.44 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 135.8, 134.8, 134.5, 130.7, 130.3, 129.5, 129.4, 126.0, 124.6, 119.2, 111.2, 102.6, 21.4, 20.9; Anal. Calcd for $C_{16}H_{15}NS$ (253.09): C, 75.85; H, 5.97; N, 5.53; Found: C, 75.71; H, 5.87; N, 5.38; MS *m/z* (EI) (relative intensity, %): 253 (100, M^+), 254 (17), 152 (11).

2-(4-Methylphenylthio)-benzothiazole (180l)[208]



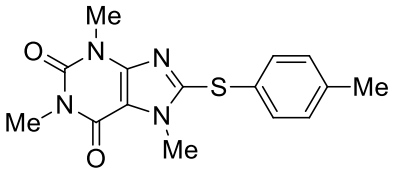
White solid, m.p. 72–73 °C (lit.[208] 73–74 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 8.0 Hz, 3H), 7.40 (t, J = 7.7 Hz, 1H), 7.31–7.23 (m, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.8, 154.0, 141.2, 135.6, 130.8, 126.3, 126.1, 124.2, 121.8, 120.7, 21.5; Anal. Calcd for $C_{14}H_{11}NS_2$ (257.03): C, 65.33; H, 4.31; N, 5.44; Found: C, 65.31; H, 4.09; N, 5.36; IR: 3057, 2913, 2110, 1988, 1591, 1491, 1452, 1420, 1235, 1083, 1003, 847, 814, 755, 725, 669; MS *m/z* (EI) (relative intensity, %): 256 (100, M^+), 257 (73), 128 (11).

1-Phenyl-2-(4-methylphenylthio)-benzimidazole (180m)



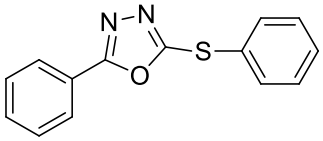
White solid, m.p. 122–124 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, J = 8.4 Hz, 1H), 7.54–7.50 (m, 3H), 7.37–7.36 (m, 2H), 7.31 (d, J = 7.8 Hz, 2H), 7.27–7.25 (m, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.12–7.09 (m, 3H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 150.2, 143.1, 138.7, 137.3, 135.5, 133.0, 130.0, 129.5, 128.9, 127.5, 126.7, 123.1, 122.5, 119.3, 109.8, 21.2; Anal. Calcd for $C_{20}H_{16}N_2S$ (316.42): C, 75.92; H, 5.10; N, 8.85; Found: C, 75.54; H, 5.11; N, 8.68; IR: 3011, 2945, 2319, 2100, 1903, 1703, 1591, 1491, 1438, 1369, 1304, 1266, 1176, 1073, 1005, 905, 807, 750, 697; MS *m/z* (EI) (relative intensity, %): 316 (95, M^+), 317 (24), 315 (100), 283 (17).

2-(4-Methylphenylthio)-caffeine (180n)



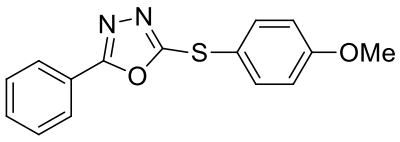
White solid, m.p. 144–146 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.28–7.26 (m, 2H), 7.14 (d, J = 7.8 Hz, 2H), 3.91–3.90 (m, 3H), 3.54 (m, 3H), 3.38 (m, 3H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 154.9, 151.4, 148.0, 147.2, 136.7, 131.2, 130.3, 126.8, 109.4, 33.0, 29.8, 27.9, 21.1; Anal. Calcd for $C_{15}H_{16}N_4O_2S$ (316.38): C, 56.94; H, 5.10; N, 17.71; Found: C, 56.88; H, 4.85; N, 17.75; IR: 3034, 2953, 2130, 1701, 1658, 1540, 1447, 1336, 1219, 1035, 971, 811, 744, 668; MS *m/z* (EI) (relative intensity, %): 316 (100, M^+), 317 (24), 105 (35), 67 (21).

2-Phenyl-5-phenylthio-1,3,4-oxadiazole (180o)[169c]



Colorless oil (lit.[169c] 62.4–63.1 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.97–7.95 (m, 2H), 7.68–7.67 (m, 2H), 7.51–7.43 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 166.4, 162.9, 133.6, 131.8, 129.8, 129.7, 129.0, 127.1, 126.8, 123.5; Anal. Calcd for $C_{14}H_{10}N_2OS$ (254.05): C, 66.12; H, 3.96; N, 11.02; Found: C, 66.11; H, 3.76; N, 11.42; MS *m/z* (EI) (relative intensity, %): 254 (78, M^+), 255 (18), 145 (100), 105 (22), 77 (61).

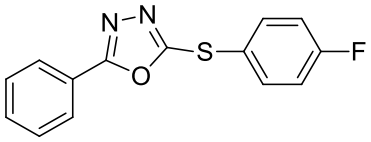
2-Phenyl-5-(4-methoxyphenylthio)-1,3,4-oxadiazole (180p)[169c]



White solid, m.p. 89–90 °C (lit.[169c] 85.5–86.5 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.94 (d, J = 7.7 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H), 7.50–7.45 (m, 3H), 6.96 (d, J = 8.3 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 166.1, 163.9, 161.3, 136.3, 131.7, 129.0, 126.7, 123.6, 116.7, 115.3, 55.4; Anal. Calcd for $C_{15}H_{12}N_2O_2S$ (284.06): C, 63.36; H, 4.25; N, 9.85; Found: C, 63.25; H, 4.16;

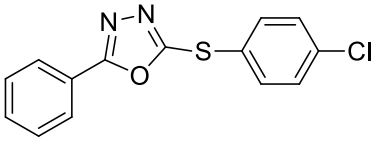
N, 9.79; MS *m/z* (EI) (relative intensity, %): 284 (97, M^+), 285 (17), 181 (14), 145 (100), 139 (61), 121 (43), 77 (78).

2-Phenyl-5-(4-fluorophenylthio)-1,3,4-oxadiazole (180q)



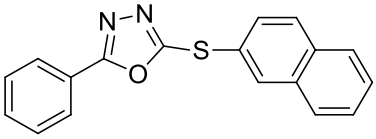
White solid, m.p. 96–97 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.95 (d, J = 7.5 Hz, 2H), 7.71–7.68 (m, 2H), 7.53–7.51 (m, 1H), 7.47 (t, J = 7.2 Hz, 2H), 7.14 (t, J = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.3, 164.7, 163.0 ($J_{F\text{-}C}$ = 9.6 Hz), 136.4 ($J_{F\text{-}C}$ = 8.7 Hz), 131.8, 129.0 ($J_{F\text{-}C}$ = 13.1 Hz), 126.7, 123.5, 121.9 ($J_{F\text{-}C}$ = 3.2 Hz), 117.1 ($J_{F\text{-}C}$ = 22.4 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ = –109.8 (m, 1F); Anal. Calcd for $C_{14}H_9FN_2OS$ (272.04): C, 61.75; H, 3.33; N, 10.29; Found: C, 61.90; H, 3.13; N, 10.26; MS *m/z* (EI) (relative intensity, %): 272 (35, M^+), 145 (100), 127 (25), 77 (54).

2-Phenyl-5-(4-chlorophenylthio)-1,3,4-oxadiazole (180r)[169c]



White solid, m.p. 97–99 °C (lit.[169c] 95–95.5 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.97 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.53–7.51 (m, 1H), 7.49–7.47 (m, 2H), 7.42–7.40 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.5, 162.4, 136.4, 134.9, 131.9, 130.0, 129.0, 126.8, 125.4, 123.4; Anal. Calcd for $C_{14}H_9ClN_2OS$ (288.01): C, 58.23; H, 3.14; N, 9.70; Found: C, 58.31; H, 2.92; N, 9.72; MS *m/z* (EI) (relative intensity, %): 288 (67, M^+), 290 (29), 145 (100), 77 (32).

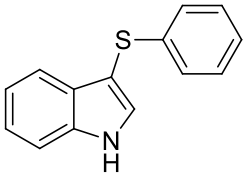
2-Phenyl-5-(2-naphthylthio)-1,3,4-oxadiazole (180s)



White solid, m.p. 114–116 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.21 (s, 1H), 7.96 (d, J = 7.8 Hz, 2H),

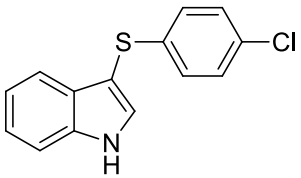
7.89 (d, *J* = 9.0 Hz, 1H), 7.86 (t, *J* = 9.6 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.58–7.54 (m, 2H), 7.51–7.49 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.4, 162.9, 133.6, 133.5, 133.4, 131.8, 129.7, 129.6, 129.0, 127.9, 127.8, 127.5, 127.0, 126.8, 124.2, 123.5; Anal. Calcd for $C_{18}H_{12}N_2OS$ (304.07): C, 71.03; H, 3.97; N, 9.20; Found: C, 71.15; H, 3.83; N, 9.23; MS *m/z* (EI) (relative intensity, %): 304 (56, M^+), 305 (12), 201 (17), 159 (31), 145 (100), 115 (55).

3-Phenylthioindole (180t)[171b]



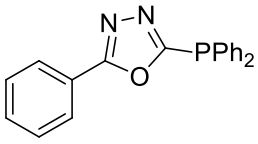
White solid, m.p. 153–154 °C (lit.[171b] 152–154 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.36 (bs, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.48 (d, *J* = 2.6 Hz, 1H), 7.45–7.43 (m, 1H), 7.31–7.26 (m, 1H), 7.20–7.11 (m, 5H), 7.09–7.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.8, 136.5, 130.7, 130.6, 128.8, 128.7, 127.1, 123.2, 121.1, 119.5, 111.7, 102.5; Anal. Calcd for $C_{14}H_{11}NS$ (225.31): C, 74.63; H, 4.92; N, 6.22; Found: C, 74.57; H, 4.74; N, 6.12; MS *m/z* (EI) (relative intensity, %): 225 (100, M^+), 224 (28), 226 (16), 193 (18), 148 (24), 121 (19), 77 (34).

3-(4-Chlorophenylthio)-indole (180u)[207]



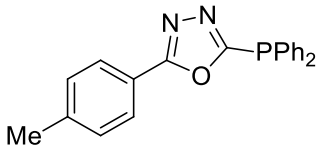
White solid, m.p. 135–136 °C (lit.[207] 134.0–135.1 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.39 (bs, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 2.4 Hz, 1H), 7.45 (t, *J* = 8.4 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.12 (dd, *J* = 8.4 Hz, 1.2 Hz, 2H), 7.04–7.03 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 137.8, 136.5, 130.7, 130.6, 128.8, 128.7, 127.1, 123.2, 121.1, 119.5, 111.7, 102.5; Anal. Calcd for $C_{14}H_{10}ClNS$ (259.02): C, 64.73; H, 3.88; N, 5.39; Found: C, 64.70; H, 3.72; N, 5.30; MS *m/z* (EI) (relative intensity, %): 259 (100, M^+), 260 (18), 261 (36), 224 (30), 223 (28), 148 (31), 121 (23), 112 (44), 77 (31).

2-Phenyl-1,3,4-oxadiazolyldiphenylphosphine (184a)[176]



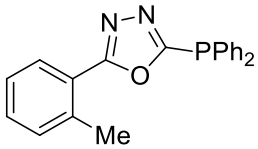
White solid, m.p. 85–86 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.96–8.00 (m, 2H), 7.62–7.55 (m, 4H), 7.47–7.43 (m, 2H), 7.42–7.36 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.8 ($^{1}J_{C\text{-}P}$ = 32.6 Hz), 167.0, 134.0 ($^{2}J_{C\text{-}P}$ = 21.1 Hz), 132.0 ($^{1}J_{C\text{-}P}$ = 6.3 Hz), 131.9, 130.2, 129.0 ($^{3}J_{C\text{-}P}$ = 2.3 Hz), 128.9, 127.2, 123.7; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –25.0; MS *m/z* (EI) (relative intensity, %): 330.1 (100, M^+), 331 (22), 226 (11), 184 (16), 183 (29), 154 (28), 77 (39); HRMS *m/z* (M^+) calcd for $C_{20}H_{15}ON_2NaP$: 353.0814, found: 353.0813; IR: 1549, 1474, 1433, 1154, 1068, 780, 745, 690.

(4-Methyl)-2-phenyl-1,3,4-oxadiazolyldiphenylphosphine (184b)



White solid, m.p. 111–112 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.90–7.88 (d, *J* = 8.2 Hz, 2H), 7.62–7.55 (m, 4H), 7.43–7.38 (m, 6H), 7.28–7.24 (d, *J* = 7.9 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.4 ($^{1}J_{C\text{-}P}$ = 32.3 Hz), 167.1, 142.4, 134.0 ($^{2}J_{C\text{-}P}$ = 21.2 Hz), 132.1 ($^{1}J_{C\text{-}P}$ = 6.2 Hz), 130.1, 129.7, 128.9 ($^{3}J_{C\text{-}P}$ = 7.9 Hz), 127.1, 121.0, 21.6; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –25.3 ppm; Anal. Calcd for $C_{21}H_{17}ON_2P$ (344.35): C, 73.03; H, 5.01; N, 8.31; Found: C, 73.25; H, 4.98; N, 8.14; MS *m/z* (EI) (relative intensity, %): 344 (100, M^+), 345 (26), 183 (22), 154 (17); IR: 3045, 1610, 1551, 1490, 1433, 1334, 1184, 1153, 1076, 1023, 954, 824, 742, 694.

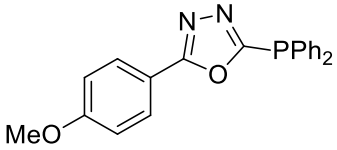
(2-Methyl)-2-phenyl-1,3,4-oxadiazolyldiphenylphosphine (184c)



White solid, m.p. 84–85 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88–7.82 (m, 1H), 7.62–7.55 (m, 4H),

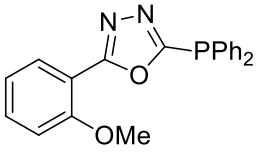
7.44–7.36 (m, 7H), 7.32–7.22 (m, 2H), 2.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.3 ($^1J_{C\text{-}P}$ = 32.4 Hz), 167.2, 138.5, 133.9 ($^2J_{C\text{-}P}$ = 21.1 Hz), 132.1 ($^1J_{C\text{-}P}$ = 6.3 Hz), 131.7, 131.4, 130.1, 129.2, 128.9 ($^3J_{C\text{-}P}$ = 7.9 Hz), 127.6, 126.1, 123.0, 22.0; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –25.3 ppm; Anal. Calcd for $C_{21}H_{17}ON_2P$ (344.11): C, 73.25; H, 4.98; N, 8.14; Found: C, 73.32; H, 4.81; N, 8.12; MS *m/z* (EI) (relative intensity, %): 344 (100, M^+), 345 (22), 184 (25), 183 (41), 154 (45), 150 (35), 91 (28), 77 (33); IR: 1604, 1542, 1480, 1434, 1053, 989, 776, 746, 694.

(4-Methoxy)-2-phenyl-1,3,4-oxadiazolyldiphenylphosphine (184d)



White solid, m.p. 94–95 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.97–7.92 (m, 2H), 7.62–7.55 (m, 4H), 7.44–7.38 (m, 6H), 7.00–6.95 (m, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.0 ($^1J_{C\text{-}P}$ = 23.8 Hz), 162.4, 133.9 ($^2J_{C\text{-}P}$ = 21.1 Hz), 132.2 ($^1J_{C\text{-}P}$ = 6.3 Hz), 130.1, 128.9 ($^3J_{C\text{-}P}$ = 2.9 Hz), 128.8, 127.6, 116.3, 114.4, 55.4; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –25.5; Anal. Calcd for $C_{21}H_{17}O_2N_2P$ (360.35): C, 70.00; H, 4.76; N, 7.77; Found: C, 69.61; H, 4.72; N, 7.81; MS *m/z* (EI) (relative intensity, %): 360 (100, M^+), 361 (26), 183 (18), 154 (14), 150 (11), 133 (12), 77 (13); IR: 1607, 1494, 1435, 1339, 1253, 1176, 1076, 1023, 953, 835, 744, 695.

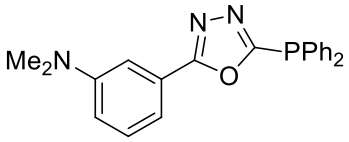
(2-Methoxy)-2-phenyl-1,3,4-oxadiazolyldiphenylphosphine (184e)



Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88–7.84 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.62–7.56 (m, 4H), 7.48–7.41 (m, 1H), 7.40–7.36 (m, 6H), 7.03–6.96 (m, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.3 ($^1J_{C\text{-}P}$ = 32.8 Hz), 165.8, 157.9, 134.0 ($^2J_{C\text{-}P}$ = 21.1 Hz), 133.2, 132.4 ($^1J_{C\text{-}P}$ = 6.6 Hz), 130.6, 130.0, 128.8 ($^3J_{C\text{-}P}$ = 7.9 Hz), 120.7, 113.0, 112.0, 55.9; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –26.0; MS *m/z* (EI) (relative intensity, %): 360 (100, M^+), 361 (30), 184 (15), 183 (27), 154 (23); HRMS *m/z* (M^+) calcd for $C_{21}H_{17}O_2N_2NaP$: 383.0920, found: 383.0923; IR: 3451, 3059, 2839, 1604,

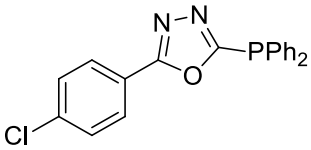
1541, 1473, 1436, 1335, 1269, 1164, 1123, 1023, 750, 696, 508.

(3-N-Dimethyl)-2-phenyl-1,3,4-oxadiazolyldiphenylphosphine (184f)



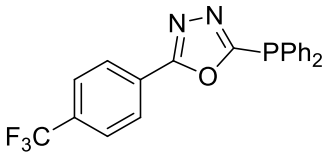
Green oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.62–7.58 (m, 1H), 7.44–7.38 (m, 6H), 7.37 (s, 1H), 7.32–7.28 (m, 2H), 6.86–6.83 (m, 1H), 2.98 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 167.7, 167.4 ($^{1}J_{C\text{-}P}$ = 32.0 Hz), 150.6, 134.0 ($^{2}J_{C\text{-}P}$ = 21.1 Hz), 132.2 ($^{1}J_{C\text{-}P}$ = 6.3 Hz), 130.1, 129.7, 128.9 ($^{3}J_{C\text{-}P}$ = 7.9 Hz), 124.3, 115.7, 115.0, 110.4, 40.4; ^{31}P NMR (243.9 MHz, $CDCl_3$) δ = –25.5; MS *m/z* (EI) (relative intensity, %): 373 (100, M^+), 374 (36), 146 (24), 145 (14); HRMS *m/z* (M^+) calcd for $C_{22}H_{21}ON_3P$: 374.1417, found: 374.1415; IR: 3439, 3055, 2915, 2808, 1604, 1546, 1495, 1437, 1360, 1231, 1184, 1091, 999, 962, 851, 784, 740, 693, 509, 465.

(4-Chloro)-2-phenyl-1,3,4-oxadiazolyldiphenylphosphine (184g)



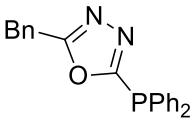
White solid, m.p. 116–117 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.95–7.90 (m, 2H), 7.62–7.54 (m, 4H), 7.45–7.36 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.1 (d, $^{1}J_{C\text{-}P}$ = 33.3 Hz), 166.2, 138.1, 134.0 (d, $^{2}J_{C\text{-}P}$ = 21.3 Hz), 131.8 ($^{1}J_{C\text{-}P}$ = 6.2 Hz), 130.2, 129.4, 129.0 ($^{3}J_{C\text{-}P}$ = 8.0 Hz), 128.5, 122.2; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –26.0; Anal. Calcd for $C_{20}H_{14}OClN_2P$ (364.76): C, 65.66; H, 3.95; N, 7.85; Found: C, 65.85; H, 3.87; N, 7.68; MS *m/z* (EI) (relative intensity, %): 364 (100, M^+), 365 (22), 366 (28), 183 (68), 154 (63), 150 (53), 91 (36), 77 (58); IR: 1603, 1475, 1433, 1401, 1089, 987, 955, 838, 741, 692.

(4-Trifluoromethyl)-2-phenyl-1,3,4-oxadiazolyldiphenylphosphine (184h)



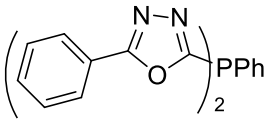
White solid, m.p. 104–105 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.15–8.10 (d, J = 8.2 Hz, 2H), 7.75–7.71 (d, J = 8.7 Hz, 2H), 7.62–7.56 (m, 4H), 7.46–7.38 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.8 (d, $^{1}J_{C\text{-}P}$ = 34.1 Hz), 165.8, 134.0 (d, $^{2}J_{C\text{-}P}$ = 21.3 Hz), 133.4 (q, $^{2}J_{C\text{-}F}$ = 32.8 Hz), 131.6 ($^{1}J_{C\text{-}P}$ = 6.1 Hz), 130.3, 129.0 ($^{3}J_{C\text{-}P}$ = 8.0 Hz), 127.5, 127.0, 126.1 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 123.5 (q, $^{1}J_{C\text{-}F}$ = 272.6 Hz); ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –24.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ = –63.1; Anal. Calcd for $C_{21}H_{14}F_3N_2OP$ (398.08): C, 63.32; H, 3.54; N, 7.03; Found: C, 63.47; H, 3.65; N, 7.09; MS *m/z* (EI) (relative intensity, %): 398 (100, M^+), 399 (22), 226 (16), 184 (27), 183 (65), 154 (62), 77 (36); IR: 3064, 1558, 1467, 1436, 1413, 1320, 1163, 1121, 1072, 1018, 848, 744, 693.

2-Benzyl-1,3,4-oxadiazolyldiphenylphosphine (184i)



Light green liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.51–7.44 (m, 4H), 7.42–7.31 (m, 6H), 7.29–7.19 (m, 5H), 4.18 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.4 ($^{1}J_{C\text{-}P}$ = 32.1 Hz), 167.7, 133.9 ($^{2}J_{C\text{-}P}$ = 21.2 Hz), 131.9 ($^{1}J_{C\text{-}P}$ = 6.4 Hz), 130.0, 128.9, 128.8 ($^{3}J_{C\text{-}P}$ = 7.9 Hz), 128.7, 127.4, 31.7; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –25.3; MS *m/z* (EI) (relative intensity, %): 344 (100, M^+), 345 (22), 184 (17), 183 (28), 154 (29), 150 (20), 91 (42); HRMS *m/z* (M^+) calcd for $C_{21}H_{17}ON_2NaP$: 367.0971, found: 367.0970; IR: 3446, 3059, 1961, 1564, 1481, 1433, 1313, 1124, 1020, 960, 745, 696, 569, 508.

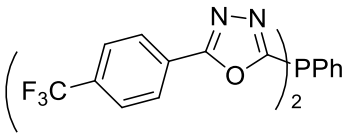
Di-(2-phenyl-1,3,4-oxadiazolyl)-phenylphosphine (185a)



White solid, m.p. 129–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.06–8.00 (m, 4H), 7.98–7.91 (m,

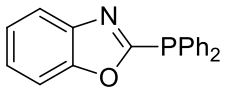
2H), 7.55–7.43 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.7, 163.5 ($^1J_{C\text{-}P}$ = 20.8 Hz), 135.5 ($^2J_{C\text{-}P}$ = 24.9 Hz), 132.3, 132.2, 129.4 ($^3J_{C\text{-}P}$ = 9.9 Hz), 129.1, 127.3, 125.7 ($^1J_{C\text{-}P}$ = 2.7 Hz), 123.3; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –52.5; Anal. Calcd for $C_{22}H_{15}O_2N_4P$ (398.35): C, 66.33; H, 3.80; N, 14.06; Found: C, 66.23; H, 3.80; N, 14.40; MS *m/z* (EI) (relative intensity, %): 398 (100, M^+), 399 (30), 150 (11), 145 (89), 105 (35), 77 (77); IR: 1605, 1546, 1448, 1334, 1159, 1065, 954, 780, 749, 688.

Di-[(4-trifluoromethyl)-2-phenyl-1,3,4-oxadiazolyl]-phenylphosphine (185b)



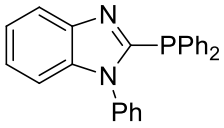
White solid, m.p. 192–194 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.20–8.16 (d, *J* = 8.4 Hz, 4H), 7.97–7.92 (m, 2H), 7.78–7.75 (d, *J* = 8.0 Hz, 4H), 7.62–7.58 (m, 1H), 7.55–7.52 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.6, 164.1 ($^1J_{C\text{-}P}$ = 21.3 Hz), 135.7 ($^2J_{C\text{-}P}$ = 25.2 Hz), 133.9 (q, $^2J_{C\text{-}F}$ = 33.0 Hz), 132.6, 129.6 ($^3J_{C\text{-}P}$ = 10.1 Hz), 127.7, 126.5, 126.2 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.2 (q, $^1J_{C\text{-}F}$ = 272.8 Hz), 124.9 ($^1J_{C\text{-}P}$ = 2.7 Hz); ^{31}P NMR (243.9 MHz, $CDCl_3$) δ = –51.5; ^{19}F NMR (564 MHz, $CDCl_3$) δ = –63.2; MS *m/z* (EI) (relative intensity, %): 534 (100, M^+), 535 (30), 320 (17), 213 (87), 173 (26), 145 (48); HRMS *m/z* (M^+) calcd for $C_{24}H_{13}O_2N_4F_6N_aP$: 557.0573, found: 557.0573; IR: 1738, 1557, 1416, 1322, 1256, 1116, 1077, 1016, 846, 752, 695.

Benzoxazolyldiphenylphosphine (187)



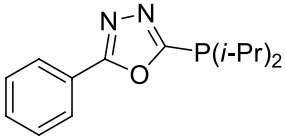
Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89–7.84 (d, *J* = 8.4 Hz, 1H), 7.50–7.46 (m, 4H), 7.44–7.40 (m, 1H), 7.42–7.36 (m, 6H), 7.33–7.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.3 ($^1J_{C\text{-}P}$ = 19.8 Hz), 152.3, 141.8, 134.2 ($^2J_{C\text{-}P}$ = 21.0 Hz), 132.9 ($^1J_{C\text{-}P}$ = 6.5 Hz), 129.9, 128.8 ($^3J_{C\text{-}P}$ = 7.9 Hz), 125.4, 124.3, 120.4, 110.8; ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –17.3 ppm; MS *m/z* (EI) (relative intensity, %): 303 (100, M^+), 304 (28), 302 (56), 185 (23), 183 (61); HRMS *m/z* (M^+) calcd for $C_{19}H_{15}ONP$: 304.0886, found: 304.0885; IR: 3439, 3057, 2921, 1587, 1482, 1442, 1383, 1332, 1239, 1116, 1086, 1000, 916, 798, 745, 695, 584, 502.

_N_-Phenylbenzoimidazolyldiphenylphosphine (189)



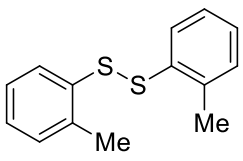
White solid, m.p. 164–165 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.78–7.73 (m, 1H), 7.62–7.54 (m, 4H), 7.44–7.40 (m, 3H), 7.35–7.26 (m, 7H), 7.24–7.14 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.7, 154.9 ($^{1}J_{C\text{-}P}$ = 11.1 Hz), 144.1, 137.7, 136.1, 134.3 ($^{2}J_{C\text{-}P}$ = 20.8 Hz), 129.3 ($^{1}J_{C\text{-}P}$ = 3.8 Hz), 128.8, 128.5 ($^{3}J_{C\text{-}P}$ = 7.8 Hz), 127.9, 123.5, 122.5, 120.4, 110.3; ^{31}P NMR (243.9 MHz, $CDCl_3$) δ = –24.5; Anal. Calcd for $C_{25}H_{19}N_2P$ (378.41): C, 79.35; H, 5.06; N, 7.40; P, 8.19; Found: C, 79.12; H, 5.43; N, 7.03; MS *m/z* (EI) (relative intensity, %): 378 (M^+), 379 (28), 377 (86), 302 (3), 301 (17), 300 (11), 183 (19); HRMS *m/z* (M^+) calcd for $C_{25}H_{20}N_2P$: 379.1359, found: 379.1357.

2-Phenyl-1,3,4-oxadiazolyldiisopropylphosphine (191)



Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.08–8.04 (m, 2H), 7.51–7.48 (m, 3H), 2.41–2.32 (m, 2H), 1.25–1.11 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.2 ($^{1}J_{C\text{-}P}$ = 43.7 Hz), 166.5, 131.7, 129.0, 127.0, 123.9, 23.1 ($^{1}J_{C\text{-}P}$ = 10.3 Hz), 19.5 (dd, $^{2}J_{C\text{-}P}$ = 4.4, 12.7 Hz); ^{31}P NMR (122.0 MHz, $CDCl_3$) δ = –4.2; MS *m/z* (EI) (relative intensity, %): 262 (85, M^+), 263 (74), 219 (100), 188 (44), 178 (37), 105 (47), 104 (33), 77 (39); HRMS *m/z* (M^+) calcd for $C_{14}H_{20}ON_2P$: 263.13078, found: 263.13071.

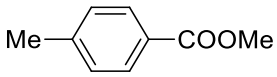
Bis(2-methylphenyl)disulfide (200)[209]



Prepared according the reported procedure.[170] Light yellow solid, yield 90%, m.p. 36–37 °C (lit.[209]

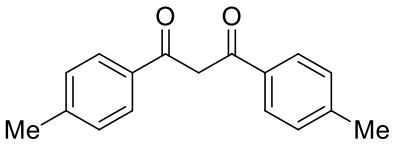
36–38 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.55–7.53 (m, 2H), 7.18–7.14 (m, 6H), 7.45 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.4, 135.4, 130.3, 128.6, 127.3, 126.7, 20.0; MS *m/z* (EI) (relative intensity, %): 246 (100, M^+), 247 (16), 123 (95), 77 (23).

Methyl 4-methylbenzoate (198b-2)[210]



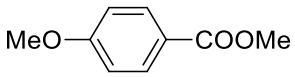
White solid, m.p. 34–35 °C (lit.[210] 35.5–36.0 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91–7.89 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 3.86 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.1, 143.4, 129.5, 129.0, 127.4, 51.8, 21.5; MS *m/z* (EI) (relative intensity, %): 150 (38, M^+), 151 (3), 119 (100), 92 (5), 91 (68), 90 (10), 89 (24), 77 (5), 65 (58), 63 (33), 62 (12), 51 (18), 50 (18), 47 (6).

1,3-di-*p*-Tolylpropane-1,3-dione (198b)[211]



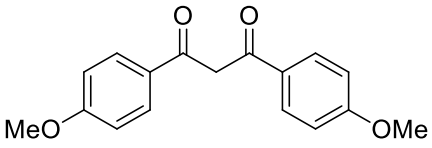
Yellow needles, m.p. 126–128 °C (lit.[211] 122 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 17.02 (bs, 0.9H), 7.89 (d, *J* = 8.4 Hz, 4H), 7.28 (d, *J* = 8.0 Hz, 4H), 6.81 (s, 1H), 4.56 (s, 0.1H), 2.42 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 185.5, 143.1, 132.9, 129.4, 127.2, 92.5, 21.6; MS *m/z* (EI) (relative intensity, %): 252 (100, M^+), 251 (92), 253 (36), 119 (40).

Methyl 4-methoxybenzoate (198c-2)[212]



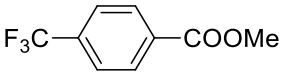
White solid, m.p. 46–47 °C (lit.[212] 47–48 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00–7.97 (m, 2H), 6.92–6.89 (m, 2H), 3.87 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.8, 163.3, 131.5, 122.6, 113.6, 55.4, 51.8; MS *m/z* (EI) (relative intensity, %): 166 (53, M^+), 135 (100), 77 (16).

1,3-Bis(4-methoxyphenyl)propan-1,3-dione (198c)[190]



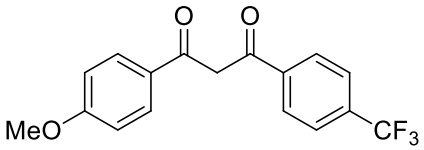
Yellow needles, m.p. 118–119 °C (lit.[190] 76 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 17.15 (bs, 0.8H), 7.95 (d, J = 8.8 Hz, 4H), 6.96 (d, J = 8.7 Hz, 4H), 6.72 (s, 1H), 4.52 (s, 0.2H), 3.87 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 184.6, 163.0, 131.3, 129.1, 128.2, 113.9, 91.5, 55.5; MS *m/z* (EI) (relative intensity, %): 284 (100, M^+), 285 (25), 283 (40), 177 (10), 136 (5), 135 (64), 109 (8), 108 (37), 78 (4), 77 (14), 69 (8).

Methyl 4-(trifluoromethyl)benzoate (198g-2)[213]



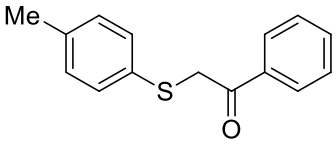
Colorless liquid, (lit.[213] 13–14 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.16–8.14 (m, 2H), 7.71–7.69 (m, 2H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.8, 134.4 ($J_{C\text{-}F}$ = 32.7 Hz), 133.3, 129.9, 125.3 (q, $J_{C\text{-}F}$ = 3.8 Hz), 123.6 ($J_{C\text{-}F}$ = 272.7 Hz), 52.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ = –63.2; MS *m/z* (EI): 204 (M^+).

1-(4-Methoxyphenyl)-3-(4-[trifluoromethyl)phenyl]propane-1,3-dione (198g)



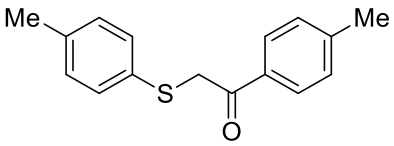
White solid**,** m.p. 121–122 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ = 17.16 (bs, 0.9H), 8.27 (d, J = 8.3 Hz, 2H), 8.13 (d, J = 8.9 Hz, 2H), 7.82 (d, J = 8.4 Hz, 2H), 7.28 (s, 1H), 7.04 (d, J = 8.9 Hz, 2H), 4.87 (s, 0.1H), 3.83 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ = 187.1, 180.5, 163.5, 138.2, 131.9 (q, $J_{C\text{-}F}$ = 32.0 Hz), 130.9, 130.0, 129.2, 127.8, 127.1, 125.5 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.8 (q, $J_{C\text{-}F}$ = 272.6 Hz), 114.1, 93.4, 55.5; ^{19}F NMR (564 MHz, DMSO-d_6) δ = –61.7; MS *m/z* (EI) (relative intensity, %): 322 (100, M^+), 323 (20), 321 (51), 108 (29).

1-Phenyl-2-(*p*-tolylthio)ethanone (199a)[214]



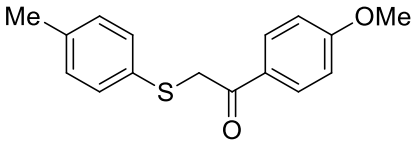
Yellow solid after recrystallization from ethanol, m.p. 38–39 °C (lit.[214] 38–39 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95–7.93 (m, 2H), 7.60–7.55 (m, 1H), 7.48–7.44 (m, 2H), 7.32–7.30 (m, 2H), 7.11–7.09 (m, 2H), 4.22 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.1, 137.5, 135.4, 133.4, 131.5, 130.9, 129.9, 128.7, 128.6, 41.8, 21.1; MS *m/z* (EI) (relative intensity, %): 242 (61, M^+), 137 (20), 105 (100), 77 (30); IR: 3437, 2919, 1679, 1596, 1492, 1447, 1385, 1276, 1197, 1011, 804, 748, 688, 497.

1-(*p*-Tolyl)-2-(*p*-tolylthio)ethanone (199b)



Yellow solid after recrystallization from ethanol, m.p. 55–56 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84–7.81 (m, 2H), 7.30–7.27 (m, 2H), 7.25–7.23 (m, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 4.18 (s, 2H), 2.40 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.9, 144.3, 137.4, 134.3, 131.4, 131.0, 129.8, 129.3, 128.8, 41.8, 21.7, 21.1; MS *m/z* (EI) (relative intensity, %): 256 (35, M^+), 119 (100), 91 (28), 65 (14); HRMS *m/z* (M^+) calcd for $C_{16}H_{16}ONaS$: 279.0814, found: 279.0814.

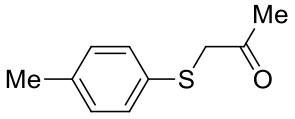
1-(4-Methoxyphenyl)-2-(*p*-tolylthio)ethanone (199c)



Yellow solid after recrystallization from ethanol, m.p. 55–56 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.93–7.92 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.93–6.92 (m, 2H), 4.17 (s, 2H), 3.87 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 192.8, 163.7, 137.3, 131.3, 131.1, 131.0, 129.8, 128.4, 113.8, 55.5, 41.6, 21.1; Anal. Calcd for $C_{16}H_{16}O_2S$ (272.36): C, 70.56; H, 5.92; Found: C, 70.42; H, 5.97; MS *m/z* (EI) (relative intensity, %): 272 (27, M^+), 135 (100), 77 (13);

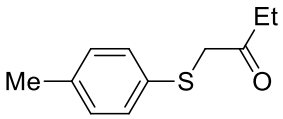
HRMS *m/z* (M^+) calcd for $C_{16}H_{16}O_2NaS$: 295.0763, found: 295.0763.

1-(*p*-Tolylthio)propan-2-one (199d)[215]



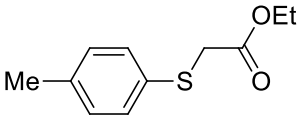
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25–7.22 (m, 2H), 7.10–7.07 (m, 2H), 3.59 (s, 2H), 2.29 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.6, 137.2, 130.8, 130.4, 129.9, 45.3, 27.9, 21.0; MS *m/z* (EI) (relative intensity, %): 180 (100, M^+), 181 (20), 138 (14), 137 (93), 91 (15), 45 (22); IR: 3440, 2921, 1710, 1493, 1355, 1230, 1149, 1013, 805, 496.

1-(*p*-Tolylthio)butan-2-one (199e)



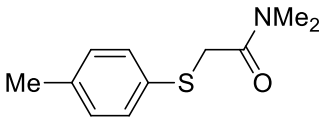
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25–7.23 (m, 2H), 7.09–7.07 (m, 2H), 3.60 (s, 2H), 2.58 (q, J = 7.3 Hz, 2H), 2.29 (s, 3 H), 3.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 206.3, 137.2, 131.0, 130.4, 129.9, 44.3, 33.9, 21.0, 7.8; MS *m/z* (EI) (relative intensity, %): 194 (97, M^+), 195 (15), 137 (100), 91 (22); HRMS *m/z* (M^+) calcd for $C_{11}H_{15}OS$: 195.0838, found: 195.0840.

Ethyl 2-(*p*-tolylthio)acetate (199f)[216]



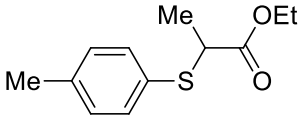
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34–7.32 (m, 2H), 7.11 (d, J = 7.9 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.58 (s, 2H), 2.32 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.8, 137.3, 131.1, 130.9, 129.8, 61.4, 37.4, 21.0, 14.1; MS *m/z* (EI) (relative intensity, %): 210 (96, M^+), 211 (25), 137 (100); IR: 2981, 1734, 1493, 1273, 1135, 1028, 806, 497.

***N,N*-Dimethyl-2-(*p*-tolylthio)acetamide (199g)[217]**



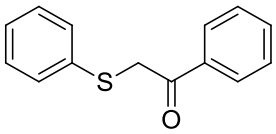
Colorless liquid (lit.[217] 45 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.34 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 7.9 Hz, 2H), 3.68 (s, 2H), 3.01 (s, 3H), 2.93 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 168.5, 137.2, 131.3, 131.1, 129.8, 37.8, 37.5, 35.8, 21.1; MS *m/z* (EI) (relative intensity, %): 209 (100, M^+), 210 (18), 137 (43), 86 (22), 72 (73); IR: 3485, 2925, 1647, 1493, 1451, 1396, 1264, 1198, 1122, 806, 495.

Ethyl 2-(*p*-tolylthio)propanoate (199h)



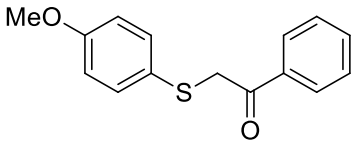
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37–7.34 (m, 2H), 7.13–7.11 (m, 2H), 4.14–4.09 (m, 2H), 3.71 (q, J = 7.13 Hz, 1H), 2.33 (s, 3H), 1.45 (d, J = 7.13 Hz, 3H), 1.19 (t, J = 7.13 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.6, 138.3, 133.8, 129.6, 129.3, 61.0, 45.6, 21.1, 17.3, 14.0; MS *m/z* (EI) (relative intensity, %): 224 (57, M^+), 151 (100), 123 (31), 91 (26); HRMS *m/z* (M^+) calcd for $C_{12}H_{16}O_2NaS$: 247.0763, found: 247.0765; IR: 2980, 2929, 1732, 1492, 1450, 1376, 1163, 1068, 809, 501.

1-Phenyl-2-(phenylthio)ethanone (199i)[214]



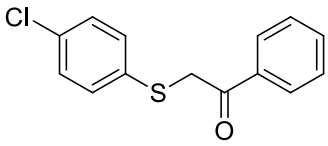
Yellow solid after recrystallization from ethanol, m.p. 49–50 °C (lit.[214] 52–53 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96–7.94 (m, 2H), 7.59–7.57 (m, 1H), 7.48–7.45 (m, 2H), 7.41–7.39 (m, 2H), 7.30–7.27 (m, 2H), 7.24–7.22 (m, 1H), 4.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.0, 135.4, 134.8, 133.9, 133.4, 130.5, 129.0, 128.7, 127.1, 41.2; MS *m/z* (EI) (relative intensity, %): 228 (46, M^+), 123 (12), 105 (100), 77 (62), 51 (53).

2-[(4-Methoxyphenyl)thio]-1-phenylethanone (199j)[218]



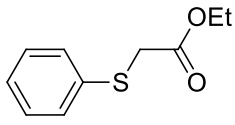
Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92–7.91 (m, 2H), 7.57–7.55 (m, 1H), 7.46–7.43 (m, 2H), 7.37–7.34 (m, 2H), 6.83–6.80 (m, 2H), 4.13 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.3, 159.7, 135.5, 134.6, 133.3, 128.7, 128.6, 124.6, 114.7, 55.3, 42.8; MS *m/z* (EI) (relative intensity, %): 258 (100, M^+), 259 (19), 153 (30), 105 (72).

2-[(4-chlorophenyl)thio]-1-phenylethanone (199k)[219]



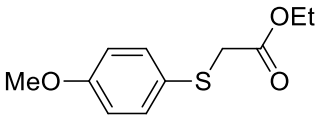
Yellow solid, m.p. 80–81 °C (lit.[219] 78–79 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.94 (d, *J* = 7.4 Hz, 2H), 7.60–7.58 (m, 1H), 7.49–7.46 (m, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 4.25 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 193.72, 135.21, 133.60, 133.21, 131.97, 129.20, 128.73, 128.65, 127.15, 41.21; MS *m/z* (EI) (relative intensity, %): 262 (39, M^+), 264 (15), 263 (9), 106 (8), 105 (100), 78 (2), 77 (20); IR: 3060, 2902, 2321, 2110, 1892, 1681, 1589, 1471, 1373, 1316, 1285, 1193, 1088, 986, 878, 813, 741, 685.

Ethyl 2-(phenylthio)acetate (199l)[182a]



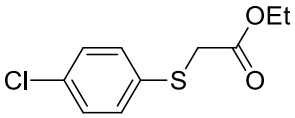
Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.42–7.40 (m, 2H), 7.31–7.29 (m, 2H), 7.24–7.21 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.63 (s, 2H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 169.7, 135.0, 130.0, 129.0, 126.9, 61.5, 36.7, 14.1; MS *m/z* (EI) (relative intensity, %): 196 (93, M^+), 123 (100), 109 (13).

Ethyl 2-[(4-methoxyphenyl)thio]acetate (199m)



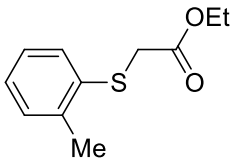
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43–7.39 (m, 2H), 6.85–6.81 (m, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.50 (s, 2H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.9, 159.6, 134.2, 124.9, 114.8, 61.3, 55.3, 38.6, 14.1; MS *m/z* (EI) (relative intensity, %): 226 (100, M^+), 153 (67), 139 (43), 109 (36); IR: 2980, 1733, 1592, 1493, 1283, 1172, 1134, 1029, 827, 523.

Ethyl 2-[(4-chlorophenyl)thio]acetate (199n)[220]



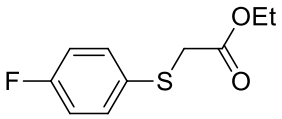
Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.35–7.33 (m, 2H), 7.27–7.25 (m, 2H), 4.16 (q, J = 7.2 Hz, 2H), 3.59 (s, 2H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 169.4, 133.4, 133.1, 131.4, 129.1, 61.6, 36.8, 14.1; MS *m/z* (EI) (relative intensity, %): 230 (63, M^+), 157 (100), 108 (39); IR: 1448, 2983, 1734, 1477, 1388, 1280, 1140, 1097, 1023, 817, 492.

Ethyl 2-(*o*-tolylthio)acetate (199o)



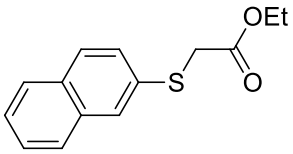
Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37–7.35 (m, 1H), 7.19–7.13 (m, 3H), 4.16 (q, J = 7.1 Hz, 2H), 3.61 (s, 2H), 2.42 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.6, 138.3, 134.1, 130.2, 129.5, 126.8, 126.6, 61.5, 35.9, 20.3, 14.0; MS *m/z* (EI) (relative intensity, %): 210 (99, M^+), 164 (38), 137 (100), 91 (28); IR: 3448, 2981, 1735, 1588, 1465, 1383, 1276, 1137, 1030, 749.

Ethyl 2-[(4-fluorophenyl)thio]acetate (199p)[220]



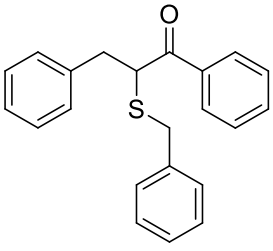
Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.45–7.43 (m, 2H), 7.02–6.99 (m, 2H), 4.15 (q, J = 7.2 Hz, 2H), 3.56 (s, 2H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.6, 162.4 ($J_{C\text{-}F}$ = 248.0 Hz), 133.4 ($J_{C\text{-}F}$ = 8.1 Hz), 129.7 ($J_{C\text{-}F}$ = 3.4 Hz), 116.1 ($J_{C\text{-}F}$ = 21.8 Hz), 61.5, 37.8, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ = –114.02; MS *m/z* (EI) (relative intensity, %): 214 (100, M^+), 215 (30), 141 (100), 127 (25), 83 (24), 45 (44); IR: 3449, 2983, 1734, 1589, 1490, 1398, 1278, 1226, 1151, 1027, 828, 628, 512.

Ethyl 2-(naphthalen-2-ylthio)acetate (199q)



Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.86 (s, 1H), 7.80–7.75 (m, 3H), 7.50–7.44 (m, 3H), 4.18 (q, J = 7.1 Hz, 2H), 3.74 (s, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 169.6, 133.7, 132.4, 132.1, 128.6, 128.2, 127.7, 127.6, 127.3, 126.6, 126.1, 61.6, 36.6, 14.1; MS *m/z* (EI) (relative intensity, %): 246 (100, M^+), 247 (40), 173 (73), 159 (31), 129 (57), 115 (68); HRMS *m/z* (M^+) calcd for $C_{14}H_{14}O_2NaS$: 269.0607, found: 269.0608; IR: 3053, 2982, 1733, 1587, 1372, 1278, 1136, 1027, 851, 813, 747, 474.

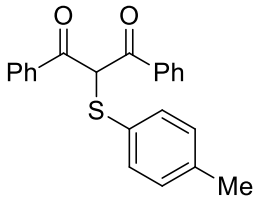
2-(Benzylthio)-1,3-diphenylpropan-1-one (202)



White solid after recrystallization from ethanol, m.p. 71–72 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ =

7.86–7.84 (m, 2H), 7.54–7.51 (m, 1H), 7.42–7.38 (m, 4H), 7.32–7.30 (m, 2H), 7.28–7.25 (m, 2H), 7.24–7.20 (m, 4H), 4.47–4.45 (m, 1H), 3.58–3.45 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 196.7, 141.7, 137.8, 136.7, 133.1, 128.9, 128.5, 128.5, 128.4, 128.0, 127.3, 127.0, 45.2, 44.1, 35.9; Anal. Calcd for $C_{22}H_{20}OS$ (332.46): C, 79.48; H, 6.06; Found: C, 79.12; H, 6.21; MS *m/z* (EI) (relative intensity, %): 332 (17, M^+), 241 (27), 210 (19), 105 (100), 77 (19); HRMS *m/z* (M^+) calcd for $C_{22}H_{20}ONaS$: 355.1127, found: 355.1127; IR: 3451, 3357, 3060, 3029, 2916, 1957, 1685, 1595, 1492, 1449, 1333, 1228, 1073, 982, 916, 752, 697, 544.

1,3-Diphenyl-2-(*p*-tolylthio)propane-1,3-dione (208)



Yellow solid, m.p. 88–89 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.97–7.94 (m, 4H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.42-7.38 (m, 4H), 7.36–7.32 (m, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 6.02–6.01 (m, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 191.8, 139.1, 135.2, 134.3, 133.7, 130.0, 129.1, 128.7, 128.7, 65.1, 21.2; Anal. Calcd for $C_{22}H_{18}O_2S$ (346.44): C, 76.27; H, 5.24; Found: C, 75.87; H, 5.09; MS *m/z* (EI) (relative intensity, %): 346 (66, M^+), 347 (20), 223 (56), 105 (100), 77 (39); IR: 3036, 2322, 1906, 1664, 1591, 1489, 1446, 1315, 1254, 1179, 1102, 997, 933, 869, 802, 756, 685.

References

[1] a) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381; b) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792; c) J. A. Ashenhurst, *Chem. Soc. Rev.* **2010**, *39*, 540; d) R. Chinchilla, C. Najera, *Chem. Rev.* **2007**, *107*, 874; e) K. M. Gligorich, M. S. Sigman, *Chem. Commun.* **2009**, 3854; f) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780; g) M. J. Schultz, M. S. Sigman, *Tetrahedron* **2006**, *62*, 8227; h) N. Yoshikai, E. Nakamura, *Chem. Rev.* **2012**, *112*, 2339.

[2] a) K. A. Horn, *Chem. Rev.* **1995**, *95*, 1317; b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; c) R. Zimmer, C. U. Dinesh, E. Nandanan, F. A. Khan, *Chem. Rev.* **2000**, *100*, 3067; d) E. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979; e) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644; f) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; g) R. I. McDonald, G. S. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981; h) X.-F. Wu, H. Neumann, M. Beller, *Chem. Rev.* **2013**, *113*, 1; i) H. F. Sore, W. R. J. D. Galloway, D. R. Spring, *Chem. Soc. Rev.* **2012**, *41*, 1845; j) Q.-A. Chen, Z.-S. Ye, Y. Duan, Y.-G. Zhou, *Chem. Soc. Rev.* **2013**, *42*, 497.

[3] a) V. B. Phapale, D. J. Cardenas, *Chem. Soc. Rev.* **2009**, *38*, 1598; b) J. Yamaguchi, K. Muto, K. Itami, *Eur. J. Org. Chem.* **2013**, 19.

[4] a) L. M. Stanley, M. P. Sibi, *Chem. Rev.* **2008**, *108*, 2887; b) A. Alexakis, J. E. Backvall, N. Krause, O. Pamies, M. Dieguez, *Chem. Rev.* **2008**, *108*, 2796; c) K. Yamada, K. Tomioka, *Chem. Rev.* **2008**, *108*, 2874; d) S. Reymond, J. Cossy, *Chem. Rev.* **2008**, *108*, 5359; e) T. Jerphagnon, M. G. Pizzuti, A. J. Minnaard, B. L. Feringa, *Chem. Soc. Rev.* **2009**, *38*, 1039; f) J. E. Hein, V. V. Fokin, *Chem. Soc. Rev.* **2010**, *39*, 1302; g) C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3464; h) I. P. Beletskaya, A. V. Cheprakov, *Coord. Chem. Rev.* **2004**, *248*, 2337; i) S. E. Allen, R. R. Walvoord, R. Padilla-Salinas, M. C. Kozlowski, *Chem. Rev.* **2013**, *113*, 6234; For an example on copper-catalyzed enantioselective synthesis of dihydropyrazoles by cycloaddition, see: J.-R. Chen, W.-R. Dong, M. Candy, F.-F. Pan, M. Jörres, C. Bolm, *J. Am. Chem. Soc.* **2012**, *134*, 6924.

[5] a) F. Hebrard, P. Kalck, *Chem. Rev.* **2009**, *109*, 4272; b) G. Cahiez, A. Moyeux, *Chem. Rev.* **2010**, *110*, 1435; c) G. Pattenden, *Chem. Soc. Rev.* 1988, *17*, 361; d) X.-B. Lu, D. J. Darensbourg, *Chem. Soc. Rev.* **2012**, *41*, 1462; e) C. Gosmini, J. M. Begouin, A. Moncomble, *Chem. Commun.* **2008**, 3221.

[6] a) A. Correa, O. G. Mancheno, C. Bolm, *Chem. Soc. Rev.* **2008**, *37*, 1108; b) A. A. O. Sarhan, C. Bolm, *Chem. Soc. Rev.* **2009**, *38*, 2730; c) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217; d) C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Rev.* **2011**, *111*, 1293.

[7] a) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180; b) B. K. Min, C. M. Friend, *Chem. Rev.* **2007**, *107*, 2709; c) Z. Li, C. Brouwer, C. He, *Chem. Rev.* **2008**, *108*, 3239; d) N. Krause, C. Winter, *Chem. Rev.* **2011**, *111*, 1994; e) A. Corma, A. Leyva-Perez, M. J. Sabater, *Chem. Rev.* **2011**, *111*, 1657; f) Y. Zhang, X. Cui, F. Shi, Y. Deng, *Chem. Rev.* **2012**, *112*, 2467; g) M. Stratakis, H. Garcia, *Chem. Rev.* **2012**, *112*, 4469; h) M. Bandini, *Chem. Soc. Rev.* **2011**, *40*, 1358; i) B.-L. Lu, L. Dai, M. Shi, *Chem. Soc. Rev.* **2012**, *41*, 3318; j) L. T. Ball, G. C. Lloyd-Jones, C. A. Russell, *Science* **2012**, *337*, 1644.

[8] a) P. Saisaha, J. W. de Boer, W. R. Browne, *Chem. Soc. Rev.* **2013**, *42*, 2059; b) B. Zhou, H. Chen, C. Wang, *J. Am. Chem. Soc.* **2013**, *135*, 1264.

[9] a) K. Fagnou, M. Lautens, *Chem. Rev.* **2003**, *103*, 169; b) T. Hayashi, K. Yamasaki, *Chem. Rev.* **2003**, *103*, 2829; c) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; d) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651; e) P. Etayo, A. Vidal-Ferran, *Chem. Soc. Rev.* **2013**, *42*, 728.

[10] a) G. Maas, *Chem. Soc. Rev.* **2004**, *33*, 183; b) S. I. Murahashi, D. Zhang, *Chem. Soc. Rev.* **2008**, *37*, 1490; c) T. Naota, H. Takaya, S. I. Murahashi, *Chem. Rev.* **1998**, *98*, 2599; d) B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067; e) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879; f) P. Zhao, F. Wang, K. L. Han, X. Li, *Org. Lett.* **2012**, *14*, 5506.

[11] a) C. Zhu, J. R. Falck, *Angew. Chem. Int. Ed.* **2011**, *50*, 6626; b) Y. Wei, N. Yoshikai, *Org. Lett.* **2011**, *13*, 5504; c) Y. Chen, F. Wang, A. Jia, X. Li, *Chem. Sci.* **2012**, *3*, 3231; d) A. Hajra, Y. Wei, N. Yoshikai, *Org. Lett.* **2012**, *14*, 5488; e) Y. Wei, I. Deb, N. Yoshikai, *J. Am. Chem. Soc.* **2012**, *134*, 9098; f) X. Jie, Y. Shang, P. Hu, W. Su, *Angew. Chem. Int. Ed.* **2013**, *52*, 3630; g) Y. Shang, X. Jie, J. Zhou, P. Hu, S. Huang, W. Su, *Angew. Chem. Int. Ed.* **2013**, *52*, 1299; h) B. Xiao, Z.-J. Liu, L. Liu, Y. Fu, *J. Am. Chem. Soc.* **2013**, *135*, 616; i) D. Yu, L. Lu, Q. Shen, *Org. Lett.* **2013**, *15*, 940.

[12] a) W.-W. Chan, S.-F. Lo, Z. Zhou, W.-Y. Yu, *J. Am. Chem. Soc.* **2012**, *134*, 13565; b) P. Zhao, F. Wang, K. Han, X. Li, *Org. Lett.* **2012**, *14*, 3400; c) C. Zhu, J. R. Falck, *Chem. Commun.* **2012**, *48*, 1674; d) Y. Chen, F. Wang, W. Zhen, X. Li, *Adv. Synth. Catal.* **2013**, *355*, 353; e) X. Li, S. Yu, F. Wang, B. Wan, X. Yu, *Angew. Chem. Int. Ed.* **2013**, *52*, 2577; f) F. Pan, Z.-Q. Lei, H. Wang, H. Li, J. Sun, Z.-J. Shi, *Angew. Chem. Int. Ed.* **2013**, *52*, 2063.

[13] a) B. Li, H. Feng, S. Xu, B. Wang, *Chem. Eur. J.* **2011**, *17*, 12573; b) L. Ackermann, S. I. Kozhushkov, D. S. Yufit, *Chem. Eur. J.* **2012**, *18*, 12068; c) L. Ackermann, L. H. Wang, A. V. Lygin, *Chem. Sci.* **2012**, *3*, 177; d) L. Ackermann, L. Wang, R. Wolfram, A. V. Lygin, *Org. Lett.* **2012**, *14*, 728; e) Y. Imazaki, E. Shirakawa, R. Ueno, T. Hayashi, *J. Am. Chem. Soc.* **2012**, *134*, 14760; f) B. Li, J. Ma, N. Wang, H. Feng, S. Xu, B. Wang, *Org. Lett.* **2012**, *14*, 736; g) K. Parthasarathy, N. Senthilkumar, J. Jayakumar, C.-H. Cheng, *Org. Lett.* **2012**, *14*, 3478; h) Y. Aihara, N. Chatani, *Chem. Sci.* **2013**, *4*, 664; i) P. B. Arockiam, C. Fischmeister, C. Bruneau, P. H. Dixneuf, *Green Chem.* **2013**, *15*, 67; j) F. Yang, L. Ackermann, *Org. Lett.* **2013**, *15*, 718.

[14] J. Legros, C. Bolm, *Angew. Chem. Int. Ed.* **2003**, *42*, 5487.

[15] A. Korte, J. Legros, C. Bolm, *Synlett* **2004**, 2397.

[16] V. Lecomte, C. Bolm, *Adv. Synth. Catal.* **2005**, *347*, 1666.

[17] a) C. Pavan, J. Legros, C. Bolm, *Adv. Synth. Catal.* **2005**, *347*, 703; b) M. Nakanishi, C. Bolm, *Adv. Synth. Catal.* **2007**, *349*, 861.

[18] a) O. G. Mancheno, C. Bolm, *Org. Lett.* **2006**, *8*, 2349; b) O. G. Mancheno, C. Bolm, *Chem. Eur. J.* **2007**, *13*, 6674; c) O. G. Mancheno, J. Dallimore, A. Plant, C. Bolm, *Org. Lett.* **2009**, *11*, 2429; d) O. G. Mancheno, J. Dallimore, A. Plant, C. Bolm, *Adv. Synth. Catal.* **2010**, *352*, 309.

[19] A. Correa, C. Bolm, *Adv. Synth. Catal.* **2008**, *350*, 391.

[20] a) A. Correa, C. Bolm, *Angew. Chem. Int. Ed.* **2007**, *46*, 8862; b) A. Correa, S. Elmore, C. Bolm, *Chem. Eur. J.* **2008**, *14*, 3527; c) O. Bistri, A. Correa, C. Bolm, *Angew. Chem. Int. Ed.* **2008**, *47*, 586; d) A. Correa, M. Carril, C. Bolm, *Angew. Chem. Int. Ed.* **2008**, *47*, 2880.

[21] a) M. Nakanishi, A. F. Salit, C. Bolm, *Adv. Synth. Catal.* **2008**, *350*, 1835; b) A. C. Mayer, A. F. Salit, C. Bolm, *Chem. Commun.* **2008**, 5975; c) J. Bonnamour, C. Bolm, *Org. Lett.* **2008**, *10*, 2665; d) J. Bonnamour, C. Bolm, *Org. Lett.* **2011**, *13*, 2012.

[22] a) C. Qin, N. Jiao, *J. Am. Chem. Soc.* **2010**, *132*, 15893; b) C. Qin, W. Zhou, F. Chen, Y. Ou, N. Jiao, *Angew. Chem. Int. Ed.* **2011**, *50*, 12595; c) T. Wang, S.-K. Xiang, C. Qin, J.-A. Ma, L.-H. Zhang, N. Jiao, *Tetrahedron Lett.* **2011**, *52*, 3208; d) T. Wang, W. Zhou, H. Yin, J.-A. Ma, N. Jiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 10823.

[23] a) Z. Li, R. Yu, H. Li, *Angew. Chem. Int. Ed.* **2008**, *47*, 7497; b) H. Li, W. Li, Z. Li, *Chem. Commun.* **2009**, 3264; c) H. Li, Z. He, X. Guo, W. Li, X. Zhao, Z. Li, *Org. Lett.* **2009**, *11*, 4176; d) X. Guo, R. Yu, H. Li, Z. Li, *J. Am. Chem. Soc.* **2009**, *131*, 17387; e) S. Pan, J. Liu, H. Li, Z. Wang, X. Guo, Z. Li, *Org. Lett.* **2010**, *12*, 1932; f) H. Li, W. Li, W. Liu, Z. He, Z. Li, *Angew. Chem. Int. Ed.* **2011**, *50*, 2975; g) W. Liu, Y. Li, K. Liu, Z. Li, *J. Am. Chem. Soc.* **2011**, *133*, 10756; h) W. Liu, J. Liu, D. Ogawa, Y. Nishihara, X. Guo, Z. Li, *Org. Lett.* **2011**, *13*, 6272; i) Y. Li, F. Jia, Z. Li, *Chem. Eur. J.* **2013**, *19*, 82; j) W. Li, X. Zheng, Z. Li, *Adv. Synth. Catal.* **2013**, *355*, 181.

[24] a) P. P. Singh, S. Gudup, S. Ambala, U. Singh, S. Dadhwal, B. Singh, S. D. Sawant, R. A. Vishwakarma, *Chem. Commun.* **2011**, *47*, 5852; b) P. P. Singh, S. Gudup, H. Aruri, U. Singh, S. Ambala, M. Yadav, S. D. Sawant, R. A. Vishwakarma, *Org. Biomol. Chem.* **2012**, *10*, 1587; c) P. P. Singh, S. K. Aithagani, M. Yadav, V. P. Singh, R. A. Vishwakarma, *J. Org. Chem.* **2013**, *78*, 2639.

[25] L. Adak, W. C. Chan, N. Yoshikai, *Chem. Asian J.* **2011**, *6*, 359.

[26] H. Shiota, Y. Ano, Y. Aihara, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 14952.

[27] T. Yamamoto, K. Muto, M. Komiyama, J. Canivet, J. Yamaguchi, K. Itami, *Chem. Eur. J.* **2011**, *17*, 10113.

[28] K. Amaike, K. Muto, J. Yamaguchi, K. Itami, *J. Am. Chem. Soc.* **2012**, *134*, 13573.

[29] K. Muto, J. Yamaguchi, K. Itami, *J. Am. Chem. Soc.* **2012**, *134*, 169.

[30] A. Correa, J. Cornella, R. Martin, *Angew. Chem. Int. Ed.* **2013**, *52*, 1878.

[31] A. Ghaderi, T. Iwasaki, A. Fukuoka, J. Terao, N. Kambe, *Chem. Eur. J.* **2013**, *19*, 2951.

[32] a) K. Gao, P. S. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc.* **2010**, *132*, 12249; b) Z. Ding, N. Yoshikai, *Org. Lett.* **2010**, *12*, 4180; c) Z. Ding, N. Yoshikai, *Synthesis* **2011**, 2561; d) P. S. Lee, T. Fujita, N. Yoshikai, *J. Am. Chem. Soc.* **2011**, *133*, 17283; e) T. Yamakawa, N. Yoshikai, *Org. Lett.* **2013**, *15*, 196.

[33] a) K. Gao, N. Yoshikai, *J. Am. Chem. Soc.* **2011**, *133*, 400; b) K. Gao, N. Yoshikai, *Angew. Chem. Int. Ed.* **2011**, *50*, 6888; c) P. S. Lee, N. Yoshikai, *Angew. Chem. Int. Ed.* **2013**, *52*, 1240.

[34] K. Gao, P. S. Lee, C. Long, N. Yoshikai, *Org. Lett.* **2012**, *14*, 4234.

[35] a) T. Sawano, A. Ashouri, T. Nishimura, T. Hayashi, *J. Am. Chem. Soc.* **2012**, *134*, 18936; b) T. Nishimura, T. Sawano, K. Y. Ou, T. Hayashi, *Chem. Commun.* **2011**, *47*, 10142; c) T. Sawano, K. Ou, T. Nishimura, T. Hayashi, *Chem. Commun.* **2012**, *48*, 6106; d) T. Tachinami, T. Nishimura, R. Ushimaru, R. Noyori, H. Naka, *J. Am. Chem. Soc.* **2013**, *135*, 50.

[36] W. Song, L. Ackermann, *Angew. Chem. Int. Ed.* **2012**, *51*, 8251.

[37] Q. Jiang, W. Sheng, M. Tian, J. Tang, C. Guo, *Eur. J. Org. Chem.* **2013**, 1861.

[38] J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359.

[39] a) R. G. Bergman, *Science* **1984**, *223*, 902; b) R. H. Crabtree, *Chem. Rev.* **1985**, *85*, 245.

[40] Y. Taniguchi, S. Horie, K. Takaki, Y. Fujiwara, *J. Organomet. Chem.* **1995**, *504*, 137.

[41] H.-F. He, Z.-J. Wang, W. Bao, *Adv. Synth. Catal.* **2010**, *352*, 2905.

[42] Y. Wei, H. Zhao, J. Kan, W. Su, M. Hong, *J. Am. Chem. Soc.* **2010**, *132*, 2522.

[43] H. Q. Do, O. Daugulis, *J. Am. Chem. Soc.* **2011**, *133*, 13577.

[44] M. Kitahara, N. Umeda, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2011**, *133*, 2160.

[45] G. S. Kumar, C. U. Maheswari, R. A. Kumar, M. L. Kantam, K. R. Reddy, *Angew. Chem. Int. Ed.* **2011**, *50*, 11748.

[46] J. Li, S. Bénard, L. Neuville, J. Zhu, *Org. Lett.* **2012**, *14*, 5980.

[47] a) V. G. Zaitsev, D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2005**, *127*, 13154; b) D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2010**, *132*, 3965.

[48] S.-Y. Zhang, G. He, W. A. Nack, Y. Zhao, Q. Li, G. Chen, *J. Am. Chem. Soc.* **2013**, *135*, 2124.

[49] Y. Ano, M. Tobisu, N. Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 12984.

[50] L. D. Tran, I. Popov, O. Daugulis, *J. Am. Chem. Soc.* **2012**, *134*, 18237.

[51] S.-Y. Zhang, G. He, Y. Zhao, K. Wright, W. A. Nack, G. Chen, *J. Am. Chem. Soc.* **2012**, *134*, 7313.

[52] a) M. Iwasaki, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2007**, *129*, 4463; b) W. Zhou, H. Li, L. Wang, *Org. Lett.* **2012**, *14*, 4594; c) Y. Zhang, M. Wang, P. Li, L. Wang, *Org. Lett.* **2012**, *14*, 2206; d) P. Zhao, C. D. Incarvito, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 3124; e) R. M. Cicchillo, H. Zhang, J. A. V. Blodgett, J. T. Whitteck, G. Li, S. K. Nair, W. A. van der Donk, W. W. Metcalf, *Nature* **2009**, *459*, 871.

[53] T. Sugiishi, A. Kimura, H. Nakamura, *J. Am. Chem. Soc.* **2010**, *132*, 5332.

[54] C. A. He, S. Guo, L. Huang, A. Lei, *J. Am. Chem. Soc.* **2010**, *132*, 8273.

[55] W. Zhou, Y. Yang, Y. Liu, G.-J. Deng, *Green Chem.* **2013**, *15*, 76.

[56] G. Evano, M. Toumi, A. Coste, *Chem. Commun.* **2009**, 4166.

[57] R. Bernini, S. Cacchi, G. Fabrizi, E. Filisti, A. Sferrazza, *Synlett* **2009**, 1480.

[58] M. Nishino, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 6447.

[59] B.-X. Tang, R.-J. Song, C.-Y. Wu, Y. Liu, M.-B. Zhou, W.-T. Wei, G.-B. Deng, D.-L. Yin,

J.-H. Li, *J. Am. Chem. Soc.* **2010**, *132*, 8900.

[60] Z.-Q. Wang, W.-W. Zhang, L.-B. Gong, R.-Y. Tang, X.-H. Yang, Y. Liu, J.-H. Li, *Angew. Chem. Int. Ed.* **2011**, *50*, 8968.

[61] G. Zhang, J. Miao, Y. Zhao, H. Ge, *Angew. Chem. Int. Ed.* **2012**, *51*, 8318.

[62] K. Kubota, E. Yamamoto, H. Ito, *J. Am. Chem. Soc.* **2013**, *135*, 2635.

[63] L. Huang, H. Jiang, C. Qi, X. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 17652.

[64] C. Wan, J. Zhang, S. Wang, J. Fan, Z. Wang, *Org. Lett.* **2010**, *12*, 2338.

[65] M. Jithunsa, M. Ueda, O. Miyata, *Org. Lett.* **2011**, *13*, 518.

[66] C. W. Cheung, S. L. Buchwald, *J. Org. Chem.* **2012**, *77*, 7526.

[67] Y. Li, Z. Li, T. Xiong, Q. Zhang, X. Zhang, *Org. Lett.* **2012**, *14*, 3522.

[68] A. E. Wendlandt, S. S. Stahl, *Org. Biomol. Chem.* **2012**, *10*, 3866.

[69] S. Ueda, H. Nagasawa, *J. Am. Chem. Soc.* **2009**, *131*, 15080.

[70] X. Lv, W. Bao, *J. Org. Chem.* **2009**, *74*, 5618.

[71] Y. Ohta, H. Chiba, S. Oishi, N. Fujii, H. Ohno, *J. Org. Chem.* **2009**, *74*, 7052.

[72] J. Barluenga, G. Lonzi, L. Riesgo, L. A. López, M. Tomás, *J. Am. Chem. Soc.* **2010**, *132*, 13200.

[73] G. Zhang, Y. Zhao, H. Ge, *Angew. Chem. Int. Ed.* **2013**, *52*, 2559.

[74] A. L. Stein, D. Alves, J. T. da Rocha, C. W. Nogueira, G. Zeni, *Org. Lett.* **2008**, *10*, 4983.

[75] E. A. Jaseer, D. J. C. Prasad, A. Dandapat, G. Sekar, *Tetrahedron Lett.* **2010**, *51*, 5009.

[76] Z. Xia, K. Wang, J. Zheng, Z. Ma, Z. Jiang, X. Wang, X. Lv, *Org. Biomol. Chem.* **2012**, *10*, 1602.

[77] a) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; b) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; c) P. Jeschke, *ChemBioChem* **2004**, *5*, 570.

[78] M. H. Hung, W. B. Farnham, A. E. Feiring, S. Rozen, in Fluoropolymers: Synthesis Vol. 1 (eds G. Hougham, P. E. Cassidy, K. Johns, T. Davidson) 51–66 (Plenum, **1999**).

[79] a) K. L. Kirk, *Org. Process Res. Dev.* **2008**, *12*, 305; b) T. Furuya, C. A. Kuttruff, T. Ritter, *Curr. Opin. Drug Disc.* **2008**, *11*, 803; c) V. V. Grushin, *Acc. Chem. Res.* **2010**, *43*, 160; d) T. Furuya, J. E. M. N. Klein, T. Ritter, *Synthesis* **2010**, 1804.

[80] W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359.

[81] P. Kirsch, Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications (Wiley, **2004**).

[82] T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470.

[83] D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224.

[84] J.-A. Ma, D. Cahard, *Tetrahedron: Asymmetry* **2004**, *15*, 1007.

[85] P. S. Fier, J. F. Hartwig, *J. Am. Chem. Soc.* **2012**, *134*, 10795.

[86] P. S. Fier, J. W. Luo, J. F. Hartwig, *J. Am. Chem. Soc.* **2013**, *135*, 2552.

[87] Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2013**, *135*, 4648.

[88] A. Narayama, K. Shibatomi, Y. Soga, T. Muto, S. Iwasa, *Synlett* **2013**, 375.

[89] I. Ruppert, K. Schlich, W. Volbach, *Tetrahedron Lett.* **1984**, *25*, 2195.

[90] L. Chu, F.-L. Qing, *J. Am. Chem. Soc.* **2010**, *132*, 7262.

[91] a) X. Jiang, L. Chu, F.-L. Qing, *J. Org. Chem.* **2012**, *77*, 1251; b) K. Zhang, X.-L. Qiu, Y. Huang, F.-L. Qing, *Eur. J. Org. Chem.* **2012**, 58.

[92] L. Chu, F.-L. Qing, *Org. Lett.* **2010**, *12*, 5060.

[93] T. D. Senecal, A. T. Parsons, S. L. Buchwald, *J. Org. Chem.* **2011**, *76*, 1174.

[94] L. Chu, F.-L. Qing, *Org. Lett.* **2012**, *14*, 2106.

[95] L. Chu, F.-L. Qing, *J. Am. Chem. Soc.* **2012**, *134*, 1298.

[96] L. Chu, F.-L. Qing, *Synthesis* **2012**, *44*, 1521.

[97] Y. Miyake, S. Ota, Y. Nishibayashi, *Chem. Eur. J.* **2012**, *18*, 13255.

[98] M. Hu, C. Ni, J. Hu, *J. Am. Chem. Soc.* **2012**, *134*, 15257.

[99] J. Xu, B. Xiao, C.-Q. Xie, D.-F. Luo, L. Liu, Y. Fu, *Angew. Chem. Int. Ed.* **2012**, *51*, 12551.

[100] R. Shimizu, H. Egami, T. Nagi, J. Chae, Y. Hamashima, M. Sodeoka, *Tetrahedron Lett.* **2010**, *51*, 5947.

[101] X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*, 16410.

[102] A. T. Parsons, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2011**, *50*, 9120.

[103] T. Liu, Q. Shen, *Org. Lett.* **2011**, *13*, 2342.

[104] Y. Huang, X. Fang, X. Lin, H. Li, W. He, K.-W. Huang, Y. Yuan, Z. Weng, *Tetrahedron* **2012**, *68*, 9949.

[105] C. Feng, T. P. Loh, *Chem. Sci.***2012**, *3*, 3458.

[106] S. Mizuta, O. Galicia-Lopez, K. M. Engle, S. Verhoog, K. Wheelhouse, G. Rassias, V. Gouverneur, *Chem. Eur. J.* **2012**, *18*, 8583.

[107] Q.-H. Deng, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* **2012**, *134*, 10769.

[108] P. G. Janson, I. Ghoneim, N. O. Ilchenko, K. J. Szabo, *Org. Lett.* **2012**, *14*, 2882.

[109] a) Z. Weng, H. Li, W. He, L.-F. Yao, J. Tan, J. Chen, Y. Yuan, K.-W. Huang, *Tetrahedron* **2012**, *68*, 2527; b) H. Zheng, Y. Huang, Z. Wang, H. Li, K.-W. Huang, Y. Yuan, Z. Weng, *Tetrahedron Lett.* **2012**, *53*, 6646.

[110] X. Lin, G. Wang, H. Li, Y. Huang, W. He, D. Ye, K.-W. Huang, Y. Yuan, Z. Weng, *Tetrahedron* **2013**, *69*, 2628.

[111] a) T. Umemoto, S. Ishihara, *Tetrahedron Lett.* **1990**, *31*, 3579; b) T. Umemoto, S. Ishihara, *J.*

Am. Chem. Soc. **1993**, *115*, 2156.

[112] H. Li, *Synlett* **2012**, *23*, 2289.

[113] J. Xu, Y. Fu, D.-F. Luo, Y.-Y. Jiang, B. Xiao, Z.-J. Liu, T.-J. Gong, L. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 15300.

[114] J. Xu, D.-F. Luo, B. Xiao, Z.-J. Liu, T.-J. Gong, Y. Fu, L. Liu, *Chem. Commun.* **2011**, *47*, 4300.

[115] D.-F. Luo, J. Xu, Y. Fu, Q.-X. Guo, *Tetrahedron Lett.* **2012**, *53*, 2769.

[116] J.-J. Dai, C. Fang, B. Xiao, J. Yi, J. Xu, Z.-J. Liu, X. Lu, L. Liu, Y. Fu, *J. Am. Chem. Soc.* **2013**, *135*, 8436.

[117] C.-P. Zhang, J. Cai, C.-B. Zhou, X.-P. Wang, X. Zheng, Y.-C. Gu, J.-C. Xiao, *Chem. Commun.* **2011**, *47*, 9516.

[118] C.-P. Zhang, Z.-L. Wang, Q.-Y. Chen, C.-T. Zhang, Y.-C. Gu, J.-C. Xiao, *Angew. Chem. Int. Ed.* **2011**, *50*, 1896.

[119] K. A. McReynolds, R. S. Lewis, L. K. G. Ackerman, G. G. Dubinina, W. W. Brennessel, D. A. Vicic, *J. Fluorine Chem.* **2010**, *131*, 1108.

[120] Y. Li, T. Chen, H. Wang, R. Zhang, K. Jin, X. Wang, C. Duan, *Synlett* **2011**, 1713.

[121] B. R. Langlois, E. Laurent, N. Roidot, *Tetrahedron Lett.* **1991**, *32*, 7525.

[122] Y. Ji, T. Brueckl, R. D. Baxter, Y. Fujiwara, I. B. Seiple, S. Su, D. G. Blackmond, P. S. Baran, *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 14411.

[123] Y. Ye, S. A. Kuenzi, M. S. Sanford, *Org. Lett.* **2012**, *14*, 4979.

[124] Y. Li, L. Wu, H. Neumann, M. Beller, *Chem. Commun.* **2013**, *49*, 2628.

[125] H. Kondo, M. Oishi, K. Fujikawa, H. Amii, *Adv. Synth. Catal.* **2011**, *353*, 1247.

[126] T. Knauber, F. Arikan, G. V. Roschenthaler, L. J. Goossen, *Chem. Eur. J.* **2011**, *17*, 2689.

[127] Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2012**, *134*, 9034.

[128] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467.

[129] a) A. Soheili, J. Albaneze-Walker, J. A. Murry, P. G. Dormer, D. L. Hughes, *Org. Lett.* **2003**, *5*, 4191; b) T. Hundertmark, A. F. Littke, S. L. Buchwald, G. C. Fu, *Org. Lett.* **2000**, *2*, 1729; c) V. P. W. Bohm, W. A. Herrmann, *Eur. J. Org. Chem.* **2000**, 3679; d) A. D. Finke, E. C. Elleby, M. J. Boyd, H. Weissman, J. S. Moore, *J. Org. Chem.* **2009**, *74*, 8897.

[130] a) J. Liu, J. W. Y. Lam, B. Z. Tang, *Chem. Rev.* **2009**, *109*, 5799; b) M. M. Heravi, S. Sadjadi, *Tetrahedron* **2009**, *65*, 7761; c) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4442; d) R. Chinchilla, C. Najera, *Chem. Soc. Rev.* **2011**, *40*, 5084.

[131] L. Yin, J. Liebscher, *Chem. Rev.* **2007**, *107*, 133.

[132] O. Vechorkin, D. Barmaz, V. Proust, X. Hu, *J. Am. Chem. Soc.* **2009**, *131*, 12078.

[133] a) C. González-Arellano, A. Abad, A. Corma, H. García, M. Iglesias, F. Sánchez, *Angew. Chem. Int. Ed.* **2007**, *46*, 1536; b) A. Corma, R. Juarez, M. Boronat, F. Sanchez, M. Iglesias, H. Garcia, *Chem. Commun.* **2011**, *47*, 1446.

[134] a) A. Tougerti, S. Negri, A. Jutand, *Chem. Eur. J.* **2007**, *13*, 666; b) Y. Liang, Y.-X. Xie, J.-H. Li, *J. Org. Chem.* **2006**, *71*, 379.

[135] a) M. Carril, A. Correa, C. Bolm, *Angew. Chem. Int. Ed.* **2008**, *47*, 4862; b) H. Huang, H. Jiang, K. Chen, H. Liu, *J. Org. Chem.* **2008**, *73*, 9061; c) D. N. Sawant, P. J. Tambade, Y. S. Wagh, B. M. Bhanage, *Tetrahedron Lett.* **2010**, *51*, 2758; d) H. Firouzabadi, N. Iranpoor, M. Gholinejad, J. Hoseini, *Adv. Synth. Catal.* **2011**, *353*, 125.

[136] a) K. Okuro, M. Furuune, M. Miura, M. Nomura, *Tetrahedron Lett.* **1992**, *33*, 5363; b) K. Okuro, M. Furuune, M. Enna, M. Miura, M. Nomura, *J. Org. Chem.* **1993**, *58*, 4716; c) C.-H. Lin, Y.-J. Wang, C.-F. Lee, *Eur. J. Org. Chem.* **2010**, 4368; d) F. Monnier, F. Turtaut, L. Duroure, M. Taillefer, *Org. Lett.* **2008**, *10*, 3203; e) H.-J. Chen, Z.-Y. Lin, M.-Y. Li, R.-J. Lian, Q.-W. Xue, J.-L. Chung, S.-C. Chen, Y.-J. Chen, *Tetrahedron* **2010**, *66*, 7755.

[137] L. Feng, F. Liu, P. Sun, J. Bao, *Synlett* **2008**, 1415.

[138] E. Zuidema, C. Bolm, *Chem. Eur. J.* **2010**, *16*, 4181.

[139] D. J. Berrisford, C. Bolm, K. B. Sharpless, *Angew. Chem. Int. Ed.* **1995**, *34*, 1059.

[140] L.-H. Zou, A. J. Johansson, E. Zuidema, C. Bolm, *Chem. Eur. J.* **2013**, *19*, 8144.

[141] a) J. W. Tye, Z. Weng, A. M. Johns, C. D. Incarvito, J. F. Hartwig, *J. Am. Chem. Soc.* **2008**, *130*, 9971; b) L. M. Huffman, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 9196; c) S.-L. Zhang, L. Liu, Y. Fu, Q.-X. Guo, *Organometallics* **2007**, *26*, 4546.

[142] B. A. Arndtsen, R. G. Bergman, T. A. Mobley, T. H. Peterson, *Acc. Chem. Res.* **1995**, *28*, 154.

[143] G. S. Chen, J. A. Labinger, J. E. Bercaw, *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 6915.

[144] J. Chatt, J. M. Davidson, *J. Chem. Soc.* **1965**, 843.

[145] a) P. Foley, G. M. Whitesides, *J. Am. Chem. Soc.* **1979**, *101*, 2732; b) A. H. Janowicz, R. G. Bergman, *J. Am. Chem. Soc.* **1982**, *104*, 352.

[146] a) F. Kakiuchi, N. Chatani, *Adv. Synth. Catal.* **2003**, *345*, 1077; b) A. R. Dick, M. S. Sanford, *Tetrahedron* **2006**, *62*, 2439; c) K. Godula, D. Sames, *Science* **2006**, *312*, 67; d) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173; e) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094.

[147] a) P. Xi, F. Yang, S. Qin, D. Zhao, J. Lan, G. Gao, C. Hu, J. You, *J. Am. Chem. Soc.* **2010**, *132*, 1822; b) D. R. Stuart, K. Fagnou, *Science* **2007**, *316*, 1172.

[148] a) C.-Y. He, S. Fan, X. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 12850; b) Y. Wei, W. Su, *J. Am. Chem. Soc.* **2010**, *132*, 16377; c) H. Li, J. Liu, C.-L. Sun, B.-J. Li, Z.-J. Shi, *Org. Lett.* **2011**, *13*, 276.

[149] a) Y. Li, J. Jin, W. Qian, W. Bao, *Org. Biomol. Chem.* **2010**, *8*, 326; b) H. Q. Do, O. Daugulis, *J. Am. Chem. Soc.* **2009**, *131*, 17052.

[150] a) Z. Mao, Z. Wang, Z. Xu, F. Huang, Z. Yu, R. Wang, *Org. Lett.* 2012, *14*, 3854; b) S. Fan, Z. Chen, X. Zhang, *Org. Lett.* **2012**, *14*, 4950.

[151] A. T. Prudchenko, S. A. Vereshchagina, V. A. Barkhash, N. N. Vorozhtsov, *Zh. Obshch. Khim.* **1967**, *37*, 2195.

[152] T. Kawano, T. Yoshizumi, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2009**, *11*, 3072.

[153] a) T. Hamada, X. Ye, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 833; b) Y. Gao, G. Wang, L. Chen, P. Xu, Y. Zhao, Y. Zhou, L.-B. Han, *J. Am. Chem. Soc.* **2009**, *131*, 7956.

[154] L.-H. Zou, J. Mottweiler, D. L. Priebbenow, J. Wang, J. A. Stubenrauch, C. Bolm, *Chem. Eur. J.* **2013**, *19*, 3302.

[155] I. Thomé, A. Nijs, C. Bolm, *Chem. Soc. Rev.* **2012**, *41*, 979.

[156] FM 3-8 Chemical Reference Handbook, US Army, **1967**.

[157] S. R. Dubbaka, P. Vogel, *Angew. Chem. Int. Ed.* **2005**, *44*, 7674.

[158] S. G. Modha, V. P. Mehtazb, E. V. Van der Eycken, *Chem. Soc. Rev.* **2013**, *42*, 5042.

[159] J. P. Corbet, G. Mignani, *Chem. Rev.* **2006**, *106*, 2651.

[160] a) M. A. Fernández-Rodríguez, Q. Shen, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 2180; b) M. A. Fernández-Rodríguez, Q. Shen, J. F. Hartwig, *Chem. Eur. J.* **2006**, *12*, 7782.

[161] a) Y. Zhang, K. C. Ngeow, J. Y. Ying, *Org. Lett.* **2007**, *9*, 3495; b) A. Saxena, A. Kumar, S. Mozumdar, *Appl. Catal. A: Gen.* **2007**, *317*, 210; c) S. Jammi, P. Barua, L. Rout, P. Saha, T. Punnlyamurthy, *Tetrahedron Lett.* **2008**, *49*, 1484.

[162] a) Y.-J. Chen, H.-H. Chen, *Org. Lett.* **2006**, *8*, 5609; b) L. Rout, T. K. Sen, T. Punniyamurthy, *Angew. Chem. Int. Ed.* **2007**, *46*, 5583; c) X. Lv, W. Bao, *J. Org. Chem.* **2007**, *72*, 3863; d) E. Sperotto, G. P. M. van Klink, J. G. de Vries, G. van Koten, *J. Org. Chem.* **2008**, *73*, 5625; e) P. F. Larsson, A. Correa, M. Carril, P. O. Norrby, C. Bolm, *Angew. Chem. Int. Ed.* **2009**, *48*, 5691; f) C.-K. Chen, Y.-W. Chen, C.-H. Lin, H.-P. Lin, C.-F. Lee, *Chem. Commun.* **2010**, *46*, 282.

[163] a) C. Mispelaere-Canivet, J. F. Spindler, S. Perrio, P. Beslin, *Tetrahedron* **2005**, *61*, 5253; b) T. Itoh, T. Mase, *Org. Lett.* **2004**, *6*, 4587; c) N. Zheng, J. C. McWilliams, F. J. Fleitz, J. D. Armstrong, R. P. Volante, *J. Org. Chem.* **1998**, *63*, 9606.

[164] a) C. Savarin, J. Srogl, L. S. Liebeskind, *Org. Lett.* **2002**, *4*, 4309; b) P. S. Herradura, K. A. Pendola, R. K. Guy, *Org. Lett.* **2000**, *2*, 2019.

[165] a) S. Kumar, L. Engman, *J. Org. Chem.* **2006**, *71*, 5400; b) N. Taniguchi, T. Onami, *J. Org. Chem.* 2004, *69*, 915.

[166] a) T. Mukai, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2009**, *74*, 6410; b) F. Besselievre, S. Piguel, *Angew. Chem. Int. Ed.* **2009**, *48*, 9553; c) M. Kitahara, K. Hirano, H. Tsurugi, T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 1772; d) T. Mukai, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2010**, *12*, 1360; e) T. Kawano, N. Matsuyama, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2010**, *75*, 1764; f) S. Guo, B. Chan, Y. Xie, C. Xia, H. Huang, *Org. Lett.* **2011**, *13*, 522; g) J. Wang, J.-T. Hou, J. Wen, J. Zhang, X.-Q. Yu, *Chem. Commun.* **2011**, *47*, 3652; h) M. Miyasaka, K. Hirano, T. Satoh, R. Kowalczyk, C. Bolm, M. Miura, *Org. Lett.* **2011**, *13*, 359.

[167] a) M. A. Khanfar, R. A. Hill, A. Kaddoumi, K. A. El Sayed, *J. Med. Chem.* **2010**, *53*, 8534; b) H. Chen, Z. Li, Y. Han, *J. Agric. Food Chem.* **2000**, *48*, 5312; c) X.-J. Zou, L.-H. Lai, G.-Y. Jin, Z.-X. Zhang, *J. Agric. Food Chem.* **2002**, *50*, 3757.

[168] Y. Zhang, C. Zuniga, S.-J. Kim, D. Cai, S. Barlow, S. Salman, V. Coropceanu, J.-L. Brédas,

B. Kippelen, S. Marder, *Chem Mater* **2011**, *23*, 4002.

[169] a) A. Alemagna, Bacchett.T, P. Beltrame, *Tetrahedron* **1968**, *24*, 3209; b) S. H. Wunderlich, P. Knochel, *Angew. Chem. Int. Ed.* **2007**, *46*, 7685; c) L.-F. Niu, Y. Cai, C. Liang, X.-P. Hui, P.-F. Xu, *Tetrahedron* **2011**, *67*, 2878; d) A.-X. Zhou, X.-Y. Liu, K. Yang, S.-C. Zhao, Y.-M. Liang, *Org. Biomol. Chem.* **2011**, *9*, 5456.

[170] L.-H. Zou, J. Reball, J. Mottweiler, C. Bolm, *Chem. Commun.* **2012**, *48*, 11307.

[171] a) X.-L. Fang, R.-Y. Tang, X.-G. Zhang, J.-H. Li, *Synthesis* **2011**, 1099; b) C. C. Silveira, S. R. Mendes, L. Wolf, G. M. Martins, *Tetrahedron Lett.* **2010**, *51*, 2014.

[172] Phosphorus Ligands in Asymmetric Catalysis; A. Börner, Ed.; Wiley-VCH: Weinheim, **2008**.

[173] M. Jia, X. Li, W. S. Lam, S. H.L Kok, L. Xu, G. Lu, C.-H. Yeung, A. S.C Chan, *Tetrahedron: Asymmetry* **2004**, *15*, 2273.

[174] a) T. Schulz, C. Torborg, B. Schäffner, J. Huang, A. Zapf, R. Kadyrov, A. Börner, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 918; b) S. Harkal, F. Rataboul, A. Zapf, C. Fuhrmann, T. Riermeier, A. Monsees, M. Beller, *Adv. Synth. Catal.* **2004**, *346*, 1742.

[175] E. V. Zarudnitskii, I. I. Pervak, A. S. Merkulov, A. A. Yurchenko, A. A. Tolmachev, A. M. Pinchuk, *Synthesis* **2006**, 1279.

[176] A. A. Tolmachev, E. V. Zarudnitskii, A. A. Yurchenko, A. M. Pinchuk, *Chem. Heterocycl. Compd*. **1999**, *35*, 1117.

[177] L.-H. Zou, Z.-B. Dong, C. Bolm, *Synlett* **2012**, *23*, 1613.

[178] a) B. M. Trost, *Chem. Rev.* **1978**, *78*, 363; b) B. M. Trost, *Acc. Chem. Res.* **1978**, *11*, 453.

[179] a) P. Groenewegen, H. Kallenberg, A. Vandergen, *Tetrahedron Lett.* **1979**, *20*, 2817; b) B. M. Trost, T. N. Salzmann, K. Hiroi, *J. Am. Chem. Soc.* **1976**, *98*, 4887.

[180] D. Seebach, M. Teschner, *Tetrahedron Lett.* **1973**, *14*, 5113.

[181] B. C. Ranu, R. Jana, *Adv. Synth. Catal.* **2005**, *347*, 1811.

[182] a) B. C. Ranu, T. Mandal, *J. Org. Chem.* **2004**, *69*, 5793; b) C. Peppe, L. B. de Castro, *Can. J. Chem.* **2009**, *87*, 678; c) S. Padmanabhan, T. Ogawa, H. Suzuki, *Bull. Chem. Soc. Jpn.* 1989, *62*, 1358; d) X. Huang, W. X. Zheng, *Synth. Commun.* **1999**, *29*, 1297.

[183] a) M. A. Mckervey, P. Ratananukul, *Tetrahedron Lett.* **1982**, *23*, 2509; b) S. Sengupta, S. Mondal, *Tetrahedron Lett.* **1999**, *40*, 8685.

[184] H. Anbou, R. Umeda, Y. Nishiyama, *Bull. Chem. Soc. Jpn.* **2011**, *84*, 1248.

[185] a) B. Rybtchinski, D. Milstein, *Angew. Chem. Int. Ed.* **1999**, *38*, 870; b) C. H. Jun, *Chem. Soc. Rev.* **2004**, *33*, 610; c) Y. J. Park, J. W. Park, C. H. Jun, *Acc. Chem. Res.* **2008**, *41*, 222.

[186] a) A. Kawata, K. Takata, Y. Kuninobu, K. Takai, *Angew. Chem. Int. Ed.* **2007**, *46*, 7793; b) S. Biswas, S. Maiti, U. Jana, *Eur. J. Org. Chem.* **2010**, 2861; c) C. B. Rao, D. C. Rao, D. C. Babu, Y. Venkateswarlu, *Eur. J. Org. Chem.* **2010**, 2855.

[187] L.-H. Zou, D. L. Priebbenow, L. Wang, J. Mottweiler, C. Bolm, *Adv. Synth. Catal.* **2013**, *355*, 2558.

[188] B. Floris, V. Rosnati, *J. Chem. Res.* **1994**, 72.

[189] M. Abarbri, P. Knochel, *Synlett* **1999**, 1577.

[190] A. Schäfer, A. Wellner, R. Gust, *ChemMedChem* **2011**, *6*, 794.

[191] P. Li, L. Wang, H. Li, *Tetrahedron* **2005**, *61*, 8633.

[192] B. H. Lipshutz, D. W. Chung, B. Rich, *Org. Lett.* **2008**, *10*, 3793.

[193] N. Inoue, O. Sugimoto, K. Tanji, *Heterocycles* **2007**, *72*, 665.

[194] J. Moon, M. Jang, S. Lee, *J. Org. Chem.* **2009**, *74*, 1403.

[195] M. A. De la Rosa, E. Velarde, A. Guzmán, *Synth. Commun.* **1990**, *20*, 2059.

[196] K. G. Thakur, G. Sekar, *Synthesis* **2009**, 2785.

[197] T. Kawano, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2010**, *132*, 6900.

[198] C. Ainsworth, *J. Am. Chem. Soc.* **1955**, *77*, 1148.

[199] J. Maillard, M. Vincent, Vovantri, *Bull. Soc. Chim. Fr.* **1966**, 376.

[200] M. C. Kloetzel, F. L. Chubb, *J. Am. Chem. Soc.* **1957**, *79*, 4226.

[201] F. A. Adekunle, J. A. O. Woods, O. O. E. Onawumi, O. A. Odunola, *Asian J. Chem.* **2010**, *22*, 5543.

[202] T. Mino, Y. Harada, H. Shindo, M. Sakamoto, T. Fujita, *Synlett* **2008**, 614.

[203] M. Oba, K. Tanaka, K. Nishiyama, W. Ando, *J. Org. Chem.* **2011**, *76*, 4173.

[204] D. R. Dreyer, H.-P. Jia, A. D. Todd, J. Geng, C. W. Bielawski, *Org. Biomol. Chem.* **2011**, *9*, 7292.

[205] J. L. G. Ruano, A. Parra, J. Aleman, *Green Chem.* **2008**, *10*, 706.

[206] L. Wang, D. L. J. Clive, *Org. Lett.* **2011**, *13*, 1734.

[207] X.-L. Fang, R.-Y. Tang, P. Zhong, J.-H. Li, *Synthesis* **2009**, 4183.

[208] M. Arisawa, F. Toriyama, M. Yamaguchi, *Tetrahedron Lett.* **2011**, *52*, 2344.

[209] F. Barba, F. Ranz, B. Batanero, *Tetrahedron Lett.* **2009**, *50*, 6798.

[210] C. C. Price, W. J. Belanger, *J. Am. Chem. Soc.* **1954**, *76*, 2682.

[211] S. Yildirim, R. Koca, *Asian J. Chem.* **2004**, *16*, 899.

[212] N. Maras, S. Polanc, M. Kocevar, *Tetrahedron* **2008**, *64*, 11618.

[213] Y. Okamoto, T. Inukai, H. C. Brown, *J. Am. Chem. Soc.* **1958**, *80*, 4972.

[214] H. Loghmani-Khouzani, M. R. Poorheravi, M. M. M. Sadeghi, L. Caggiano, R. F. W. Jackson, *Tetrahedron* **2008**, *64*, 7419.

[215] A. Shafiee, S. Toghraie, F. Aria, G. Mortezaei-Zandjani, *J. Heterocycl. Chem.* **1982**, *19*, 1305.

[216] I. Aviv, Z. Gross, *Chem. Eur. J.* **2008**, *14*, 3995.

[217] S. Colonna, S. Banfi, F. Fontana, M. Sommaruga, *J. Org. Chem.* **1985**, *50*, 769.

[218] J. Ham, I. Yang, H. Kang, *J. Org. Chem.* **2004**, *69*, 3236.

[219] R.-Y. Tang, P. Zhong, Q.-L. Lin, *Synthesis* **2007**, 85.

[220] V. Hugenberg, G. Haufe, *J. Fluorine Chem.* **2010**, *131*, 942.

Appendix

1. List of Abbreviations

Å	Angstrom
Ac	acetyl
aq.	aqueous (solution)
Ar	aromatic substituent
Bn	benzyl
br	broad (NMR signal)
Bu	butyl
*t*Bu	*tert*-butyl
Calc.	Calculated
C	centigrade
Cy	cyclohexyl
δ	chemical shift
d	doublet (NMR signal)
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DMF	*N*,*N*-dimethylformamide
DMEDA	*N,N'*-dimethylethylene diamine
DMSO	dimethylsulfoxide
Ed.	Edition
EI	electronic impact (in mass spectroscopy)
equiv	equivalent
Et	ethyl
eV	electron volt
GC	gas chromatography
HRMS	high resolution mass spectroscopy

Hz	Hertz
ICP-MS	inductively coupled plasma mass spectrometry
IR	infrared spectroscopy
J	coupling constant (in NMR spectroscopy)
L	ligand
M	molar
MCPBA	3-chloroperoxybenzoic acid
Me	methyl
min	minutes
mol	mole
m.p.	melting point
MS	mass spectroscopy
Naphth	naphthyl
NCS	*N*-chlorosuccinimide
NMI	*N*-methylimidazole
NMR	nuclear magnetic resonance (spectroscopy)
phen	1,10-phenanthroline
ppb	parts per billion
ppm	parts per million
*i*Pr	*iso*-propyl
rt	room temperature
s	singlet (NMR signal)
Selectfluor	1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane
TBAB	tetrabutylammonium bromide
TBHP	*tert*-Butylhydroperoxide
Temp	temperature
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl

2. Curriculum Vitae

Personal Information

Nationality:	Chinese
Gender:	Male
Marital Status:	Married
Date of Birth:	Sep. 21, 1982
Place of Birth:	Loudi, China

Education Background

Sep. 2009–Aug. 2013	Doctoral thesis, Organic Chemisty, Institute of Organic Chemistry, RWTH Aachen University, Germany; Supervisor: Prof. Dr. Carsten Bolm
Sep. 2006–Jun. 2009	Master of Science, Organic Chemistry, College of Chemistry and Chemical Engineering, Hunan University, China; Supervisor: Prof. Dr. Qiuan Wang
Sep. 2002–Jun. 2006	Bachelor of Science, Chemistry, College of Chemistry and Chemical Engineering, Hunan University of Arts and Science, China

Awards and Scholarships

Unversity Scholarship, Second and Third Class, twice respectively (**2002-2006**)

"The Third Class of English Contest" Award (**2004**)

"The Third Class of Mathematic Modeling" Award (**2005**)

Provincial Government Scholarships of Hunan Province (**2005**)

"Excellent College Student" Award (**2006**)

China Scholarship Council (CSC) Scholarship for Studying Abroad (**2009-2013**)

Academic Symposium Participated and Presentations

[1] The 10th International Symposium for Chinese Organic Chemists, Shanghai, China, July **2008**.

[2] Copper-mediated direct oxidative cross-coupling of polyfluoroarenes with heteroarenes using O_2 as an oxidant. Poster presented at "The 4th Annual New Year's Symposium", RWTH Aachen University, Germany, January **2012**.

[3] Copper-catalyzed selective cross-coupling of diaryl disulfides and β-diketones: a

new approach towards α-thiophenyl carbonyl compounds and diaryl thioethers. Poster presented at "The 5th Annual New Year's Symposium", RWTH Aachen University, Germany, January **2013**.

[4] Mechanistic insights into copper-catalyzed Sonogashira-Hagihara-type cross-coupling reactions: sub-mol% catalyst loadings and ligand effects. Poster presented at "The 4th Münster Symposium on Cooperative Effects in Chemistry", Münster University, Germany, May **2013**.

[5] Copper-catalyzed synthesis of α-thiophenyl carbonyl compounds through S–S bond cleavage and C–C bond activation. Poster presented at Holland Research School of Molecular Chemistry (HRSMC), Maastricht, Netherlands, July **2013**.

Foreign Languages

English: Good at listening, speaking, reading and writing

German: B2 level

Publications

[1] **L.-H. Zou**, Z.-B. Dong, C. Bolm*, *Synlett* **2012**, *23*, 1613.

[2] **L.-H. Zou**, J. Reball, J. Mottweiler, C. Bolm*, *Chem. Commun.* **2012**, *48*, 11307.

[3] **L.-H. Zou**, J. Mottweiler, D. L. Priebbenow, J. Wang, J. A. Stubenrauch, C. Bolm*, *Chem. Eur. J.* **2013**, *19*, 3302.

[4] **L.-H. Zou**, A. J. Johansson, E. Zuidema, C. Bolm*, *Chem. Eur. J.* **2013**, *19*, 8144.

[5] **L.-H. Zou**, D. L. Priebbenow, L. Wang, J. Mottweiler, C. Bolm*, *Adv. Synth. Catal.* **2013**, *355*, 2558.

[6] D. L. Priebbenow, **L.-H. Zou**, P. Becker, C. Bolm*, *Eur. J. Org. Chem.* **2013**, 3965.

[7] L. Wang, D. L. Priebbenow, **L.-H. Zou**, C. Bolm*, *Adv. Synth. Catal.* **2013**, *355*, 1490.

[8] Q.-A. Wang*, Z. Wu, L. Liu, **L.-H. Zou**, M. Luo, Youji Huaxue (*Chin. J. Org. Chem. in Chinese)*, **2010**, *30*, 1682.

[9] Q.-A. Wang*, L. Wang, **L.-H. Zou,** Z.-J. Zhang, *Journal of Hunan University*, **2009**, *36*, 59.

[10] W.-Q. Zhang*, **L.-H. Zou**, S.-B. Zhou, R.-X. Zhang, *Chemical Industry Times*, **2006**, *20*, 37.