University of Warsaw
Faculty of Chemistry

Novel synthetic reactions employing hypervalent iodine compounds: oxidations and arylations

Sudeep Sarkar

Doctoral Thesis
in the field of Natural Sciences
in the discipline of Chemical Sciences

Doctoral Advisor: Dr. hab. Marcin Kalek

Warsaw 2023

Oświadczenie kierującego pracą/Doctoral advisor's statement

Oświadczam, że niniejsza praca została przygotowana pod moim kierunkiem i stwierdzam, że spełnia ona warunki do przedstawienia jej w postępowaniu o nadanie stopnia doktora nauk chemicznych w dziedzinie nauk ścisłych i przyrodniczych.

I declare that this work has been prepared under my supervision and that it meets the criteria required to submit it for the proceedings for conferring of the degree of doctor of Chemical Sciences in the field of Natural Sciences.

Data/Date Podpis kierującego pracą/Signature of the doctoral advisor

Author's statement

Świadom odpowiedzialności prawnej oświadczam, że niniejsza rozprawa doktorska została napisana przeze mnie samodzielnie i nie zawiera treści uzyskanych w sposób niezgodny z obowiązującymi przepisami. Oświadczam również, że przedstawiona praca nie była wcześniej przedmiotem procedur związanych z uzyskaniem stopnia doktora w innej jednostce.

Oświadczam ponadto, że niniejsza wersja pracy jest identyczna z załączoną wersją elektroniczną.

Aware of legal liability, I declare that this doctoral thesis was written by me independently and does not contain any content obtained in a manner inconsistent with applicable regulations. I also declare that the submitted thesis has not been previously subjected to procedures for obtaining a doctoral degree in another unit.

I also declare that this version of the thesis is identical to the enclosed electronic version.

Data/Date Podpis autora pracy/Signature of the author

ॐ सर्वे भवन्तु सुखिनः।
सर्वे सन्तु निरामयाः।
सर्वे भद्राणि पश्यन्तु मा कश्चिद्दुःखभाग्भवेत।
ॐ शान्तिः शान्तिः शान्तिः॥

oṃ sarve bhavantu sukhinaḥ ।
sarve santu nirāmayāḥ ।
sarve bhadrāṇi paśyantu mā kaścidduḥ khabhāgbhaveta ।
oṃ śāntiḥ śāntiḥ śāntiḥ ॥

May all sentient beings be at peace.
May all be free from illness.
May all see what is auspicious, may no one suffer from sorrow.
Om peace, peace, peace.

Abstract

Due to the challenges facing the humanity in the 21st century, the requirements for chemical synthesis are growing, especially in terms of reducing cost and environmental impact. One of the changes in line with the above directions is to limit the use of metal compounds, especially these of heavy and noble metals. In this context, hypervalent iodine species offer great opportunities. On one hand they have properties that allow them to replace metal-based oxidants and catalysts, and on the other, they possess a number of advantages, such as low toxicity and moderate price. Although the chemistry of hypervalent iodine compounds has a long history, the intensive development of their applications in organic synthesis has taken place over the period of the last 40 years, of which the last decade has seen a leap forward in the emergence of new chemical processes utilizing this class of reagents.

The two most important types of organic reactions promoted by hypervalent iodine-based reagents are oxidations reactions, often accompanied by the formation of new bonds and building the molecular complexity, and electrophilic group transfers. This thesis presents the overview of such transformations (Chapter 1) and describes the development of several new synthetic methods based on both above reaction types.

The first of the implemented projects, described in Chapter 2, concerns the synthesis of Pummerer's ketone and its analogs by the oxidative coupling of *para*-substituted phenols using iodine(III) compounds as oxidants. The rigid tricyclic Pummerer's ketone system is a common motif in substances of pharmaceutical interest. Existing procedures for the oxidative coupling of phenols to Pummerer ketone use a variety of oxidizing agents, but hypervalent iodine compounds have never been used in this context. The chapter presents the development of conditions and the exploration of the scope of the method, delivering a variety of Pummerer's ketone analogs by iodosobenzene-promoted oxidative phenolic coupling.

As a continuation of research on the oxidative transformations of phenols employing iodine(III) reagents, Chapter 3 explores a design of a new reaction, during which phenols with pendant aldehyde undergo an enantioselective intramolecular cyclization-dearomatization organocatalyzed by chiral proline derivatives. The resulting spiro-[6,5]-bicyclic products, rich in functional groups, are suitable building blocks for the synthesis of many natural and bioactive compounds. Despite a partial success, the transformation could not be developed into an efficient and general synthetic method.

The following three chapters deal with the development of aryl transfer reactions using diaryliodonium salts. The transfer of groups, *e.g.*, aryl, vinyl, alkynyl, CF_3, CN, N_3, F, or NTs_2, to organic acceptors is an intensively investigated class of reactions employing hypervalent iodine compounds, constituting an alternative to cross-couplings catalyzed by transition metal complexes. Thus, Chapters 4 and 5 present studies on the aryl transfer to a sulfur atom, leading to aryl sulfides and *S*-aryl phosphorothioates, respectively. The developed reactions are metal-free, high-yielding, and experimentally simple. They create handy and general entries to biologically relevant compounds containing S–Ar moiety. Importantly, the process described in Chapter 5 allowed for the first time for the stereospecific *S*-arylation of P-stereogenic compounds.

Along the same lines, but on another front, Chapter 6 addresses the arylation of phosphorus nucleophiles, specifically secondary phosphines, with diaryliodonium salts. The reaction conditions have been preliminarily optimized and the scope of the process briefly explored, providing a strong basis for the development of a universal method for the metal-free preparation of unsymmetrical tertiary phosphines under mild conditions.

Keywords: hypervalent iodine, synthetic methodology, oxidation, group-transfer reactions, phenolic coupling, Pummerer's ketone, spirocyclization, *S*-arylation, *P*-arylation

Streszczenie

Tytuł w języku polskim: ***Nowe reakcje syntetyczne wykorzystujące związki jodu hiperwalencyjnego: utleniania i arylowania***

Z uwagi na wyzwania stojące przed ludzkością w XXI wieku, rosną wymagania stawiane syntezie chemicznej, szczególnie w zakresie obniżenia kosztów i wpływu na środowisko. Jedną ze zmian zgodnych z powyższymi kierunkami jest ograniczenie stosowania w syntezie związków metali, zwłaszcza ciężkich i szlachetnych. W tym kontekście duże możliwości oferują związki jodu hiperwalencyjnego. Z jednej strony posiadają one właściwości pozwalające na zastąpienie utleniaczy i katalizatorów opartych na metalach, z drugiej mają szereg zalet, takich jak niska toksyczność i umiarkowana cena. Chociaż chemia hiperwalencyjnych związków jodu ma długą historię, intensywny rozwój ich zastosowań w syntezie organicznej przypada na okres ostatnich 40 lat, z czego w ostatniej dekadzie nastąpił skokowy wzrost liczby nowych procesów chemicznych z wykorzystaniem tego typu reagentów.

Dwa najważniejsze rodzaje reakcji organicznych promowanych przez odczynniki oparte na jodzie hiperwalncyjnym to reakcje utleniania, którym często towarzyszy tworzenie nowych wiązań chemicznych i budowanie złożoności molekularnej, oraz elektrofilowe transfery grup. W niniejszej rozprawie przedstawiono przegląd tych transformacji (Rozdział 1) oraz opisano opracowanie kilku nowych metod syntetycznych opartych na obu powyższych typach reakcji.

Pierwszy ze zrealizowanych projektów, opisany w Rozdziale 2, dotyczy syntezy ketonu Pummerera i jego analogów na drodze utleniającego sprzęgania *para*-podstawionych fenoli z wykorzystaniem związków jodu(III) jako utleniaczy. Sztywny trójpierścieniowy układ ketonu Pummerera jest częstym motywem w substancjach o znaczeniu farmaceutycznym. Istniejące procedury utleniającego sprzęgania fenoli do ketonu Pummerera wykorzystują różne czynniki utleniające, ale związki jodu hiperwalencyjnego nigdy nie były dotąd stosowane w tym kontekście. W rozdziale przedstawiono opracowanie warunków i określenie zakresu stosowalności metody dostarczającej różnorodnych analogów ketonu Pummerera poprzez promowane jodozobenzenem utleniające sprzęganie fenoli.

W ramach kontynuacji badań nad utleniającymi transformacjami fenoli z wykorzystaniem odczynników jodu(III), w Rozdziale 3 badano zamysł nowej reakcji, podczas której fenole z

dołączonym ugrupowaniem aldehydowym ulegają enancjoselektywnej wewnątrzcząsteczkowej cyklizacji-dearomatyzacji organokatalizowanej przez chiralne pochodne proliny. Powstałe w ten sposób bogate w grupy funkcyjne produkty spiro-[6,5]-bicykliczne stanowią wygodne bloki budulcowe do syntezy wielu związków naturalnych i bioaktywnych. Pomimo częściowego sukcesu, reakcji nie udało się rozwinąć w wydajną i ogólną metodę syntetyczną.

Kolejne trzy rozdziały dotyczą opracowania reakcji przeniesienia grupy arylowej z wykorzystaniem soli diarylojodoniowych. Przeniesienie grup, np. arylowych, winylowych, alkynylowych, CF_3, CN, N_3, F czy NTs_2, na organiczne akceptory jest intensywnie badaną klasą reakcji z udziałem hiperwalencyjnych związków jodu, stanowiącą alternatywę dla sprzęgań krzyżowych katalizowanych przez kompleksy metali przejściowych. W Rozdziałach 4 i 5 przedstawiono badania dotyczące przeniesienia arylu na atom siarki, prowadzące do, odpowiednio, sulfidów arylowych i *S*-arylowych tiofosforanów. Opracowane reakcje nie wykorzystują związków metali, są wysokowydajne oraz proste pod względem doświadczalnym. Stanowią one wygodną i ogólną drogę syntezy związków, w tym biologicznie istotnych, zawierających ugrupowanie S–Ar. Co ważne, proces opisany w Rozdziale 5 pozwolił po raz pierwszy stereospecyficzne *S*-arylowanie związków P-stereogenicznych.

W tym samym kierunku, ale na innym froncie, Rozdział 6 dotyczy arylowania nukleofili fosforowych, konkretnie drugorzędowych fosfin, za pomocą soli diarylojodoniowych. Warunki reakcji zostały wstępnie zoptymalizowane, a zakres stosowalności procesu pokrótce przebadany, dając solidne podstawy do opracowania uniwersalnej metody otrzymywania niesymetrycznych fosfin trzeciorzędowych w łagodnych warunkach i bez użycia związków metali przejściowych.

Słowa kluczowe: jod hiperwalencyjny, metodologia syntetyczna, utlenianie, reakcje przeniesienia grup, kondensacja fenoli, keton Pummerera, spirocykilzacja, *S*-arylowanie, *P*-arylowanie

List of Publications

This thesis is in part based on the following publications:

I. Synthesis of Pummerer's Ketone and Its Analogs by Iodosobenzene-Promoted Oxidative Phenolic Coupling.
Sarkar, S.; Ghosh, M. K.; Kalek, M. *Tetrahedron Lett.* **2020**, *61* (43), 152459.

II. Synthesis of Aryl Sulfides by Metal-Free Arylation of Thiols with Diaryliodonium Salts under Basic Conditions.
Sarkar, S.; Wojciechowska, N.; Rajkiewicz, A. A.; Kalek, M. *Eur. J. Org. Chem.* **2022**, e202101408.

III. Metal-free *S*-arylation of Phosphorothioate Diesters and Related Compounds with Diaryliodonium Salts
Sarkar, S.; Kalek, M. *Org. Lett.* **2023**, *25 (4)*, 671–675

Reprints (**Appendix A**) were made with the kind permission from the publishers. The contributions of the authors to each publication are clarified in **Appendix B**.

Some of the results presented in Chapter 4 (Paper II) have been used in Master's degree thesis of Natalia Wojciechowska (University of Warsaw, 2021). Similarly, selected results from Chapter 6 will be used in Master's degree thesis of Kacper Szczepański.

This work has been supported by the funding from the National Science Center, Poland (grant SONATA BIS 2016/22/E/STS/00566 to Marcin Kalek)

Table of Contents

Abbreviations

2c-2e = two-center two-electron
3c-2e = three-center two-electron
3c-4e = three-center four-electron
bmim = 1-butyl-3-methylimidazolium
Boc = *tert*-butyloxycarbonyl
BODIPY = 5,5-difluoro-5*H*-4λ^5-dipyrrolo[1,2-*c*:2′,1′-*f*][1,3,2]diazaborinin-4-ylium-5-uide
CAN = ceric ammonium nitrate
Cbz = benzyloxycarbonyl
CPME = cyclopentyl methyl ether
Cy = cyclohexyl
DABCO = 1,4-diazabicyclo[2.2.2]octane
DABSO = 1,4-diazabicyclo[2.2.2]acetate bis(sulfur dioxide) adduct
DBN = 1,5-diazabicyclo[4.3.0]non-5-ene
DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene
DCA = dichloroacetate
DCE = 1,2-dichloroethane
DCM = dichloromethane
DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DFT = density functional theory
DIBAL-H = diisobutylaluminum hydride
DIPA = diisopropylamine
DIPEA = *N*,*N*-diisopropylethylamine
DMA = dimethylacetamide
DMAP = 4-dimethylaminopyridine
DME = 1,2-dimethoxyethane
DMEDA = *N*,*N*′-dimethylethane-1,2-diamine
DMF = *N*,*N*-dimethylformamide
DMP = Dess–Martin periodinane
DMSO = dimethyl sulfoxide
DMT = 4,4′-dimethoxytrityl

DPE = 1,1-diphenylethylene
HFIP = 1,1,1,3,3,3-hexafluoropropan-2-ol
HIRs = hypervalent iodine reagents
IBX = 2-iodoxybenzoic acid
LED = light emitting diode
***m*-CPBA** = *meta*-chloroperoxybenzoic acid
Mes = mesityl
MTBE = methyl *tert*-butyl ether
MW = microwave
NaHMDS = sodium hexamethyldisilazide
NBS = *N*-bromosuccinimide
OTf = trifluoromethanesulfonate, triflate
Oxone = potassium peroxymonosulfate
PET = positron emission tomography
PIDA = phenyliodine diacetate
PIFA = phenyliodine bis(trifluoroacetate)
PPHF = pyridinium poly(hydrogen fluorde), Olah's reagent
RT = room temperature
Selectfluor = 1-(chloromethyl)-4-fluoro-1,4-diazabicyclo[2.2.2]octane-1,4-diium ditetrafluoroborate
SET = single electron transfer
TADDOL = α,α,α',α'-tetraaryl-2,2-dimethyl 1,3-dioxolane-4,5-dimethanol
TBAF = tetrabutylammonium fluoride
TBS = *tert*-butyldimethylsilyl
TDS = dimethylthexylsilyl
TEMPO = (2,2,6,6-tetramethylpiperidin-1-yl)oxyl
TFA = trifluoroacetic acid
TFE = 2,2,2-trifluoroethanol
THF = tetrahydrofuran
TMAF = tetramethylammonium fluoride
TMG = *N*,*N*,*N*′,*N*′-tetramethylguanidine
TMS = trimethylsilyl
TMSOTf = trimethylsilyl triflate
TsOH = *para*-toluenesulfonic acid
μ-oxoBTI = μ-oxobis(trifluoroacetoxyiodobenzene)

Preface

We, chemists, make and break bonds, and this process has been happening throughout the span of mankind. Since ancient times, humans have been transforming matter as a means to prepare food, medicines, dyes, tools, and weapons. Our curiosity about nature led us to speculate matter, which was marked by milestones, such as the development of atomic theory or the identification of various elements and several organic acids. Collectively these landmarks have established the field of chemistry.

Among them, the first synthesis of urea, a naturally occurring organic compound, by Friedrich Wöhler in 1828, meant that man could construct organic compounds, the molecules of living nature, in the laboratory and without the aid of living creatures or their organs. This was followed by the total synthesis of acetic acid by Kolbe. Thus, the art of construction of nature's organic molecules has started. Technologies derived from it, known in general as organic synthesis, are benefitting the society and have led to the development of useful products in fields ranging from medicine, dyes, cosmetics, and agriculture to diagnostics and high technology materials used in computers, mobile phones, and spaceships.

Despite the significant advancements, there are always some drawbacks and room for improvement. This thesis entitled "Novel synthetic reactions employing hypervalent iodine compounds: oxidations and arylations" is my small effort towards the advancement of organic synthesis, in particular by using hypervalent iodine chemistry, and eventually for the betterment of society.

Chapter 1
Introduction

1.1. Hypervalency and hypervalent iodine compounds

The reactivity of main-group elements has been traditionally described by the octet rule, which states that these elements tend to bond with other atoms in such a way that they attain a stable noble gas 8-electron configuration.[1] Although bonding in the majority of molecules satisfies the octet rule, certain compounds, such as nitric oxide (NO; having an odd number of electrons), diborane (B_2H_6; 6 valence electrons at boron), or phosphorus pentachloride (PCl_5; 10 valence electrons at phosphorus), do not adhere to it. The two former examples are so-called hypovalent compounds, and their electronic structure can be explained invoking two-center three-electron (2c-3e) and three-center two-electron (3c-2e) bonding, respectively. The latter one, on the other hand, is the case of an expanded-valence or hypervalent molecule, the term coined by J. I. Musher in 1969, referring to species of the elements of Groups 13–18 bearing more than eight electrons within the valence shell.[2]

The initial proposal for explaining the ability of main-group elements to hold more than the octet of electrons within a valence shell was put forward by L. Pauling in 1931. It assumed the involvement of the higher lying d orbitals, resulting in dsp^3 or d^2sp^3 hybridization.[3] According to the current knowledge, however, the contribution of d orbitals is not essential to form hypervalent compounds and the hypervalent bonding is best explained by a molecular orbital description involving a three-center four-electron (3c-4e) bond, first proposed by G. Pimentel and R. E. Rundle in 1951, rationalizing the bonding in trihalide ions (X_3^-, X = F, Br, Cl, I).[4,5] In this description, often referred to as a hypervalent bond, two pairs of electrons occupy molecular orbitals delocalized on all three atoms of the linear L–X–L moiety (Figure 1.1). Such bonding picture was later proven to be correct by quantum-chemical calculations.[6] Importantly, only one of the two occupied orbitals has a bonding character, while the other is nonbonding (it can be viewed as a delocalized lone pair of electrons). This results in each of the X–L bonds having a formal bond order of 0.5, rendering the hypervalent bond relatively weak, and making hypervalent compounds highly reactive, both kinetically and thermodynamically. That is, the

breaking of the hypervalent 3c-4e bond, and forming two regular 2c-2e bonds instead, is associated with a low energy barrier and results in a large downhill energy change.

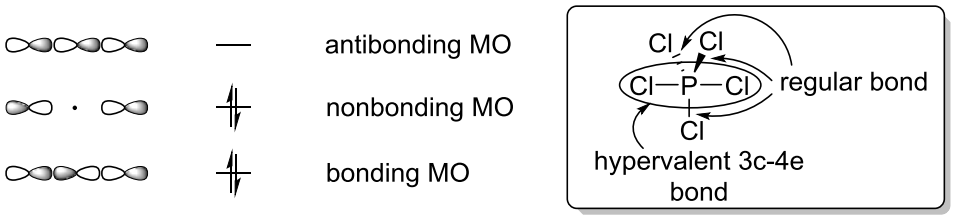


Figure 1.1. Molecular orbital description of three-center four-electron bond in hypervalent molecules, exemplified by PCl_5 (10 valence electrons).

Iodine is a remarkable element, first isolated from the ash of seaweed by industrial chemist B. Courtois in 1811. Its name, introduced by J. L. Gay Lussac in 1813,[7,8] derives from the Greek word ιωδες (iodes) for violet, due to the color of iodine vapor. Iodine is most commonly present in a monovalent form, having the octet of electrons. However, because iodine is the largest, most polarizable, and most electropositive of Group 17 elements, it forms also many stable hypervalent compounds. Here, a note on assigning the formal oxidation state is necessary. Namely, the convention (also followed in this thesis) is to count electrons in organic compounds of iodine such as iodine atom was a metal in a complex and the groups attached to it, including carbon-based moieties, were ligands. This is due to similar electronegativities of carbon and iodine, and more importantly, because hypervalent iodine compounds display striking resemblance in properties and reactivity to late transition metal complexes (see section 1.2, below). Hence, the monovalent iodine atom, for example in PhI, has the formal oxidation state of +I, while the hypervalent iodine adopts higher oxidation states, up to +VII.

Inorganic polyvalent iodine derivatives have been prepared since the beginning of the 19th century, and in 1886 the first organic hypervalent iodine compound, phenyliodine dichloride $PhICl_2$ (with iodine having 10 valence electrons and +III oxidation state), was synthesized. Although hundreds of hypervalent organoiodine compounds have been prepared by the early 20th century, it was not until later in that century that interest in these molecules was revived due to their unique chemical properties. With the increasing demand to develop new greener synthetic procedures, organic Hypervalent Iodine Reagents (HIRs) have gained a considerable recognition, serving an excellent synthetic tools with rich reactivity, low toxicity, easy handling, and, in particular, allowing to replace compounds of heavy metals in many synthetic applications. They have been employed in diverse transformations, both for simple functional

group interconversions as well as to create new chemical bonds during synthesis of complex molecules.[9–12] The two major areas that HIRs have found synthetic use are selective oxidations and electrophilic group-transfer reactions. In the former context, in the recent years they have been also used as oxidation organocatalysts, combined with a stoichiometric terminal oxidant or an anodic reoxidation.[13–16] Finally, there is a recent example wherein HIRs were used in a flow chemistry setting.[17]

Iodine can form stable trivalent, pentavalent, and heptavalent compounds, with the I oxidation states of +III, +V, and +VII, respectively. To maintain the high oxidation states of iodine atom, the presence of electronegative substituents (*e.g.*, halide- or oxygen-based) is necessary. The higher the oxidation state, the more such substituents are needed. Thus, for iodine(III), as many as two carbon-based ligands are acceptable; for iodine(V), only one carbon-based ligand can be present in stable compounds; for iodine(VII), all the substituents must be strongly electronegative (for example, as in IF_7). Therefore, only the former two classes have been widely used in organic chemistry.

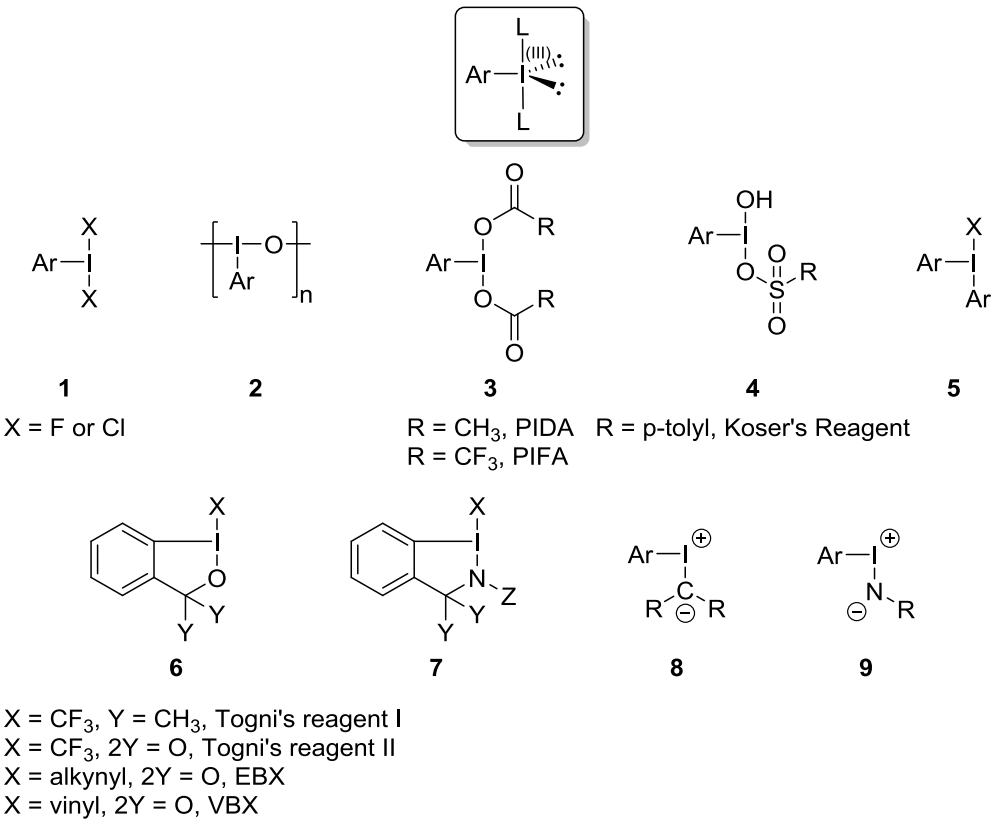


Figure 1.2. General classes of organoiodine(III) compounds and some important examples.

Depending on the type of ligands present at the iodine atom, organoiodine(III) compounds are conventionally classified into the following general categories: (dihaloiodo)arenes **1**, iodosoarenes (also called iodosylarenes) **2**, bis(acyloxy)iodoarenes **3**, aryliodine(III) organosulfonates **4**, iodonium salts **5**, benziodoxoles **6** and benziodoazoles **7**, iodonium ylides **8** and imides **9** (Figure 1.2). These reagents are used both for oxidations, *e.g.*, oxidative coupling, phenol dearomatization, oxidative heterocycle formation, including asymmetric reactions, as well as for group-transfer reactions, such as amination, arylation, trifluoromethylation, alkynylation, and vinylation.[12] Due to the electronic structure of the 3c-4e bond and its underlying molecular orbitals (Figure 1.1), the three atoms forming the hypervalent bond are collinear, resulting in a T-shaped geometry of iodine(III)-containing molecules. As visible in Figure 1.2, typically, the electronegative groups are more stable participating in the hypervalent bond, as the nonbonding orbital is localized at its termini. However, if there are two carbon substituents present, one of them has to occupy the hypervalent ligand position, creating an opportunity to use I(III) compounds as organic group-transfer reagents. The cyclic species with iodine atom being part of the ring (**6**-**7**) have considerably higher thermal stability compared to the noncyclic analogs, due to a positive entropy effect.[18]

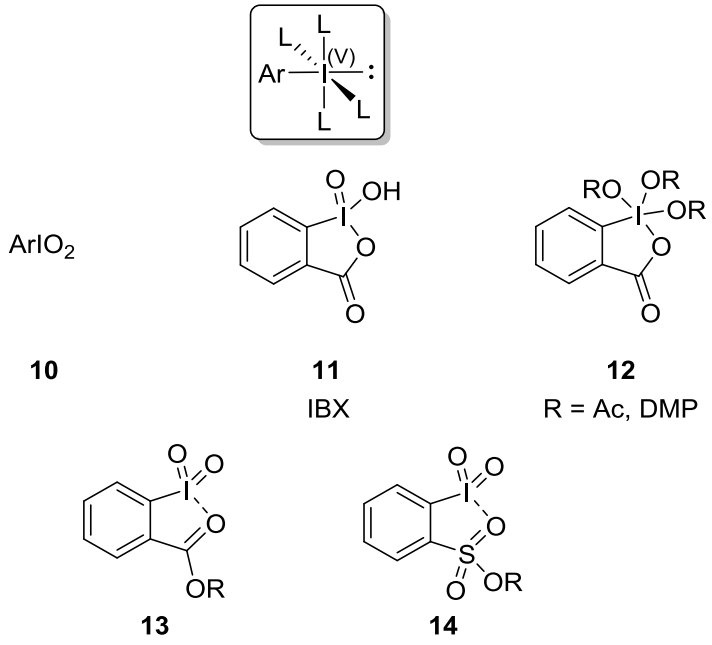


Figure 1.3. General classes of organoiodine(V) compounds and some important examples.

Organoiodine(V) compounds have found applications mostly as powerful and selective oxidants. Important examples are iodoxyarenes (also called iodylarenes) **10**, and the cyclic benziodoxole derivatives, such as IBX **11** and DMP **12** (Figure 1.3). A special class are *ortho*-substituted iodoxyarenes, *e.g.*, **13** and **14**, in which a pseudocycle is formed with the oxygen atom of an adjacent carbonyl or sulfonyl group.[19] Similarly as in the case of cyclic iodine(III) compounds, the cyclic and pseudeocyclic I(V) species are characterized by an increased stability, which is of importance as iodoxyarenes may be explosive. In iodine(V) compounds two perpendicular hypervalent bonds are present, hence their molecules adopt a (full or reduced) square pyramidal geometry.

1.2. Reactivity of hypervalent iodine compounds

The overall reactivity patterns of hypervalent iodine compounds in reactions such as oxidations and electrophilic group-transfers, can be explained by a number elementary steps that these species can undergo. Specifically, these are: ligand exchange, reductive elimination, attack of a nucleophile on a ligand, reductive α- and β-eliminations, homolytic R–I bond cleavage, and single-electron transfer to iodine.[20] It is impossible to fail to notice that organometallic transition metal complexes can participate in very similar elementary steps, making the hypervalent iodine chemistry closely resembling the organometallic chemistry. An important common feature of many of the elementary steps is that they lead to the reduction of the iodine atom and, thus, the loss of the hypervalency. As mentioned above, this is a highly exothermic process and it provides the driving force for the reaction.

For clarity, the description and examples below involve I(III) species, but the same processes are applicable in the case of I(V) compounds, as well.

Ligand exchange: The ligands in hypervalent iodine compounds can be displaced with external nucleophiles. The reaction is particularly facile for heteroatom-based ligands. The ligand exchange may occur either via an associative or a dissociative pathway (Figure 1.4). The associative pathway initiates by the addition of a nucleophile to the iodine atom that for I(III) compounds generates a 12-I-4 square-planar intermediate. Such species has been experimentally characterized for the reaction between ICl_3 and benzyltrimethylammonium chloride, which resulted in the formation of benzyltrimethylammonium tetrachloroiodate[21] that was analyzed by X-ray crystallography.[22] However, typically the tetra-coordinate 12-I-4 intermediate is not stable and it rapidly dissociates one of the ligands to regenerate the tri-

coordinate T-shaped I(III) species. Conversely, the alternative dissociative ligand exchange pathway proceeds via the initial departure of a ligand to form a di-coordinate 8-I-2 species, iodonium ion, which then binds the incoming nucleophile (Figure 1.4b).

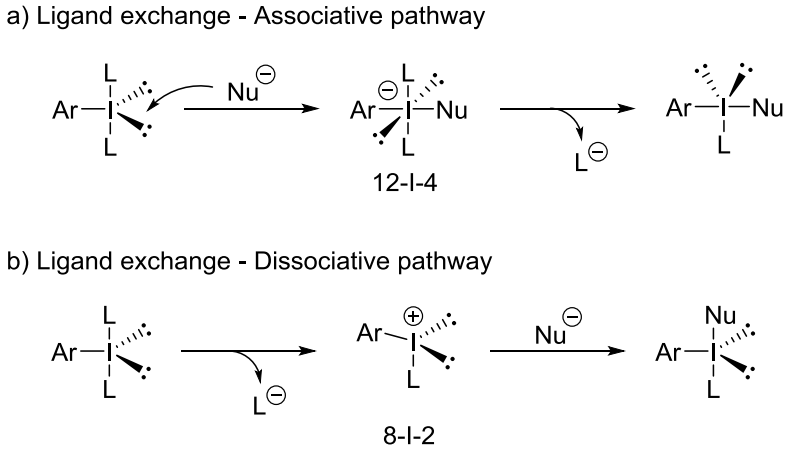


Figure 1.4. Ligand exchange - dissociative and associative pathways.

The ligand exchange process allows for the fast interchange of the substituents' positions, so only the most stable isomer of a given hypervalent iodine compound can be observed and isolated. However, the other, less stable isomers (with alternative arrangements of substituents around iodine) are accessible by fast equilibrium in solution and they may also engage in reactions.

The ligand exchange has been utilized for the synthesis of various iodine(III) species which could be further used for other synthetic applications. For example, [hydroxy(tosyloxy)iodo]arenes react with aryltrimethylsilanes in acetonitrile to give diaryliodonium tosylates (Figure 1.5a).[23] The reaction of (*E*)-styrylboronic acid and 2-iodosylbenzoic acid in the presence of TMSOTf produces vinylbenziodoxolones via ligand exchange (Figure 1.5b).[24] [[(+)-Menthyloxy](tosyloxy)iodo]benzene could be synthesized by the exchange of methoxyl ligand of [methoxy(tosyloxy)iodo]benzene with menthyloxy ligand (Figure 1.5c).[25]

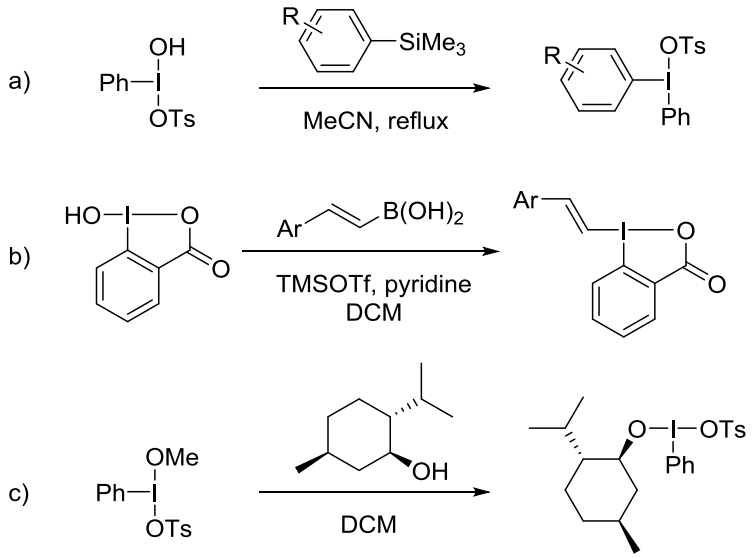


Figure 1.5. Selected examples of ligand exchange.

Reductive elimination: During the reductive elimination a bond is formed between two adjacent ligands and the iodine atom undergoes a 2-electron reduction (Figure 1.6). Computational studies have demonstrated that this process is concerted and proceeds via a 3-membered cyclic transition state.[26]

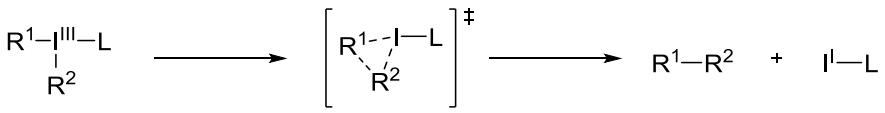


Figure 1.6. Reductive elimination.

The reductive elimination is the key elementary step in many of the group-transfer reactions, as it is one of the major ways via which hypervalent iodine can promote the formation of a new bond between two organic moieties. Thus, a typical group-transfer reaction employing a hypervalent iodine reagent involves a two-step mechanism composed of a ligand exchange, followed by a reductive elimination (Figure 1.7).[26] Such pathway can be considered as analogous to the mechanism of a transition metal-catalyzed cross-coupling that has been "truncated" by removing the oxidative addition step, making it a linear sequence instead of a catalytic cycle. Although this necessitates the use of a stoichiometric amount of the hypervalent iodine reagent, it is often still advantageous compared to metal-catalyzed cross-coupling due to environmental and economic advantages of iodine relative to transition metals (iodine is not

inherently toxic, much higher levels are allowed in pharmaceutical products; 2018-2023 prices: \$20-30/kg for I_2 vs. \$50 000-90 000/kg for Pd).

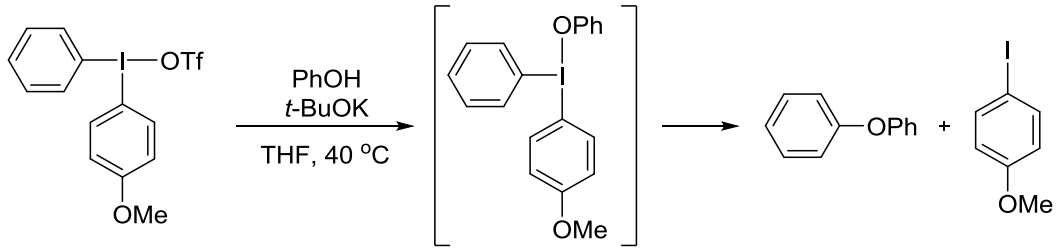


Figure 1.7. An example of arylation of phenol with diaryliodonium salt proceeding via ligand substitution/reductive elimination sequence.

Nucleophilic attack on a ligand: Hypervalent iodine atom is highly electron-deficient and it may induce an attack of a nucleophile on one of the ligands, resulting in the transfer of the electron density toward the iodine center. Depending on the nature of the ligand, the reaction may or may not lead to the loss of the hypervalency (Figure 1.8). In the former case, the iodine atom becomes a leaving group and undergoes a two-electron reduction in the process (Figure 1.8a).

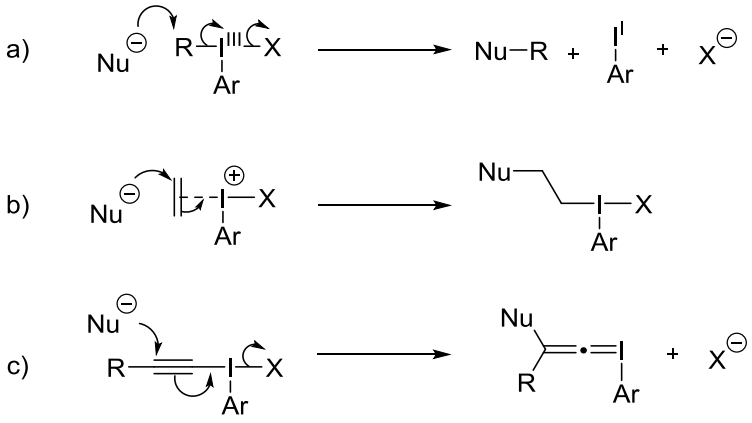


Figure 1.8. Different nucleophilic attacks on a ligand in iodine(III) compounds (other options are also possible).

The nucleophilic attack on a ligand occurring with the loss of hypervalency (sometimes referred to as the "outer sphere mechanism") gives similar overall outcome as the ligand exchange/reductive elimination sequence (the "inner sphere mechanism") and these two alternative pathways can typically only be distinguished through computations. In some cases, however, they are discernible by the stereochemical course of a reaction, as for example during

the bis(trifluoroacetoxylation) of cyclohexene, which needs to proceed via two consecutive attacks on the ligand in order to afford the observed *cis* product (Figure 1.9a).[27]

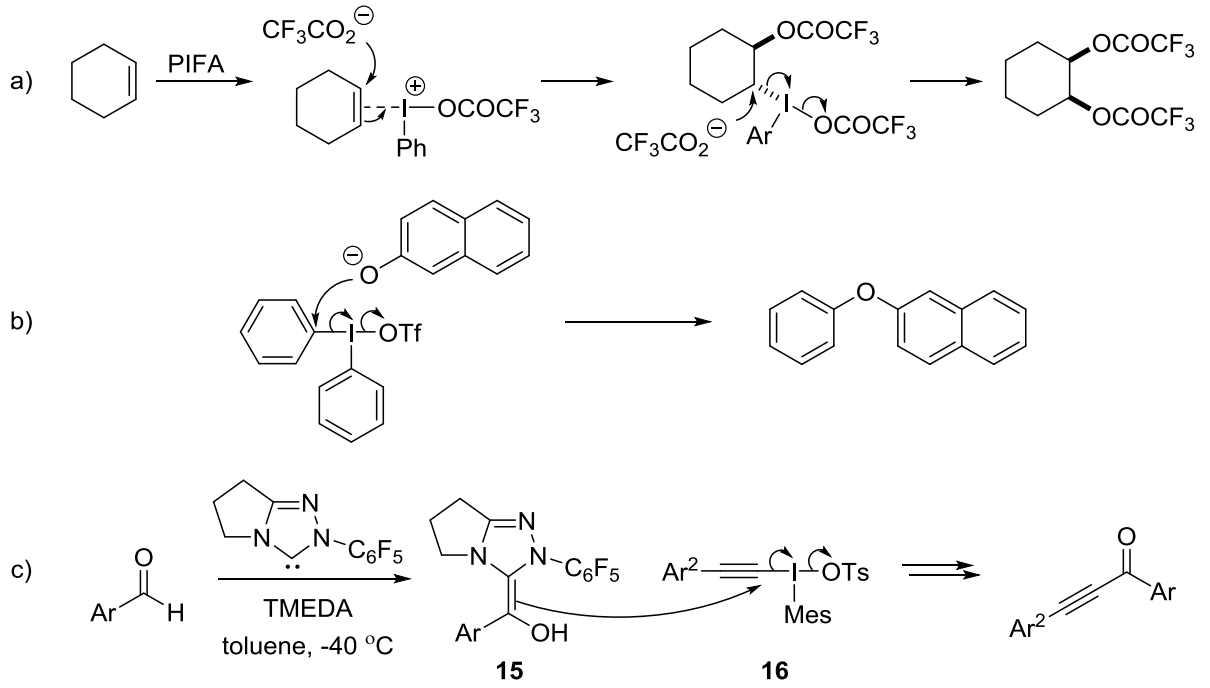


Figure 1.9. Examples of reactions involving the nucleophilic attack on a ligand.

The leaving group ability of the hypervalent iodine atom is so high that it may undergo a direct substitution not only at sp^3-, but also at sp^2-, or at even sp-hybridized carbon. For instance, a 2-naphtholate ion directly attacks the *ipso* position in a diaryliodonium salt displacing iodine and generating the corresponding diaryl ether (Figure 1.9b), as evidenced by DFT calculations.[28] Recently, the Kalek group reported the alkynylation of aldehydes with alkynyl(aryl)iodonium salts **16** catalyzed by an *N*-heterocyclic carbene (Figure 1.9c). This transformation proceeds via a direct substitution of iodine at an acetylenic carbon by a nucleophilic Breslow intermediate **15**. Such a course of the reaction has been supported both experimentally and computationally.[29]

Reductive α- and β-elimination: Due to the electron-poor character of the hypervalent iodine atom and its superior leaving group ability, ligands containing alkyl groups with hydrogens in α- or β-positions undergo a facile elimination with the simultaneous two-electron reduction of the iodine (Figure 1.10a-b). The α-elimination yields a carbene (Figure 1.10a), while depending on the M atom, the β-elimination produces a C–C multiple bond, carbonyl, or imine (Figure

1.10b). A very weak base, such as a solvent molecule or even another ligand on iodine, is sufficient to abstract the proton, hence, hypervalent iodine compounds with alkyl substituents are inherently labile and they can only exist as short-lived intermediates (as, for example, in the reaction depicted in Figure 1.9a). Thus, the only stable hypervalent iodine derivatives with alkyl ligands are those not containing hydrogens, for example perfluorinated ones, such as the Togni reagents (**6** in Figure 1.2).

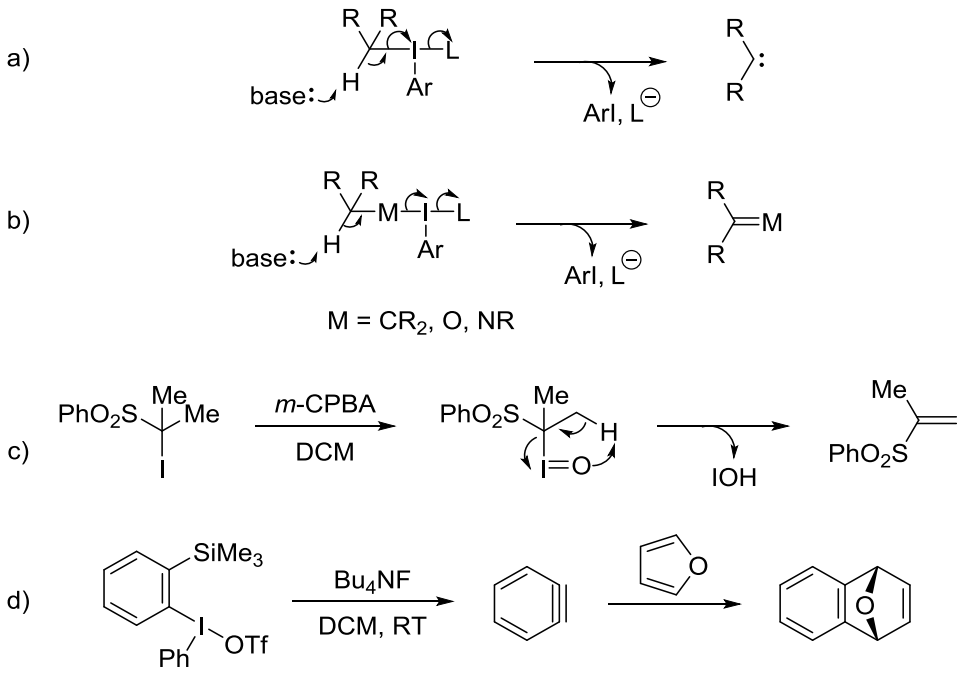


Figure 1.10. α- and β-elimination and selected examples.

A synthetic example of the application of the β-elimination is the preparation of olefins from alkyl iodides upon treatment with *m*-CPBA. Under these conditions, the iodine is oxidized to the hypervalent iodoso species, which then spontaneously undergoes a β-elimination, with the oxygen atom playing the role of an internal base, to give unsaturated compounds (Figure 1.10c).[30] Not only a base-assisted deprotonation can lead to the elimination. Kitamura and co-workers reported a fluoride ion-induced reductive β-elimination from [2-(trimethylsilyl)phenyl]iodonium triflate to generate benzyne, further using it for Diels-Alder reaction, affording cycloadducts in high yields (Figure 1.10d).[31]

Homolytic cleavage of I–X bond: Bond dissociation energies of the hypervalent bonds, including these in present hypervalent iodine compounds, are relatively low and their homolytic cleavage under photochemical or thermal conditions is often facile (Figure 1.11a).

Various synthetic transformations such as chlorination, bromination, azidation of C–H bonds, and oxidation of alcohols, employ iodine(III) reagents as the source of free-radicals. For example, bromobenziodoxoles **17** have been used for the allylic and benzylic bromination via the generation of a bromine radical (Figure 1.11b).[18,32] The homolytic bond cleavage in diaryliodonium salts has also been employed to photoinitiate polymerization processes.[33]

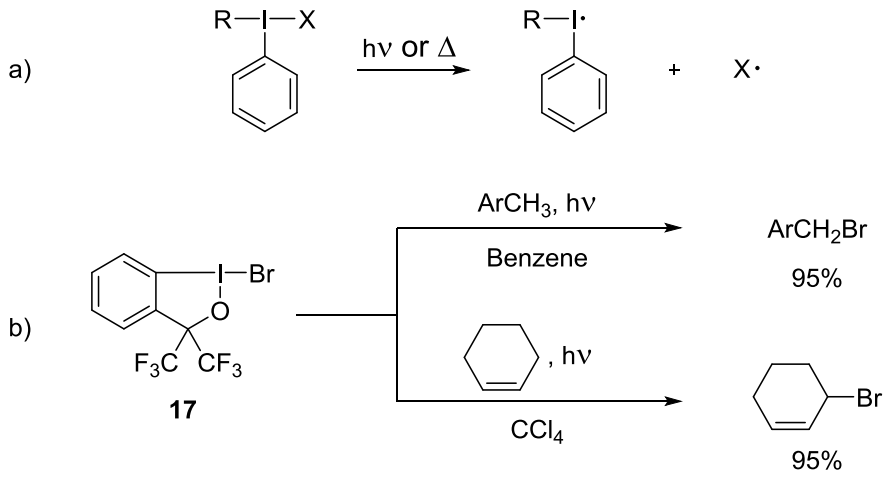


Figure 1.11. Homolytic cleavage of I–X bond and a synthetic example.

Single electron transfer to iodine: Hypervalent iodine(III) compounds have been utilized as selective and efficient SET oxidizing agents. Under the SET reduction conditions, first a iodanyl(II) intermediate is formed, which subsequently undergoes a fragmentation to generate R• radical (Figure 1.12a). R•, in turn, can further engage in typical radical processes, such as addition to arenes, heteroarenes, alkenes and alkynes, hydrogen atom transfer, etc.

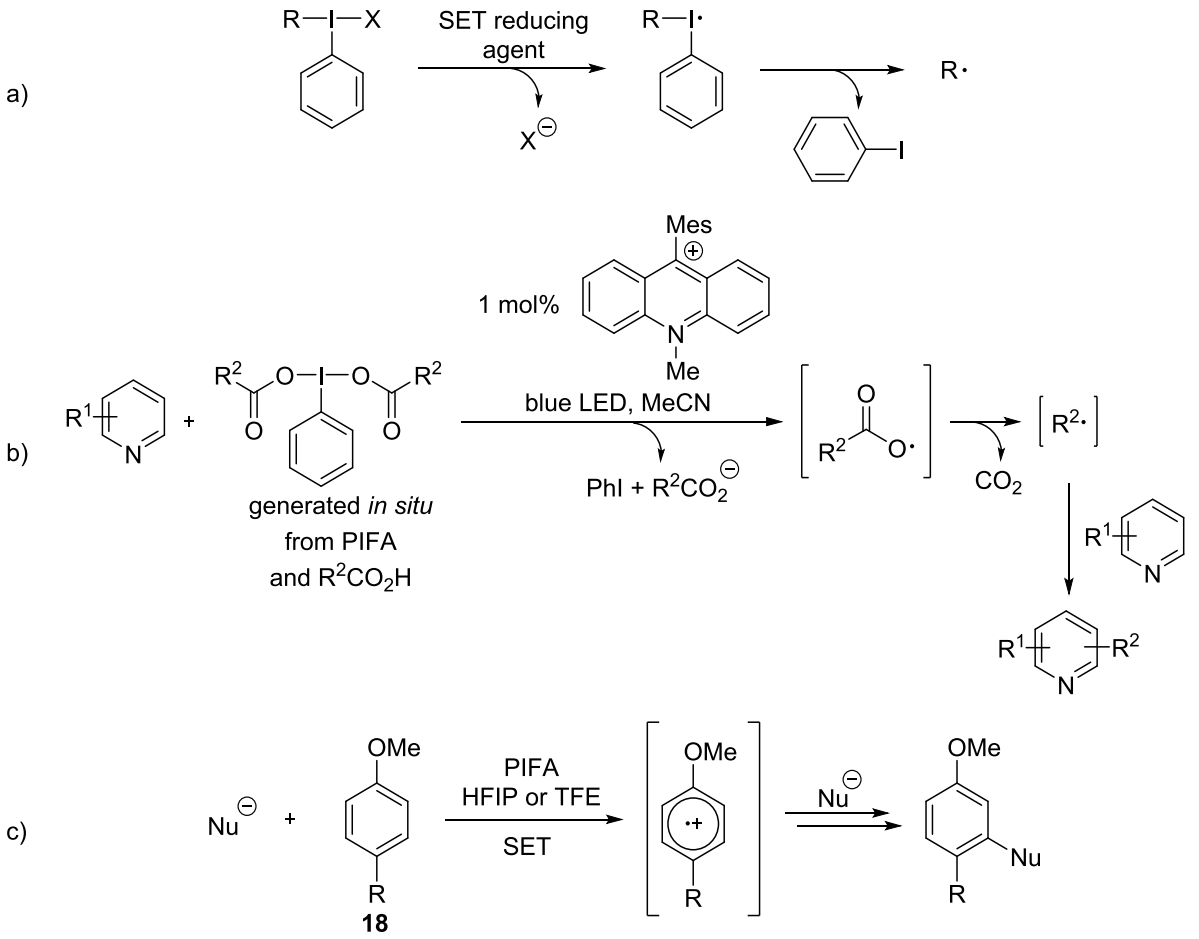


Figure 1.12. SET reduction of I(III) compound and examples of its synthetic applications.

Various single electron transfer (SET) reducing reagents, such as transition metal complexes, photocatalysts, and organic reductants, have been used in this type of reactions. For instance, 9-mesityl-10-methylacridinium was used by Genovino as a photocatalyst for the alkylation of nitrogen heteroaromatics with phenyliodine dicarboxylates (Figure 1.12b).[34] The key alkyl radical intermediates are generated through the decarboxylation of the incipient carboxylic radicals originating from the SET reduction of I(III) reagents with the excited photocatalyst. Kita has reported an interesting example, wherein the PIFA is used as a SET oxidant to effect a nucleophilic substitution in *para*-substituted anisoles **18** (Figure 1.12c).[35]

1.3. Hypervalent iodine-promoted oxidations

One of the most important applications of the hypervalent iodine compounds in organic synthesis are oxidation reactions. Due to the large energy gain associated with the loss of hypervalency, both iodine(III) and (V) reagents display high potency to accept electrons from organic substrates. Despite the high oxidative power, the hypervalent iodine-promoted oxidations are often very selective and confined to specific parts of the substrate molecule. Importantly, the oxidation reactions involving the hypervalent iodine reagents are not limited to simple functional group interconversions (*e.g.*, alcohol→ketone), but they also allow for the formation of new chemical bonds, increasing the molecular complexity.

The hypervalent iodine-promoted oxidations are, by convention, conceptually distinguished from the group transfer reactions (outlined in section 1.4, below). Although from the organic reactant viewpoint these are both oxidative transformations, during "pure" oxidations technically no part of the iodine-containing reagent gets incorporated into the reaction product and its sole role is to accept the electrons. However, this definition is not clear cut and the border between the two reaction types is somewhat blurred. One feature that can be considered characteristic for at least some of the oxidation reactions is that they can be made catalytic in the iodine reagent. That is, it is applied in a substoichiometric quantity in a combination with a stoichiometric terminal oxidant in order to *in situ* regenerate the hypervalent iodine species. This is particularly valuable when using precious chiral iodine oxidants (see below).

In section 1.3.1, the most eminent hypervalent iodine-promoted oxidations, namely of alcohols and olefins, are briefly presented. Then, section 1.3.2 discusses in detail the oxidative dearomatization of phenols, which is relevant for this thesis.

1.3.1. Oxidation of alcohols and olefins

Hypervalent iodine reagents are commonly used for the oxidation of alcohols to the corresponding carbonyl compounds (and amines to imines). The mechanism of the reaction involves, first, the coordination of the substrate to the iodine center via the ligand exchange. Subsequently, a β-elimination takes place, leading to the carbonyl (or imine) product. As the carbonyl group has practically no affinity for the hypervalent iodine atom, the oxidation of primary alcohols selectively affords aldehydes with no over-oxidation.

For example, benzyl and allyl alcohols are oxidized with iodosobenzene to aldehydes (Figure 1.13a). Interestingly, this I(III) reagent does not oxidize aliphatic alcohols.[36] However, Kita reported that the combination of iodosobenzene and potassium bromide in water is a powerful oxidant for both primary and secondary alcohols (Figure 1.13b), probably due to KBr partially depolymerizing $(PhIO)_n$.[37] Lewis acids such as $BF_3{\cdot}OEt_2$ accelerate the oxidation of alcohols with iodine(III) reagents by the coordination of BF_3 to the acetoxy ligand, increasing the propensity of I(III) center to accept electrons (Figure 1.13c).[38] Combination of a catalytic amount of TEMPO with PIDA as a stoichiometric oxidant was used to convert primary and secondary alcohols to carbonyl compounds, without over-oxidation.[39] The PIDA-TEMPO system selectively converts primary alcohols into aldehydes in the presence of secondary alcohols (Figure 1.13d). To achieve the oxidation of primary alcohols all the way to carboxylic acids and their derivatives, PIDA is combined with molecular iodine in acetonitrile.[40] Primary alcohols can be converted to methyl esters directly by the same system in methanol (Figure 1.13e).

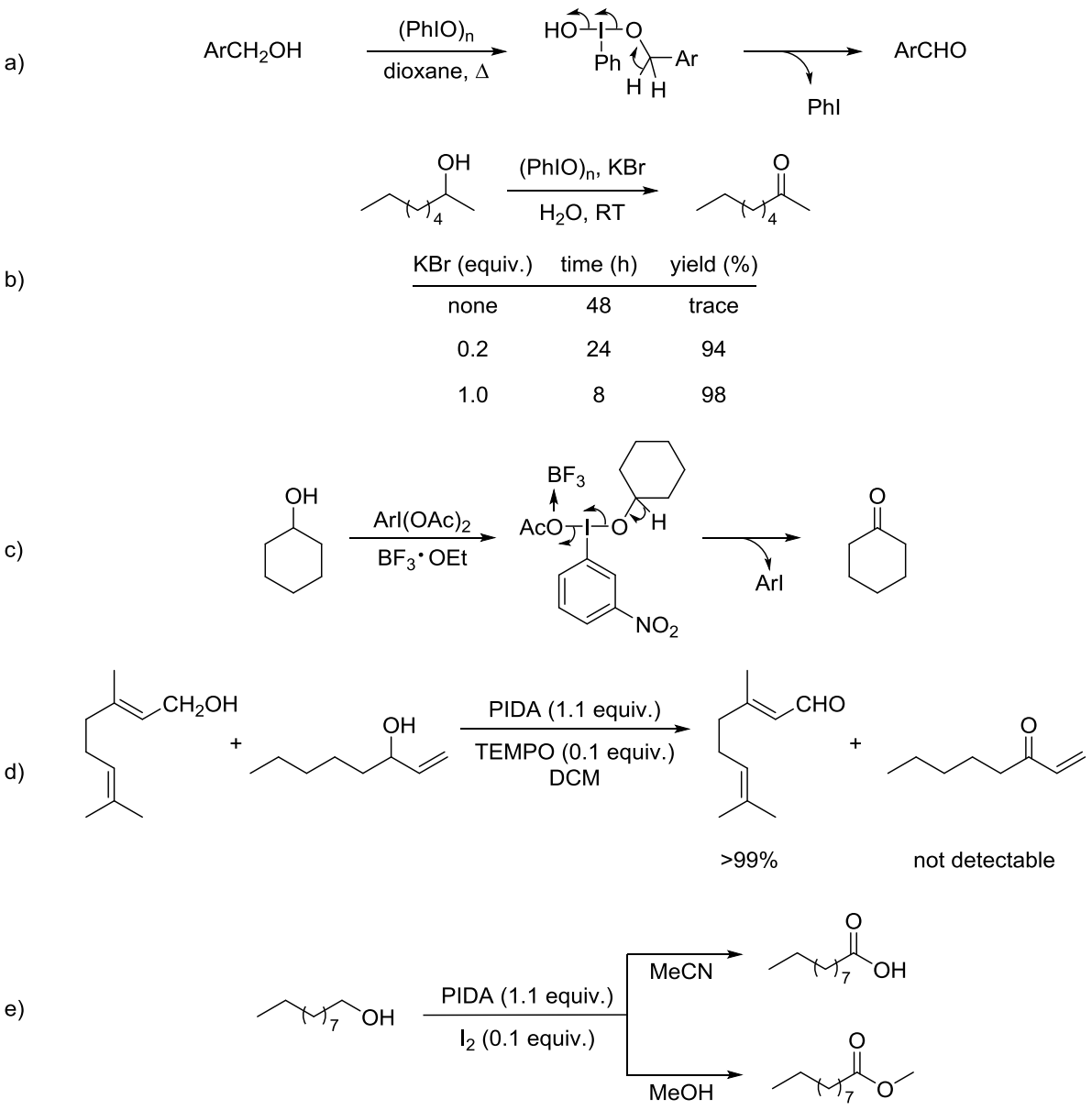


Figure 1.13. Oxidation of alcohols by iodine(III) reagents.

The prominent reagents for the oxidation of alcohols are Dess-Martin periodinane and its cyclic precursor *ortho*-iodoxybenzoic acid (IBX).[41,42] The mild reaction conditions and the broad functional group tolerance make these iodine(V) reagents highly attractive (Figure 1.14). Although Dess-Martin reagent is used as a highly efficient oxidant in many syntheses, IBX may be a cheaper alternative in some cases, but it is potentially explosive and insoluble in common organic solvents. For example, IBX smoothly oxidizes 1,2-glycols to α-ketols or α-diketones without cleaving the C-C bond (Figure 1.14b). Iodine(V) reagents are more potent oxidants

compared to I(III) compounds, which usually require an additional activator, as mentioned above.

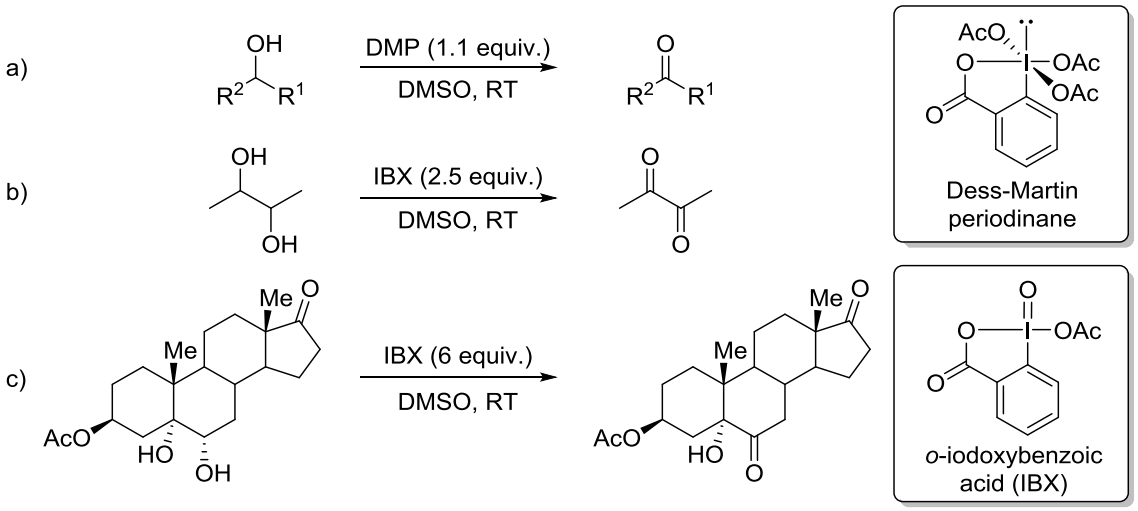


Figure 1.14. Oxidation of alcohols by iodine(V) reagents.

Alkenes can be oxidatively difunctionalized by hypervalent iodine reagents with the introduction of two vicinal functional groups, often in a stereoselective manner. A wide range of carbon nucleophiles as well as heteroatom functional groups can be attached to a carbon–carbon double bond in this way. A typical reaction mechanism for the oxidative functionalization of an alkene with hypervalent iodine(III) involves the initial formation of a complex with the olefin's π-orbital and the electron-deficient iodine center. This complex undergoes a nucleophilic attack on the alkene ligand, affording an intermediate containing an alkyl substituent at iodine(III). Although such species are inherently unstable due to possible β-elimination, the nucleophilic substitution of iodine via the attack on the alkyl ligand is much faster, leading to the 1,2-difunctionalized product (Figure 1.15a). For example, aminofluorination of styrenes in good yields with a complete regioselectivity was achieved using 2,5-dimethylphenyliodonium difluoride in the presence of *N*-methyl tosylamide (Figure 1.15b).[43,44] The diamination products formed in minor quantity.

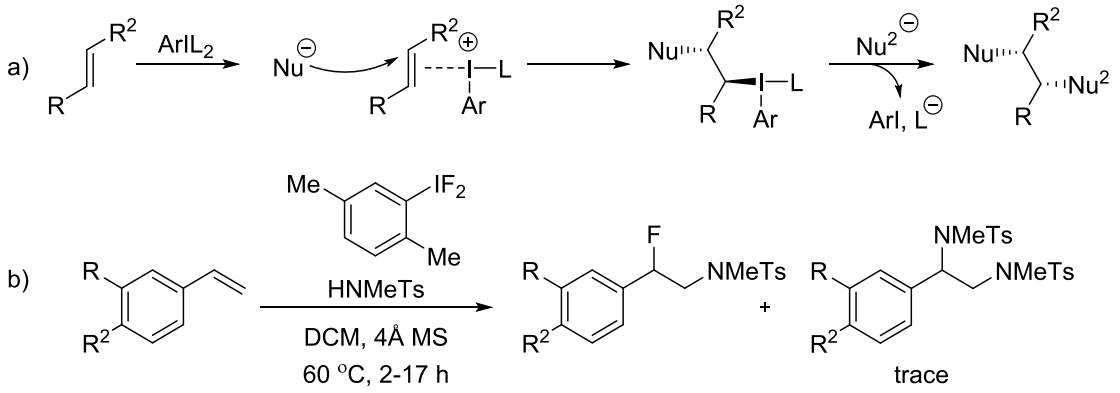


Figure 1.15. Alkene oxidation.

In the last decade, the olefin oxidation reactions have been turned catalytic, wherein the active iodine(III) reagent is generated *in situ* by the use of stoichiometric amounts of terminal oxidants. Chiral iodoarenes (having central, axial, and helical chirality) have been used to develop enantioselctive protocols. One of the first examples was Kita's asymmetric spiro-oxocyclization, which will be discussed more in section 1.3.2. In the context of asymmetric olefin oxidations, Fujita developed an asymmetric difunctionalization of *ortho*-alkenylbenzoates employing a 10 mol% catalyst loading of chiral iodoarene **19** and *m*-CPBA as the co-oxidant, providing an efficient route toward 4-hydroxyisochroman-1-one motif (Figure 1.16a).[45] Vicinal difluorination of alkenes was also achieved in an enantioselective manner with iodoarene catalyst **20** (Figure 1.16b).[46] Recently, many related reactions have been reported.[47]

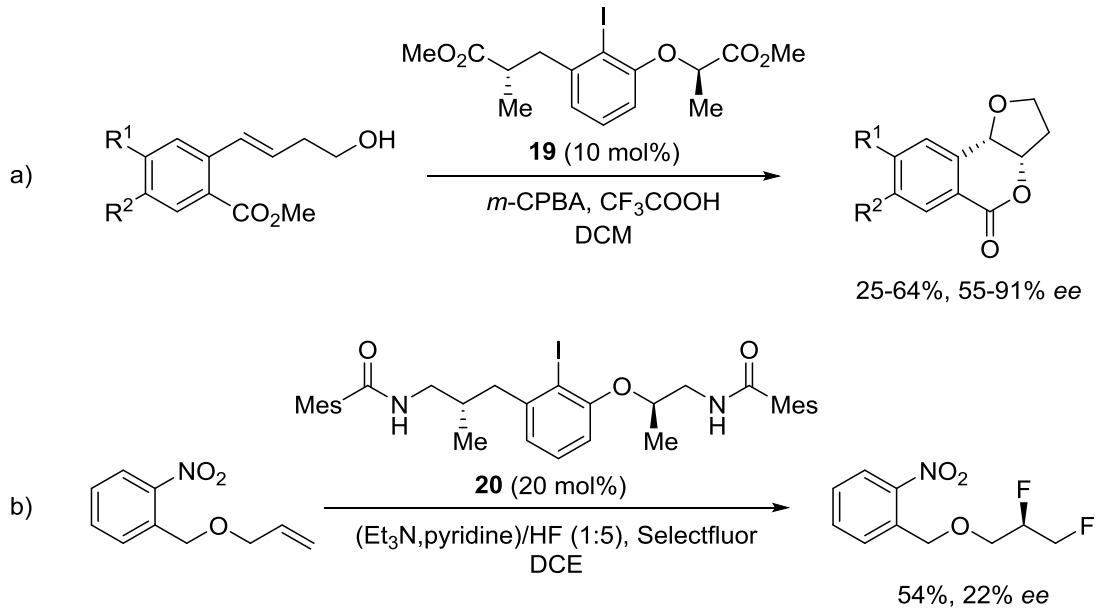


Figure 1.16. Examples of catalytic asymmetric oxidations of alkenes.

1.3.2. Oxidative dearomatization of phenols

Aromatic compounds can serve as valuable building blocks for the construction of alicyclic moieties in complex molecules. The oxidative dearomatization of phenols promoted by hypervalent iodine reagents has been particularly successful in this context (Figure 1.17).[48] This stems from several advantageous features of the reaction. First, the transformation is facile and universal, it can engage an array of nucleophiles, both carbon- and heteroatom-based. Secondly, the resulting cyclohexadienone products are versatile synthetic intermediates, suitable for a variety of further functionalizations to rapidly construct diverse and complex carbo- and heteropolycyclic architectures. Finally upon losing the aromaticity, a planar arenol transforms into a three-dimensional structure, possessing a stereogenic carbon, the configuration of which may be controlled by adopting asymmetric protocols.

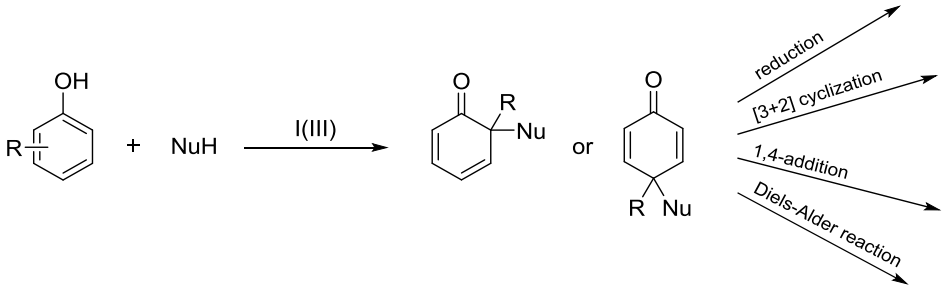


Figure 1.17. Oxidative dearomatization of phenols promoted by hypervalent iodine reagents.

There have been two major general mechanisms proposed in literature for the dearomatization of phenols with iodine(III) reagents. In the first scenario, referred to as associative, following the incipient coordination of the phenolic oxygen to the iodine(III) center, intermediate **21** undergoes a nucleophilic attack at the *ortho*- or *para*-position of the ring with a simultaneous dearomatization and a reduction of iodine (Figure 1.18a).[49] Alternatively, intermediate **21** may undergo a unimolecular fragmentation with the reduction of iodine, leading to the formation of phenoxenium ion, which upon the addition of the nucleophile affords the dearomatized products (dissociative pathway; Figure 1.18b).[50,51] Neither of these pathways is universal, as they cannot fully account for the observed features of all reactions. For instance, the associative pathway does not provide explanation why in some reactions the addition of a nucleophile exhibits a clear preference to occur at the position of the phenolic ring containing a substituent, while the other *ortho* or *para* sites are unsubstituted, thus more sterically available. On the other hand, the dissociative pathway cannot rationalize the enantioselectivity of the reactions carried out in the presence of chiral iodine(III) regents or catalysts.

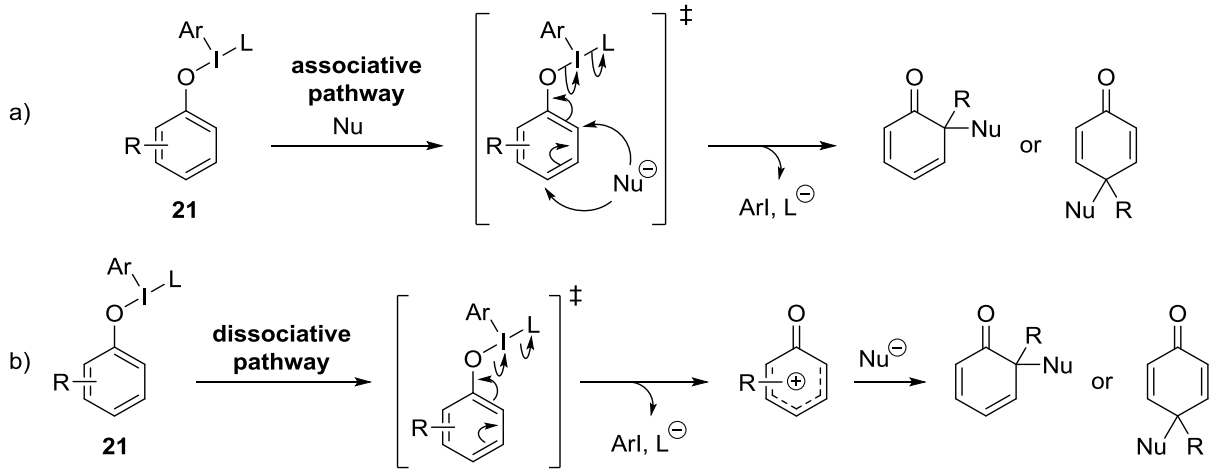


Figure 1.18. General mechanistic pathways proposed for the oxidative dearomatizing addition of nucleophiles to phenols.

Kalek's recent work on iodine(III)-promoted oxidative dearomatizing hydroxylation of 2,4-di(*tert*-butyl)phenol has demonstrated that there exists also a possibility of a radical chain pathway.[52] The phenol substrate is converted into the corresponding aryloxyl radical **23**, which constitutes the key chain-carrying intermediate. The nucleophile (H_2O) is activated by the coordination to the I(III) center to form the actual oxidant **22**, which reacts with the aryloxyl radical **23**, to generate the product together with a iodanyl(II) radical **24** that further propagates the chain (Figure 1.19).

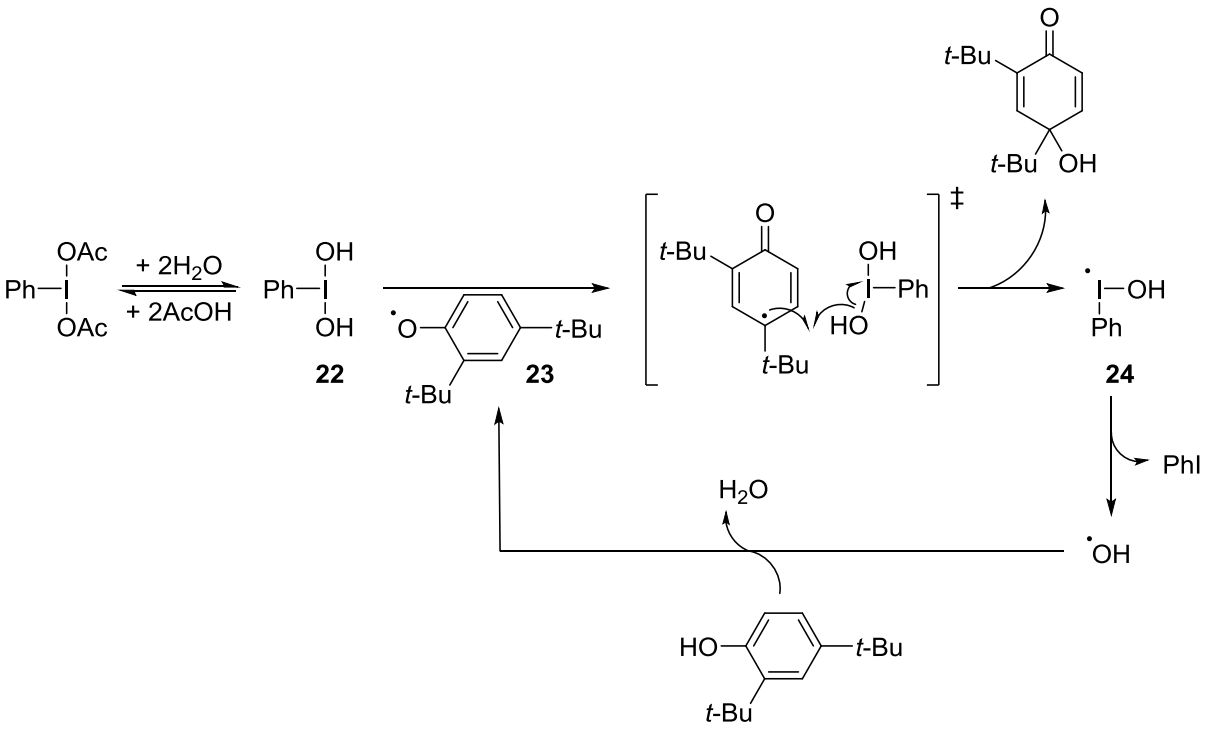


Figure 1.19. Radical-chain pathway of the oxidative dearomatizing hydroxylation of phenols.

Overall, depending on the exact structure of the arenol and the nucleophile, the iodine(III)-promoted dearomatization can follow either of the mechanistic routes depicted in Figures 1.18 and 1.19, as shown by mechanistic investigations using experimental and computational techniques.[49,52,53]

The simplest dearomatizing transformation is the conversion of hydroquinones into the corresponding benzoquinones (Figure 1.20).[54] Usually PIDA is used for such reactions to afford the products in excellent yields. The application of polyiodostyrene and aminomethylated polystyrene based polymer-supported reagents has led to a cleaner oxidation, additionally allowing for the easy recycling of the reagent.[55,56] Kita found that in aqueous oxidations of phenolic substrates, μ-oxobridged hypervalent iodine trifluoroacetate reagent **25** is generally more reactive than the corresponding monomeric species.[57]

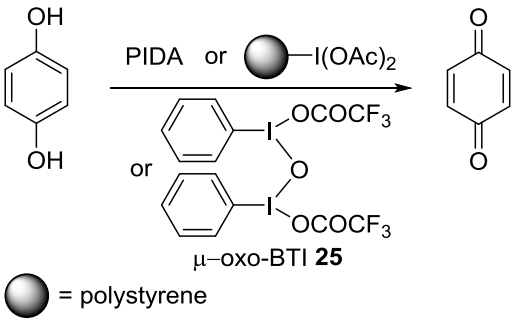


Figure 1.20. Iodine(III)-mediated oxidation of hydroquinone.

Phenols can be oxidatively dearomatized in the presence of various external nucleophiles. Figure 1.21a presents the oxidation of substituted phenols **26** with PIDA in aqueous acetonitrile to afford *para*-quinols.[58] Similarly, quinone monoketals can be obtained from *para*-alkoxyphenols and *para*-alkoxynaphthols in the presence of alcohols (Figure 1.21b).[59]

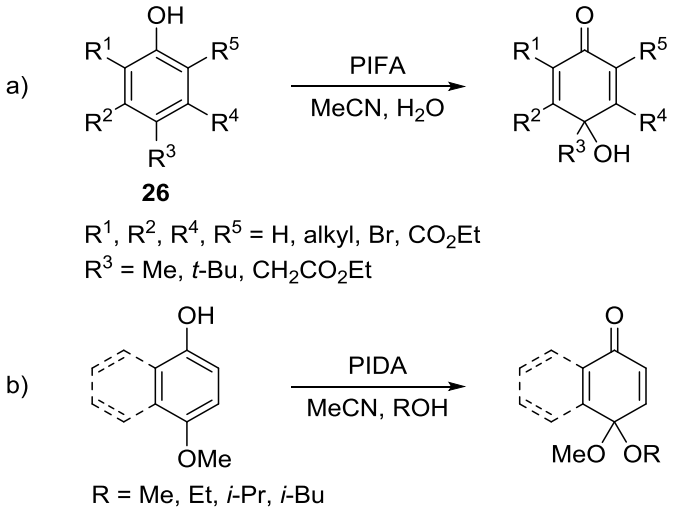


Figure 1.21. Intermolecular oxidative dearomatization of phenols by oxygen nucleophiles.

Acetamides can be obtained in synthetically useful yields by PIDA oxidation of phenolic substrates in a 1:1 mixture of acetonitrile and HFIP through a Ritter type reaction. Nitrile solvents other than MeCN can also be used in the reaction.[60] For instance, the oxidation of *para*-cresol in the presence of propionitrile deliveres the corresponding propionamide (Figure 1.22).

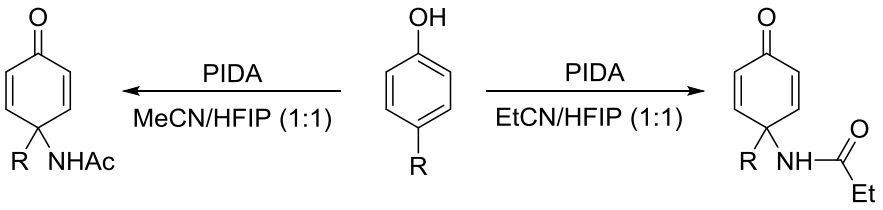


Figure 1.22. Intermolecular oxidative dearomatization of phenols by nitrogen nucleophiles.

Carbon nucleophiles can also be used in the reaction. Canesi reported the oxidative allylation of polysubstituted phenols **27**.[61] This reaction, occurring in useful to good yields, either in trifluoroethanol or hexafluoro-2-propanol provides a rapid access to dienones containing a quaternary carbon center (Figure 1.23).

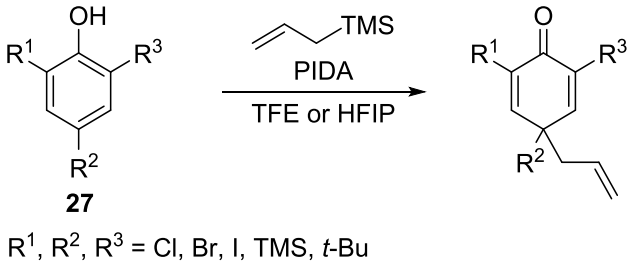


Figure 1.23. Intermolecular oxidative dearomatization of phenols with carbon nucleophiles.

Nucleophilic *para*-fluorination of 4-alkylphenols by hypervalent iodine reagent and pyridinium polyhydrogen fluoride (PPHF), as a fluoride anion source, afforded 4-fluorocyclohexa-2,5-dienones (Figure 1.24a).[62] The method was extended to the fluorination of bicyclic and polycyclic phenols (Figure 1.24b).[63,64]

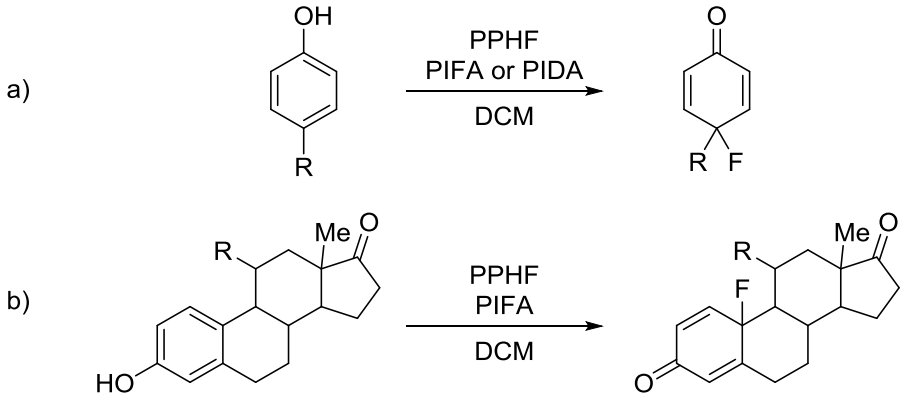


Figure 1.24. Intermolecular oxidative dearomatization of phenols by fluoride anion.

Oxidative dearomatization of phenols containing tethered nucleophilic groups at *ortho*- or *para*- positions is a powerful strategy in the synthesis of spirocyclic compounds. Kita's pioneering work on the synthesis of spirodienones from *N*-acyltyramines using iodine(III) reagent has paved the way for many spirocyclization reactions.[65] Various oxo-, aza-, and carbo-spirocyclizations were accomplished using this apporach, and new methods continue to be reported, either by using iodine(III) reagent in a stoichiometric or catalytic amount with a terminal oxidant.[66]

Wipf and Kim employed PIDA for the spirocyclization of *N*-protected tyrosine **28** to spirolactone **29**. The spirocyclization reaction was carried out in methanol using the stoichiometric amount of PIDA and spirolactone **29** was isolated in 35% yield (Figure 1.25a).[67] Fan combined iodosobenzene-mediated oxidative dearomatization of 3-(3-alkynyl-4-hydroxyphenyl)propanoic **30** acid with a cascade transition metal-catalyzed cyclization/addition/aromatization/lactamization, to synthesize furoquinolinone **31** and angelicin derivatives (Figure 1.25b).[68]

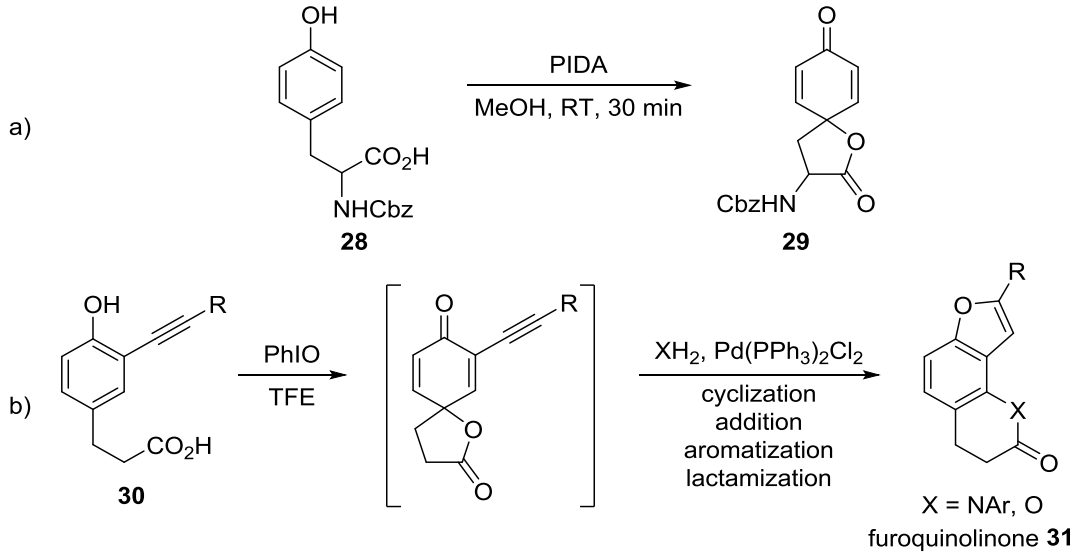


Figure 1.25. Examples of oxo-spirocyclization.

Ciufolini reported various methods for the oxidative spiro-amination/amidation of phenols to form *N*-substituted spiro compounds (Figure 1.26).[69–73]

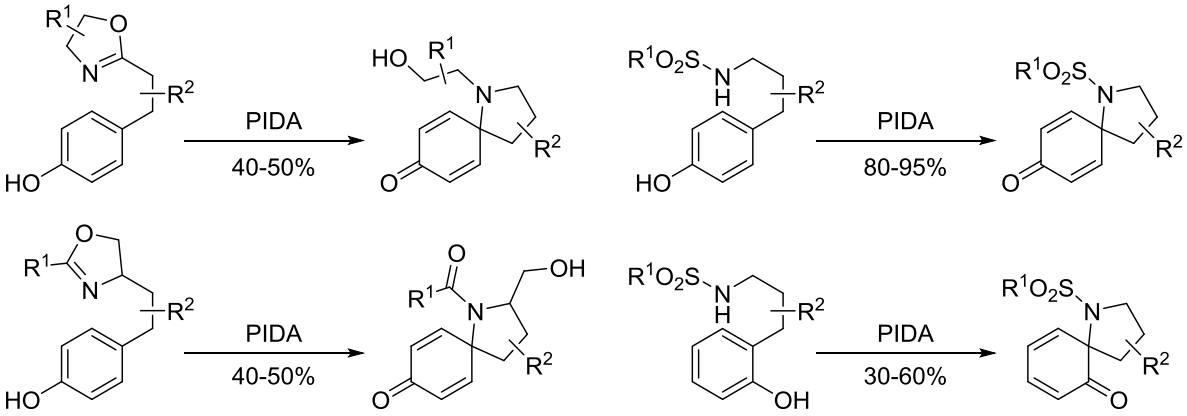


Figure 1.26. Ciufolini's various modes of oxidative spiro-amination/amidation.

In the course of synthetic studies toward discorhabdin alkaloids, Kita used PIFA for the dearomatization of *ortho*- and *para*-substituted phenol derivatives bearing aminoquinones to access azacarbocyclic spirodienones (Figure 1.27).[74–76]

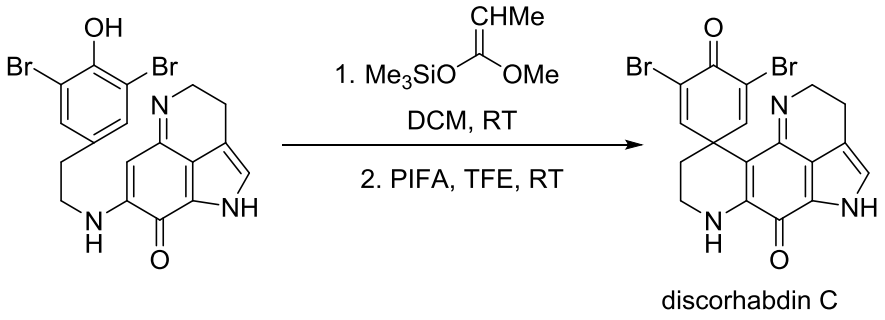


Figure 1.27. Synthesis of discorhabdin C using PIFA.

Phenolic amides **32**, phenolic benzyl amide **34,** and phenolic benzamido-acrylate homolog **36** have been carbo-spirocyclized, leading to β-lactam spirocyclohexa-2,5-dienones **33**, carbo-spirocyclic pyrrolidone derivative **35**, and carbo-spirocycles **37**, respectively (Figure 1.28).[77,78]

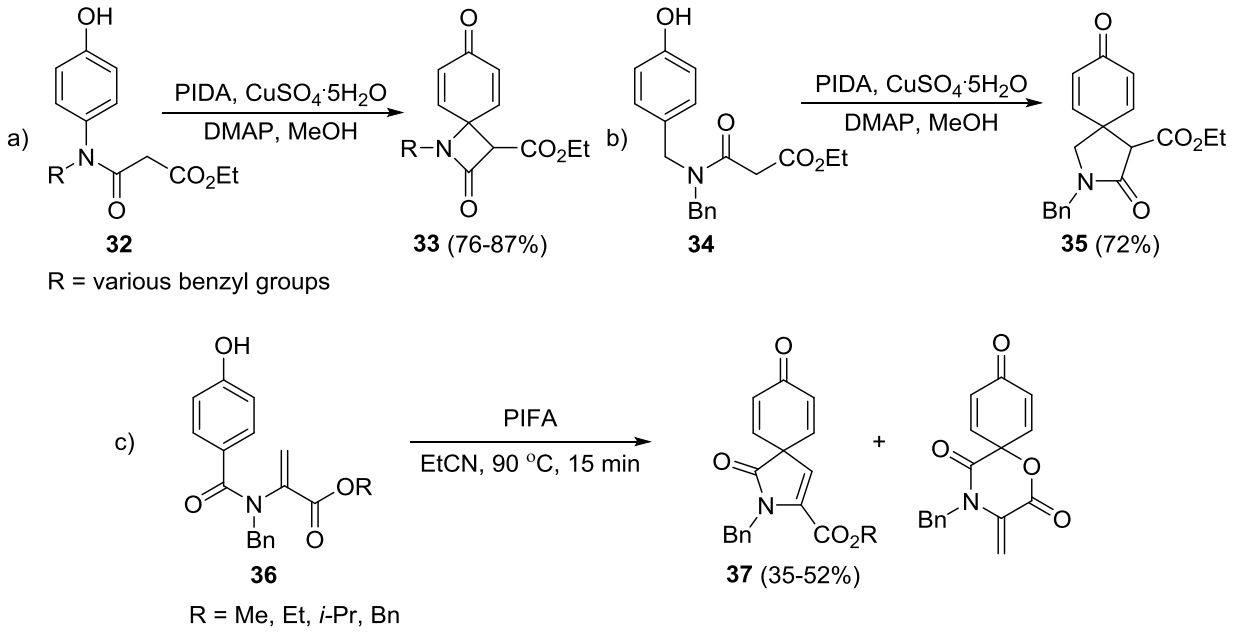


Figure 1.28. Examples of carbo-spirocyclizations.

Wang reported an intramolecular variant of the reaction depicted in Figure 1.23 to access all-carbon spirobicycles.[79] Phenols that are *ortho*-substituted by a pendant allylsilane **38** were converted to spirocycle **39** with PIDA in TFE/DCM solvent mixture at -40 °C (Figure 1.29a). Similarly, under slightly modified reaction conditions, vinyl methyl ether-functionalized phenols **40** gave acetal terminated spiro-carbocyclization products **41** (Figure 1.29b).

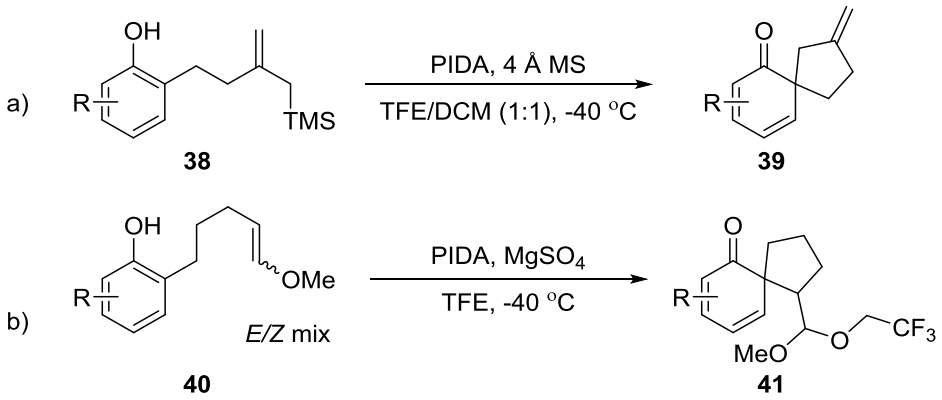


Figure 1.29. Wang's *ortho*-dearomative spiro-carbocyclization of phenols.

In 2011, Kita suggested the use of μ-oxoBTI **25** over PIDA or PIFA to generate spirocyclic cyclohexadienones via the dearomatization (Figure 1.30).[80] A comparative study between the

bridged iodine(III) reagent **25** and PIFA showed that the reaction products were obtained in higher yields using the former compound.

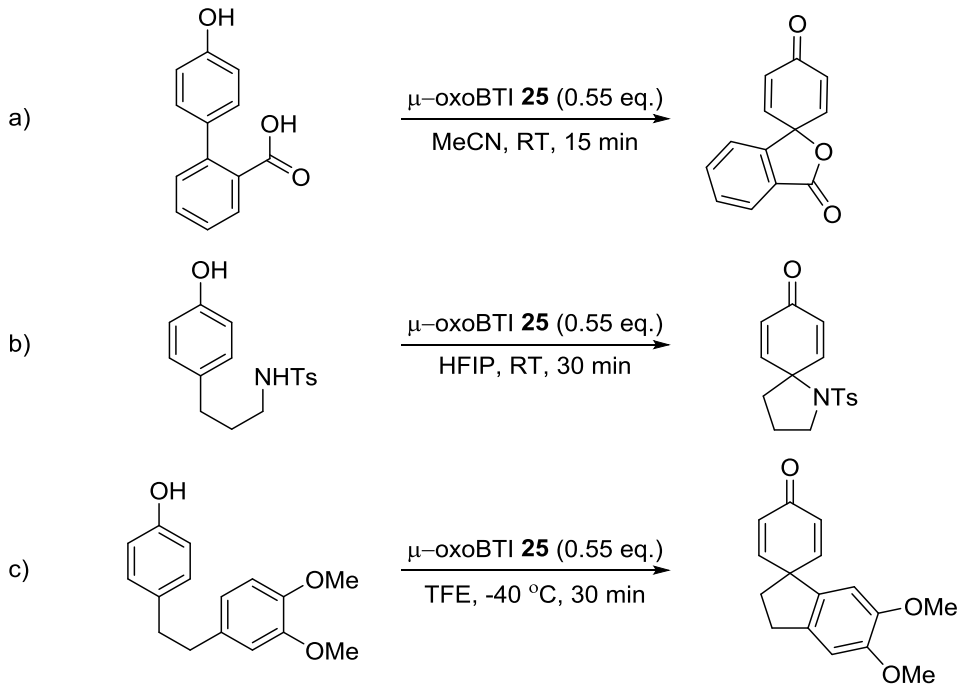


Figure 1.30. Kita's μ-oxoBTI-mediated oxo-, aza-, and carbo-spirocyclization.

It is possible to carry out the spirocyclization using catalytic amounts of hypervalent iodine species, generated *in situ*, by the oxidation of catalytic amounts of iodoarene with a terminal oxidant, such as *m*-CPBA or Oxone. Kita established the efficient catalytic reactions involving hypervalent iodine(III) species at room temperature by using *m*-CPBA as an effective chemical cooxidant and TFA as an additive (Figure 1.31).[81]

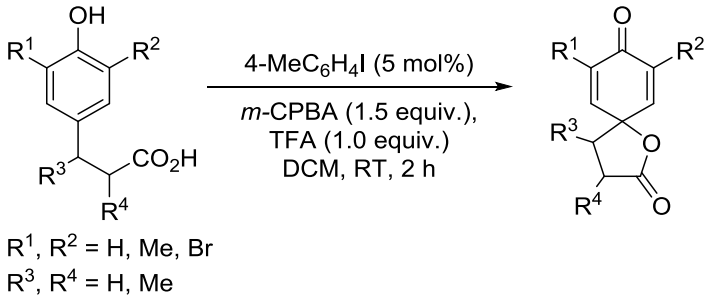


Figure 1.31. Iodoarene-catalyzed spirolactonization of *para*-substituted phenols to spirolactones.

One of the most important developments in area of spirocyclization has been the asymmetric synthesis of spirolactones via phenol dearomatization, using catalytic amounts of the chiral spirobiindane-based bis(iodoarene) **42** in the presence of *m*-CPBA as the terminal oxidant (Figure 1.32).[82] The *in situ* regeneration of the catalyst iodine(III) form **43** allows for the economical use of the precious chiral iodoarene **42**. Ishihara and Uyanik have further developed many spirolactonization variants using more conformationally flexible and easier to access chiral iodoarene catalysts **44**, obtaining the products with enantiomeric excesses up to 92% (Figure 1.32).[83,84]

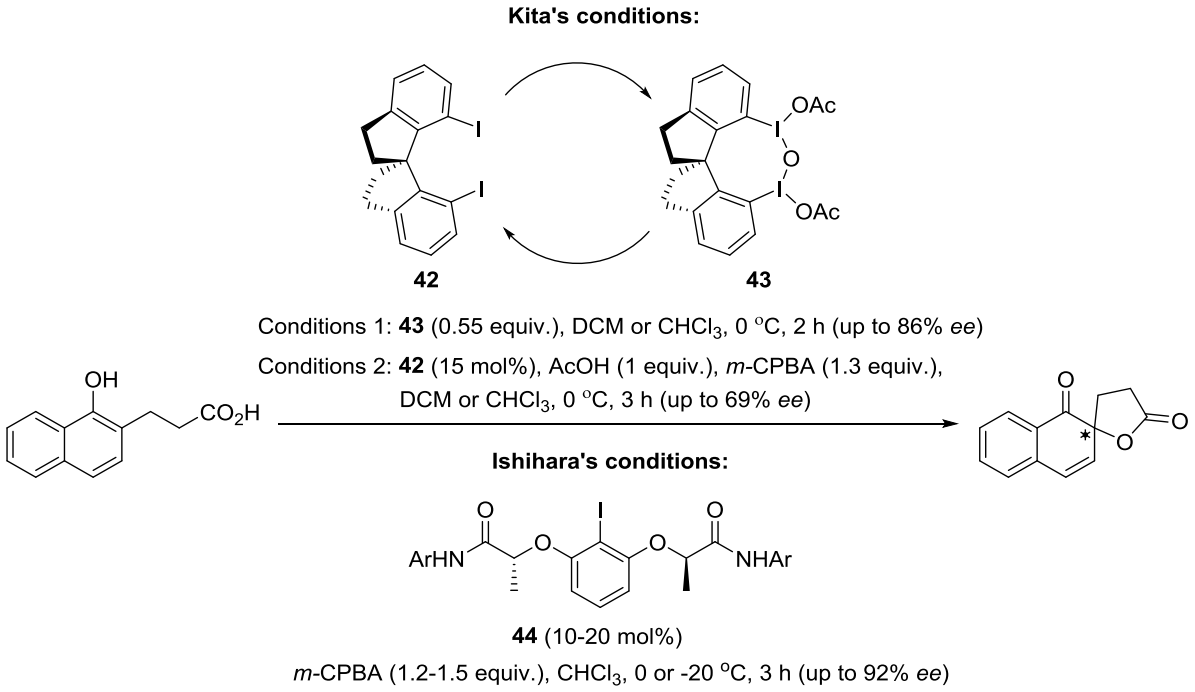


Figure 1.32. Asymmetric catalytic versions of oxo-spirocyclization.

1.4. Group-transfer reactions using I(III) reagents

The second class of transformations, wherein the hypervalent iodine reagents have found widespread applications are so-called group-transfer reactions. In contrast to the oxidation reactions discussed above, making use of both I(III) and I(V) species with a single carbon-based ligand that remains bound to the I atom, the group transfers typically employ only iodine(III) compounds, such as aryl(R)iodonium salts or R-benziodoxol(on)es (**5**-**7** in Figure 1.2), containing two carbon ligands, one of each (R) is delivered to an organic substrate. Since the iodine atom accepts two-electrons in the course of the reaction and it is reduced to I(I), originally the R group has an electrophilic character, hence, the organic acceptor needs to be a

nucleophile. As the group-transfer process involves the loss of hypervalency, it is favorable both kinetically and thermodynamically, making the iodonium derivatives highly reactive compared to conventional electrophiles. Thus, the transfer of various moieties, whose, for instance, halide derivatives are not particularly reactive, such as aryl, alkenyl, alkynyl, and other, can be achieved.The last two decades witnessed a tremendous development in the area of group-transfer reactions from hypervalent iodine reagents, wherein an array of groups has been transferred to a variety of acceptors.[85–90]

Mechanistically, the group-transfer reactions can follow one of the three general pathways, as described in section 1.2. Namely, these are: (1) the inner sphere mechanism, proceeding through the incorporation of the nucleophile into the I(III) coordination sphere via the ligand exchange, followed by the reductive elimination; (2) the outer sphere mechanism, proceeding through the direct nucleophilic attack of the nucleophile on the ligand, substituting the iodine leaving group; (3) the radical mechanism, wherein one of the ligands is converted into a radical, either via the homolytic cleave of R–I bond or the SET reduction, and subsequently reacts with the organic acceptor.

In this thesis, the transfer of aryl groups from diaryliodonium salts has been investigated. Therefore, the following sections survey this area in detail, including the methods for the preparation of diaryliodonium salts. Figure 1.33 depicts few selected examples employing the second class of hypervalent iodine reagents most commonly used for the group transfer, the cyclic benziodoxol(on)es. Perhaps the most famous of them is the Togni reagent, allowing for the electrophilic trifluoromethylation of both *C*- and heteroatom-centered nucleophiles (Figure 1.33a).[91] Another compound with a broad scope of applications is ethynylbenziodoxolone **45** (EBX) developed by Waser. It is capable of transferring the alkynyl moiety to a variety of acceptors (Figure 1.33b). [92–94] The corresponding vinyl analog, vinylbenziodoxolone (VBX), has been prepared by Olofsson. The reagent displays a peculiar regioselectivity of the vinyl transfer, preferably affording the branched product, opposite to the related phenyl(vinyl)iodonium salt (Figure 1.33c).[95]

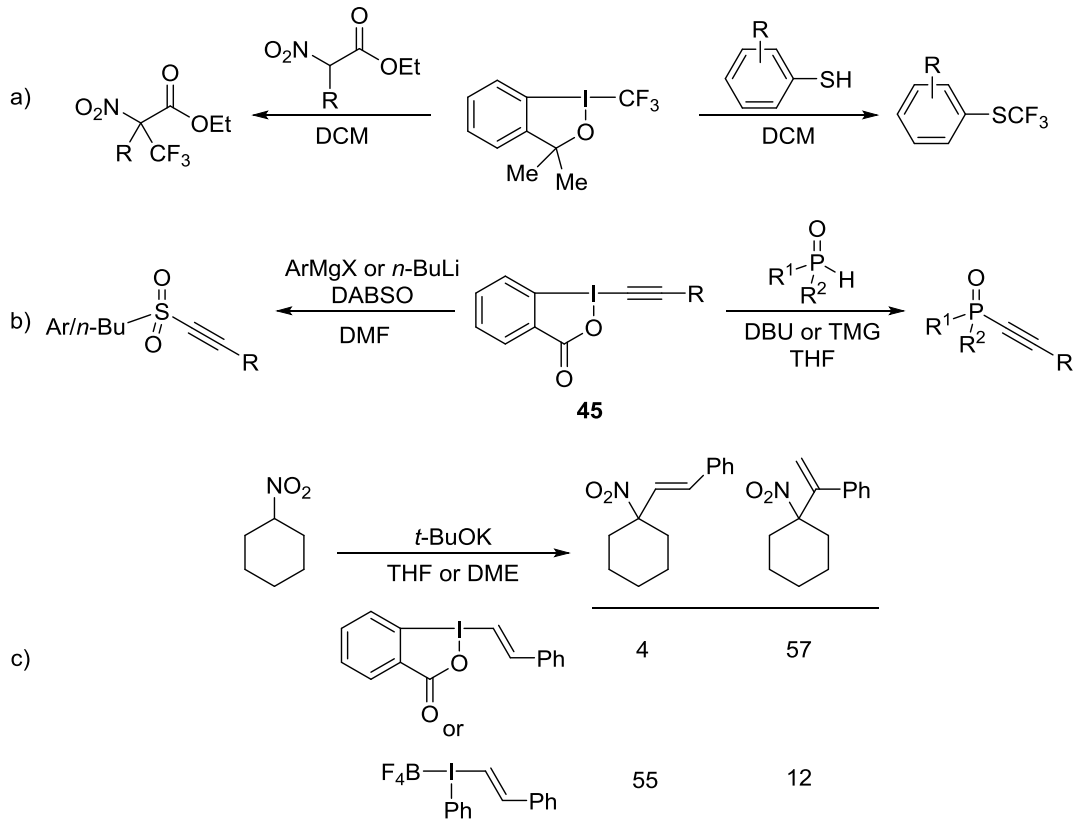


Figure 1.33. Selected examples of group-transfer reactions employing cyclic benziodoxol(on)es.

1.4.1. Diaryliodonium salts

In 1894, Meyer and Hartmann reported the first synthesis of diaryliodonium salts, Ar_2IX, as air- and moisture-stable compounds.[96] This class of hypervalent iodine reagents has found diverse applications as electrophilic aryl-transfer agents, capable of delivering aryl groups to a variety of nucleophiles. The following sections provide an overview of transition metal-free arylation reactions employing diaryliodonium salts, that is, the reactions which do not require intermediate transfer of the aryl onto a metal center. The application of transition metal catalysts is possible and sometimes necessary to effect the aryl transfer from diaryliodonium salts, but it is clearly disadvantageous, as it compromises the environmental and economic benefits inherent to these hypervalent iodine reagents. Fortunately, the direct arylation using diaryliodonium salts is often kinetically feasible (and always very favorable thermodynamically), allowing for an array of reactions without the need to involve the additional activation by transition metal catalysts.

According to X-ray crystallographic measurements the prototypic diaryliodonium salt, Ph_2ICl, in solid state has a T-shaped structure with the Cl atom sharing a three-center four-electron (3c-4e) bond with the iodine and one phenyl group.[97,20] Similar solid-state structures have been obtained for other compounds of this type, in line with the molecular orbital picture of hypervalent molecules described in section 1.1. However, in solution the anionic ligand can relatively easily dissociate, thus justifying the name of this class of hypervalent iodine compounds. Studies have shown that the degree of dissociation depends on both the solvent and the counterion.[98] Importantly, the dissociated cation Ar_2I^+ retains the ~90° angle between the two aryl moieties and remains hypervalent, as a solvent molecule (or another species) coordinates to I center instead of the original anion.

1.4.2. Preparation of diaryliodonium salts

Since the initial discovery, several synthetic routes to diaryliodonium salts have been reported. Stepwise synthesis of diaryliodonium salts involves two or three steps. First an iodoarene is oxidized to an iodine(III) compound under acidic conditions. It is then reacted with a nucleophilic aryl source, such as electron-rich arene or arylstannane, arylboronic acid, or arylsilane (Figure 1.34a), transferring the second aryl group to iodine via a Friedel-Crafts type process or transmetallation, respectively. In many cases a subsequent anion exchange is needed. Commercially available iodine(III) compounds, such as PIDA, PIFA, and Koser reagent are very convenient precursors in the step-by-step synthesis of aryl(phenyl)iodonium salts.

One-pot synthesis of diaryliodonium salts was limited in scope and required harsh conditions[99] until efficient protocols were developed by the Olofsson's group in the beginning of the 20th century.[100–104] In these one-pot routes to symmetric and unsymmetric diaryliodonium salts, an iodoarene is mixed with an arene and an oxidant (typically *m*-CPBA), in a combination with TfOH, TsOH, or $BF_3{\cdot}OEt_2$. For unsymmetric salts, the more electron-deficient aryl group should originate from ArI, and the more electron-rich aryl group should come from the arene to avoid byproducts formation. The method employing TfOH is more versatile (Figure 1.34b), whereas the one with TsOH is more suitable for electron-rich salts (Figure 1.34c). $BF_3{\cdot}OEt_2$ can be applied for the one-pot synthesis of symmetric and unsymmetric diaryliodonium tetrafluoroborates from iodoarenes and arylboronic acids (Figure 1.34d). Both electron-deficient and electron-rich salts can be synthesized in a regiospecific manner this way, and the substitution pattern can be varied easily. Symmetric diaryliodonium salts can also be prepared directly from molecular iodine and arene (Figure 1.34e). Other

oxidants, such as $K_2S_2O_8$/TFA,[105,106] H_2O_2/Tf_2O,[107] AcOOH/TsOH,[108] and Oxone/H_2SO_4,[109] have also been used for the one-pot synthesis of diaryliodonium salts.

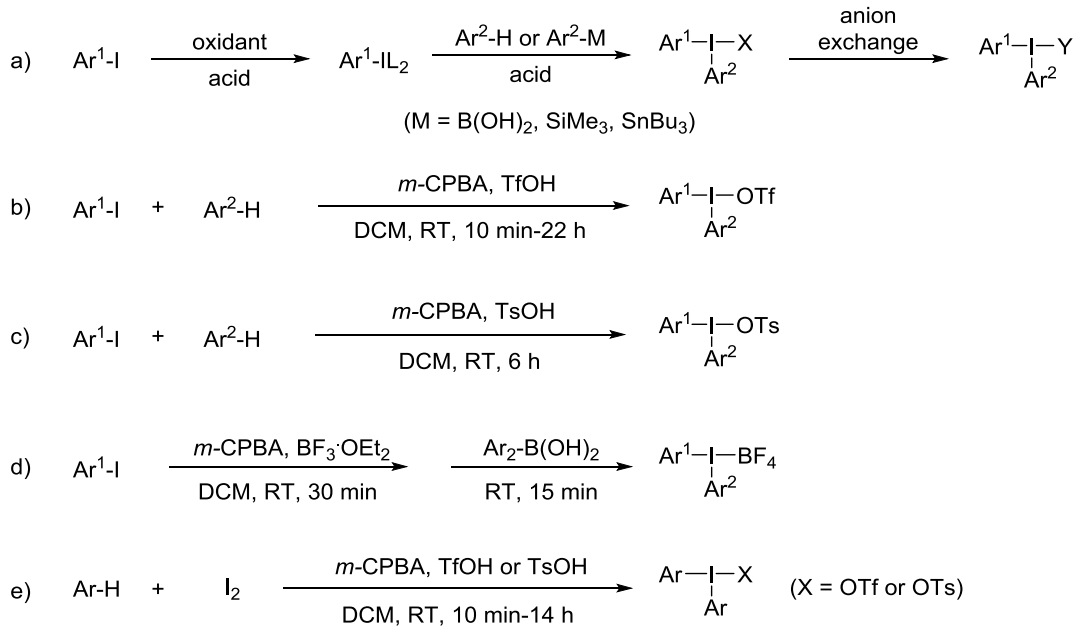


Figure 1.34. Synthetic strategies for the preparation of diaryliodonium salts.

1.4.3. Arylation of carbon nucleophiles

Several classes of *C*-nucleophiles have been successfully arylated using diaryliodonium salts under metal-free conditions.

The first class are electron-rich arenes. In 2010, Kita and co-workers reported using diaryliodonium salts **46** as selective heteroaryl transfer agents to functionalize dimethoxybenzenes (Figure 1.35a).[110] Building on a seminal work by Quideau *et al.*,[111] Kalek group developed transition metal-free C−H arylation of 2-naphthols using diaryliodonium salts as aryl donors (Figure 1.35b).[28] The reaction displays a complete regioselectivity with regard to C1 carbon, providing access to an important biaryl scaffold with many possible substitution patterns. A double *C1*- and *O*-arylation of the same substrates was reported by Solorio-Alvarado and co-workers, using **47** as a radical initiator (Figure 1.35c).[112] Diaryliodonium salts were also used in metal-free *C*-arylations of naphthalene and other unbiased arenes under microwave heating conditions. (Figure 1.35d).[113]

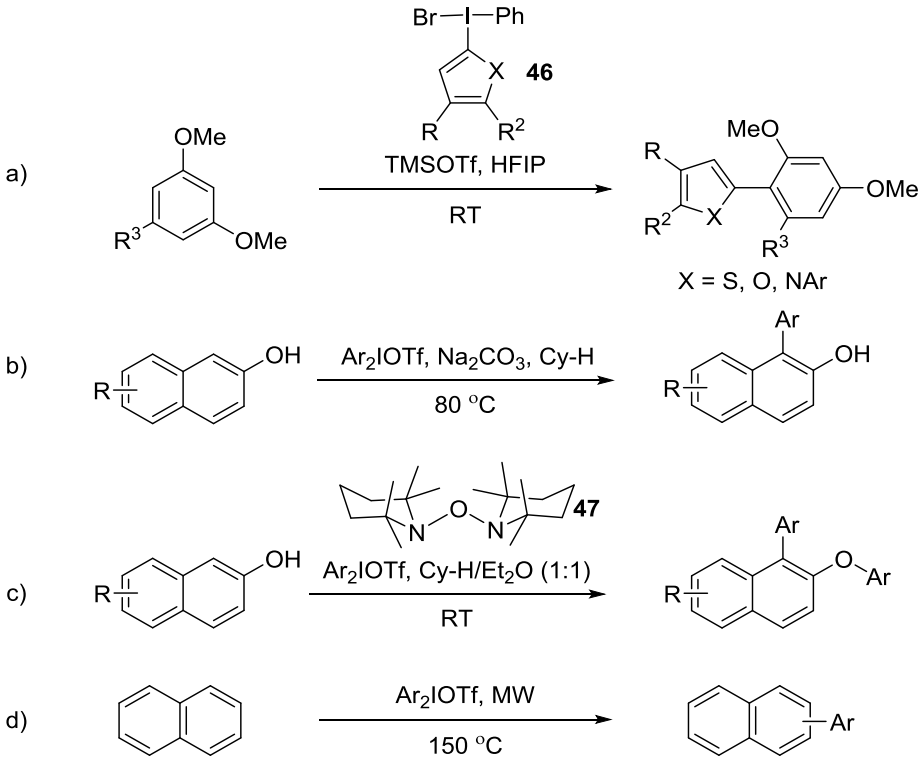


Figure 1.35. Arylation of electron-rich arenes.

The scope of the *C*-arylation reaction was further extended to aromatic heterocycles. In 2012, Yu developed a metal-free arylation of various 5- and 6-membered *N*-heteroarenes with diaryliodonium salts using an inorganic base (Figure 1.36a).[114] Ackermann's group reported the *C3* arylation of pyrroles and indoles with diaryliodonium salts in DMF at high temperature (Figure 1.36b).[115] Later, the *C2*-arylation of engineered indole-3-acetamides **48** with diaryliodonium salts was also reported by the same group (Figure 1.36c).[116] This arylation reaction was shown to be applicable for a late-stage diversification of complex peptides.

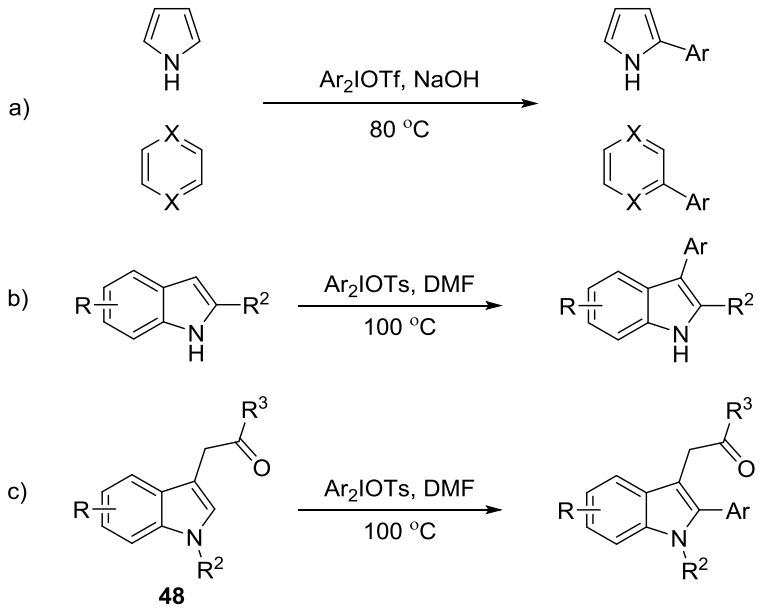


Figure 1.36. Arylation of heterocycles.

Diaryliodonium salts were also used for the direct modification of pyrrole rings in the fluorescent dye BODIPY. Both mono- and di-α-aryl-BODIPYs were accessed via a base mediated direct C−H α-arylation in refluxing DCE (Figure 1.37).[117] The resultant α-aryl-BODIPYs showed strong absorption and intense fluorescence emission over a broad range of the spectra and may be easily tuned via the variation of the diaryliodonium salt.

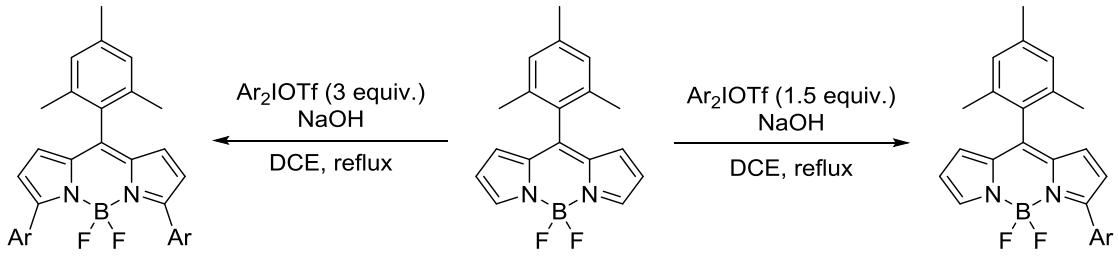


Figure 1.37. α‑Selective arylation of boron dipyrrolmethenes.

The arylations of arenes with diaryliodonium salts may follow either a Friedel-Crafts-type or a radical mechanism depending on the particular case.

The second general class of carbon nucleophiles, which have been used as substrates for the arylation with diaryliodonium salts are carbonyl compounds. Already in 1991, Koser discovered that diphenyliodonium fluoride could be utilized in the α-phenylation of silyl enol

ethers **49**. The fluoride counter-ion in this case was conveniently chosen to facilitate the removal of the silyl moiety (Figure 1.38a).[118] Oh and co-workers developed a metal-free α-arylation of β-keto esters and malonates (Figure 1.38b).[119] Agrawal and co-workers reported the first asymmetric α-arylation of cyclohexanones, employing Simpkin's base to generate the chiral nucleophilic enolate intermediate (Figure 1.38c).[120] This approach has been applied in a short and efficient total synthesis of (−)-epibatidine **50** and a formal synthesis of (+)-epibatidine. The *C2*-arylation of quinone systems (Figure 1.38d),[121] *C*-arylation of ethyl acetoacetate (Figure 1.38e),[122] *C2*-arylation of indolinone derivatives (Figure 1.38f),[123] *C4*-arylation of 4-substituted-pyrazolin-5-ones (Figure 1.38g),[124] *C*-arylation of α-cyano-α-phenyl esters (Figure 1.38h),[125] and 2-substituted cyanoacetates (Figure 1.38i)[126] are some other prominent examples of the α-arylations of carbonyl compounds.

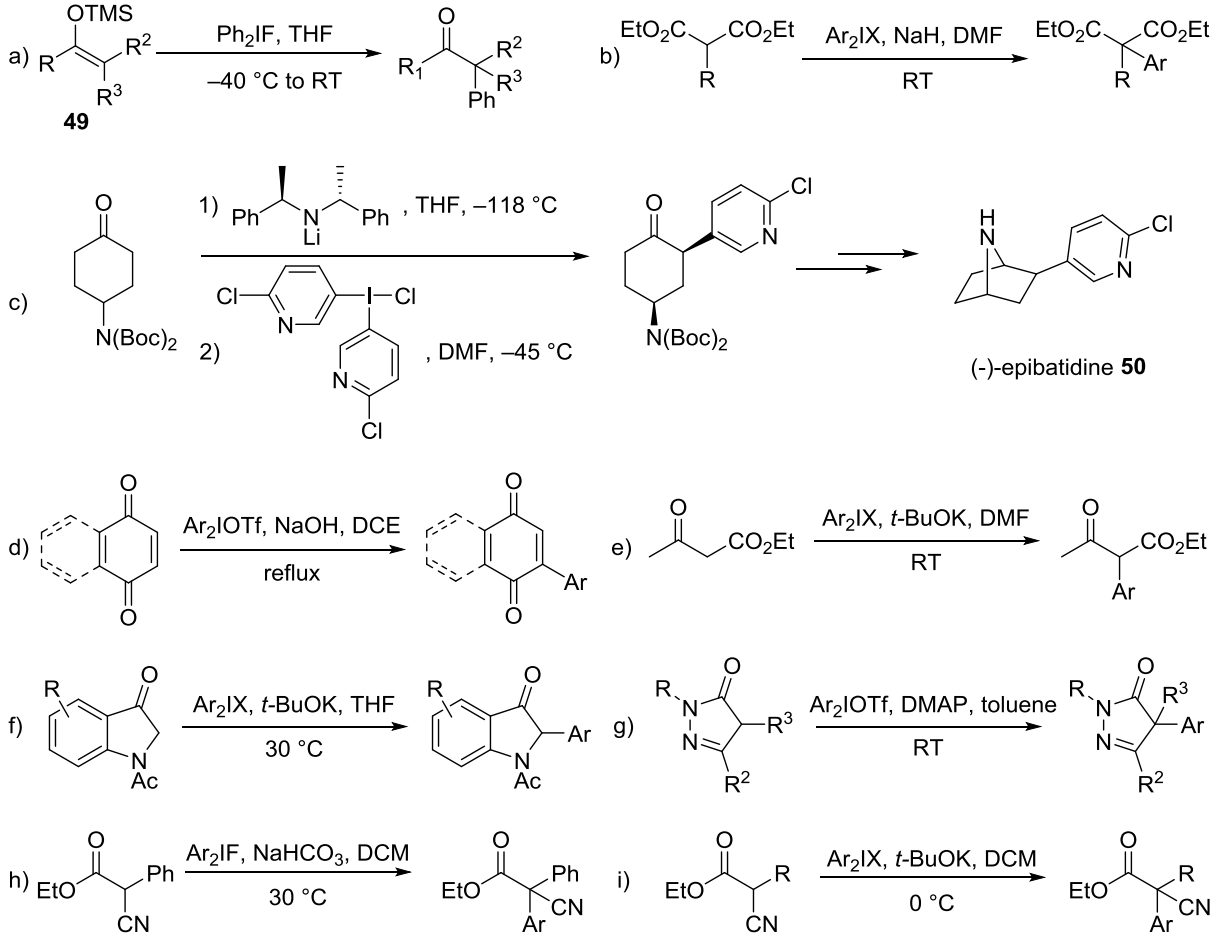


Figure 1.38. α-Arylation of carbonyl compounds.

Similarly, the metal-free α-arylations of aliphatic nitro compounds, such as nitroalkanes and nitroesters (Figure 1.39a),[127] α-nitroketones (Figure 1.39b)[128] and α-fluoro-α-nitroacetamides (Figure 1.39c),[129] using diaryliodonium salts were also reported.

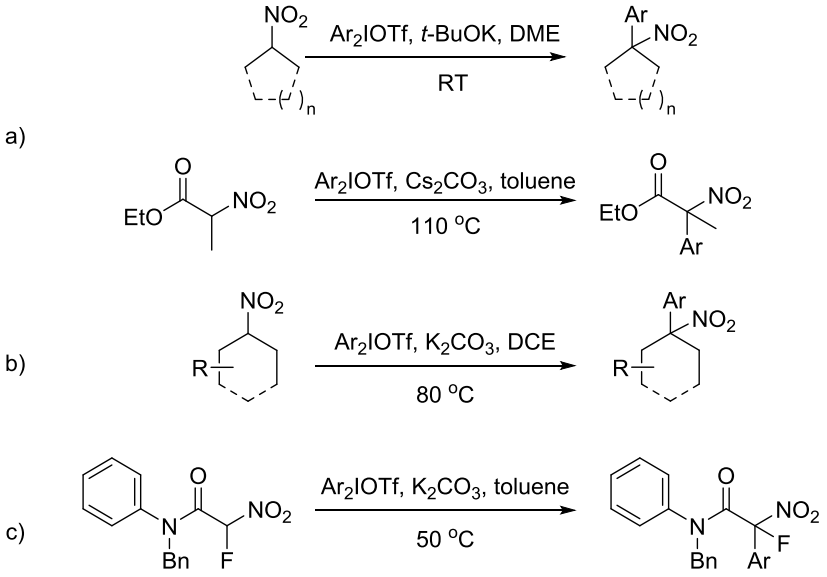


Figure 1.39. Arylation of aliphatic nitro compounds.

Finally, Gaunt and co-workers discovered that heteroaromatic aldehydes **51** can be arylated at the carbonyl carbon with diaryliodonium salts, employing the catalysis by *N*-heterocyelcic carbenes that convert the aldehydes into nucleophilic Breslow intermediates (Figure 1.40).[130]

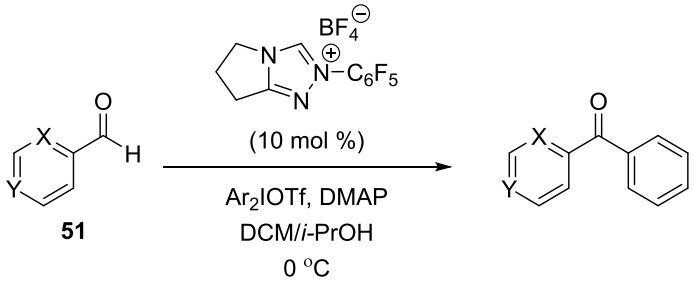


Figure 1.40. N-heterocyclic carbene-catalyzed arylation of heteroaromatic aldehydes.

1.4.4. Arylation of oxygen nucleophiles

Beringer's pioneering investigation on the arylation of organic and inorganic bases by diaryliodonium salts paved the way for the synthesis of many synthetically useful motifs via *O*-arylation (Figure 1.41).[131,132]

The first class are diaryl ethers, whose synthesis via aryl transfer from diaryliodonium salts to phenols in the presence of aqueous sodium hydroxide was first reported by Crowder.[133] The resulting products were used as intermediates in the synthesis of bis(benzyl)isoquinoline alkaloids. A faster, milder, and high yielding protocol for the synthesis of diaryl ethers was reported by Olofsson and co-workers (Figure 1.41a).[134] Sterically crowded *ortho*-substituted diaryl ethers, which are difficult to obtain by a metal-catalyzed arylation, halogen substituted, racemization-prone amino acid derivatives, and heteroaromatics were all tolerated in this reaction. 4-Methoxyphenyl and 2,4-dimethoxyphenyl were found to be suitable auxiliary aryl groups that do not undergo the transfer, thus allowing for the chemoselective reactions using unsymmetrical diaryliodonium salts.[26,135,136] Gaunt and co-workers reported a counter-anion triggered arylation strategy with diaryliodonium fluorides under weakly basic conditions.[125] The fluoride counter-anion forms a hydrogen bond with the phenolic OH, which enhances the nucleophilicity of the phenol and triggers the attack at the iodine(III) center displacing the fluoride as a leaving group. Olofsson reported the synthesis of aryl ethers in water, which in addition to phenols was also applicable to allylic and benzylic alcohols (Figure 1.41b).[137] The transition metal-free synthesis of phenoxazine **52** was carried out via *O*-arylation of *ortho*-iodo phenol with unsymmetrical diaryliodonium salt to provide substituted diaryl ether as the key step (Figure 1.41c).[138]

In 1975, McEwen published an etherification of aliphatic alcohols using diphenyliodonium salts and sodium alkoxide, in which a complex mixture of products arising from a radical chain reaction was formed.[139] The yields of the alkyl aryl ethers were increased by the use of 1,1-diphenylethylene (DPE) as radical trap. Solvolysis of diaryliodonium salts with trifluoroethanol and methanol led to the corresponding arylated products.[140] Only in 2014, Olofsson reported a practical and efficient synthesis of alkyl aryl ethers using sodium *tert*-butoxide as a base in toluene. Primary alcohols were the best reaction partners, though secondary, tertiary, allylic, benzylic, and other functionalized alcohols were also tolerated.[141] Stuart group also reported a similar transformation, with an extended scope and better tolerance of various alcohols using sodium hydride as the base and methyl *tert*-butyl ether (MTBE) as the solvent, at 50 °C.[142] The

arylation of tertiary alcohols with *ortho*-substituted diaryliodonium salts to obtain highly sterically hindered ethers was also developed. The substrate scope includes cyclic, acyclic, propargylic, and allylic alcohols.[143] Olofsson group reported a general method for the synthesis of carbohydrate-derived aryl ethers **53**, with aryl group containing both electron donating and withdrawing groups (Figure 1.41d).[144] This method is of a special importance, as *O*-arylated carbohydrate derivatives have diverse applications in medicine and glycobiology.

Olofsson also reported the arylation of other oxygen nucleophiles such as *N*-hydroxysuccinimide and *N*-hydroxyphthalimide to the corresponding *N*-aryloximides (Figure 1.41e).[145] A fast and operationally simple one-pot synthesis of substituted benzofurans was achieved by the *O*-arylation of ethyl acetohydroxamate, followed by an *in situ* reaction with ketones under acidic conditions (Figure 1.41f).[146]

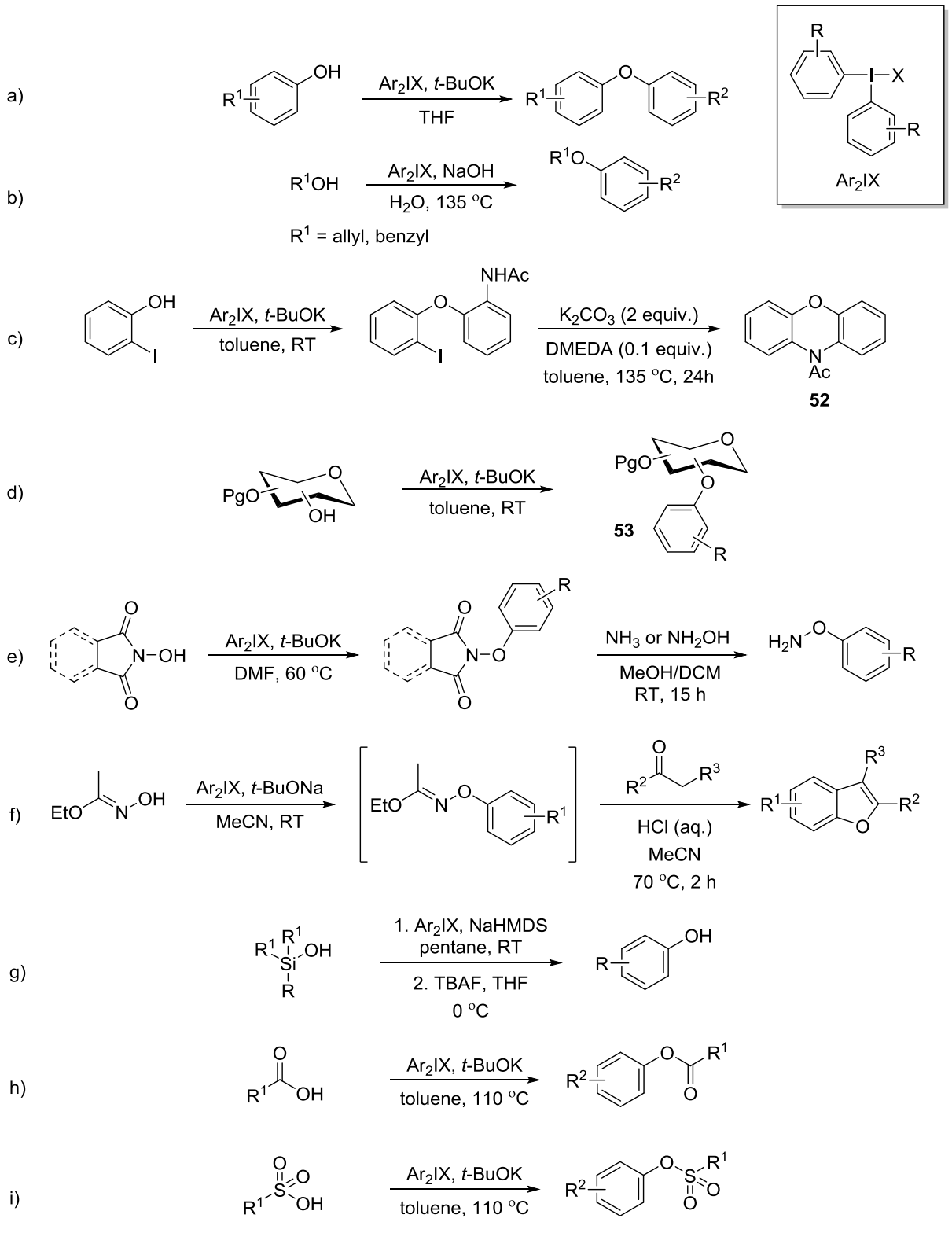


Figure 1.41. Olofsson's *O*-arylations by diaryliodonium salts.

Olofsson also developed an interesting pathway for the synthesis of phenols, based on the *O*-arylation of silanols with diaryliodonium salts, followed by the removal of the silyl group (Figure 1.41g).[147]

Finally, diaryliodonium salts can be used for the preparation of aryl esters via aryl transfer to oxygen atom of acids, including carboxylic acids (Figure 1.41h), sulfonic acids (Figure 1.41i), [135,148] and phosphoric acids (Figure 1.42).[149]

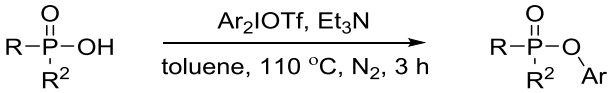


Figure 1.42. Arylation of P(O)–OH by diaryliodonium salts.

1.4.5. Arylation of nitrogen nucleophiles

The first report of *N*-arylation using diaryliodonium salts was the Beringer's work on the arylation of sodium nitrite, sulfonamides, and amines. However, only low to moderate yields were achieved in this reaction.[131] In 1977, McEwen obtained nitrobenzene in ~75% yield and phenyl azide in ~98% by the arylation of sodium nitrite and sodium azide, respectively.[150] Later an efficient arylation of ammonia with diaryliodonium salts in aqueous media at 80 °C was developed, providing anilines.[151]

Concerning the arylation of organic nitrogen nucleophiles with diaryliodonium salts, Carroll and Wood were the first to use substituted anilines, obtaining a range of diarylamines in good yields.[152] Trifluoroacetate was used as preferred counter-ion for the iodonium salts and the reaction was carried out in DMF at 130 °C. The presence of electron-withdrawing groups, *e.g.*, NO_2, at the aniline ring decreased the yields, while anilines with electron-donating groups gave the corresponding products with high efficiency. Olofsson group performed a systematic chemoselectivity study with anilines and diaryliodonium triflates, which showed that 2,4- and 2,6-dimethoxyphenyl, as well as 2,4,6-trimethoxyphenyl groups are the most efficient auxiliary groups for the *N*-arylation of *meta*-anisidine, using unsymmetrical diaryliodonium salts (Figure 1.43a).[26] Chen reported the synthesis of acridine derivative from *ortho*-acylanilines via a tandem *N*-arylation/Friedel–Crafts reaction pathway (Figure 1.42b).[153]

The arylation of aliphatic amines, both primary and secondary, was reported by Olofsson in 2018 (Figure 1.42c).[154] Cyclic and acyclic amines were well tolerated, providing a range of *N*-

alkylanilines. The reaction employs Na_2CO_3 as the base in toluene at 110 °C. The *N*-arylation of amino esters with unsymmetrical aryl(anisyl)iodonium salts was also developed, delivering the products in high yields (Figure 1.42d).[155] Chi and co-workers reported an intramolecular arylation of iodonium salts **54**, leading to indoline derivatives (Figure 1.42e).[156] Amines containing other substituents were also successfully subjected to arylation with diaryliodonium salts. For example, Wang and co-workers demonstrated the facile arylation of hydroxylamines in the presence of Cs_2CO_3 at room temperature (Figure 1.42f).[157]

Further extension was the arylation of amides. A one-pot synthesis of multiply substituted ureas **55** from *N*-arylcyanamide and diaryliodonium salts was developed by arylation of *N*-substituted cyanamides under metal-free conditions, followed by a second *N*-arylation under copper-catalyzed conditions (Figure 1.42g).[158] The high reactivity of diaryliodonium salts has been utilized in metal-free arylations of acyclic secondary amides at room temperature using NaH as the base (Figure 1.42h),[159] as well as a benzyne precursor for *N*-arylation of challenging acyclic secondary amides (Figure 1.42i).[160] The reaction of thiolactams with diaryliodonium salts delivered *N*-arylated thioamides (Figure 1.42j).[161]

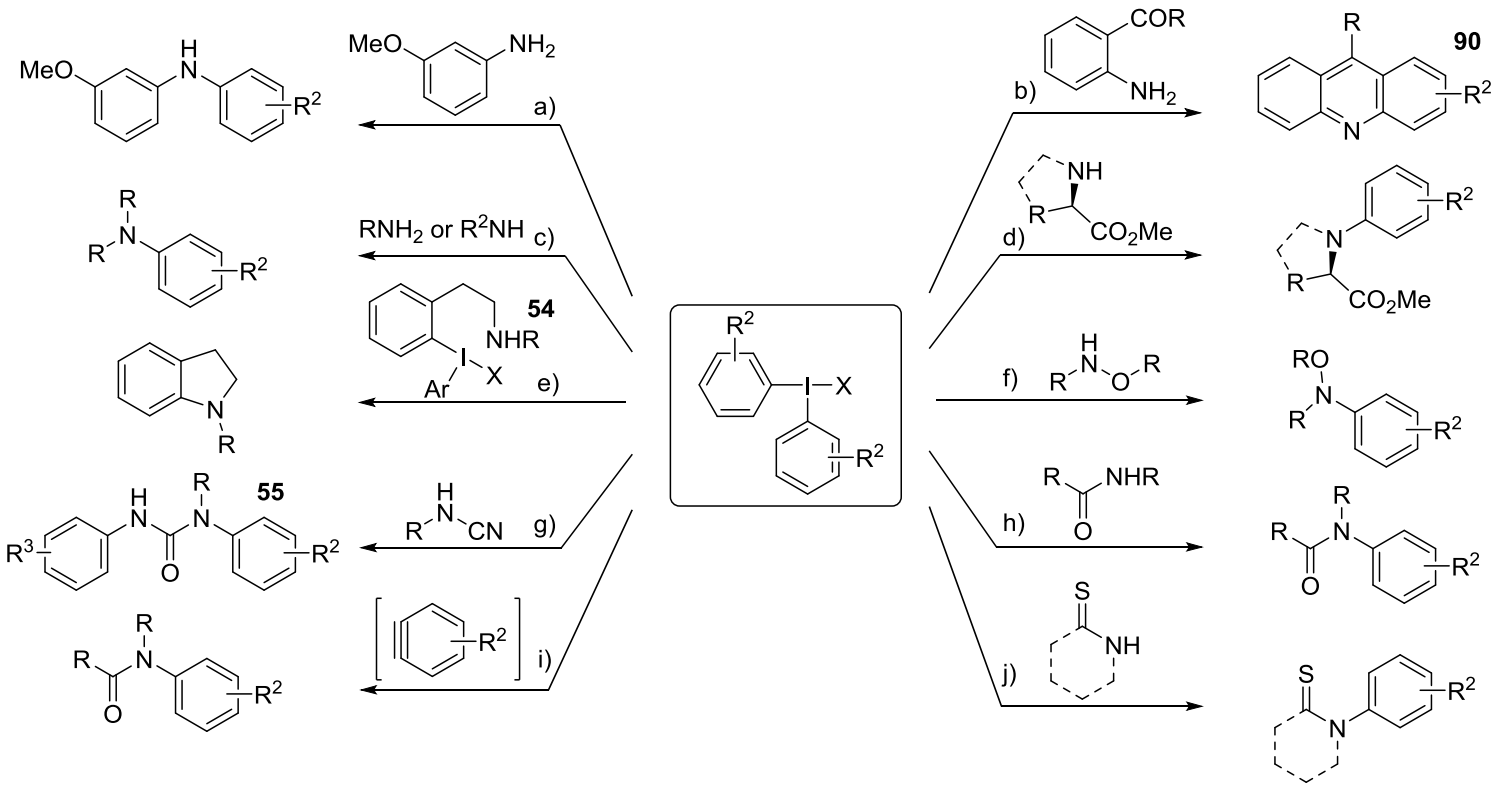


Figure 1.42. Metal-free *N*-arylations: a) DMF, 130 °C, 24 h; b) DCE, 130 °C, 12 h; c) Na_2CO_3, toluene, 110 °C, 4 – 22 h; d) Na_2CO_3, toluene, 150 °C, 4 – 24 h; e) Cs_2CO_3, TEMPO (0.1 equiv.), DMF, 80 °C, 1 h; f) Cs_2CO_3, toluene, RT, 6 h; g) 1. Cs_2CO_3, toluene, RT, 5 h; 2. AcOH (4 equiv.), 0.5 h; 3. $Cu(OTf)_2$ (20 mol%), 60 °C, 21 h; h) NaH, toluene, RT, 24 h; i) *t*-BuOK, THF, RT; j) *t*-BuOLi, toluene, 80 °C, 1 h.

Heterocycles, such as pyrazole, carbazole, and indolines, were efficiently arylated at nitrogen by diaryliodonium salts (Figure 1.43a-c).[162–164] Karchava and co-workers developed the first synthetic approach to quaternary *N*-aryl-DABCO salts **56**, based on the arylation with aryl(mesityl)iodonium triflates and demonstrated a one-pot procedure for the synthesis of flibanserin **57**, the active agent of recently approved drug Addyi (Figure 1.43d).[165]

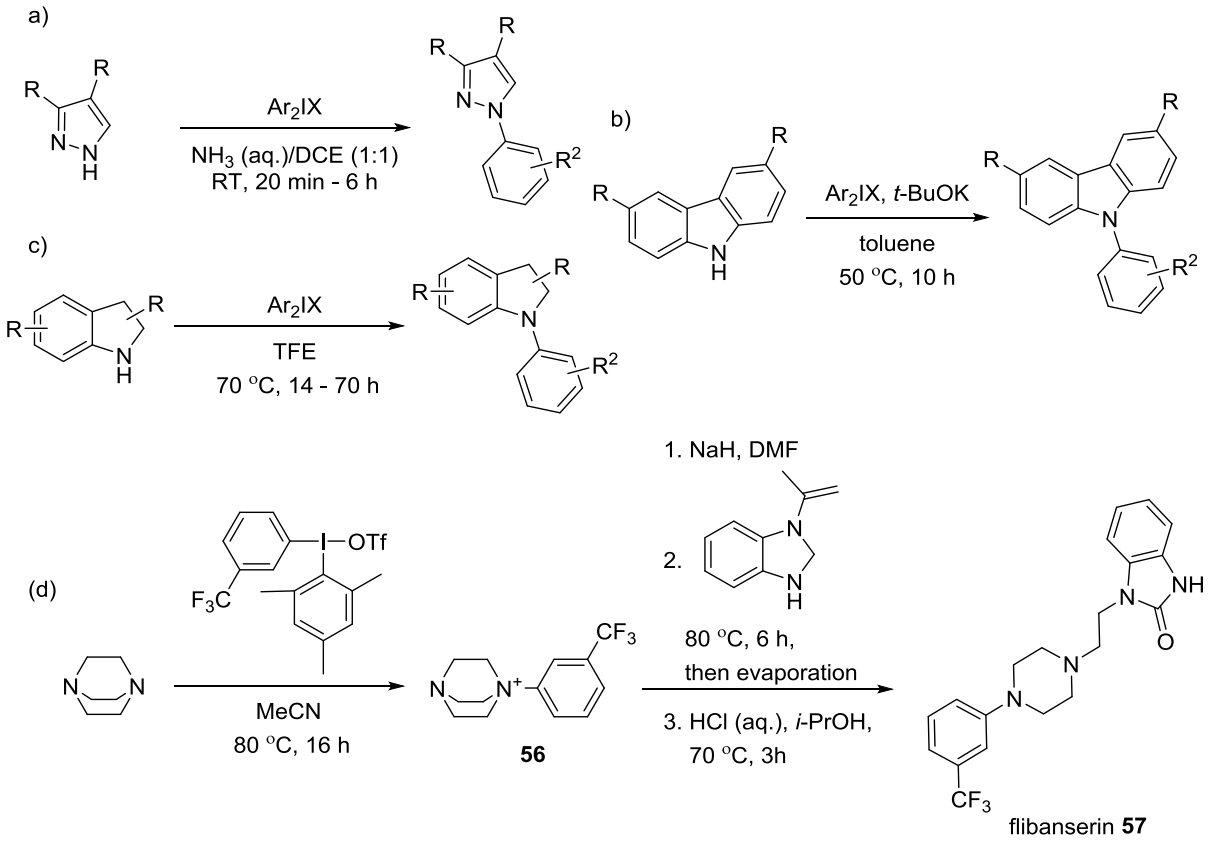


Figure 1.43. Metal-free *N*-arylation of nitrogen-containing heterocycles.

1.4.6. Arylation of sulfur nucleophiles

In 1947, Sandin and co-workers reported the reaction of diphenyliodonium chloride with thiophenol, cysteine, and thioglycolic acid in refluxing aqueous solutions, giving *S*-arylated products.[166] Crivello and Lam accessed triarylsulfonium salts via a double arylation of thiols.[167] Chen used diaryliodonium salts to arylate several sulfur nucleophiles to synthesize aryl esters of dithiocarbamic acids (Figure 1.44a),[168] aryl arenedithiocarboxylates (Figure 1.44b),[169] *S*-aryl

thiocarboxylates (Figure 1.44c),[170] *O*,*O*-dialkyl *S*-aryl phosphorothioates (Figure 1.44d),[171] and unsymmetric *S*-aryl thiosulfonates (Figure 1.44e).[172]

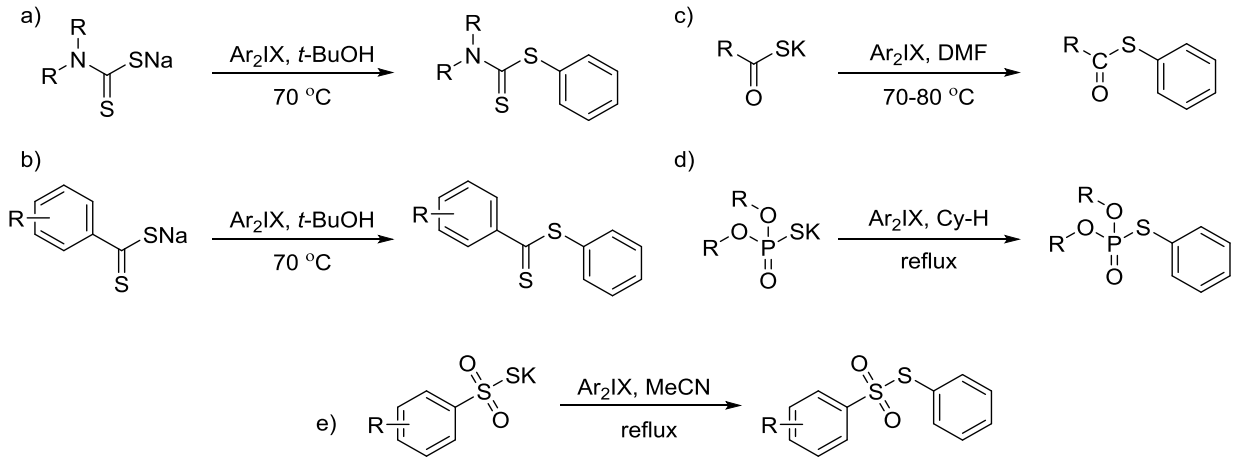


Figure 1.44. Chen's work on the arylation of various *S*-centered nucleophiles.

Huang et al. synthesized polymeric diaryliodonium salts and applied them to the preparation of diaryl ethers and diaryl sulfides under mild conditions. The polymeric support, polyiodostyrene, could be recycled and reused.[173] Sanford and co-workers reported the preparation of diaryl and alkyl aryl sulfides via acid-mediated coupling of thiols and thioethers with diaryliodonium salts in dioxane at 110 °C.[174] Ciufolini reported a high yielding preparation of triarylsulfonium salts via metal-free arylation of diaryl sulfides.[175]

In 2013, Manolikakes and Umierski reported the synthesis of diaryl sulfones by the arylation of arylsulfinites (Figure 1.45a).[176] The transfer of electron-poor and bulky, *ortho*-substituted, aryl groups was favored over the transfer of electron-rich aryl groups and less bulky aryl groups, respectively. The same researchers subsequently reported a one-pot synthesis of aryl sulfones by the arylation of sulfonate salts, generated *in situ* from organometallic reagents and SO_2 (Figure 1.45b-c).[177,178] A safer version of this reaction, using DABSO instead of SO_2, was published by Willis and co-workers (Figure 1.45d).[179] Olofsson reported the chemoselective *S*-arylation (over *N*-arylation) of secondary thioamides with diaryliodonium salts. Equimolar amounts of thioamide, base, and diaryliodonium salt were sufficient to obtain a diverse selection of products within short reaction times.[161] Le and co-workers developed a base-promoted synthesis of diarylsulfones from sulfonyl hydrazines and symmetrical or unsymmetrical diaryliodonium salts (Figure 1.45e).[180]

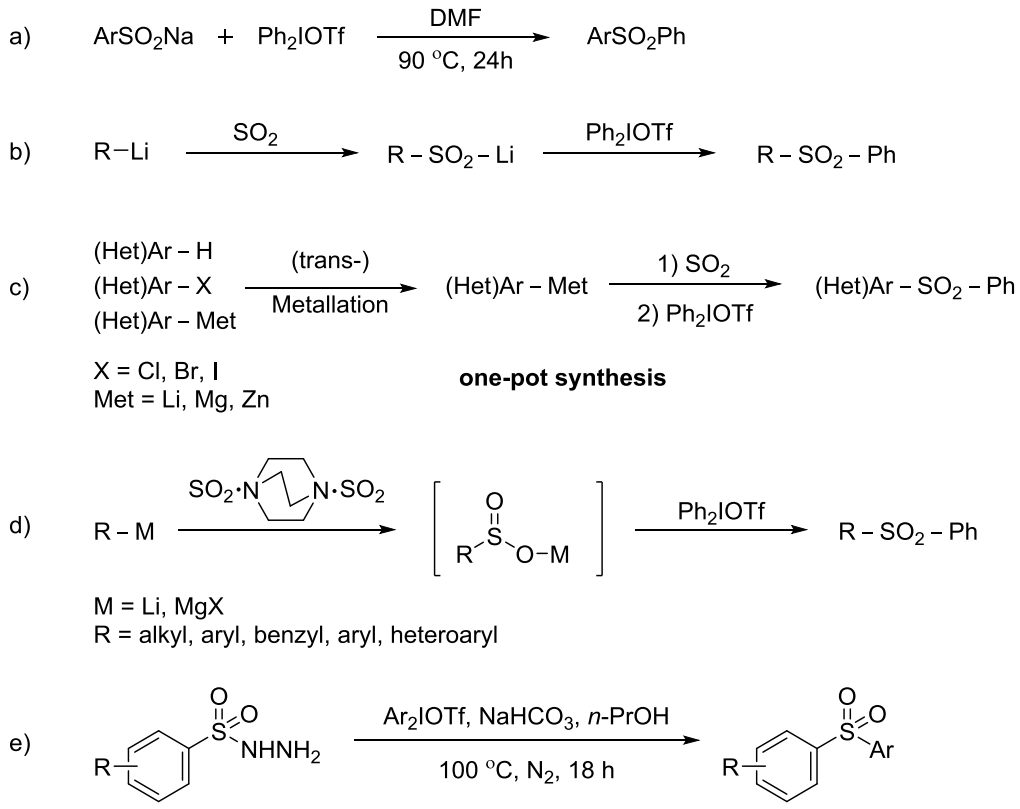


Figure 1.45. Synthesis of aryl sulfones by *S*-arylation with diaryliodonium salts.

1.4.7. Arylation of other heteroatom nucleophiles

Various other heteroatoms, such as phosphorus, boron, and halogens have also been arylated using diaryliodonium salts.

Chen reported the efficient synthesis of arylphosphonates by the reaction of dialkyl phosphite salts with diaryliodonium salts in DMF (Figure 1.46a).[181] Recently, a transition metal-free synthesis of aryl phosphonates by a simple combination of diaryliodonium salts with phosphites, using K_2CO_3 in acetonitrile and under blue-light irradiation, was reported (Figure 1.46b).[182] Karchava and co-workers developed another visible light-induced arylation of tertiary phosphines with aryl(mesityl)iodonium triflates to produce the quaternary phosphonium salts occurs under mild, metal- and catalyst-free conditions (Figure 1.46c).[183]

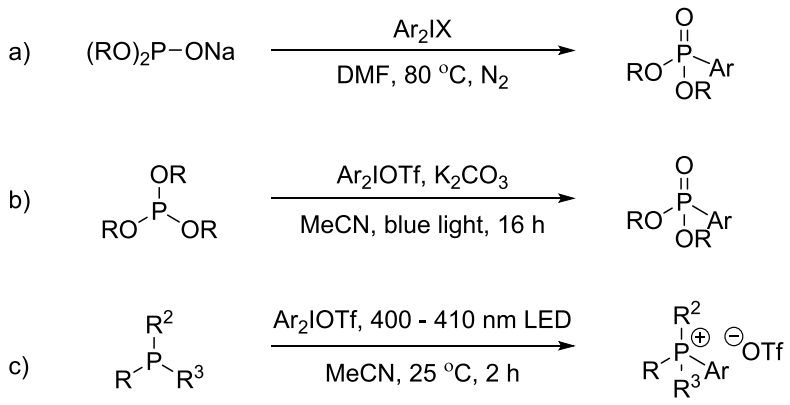


Figure 1.46. Arylation of phosphorus by diaryliodonium salts.

Muñiz and co-workers developed the arylation of diboron reagents with diaryliodonium salts proceeding without the use of any catalysts or additives.[184] Diboron reagents in a methanol solution engage in direct aryl–boron bond formation through a formal Umpolung of the electrophilic boron center (Figure 1.47).

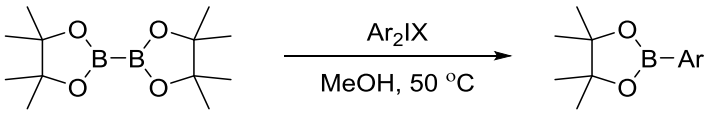


Figure 1.47. Metal-free borylation of diaryliodonium salts.

In 1982, Puy reported the synthesis of aryl fluorides by the reaction of KF with diaryliodonium salts having non-nucleophillic counter-anions.[185] The thermal decomposition of tetrafluoroborate salts also resulted in the formation of aryl fluorides. The best results were obtained when the salt Ar_2IX was heated with KF in the absence of solvent (Figure 1.48a).

Noninvasive imaging in living subjects with positron emission tomography (PET) provides early detection of diseases in humans by the detection of positron-emitting radiopharmaceuticals labeled with the short-lived positron-emitting radionuclides ^{11}C, ^{18}F, ^{15}O, and ^{13}N.[186] Fluorine-18 is the most widely used radionuclide in PET because of its favorable physical and nuclear characteristics, such as a short, but manageable half-life ($t_{1/2}$ = 109.7 min). In this regard, Pike and Aigbirhio reported the first radiofluorination of diaryliodonium salts (Figure 1.48b).[187] Several other groups reported the synthesis of various diaryliodonium salts for the efficient synthesis of wide range of substituted radiofluorinated arenes.[188–190] DiMagno and co-workers reported an improved fluorination of Ar_2IPF_6 achieved upon a filtration of

inorganic salts after an *in situ* formation of Ar_2IF, followed by heating to 140 °C in benzene (Figure 1.46c).[191] Radical scavengers were found to increase the reproducibility in the fluorinations with electron-rich salts.[192]

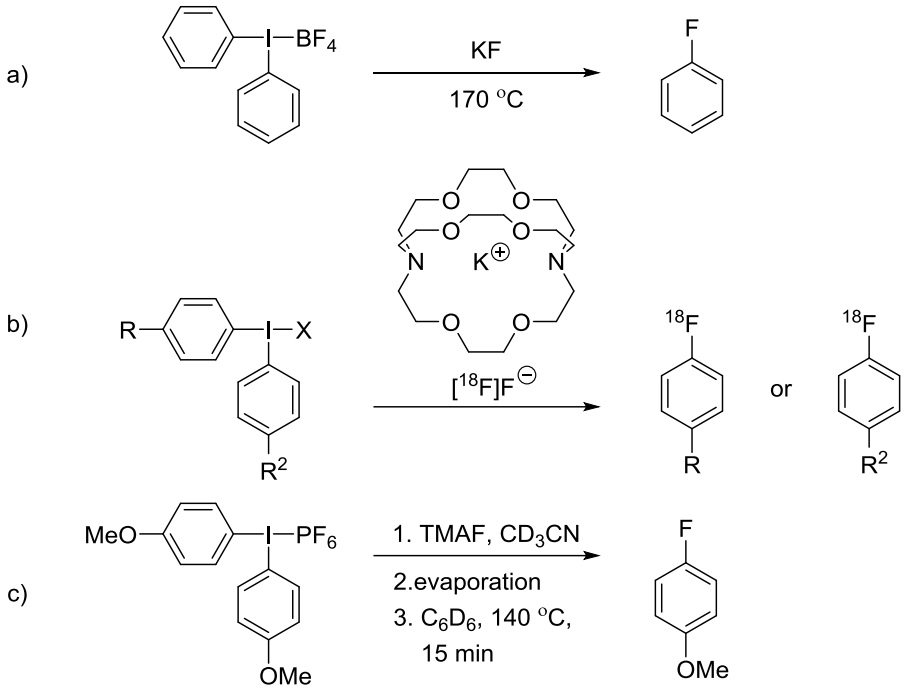


Figure 1.48. Fluorination of diaryliodonium salts.

Finally, Hartmann and Meyer reported the decomposition of diphenyliodonium chloride into chlorobenzene and iodobenzene at higher temperatures.[96] Similarly, diaryliodonium bromide in DMF at 100 °C gave aryl bromides.[193–195] DiMagno and co-workers published a two-step synthesis of iodoarenes via the formation of unsymmetric diaryliodonium salts, which were treated with excess NaI to yield two different iodoarenes upon heating to 80-120 °C.[196]

1.5. Objectives of the thesis

The primary objective of the thesis is to develop new synthetically useful reactions employing hypervalent iodine compounds and to understand their underlying mechanisms. In particular, the novel reactions will represent the two major domains of reactivity: the oxidations and the arylations.

With respect to the former reaction type, the first goal is to evaluate HIRs for their ability to promote the oxidative phenolic coupling leading to Pummerer's ketone. This important building block has been reported to form as a side product in processes involving I(III) reagents and I envisioned that they may be applied to prepare it synthetically. The second specific objective is to use organocatalytically generated enamine nucleophiles in the hypervalent iodine-promoted dearomatization of phenols. As organocatalysts and HIRs share common advantages in terms of low toxicity and cost, they seem to be an excellent match and their combined use should allow to benefit from the best of both worlds.

Concerning the arylation reactions, I believe that the application of HIRs could fill existing gaps in a metal-free access to certain *S*- and *P*-aryl compounds. Thus, I set out to develop protocols for the arylation of sulfur and phosphorus nucleophiles with diaryliodonium salts. The first project regarded the synthesis of aryl sulfides. Although the envisioned transformation has already been achieved using an activation by acid, we thought that basic conditions should allow for a broader scope, including biologically-relevant heterocyclic products. Secondly, I decided to investigate the aryl transfer onto the sulfur atom of phosphorothioate diesters leading to *S*-aryl phosphorothioates. Due to the importance of phosphorothioate derivatives in biology and medicine, as well as, an easy access to P-stereogenic phosphorothioate diesters in stereopure form, the proposed method should provide facile and metal-free entry to an interesting class of compounds. Finally, I decided to examine the metal-free arylation of secondary phosphines, since no reports on such a reaction have existed at the time.

Chapter 2
Synthesis of Pummerer's ketone and its analogs by iodosobenzene-promoted oxidative phenolic coupling (Paper I)

2.1. Background

Heterocyclic compounds have found numerous applications as pharmaceuticals, agrochemicals, cosmetics, and polymers, resulting in the continuous interest from the synthetic organic chemistry perspective. Development of efficient strategies for the synthesis of these scaffolds is an ever-increasing field of research. In this regard, hypervalent iodine chemistry has emerged as an elegant and powerful tool for the construction of a plethora of bioactive heterocyclic compounds and natural products ranging from three- to seven-membered ring systems.[197,198] In particular, the properties of iodine(III) compounds, such as (difluoroiodo)arenes and (dichloroiodo)arenes **1**, iodosylarenes **2**, aryliodine(III) carboxylates **3** and organosulfonates **4** (Figure 1.2) have been exploited in a many oxidative functionalizations of organic substrates, leading to the formation of new carbon-carbon, carbon-heteroatom, and heteroatom-heteroatom bonds.[11,12,199–202]

Arenols constitute valuable starting materials for the synthesis of heterocycles, in particular, the susceptibility of phenols to undergo oxidation has been utilized in numerous synthetically useful transformations.[203] The oxidative phenolic couplings, wherein two or more molecules of a phenol become linked together, constitute an important class of reactions. Many biosynthetic pathways, for instance these leading to usnic acid, dinapionones, and vancomycin, proceed via the phenolic coupling.[204–206] Not surprisingly, biomimetic total syntheses of multiple natural products have employed such process as the key steps.[207–209]

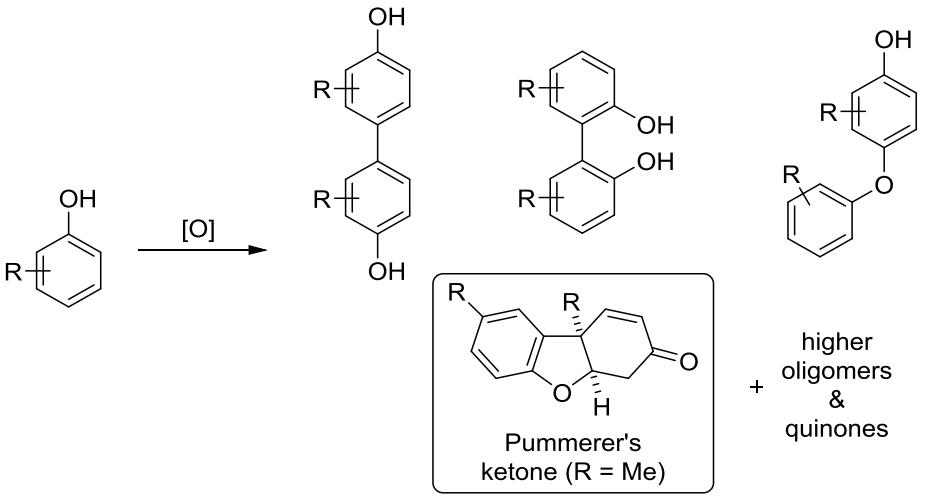


Figure 2.1. Possible products of an oxidative phenolic coupling, including Pummerer's ketone.

The major challenge in the development of oxidative phenolic coupling, especially its intermolecular variants, is controlling the selectivity of the reaction. Namely, the oxidation involves the removal of one hydrogen atom from each phenol molecule and creating linkages between *ortho* and *para* carbon atoms, and more rarely oxygen, possibly yielding a mixture of various dimers and higher oligomers, as well as quinone side-products (Figure 2.1).[210] Important products of the oxidations of *para*-substituted phenols are Pummerer's ketone and its analogs, which originate from the incipient *ortho-para* coupling, followed by the conjugate addition of the residual hydroxyl group to the resulting cyclohexadienone ring. The rigid tricyclic ring system of Pummerer's ketone constitutes a common pharmacophoric motif. It is present among the morphine family of narcotic analgesics, for example in codeine **58**, and in an Alzheimer's disease drug galanthamine **59** (Figure 2.2).

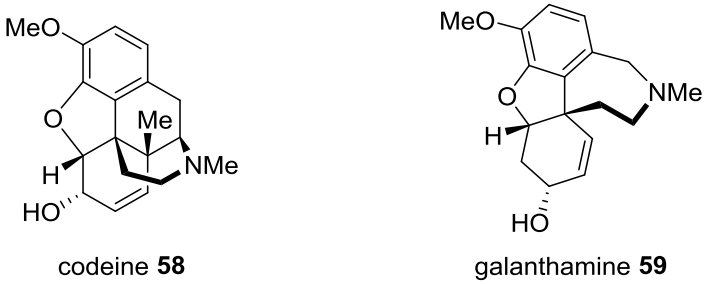


Figure 2.2. Examples of pharmaceuticals containing Pummerer's ketone motif.

Pummerer's ketone and its analogs have been reported to form in 5–30% yield during intermolecular oxidative phenolic couplings promoted electrochemically,[211–213] enzymatically,[214–216] and with chemical oxidants, such as iron(III),[217,218] silver(II),[219] persulfates,[220] and organic peroxides.[221] There have been also catalytic procedures developed, the best one affording as much as 65% of the product, but only for a few very specific phenol substrates.[222] Somewhat better yields of Pummerer's ketone analogs, in the range of 40–60%, have been obtained in several intramolecular phenolic couplings (Figure 2.3).[223–228] Alternative approaches to the synthesis of Pummerer's ketone have also been devised. These are usually more efficient compared to the direct phenolic coupling, however, on the downside, they involve multistep synthetic sequences.[229–232]

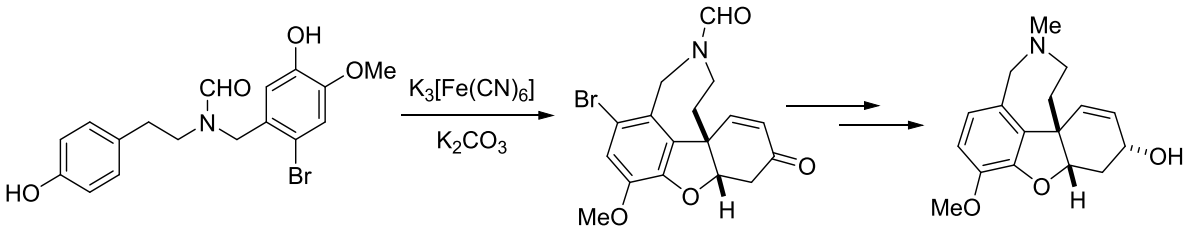


Figure 2.3. Synthesis of (±)-galanthamine by an intramolecular phenolic coupling.

Because of the considerable advantage of the intermolecular oxidative phenolic coupling leading to Pummerer's ketone in terms of the large increase of the molecular complexity during the single-step, we decided to investigate this reaction further. Also, up to date only the simplest analogs of Pummerer's ketone have been prepared by the oxidative phenolic coupling, hence we intended to assess the scope of this method for the synthesis of a broader array of compounds. In particular, we set out to explore the application of hypervalent iodine(III) oxidants to promote the phenolic coupling. The low toxicity and environmental friendliness of these reagents make them ideal for the synthesis of bioactive compounds, such as ones containing the Pummerer's ketone scaffold.[15] Hypervalent iodine(III) reagents have been reported to generate small amounts of Pummerer's ketone as a side-product during the oxidative dearomatizing fluorination of phenols.[62,64] Also, a promising performance of a hypervalent iodine(III) oxidant has been observed in an intramolecular coupling leading to polycylic Pummerer's ketone analogs, including a galanthamine precursor.[224] Finally, the hypervalent iodine(III) species are a prominent class of reagents used in multiple oxidative transformations of phenols.[48,86,233]

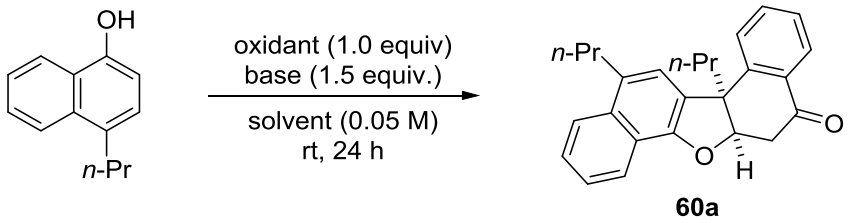
2.2. Optimization of reaction conditions

We started our investigations by examining the effect of reaction parameters on the model phenolic coupling of 4-propyl-1-naphthol (Table 2.1). The reaction using PIFA, the reagent that has been employed before in the oxidative dearomatizing fluorination of phenols,[62,64] affords 26% of the desired Pummerer's ketone analog **60a** (entry 1). Very interestingly, although the conversion of starting material is practically complete (>95%), compound **60a** is the only product observed in the reaction mixture by ^{1}H NMR (apart from iodobenzene). Presumably, the remainder of the substrate is transformed into polymeric products, as evidenced by the presence of some polar material showing very low mobility in TLC.

Testing other hypervalent iodine(III) reagents (Table 2.1, entries 2-4) identified iodosobenzene as the optimal oxidant, furnishing ketone **60a** in 35% yield. An iodine(V) Dess-Martin reagent was found to be less efficient (entry 5). The choice of solvent affects the efficiency of the reaction only to a moderate degree (entries 6-15), except for highly polar solvents, such as DMSO and MeOH (entries 7-8), which completely hinder the reaction. The best results were obtained in toluene (entry 4) and DCE (entry 15). As far as the bases are concerned, the replacement of Et_3N with K_3PO_4 lead to a slight improvement in the yield (entry 21). Other examined bases, both organic and inorganic, had a detrimental effect on the yield (entries 16-20). In the absence of base, only traces of the compound are formed. (entry 22). Finally, we have briefly explored altering the equivalents of the oxidant (entry 23) and the reaction temperature (entries 24-25), but not further enhancement could be achieved. Moreover, it was established that the reaction time can be shortened to 2 h without any appreciable loss in the yield.Although 38% yield of Pummerer's ketone analog **60a** might not be considered impressive, it is still surpassing the other existing protocols for the intermolecular oxidative phenolic coupling.[211–221]

Many of the hypervalent iodine(III)-mediated oxidations, including phenolic couplings, have been turned catalytic in the iodine-containing compound by the application of a stoichiometric terminal oxidant, typically *m*-CPBA.[14,234] Unfortunately, the attempted reaction using 10 mol% of PhIO did not show a catalytic turnover (entry 26). This most likely originates from the presence of a base in the mixture, which is an indispensable reaction component (entry 22), but it hampers the reoxidation of iodoarene back to iodine(III).[14]

Table 2.1. Effect of reaction parameters on the model phenolic coupling.



60a

Entry	Reaction conditions	Yield %[a]
1	PIFA, Et_3N, toluene	26
2	PIDA, Et_3N, toluene	33
3	PhI(OH)OTs, Et_3N, toluene	21
4	PhIO, Et_3N, toluene	35
5	Dess-Martin reagent, Et_3N, toluene	10
6	PhIO, Et_3N, MeCN	24
7	PhIO, Et_3N, DMSO	0
8	PhIO, Et_3N, MeOH	0
9	PhIO, Et_3N, Cy-H	26
10	PhIO, Et_3N, Et_2O	26
11	PhIO, Et_3N, THF	33
12	PhIO, Et_3N, CPME	31
13	PhIO, Et_3N, AcOEt	25
14	PhIO, Et_3N, CH_2Cl_2	30
15	PhIO, Et_3N, DCE	35
16	PhIO, pyridine, DCE	30
17	PhIO, 4-DMAP, DCE	32
18	PhIO, *t*-BuOK, DCE	0
19	PhIO, Na_2CO_3, DCE	12
20	PhIO, AcONa, DCE	9
21	PhIO, K_3PO_4, DCE	38
22	PhIO, no base, DCE	3
23	PhIO (1.5 equiv.), K_3PO_4, DCE	15
24	PhIO, K_3PO_4, DCE, 0 °C	25
25	PhIO, K_3PO_4, DCE, 80 °C	27
26	PhIO (10 mol%), K_3PO_4, DCE, *m*-CPBA (2.0 equiv.)	4

[a] Determined through analysis by ^1H NMR spectroscopy

2.3. Scope and limitations

Having established the optimal reaction conditions, we continued to examine the scope of the procedure (Figure 2.4). 4-Alkyl-subsituted naphthols could be oxidatively coupled, providing benzannulated Pummerer's ketone analogs **60a**-**60d**. Specifically, *n*-propyl- (**60a**), methyl- (**60b**), and 2-phenylethyl-containing (**60d**) products were obtained in over 30% yield. A somewhat reduced yield of 22% was achieved for the benzyl-containing compound **60c**. The standard Pummerer's ketone **60e** was synthesized from *para*-cresol in 36%, while its analogs having larger alkyl groups, such as ethyl (**60f**), *n*-pentyl (**60g**), 2-phenylethyl (**60h**), and benzyl (**60i**) were afforded in synthetically acceptable yields of 22-28%. As far as the oxidative coupling of phenols with additional substituents is concerned, the introduction of an extra group into the ring lead to a slight improvement in the formation of the Pummerer's ketone analogs. Namely, 2-methyl- (**60j**), 2-*n*-propyl- (**60k**), 2-allyl- (**60l**), and 2-benzyl-4-methylphenols (**60m**) were transformed into the corresponding Pummerer's ketone-type products in moderate 30-38% yields. Compound **60l**, bearing the allyl substituents, is particularly noteworthy, as it demonstrates the compatibility of this methodology with terminal olefins, allowing, for instance, for further functionalization of the peripheries. Finally, 3,4-dimethylphenol could also be oxidatively coupled under the developed conditions, affording product **60n** in 35% yield, showing that such substitution pattern in the substrate is also tolerated. In all the cases, excellent diastereoselectivity was observed – the reactions provided the *cis* isomers exclusively.

Importantly, as noticed before during the optimization, compounds **60a**-**60n** were the sole low molecular weight products of the reaction. The process selectively generates the Pummerer's ketone analogs, while the rest of the substrate is converted into polymeric material. This constitutes a considerable advantage from the practical viewpoint, because it allows for an easy isolation of the desired product, which needs just to be separated from iodobenzene side-product. We speculate that such outcome stems from consecutive subsequent oxidative couplings of any products, which still contain free phenol moieties (*e.g.*, these originating from the *ortho*-*ortho* or C–O couplings; see Figure 2.1). On the other hand, Pummerer's ketone is a "dead end", since it cannot undergo further oxidation under the reaction conditions.

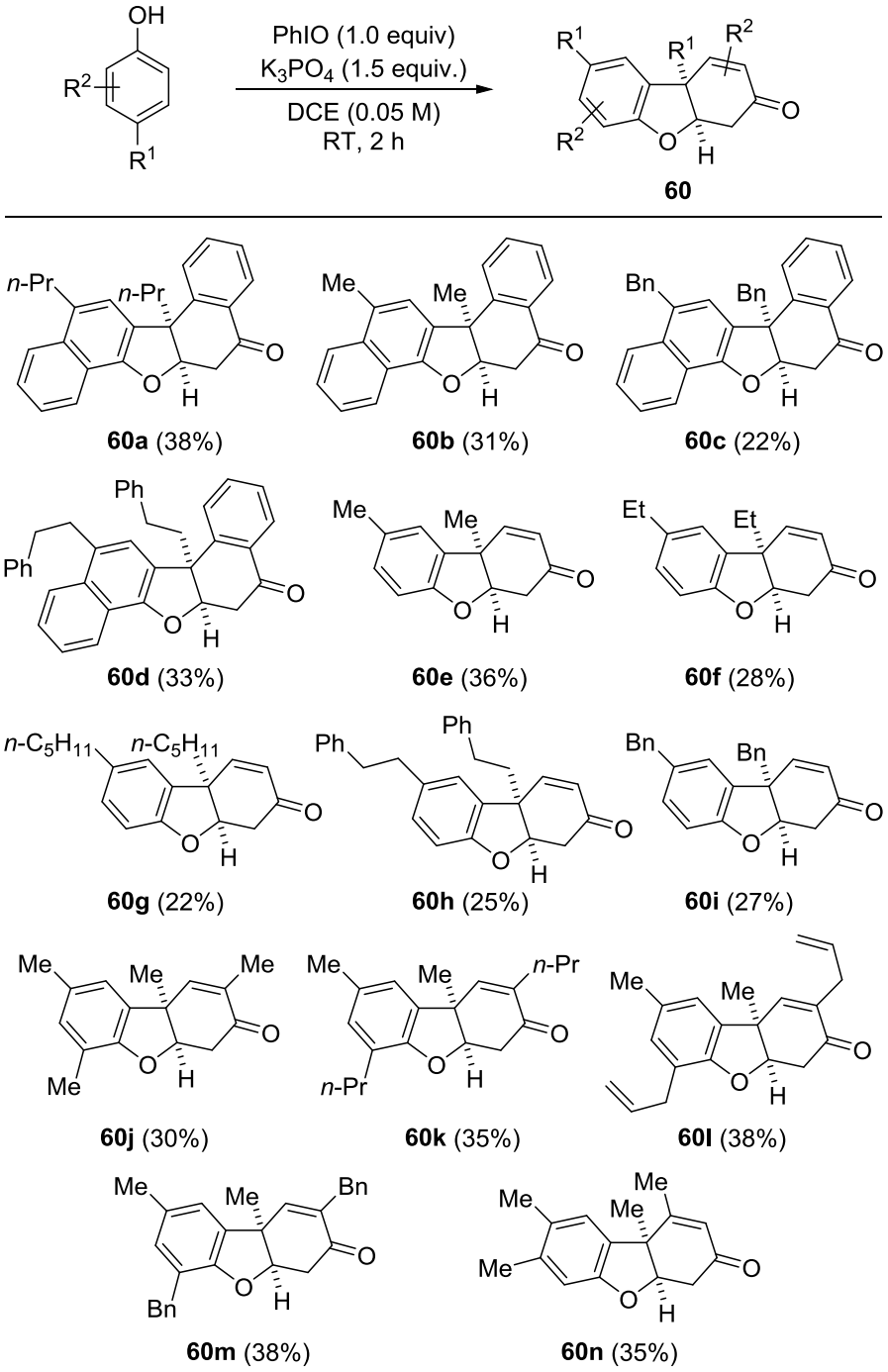


Figure 2.4. Scope of the PhIO-promoted oxidative phenolic coupling (isolated yields).

2.4. Plausible mechanism

Although for most of the oxidative reactions of phenols promoted by hypervalent iodine(III) reagents two-electron mechanisms have usually been implicated,[203,233] recent investigations on the dearomatizing phenol hydroxylation (Figure 1.19) demonstrate that a radical pathway is also a viable option.[52] Additionally, the similarity of the PhIO-promoted reaction to the other phenolic couplings employing single-electron oxidants, such as Fe(III), Ag(II), or peroxides,[217–221] lends support for a radical mechanism. Therefore, we propose that the PhIO-promoted phenolic coupling follows a radical pathway depicted in Figure 2.5.

In order to efficiently undergo a single-electron oxidation the phenol substrate needs to be deprotonated,[235] thus, the presence of a base in the reaction mixture is necessary, despite that the stoichiometry of the reaction does not require extra base (phenolic protons recombine eventually with the oxygen of PhIO, becoming H_2O). The single-electron transfer from PhIO to phenolate anion is deemed favorable as it results in the formation of a resonance-stabilized phenoxyl radical and the cleavage of the weak hypervalent bond in PhIO, yielding iodanyl(II) radical, presumably PhI(OH)•. The latter species can in turn oxidize another phenolate, producing the second equivalent of the phenoxyl radical. The recombination of two phenoxyl radicals may take place in *ortho-para*, *ortho-ortho*, or C–O fashion, while *para-para* coupling is prevented by the steric hindrance. The respective dearomatized intermediates convert into their more stable aromatic tautomers. In the case of the *ortho-para* adduct, a subsequent intramolecular conjugate addition affords the Pummerer's ketone. Conversely, the phenol-containing products may undergo following successive oxidative couplings leading to higher oligomers.

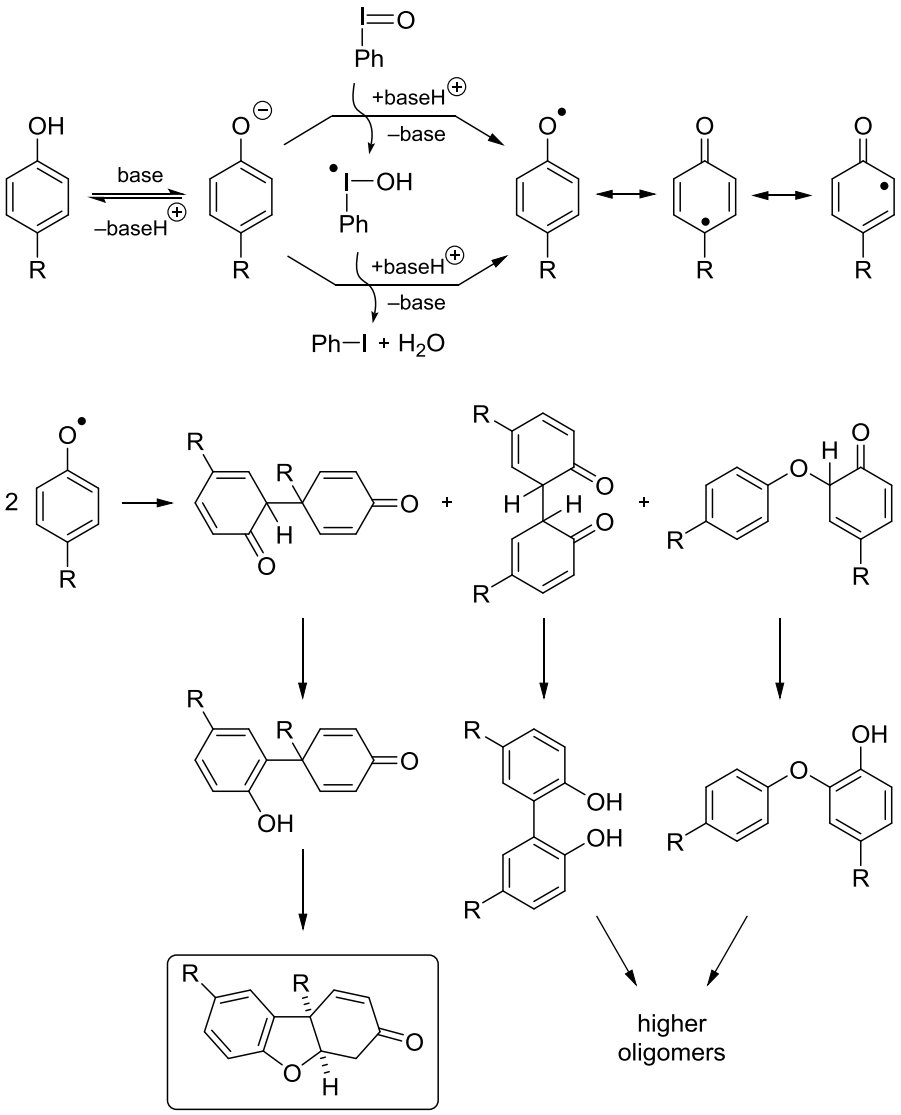


Figure 2.5. Plausible mechanism for the PhIO-promoted phenolic coupling leading to Pummerer's ketone.

2.5. Conclusions

In summary, we have developed an iodosobenzene-promoted oxidative phenolic coupling, which affords Pummerer's ketone and its analogs. The method enables the synthesis of an array of compounds, derived both from phenols and naphthols, and containing various substitution patterns, with excellent diastereoselctivity. The products are formed in 20-40% yield, which is synthetically useful considering the large increase of the molecular complexity during this one-step process. Importantly, the Pummerer's ketone analogs are selectively formed under the developed conditions, adding to the practical synthetic usefulness of the method.

Chapter 3

Intramolecular enantioselective and distereoselective oxidative dearomatization of naphthols and phenols: Synthesis of spirocarbocycles by the merger of I(III)-promoted oxidation and organocatalysis

3.1. Background

According to IUPAC, "spiro ring systems have two or more rings linked by one common atom".[236] They were first postulated by Adolf Baeyer in 1900.[237] Spriocycles frequently occur in natural products[238–240] and spirocyclic compounds are the focus of modern drug discovery due to their presence in a variety of medicinally important molecules exhibiting a broad range of biological activities. The structure of some bioactive natural products, such as anticardiovascular magellanine **61**, cytotoxic daphnilongeranin C **62**, neurotrophic tricycloillicinone **63**, and antitubercular colombiasin A **64**, which contain *ortho*-fused spiro-[6-5]-bicycles are depicted in Figure 3.1.The design of new spirocyclic scaffolds and methods for their preparation is one of the central themes in modern organic synthesis. Importantly, spirocycles by definition contain a tetra-substituted carbon atom and often possess central or axial chirality. This, combined with the high degree of rigidity imparted by the spiro ring junction, lead to the development of a number of spirocyclic chiral ligands and catalysts, such as **65**-**68** (Figure 3.1), that have found applications in various asymmetric transformations.[241–246]

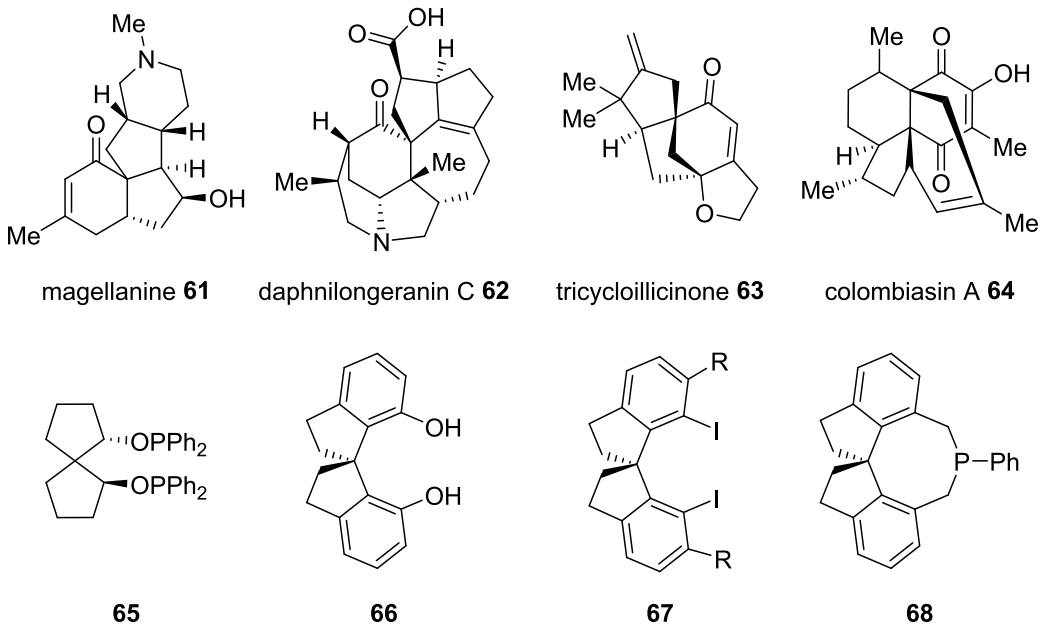


Figure 3.1. Biologically active natural products and chiral ligands/catalysts containing spiro linkages.

Oxidative dearomatization of phenols by hypervalent iodine reagents is one of the synthetic strategies to access various functionalized spirocycles. As discussed in section 1.3.2, upon the treatment with iodine(III) compounds, typically PIDA or PIFA, phenols undergo an oxidative dearomatization coupled with the addition of a nucleophile to either *ortho*- or *para*-position. By tethering the nucleophilic group to the phenol, several dearomatizing transformations resulting in the formation of spirocycles have been developed (see section 1.3.2). This chapter focusses on our attempts to obtain carbospirocycles via a I(III)-promoted phenol dearomatization, using as the nucleophiles tethered enamines that would be generated upon the action of secondary amine catalysts on aldehydes (Figure 3.2).

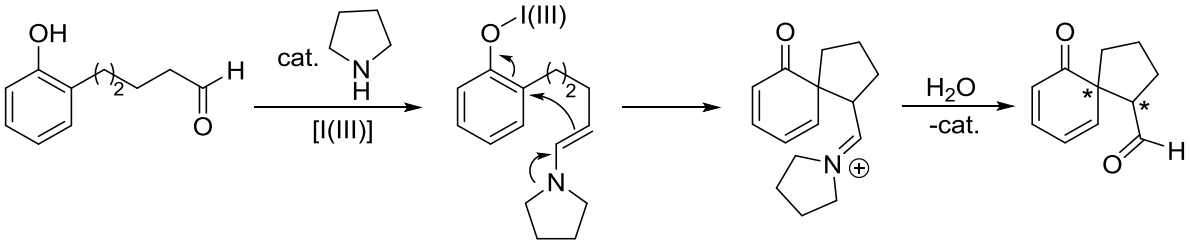


Figure 3.2. Proposed synthesis of spirocycles by combining iodine(III)-promoted phenol dearomatization with the catalytic enamine activation of aldehydes.

The catalytic Umpolung activation of aldehydes to form nucleophilic enamines is the classic approach in asymmetric organocatalysis that has revolutionized organic synthesis since the beginning to the 21st century and was eventually acknowledged by the Nobel Prize in 2021.[247–249] Application of chiral secondary amine catalysts, such as proline derivatives, may allow for the controlled formation of the stereogenic centers created during the envisioned reaction.

3.2. Development of reaction conditions

We started the project with synthesizing five suitable substrates for the dearomatization, **69-73**, shown in Figure 3.3. The synthetic route, exemplified for **69**, involved an initial Wittig olefination of a naphthol aldehyde. Next, the phenol group was protected as TBS ether, followed by a hydrogenation of the double bond and a DIBAL reduction of the ester to the aldehyde. Finally, the silyl protection was removed by TBAF. Similarly, the other four substrates **70-73** were synthesized from the respective hydroxy-naphathaldehydes or benzaldehydes.

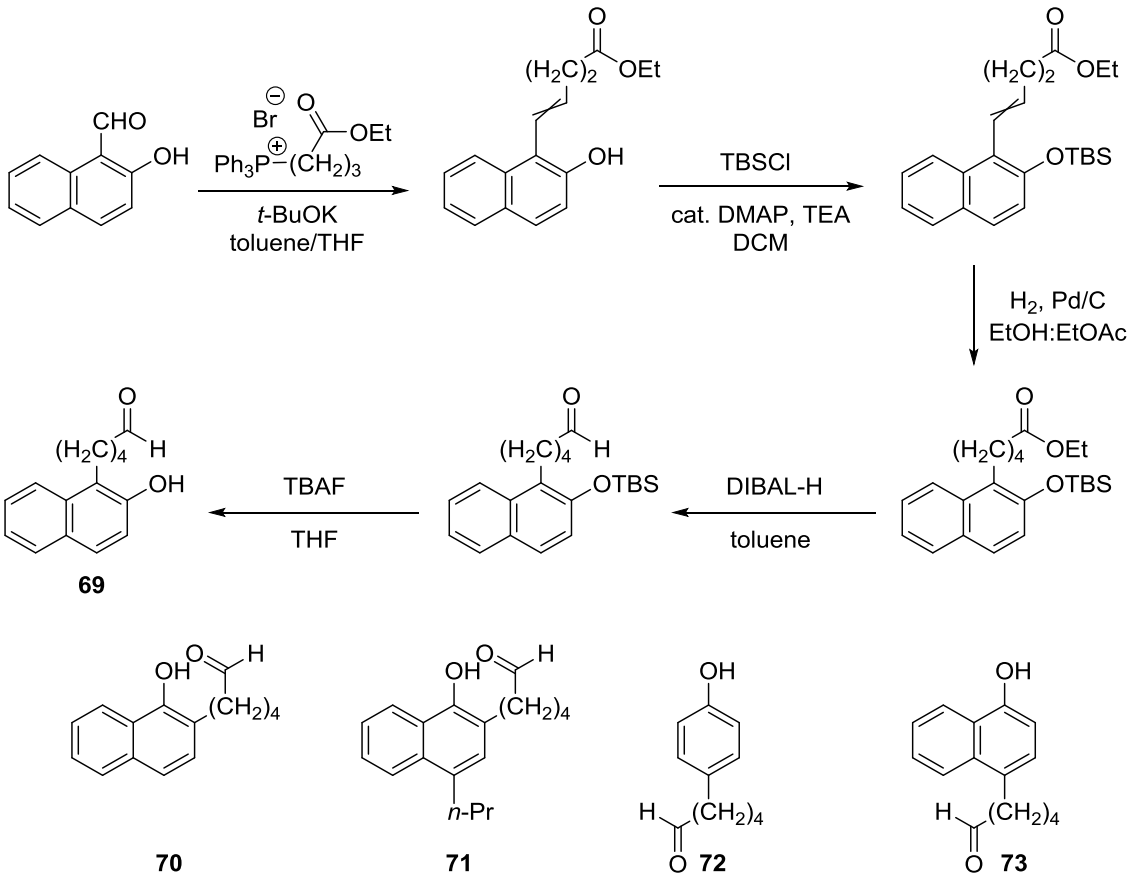
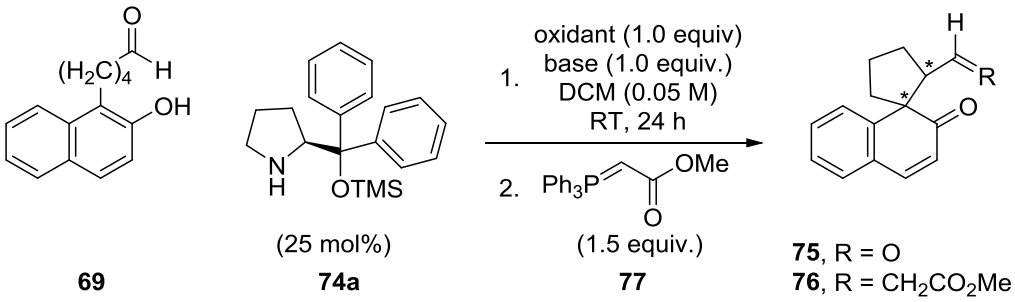


Figure 3.3. Synthetic route to the starting materials.

The initial testing of the reaction conditions was performed on substrate **69**, using 25 mol% of the canonical secondary amine organocatalyst – TMS-protected diphenylprolinol **74a**. Several commercially available hypervalent iodine(III) reagents, such as PIDA, PIFA, and Koser reagent were screened, but unfortunately no desired product **75** was obtained (Table 3.1, entries 1-3). The use of iodine(V) reagents yielded similar results (entries 4 and 5). Although the use of iodosobenzene resulted in trace amounts of the desired spirocycle (entry 6), an increase to 8% was observed when the reaction was performed in the presence of 1 equivalent of trimethylamine (entry 7). Repeating this reaction resulted variable erratic yields each time, probably due to the inherent instability of the aldehyde product (*e.g.*, toward an aldol reaction). Therefore, we decided to convert the product to the corresponding alkene **76**, via a one-pot Wittig olefination with phosphorane **77**, after the reaction. We have since tested *ortho*-iodosoanisole and iodosomesitylene, and to our delight, the former resulted in a two-fold increase in the yield (entries 8 and 9).

Table 3.1. Initial screening of oxidants.



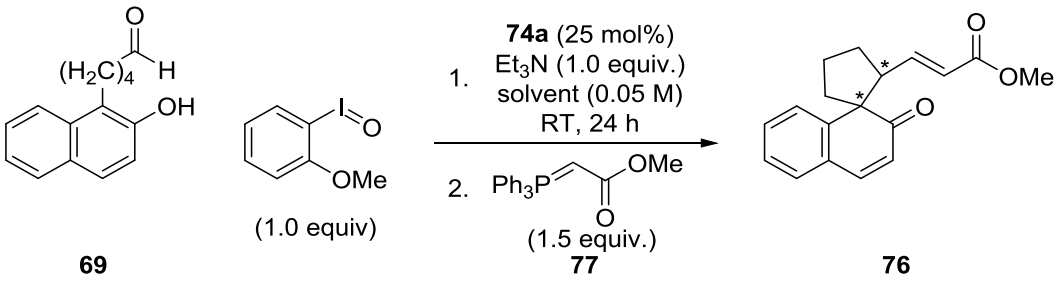
69 **74a** **77**

Entry	Reaction conditions	Yield %[a] (**75**/**76**)
1	PIDA, no base	0 (**75**)
2	PIFA, no base	0 (**75**)
3	Kosher reagent, no base	0 (**75**)
4	Dess-Martin reagent, no base	0 (**75**)
5	IBX, no base	0 (**75**)
6	PhIO, no base	<3 (**75**)
7	PhIO, Et_3N; then **77**	8; 8 (**75**; **76**)
8	*o*-iodosoanisole, Et_3N; then **77**	17 (**76**)
9	iodosomesitylene, Et_3N; then **77**	6 (**76**)

[a] Determined through analysis by ^1H NMR spectroscopy.

An assessment the reaction media on the reaction outcome showed that polar solvents, both protic and aprotic, have an adverse effect on the yield (Table 3.2, entries 1-7). The other tested solvents provided the product in comparable amounts (entries 8-17).

Table 3.2. Effect of solvents on the reaction outcome.



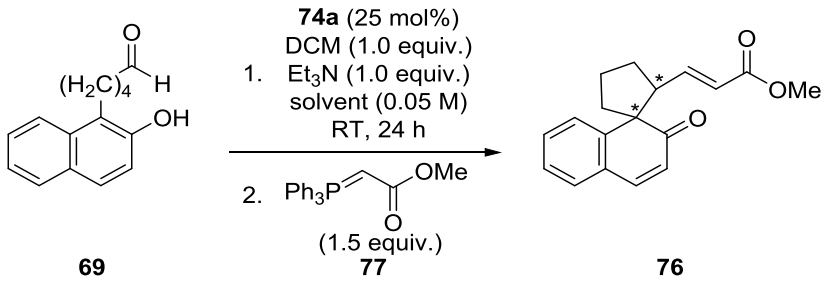
Entry	Solvents	Yield %[a]
1	DMA	0
2	DMF	2
3	DMSO	1
4	TFE	0
5	HFIP	4
6	EtOH	4
7	MeOH	4
8	Et_2O	19
9	$CDCl_3$	16
10	$CHCl_3$	18
11	DCE	16
12	THF	16
13	1,4-dioxane	13
14	Cy-H	15
15	pentane	10
16	toluene	22
17	MeCN	10

[a] Determined through analysis by ^{1}H NMR spectroscopy.

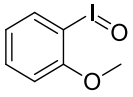
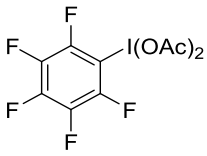
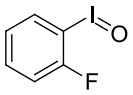
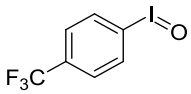
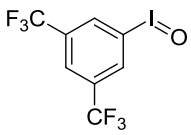
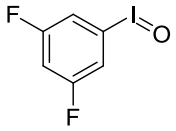
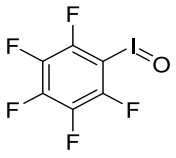
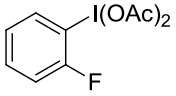
Therefore, we returned to a more extensive screening of the oxidants (Table 3.3). To this end, we synthesized and tested a series of iodosoarenes and aryliodo diacetates, and other oxidants used for the phenol dearomatization. 3,5-Bis(trifluoromethyl)iodosobenzene **78** worked best, resulting in 25% of desired product (entry 4). In general, iodosoarenes performed better than aryliodo diacetates. The other tested oxidants that have delivered some product were: $(PhIO)_3{\bullet}SO_3$, which can be considered as a modified, partially depolymerized, and activated form of iodosobenzene (entry 12)[250]; iminoiodane, an iodosobenzene surrogate (entry

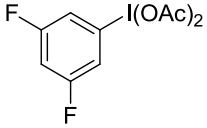
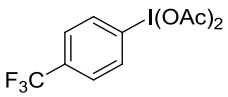
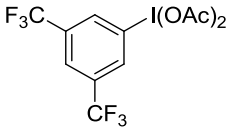
13)[251]; iodylbenzene (entry 14); NBS (entry 17); and, sodium hypochlorite (entry 19). However, they provided results not better than 3,5-bis(trifluoromethyl)iodosobenzene.

Table 3.3. Second screening of oxidants.



69 **77** **76**

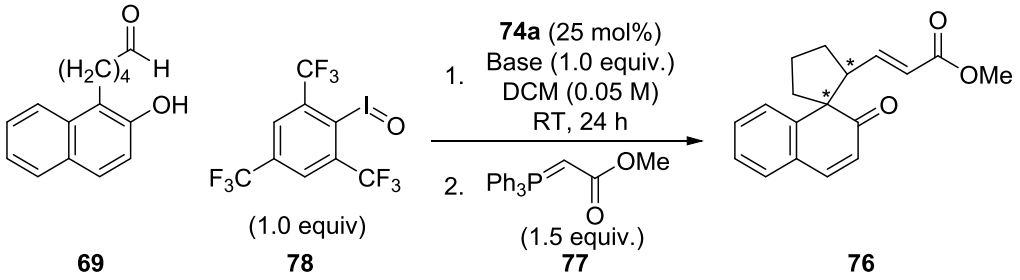
Entry	Oxidants	Yield %[a]	Entry	Oxidants	Yield %[a]
1		17	11		11
2		23	12	$(PhIO)_3*SO_3$	4
3		4	13	PhINTs	6
4		25	14	$PhIO_2$	16
5		12	15	CAN	<1
6		15	16	DDQ	2
7		13	17	NBS	19

Entry	Oxidants	Yield %[a]	Entry	Oxidants	Yield %[a]
8		15	18	Oxone	4
9		18	19	$NaClO•5H_2O$ (2.0 equiv.)	21
10		14			

[a] Determined through analysis by ^1H NMR spectroscopy.

Table 3.4 presents the effect of various inorganic and organic bases on the efficiency of the reaction. Inorganic bases were all found to be unsuitable for this transformation (entries 1-5). Slight increase in yield was observed with the increase in the amount of Et_3N (entries 13 and 14), while other organic bases provided inferior results.

Table 3.4. Screening of bases.

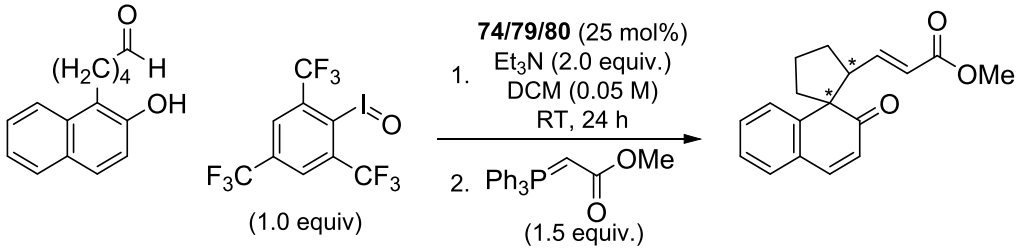


Entry	Base	Yield %[a]
1	Li_2CO_3	5
2	Ca_2CO_3	5
3	K_3PO_4	8
4	$NaHCO_3$	3
5	KOH	2
6	NaOAc	6
7	*t*-BuOK	0
8	DIPA	22
9	pyridine	6
10	DMAP	15
11	DABCO	18
12	DBU	8
13	Et_3N (1.5 equiv.)	26
14	Et_3N (2.0 equiv.)	28

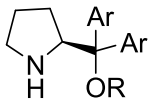
[a] Determined through analysis by ^1H NMR spectroscopy.

Subsequently, various chiral organocatalysts were evaluated, both in terms of the yield as well as the enantioselectivity (Table 3.5). Unfortunately, the results could not be improved. In particular, similar levels of efficiency and enantioselectivity were obtained using the catalysts with more bulky 3,5-dimethylphenyl, 2-naphthyl, and 3,5-bis(trifluoromethyl)phenyl moieties and larger silyl groups (**74a**-**g**, entries 1-7). We also tried to activate the tethered aldehyde with MacMillan's imidazolidinone organocatalysts of type **79**, but to our disappointment they did not work better than the proline-derived catalysts (entries 8-12). Other potential catalysts, including amino acids: L-proline, D-valine, L-*t*-Bu-leucine, L-α-phenylglycine, L-phenylalanine, and L-alanine provided the desired product in trace amounts (not shown). Finally, the bifunctional squaramide-based secondary amine **80** catalyst gave no product, as well (entry 13).

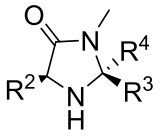
Table 3.5. Effect of organocatalysts on the reaction outcome.



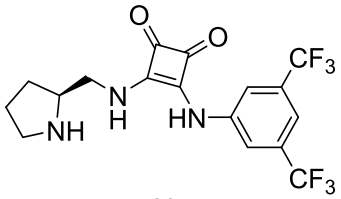
69 **78** **77** **76**



146



79



80

74a, Ar = Ph, R = TMS
74b, Ar = Ph, R = TBS
74c, Ar = 2-naphthyl, R = TMS
74d, Ar = 2-naphthyl, R = TBS
74e, Ar = 3,5-dimethylphenyl, R = TMS
74f, Ar = 3,5-bis(trifluoromethyl)phenyl, R = TMS
74g, Ar = 3,5-bis(trifluoromethyl)phenyl, R = TDS

79a, R^2 = Bn, R^3 = *t*-Bu, R^4 = H
79b*TFA, R^2 = H, R^3 = *t*-Bu, R^4 = H
79c*DCA, R^2 = Bn, R^3 = Me, R^4 = Me
79d*HCl, R^2 = Bn, R^3 = Me, R^4 = Me
79e, R^2 = Bn, R^3 = 5-methyl-2-furyl, R^4 = H

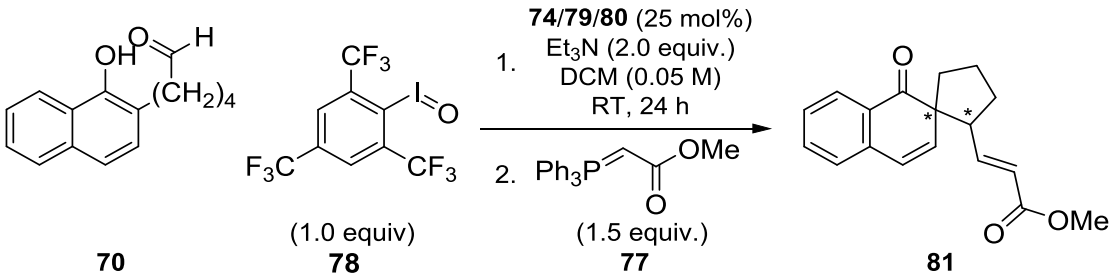
Entry	Catalyst	Yield %[a]	dr[a]	*ee*[b]
1	**74a**	27	6:1	72
2	**74b**	30	7:1	68
3	**74c**	26	6:1	68
4	**74d**	30	7:1	70
5	**74e**	27	4:1	72
6	**74f**	15	14:1	16
7	**74g**	20	9:1	0
8	**79a**	6	3:1	-
9	**79b**	7	3:1	-
10	**79c**	4	3:1	-
11	**79d**	7	3.4:1	-
12	**79e**	7	3:1	-
13	**80**	0	-	-

[a] Determined through analysis by ^{1}H NMR spectroscopy; [b] *ee* of the major diastereomer, determined by HPLC with a chiral column.

So far, the best results observed for the β-naphthol substrate were the yield up to 30% *i.e.*, no catalytic turnover and the *ee* up to 72% (Table 3.5, entries 2 and 1, respectively). Thus, we decided to apply these conditions for the other synthesized substrates **70**-**73**.

The yields as well as the enantioselectivities for the α-naphthol derivative **70,** using various catalysts were worse compared to those obtained for the **69** (Table 3.6).

Table 3.6. Effect of organocatalyst on the reaction outcome for substrate **70**.



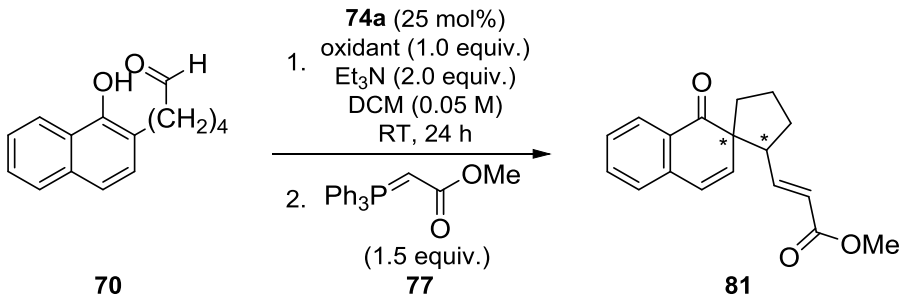
Entry	Catalyst	Yield %[a]	*ee*[b]
1	**74a**	13	52
2	**74b**	6	-
3	**74c**	14	50
4	**74d**	8	-
5	**74e**	13	50
6	**74f**	13	50
7	**74g**	14	50
8	**79a**	12	-
9	**79b**	10	-
10	**79c**	11	-
11	**79d**	12	-
12	**79e**	11	-
13	**80**	4	-

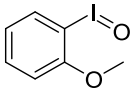
[a] Determined through analysis by ^{1}H NMR spectroscopy. The diastereomeric ratio could not be determined due to signal overlapping in crude NMR spectra. [b] *ee* of the major diastereomer, determined by HPLC with a chiral column.

A re-evaluation of oxidants, however, have identified sodium hypochlorite as a better choice in the case of substrate **70**, however, the results were still far from satisfactory (Table 3.7).

Specifically, it provided 34% yield and 80% enantiomeric excess of the desired product at 0 °C (entry 6).

Table 3.7. Effect of oxidant on reaction outcome for substrate **70**.



Entry	Oxidant	Yield %[a]	*ee*[b]
1	PhIO	0	-
2		0	-
3	PIDA	0	-
4	$NaClO{\bullet}5H_2O$ (2.0 equiv.)	20	80
5	$NaClO{\bullet}5H_2O$ (2.0 equiv.), 0 °C	14	62
6	$NaClO{\bullet}5H_2O$ (2.0 equiv.), no base, 0 °C	34	80

[a] Determined through analysis by ^1H NMR spectroscopy. The diastereomeric ratio could not be determined due to signal overlapping in crude NMR spectra. [b] *ee* of the major diastereomer, determined by HPLC with a chiral column.

The related α-naphthol substrate **71**, containing an additional *para*-substituent, did not deliver any promising results irrespective of the applied conditions (up to 6% yield of product). Similarly, phenol **72** and naphthol **73**, with the aliphatic aldehyde tethered at the *para*-position, gave no spirocyclic products **82** and **84**. Instead, they yielded up to 8% of the corresponding Pummerer's ketones **83** and **84**, respectively (Figure 3.10). In the case of **72**, most of the substrate was recovered, while for **73**, it was presumably fully converted to some polar polymeric material.

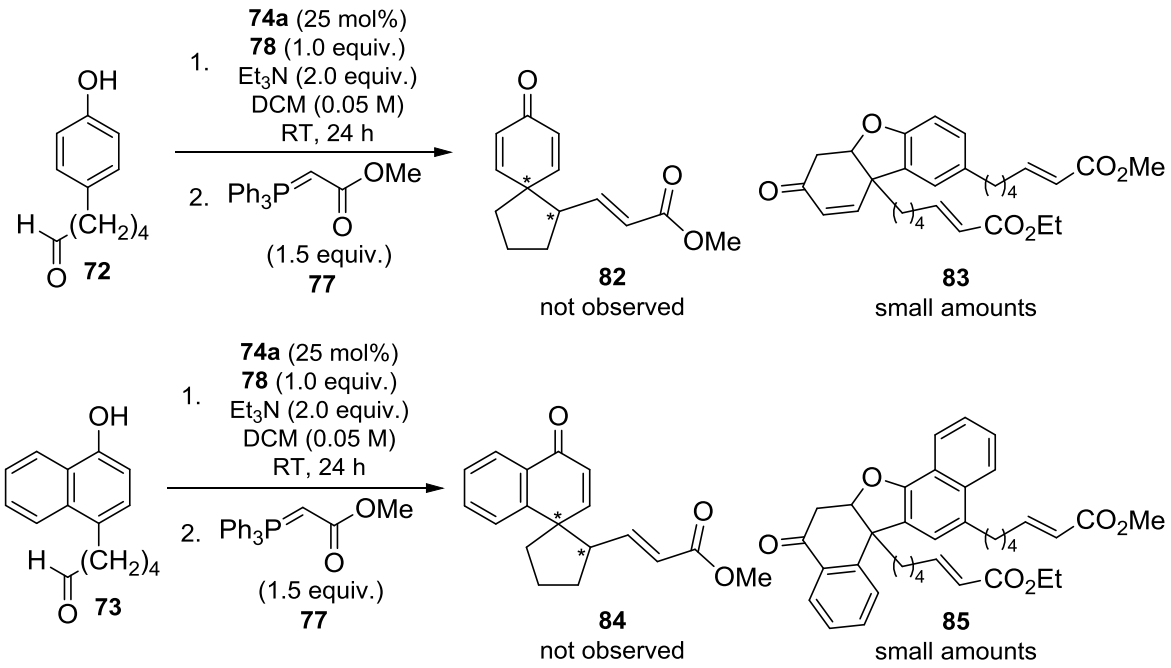


Figure 3.10. Reaction of substrates **72** and **73** under the developed reaction conditions.

3.3. Conclusions

In conclusion, we attempted to develop a hypervalent iodine-mediated, amine organocatalyzed protocol to synthesize all-carbon spirocycles via the dearomatization of naphthols and phenols with tethered aldehydes. Though we succeeded in obtaining some of the desired products with modest to good enantioselectivity, the yields of the reactions were unsatisfactory. We speculate that such outcome may be due to the oxidation of the phenol moiety by the stoichiometric oxidant being too fast compared to the catalytic generation of the enamine nucleophile, leading to substrate decomposition.

Chapter 4
Synthesis of aryl sulfides by metal-free arylation of thiols with diaryliodonium salts (Paper II)

4.1. Background

Aryl sulfide moiety is ubiquitous in natural products and bioactive molecules.[252,253] These include several pharmaceuticals and drug candidates, exhibiting for example anti-Alzheimer, antiviral, antiinflammatory, and antidepressant activities (Figure 4.1).[254–257] Moreover, aryl sulfides constitute important reagents for organic synthesis[258–262] and building blocks in material chemistry.[263–265]

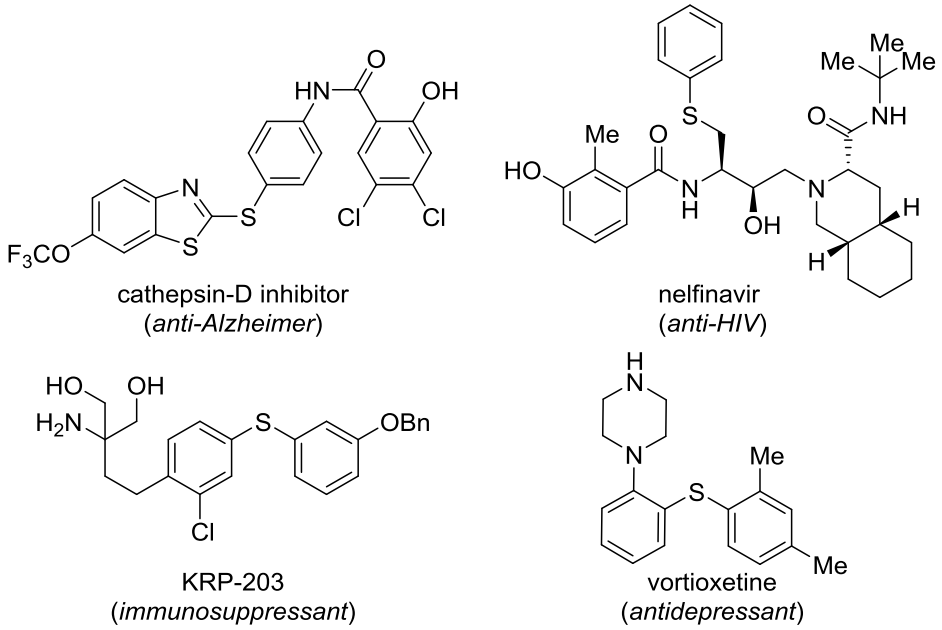


Figure 4.1. Examples of bioactive compounds containing an aryl sulfide moiety.

Among the existing methods for the preparation of aryl sulfides, the most general and widely used is the transition metal-catalyzed C–S cross-coupling.[266–268] Complexes of a variety of metals, such as palladium, nickel, copper, cobalt, iron, gold, and indium, have been used as catalysts in these reactions.[269–277] Apart from the typical couplings of aryl halides with thiols, oxidative and reductive variants also exist.[278–281] Despite their high versatility, the inherent drawbacks of the transition metal catalyzed cross-couplings, especially in the context of pharmaceutical applications, are high price of the catalysts and possible contamination of products with trace metal residues. Therefore, the development of metal-free methods for the synthesis of aryl sulfides is an outstanding challenge and a number of such processes, for instance organocatalytic or photoinduced, has been recently reported.[282–285]

One possible approach to eliminate the need of transition metal catalysis during Ar–S bond formation is the application of aryl transfer reagents based on hypervalent iodine. The steep downhill thermodynamics of I(III) to I(I) reduction has allowed for the arylation of various carbon and heteroatom nucleophiles (*e.g.*, N-, O-, and P-centered) under metal-free conditions (see sections 1.4.4-1.4.5 and 1.4.7), however, the reports of aryl transfers to sulfur are scarce (section 1.4.6).[86,87,286–289] In particular, as far as the synthesis of aryl sulfides from thiols is concerned, there exist only three such methods, employing diaryliodonium salts. Two of them, developed by Zheng and Chen, have the advantage of not requiring any extra reagents, but their

scope is strictly limited to 2-mercaptobenzazole substrates (Figure 4.2a).[290,291] A more general procedure reported by Sanford utilizes an acid activation (Figure 4.2b).[174] Albeit it constituted a considerable advancement, that protocol is still restricted to simple thiols, mainly due to relatively harsh reaction conditions and long reaction times.

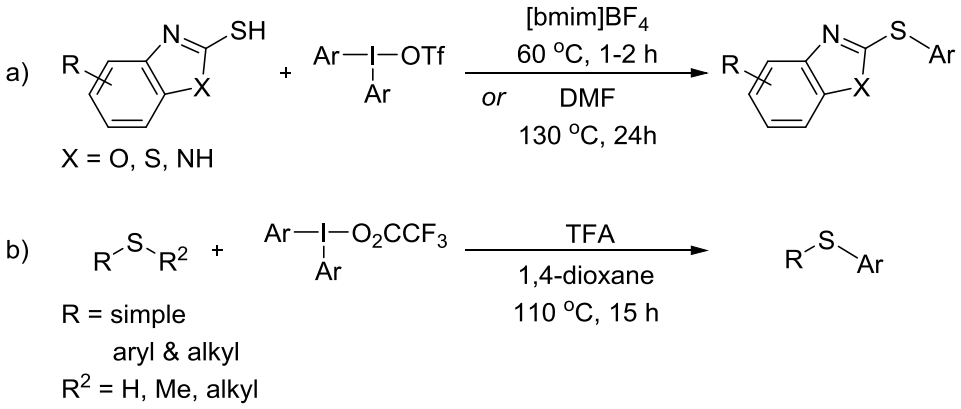


Figure 4.2. Transition metal-free synthesis of aryl sulfides using diaryliodonium salts.

Diaryliodonium salts have also been used for synthesis of aryl sulfides under palladium catalysis conditions (Figure 4.3a).[292] In another report, Mossadegh reported the preparation of various alkyl-, aryl-, and diaryl sulfides via the reaction of diphenyliodonium iodide and disulfides promoted by a $Zn/AlCl_3$ system (Figure 4.3b).[293]

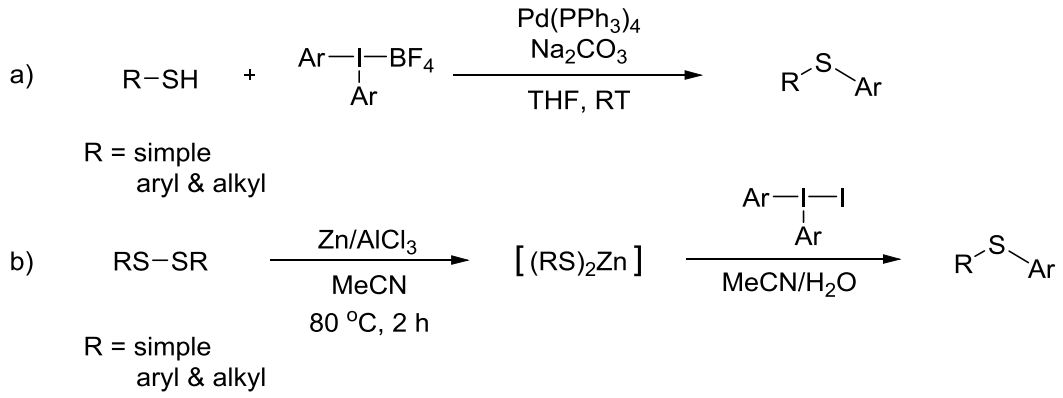


Figure 4.3. Transition metal-catalyzed/promoted synthesis of aryl sulfides using diaryliodonium salts.

We hypothesized that the activation of the thiol nucleophile by a base, commonly applied in other reactions employing hypervalent iodine group transfer reagents,[161,168,172,86,286–289,294–296]

may lead to a facile formation of aryl sulfides under mild conditions, allowing for the synthesis of complex products, relevant to pharmaceutical applications (Figure 4.4).

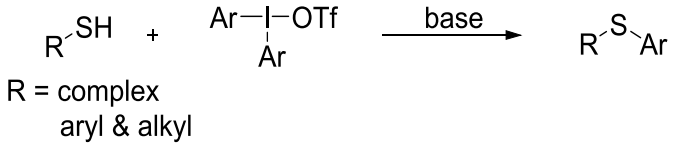
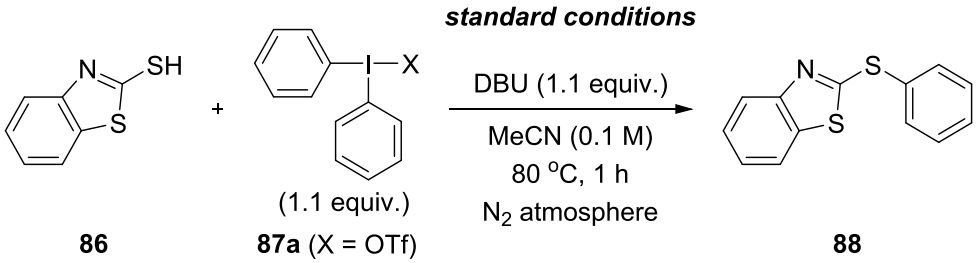


Figure 4.4. Proposed synthesis of aryl sulfides by the arylation of thiols with diaryliodonium salts under basic conditions.

4.2. Optimization of reaction conditions

Using 2-mercaptobenzothiazole **86** and diphenyliodonium trilfate **87a** as model substrates, we were able to establish a set of conditions for the *S*-arylation in quantitative yield (Table 4.1, entry 1). In particular, the reaction is carried out in the presence of DBU in MeCN at 80 °C, under the atmosphere of nitrogen. The arylation also proceeds well with a range of other bases, both organic and inorganic (entries 2-7), however, these were later found to provide lower yields than DBU, when other starting materials were used. As far as solvents are concerned, application of toluene and DCE led to slightly decreased yields (entries 11-12), while further decline was observed for the other tested solvents (entries 13-15). We have also evaluated diphenyliodonium salts bearing various counter-anions, all of which delivered the product in excellent yields (entries 16-20). However, the use of phenylbenziodoxolone as the aryl transfer reagent had a detrimental effect on the reaction outcome (entry 21). Finally, it was determined that the efficiency of the arylation drops significantly at lower temperature (entry 22) and that the inert atmosphere is compulsory to attain quantitative product formation (entry 23).

Table 4.1. Effect of reaction parameters.



Entry	Change from the standard conditions	Yield %[a]
1	none	95
2	TMG, instead of DBU	99
3	Et_3N, instead DBU	87
4	*t*-BuOK, instead of DBU	84
5	AcONa, instead of DBU	91
6	Cs_2CO_3, instead of DBU	97
7	K_3PO_4, instead of DBU	98
8	$NaHCO_3$, instead of DBU	34
9	pyridine, instead of DBU	27
10	DABCO, instead of DBU	56
11	toluene, instead of MeCN	82
12	DCE, instead of MeCN	85
13	CPME, instead of MeCN	72
14	DMSO, instead of MeCN	72
15	Cy-H, instead of MeCN	57
16	X = BF_4 (**87b**), instead of X = OTf	100
17	X = $OOCCF_3$ (**87c**), instead of X = OTf	97
18	X = Cl (**87d**), instead of X = OTf	100
19	X = OTs (**87e**), instead of X = OTf	95
20	X = AsF_6 (**87f**), instead of X = OTf	91
21	phenylbenziodoxolone (**87g**), instead of **87a**	0
22	RT, instead of 80 °C	46
23	under air, instead of N_2	80

[a] Yields are average of two experiments and were determined by ^1H NMR spectroscopy.

4.3. Scope and limitations

Having optimized the reactions conditions, we explored the scope and limitations of this transition metal-free *S*-arylation of thiols. With regard to the thiol coupling partner (Figure 4.5), good to excellent yields were obtained for five-membered heterocyclic thiols. These include thiols derived from pharmaceutically-relevant benzazoles (**88a**, **88b**),[297] as well as thiazole (**88c**), 2-thiazoline (**88d**), and 1,3,4-oxadiazole (**88e**). 2-Mercaptoimidazole furnished the product with moderate efficiency (**88f**), likely due to the presence of a free NH group, although no aryl transfer to the nitrogen could be detected. The method is also applicable to the synthesis of aryl sulfides containing six-membered heterocycles, such as pyridine (**88g**, **88h**) and pyrimidine (**88i**). The arylation of thiophenols is possible for unsubstituted, electron-poor, and electron-rich substrates (**88j-88l**). As far as the aliphatic thiols are concerned, they undergo the arylation under the developed conditions in somewhat lower, albeit still synthetically useful, overall yields compared to the aromatic counterparts. However, the reaction has proven to be quite general, tolerating starting materials ranging from simple alkyl (**88m**), through benzyl (**88n**), to functional group-containing thiols (**88o**). Noteworthy, 1-thio-β-D-glucose derivative could be *S*-arylated in good yield (**88p**), demonstrating the usefulness of the method for the preparation of complex, biologically-relevant aryl sulfides.

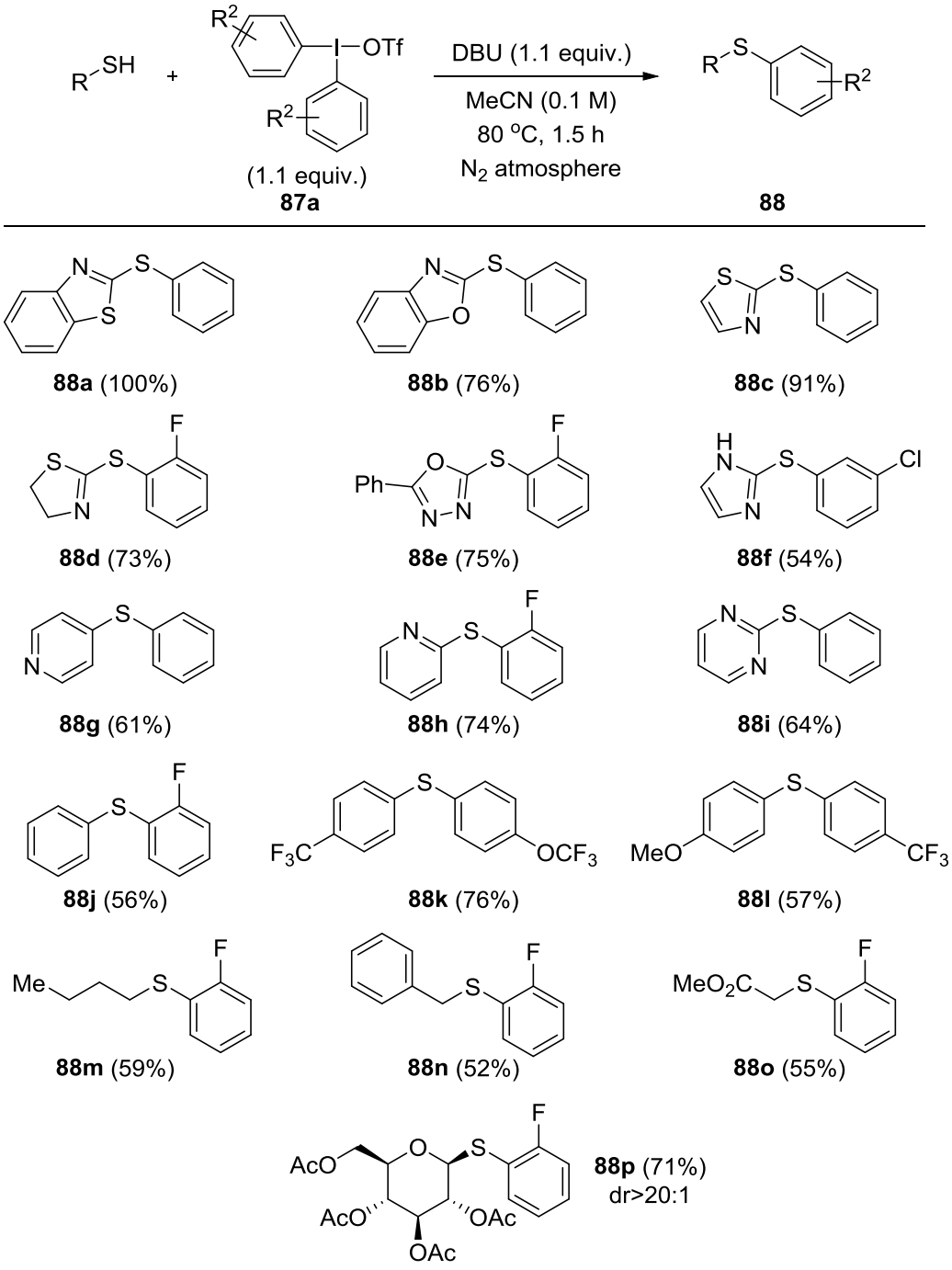


Figure 4.5. Scope with regard to the thiol (isolated yields).

Some thiols (Figure 4.6), such as 2-mercaptopurine (**88q**), 2-quinolinethiol (**88r**), and 1,2,4-triazole-3-thiol (**88s**) gave low yields of *S*-arylated products under the developed conditions. Compared to thiophenol, the arylation of 2-naphthalenethiol (**88t**) proceeded in slightly reduced

yield. The synthesis of *S*-aryl thiocarboxylates (**88u**), and aryl esters of thio- and dithiocarbamic acids (**88v**, **88w**) was also achieved. Though no product was observed for L-cysteine ethyl ester (**88x**) and captopril (**88y**).

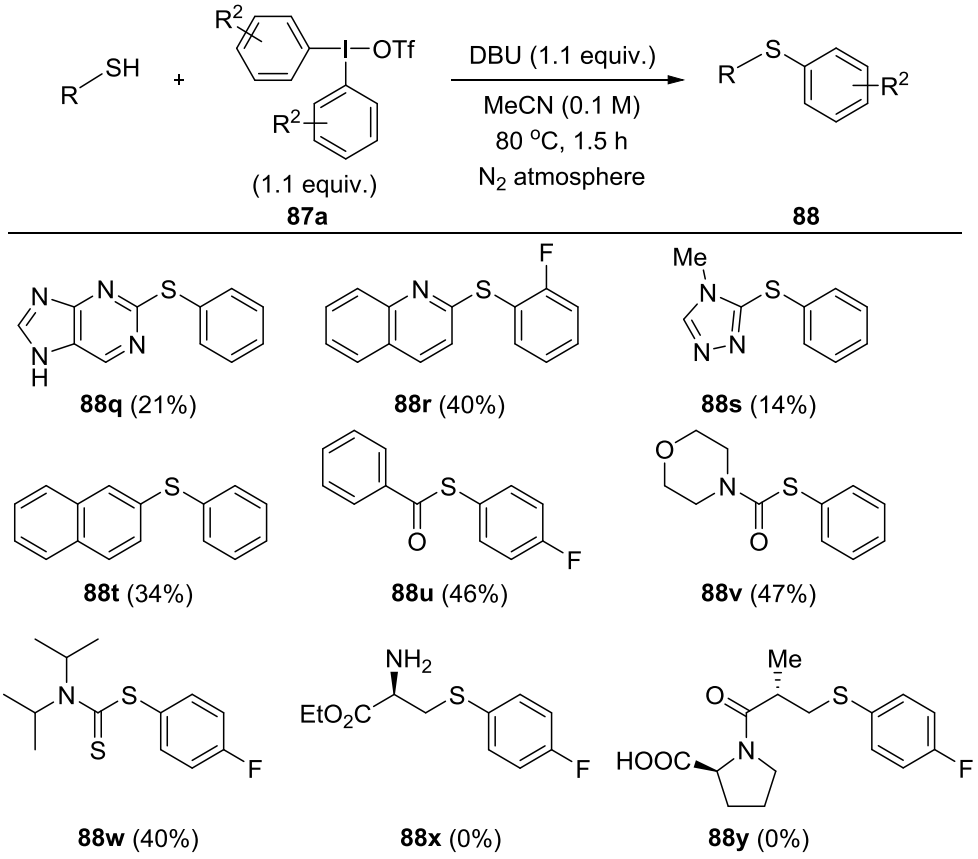


Figure 4.6. Unsuccessful substrates (NMR yields).

Next, we examined the scope with respect to diaryliodonium salts (Figure 4.7). The reaction works well for 2- and 3-halide substituted aryl rings (**88z**, **88aa**), however, 4-fluorophenyl is transferred in a low yield (**88ab**). All evaluated trifluoromethyl-containing aryl groups furnished desired sulfides with high efficiency (**88ac**-**88ae**), displaying the applicability of the developed methodology to prepare compounds of potential pharmaceutical interest.[298–300] The presence of other electron-withdrawing substituents, such as nitro (**88af**) and ester (**88ag**), also resulted in excellent yields of the corresponding products. Similarly, moderately electron-rich aryls are well tolerated, as in the case of mesityl (**88ah**) and 4-(trifluoromethoxy)phenyl (**88ai**) moieties. The former example shows additionally that a considerable steric hindrance does not

interfere with the C–S bond formation. Only if a strongly electron-donating 4-methoxy substituent is present in the aryl ring, the efficiency of the coupling declines appreciably (**88aj**).

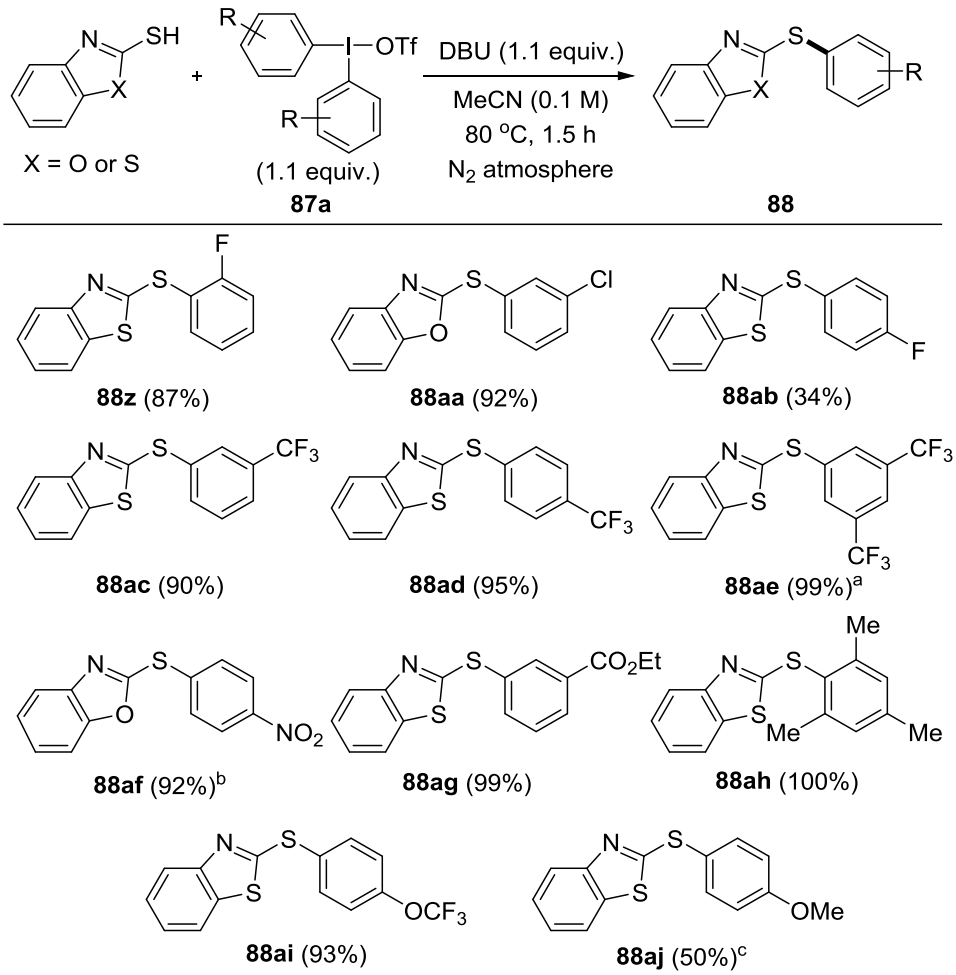


Figure 4.7. Scope with regard to the diaryliodonium salt (isolated yields).
[a] Synthesized using tetrafluoroborate salt; [b] Synthesized using unsymmetrical (4-nitrophenyl)(phenyl)iodonium triflate; [c] Synthesized using tosylate salt.

4.4. Computational mechanistic studies

In order to obtain insight into the mechanism of the developed reaction, we performed DFT calculations (Figure 4.8). The computations show that in the presence of thiolate anion **89a**, diphenyliodonium triflate **87a** is easily (via intermediate **90**) and quantitatively transformed into a much more stable (by 7.2 kcal/mol) iodonium thiolate species **91**. The latter compound can undergo a C–S bond-forming reductive elimination through **TS1** with a viable barrier of

21.5 kcal/mol, furnishing sulfide product **88a**. This process, reducing iodine from +III to +I oxidation state and leading to the loss of hypervalency, is highly exergonic (by 35.0 kcal/mol relative to **91**) providing the driving force for the reaction. We have also examined an alternative mechanistic pathway of a direct attack of thiolate nucleophile **89a** on the aryl group of iodonium salt **87a**. However, the corresponding transition state, **TS2**, is found to have a prohibitively high energy barrier (28.2 kcal/mol relative to **87a**). Therefore, the studied reaction follows preferentially the inner sphere pathway, reported for several other reactions employing iodine(III) group transfer reagents,[26,28,301,302] rather than a less common direct substitution route, wherein iodine constitutes a leaving group.[29,303,304]

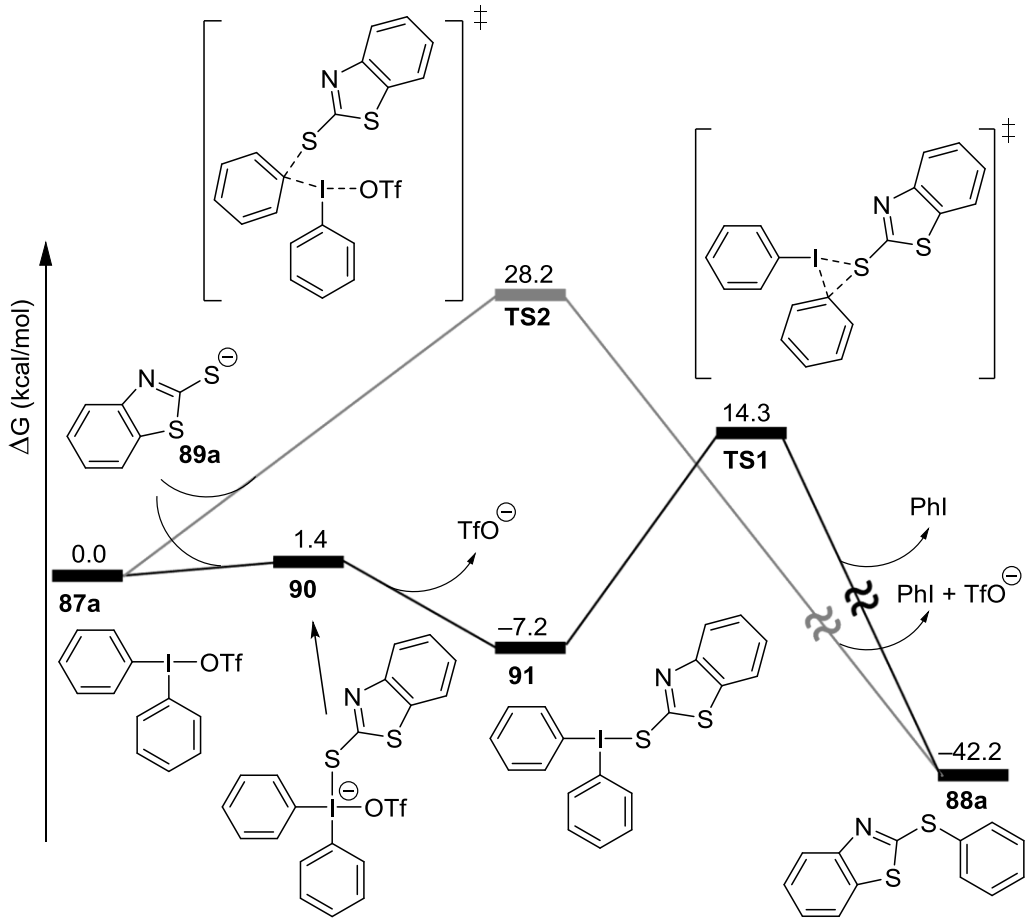


Figure 4.8. Calculated free-energy profile for the arylation of thiolate **89a** with diaryliodonium salt **87a** in MeCN.

4.5. Conclusions

In summary, we have developed an efficient method for the synthesis of aryl sulfides by the arylation of thiols with diaryliodonium salts. The reaction proceeds without the need of metal catalysis, under mild conditions, and it is experimentally simple. It delivers a range of products containing various moieties, including pharmacophoric groups, such as heteroaryls and a sugar derivative. The performed DFT calculations demonstrate that the process follows an inner-sphere mechanism via C–S bond-forming reductive elimination at iodine center.

Chapter 5
Metal-free *S*-arylation of phosphorothioate diesters and related compounds with diaryliodonium salts (Paper III)

5.1. Background

Sulfur-containing organophosphorus compounds display an array of interesting and valuable properties from both biological and chemical viewpoints. Accordingly, they have found widespread applications ranging from agrochemicals and pharmaceuticals (including oligonucleotide therapeutics), through building blocks for material and synthetic chemistry, to chiral catalysts.[305–311]

An important subset of the sulfur-containing organophosphorus compounds are *S*-aryl phosphorothioates (also referred to as aryl phosphorothiolates). Many of them are useful in their own right as pesticides (for example Edifenphos and Fonofos)[312–314] as well as biologically active agents (Figure 5.1).[315–317] Moreover, due to the intrinsic lability of the P–S–Ar linkage, this class of compounds have received considerable interest as intermediates in synthetic organic chemistry. In this context, *S*-aryl phosphorothioate moiety has been used, for instance, as a protecting group during the synthesis of modified oligonucleotides.[318–320] Their other synthetic applications include serving as convenient precursor for the construction of diverse classes of organophosphorus compounds, such as phosphates,[321] pyrophosphates,[322–324] phosphine oxides,[325] and aryl-[309,326] and vinylphosphonates.[327]

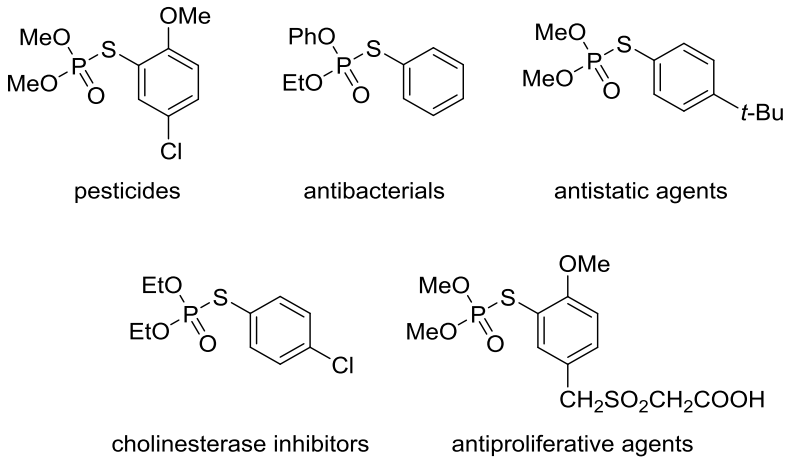


Figure 5.1. Examples of biologically active *S*-aryl phosphorothioates.

The traditional approaches for the synthesis of *S*-aryl phosphorothioates involve the construction of the P–S bond,[328] either via the phosphorylation of aryl thiols[329–332] or by the reaction of P(III) species with sulfur-centered electrophiles.[333–337] Except for a single isolated example,[338] none of these methods allows for effective stereoselective access to P-chiral molecules. Conversely, in the context of recent developments in the stereoselective preparation of P-chiral phosphorothioate diesters,[339–342] the alternative synthetic strategy, that is via the formation of the S–Ar bond, would provide a superior entry to *S*-aryl phosphorothioates in a stereopure form. Such synthetic pathway has, however, been explored to a much lesser extent. This state of affairs stems from the difficulty associated with the functionalization of an aromatic sp^2-hybridized carbon center and bonding it to sulfur. Specifically, there exist few reports on oxidative couplings of phosphorothioate diesters with arylboronic acids or electron-rich arenes, as well as Sandmeyer reactions employing diazonium and iodonium salts.[343–347] Yet most of these processes employ phosphorothioates generated *in situ* by the sulfurization of corresponding *H*-phosphonates, which cannot be readily accessed as pure enantiomers. Moreover, a probable free-radical mechanisms of some of these reactions create additional challenges for performing them in a stereocontrolled manner. Indeed, the synthesis of even a single example of chiral *S*-aryl phosphorothioate (with stereogenic elements either in carbon skeleton or at phosphorus) using above methods has not been demonstrated.

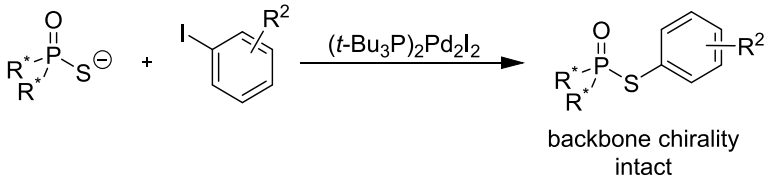


Figure 5.2. Palladium-catalyzed synthesis of *S*-aryl phosphorothioates by direct *S*-arylation.

In this context, the group of Schoenebeck has disclosed in 2019 a direct *S*-arylation of phosphorothioate diesters with aryl iodides using a dinuclear Pd(I) catalyst (Figure 5.2). Although it has been shown that this cross-coupling conditions preserve the stereochemical configuration of chiral centers in the carbon backbone, it has still not been applied to molecules, in which the phosphorus atom itself is a stereocenter.[348]

Building on previous studies by us and others showing that hypervalent iodine(III) reagents allow for a highly efficient aryl transfer to sulfur-based nucleophiles,[161,174,291,296,349] as well as on seminal preliminary results by Chen et al. (Figure 1.44d),[171] we came up with the idea for the synthesis of *S*-aryl phosphorothioates by the direct arylation of phosphorothioate diesters with diaryliodonium salts (Figure 5.3). Apart from being metal-free, the envisioned reaction should maintain the stereochemical integrity of P-chiral compounds, enabling for the first time to harness the potential provided by the access to enantiopure phosphorothioate diesters.[339–342]

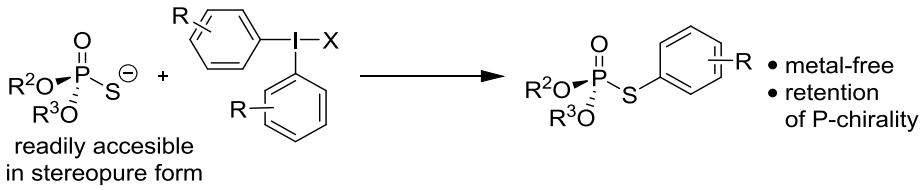


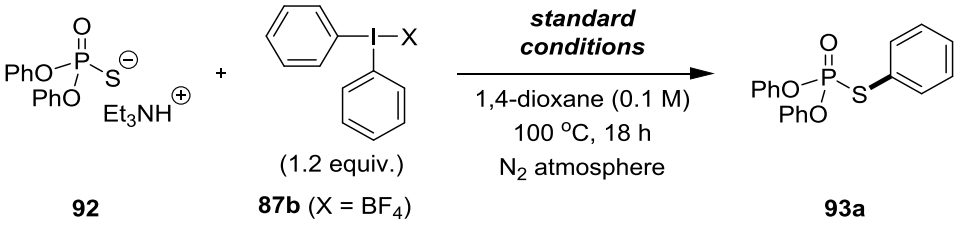
Figure 5.3. Proposed synthesis of *S*-aryl phosphorothioates by metal-free *S*-arylation with diaryliodonium salts.

5.2. Optimization of reaction conditions

Table 5.1 presents the effect of reaction parameters on the efficiency of the arylation of model diphenyl phosphorothioate **92a** with diphenyliodonium tetrafluoroborate **87b**. Under the optimized conditions, consisting simply of heating the starting materials overnight in 1,4-dioxane at 100 °C under inert atmosphere, the reaction provides a quantitative yield of the desired product (entry 1). The arylation sharply decelerates with decreasing temperature (entries 2-3). Regarding the reaction solvents, the application of toluene and CPME led to

slightly lowered yields (entries 4-5), while further decline was observed for other tested solvents (entries 6-9). We evaluated also diphenyliodonium salts bearing various counter-anions, most of which delivered the product in good to excellent yields (entries 10-15), apart from chloride, having a detrimental effect on the reaction outcome (entry 12). An alternative iodine(III)-based aryl transfer reagent, phenylbenziodoxolone, was found to be completely ineffective (entry 16). Finally, the reaction could be carried out under air, albeit in a slightly lowered yield (entry 17).

Table 5.1. Effect of reaction parameters



92 **87b** (X = BF_4) **93a**

Entry	Change from the standard conditions	Yield %[a]
1	none	99
2	80 °C, instead of 100 °C	65
3	rt, instead of 100 °C	0
4	toluene, instead of 1,4-dioxane	94
5	CPME, instead of 1,4-dioxane	90
6	DMF, instead of 1,4-dioxane	63
7	DCE, instead of 1,4-dioxane @ 80 °C	43
8	MeCN, instead of 1,4-dioxane @ 80 °C	29
9	Cy-H, instead of 1,4-dioxane	19
10	X = OTf (**87a**), instead of X = BF_4	89
11	X = $OOCCF_3$ (**87c**), instead of X = BF_4	96
12	X = Cl (**87d**), instead of X = BF_4	22
13	X = OTs (**87e**), instead of X = BF_4	97
14	X = AsF_6 (**87f**), instead of X = BF_4	88
15	X = PF_6 (**87h**), instead of X = BF_4	77
16	phenylbenziodoxolone (**87g**), instead of **87b**	0
17	under air, instead of N_2	90

[a] Yields are the average of two experiments and were determined by ^{1}H NMR spectroscopy

5.3. Scope and limitations

With the optimized reactions conditions in hand, we set out to explore the scope and limitations of this metal-free *S*-arylation of phosphorothioate diesters, first, with regard to the aryl group that can be transferred (Figure 5.4). The reaction works well for halide-substituted aryl rings (**93b**-**93e**). Noteworthy, contrary to the palladium-catalyzed counterpart,[343–347] aryl bromide is tolerated (**93d**), providing a convenient handle for further functionalization. Aryls containing both diverse electron-withdrawing (**93f**-**93i**) and electron-donating (**93j**-**93l**) substituents in various positions of the ring furnish the desired products with good efficiency. Extended aryl systems, such as 1- and 2-naphthyl, can also be transferred (**93m**-**93n**). Regarding the steric factors, though the considerably hindered mesityl does not interfere with the S–Ar bond formation **93j**, there is a slight decrease in the yield in the case of 1-naphthyl moiety **93n**.

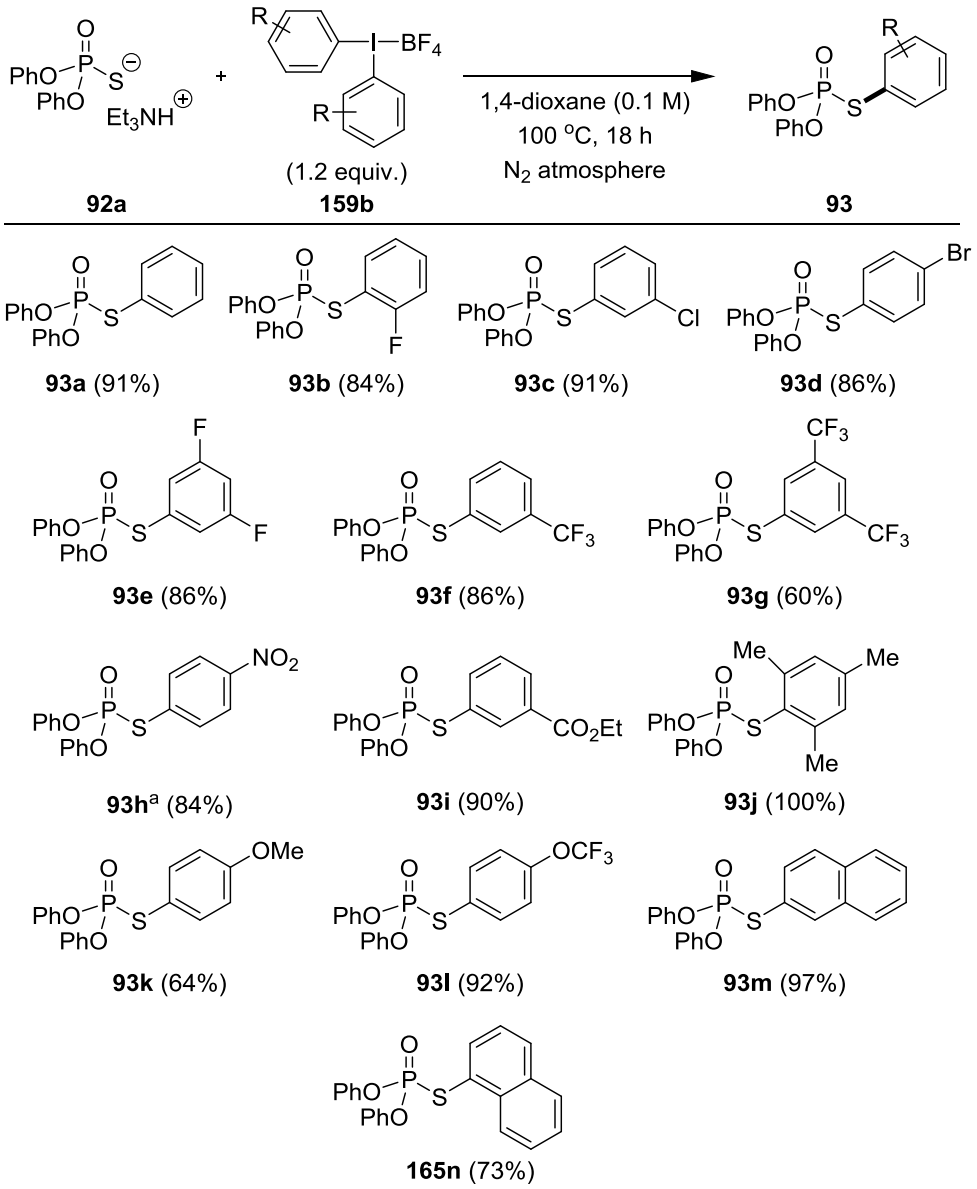


Figure 5.4 Scope with regard to the diaryliodonium salt (isolated yields).
[a] Synthesized using unsymmetrical (4-nitrophenyl)(phenyl)iodonium tetrafluoroborate.

Next, we moved to explore the scope with respect to the phosphorothioate diester (Figure 5.5). For simple starting materials the reaction is uneventful, both in the case of *O*,*O*-diaryl and *O*,*O*-dialkyl substrates (**93a**, **93o**-**93q**). However, 2,2,2-trifluoroethyl-, 2,2,2-trichloroethyl-derived phosphorothioate substrates (**93r**, **93s**) were arylated in lower yields. Moreover, the reaction with *O*,*O*-dibenzyl phosphorothioate, provides varying yields in the range of 20-40% of **93t**. This is most likely because of the partial removal of the respective groups from the oxygen atoms under the reaction conditions. A single strict limitation identified is a very

sterically hindered *O,O*-di-*tert*-butyl phosphorothioate, which was found to be completely unreactive (**93u**).

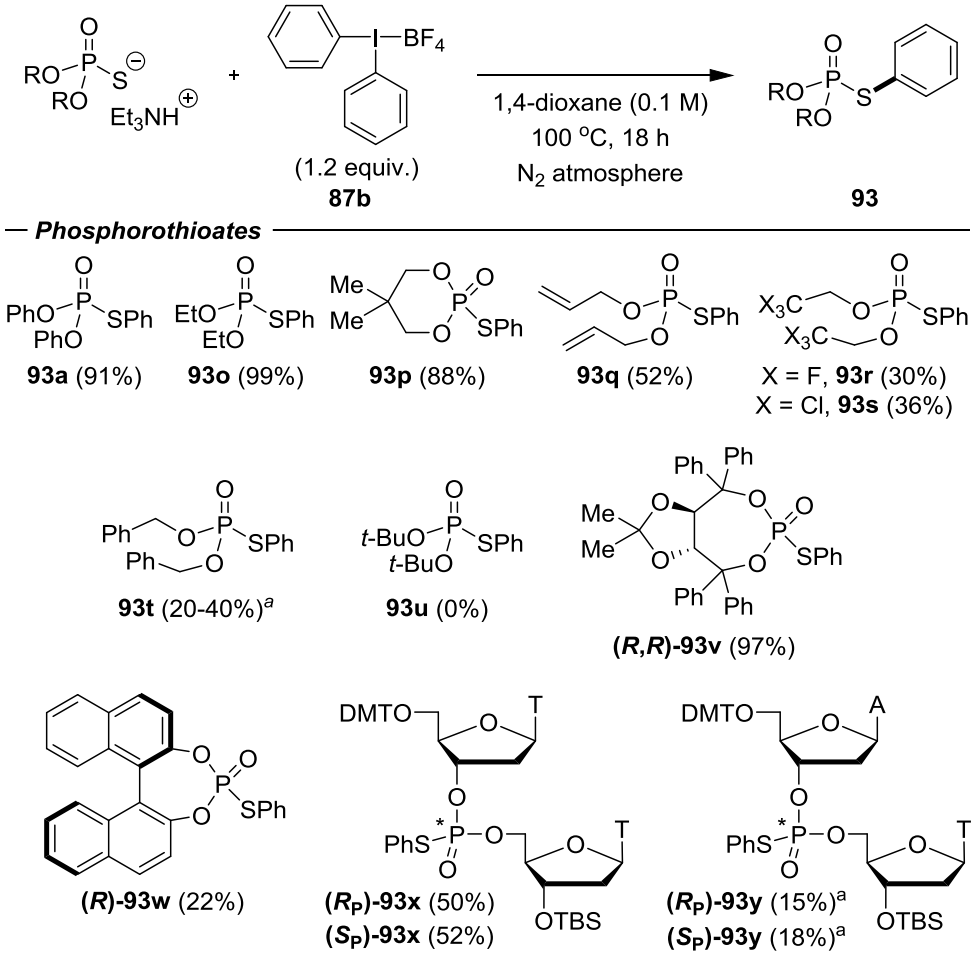


Figure 5.5 Scope with regard to the phosphorothioate diester (isolated yields).
[a] NMR yield; T=thymin-1-yl, A=adenine-9-yl

The reaction was then tested using more complex molecules, relevant to asymmetric catalysis and biological applications. To this end, a TADDOL-derived phosphorothioate could be *S*-arylated in a nearly quantitative yield without any disruption to the backbone stereocenters (**93v**). This result demonstrates that the developed method is fully interchangeable with the palladium-catalyzed cross-coupling reported previously,[348] while it avoids a possible contamination of the chiral product with trace transition metal residues, which may be of importance in downstream catalytic applications. Moreover, the enantiopurity of axially chiral BINOL-containing substrate also remained intact, although the reaction proceeds in much lower yield in this case (**93w**). Most importantly, however, the *S*-arylation with a

diaryliodonium salt could be performed with a complete stereospecificity on dinucleoside phosphorothioates having the opposite sense of chirality at the phosphorus stereocenter (**93x**) (Figure 5.6). Not only these are the first instances of such transformation, but they also show the applicability of this chemistry for a selective late-stage functionalization of complex, functional group-rich molecules. Similarly, *S*-arylation of another dinucleoside phosphorothioate also proceeded stereospecifically, though with lower yields (**93y**).

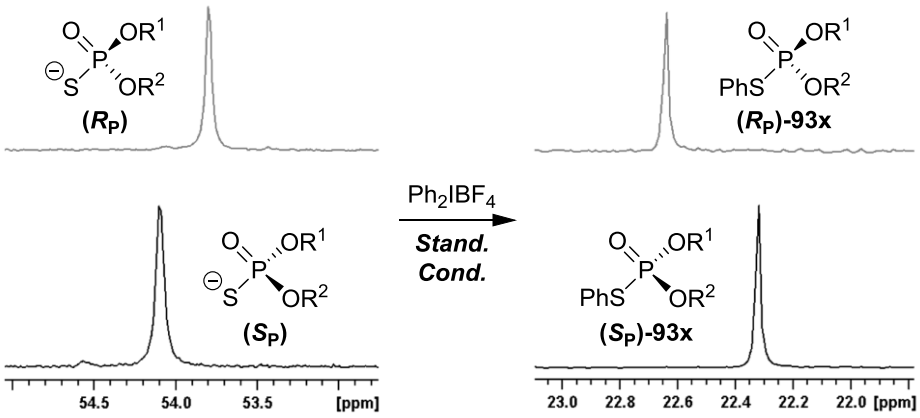


Figure 5.6 ^{31}P NMR spectra demonstrating complete stereospecificity of the reaction with P-stereogenic dinucleoside phosphorothioates.
R^1 = 5′-*O*-DMT-thymidin-3′-yl, R^2 = 3′-*O*-TBS-thymidin-5′-yl.

To further extend the scope, other possible P–S nucleophiles and related selenium compounds were subjected to the developed arylation conditions (Figure 5.7). Thus, *S*-aryl phosphorodithioates, both *O*,*O*-diaryl **94a** and *O*,*O*-dialkyl **94b** one, were successfully obtained in high yields. Moreover, the aryl transfer to the selenium atom of phosphoroselenoates could also be achieved, although with considerably lower efficacy **95a**-**95b**. Finally, it was determined that replacing alkoxy groups at phosphorus with carbon substituents gradually decreases the reactivity toward diaryliodonium salts. Namely, the introduction of a single P–C bond into the starting material resulted in a 20-30% drop in the yield of the corresponding *S*-aryl phosphonate products (**96a** vs. **93a**; **96b** vs. **93o**). However, a synthetically useful yield was obtained in the case of derivative of (–)-menthol **96c**, for which the *S*-arylation was found to also be fully stereospecific. In turn, the presence of two P–C bonds lead to the formation of only 31% of *S*-phenyl diphenylphosphinothioate **97a** and a complete loss of the reactivity for dimethylphosphinothioate substrate **97b**. Similarly, we verified this trend with other phosphinothioates and were not able to observe the formation of **97c** and **97d**.

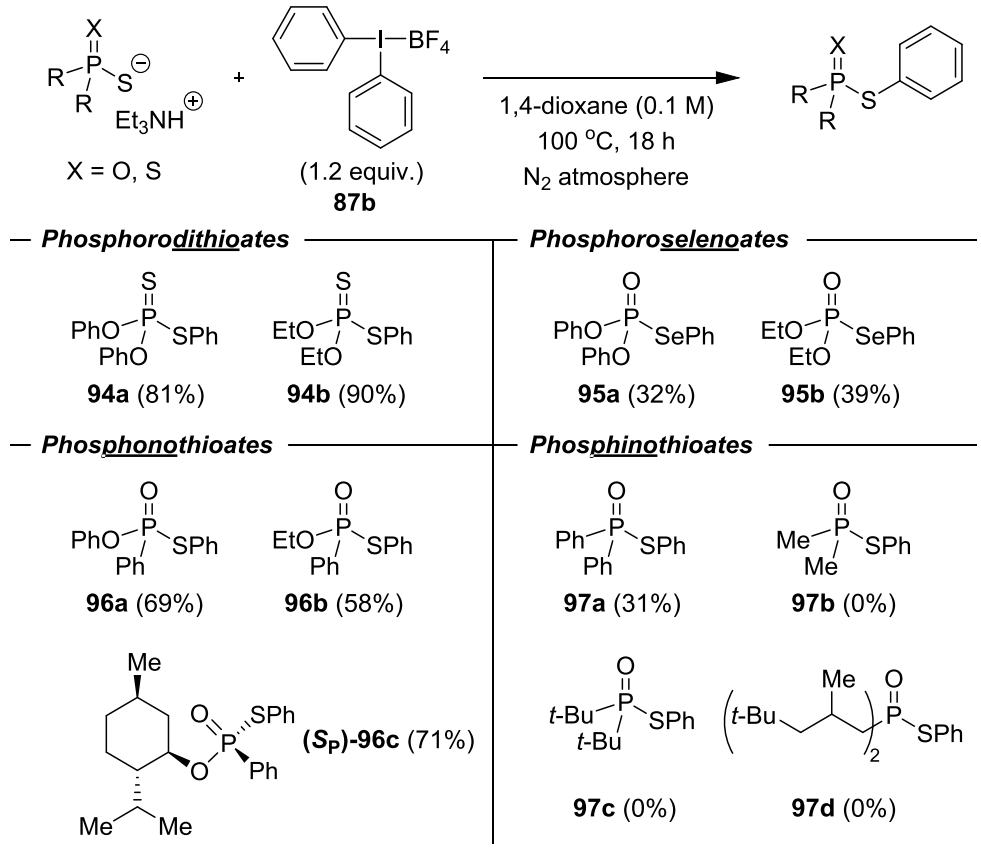


Figure 5.7 Scope with regard to other types of P-S and P-Se compounds (isolated yields).

5.4. Mechanistic investigations

To obtain some insight into the mechanism of the *S*-arylation of phosphorothioate diesters with diaryliodonium salts, the reaction between **92** and **87b** was performed in the presence of either TEMPO or DPE (1 equiv. each). In both cases the yield was not affected (>95%), speaking against the involvement of radical intermediates.

The mechanism of the reaction was also subject to computational investigations using the density functional theory calculations. In particular, we sought to elucidate the details of the S–Ar bond formation and to rationalize the selectivity in terms of *S*- over *O*-arylation. The computed free energy profile for the reaction is depicted in Figure 5.8.

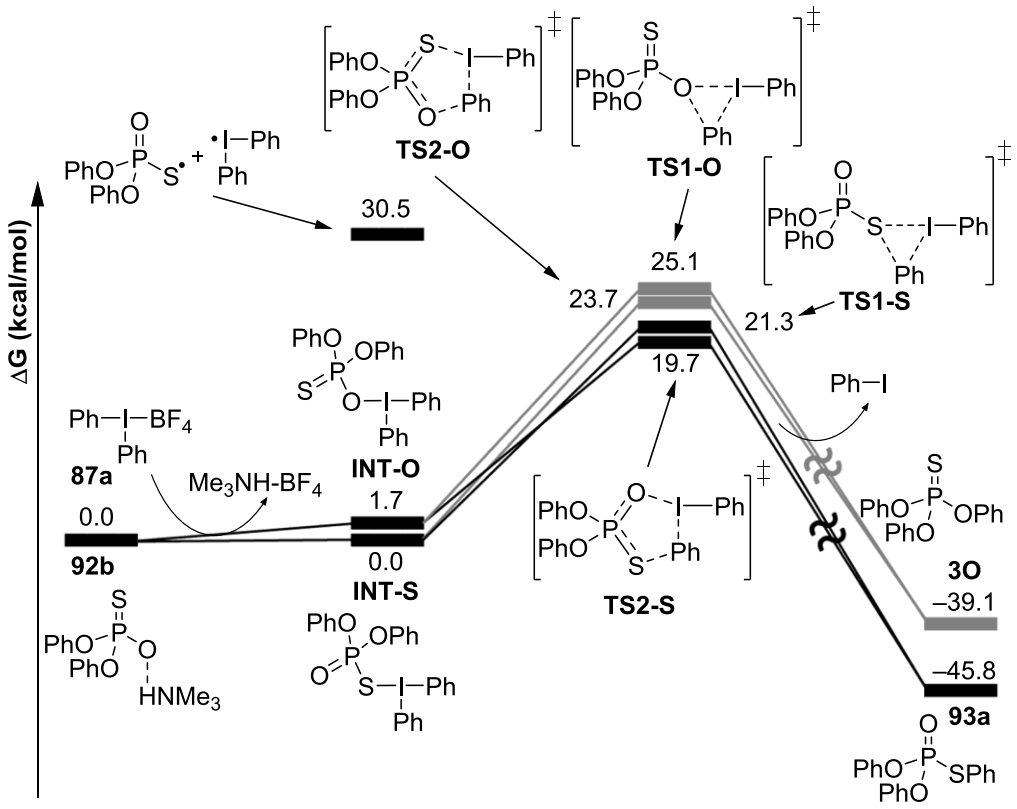


Figure 5.8 Free energy profile for the aryl transfer from diaryliodonium salt to phosphorothioate diester

Despite multiple attempts, we could not locate a transition state for the outer sphere pathway, that is, a direct nucleophilic attack of model phosphorothioate **92b**, neither with sulfur nor oxygen, on the phenyl ring of **87b**, substituting iodine-based leaving group in an S_N2 fashion.[28,29,304] Conversely, the incorporation of phosphorothioate as a ligand into the inner coordination sphere of iodine generates intermediates with either P–S–I or P–O–I linkage (**INT-S** and **INT-O**, respectively), which are relatively close in energy to both **92b** and each other, implying that these species can exist in an equilibrium. A homolytic cleavage of the S/O–I bond in **INT-S**/**INT-O** is calculated to be highly endergonic (~30 kcal/mol), precluding the radical course of the reaction, as already indicated by the experiments with TEMPO and DPE. From both intermediates the aryl transfer may take place via two distinct pathways, involving either 3- or 5-membered cyclic transition states (**TS1** and **TS2**, respectively) that diverge into the *S*- and *O*-arylation products. The S–Ar-forming **TS1-S** (from **INT-S**) and **TS2-S** (from **INT-O**) are clearly energetically preferred to the O–Ar-forming **TS1-O** (from **INT-O**) and **TS2-O** (from **INT-S**), explaining the completely selective *S*-arylation observed experimentally. Interestingly, the 5-membered cyclic structures are favored in both pairs of the respective

transition states, likely due to their less strained nature. In general, the inner sphere mechanism established by the current computations shares similarities to those found for other aryl transfers employing diaryliodonium salts.[301,26,302,349] However, the 5-membered cyclic TS is unique, attributed to intrinsic structure of a phosphorothioate diester, bearing two nucleophilic sites in an 1,3-arrangment. The computational studies also indicate that the *S*-arylation of P-chiral phosphorothioates should proceed stereospecifically, as indeed observed experimentally, with the retention of configuration at phosphorus atom, whose integrity is maintained throughout the mechanistic pathway.

5.5. Conclusions

In conclusion, we have successfully developed an efficient protocol for the direct *S*-arylation of phosphorothioate diesters with diaryliodonium salts. The method constitutes an operationally simple and metal-free entry to a variety of *S*-aryl phosphorothioates and related com-pounds that is also suitable for a late-stage functionalization of complex molecules. Very importantly, the reaction proceeds with a full retention of the stereochemical con-figuration at the phosphorus atom, as proven experimen-tally and computationally, thus, benefiting from the easily accessible pool of stereodefined P-chiral phosphorothioate diesters. Finally, with the use of DFT calculations, the arylation has been shown to proceed via an inner sphere mechanism, through a 5-membered cyclic transition state.

Chapter 6
Synthesis of tertiary phosphines and phosphine oxides by metal-free arylation with diaryliodonium salts

6.1. Background

Within the realm of organic chemistry, one of the oldest subfields is the chemistry of phosphorus. Since the discovery of phosphorus, nearly two and a half century ago, organophosphorus chemistry has emerged as an interesting and exciting field of research. Organophosphorus compounds have found applications in medicinal chemistry,[350] agrochemistry,[351] chemistry of materials,[352,353] and general organic synthesis. In the latter context, they have been used as organocatalysts, redox catalysts, excellent ligands for transition-metal catalysis, and biorthogonal reagents.[354–358]

As part of our general interest in the synthetic applications of diaryliodonium salts, we decided to explore the metal-free aryl transfer to a phosphorus atom. There exist already some reactions employing this idea, as briefly discussed in section 1.4.7. However, the great majority of the arylations of phosphorus employing diaryliodonium salts make use of transition metal catalysis. In particular, arylphosphonates,[359] tertiary phosphine oxides,[360,361] and quaternary phosphonium salts[362–364] have been synthesized by the arylation of phosphites, secondary phosphine oxides, and tertiary phosphines, respectively (Figure 6.1). However, no single report exist on the direct arylation of secondary phosphines, either metal-free or metal-catalyzed. Therefore, with the previous experience of *S*-arylation,[349,365] we hypothesized that secondary phosphines could act as suitable nucleophiles, in the reaction with diaryliodonium salts, allowing for the easy, metal-free to access tertiary phosphines (Figure 6.2).

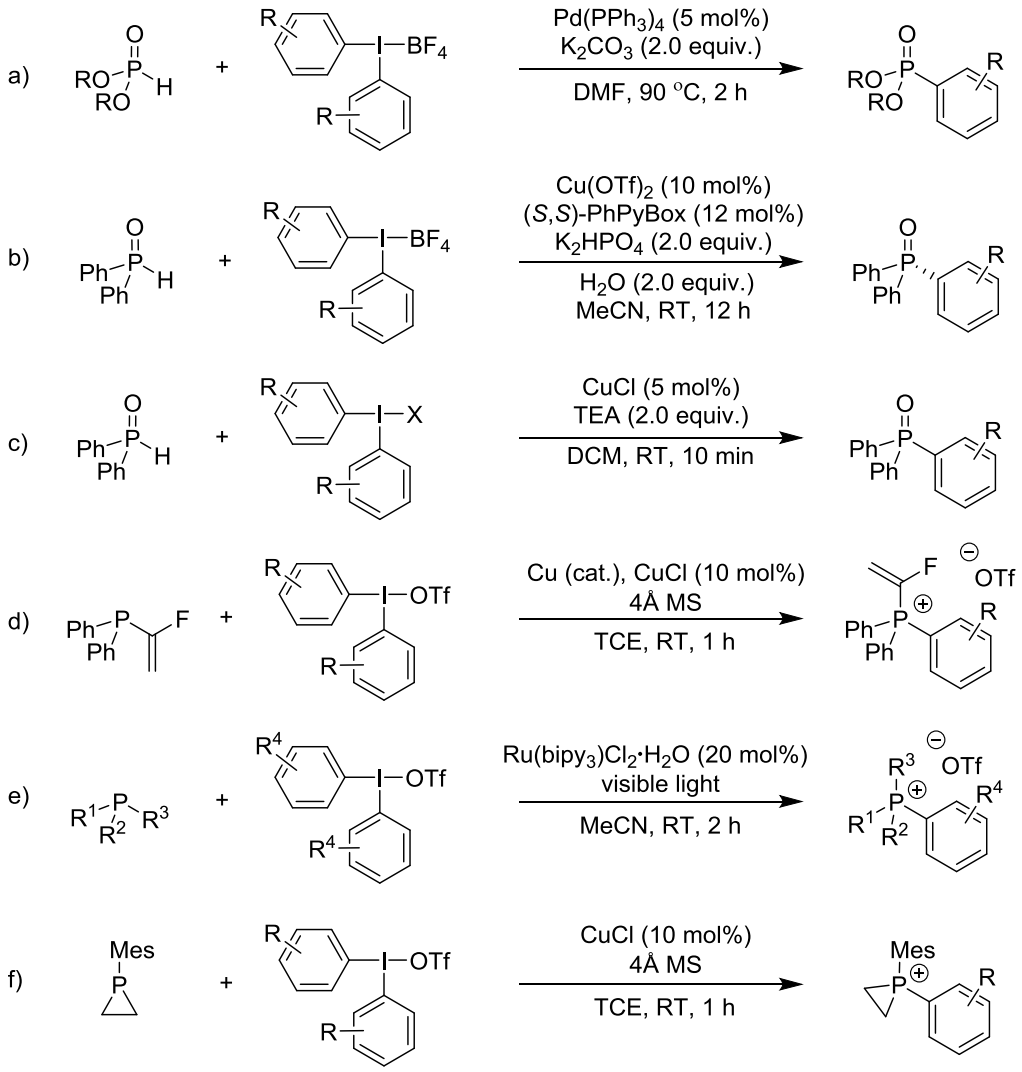


Figure 6.1. Examples of metal-catalyzed arylations of phosphorus using diaryliodonium salts.

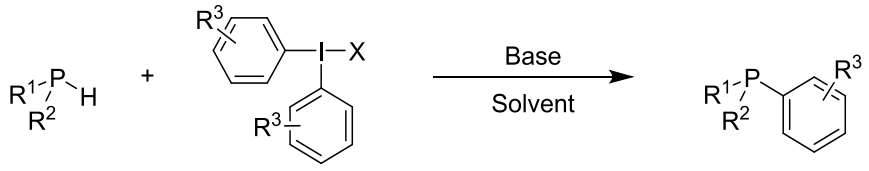


Figure 6.2. Proposed metal-free arylation of secondary phosphines with diaryliodonium salts.

Traditionally, arylphosphines are synthesized by the reactions of organometallic reagents with halophosphines or of alkali metal phosphides with aryl halides.[366–368] These protocols are often limited in scope, due to the low functional group tolerance of organometallic reagents. Several transition metal-catalyzed processes, employing palladium,[369,370] copper,[371,372] and

nickel,[370,373] for the coupling of aryl- or diarylphosphines with aryl(pseudo)halides have been developed. Acylphosphines,[374,375] (trimethylstannyl)diphenylphosphine and (trimethylsilyl)diphenylphosphine,[376] diphenylphosphine-borane[377,378] have also been used as the phosphorus coupling partners in the transition-metal mediated couplings with aryl halides. Although these methods have considerable advantages in terms of efficiency and functional group tolerance, catalyst price and the contamination with residual trace metals remain a concern. In one report, Zeitler and Wolf have reported a photoredox approach toward unsymmetrically-substituted phosphines and phosphonium salts.[379] However, the reaction is strongly substrate-dependent, as *ortho*-substituted aryl iodides delivered tertiary phosphines in moderate yields, whereas tetraarylphosphonium salts were obtained from *meta*- and *para*-substituted substrates, resulting from an over-arylation.

Recently, in the context of metal-free aryl transfer to phosphorus from diaryliodonium salts, Bugaenko and Karchava achieved the arylation of tertiary aryl- and alkylphosphines bearing 2-cyanoethyl group **98** with aryl(mesityl)iodonium triflates under a blue light irradiation, followed by a DBU-mediated retro-Michael reaction of the *in situ* generated quaternary phosphonium salts **99** (Figure 6.3).[380] Hence, (2-cyanoethyl)diphenylphosphine has been used as diphenylphosphine surrogate.

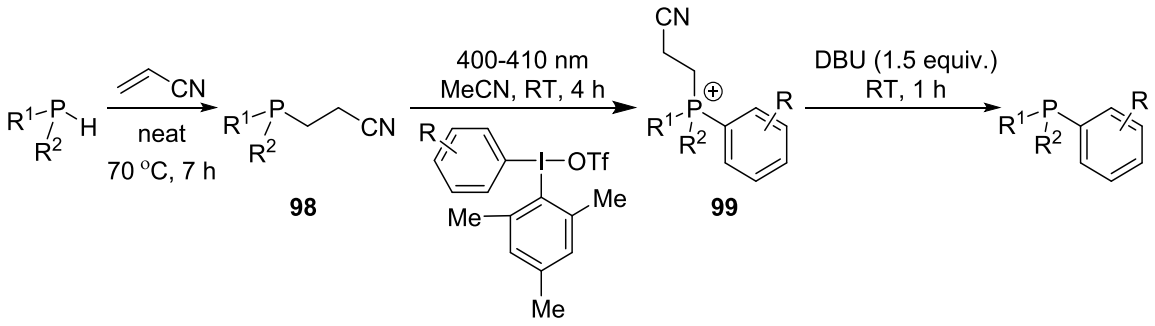


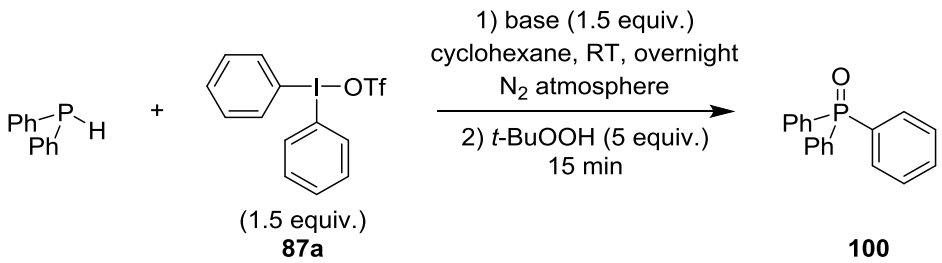
Figure 6.3. Photochemical arylation of diphenylphosphine surrogate using diaryliodonium salts.

6.2. Development of reaction conditions

We started our investigations by screening different bases in the ability to promote the arylation of model diphenylphosphine with diphenyliodonium triflate. Cylcohexane was used at the solvent and the reactions were carried out at room temperature under nitrogen atmosphere (Table 6.1). To avoid errors in the quantification of the reaction outcome due to oxidation by air, the phosphine product (and any remaining substrate) was *in situ* oxidized to

triphenylphosphine oxide with *tert*-butyl hydroperoxide. Different organic and inorganic bases were tested, of which *t*-BuOK performed best (entry 10).

Table 6.1. Initial screening of bases.

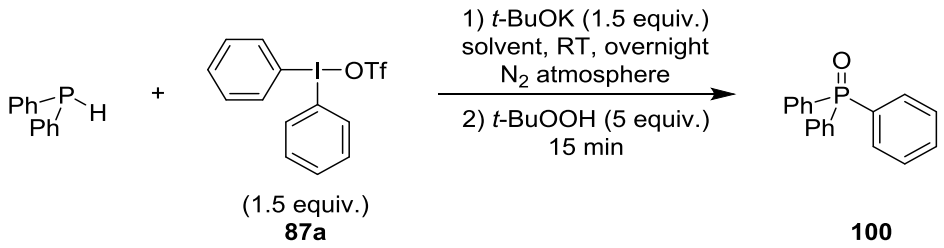


Entry	Base	Yield %[a]
1	TEA	38
2	DBU	38
3	DBN	33
4	DIPEA	10
5	DABCO	32
6	TMG	38
7	2,6-lutidine	8
8	pyridine	4
9	imidazole	21
10	*t*-BuOK	77
11	Cs_2CO_3	45
12	AcOK	36
13	$NaHCO_3$	10
14	KOH	56
15	Li_2CO_3	4
16	Na_2CO_3	2

[a] Yields are the average of two experiments and were determined by ^{31}P NMR spectroscopy

After identifying *t*-BuOK as the best base for the arylation of diphenylphosphine, we performed an extensive screening of solvents (Table 6.2). MeCN and DMSO were found to be the best reaction media (entry 12 and 13). Although the result for DMSO was slightly better than that for MeCN, the latter solvent was considered advantageous, due to more facile reaction work-up.

Table 6.2. Screening of solvents.



Entry	Solvent	Yield %[a]
1	*n*-hexane	63
2	toluene	63
3	benzene	81
4	diethyl ether	73
5	CPME	63
6	1,4-dioxane	59
7	acetone	56
8	AcOEt	46
9	DME	64
10	DCE	44
11	DMF	70
12	MeCN	88
13	DMSO	91
14	EtOH	56
15	$MeNO_2$	36
16	DCM	35
17	THF	58
18	$PhCF_3$	83

[a] Yields are the average of two experiments and were determined by ^{31}P NMR spectroscopy

Subsequent experiments showed that the reaction is sensitive to the order of addition of the reagents. For instance, if the phosphine substrate is added last to the reaction mixture, instead of the base, it has a detrimental effect on the yield, providing only 30% of product. This may be due to some undesired reaction of *t*-BuOK with the diaryliodonium salt, however further studies are needed to clarify the details. Thus, the final experimental procedure involves placing diphenylphosphine and diphenyliodonium triflate in a reaction vessel, followed by the addition of the solvent (MeCN) under the inert atmosphere and, finally, the base (*t*-BuOK). The

optimization of reaction time showed that nearly quantitative amounts of the product were formed already within an hour of stirring at RT under these conditions.

For completeness, we also tested for a possible arylation of diphenylphosphine oxide (formed from the unreacted substrate during the quenching of the reaction with *t*-BuOOH) with diphenyliodonium triflate. Thus, subjecting of diphenylphosphine oxide to the developed reaction conditions gave 15% of Ph_3PO after stirring overnight. Hence, Ph_2HPO indeed shows a limited reactivity toward the diaryliodonium salt, but it is negligible compared to the reactivity of the parent phosphine (which is fully arylated within an hour), and it should not have caused any appreciable inaccuracy in the data presented in Tables 6.1-6.2.

Finally, we examined whether, during the one-pot oxidation of the generated tertiary phosphine, chalcogenes other than oxygen can be introduced into the product. Thus, after a 2h arylation, sulfur or selenium were added to the reaction mixture instead of *t*-BuOOH. Regrettably, after an overnight stirring at RT, the corresponding triphenylphosphine sulfide **101a** and selenide **101b** were formed in only moderate yields under these conditions (Figure 6.4). Therefore, further optimization of the sulfurization and selenization reactions is necessary.

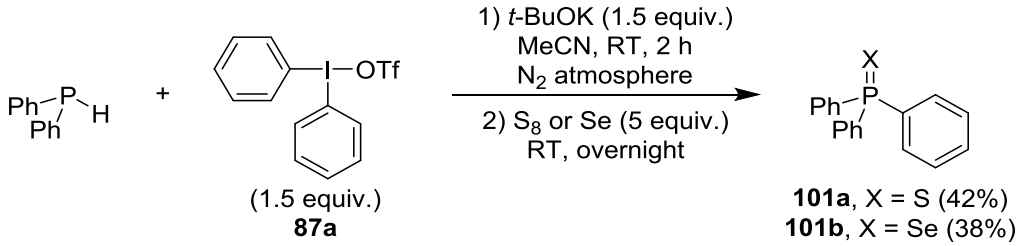


Figure 6.4. Synthesis of triphenylphosphine sulfide and selenide.

6.3. Scope and limitations

Having optimized the reactions conditions, we moved on to explore the scope and limitations of the developed reaction. Up till now, only the scope with regard to the diaryliodonium salts has been examined (Figure 6.5). In the case of aryl rings *ortho*- and *meta*-substituted with halogens (**100b** and **100c**) moderate yields were obtained, whereas the *para*-halogen-containing rings were transferred in low yields (**100d** and **100e**). All evaluated trifluoromethyl-containing aryls furnished the desired phosphine oxides with satisfactory efficiency (**100f**-**100h**). Better results were obtained for the substrate with the electron-withdrawing ester moiety (**100i**),

however, a sharp decline in the yield was observed for the transfer of the nitroarene group (**100j**). Moderately electron-rich aryls are well tolerated, as in the case of (trifluoromethoxy)phenyl (**100k**), mesityl (**100l**), and extended aryl systems, such as 1- and 2-naphthyl (**100m** and **100n**). Finally, the steric hindrance imposed by the mesityl and 1-naphthyl moieties was found to have a considerable adverse effect on the coupling efficiency.

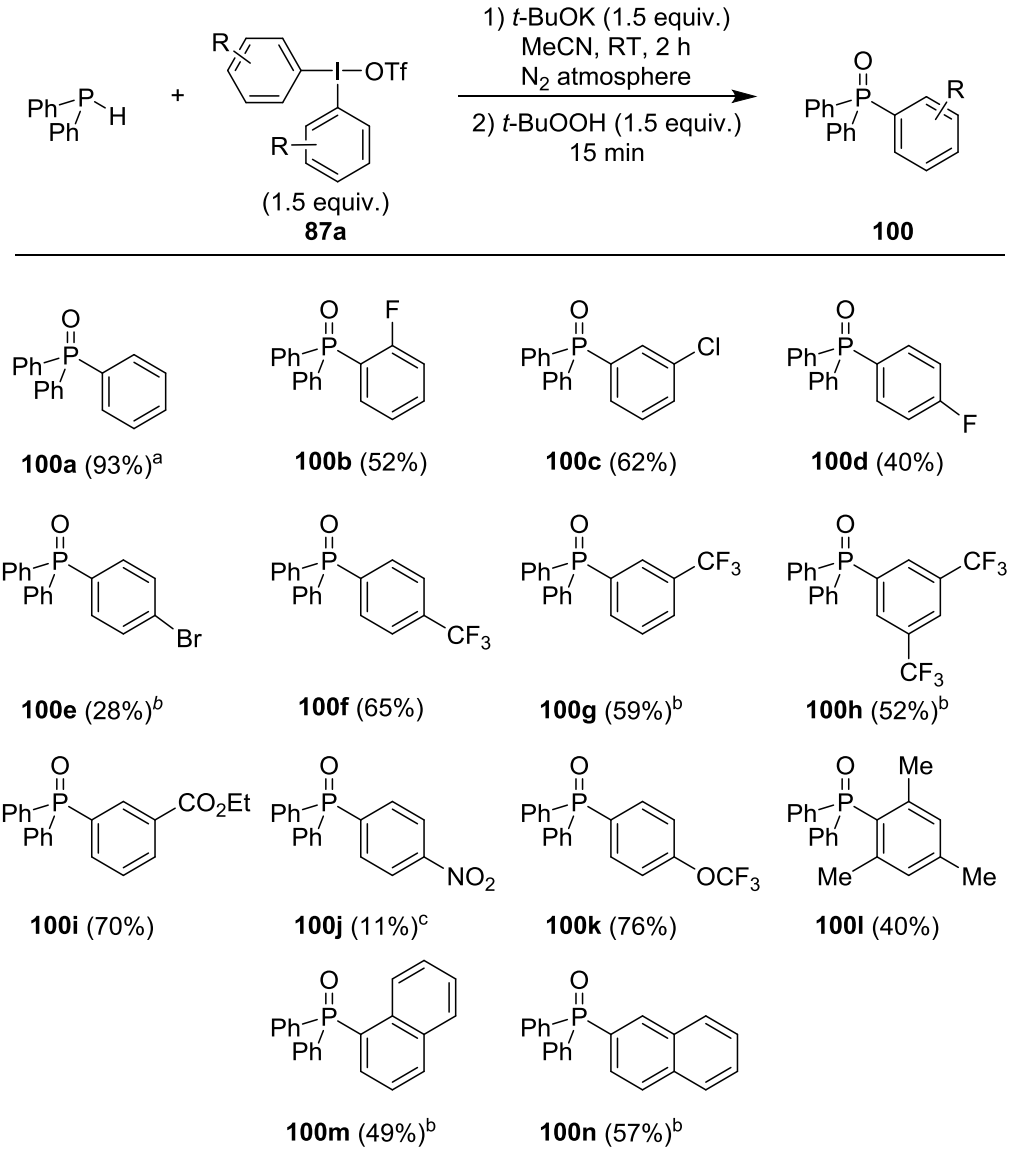


Figure 6.5. Scope with regard to the diaryliodonium salt (NMR yields).
[a] Isolated yield, [b] Synthesized using **87b**, [c] Synthesized using unsymmetrical (4-nitrophenyl)(phenyl)iodonium tetrafluoroborate.

6.4. Conclusions

In conclusion, we have developed a preliminary protocol for the direct *P*-arylation of secondary phosphines with diaryliodonium salts and briefly explored its scope. The work on this project is still in progress. In particular, the scope and limitations of the reaction with regard to the phosphine coupling partner are still to be explored, but a good tolerance toward various functional groups has already been established. Based on the results that will be obtained, additional changes to the reaction conditions may need to be implemented. Anyhow, the method already shows promise to allow for a direct access to various phosphines and phosphine oxides under simple and metal-free conditions.

Concluding Remarks

To conclude, in this thesis, the utility of hypervalent iodine regents for oxidations and arylations has been explored.

Specially, in Chapter 2, I have developed a hypervalent iodine(III)-mediated synthesis of an array of Pummerer's ketone analogs, by the oxidative phenol coupling. These compounds were derived from both phenols and naphthols, with various substitution patterns, in excellent diasteroselectivity, as sole low-molecular-weight products.

In Chapter 3, I was also able to develop an enantioselective and diastereoselective protocol for the synthesis of all carbon spirocycles through a combination of I(III)-promoted oxidative arenol dearomatization and amine organocatalysis. Unfortunately, satisfactory yields could not be obtained.

On the arylation front, Chapters 4 and 5 report metal-free transfers of an aryl group onto a sulfur atom, under mild and experimentally simple conditions. Aryl sulfides containing a broad range of aryl groups were accessed from an array of thiols, including aryl, heteroaryl, and alkyl, including ones of biological and therapeutic relevance. Similarly, diaryliodonium salts were found effective in the synthesis of an array of diverse *S*-aryl phosphorothioates and related compounds. The *S*-arylation of phosphorothioate diesters proceeded with a full retention of the stereogenic center at the phosphorus atom, opening convenient access to P-chiral products. In both cases, the mechanisms of the reactions were established using DFT calculations.

Chapter 6 describes the preliminary work on the synthesis of tertiary phosphines and phosphine oxides by the arylation of phosphorus with diaryliodonium salts. The reaction conditions have been initially optimized and its scope accessed.

I am confident that the scientific results described in this thesis will support other researchers to discover other new outstanding applications of hypervalent iodine compounds.

Acknowledgements

The PhD journey has been a truly life-changing experience for me and without the support and guidance I received from many people, this goal could not have been achieved.

It is said that, if you want to make it big, find mentor, not for weeks or months, but for years. It is a great pleasure for me to express my respect and deep sense of gratitude to my advisor **Dr. Marcin Kalek** for his continuous support and mentoring during my PhD study. I have learnt so much about chemistry and life, through his immense knowledge and experience.

No task can be completed in professional isolation without interaction with others. Discussions arising from differences of opinion or approach, and particularly criticism, can of course be time consuming and even painful to deal with, but I believe it has not only kept me from making mistakes, but also added clarity. I would like to extend my gratitude towards the past and present members of LCSM: **Dr. Manoj**, **Dr. Adam**, **Dr. Abhishek**, **Dr. Somayyeh**, **Karol**, **Natalia**, **Robert**, **Ireneusz**, **Kacper** and **Julia** for the nicest working environment, and **Grela's group members** for many fruitful discussions.

I would also like to take this opportunity to thank my friends **Kaustav**, **Anup**, **Ashutosh**, **Narjes**, **Sanjukta**, **Bohnisikha**, **Vishal**, **Vijay** for always being there and their constant encouragement. Also **Rajanish**, **Sid**, **Pandey**, **Pulak**, **Bata**, **Junnu**, **Abhijeet**, **Pradyumna**, **Bharath** and **Duds** for all the online parties during my PhD studies, especially during the tough pandemic time.

I am grateful to all the people I have met over these four years for their support and sharing their life experiences.

Finally, **Maa** and **Baba** for their understanding, patience, and immense support, and my sister **Puchu** for always being fun.

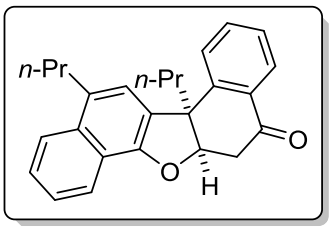
Experimental Section

Unless otherwise noted, all materials were purchased from commercial suppliers and used without purification. Iodosobenzene was prepared according to a published procedure.[381] Anhydrous tetrahydrofuran and dichloromethane were purified prior to use by passage through a column of neutral alumina under nitrogen. Triethylamine was rendered anhydrous by storing over molecular sieves 4Å. Anhydrous DCE, MeCN and 1,4-dioxane were purchased in a septa-sealed bottle and was stored under nitrogen.

^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectroscopic data were collected on Varian 400 MHz and Bruker 500 MHz spectrometers at ambient temperature. The chemical shifts are reported in ppm relative to solvent peaks. Mass spectra were recorded on Thermo QExactive mass spectrometer in ESI ionization mode with TOF mass analyzer. IR spectra were recorded on Shimadzu FT-IR spectrometer equipped with an ATR unit for direct measurements of solid and liquid samples. HPLC analysis of compound **93o** was carried out on Shimadzu LC20AD.

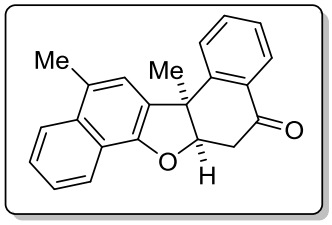
Experimental procedure and characterization of compounds for Chapter 2 (Paper I)

General Procedure A: A 20 mL vial was charged with a phenol (0.50 mmol) and K_3PO_4 (159 mg, 0.75 mmol), followed by the addition of 1,2-dichloroethane (anhydrous, 10 mL). Iodosobenzene (110 mg, 0.50 mmol) was then added and the mixture was stirred for 2 hours at room temperature. Insoluble material was filtered off and washed with dichloromethane. Combined filtrates were concentrated under reduced pressure and the product was purified by column chromatography on silica (*n*-hexane/ethyl acetate).

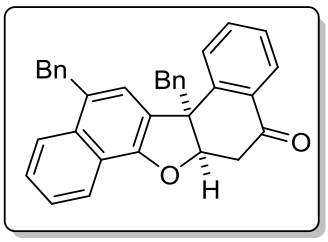


***cis*-12,13b-Dipropyl-6a,13b-dihydrodinaphtho[1,2-b:1',2'-d]furan-5(6*H*)-one** (**60a**): The title compound was prepared according to the General Procedure A from 4-propylnaphthalen-1-ol[382] in 38% yield (35 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.9 Hz, 1H), 7.96 – 7.91 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.47 – 7.39 (m, 3H), 7.27 (t, *J* = 7.4 Hz, 1H), 5.15 (t, *J* = 3.5 Hz, 1H), 3.47 (dd, *J* = 17.2, 3.2 Hz, 1H), 3.12 (dt, *J* = 17.2, 3.9 Hz, 1H), 3.07 – 2.99 (m, 2H), 2.50 – 2.40 (m, 1H), 2.30 – 2.18 (m, 1H), 1.81 – 1.68 (m, 2H), 1.55 – 1.44 (m, 2H), 1.08 – 0.95 (m, 6H). **^{13}C**

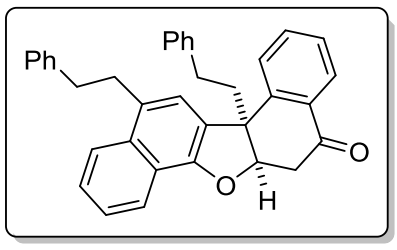
NMR (126 MHz, $CDCl_3$) δ 195.0, 152.9, 144.6, 134.4, 132.4, 132.2, 132.0, 131.4, 127.3, 126.6, 126.4, 126.0, 125.2, 124.2, 122.3, 121.0, 120.7, 86.1, 50.8, 41.6, 39.9, 35.4, 24.2, 18.5, 14.7, 14.2. **HRMS** (ESI): *m/z* 371.2007 ($[M+H]^+$, $C_{26}H_{27}O_2^+$ calcd. 371.2006).



cis **-12,13b-Dimethyl-6a,13b-dihydrodinaphtho[1,2-b:1',2'-d]furan-5(6*H*)-one** (**60b**): The title compound was prepared according to the General Procedure A from 4-methylnaphthalen-1-ol in 31% yield (24 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.9 Hz, 1H), 7.95 – 7.87 (m, 2H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.27 (t, *J* = 7.6 Hz, 1H), 4.97 (t, *J* = 3.5 Hz, 1H), 3.44 (dd, *J* = 17.0, 3.5 Hz, 1H), 3.13 (dd, *J* = 17.0, 3.5 Hz, 1H), 2.68 (s, 3H), 1.93 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.7, 153.1, 145.2, 134.5, 132.7, 130.4, 127.8, 127.70, 127.65, 126.7, 126.3, 126.1, 125.5, 124.4, 122.1, 121.0, 120.8, 88.4, 47.1, 38.3, 25.3, 19.5. **HRMS** (ESI): *m/z* 315.1378 ($[M+H]^+$, $C_{22}H_{19}O_2^+$ calcd. 315.1380).

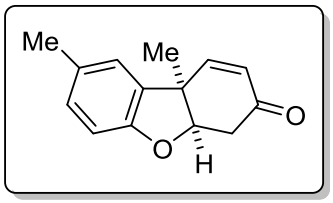


***cis*-12,13b-diBenzyl-6a,13b-dihydrodinaphtho[1,2-b:1',2'-d]furan-5(6*H*)-one** (**60c**): The title compound was prepared according to the General Procedure A from 4-benzylnaphthalen-1-ol[383] in 22% yield (26 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.94 – 7.91 (m, 1H), 7.90 – 7.85 (m, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.64 (ddd, *J* = 8.2, 7.2, 1.5 Hz, 1H), 7.57 (s, 1H), 7.42 – 7.36 (m, 2H), 7.34 – 7.28 (m, 3H), 7.25 – 7.13 (m, 6H), 6.88 – 6.84 (m, 2H), 5.16 (dd, *J* = 3.7, 3.1 Hz, 1H), 4.52 – 4.44 (AB system, 2H), 3.95 (d, *J* = 13.8 Hz, 1H), 3.48 (d, *J* = 13.8 Hz, 1H), 3.14 (dd, *J* = 17.3, 3.0 Hz, 1H), 2.06 (dd, *J* = 17.3, 3.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.6, 153.5, 143.9, 141.0, 135.9, 134.3, 132.4, 131.6, 130.1, 129.5, 128.6, 128.5, 127.9, 127.3, 127.2, 127.0, 126.4, 126.1, 125.5, 124.6, 122.31, 122.25, 121.1, 86.4, 51.3, 45.4, 39.1, 38.9. **HRMS** (ESI): *m/z* 467.2010 ($[M+H]^+$, $C_{34}H_{27}O_2^+$ calcd. 467.2006).

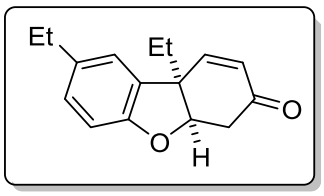


***cis*-12,13b-Diphenethyl-6a,13b-dihydrodinaphtho[1,2-b:1',2'-d]furan-5(6*H*)-one** (**60d**): The title compound was prepared according to the General Procedure A from 4-phenethylnaphthalen-1-ol[383] in 33% yield (41 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 – 7.97 (m, 3H), 7.59 – 7.54 (m, 1H), 7.52 – 7.44 (m, 3H), 7.34 – 7.11 (m, 12H), 5.26 (t, *J* = 3.7 Hz, 1H), 3.49 (dd, *J* = 17.1, 3.5 Hz, 1H), 3.35 (t, *J* = 7.8 Hz, 2H), 3.13 (dd, *J* = 17.1, 4.0 Hz, 1H), 3.04 (t, *J* = 7.8 Hz, 2H), 2.73 – 2.61 (m, 2H), 2.57 – 2.46 (m, 3H). **^{13}C NMR** (126

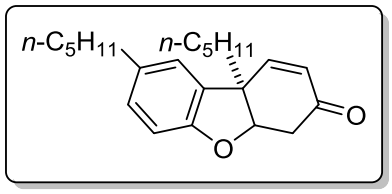
MHz, $CDCl_3$) δ 194.8, 153.2, 144.0, 141.7, 141.2, 134.7, 132.0, 131.4, 131.1, 128.6, 128.5, 128.4, 128.1, 127.2, 126.8, 126.5, 126.31, 126.30, 126.25, 125.9, 125.4, 123.9, 122.4, 121.04, 121.00, 86.0, 50.8, 41.1, 39.9, 37.2, 35.1, 31.4. **HRMS** (ESI): *m/z* 495.2319 ($[M+H]^+$, $C_{36}H_{31}O_2^+$ calcd. 495.2319).



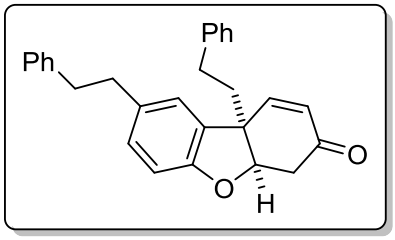
***cis*-8,9b-Dimethyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60e**): The title compound was prepared according to the General Procedure A from 4-methylphenol in 36% yield (19 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.02 (s, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 6.47 (dd, *J* = 10.2, 1.9 Hz, 1H), 5.93 (d, *J* = 10.2 Hz, 1H), 4.72 – 4.68 (m, 1H), 3.05 (dd, *J* = 17.5, 2.8 Hz, 1H), 2.80 (dd, *J* = 17.5, 3.8 Hz, 1H), 2.33 (s, 3H), 1.58 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.1, 156.6, 149.6, 132.2, 131.1, 129.7, 125.8, 123.2, 110.1, 86.5, 45.1, 37.5, 21.4, 20.9.



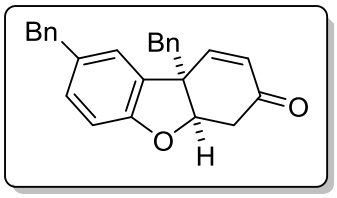
***cis*-8,9b-diethyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60f**): The title compound was prepared according to the General Procedure A from 4-ethylphenol in 28% yield (17 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.04 – 6.98 (m, 2H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.47 (dd, *J* = 10.2, 1.8 Hz, 1H), 6.02 (d, *J* = 10.2 Hz, 1H), 4.86 – 4.83 (m, 1H), 3.05 (dd, *J* = 17.6, 2.8 Hz, 1H), 2.77 (dd, *J* = 17.6, 4.2 Hz, 1H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.11 – 1.93 (m, 2H), 1.23 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.5, 156.8, 149.4, 137.5, 131.2, 128.5, 127.1, 122.3, 110.0, 84.2, 49.2, 39.1, 28.8, 28.4, 16.0, 9.1. **HRMS** (ESI): *m/z* 243.1379 ($[M+H]^+$, $C_{16}H_{19}O_2^+$ calcd. 243.1380).



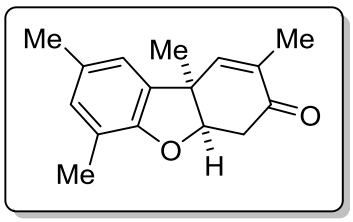
***cis*-8,9b-Dipentyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60g**): The title compound was prepared according to the General Procedure A from 4-pentylphenol[382] in 22% yield (18 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.00 – 6.96 (m, 2H), 6.72 (dd, *J* = 7.9, 0.6 Hz, 1H), 6.46 (dd, *J* = 10.2, 1.9 Hz, 1H), 6.00 (dd, *J* = 10.2, 0.6 Hz, 1H), 4.85 – 4.82 (m, 1H), 3.05 (dd, *J* = 17.6, 2.9 Hz, 1H), 2.78 (dd, *J* = 17.6, 4.2 Hz, 1H), 2.56 (t, *J* = 7.8 Hz, 2H), 2.02 – 1.85 (m, 2H), 1.62 – 1.55 (m, 2H) 1.44 – 1.25 (m, 10H), 0.91 (t, *J* = 7.0 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.5, 156.7, 149.6, 136.2, 131.4, 129.0, 126.9, 122.7, 109.9, 84.6, 48.9, 39.1, 36.1, 35.5, 32.3, 31.6, 31.5, 24.4, 22.5, 22.4, 14.04, 13.97. **HRM**S (ESI): *m/z* 327.2317 ($[M+H]^+$, $C_{22}H_{31}O_2^+$ calcd. 327.2319).



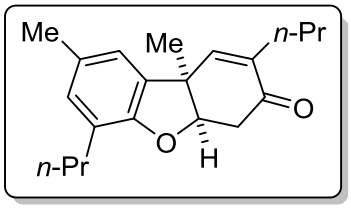
***cis*-8,9b-Diphenethyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60h**): The title compound was prepared according to the General Procedure A from 4-(2-pheneth-1-yl)phenol[384] in 25% yield (25 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.12 (m, 10H), 7.03 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.88 (d, *J* = 1.8 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.47 (dd, *J* = 10.2, 1.8 Hz, 1H), 6.06 (d, *J* = 10.2 Hz, 1H), 4.98 – 4.93 (m, 1H), 3.09 (dd, *J* = 17.6, 2.9 Hz, 1H), 2.89 (s, 4H), 2.81 (dd, *J* = 17.6, 4.2 Hz, 1H), 2.72 – 2.65 (m, 2H), 2.29 – 2.16 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.2, 156.9, 148.9, 141.5, 140.8, 135.1, 130.9, 129.3, 128.6, 128.5, 128.2, 128.1, 127.2, 126.4, 125.9, 123.1, 110.2, 84.4, 48.9, 39.0, 38.4, 37.9, 37.5, 31.0**. HRMS** (ESI): *m/z* 395.2007 ($[M+H]^+$, $C_{28}H_{27}O_2^+$ calcd. 395.2006).



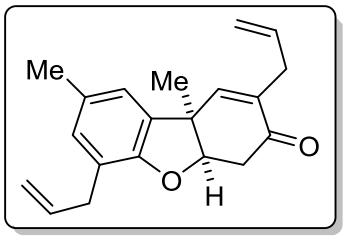
***cis*-8,9b-Dibenzyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60i**): The title compound was prepared according to the General Procedure A from 4-benzylphenol in 27% yield (25 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36 – 7.03 (m, 13H), 6.59 (dd, *J* = 10.2, 1.9 Hz, 1H), 5.96 (d, *J* = 10.2 Hz, 1H), 4.90 – 4.86 (m, 1H), 3.98 (s, 2H), 3.39 (d, *J* = 13.7 Hz, 1H), 3.14 (d, *J* = 13.7 Hz, 1H), 2.73 (dd, *J* = 17.5, 2.7 Hz, 1H), 1.81 (dd, *J* = 17.5, 4.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.3, 156.9, 148.3, 141.3, 135.3, 134.5, 131.6, 129.7, 128.8, 128.6, 128.5, 127.4, 127.2, 126.2, 123.5, 115.3, 110.3, 84.9, 49.7, 42.8, 41.4, 38.3. **HRMS** (ESI): *m/z* 367.1696 ($[M+H]^+$, $C_{26}H_{23}O_2^+$ calcd. 367.1693).



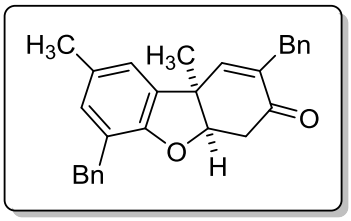
***cis*-2,6,8,9b-Tetramethyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60j**): The title compound was prepared according to the General Procedure A from 2,4-dimethylphenol in 30% yield (18 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.84 – 6.80 (m, 2H), 6.23 – 6.19 (m, 1H), 4.64 – 4.61 (m, 1H), 3.08 (dd, *J* = 17.4, 2.6 Hz, 1H), 2.78 (dd, *J* = 17.4, 3.8 Hz, 1H), 2.89 (s, 3H), 2.15 (s, 3H), 1.72 (d, *J* =1.1 Hz, 3H), 1.52 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.7, 155.2, 145.4, 132.4, 132.0, 132.8, 132.7, 120.22, 120.20, 86.5, 45.5, 37.8, 21.9, 20.8, 16.1, 15.0. **HRMS** (ESI): *m/z* 243.1379 ($[M+H]^+$, $C_{16}H_{19}O_2^+$ calcd. 243.1380).



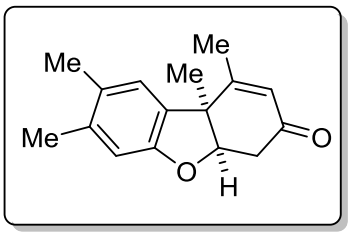
***cis*-8,9b-Dimethyl-2,6-dipropyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60k**): The title compound was prepared according to the General Procedure A from 4-methyl-2-propylphenol[385] in 35% yield (26 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.84 (s, 1H), 6.82 (s, 1H), 6.16 (s, 1H), 4.63 – 4.59 (m, 1H), 3.06 (dd, *J* = 17.2, 3.0 Hz, 1H), 2.78 (dd, *J* = 17.4, 3.8 Hz, 1H), 2.49 (t, *J* = 7.7, 2H), 2.31 (s, 3H), 2.21 – 2.13 (m, 1H), 2.09 – 2.01 (m, 1H), 1.62 – 1.55 (m, 2H), 1.54 (s, 3H), 1.40 –1.31 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.80 91 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.5, 155.0, 144.9, 135.8, 132.5, 130.6, 129.8, 125.0, 120.3, 86.2, 45.4, 38.1, 31.6, 31.4, 22.9, 22.1, 21.3, 20.9, 13.9, 13.6. **HRMS** (ESI): *m/z* 299.2003 ($[M+H]^+$, $C_{20}H_{27}O_2^+$ calcd. 299.2006).



***cis*-2,6-Diallyl-8,9b-dimethyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60l**): The title compound was prepared according to the General Procedure A from 2-allyl-4-methylphenol[385] in 38% yield (28 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.83 (s, 1H), 6.21 – 6.18 (m, 1H), 5.94 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.74 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.10 – 5.00 (m, 3H), 4.97 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.67 – 4.62 (m, 1H), 3.36 – 3.23 (m, 2H), 3.09 (dd, *J* = 17.3, 2.9 Hz, 1H), 2.99 (dddd, *J* = 16.2, 6.6, 2.7, 1.3 Hz, 1H), 2.88 – 2.76 (m, 2H), 2.31 (s, 3H), 1.55 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.8, 154.7, 145.4, 136.1, 135.1, 134.2, 132.5, 130.9, 129.7, 122.3, 120.9, 116.7, 115.8, 86.4, 45.5, 38.0, 33.6, 33.1, 22.0, 20.9. **HRMS** (ESI): *m/z* 295.1690 ($[M+H]^+$, $C_{20}H_{23}O_2^+$ calcd. 295.1693).

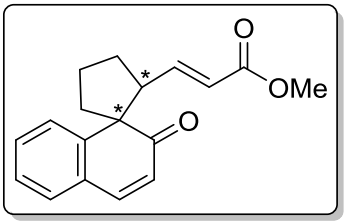


***cis*-2,6-Dibenzyl-8,9b-dimethyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one** (**60m**): The title compound was prepared according to the General Procedure A from 2-benzyl-4-methylphenol[386] in 38% yield (41 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.16 (m, 8H), 7.08 – 7.05 (m, 2H), 6.80 (s, 1H), 6.74 (s, 1H), 6.16 – 6.12 (m, 1H), 4.68 – 4.64 (m, 1H), 3.94 – 3.82 (AB system, 2H), 3.61 (d, *J* = 15.4 Hz, 1H), 3.36 (d, *J* = 15.4 Hz, 1H), 3.09 (dd, *J* = 17.2, 3.1 Hz, 1H), 2.79 (dd, *J* = 17.2, 3.8 Hz, 1H), 2.24 (s, 3H), 1.52 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.9, 154.8, 146.1, 140.4, 139.1, 135.5, 132.5, 131.0, 130.1, 128.9, 128.8, 128.4, 128.3, 126.1, 126.0, 123.5, 121.0, 86.5, 45.7, 38.2, 35.4, 35.2, 22.0, 20.9**. HRMS** (ESI): *m/z* 395.2004 ($[M+H]^+$, $C_{28}H_{27}O_2^+$ calcd. 395.2006).

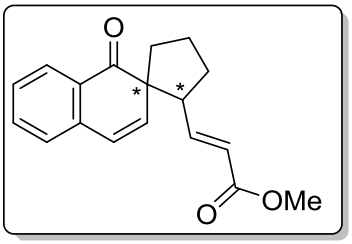


(4aR,9bR)-1,7,8,9b-Tetramethyl-4a,9b-dihydrodibenzo[b,d]furan-3(4*H*)-one (**60n**): The title compound was prepared according to the General Procedure A from 3,4-dimethylphenol in 35% yield (21 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.64 (s, 1H), 5.87 (s, 1H), 4.62 (t, J = 3.2 Hz, 1H), 3.02 (dd, *J* = 17.4, 2.6 Hz, 1H), 2.75 (dd, *J* = 17.4, 3.8 Hz, 1H), 2.25 (s, 3H), 2.22 (s, 3H), 1.93 (s, 3H), 1.58 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 194.7, 158.7, 157.2, 137.8, 129.04, 128.98, 125.9, 125.1, 111.7, 87.8, 47.9, 37.0, 20.5, 20.1, 19.53, 19.50. **HRMS** (ESI): *m/z* 243.1377 ($[M+H]^+$, $C_{16}H_{19}O_2^+$ calcd. 243.1380).

Experimental procedures for Chapter 3



Methyl (*E*)-3-(2'-oxo-2'*H*-spiro[cyclopentane-1,1'-naphthalen]-2-yl)acrylate (**76**); Table 3.5, entry 1: A 4 mL vial was charged with 5-(2-hydroxynaphthalen-1-yl)pentanal **69** (11.4 mg, 0.05 mmol), catalyst **74a** (4.19 mg, 25 mol%) and oxidant **78** (17.8 mg, 0.05 mmol), followed by the addition of DCM (anhydrous, 1 mL). Et_3N (13.9 μl, 0.10 mmol) was then added and the mixture was stirred for 24 hours at room temperature. Then, phosphorane **77** (25.1 mg, 0.15 mmol) was added and stirred for additional 4 hours. The reaction mixture was filtered through a short silica plug eluting with diethyl ether. Combined filtrates were concentrated under reduced pressure, and the yield (27%) and dr (6:1) were assessed by ^{1}H NMR relative to an internal standard. The product was purified by preparative TLC (*n*-hexane/ethyl acetate). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.50 – 7.43 (m, 2H), 7.37 (d, *J* = 9.8 Hz, 1H), 7.30 – 7.27 (m, 2H), 6.63 (dd, *J* = 15.6, 7.9 Hz, 1H), 6.07 (d, *J* = 9.8 Hz, 1H), 5.45 (dd, *J* = 15.6, 1.3 Hz, 1H), 3.64 (s, 3H), 2.65 – 2.54 (m, 1H), 2.26 – 2.18 (m, 2H), 2.16 – 1.99 (m, 2H), 1.97 – 1.86 (m, 2H). **HPLC** (CHIRALART Cellulose-SC (equivalent to CHIRALPAK IC), hexanes/2-propanol = 17/3, flow rate = 1.0 mL/min, λ = 227 nm, 30 °C): t_R = 19.0 min (*rac*-**76**: t_R = 19.0 min, 22.0 min).

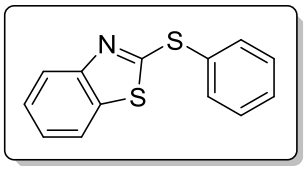


Methyl (*E*)-3-(1'-oxo-1'H-spiro[cyclopentane-1,2'-naphthalen]-2-yl)acrylate (**81**); Table 3.7, entry 6: A 4 mL vial was charged with 5-(1-hydroxynaphthalen-2-yl)pentanal **70** (11.4 mg, 0.05 mmol), catalyst **74a** (4.19 mg, 25 mol%), followed by the addition of DCM (anhydrous, 1 mL). $NaClO{\bullet}5H_2O$ (16.5 mg, 0.10 mmol) was then added at 0 °C and

the mixture was stirred for 24 hours at 0 °C. Then, phosphorane **77** (25.1 mg, 0.15 mmol) was added and stirred for additional 4 hours at room temperature. The reaction mixture was filtered through a short silica plug eluting with diethyl ether. Combined filtrates were concentrated under reduced pressure, and the yield (34%) were assessed by ^{1}H NMR relative to an internal standard. The product was purified by preparative TLC (*n*-hexane/ethyl acetate). **^{1}H NMR** (400 MHz, $CDCl_3$, for the mixture of diastereomers): δ 8.04 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.57 (td, *J* = 7.5, 1.4 Hz, 1H), 7.51 (td, *J* = 7.5, 1.4 Hz, 1H), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 6.73 (dd, *J* = 15.6, 7.9 Hz, 1H), 6.62 (d, *J* = 10.1 Hz, 2H), 6.63 – 6.56 (m, 1H), 6.20 (d, *J* = 9.9 Hz, 1H), 6.04 (d, *J* = 9.7 Hz, 1H), 5.71 (dd, *J* = 15.6, 1.2 Hz, 1H), 5.69 (dd, *J* = 15.6, 1.2 Hz, 1H), 3.62 (s, 3H), 3.55 (s, 3H), 3.46 – 3.34 (m, 1H), 2.79 – 2.67 (m, 1H), 2.30 – 2.10 (m, 4H), 2.08 – 1.76 (m, 8H). **HPLC** (CHIRALART Cellulose-SC (equivalent to CHIRALPAK IC), hexanes/2-propanol = 17/3, flow rate = 1.0 mL/min, λ = 227 nm, 30 °C): t_R = 9.3 min (*rac*-**76**: t_R = 7.9 min, 9.3 min).

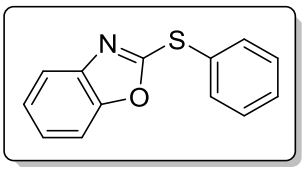
Experimental procedure and characterization of compounds for Chapter 4 (Paper II)

General Procedure B: A 20 mL vial was charged with thiol (0.70 mmol) and diaryliodonium triflate (0.77 mmol). The vial was capped and evacuated/back-filled with nitrogen three times. Acetonitrile (anhydrous, 7 mL) was added via syringe, followed by DBU (115 μL, 117 mg, 0.77 mmol), and the reaction mixture was stirred at 80 °C for 1.5 hours. After cooling to room temperature, the solvent was evaporated under reduced pressure. Dichloromethane (2 mL) was added to the residue, followed by a small amount of silica. The solvent was evaporated under reduced pressure, the solid residue was applied on the top of silica column, and the product was purified by column chromatography.

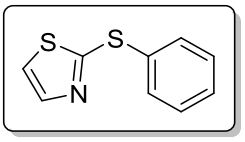


2-(Phenylthio)benzo[d]thiazole (**88a**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol (**1a**) and diphenyliodonium trifluoromethanesulfonate[100] (**2a**) in 100% yield (171 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.2 Hz, 1H), 7.77 – 7.72 (m, 2H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 169.9, 154.1, 135.7, 135.6, 130.7, 130.13, 130.10, 126.3, 124.5, 122.1, 121.0. **FT-**

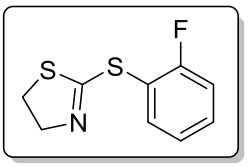
IR (ATR): 1455, 1440, 1424, 1310, 1019, 1007, 999, 983, 748, 725, 705, 689, 665 cm^{-1}. **HRMS** (ESI): *m/z* 244.0248 ($[M+H]^+$, $C_{13}H_{10}NS_2^+$ calcd. 244.0249).



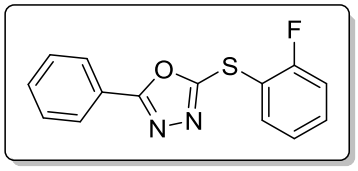
2-(Phenylthio)benzo[d]oxazole (**88b**): The title compound was prepared according to the General Procedure B from benzo[d]oxazole-2-thiol and diphenyliodonium trifluoromethanesulfonate[100] (**2a**) in 76% yield (121 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.75 – 7.69 (m, 2H), 7.64 – 7.60 (m, 1H), 7.50 – 7.45 (m, 3H), 7.44 – 7.41 (m, 1H), 7.31 – 7.24 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.5, 152.0, 142.2, 134.6, 130.2, 129.8, 127.3, 124.54, 124.46, 119.3, 110.2. **FT-IR** (ATR): 1496, 1476, 1451, 1441, 1240, 1233, 1209, 1124, 1094, 1088, 1024, 1002, 925, 805, 740, 704, 687 cm^{-1}. **HRMS** (ESI): *m/z* 228. 0477 ($[M+H]^+$, $C_{13}H_{10}NOS^+$ calcd. 228.0478).



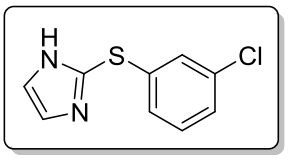
2-(Phenylthio)thiazole (**88c**): The title compound was prepared according to the General Procedure B from thiazole-2-thiol and diphenyliodonium trifluoromethanesulfonate[100] (**2a**) in 91% yield (123 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 3.4 Hz, 1H), 7.66 – 7.61 (m, 2H), 7.44 – 7.40 (m, 3H), 7.23 (d, *J* = 3.4 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 166.1, 143.7, 133.9, 132.1, 129.9, 129.7, 120.6. **FT-IR** (ATR): 1472, 1440, 1384, 1303, 1052, 1038, 1018, 1015, 1000, 754, 742, 722, 716, 713, 704, 689 cm^{-1}. **HRMS** (ESI): *m/z* 194.0093 ($[M+H]^+$, $C_9H_8NS_2^+$ calcd. 194.0093).



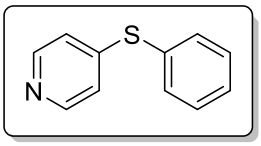
2-((2-Fluorophenyl)thio)-4,5-dihydrothiazole (**88d**): The title compound was prepared according to the General Procedure B from 4,5-dihydrothiazole-2-thiol and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 72% yield (108 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.69 – 7.59 (m, 1H), 7.50 – 7.44 (m, 1H), 7.22 – 7.15 (m, 2H), 4.26 (t, *J* = 8.1 Hz, 2H), 3.35 (t, *J* = 8.1 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.9, 162.8 (d, *J* = 250.3 Hz), 137.5, 132.9 (d, *J* = 8.2 Hz), 124.8 (d, *J* = 3.7 Hz), 117.0 (d, *J* = 18.2 Hz), 116.5 (d, *J* = 22.7 Hz), 65.6, 35.5. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -104.91 – -105.02 (m, 1F). **FT-IR** (ATR): 1594, 1576, 1570, 1469, 1438, 1437, 1262, 1221, 1072, 977, 958, 917, 820, 770, 717, 679 cm^{-1}. **HRMS** (ESI): *m/z* 214.0155 ($[M+H]^+$, $C_9H_9FNS_2^+$ calcd. 214.0155).



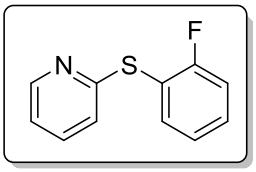
2-((2-Fluorophenyl)thio)-5-phenyl-1,3,4-oxadiazole (**88e**): The title compound was prepared according to the General Procedure B from 5-phenyl-1,3,4-oxadiazole-2-thiol and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 75% yield (142 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.98 – 7.94 (m, 2H), 7.70 (td, *J* = 7.5, 1.8 Hz, 1H), 7.55 – 7.44 (m, 4H), 7.26 – 7.21 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 166.5, 162.3 (d, *J* = 251.2 Hz), 161.9, 136.2, 132.8 (d, *J* = 8.2 Hz), 132.0, 129.2, 127.0, 125.4 (d, *J* = 4.5 Hz), 123.6, 116.9 (d, *J* = 21.8 Hz), 114.3 (d, *J* = 18.3 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -105.77 – -105.86 (m, 1F). **FT-IR** (ATR): 1473, 1469, 1450, 1266, 1187, 1059, 953, 824, 767, 699, 686, 678, 673 cm^{-1}. **HRMS** (ESI): *m/z* 273.0490 ($[M+H]^+$, $C_{14}H_{10}FN_2OS^+$ calcd. 273.0492).



2-((3-Chlorophenyl)thio)-1*H*-imidazole (**88f**): The title compound was prepared according to the General Procedure B from 1*H*-imidazole-2-thiol and bis(3-chlorophenyl)iodonium trifluoromethanesulfonate[387] in 54% yield (79 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.13 (s, 2H), 7.12 – 7.08 (m, 3H), 7.01 – 6.96 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 137.4, 136.0, 135.1, 130.3, 128.0, 127.0, 126.4, 125.5 (broad). **FT-IR** (ATR): 2558, 1860, 1576, 1565, 1550, 1461, 1457, 1419, 1405, 1328, 1099, 964, 944, 941, 769, 764, 704, 674, 660 cm^{-1}. **HRMS** (ESI): *m/z* 211.0092 ($[M+H]^+$, $C_9H_8N_2SCl^+$ calcd. 211.0091).

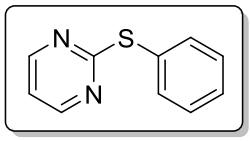


4-(Phenylthio)pyridine (**88g**): The title compound was prepared according to the General Procedure B from pyridine-4-thiol and diphenyliodonium trifluoromethanesulfonate[100] (**2a**) in 61% yield (80 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.35 (d, *J* = 5.2 Hz, 2H), 7.59 – 7.52 (m, 2H), 7.49 – 7.44 (m, 3H), 6.98 – 6.89 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.5, 149.6, 135.4, 130.1, 129.9, 129.6, 121.0. **FT-IR** (ATR): 1570, 1540, 1476, 1440, 1406, 1220, 1087, 1066, 1024, 802, 749, 726, 705, 690 cm^{-1}. **HRMS** (ESI): *m/z* 188.0529 ($[M+H]^+$, $C_{11}H_{10}NS^+$ calcd. 188.0529).

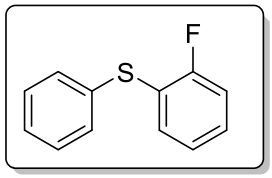


2-((2-Fluorophenyl)thio)pyridine (**88h**): The title compound was prepared according to the General Procedure B from pyridine-2-thiol and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 73% yield (105 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.42 (ddd, *J* = 4.9, 1.0, 0.9 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.51 – 7.42 (m, 2H), 7.24 – 7.17 (m, 2H), 7.02 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 162.9 (d, *J* = 249.1 Hz),

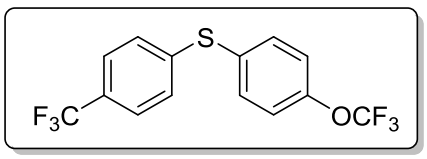
159.5, 149.9, 137.2, 136.9, 131.9 (d, *J* = 8.1 Hz), 125.2 (d, *J* = 4.5 Hz), 121.3, 120.3, 118.3 (d, *J* = 18.2 Hz), 116.6 (d, *J* = 22.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -105.60 – -105.70 (m, 1F). **FT-IR** (ATR): 1574, 1558, 1473, 1447, 1417, 1261, 1225, 1116, 1070, 985, 823, 753, 734, 723 cm^{-1}. **HRMS** (ESI): *m/z* 206.0435 ($[M+H]^+$, $C_{11}H_9FNS^+$ calcd. 206.0434).



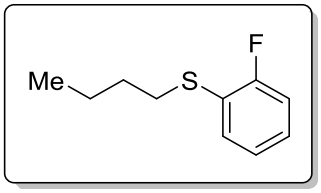
2-(Phenylthio)pyrimidine (**88i**): The title compound was prepared according to the General Procedure B from pyrimidine-2-thiol and diphenyliodonium trifluoromethanesulfonate[100] (**2a**) in 64% yield (84 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.50 (d, *J* = 4.9 Hz, 2H), 7.68 – 7.62 (m, 2H), 7.47 – 7.43 (m, 3H), 6.97 (t, *J* = 4.9 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 173.0, 157.7, 135.4, 129.6, 129.5, 129.4, 117.1. **FT-IR** (ATR): 1559, 1547, 1476, 1376, 1184, 1171, 772, 751, 705, 689, 629 cm^{-1}. **HRMS** (ESI): *m/z* 189.0481 ($[M+H]^+$, $C_{10}H_9N_2S^+$ calcd. 189.0481).



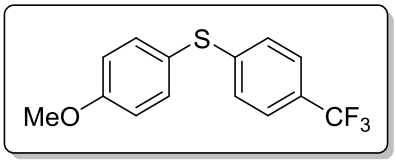
(2-Fluorophenyl)(phenyl)sulfane (**88j**): The title compound was prepared according to the General Procedure B from benzenethiol and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 56% yield (80 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.37 – 7.24 (m, 7H), 7.15 – 7.06 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.3 (d, *J* = 248.9 Hz), 134.4, 133.6, 131.1, 129.6 (d, *J* = 7.6 Hz), 129.5, 127.5, 124.9 (d, *J* = 3.6 Hz), 122.9 (d, *J* = 17.5 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -108.71 – -108.81 (m, 1F). **FT-IR** (ATR): 1581, 1472, 1446, 1440, 1260, 1221, 1068, 1024, 822, 819, 747, 738, 716, 707, 689, 675 cm^{-1}. **HRMS** (ESI): *m/z* 204.0406 ($[M]^+$, $C_{12}H_9FS^+$ calcd. 204.0404).



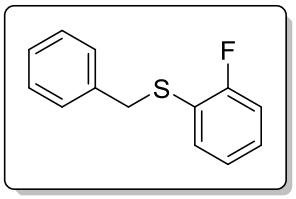
(4-(Trifluoromethoxy)phenyl)(4-(trifluoromethyl) phenyl)sulfane (**88k**): The title compound was prepared according to the General Procedure B from 4-(trifluoromethyl)benzenethiol and bis(4-(trifluoromethoxy)phenyl)iodonium trifluoromethanesulfonate[161] in 76% yield (180 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.56 – 7.51 (m, 2H), 7.51 – 7.46 (m, 2H), 7.34 – 7.29 (m, 2H), 7.27 – 7.21 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 149.5, 141.9, 134.7, 131.8, 129.1, 126.8, 126.2 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 272.5 Hz), 122.2, 120.6 (q, *J* = 259.3 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -57.9 (s, 3F), -62.6 (s,3F). **FT-IR** (ATR): 1607, 1491, 1324, 1254, 1208, 1161, 1122, 1107, 1099, 1085, 1063, 1013, 922, 827, 806, 703, 699 cm^{-1}. **HRMS** (EI): *m/z* 338.0196 ($[M]^+$, $C_{14}H_8F_6OS^+$ calcd. 338.0195).



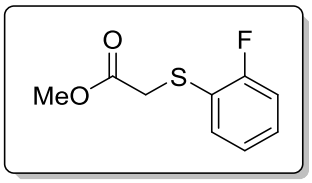
(4-Methoxyphenyl)(4-(trifluoromethyl)phenyl)sulfane (**88l**): The title compound was prepared according to the General Procedure B from 4-methoxybenzenethiol and bis(4-(trifluoromethyl)phenyl)iodonium trifluoromethanesulfonate[388] in 57% yield (113 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.51 – 7.42 (m, 4H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 3.86 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 160.8, 145.0, 136.9, 127.4 (q, *J* = 32.6 Hz), 126.6, 125.8 (q, *J* = 3.6 Hz), 124.4 (q, *J* = 271.6 Hz), 121.8, 115.6, 55.6. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.34 – -62.44 (s, 3F). **FT-IR** (ATR): 1602, 1492, 1324, 1314, 1290, 1252, 1166, 1153, 1109, 1097, 1083, 1062, 1031, 1011, 838, 831, 813, 801, 590 cm^{-1}. **HRMS** (EI): *m/z* 284.0485 ($[M]^+$, $C_{14}H_{11}F_3OS^+$ calcd. 284.0483).



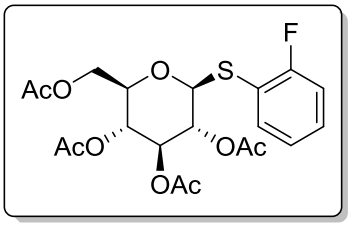
Butyl(2-fluorophenyl)sulfane (**88m**): The title compound was prepared according to the General Procedure B from butane-1-thiol and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 59% yield (76 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.37 (td, *J* = 7.6, 1.7 Hz, 1H), 7.24 – 7.16 (m, 1H), 7.11 – 7.03 (m, 2H), 2.92 (t, *J* = 7.4 Hz, 2H), 1.62 (quintet, *J* = 7.5 Hz, 2H), 1.46 (sextet, *J* = 7.5 Hz, 2H), 0.93 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.5 (d, *J* = 244.6 Hz), 131.8 (d, *J* = 1.8 Hz), 128.1 (d, *J* = 7.3 Hz), 124.5 (d, *J* = 3.6 Hz), 123.9 (d, *J* = 17.3 Hz), 115.7 (d, *J* = 22.4 Hz), 33.1 (d, *J* = 2.8 Hz), 31.5, 22.0, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -109.81 – -109.90 (m, 1F). **FT-IR** (ATR): 2923, 1472, 1446, 1437, 1275, 1259, 1218, 1123, 1072, 821, 747, 673 cm^{-1}. **HRMS** (EI): *m/z* 184.0724 ($[M]^+$, $C_{10}H_{13}FS^+$ calcd. 184.0722).



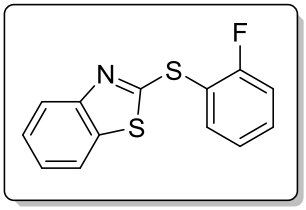
Benzyl(2-fluorophenyl)sulfane (**88n**): The title compound was prepared according to the General Procedure B from phenylmethanethiol and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 52% yield (79 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.31 – 7.19 (m, 7H), 7.09 – 7.00 (m, 2H), 4.12 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.9 (d, *J* = 245.6 Hz), 137.4, 133.2 (d, *J* = 1.8 Hz), 129.02, 128.96, 128.6, 127.4, 124.5 (d, *J* = 3.6 Hz), 122.9 (d, *J* = 18.4 Hz), 115.8 (d, *J* = 22.7 Hz), 38.6 (d, *J* = 2.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -166.82 – -167.00 (m, 1F). **FT-IR** (ATR): 1569, 1496, 1473, 1465, 1454, 1450, 1439, 1437, 1263, 1215, 1197, 1068, 1031, 782, 745, 715, 693, 677, 667 cm^{-1}. **HRMS** (EI): *m/z* 218.0567 ($[M]^+$, $C_{13}H_{11}FS^+$ calcd. 218.0566).



Methyl 2-((2-fluorophenyl)thio)acetate (**88o**): The title compound was prepared according to the General Procedure B from methyl 2-mercaptoacetate and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 55% yield (77 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.47 (td, *J* = 7.6, 1.8 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.14 – 7.06 (m, 2H), 3.70 (s, 3H), 3.64 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 170.0, 162.0 (d, *J* = 246.8 Hz), 133.5, 129.9 (d, *J* = 8.1 Hz), 124.8 (d, *J* = 3.7 Hz), 121.5 (d, *J* = 18.1 Hz), 116.0 (d, *J* = 22.7 Hz), 52.7, 36.0 (d, *J* = 3.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -108.65 – -108.76 (m, 1F). **FT-IR** (ATR): 1735, 1730, 1473, 1437, 1277, 1260, 1222, 1153, 1150, 1143, 1131, 1124, 1072, 1008, 821, 753 cm^{-1}. **HRMS** (EI): *m/z* 200.0311 ($[M]^+$, $C_9H_9FO_2S^+$ calcd. 200.0307).

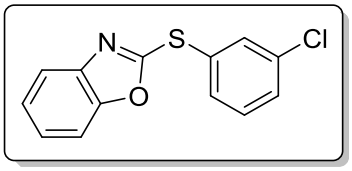


(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((2-fluorophenyl)thio)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (**88p**): The title compound was prepared according to the General Procedure B from (2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-mercaptotetrahydro-2*H*-pyran-3,4,5-triyl triacetate and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 71% yield (228 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.58 (td, *J* = 7.5, 1.6 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.15 – 7.07 (m, 2H), 5.22 (t, *J* = 9.4 Hz, 1H), 5.05 (t, *J* = 9.8 Hz, 1H), 4.95 (t, *J* = 9.7 Hz, 1H), 4.72 (d, *J* = 10.1 Hz, 1H), 4.22 (dd, *J* = 12.3, 5.3 Hz, 1H), 4.14 (dd, *J* = 12.3, 2.3 Hz, 1H), 3.71 (ddd, *J* = 10.2, 5.2, 2.4 Hz, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 170.7, 170.3, 169.54, 169.52, 162.3 (d, *J* = 247.9 Hz), 136.0, 131.0 (d, *J* = 8.2 Hz), 124.7 (d, *J* = 4.5 Hz), 118.5 (d, *J* = 17.4 Hz), 116.2 (d, *J* = 22.8 Hz), 85.2, 76.0, 74.1, 70.1, 68.3, 62.2, 20.9, 20.8, 20.75, 20.73. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -106.83 – -106.93 (m, 1F). **FT-IR** (ATR): 1739, 1735, 1473, 1366, 1250, 1213, 1088, 1042, 1031, 980, 913, 827, 819, 758, 754, 679, 621 cm^{-1}. **HRMS** (ESI): *m/z* 459.1122 ($[M+H]^+$, $C_{20}H_{24}FO_9S^+$ calcd. 459.1120).

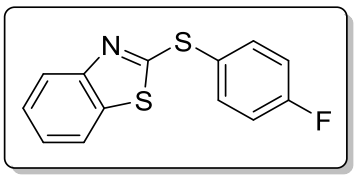


2-((2-Fluorophenyl)thio)benzo[d]thiazole (**88z**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(2-fluorophenyl)iodonium trifluoromethanesulfonate[102] in 89% yield (162 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.2 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.42 (td, *J* = 7.8, 1.2 Hz, 1H), 7.32 – 7.23 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 167.5, 162.9 (d, *J* = 251.4 Hz), 154.0, 137.5, 135.8, 133.3

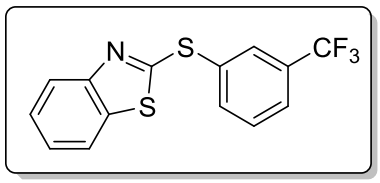
(d, *J* = 8.2 Hz), 126.4, 122.3, 121.0, 117.3 (d, *J* = 18.2 Hz), 117.0 (d, *J* = 22.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -104.85 – -104.93 (m, 1F). **FT-IR** (ATR): 1468, 1456, 1439, 1425, 1221, 1020, 1005, 816, 769, 755, 751, 723, 716, 678 cm^{-1}. **HRMS** (ESI): *m/z* 262.0155 ($[M+H]^+$, $C_{13}H_9FNS_2^+$ calcd. 262.0155).



2-((3-Chlorophenyl)thio)benzo[d]oxazole (**88aa**): The title compound was prepared according to the General Procedure B from benzo[d]oxazole-2-thiol and bis(3-chlorophenyl)iodonium trifluoromethanesulfonate[387] in 92% yield (168 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.73 (t, *J* = 1.8 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.47 – 7.42 (m, 2H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.33 – 7.26 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 162.4, 152.1, 142.0, 135.3, 134.0, 132.4, 130.8, 130.2, 129.2, 124.76, 124.72, 119.4, 110.3. **FT-IR** (ATR): 1567, 1503, 1496, 1464, 1405, 1237, 1211, 1129, 1095, 1086, 1079, 1074, 869, 808, 779, 735, 676, 671, 664 cm^{-1}. **HRMS** (ESI): *m/z* 262.0088 ($[M+H]^+$, $C_{13}H_9NOSCl^+$ calcd. 262.0088).

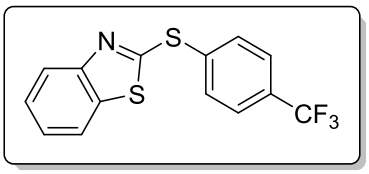


2-((4-Fluorophenyl)thio)benzo[d]thiazole (**88ab**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(4-fluorophenyl)iodonium trifluoromethanesulfonate[100] in 34% yield (62 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.89 (dt, *J* = 8.2, 0.6 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.68 (dt, *J* = 8.1, 0.6 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.22 – 7.16 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 168.7 (d, *J* = 1.8 Hz), 164.4 (d, *J* = 253.1 Hz), 154.1, 138.0 (d, *J* = 9.1 Hz), 135.6, 126.4, 125.3 (d, *J* = 3.6 Hz), 124.6, 122.2, 121.0, 117.4 (d, *J* = 22.3 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -108.84 – -109.00 (m, 1F). **FT-IR** (ATR): 1585, 1489, 1454, 1426, 1217, 1158, 1021, 1005, 833, 814, 756, 751, 726, 637 cm^{-1}. **HRMS** (ESI): *m/z* 262.0155 ($[M+H]^+$, $C_{13}H_9FNS_2^+$ calcd. 262.0155).

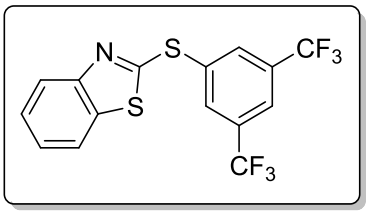


2-((3-(Trifluoromethyl)phenyl)thio)benzo[d]thiazole (**88ac**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(3-(trifluoromethyl)phenyl)iodonium tetrafluoroborate[100] in 90% yield (196 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.45 (td, *J* = 7.8, 1.2 Hz, 1H), 7.33 (td, *J* = 7.7, 1.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 166.8, 153.8, 138.1, 135.8, 132.4 (q, *J* = 33.2 Hz), 131.8, 131.5 (q, *J* = 3.7 Hz), 130.5, 127.0 (q, *J* = 3.7 Hz), 126.6, 125.0, 123.6 (q, *J* = 273.5 Hz), 122.5, 121.1. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.79 (s, 3F). **FT-IR**

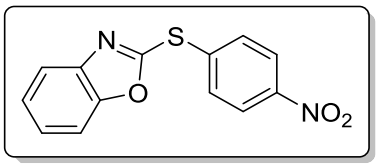
(ATR): 1455, 1417, 1315, 1304, 1164, 1156, 1123, 1106, 1081, 1069, 1019, 1006, 998, 900, 807, 757, 728, 714, 707, 696, 673, 652 cm^{-1}. **HRMS** (ESI): *m/z* 312.0122 ($[M+H]^+$, $C_{14}H_9F_3NS_2^+$ calcd. 312.0123).



2-((4-(Trifluoromethyl)phenyl)thio)benzo[d]thiazole (**88ad**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(4-(trifluoromethyl)phenyl)iodonium trifluoromethanesulfonate[388] in 95% yield (207 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 1H), 7.46 (td, *J* = 7.8, 1.2 Hz, 1H), 7.35 (td, *J* = 7.7, 1.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.9, 153.8, 136.0, 135.5, 134.3, 131.9 (q, *J* = 32.8 Hz), 126.8 (q, *J* = 3.6 Hz), 126.6, 125.2, 123.9 (q, *J* = 272.9 Hz), 122.6, 121.2. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.88 (s, 3F). **FT-IR** (ATR): 1428, 1319, 1312, 1166, 1160, 1104, 1092, 1077, 1061, 1015, 1007, 841, 834, 755, 728, 704 cm^{-1}. **HRMS** (ESI): *m/z* 312.0122 ($[M+H]^+$, $C_{14}H_9F_3NS_2^+$ calcd. 312.0123).

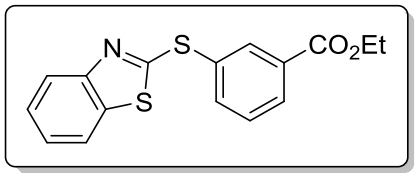


2-((3,5-Bis(trifluoromethyl)phenyl)thio)benzo[d]thiazole (**88ae**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(3,5-bis(trifluoromethyl)phenyl)iodonium tetrafluoroborate[28] in 99% yield (263 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.17 (s, 2H), 7.99 – 7.92 (m, 2H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.7 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.6, 153.6, 136.1, 134.1, 133.8 (q, *J* = 3.6 Hz), 133.1 (q, *J* = 33.8 Hz), 126.8, 125.5, 123.5 (quint., *J* = 3.6 Hz), 122.9 (q, *J* = 273.5 Hz), 121.3. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -63.0 (s, 6F). **FT-IR** (ATR): 1457, 1425, 1350, 1273, 1173, 1136, 1126, 1120, 1106, 1098, 1074, 1024, 1010, 1000, 893, 822, 754, 727, 714, 699, 680, 676 cm^{-1}. **HRMS** (ESI): *m/z* 379.9997 ($[M+H]^+$, $C_{15}H_8F_6NS_2^+$ calcd. 379.9997).

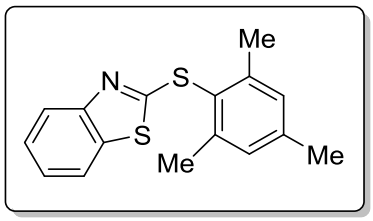


2-((4-Nitrophenyl)thio)benzo[d]oxazole (**88af**): The title compound was prepared according to the General Procedure B from benzo[d]oxazole-2-thiol and (4-nitrophenyl)(phenyl)iodonium trifluoromethanesulfonate[100] in 92% yield (175 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.31 – 8.26 (m, 2H), 7.89 – 7.84 (m, 2H), 7.69 – 7.64 (m, 1H), 7.51 – 7.46 (m, 1H), 7.37 – 7.31 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 160.5, 152.0, 148.2, 141.7, 136.9, 133.2, 125.3, 125.0, 124.6, 119.6, 110.5. **FT-IR** (ATR):

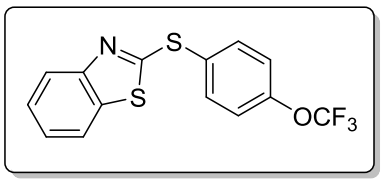
1502, 1451, 1338, 1211, 1128, 843, 807, 756, 749, 740, 727, 683 cm^{-1}. **HRMS** (ESI): *m/z* 273.0328 ($[M+H]^+$, $C_{13}H_9N_2O_3S^+$ calcd. 273.0328).



2-((3-(ethoxycarbonyl)phenyl)thio)benzo[d]thiazole (**88ag**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(3-(ethoxycarbonyl)phenyl)iodonium trifluoromethanesulfonate[125] in 99% yield (218 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.42 (t, *J* = 1.7 Hz, 1H), 8.19 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.95 – 7.87 (m, 2H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 168.3, 165.6, 154.0, 139.4, 136.2, 135.8, 132.5, 131.6, 130.8, 130.1, 126.5, 124.8, 122.3, 121.1, 61.7, 14.5. **FT-IR** (ATR): 1715, 1457, 1426, 1419, 1289, 1279, 1256, 1239, 1125, 1020, 1007, 998, 984, 749, 726, 685 cm^{-1}. **HRMS** (ESI): *m/z* 316.0459 ($[M+H]^+$, $C_{16}H_{13}NS_2^+$ calcd. 316.0460).

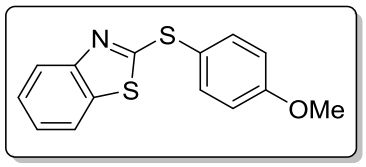


2-(Mesitylthio)benzo[d]thiazole (**88ah**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and dimesityliodonium trifluoromethanesulfonate[100] in 100% yield (200 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.40 (td, *J* = 7.8, 1.2 Hz, 1H), 7.24 (td, *J* = 7.6, 1.2 Hz, 1H), 7.10 (s, 2H), 2.51 (s, 6H), 2.38 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 171.1, 154.7, 144.2, 141.6, 135.4, 130.1, 126.2, 125.8, 124.0, 121.7, 120.9, 21.84, 21.48. **FT-IR** (ATR): 1453, 1448, 1426, 1424, 1419, 1241, 1022, 1006, 853, 754, 726, 720 cm^{-1}. **HRMS** (ESI): *m/z* 286.0717 ($[M+H]^+$, $C_{16}H_{16}NS_2^+$ calcd. 286.0719).



2-((4-(Trifluoromethoxy)phenyl)thio)benzo[d]thiazole (**88ai**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(4-(trifluoromethoxy)phenyl)iodonium trifluoromethanesulfonate[161] in 93% yield (213 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.3 Hz, 1H), 7.81 – 7.75 (m, 2H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.43 (td, *J* = 7.8, 1.2 Hz, 1H), 7.35 – 7.29 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 168.1, 154.0, 150.9 (d, *J* = 1.8 Hz), 136.9, 135.8, 128.6, 126.5, 124.8, 122.3, 122.1, 121.06, 120.5 (q, *J* = 258.4 Hz). **^{19}F NMR** (376 MHz, CDCl3): δ -57.76 (s, 3F). **FT-IR** (ATR): 1488, 1458, 1429, 1279 1258, 1257, 1241, 1215, 1202,

1165, 1154, 1127, 1102, 1090, 1087, 1074, 1021, 1008, 920, 849, 756, 728, 662, 510 cm^{-1}. **HRMS** (ESI): *m/z* 328.0072 ($[M+H]^+$, $C_{14}H_9F_3NOS_2^+$ calcd. 328.0072).



2-((4-Methoxyphenyl)thio)benzo[d]thiazole (**88aj**): The title compound was prepared according to the General Procedure B from benzo[d]thiazole-2-thiol and bis(4-methoxyphenyl)iodonium 4-methylbenzenesulfonate[103] in 50% yield (137 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.3 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.04 – 6.98 (m, 2H), 3.89 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 172.1, 161.9, 154.3, 137.8, 135.6, 126.3, 124.2, 121.9, 120.9, 120.4, 115.7, 55.6. **FT-IR** (ATR): 1588, 1493, 1460, 1453, 1427, 1291, 1250, 1175, 1172, 1027, 1019, 1006, 1002, 830, 767, 759, 731 cm^{-1}. **HRMS** (ESI): *m/z* 274.0353 ($[M+H]^+$, $C_{14}H_{12}NOS_2^+$ calcd. 274.0355).

Computational Details for Chapter 4 (Paper II)

The calculations were carried out with Gaussian 16 software package[389] using B3LYP functional,[390–394] including the D3 dispersion correction with the BJ dumping.[395,396] Geometries were optimized with SMD solvation model (in acetonitrile),[397] using Def2-SVP basis set,[398] including a pseudopotential for iodine.[399,400] For each stationary point a thorough conformational analysis was performed in order to locate the conformer with the lowest energy. This was done by identifying key rotatable bonds and manually building possible starting geometries for optimizations.

The identified lowest energy stationary points were then characterized by frequency calculations to confirm their character as minima (no imaginary frequencies) or transition states (a single imaginary frequency). The final free energies were obtained from single-point calculations on the optimized geometries with a larger Def2-QZVP basis set[398] (with SMD solvation) and were corrected for the thermodynamic effects using the quasi-harmonic approximation[401] (100 cm^{-1} cut-off) as implemented in GoodVibes program.[402]

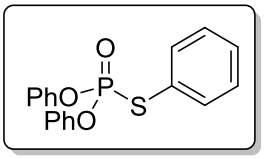
Table S1. Energies and energy corrections of stationary points (in atomic units)

Stationary point	B3LYP-D3BJ/ Def2-SVP (MeCN) optimization	B3LYP-D3BJ/ Def2-QZVP (MeCN) single-point	Thermal correction to Gibbs free energy
87a	-1721.665759	-1723.154379	0.163506
88a	-1351.406924	-1352.347485	0.148636
89a	-1120.026185	-1120.713668	0.062360
90	-2841.720875	-2843.887101	0.247171
91	-1880.658140	-1881.880890	0.227948
PhI	-529.303981	-529.582725	0.061381
TfO^-	-961.040531	-961.998903	-0.001833
TS1	-1880.628122	-1881.845896	0.227293
TS2	-2841.680576	-2843.845752	0.244306

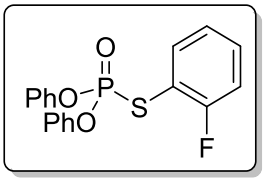
Experimental procedure and characterization of compounds for Chapter 5 (Paper III)

General Procedure C: A 20 mL vial was charged with phosphorothioate diester/related P–S/Se compound (0.40 mmol) and diaryliodonium tetrafluoroborate (1.2 equiv., 0.48 mmol). The vial was capped and evacuated/back-filled with nitrogen three times. Anhydrous 1,4-dioxane (8 mL) was added via syringe and the reaction mixture was stirred at 100 °C for 18 hours. After cooling to room temperature, the solvent was evaporated under reduced pressure. Dichloromethane (2 mL) was added to the residue, followed by a small amount of silica. The solvent was evaporated under reduced pressure, the solid residue was applied on the top of silica column, and the product was purified by column chromatography.

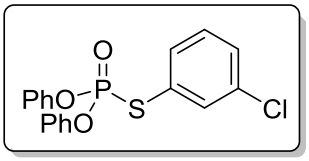
The procedure can also performed in a larger scale (see product **93w** for 1.50 mmol example). In this case, the 20 mL vial is replaced by a round-bottom flask equipped with a reflux condenser, which is closed with a rubber septum and connected via needle to a positive pressure of nitrogen (from balloon or manifold) throughout the reaction.



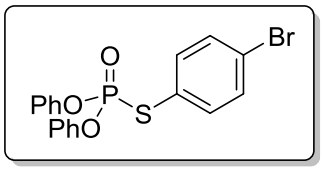
Triphenyl phosphorothioate (**93a**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and diphenyliodonium tetrafluoroborate **87a**[102] in 91% yield (124 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 – 7.45 (m, 2H), 7.42 – 7.30 (m, 7H), 7.21 (t, *J* = 7.5 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.5 (d, *J* = 8.6 Hz), 135.5 (d, *J* = 5.3 Hz), 130.0, 129.8 (d, *J* = 3.4 Hz), 129.7 (d, *J* = 2.6 Hz), 125.7, 125.2 (d, *J* = 7.6 Hz), 120.6 (d, *J* = 5.1 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 15.1. **FT-IR** (ATR): 1588, 1487, 1269, 1179, 1159, 922, 746 cm^{-1}. **HRMS** (ESI): *m/z* 343.0557 ($[M+H]^+$, $C_{18}H_{16}O_3PS^+$ calcd. 343.0552).



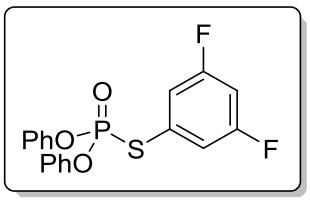
***S*-(2-Fluorophenyl) *O,O*-diphenyl phosphorothioate** (**93b**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(2-fluorophenyl)iodonium tetrafluoroborate[102]in 84% yield (121 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.57 – 7.51 (m, 1H), 7.43 – 7.38 (m, 1H), 7.38 – 7.32 (m, 1H), 7.26 – 7.19 (m, 6H), 7.15 – 7.10 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 162.9 (dd, *J* = 250.6, 5.7 Hz), 150.5 (d, *J* = 8.6 Hz), 137.9 (d, *J* = 4.6 Hz), 132.4 (dd, *J* = 8.1, 3.5 Hz), 130.0, 125.8, 125.1 (t, *J* = 3.2 Hz), 120.6 (d, *J* = 5.0 Hz), 116.7 (dd, *J* = 22.6, 2.8 Hz), 112.6 (dd, *J* = 18.6, 7.7 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 13.6. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -104.5 – -104.6 (m). **FT-IR** (ATR): 2921, 1487, 1180, 1158, 934, 756 cm^{-1}. **HRMS** (ESI): *m/z* 361.0461($[M+H]^+$, $C_{18}H_{15}FO_3PS^+$ calcd. 361.0458).



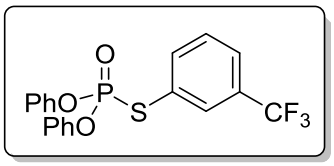
***S*-(3-Chlorophenyl) *O,O*-diphenyl phosphorothioate** (**93c**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(3-chlorophenyl)iodonium tetrafluoroborate[334] in 91% yield (137 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.45 – 7.32 (m, 7H), 7.29 – 7.20 (m, 7H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.4 (d, *J* = 8.3 Hz), 135.1 (d, *J* = 5.5 Hz), 135.1 (d, *J* = 3.2 Hz), 133.5 (d, *J* = 5.5 Hz), 130.6 (d, *J* = 2.7 Hz), 130.10, 130.07, 126.9 (d, *J* = 7.5 Hz), 126.0, 120.6 (d, *J* = 4.8 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 13.9. **FT-IR** (ATR): 1588, 1487, 1273, 1179, 1159, 933, 764 cm^{-1}. **HRMS** (ESI): *m/z* 377.0168($[M+H]^+$, $C_{18}H_{15}ClO_3PS^+$ calcd. 377.0163).



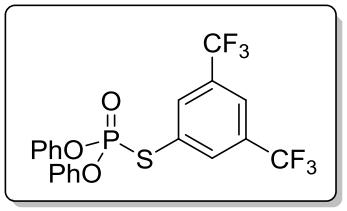
***S*-(4-Bromophenyl) *O,O*-diphenyl phosphorothioate** (**93d**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(4-bromophenyl)iodonium tetrafluoroborate[102] in 86% yield (145 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.48 – 7.43 (m, 2H), 7.38 – 7.32 (m, 6H), 7.25 – 7.19 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.4 (d, *J* = 8.4 Hz), 136.9 (d, *J* = 5.5 Hz), 132.8 (d, *J* = 2.6 Hz), 130.1, 125.9, 124.6 (d, *J* = 3.8 Hz), 124.3 (d, *J* = 8.0 Hz), 120.6 (d, *J* = 4.8 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 14.1. **FT-IR** (ATR): 1585, 1484, 1264, 1181, 1157, 926, 759 cm^{-1}. **HRMS** (ESI): *m/z* 420.9664 and 422.9635($[M+H]^+$, $C_{18}H_{15}BrO_3PS^+$ calcd. 420.9657 and 422.9637). **Mp.**: 88-89 °C.



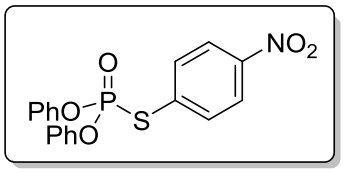
***S*-(3,5-Difluorophenyl) *O,O*-diphenyl phosphorothioate** (**93e**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(3,5-difluorophenyl)iodonium tetrafluoroborate[361] in 86% yield (130 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.40 – 7.43 (m, 4H), 7.28 – 7.21 (m, 6H), 7.06 – 7.00 (m, 2H), 6.86 (tq, *J* = 8.7, 2.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 163.8 (dd, *J* = 12.7, 2.7 Hz), 161.8 (dd, *J* = 12.7, 2.7 Hz), 150.3 (d, *J* = 8.2 Hz), 130.1. 126.1, 120.6 (d, *J* = 5.1 Hz), 118.4 – 118.0 (m, 6H), 105.8 (td, *J* = 25.1, 2.9 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 13.0. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -107.6 – -107.8 (m). **FT-IR** (ATR): 3059, 1591, 1434, 1269, 1186, 947, 847, 760 cm^{-1}. **HRMS** (ESI): *m/z* 379.0367($[M+H]^+$, $C_{18}H_{14}F_2O_3PS^+$ calcd. 379.0364). **Mp.**: 51-53 °C.



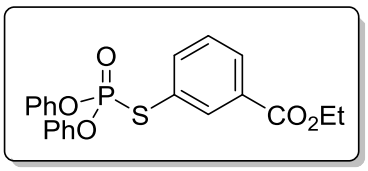
***S*-(3-Trifluoromethylphenyl) *O,O*-diphenyl phosphorothioate** (**93f**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(3-(trifluoromethyl)phenyl)iodonium tetrafluoroborate[102] in 86% yield (141 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.7 Hz, 1H), 7.67 – 7.61 (m, 2H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.39 – 7.33 (m, 4H), 7.26 – 7.17 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.3 (d, *J* = 8.3 Hz), 138.8 (d, *J* = 5.1 Hz), 132.3 – 132.0 (m), 130.10, 130.07, 126.8 (d, *J* = 7.5 Hz), 125.6 (quintet, *J* = 3.6 Hz), 126.0, 124.5 (q, *J* = 273.1 Hz), 120.5 (d, *J* = 5.4 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 13.5. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.8. **FT-IR** (ATR): 1588, 1486, 1321, 1272, 1179, 1158, 938, 762 cm^{-1}. **HRMS** (ESI): *m/z* 411.0429($[M+H]^+$, $C_{19}H_{15}F_3O_3PS^+$ calcd. 411.0426).



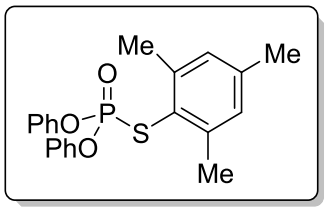
***S*-(3,5-Bis(trifluoromethyl)phenyl) *O,O*-diphenyl phosphorothioate** (**93g**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(3,5-bis(trifluoromethyl)phenyl)iodonium tetrafluoroborate[28]in 60% yield (114 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.90 – 7.81 (m, 3H), 7.34 (t, J = 7.9 Hz, 4H), 7.29 – 7.19 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.1 (d, *J* = 8.1 Hz), 135.4, 132.8 (qd, *J* = 34.3, 2.5 Hz), 130.2, 129.0 (d, *J* = 7.4 Hz), 126.3, 123.7 – 123.5 (m), 122.7 (q, *J* = 272.9 Hz), 120.5 (d, *J* = 5.4 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 12.0. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -63.0. **FT-IR** (ATR): 1588, 1484, 1348, 1273, 1118, 935, 681 cm^{-1}. **HRMS** (ESI): *m/z* 479.0301($[M+H]^+$ $C_{20}H_{14}F_6O_3PS^+$ calcd. 479.0300). **Mp.**: 51-52 °C.



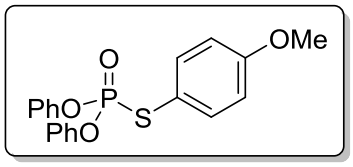
***S*-(4-Nitrophenyl) *O,O*-diphenyl phosphorothioate** (**93h**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and (4-nitrophenyl)(phenyl)iodonium tetrafluoroborate[147] in 84% yield (130 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.70 – 7.63 (m, 2H), 7.40 – 7.35 (m, 4H), 7.28 – 7.20 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.1 (d, *J* = 8.5 Hz), 148.4 (d, *J* = 2.8 Hz), 135.5 (d, *J* = 6.0 Hz), 134.4 (d, *J* = 7.2 Hz), 130.2, 126.2 (d, *J* = 1.4 Hz), 124.3 (d, *J* = 1.7 Hz), 120.6 (d, *J* = 5.3 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 12.6. **FT-IR** (ATR): 1589, 1487, 1274, 1175, 1156, 932, 847, 741 cm^{-1}. **HRMS** (ESI): *m/z* 388.0405($[M+H]^+$, $C_{18}H_{15}NO_5PS^+$ calcd. 388.0403). **Mp.**: 70-71 °C.



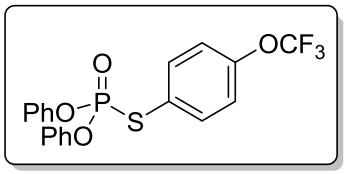
***S*-(3-Ethoxycarbonylphenyl) *O,O*-diphenyl phosphorothioate** (**93i**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(3-(ethoxycarbonyl)phenyl)iodonium tetrafluoroborat[361] in 90% yield (100 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.12 (q, *J* = 1.9 Hz, 1H), 8.09 – 8.04 (m, 1H), 7.72 – 7.66 (m, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.38 – 7.33 (m, 4H), 7.25 – 7.20 (m, 6H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 165.5, 150.4 (d, *J* = 8.3 Hz), 139.6 (d, *J* = 5.1 Hz), 136.4 (d, *J* = 5.7 Hz), 132.0 (d, *J* = 2.1 Hz), 130.9 (d, *J* = 3.2 Hz), 130.0, 129.7 (d, *J* = 2.3 Hz), 126.0 (d, *J* = 7.9 Hz), 125.9, 120.6 (d, *J* = 5.1 Hz), 61.6, 14.5. **^{31}P NMR** (203 MHz, $CDCl_3$): δ 14.2. **FT-IR** (ATR): 1719, 1266, 1127, 932, 774 cm^{-1}. **HRMS** (ESI): *m/z* 415.0768($[M+H]^+$, $C_{21}H_{20}O_5PS^+$ calcd. 415.0764). **Mp.**: 83-84 °C.



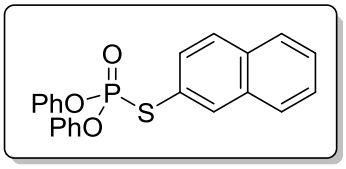
***S*-Mesityl *O,O*-diphenyl phosphorothioate** (**93j**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and dimesityliodonium tetrafluoroborate[143] in 100% yield (154 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.33 – 7.29 (m, 4H), 7.21 – 7.13 (m, 6H), 6.94 (s, 2H), 2.41 (d, *J* = 1.5 Hz, 6H), 2.27 (d, *J* = 2.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.8 (d, *J* = 9.9 Hz), 144.4 (d, *J* = 5.0 Hz), 140.2 (d, *J* = 4.3 Hz), 129.9, 129.8 (d, *J* = 3.6 Hz), 125.5, 120.7 (d, *J* = 4.7 Hz), 120.4 (d, *J* = 8.2 Hz), 22.5, 21.2. **^{31}P NMR** (203 MHz, $CDCl_3$): δ 16.4. **FT-IR** (ATR): 2931, 1589, 1487, 1270, 1180, 922, 764 cm^{-1}. **HRMS** (ESI): *m/z* 385.1026($[M+H]^+$, $C_{21}H_{22}O_3PS^+$ calcd. 385.1022).



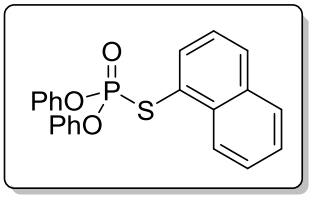
***S*-(4-Methoxyphenyl) *O,O*-diphenyl phosphorothioate** (**93k**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(4-methoxyphenyl)iodonium tetrafluoroborate[102] in 62% yield (93 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.41 – 7.32 (m, 6H), 7.24 – 7.18 (m, 6H), 6.88 – 6.84 (m, 2H), 3.81 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 161.1 (d, *J* = 2.9 Hz), 150.6 (d, *J* = 8.7 Hz), 137.2 (d, *J* = 5.0 Hz), 130.0, 125.6, 120.6 (d, *J* = 5.0 Hz), 115.2 (d, *J* = 2.7 Hz), 115.1 (d, *J* = 7.8 Hz), 55.6. **^{31}P NMR** (203 MHz, $CDCl_3$): δ 15.6. **FT-IR** (ATR): 1589, 1487, 1250, 1175, 1155, 922, 748 cm^{-1}. **HRMS** (ESI): *m/z* 373.0662 ($[M+H]^+$, $C_{19}H_{18}O_4PS^+$ calcd. 373.0658).



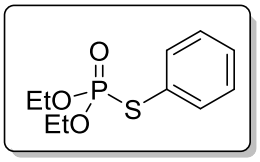
***S*-(4-Trifluoromethoxyphenyl) *O,O*-diphenyl phosphorothioate** (**93l**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(4-(trifluoromethoxy)phenyl)iodonium tetrafluoroborate[361] in 92% yield (156 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.54 – 7.48 (m, 2H), 7.39 – 7.33 (m, 4H), 7.25 – 7.13 (m, 8H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.41 (d, *J* = 1.8 Hz), 150.40 (d, *J* = 8.6 Hz), 137.1 (d, *J* = 5.4 Hz), 130.1, 125.9, 123.7 (d, *J* = 7.8 Hz), 121.9, 120.6 (d, *J* = 4.8 Hz), 120.5 (d, *J* = 258.9 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 14.2. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -57.8. **FT-IR** (ATR): 1574, 1487, 1260, 1196, 1152, 393, 902, 764 cm^{-1}. **HRMS** (ESI): *m/z* 427.0378($[M+H]^+$, $C_{19}H_{15}F_3O_4PS^+$ calcd. 427.0375).



***S*-(Naphth-2-yl) *O,O*-diphenyl phosphorothioate** (**93m**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(2-naphthyl)iodonium tetrafluoroborate[403] in 96% yield (150 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.57 – 7.49 (m, 3H), 7.37 – 7.30 (m, 4H), 7.25 – 7.18 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.6 (d, *J* = 8.2 Hz), 135.8 (d, *J* = 7.1 Hz), 133.7 (d, *J* = 2.7 Hz), 133.5 (d, *J* = 2.5 Hz), 131.5 (d, *J* = 3.9 Hz), 130.0, 129.3 (d, *J* = 2.2 Hz), 128.0 (d, *J* = 10.0 Hz), 127.6 (d, *J* = 1.3 Hz), 127.0, 125.8 (d, *J* = 1.2 Hz), 122.2 (d, *J* = 8.3 Hz), 120.7 (d, *J* = 5.3 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 14.9. **FT-IR** (ATR): 1487, 1260, 1178, 1159, 913, 764 cm^{-1}. **HRMS** (ESI): *m/z* 393.0708($[M+H]^+$, $C_{22}H_{18}O_3PS^+$ calcd. 393.0709). **Mp.**: 62-63 °C.

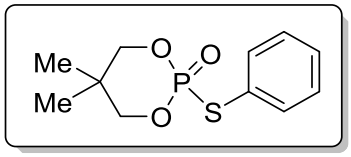


***S*-(Naphth-1-yl) *O,O*-diphenyl phosphorothioate** (**93n**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorothioate **92a** and bis(1-naphthyl)iodonium tetrafluoroborate[102] in 73% yield (114 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.53 – 7.48 (m, 1H), 7.48 – 7.41 (m, 2H), 7.33 – 7.26 (m, 4H), 7.17 (t, *J* = 7.4 Hz, 2H), 7.14 – 7.08 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.7 (d, *J* = 8.5 Hz), 136.2 (d, *J* = 5.8 Hz), 134.9 (d, *J* = 4.0 Hz), 134.5 (d, *J* = 2.6 Hz), 131.1 (d, *J* = 3.8 Hz), 129.9, 128.6, 127.4, 126.7, 126.2, 125.8 (d, *J* = 3.7 Hz), 125.6 (d, *J* = 1.1 Hz), 122.4 (d, *J* = 8.5 Hz), 120.5 (d, *J* = 5.4 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 14.7. **FT-IR** (ATR): 1487, 1260, 1178, 1159, 913, 764 cm^{-1}. **HRMS** (ESI): *m/z* 393.0709 ($[M+H]^+$, $C_{22}H_{18}O_3PS^+$ calcd. 393.0709).

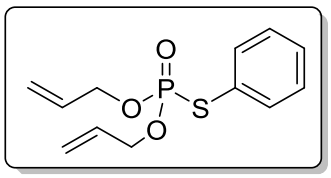


***O,O*-Diethyl *S*-phenyl phosphorothioate** (**93o**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diethyl phosphorothioate and diphenyliodonium tetrafluoroborate **87b**[102] in 99% yield (97 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.60 – 7.52 (m, 2H), 7.40 – 7.30 (m, 3H), 4.26 – 4.12 (m, 4H), 1.30 (td, *J* = 7.1, 0.7 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 134.7 (d, *J* = 5.2 Hz), 129.5 (d, *J* = 2.4 Hz), 129.2 (d, *J* = 2.7 Hz), 126.8 (d, *J* = 7.4 Hz), 64.2 (d, *J* = 6.4 Hz), 16.2 (d, *J* = 7.2 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 23.1. **FT-IR** (ATR): 1441, 1253, 1008, 970, 745 cm^{-1}. **HRMS** (ESI): *m/z* 247.0555($[M+H]^+$, $C_{10}H_{16}O_3PS^+$ calcd. 247.0552).

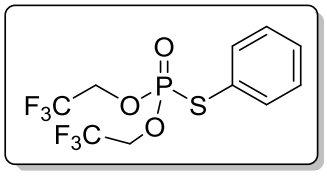
This product was also synthesized in a larger scale (1.5 mmol), from triethylammonium *O,O*-diethyl phosphorothioate and diphenyliodonium tetrafluoroborate, affording 332 mg (90%) of **93o**.



5,5-Dimethyl-2-(phenylthio)-1,3,2-dioxaphosphinane 2-oxide (**93p**): The title compound was prepared according to the General Procedure C from triethylammonium 5,5-dimethyl-1,3,2-dioxaphosphinane-2-thiolate 2-oxide and diphenyliodonium tetrafluoroborate **87b**[102] in 88% yield (91 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.68 – 7.58 (m, 2H), 7.40 – 7.32 (m, 3H), 4.20 (dd, *J* = 10.1, 3.7 Hz, 2H), 3.99 – 3.87 (m, 2H). 1.27 (s, 3H), 0.87 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 134.9 (d, *J* = 5.3 Hz), 129.7 (d, *J* = 2.2 Hz), 129.4 (d, *J* = 2.7 Hz), 124.9 (d, *J* = 6.4 Hz), 78.4 (d, *J* = 7.4 Hz), 32.7 (d, *J* = 6.7 Hz), 22.2, 20.6. **^{31}P NMR** (203 MHz, $CDCl_3$): δ 15.1. **FT-IR** (ATR): 1476, 1464, 1267, 1045, 990, 972, 782 cm^{-1}. **HRMS** (ESI): *m/z* 259.0553($[M+H]^+$, $C_{11}H_{16}O_3PS^+$ calcd. 259.0552). **Mp.**: 120-121 °C.

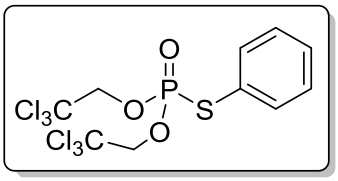


***O,O*-Diallyl *S*-phenyl phosphorothioate** (**93q**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diallyl phosphorothioate and diphenyliodonium tetrafluoroborate **87b**[102] in 52% yield (56 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.61 – 7.53 (m, 2H), 7.40 – 7.30 (m, 3H), 5.93 – 5.85 (m, 2H), 5.32 (dq, *J* = 17.1, 1.4 Hz, 2H), 5.23 (d, *J* = 10.3 Hz, 2H), 4.67 – 4.54 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 135.0 (d, *J* = 5.4 Hz), 132.2 (d, *J* = 7.5 Hz), 129.6 (d, *J* = 2.5 Hz), 129.4 (d, *J* = 2.7 Hz), 126.2 (d, *J* = 7.2 Hz), 118.8, 68.5 (d, *J* = 5.7 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 23.9. **FT-IR** (ATR): 2917, 1259, 922, 796, 745 cm^{-1}. **HRMS** (ESI): *m/z*: 271.0552 ($[M+H]^+$, $C_{12}H_{16}O_3PS^+$ calcd. 271.0552).

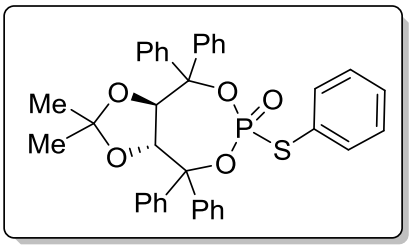


***S*-phenyl *O,O*-bis(2,2,2-trifluoroethyl) phosphorothioate** (**93r**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-bis(2,2,2-trifluoroethyl) phosphorothioate and diphenyliodonium tetrafluoroborate **87b**[102] in 30% yield (43 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.63 – 7.56 (m, 2H), 7.48 – 7.37 (m, 3H), 4.44 – 4.29 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 135.6 (d, *J* = 5.4 Hz), 130.5 (d, *J* = 3.5 Hz), 130.0 (d, *J* = 2.8 Hz), 123.3 (d, *J* = 7.6 Hz), 122.3 (qd, *J* = 277.9, 10.3 Hz), 63.8 (qd, *J* = 38.4, 5.7 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 26.5. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -75.0 (t, *J* = 7.8 Hz, 6F). **FT-IR** (ATR): 1299, 1284, 1247, 1180, 1153, 1078, 1069, 1023, 963, 956,

874, 846, 836, 808, 752, 689, 654, 586, 582, 575, 556, 552 cm^{-1}. **HRMS** (ESI): *m/z* 354.9986($[M+H]^+$, $C_{10}H_{10}F_6O_3PS^+$ calcd. 354.9987).

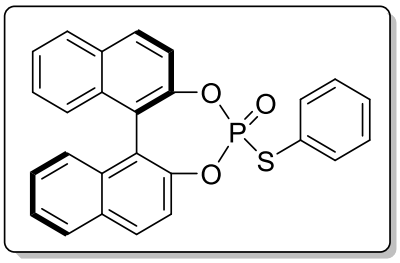


***S*-phenyl *O,O*-bis(2,2,2-trichloroethyl) phosphorothioate** (**93s**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-bis(2,2,2-trichloroethyl) phosphorothioate and diphenyliodonium tetrafluoroborate **87b**[102] in 36% yield (65 mg).**^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.63 – 7.56 (m, 2H), 7.48 – 7.37 (m, 3H), 4.64 (dd, *J* = 11.1, 7.0 Hz, 2H), 4..58 (dd, *J* = 11.1, 6.7 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 135.8 (d, *J* = 5.4 Hz), 130.3 (d, *J* = 3.5 Hz), 129.9 (d, *J* = 2.8 Hz), 128.8 (d, *J* = 7.6 Hz), 94.5 (d, *J* = 11.4 Hz), 77.1 (d, *J* = 6.3 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 23.9. **FT-IR** (ATR): 1250, 1110, 1091, 1042, 1012, 888, 883, 843, 775, 765, 757, 751, 718, 699, 692, 622, 593, 565, 561, 531 cm^{-1}. **HRMS** (ESI): *m/z* 452.8185 ($[M+H]^+$, $C_{10}H_{10}Cl_6O_3PS^+$ calcd. 452.8184).



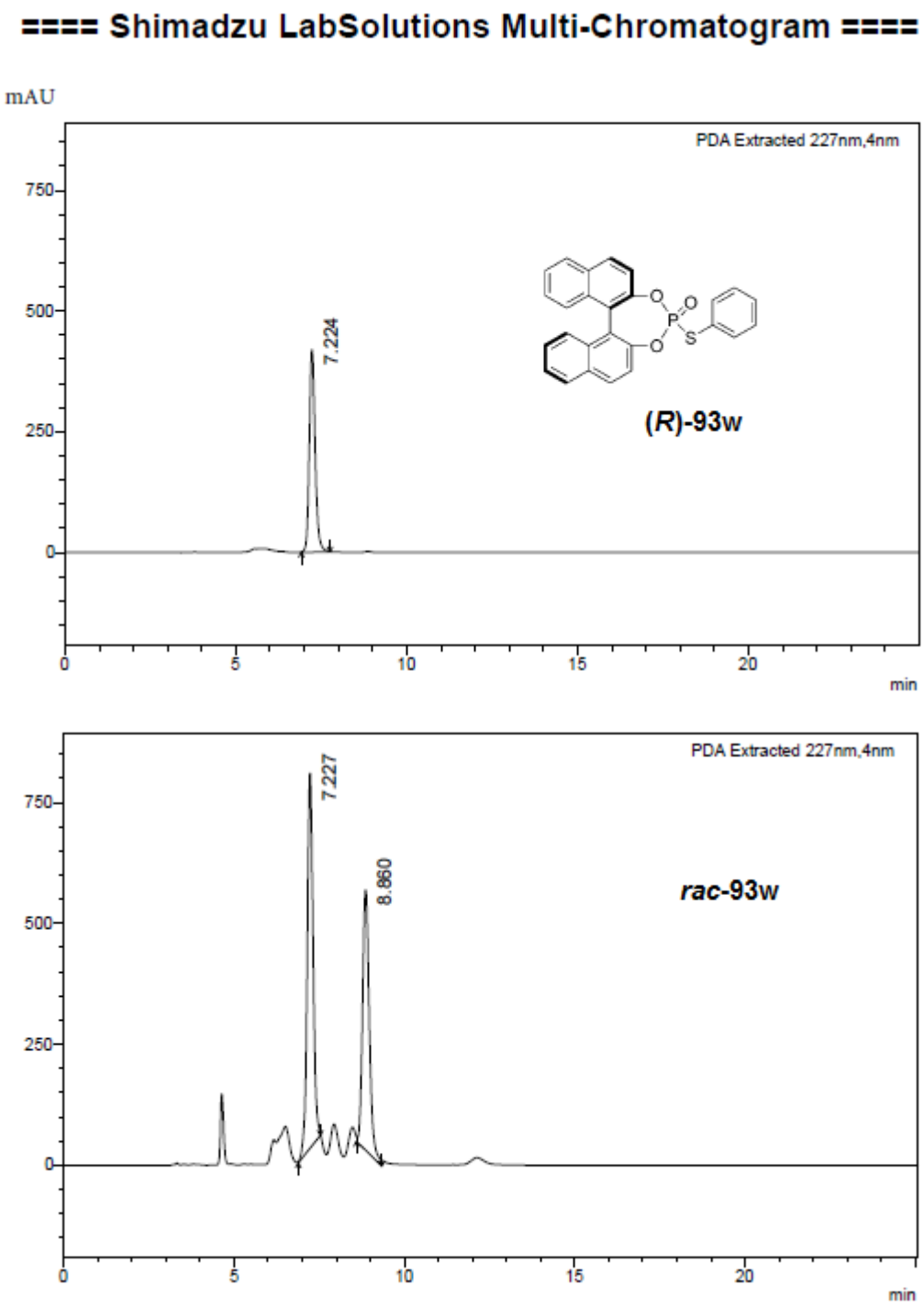
(3a*R*,8a*R*)-2,2-Dimethyl-4,4,8,8-tetraphenyl-6-(phenylthio)tetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine 6-oxide (**93v**): The title compound was prepared according to the General Procedure C from triethylammonium (3a*R*,8a*R*)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine-6-thiolate 6-oxide and diphenyliodonium tetrafluoroborate **87b**[102] in 97% yield (239 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 – 7.52 (m, 2H), 7.49 – 7.42 (m, 4H), 7.42 – 7.37 (m, 5H), 7.37 – 7.14 (m, 12H), 6.99 – 6.94 (m, 2H), 5.38 (d, *J* = 8.0 Hz, 1H), 5.09 (d, *J* = 8.0 Hz, 1H) 0.72 (s, 3H), 0.51 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 144.0 (d, *J* = 6.1 Hz), 143.3, 139.7 (d, *J* = 10.9 Hz), 139.6 (d, *J* = 3.6 Hz), 135.7 (d, *J* = 5.5 Hz), 129.9, 129.3 (d, *J* = 2.6 Hz), 129.2 (d, *J* = 3.1 Hz), 128.7, 128.5, 128.4 (d, *J* = 3.9 Hz), 127.87, 127.86 (d, *J* = 12.9 Hz), 127.3 (d, *J* = 2.4 Hz), 126.8, 126.1 (d, *J* = 8.6 Hz), 114.2, 92.0 (d, *J* = 13.6 Hz), 88.9 (d, *J* = 10.0 Hz), 79.3 (d, *J* = 1.4 Hz), 79.1 (d, *J* = 2.3 Hz), 27.0, 26.6. **^{31}P NMR** (203 MHz, $CDCl_3$): δ 15.4. **FT-IR** (ATR): 1255, 1014, 968, 744, 696 cm^{-1}. **HRMS** (ESI): *m/z* 621.1860($[M+H]^+$, $C_{37}H_{34}O_5PS^+$ calcd. 621.1859). **Mp.**: 165-167 °C (decomposition).

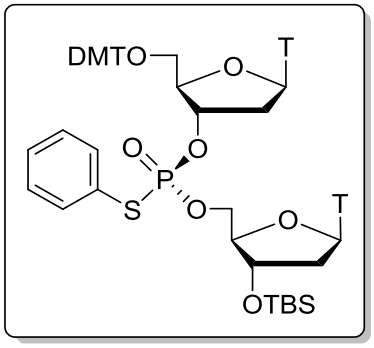
The NMR spectra (^{1}H, ^{13}C, ^{31}P) of the title compound contain a single set of signals indicating that no epimerization has occurred, demonstrating the stability of the stereocenters under the reaction conditions.



(*R*)-4-(Phenylthio)dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine 4-oxide (**(*R*)-93w**): The title compound was prepared according to the General Procedure C from triethylammonium (*R*)-dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-4-thiolate 4-oxide and diphenyliodonium tetrafluoroborate **87b**[102] in 22% yield (38 mg). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.29 (dd, *J* = 13.2, 9.0 Hz, 2H), 8.15 (dd, *J* = 8.1, 3.2 Hz, 2H), 7.78 – 7.68 (m, 4H), 7.63 – 7.55 (m, 2H), 7.54 – 7.45 (m, 3H), 7.44 – 7.38 (m, 2H), 7.25 – 7.18 (m, 2H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ 146. 4 (d, *J* = 11.7 Hz), 145.7 (d, *J* = 11.6 Hz), 135.5 (d, *J* = 5.3 Hz), 131.9 (d, *J* = 10.5 Hz), 131.6, 131.5, 130.2 (d, *J* = 2.8 Hz), 130.0 (d, *J* = 2.1 Hz), 128.8 (d, *J* = 8.6 Hz), 127.4 (d, *J* = 10.6 Hz), 126.3, 126.2 (d, *J* = 21.1 Hz), 122.8 (d, *J* = 6.3 Hz), 121.1 – 120.6 (m). **^{31}P NMR** (203 MHz, DMSO-d_6): δ 32.0. **FT-IR** (ATR): 1466, 1286, 1220, 1069, 945, 813, 745 cm^{-1}. **HRMS** (ESI): *m/z* 441.0709([M+H]$^{+}$, $C_{26}H_{18}O_3PS^{+}$ calcd. 441.0709). **Mp.**: 80-83 °C (decomposition). **HPLC** (CHIRALART Cellulose-SC (equivalent to CHIRALPAK IC), hexanes/2-propanol = 9/1, flow rate = 1.0 mL/min, λ = 227 nm, 30 °C): t_R = 7.2 min (*rac*-**93w**: t_R = 7.2 min, 8.9 min).

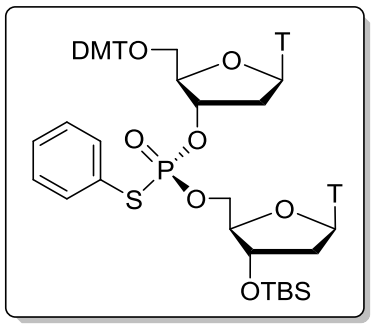
The HPLC analysis shows that the compound is enantiopure, demonstrating the stability of the axial chirality under the reaction conditions.


==== Shimadzu LabSolutions Multi-Chromatogram ====
mAU
PDA Extracted 227nm,4nm
750
500
250
0
7.224
(R)-93w
0
5
10
15
20
min
PDA Extracted 227nm,4nm
7.227
8.860
rac-93w
750
500
250
0
0
5
10
15
20
min



(R_P)-3′-*O*-(*tert*-Butyldimethylsilyl)thymidin-5′-yl 5′-*O*-dimethoxytritylthymidin-3′-yl *S*-phenyl phosphorothioate (**R_P-93x**): The title compound was prepared according to the General Procedure C from triethylammonium (R_P)-3′-*O*-(*tert*-Butyldimethylsilyl)thymidin-5′-yl 5′-*O*-Dimethoxytritylthymidin-3′-yl phosphorothioate (108 mg, 0.10 mmol) and diphenyliodonium tetrafluoroborate **87b** (44.2 mg, 0.12 mmol)[102]in 50% yield (53 mg). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.40 (s, 1H), 11.34 (s, 1H), 7.58 – 7.53 (m, 2H), 7.47 – 7.39 (m, 3H), 7.39 – 7.33 (m, 4H), 7.33 – 7.27 (m, 2H), 7.27 – 7.20 (m, 5H), 6.92 – 6.84 (m, 4H), 6.20 – 6.11 (m, 2H), 5.21 – 5.11 (m. 1H), 4.39 – 4.32 (m, 1H), 4.32 – 4.19 (m, 2H), 4.14 – 4.08 (m, 1H), 3.91 – 3.84 (m, 1H), 3.72 (s, 6H), 3.24 (dd, *J* = 27.5, 10.9 Hz, 2H), 2.49 – 2.42 (m, 1H), 2.32 (dd, *J* = 14.3, 6.0 Hz, 1H), 2.28 – 2.19 (m, 1H), 2.04 (ddd, *J* = 13.6, 6.4, 3.4 Hz, 1H), 1.72 (d, *J* = 1.0 Hz, 3H), 1.45 (d, *J* = 1.0 Hz, 3H), 0.84 (s, 9H), 0.04 (d, *J* = 6.0 Hz, 6H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ 163.6 (d, *J* = 6.4 Hz), 158.2 (d, *J* = 1.2 Hz), 150.4 (d, *J* = 11.9 Hz), 144.5, 136.0, 135.5, 135.2, 135.1, 134.6 (d, *J* = 5.1 Hz), 129.73, 129.70 (d, *J* = 1.5 Hz), 127.8 (d, *J* = 35.1 Hz), 126.9, 124.9 (d, *J* = 7.2 Hz), 113.3, 109.9 (d, *J* = 16.5 Hz), 86.2, 84.2, 84.1, 83.7, 83.6 (d, *J* = 4.8 Hz), 78.6 (d, *J* = 5.5 Hz), 71.7, 67.0 (d, *J* = 5.9 Hz), 63.1, 59.8, 55.1, 25.6, 21.1, 17.6, 14.1, 12.1, 11.7, -4.9 (d, *J* = 15.4 Hz). **^{31}P NMR** (203 MHz, DMSO-d_6): δ 22.6. **FT-IR** (ATR): 1683, 1248, 1030, 991, 828 cm^{-1}. **HRMS** (ESI): *m/z* 1055.3688([M+H]$^+$, $C_{53}H_{64}N_4O_{13}PSSi^+$ calcd. 1055.3692). **Mp.**: 115-117 °C (decomposition).

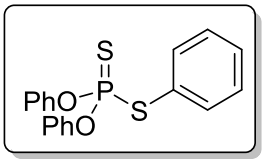
The NMR spectra (^{1}H, ^{13}C, ^{31}P) of the title compound contain a single set of signals indicating that no epimerization has occurred, demonstrating the stability of the stereocenters (both at carbons and at phosphorus) under the reaction conditions.



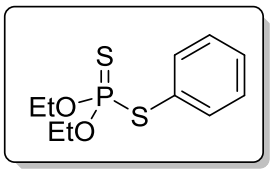
(S_P)-3′-*O*-(*tert*-Butyldimethylsilyl)thymidin-5′-yl 5′-*O*-dimethoxytritylthymidin-3′-yl *S*-phenyl phosphorothioate (**S_P-93x**): The title compound was prepared according to the General Procedure C from triethylammonium (S_P)-3′-*O*-(*tert*-Butyldimethylsilyl)thymidin-5′-yl 5′-*O*-Dimethoxytritylthymidin-3′-yl phosphorothioate (108 mg, 0.10 mmol) and diphenyliodonium tetrafluoroborate **87b** (44.2 mg, 0.12 mmol)[102] in 52% yield (55 mg). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.39 (s, 1H), 11.32 (s, 1H), 7.49 – 7.44 (m, 3H), 7.44 – 7.28 (m, 8H), 7.27 – 7.20

(m, 5H), 6.91 – 6.86 (m, 4H), 6.21 – 6.15 (m, 1H), 6.12 (t, *J* = 6.9 Hz, 1H), 5.18 – 5.05 (m. 1H), 4.36 – 4.26 (m, 2H), 4.26 – 4.19 (m, 1H), 4.06 – 3.98 (m, 1H), 3.91 – 3.85 (m, 1H), 3.72 (s, 6H), 3.22 (dd, *J* = 26.5, 10.9 Hz, 2H), 2.53 – 2.36 (m, 2H), 2.26 – 2.16 (m, 1H), 2.10 – 2.02 (m, 1H), 1.68 (d, *J* = 0.9 Hz, 3H), 1.46 (d, *J* = 0.8 Hz, 3H), 0.85 (s, 9H), 0.06 (d, *J* = 2.8 Hz, 6H). **^{13}C NMR** (126 MHz, DMSO-d_6): δ 163.6 (d, *J* = 5.8 Hz), 158.2 (d, *J* = 1.8 Hz), 150.3 (d, *J* = 3.9 Hz), 144.5, 135.8, 135.5, 135.2, 135.0, 134.4 (d, *J* = 4.8 Hz), 129.9 – 129.5 (m), 127.8 (d, *J* = 39.3 Hz), 126.9, 124.9 (d, *J* = 7.3 Hz), 113.3, 109.9 (d, *J* = 20.0 Hz), 86.2, 84.02, 83.96, 83.7, 83.3 (d, *J* = 7.1 Hz), 78.7 (d, *J* = 6.1 Hz), 71.4, 66.8 (d, *J* = 6.3 Hz), 66.3, 63.2, 59.8, 55.0, 25.6, 20.8, 17.6, 14.1, 12.1, 11.7, -4.9 (d, *J* = 19.2 Hz). **^{31}P NMR** (203 MHz, DMSO-d_6): δ 22.3. **FT-IR** (ATR): 1680, 1249, 997, 830 cm^{-1}. **HRMS** (ESI): *m/z* 1055.3687([M+H]$^+$, $C_{53}H_{64}N_4O_{13}PSSi^+$ calcd. 1055.3692). **Mp.**: 114-116 °C (decomposition).

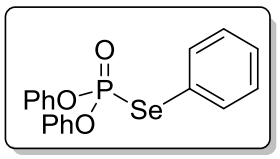
The NMR spectra (^{1}H, ^{13}C, ^{31}P) of the title compound contain a single set of signals indicating that no epimerization has occurred, demonstrating the stability of the stereocenters (both at carbons and at phosphorus) under the reaction conditions.



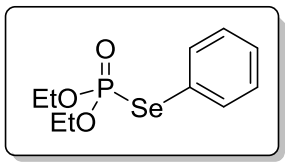
Triphenyl phosphorodithioate (**94a**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphorodithioate and diphenyliodonium tetrafluoroborate **87b**[102] in 81% yield (116 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62 – 7.54 (m, 2H), 7.46 – 7.32 (m, 7H), 7.25 – 7.17 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.8 (d, *J* = 9.6 Hz), 135.6 (d, *J* = 5.3 Hz), 130.0 (d, *J* = 3.6 Hz), 129.8 (d, *J* = 1.5 Hz), 129.6 (d, *J* = 2.8 Hz), 127.6 (d, *J* = 8.2 Hz), 125.8 (d, *J* = 1.7 Hz), 121.6 (d, *J* = 4.9 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 82.5. **FT-IR** (ATR): 1486, 1177, 1151, 913, 897, 791, 667 cm^{-1}. **HRMS** (ESI): *m/z* 359.0324([M+H]$^+$, $C_{18}H_{16}O_2PS_2^+$ calcd. 359.0324). **Mp.**: 74-75 °C.



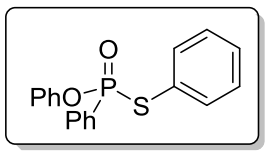
***O,O*-Diethyl *S*-phenyl phosphorodithioate** (**94b**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diethyl phosphorodithioate and diphenyliodonium tetrafluoroborate **87b**[102] in 90% yield (94 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.55 – 7.48 (m, 2H), 7.41 – 7.33 (m, 3H), 4.30 – 4.13 (m, 4H), 1.31 (td, *J* = 7.1, 0.8 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 134.9 (d, *J* = 5.1 Hz), 129.5 – 129.4 (m), 128.5 (d, *J* = 7.5 Hz), 64.4 (d, *J* = 5.6 Hz), 15.9 (d, *J* = 8.6 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 88.3. **FT-IR** (ATR): 2924, 1440, 1009, 955, 797, 744, 648 cm^{-1}. **HRMS** (ESI): *m/z* 263.0324([M+H]$^+$, $C_{10}H_{16}O_2PS_2^+$ calcd. 263.0324).



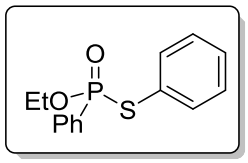
***O,O,Se*-Triphenyl phosphoroselenoate** (**95a**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diphenyl phosphoroselenoate and diphenyliodonium tetrafluoroborate **87b**[102] in 32% yield (49 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 – 7.52 (m, 2H), 7.41 – 7.27 (m, 7H), 7.24 – 7.18 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.5 (d, *J* = 8.3 Hz), 136.4 (d, *J* = 5.0 Hz), 130.0, 129.8 (d, *J* = 2.6 Hz), 129.5 (d, *J* = 3.2 Hz), 125.8 (d, *J* = 1.3 Hz), 122.9 (d, *J* = 9.1 Hz), 120.8 (d, *J* = 5.2 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 9.6. **FT-IR** (ATR): 1586, 1489, 1254, 1179, 1025, 924, 744 cm^{-1}. **HRMS** (ESI): *m/z* 390.998($[M+H]^+$, $C_{18}H_{16}O_3PSe^+$ calcd. 390.9997). **Mp.**: 51-53 °C.



***O,O*-Diethyl *Se*-phenyl phosphoroselenoate** (**95b**): The title compound was prepared according to the General Procedure C from triethylammonium *O,O*-diethyl phosphoroselenoate and diphenyliodonium tetrafluoroborate **87b**[102] in 39% yield (45 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.68 – 7.61 (m, 2H), 7.39 – 7.28 (m, 3H), 4.28 – 4.10 (m, 4H), 1.31 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 135.7 (d, *J* = 4.6 Hz), 129.7 (d, *J* = 1.7 Hz), 129.0 (d, *J* = 2.6 Hz), 124.0 (d, *J* = 8.5 Hz), 64.0 (d, *J* = 6.1 Hz), 16.1 (d, *J* = 7.5 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 18.1. **FT-IR** (ATR): 2992, 2922, 1439, 1248, 1007, 957, 739 cm^{-1}. **HRMS** (ESI): *m/z* 294.9997($[M+H]^+$, $C_{10}H_{16}O_3PSe^+$ calcd. 294.9997).

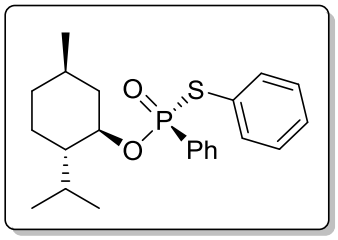


***O,S*-Diphenyl phenylphosphonothioate** (**96a**): The title compound was prepared according to the General Procedure C from triethylammonium *O*-phenyl phenylphosphonothioate and diphenyliodonium tetrafluoroborate **87b**[102] in 68% yield (89 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 – 7.74 (m, 2H), 7.57 – 7.51 (m, 1H), 7.45 – 7.39 (m, 2H), 7.37 – 7.32 (m, 2H), 7.32 – 7.24 (m, 5H), 7.23 – 7.16 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 150.9 (d, *J* = 9.4 Hz), 136.0 (d, *J* = 4.5 Hz), 133.1 (d, *J* = 3.4 Hz), 131.9 (d, *J* = 10.9 Hz), 131.2 (d, *J* = 150.5 Hz), 129.9, 129.4 (d, *J* = 2.8 Hz), 129.3 (d, *J* = 2.5 Hz), 128.5 (d, *J* = 15.1 Hz), 125.9 (d, *J* = 5.6 Hz), 125.4, 121.0 (d, *J* = 4.8 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 39.5. **FT-IR** (ATR): 1684, 1496, 1440, 1236, 922, 748, 687 cm^{-1}. **HRMS** (ESI): *m/z* 327.0604($[M+H]^+$, $C_{18}H_{16}O_2PS^+$ calcd. 327.0603). **Mp.**: 58-59 °C.



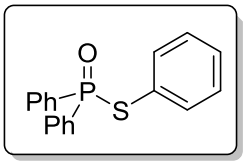
***O*-Ethyl *S*-phenyl phenylphosphonothioate** (**96b**): The title compound was prepared according to the General Procedure C from triethylammonium *O*-ethyl phenylphosphonothioate and diphenyliodonium tetrafluoroborate **87b**[102] in 58% (64 mg). **^{1}H NMR**

(500 MHz, $CDCl_3$): δ 7.69 – 7.60 (m, 2H), 7.52 – 7.47 (m, 1H), 7.40 – 7.39 (m, 2H), 7.32 – 7.26 (m, 3H), 7.24 – 7.17 (m, 2H), 4.42 – 4.28 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 135.7 (d, *J* = 4.0 Hz), 132.7 (d, *J* = 3.4 Hz), 131.7 (d, *J* = 151.3 Hz), 131.6 (d, *J* = 10.3 Hz), 129.3 (d, *J* = 1.8 Hz), 129.1 (d, *J* = 2.7 Hz), 128.4 (d, *J* = 14.8 Hz), 126.8 (d, *J* = 5.6 Hz), 62.6 (d, *J* = 7.1 Hz), 16.5 (d, *J* = 6.5 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 41.8. **FT-IR** (ATR): 1439, 1231, 1118, 1018, 952, 745, 690 cm^{-1}. **HRMS** (ESI): *m/z* 279.0604($[M+H]^+$, $C_{14}H_{16}O_2PS^+$ calcd. 279.0603).



***O*-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl) *S*-phenyl (*S*)-phenylphosphonothioate** (**(S_P)-96c**): The title compound was prepared according to the General Procedure C from triethylammonium *O*-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl) (*S*)-phenylphosphonothioate (97:3 dr at phosphorus) (62 mg, 0.15 mmol) and diphenyliodonium tetrafluoroborate **87b** (44.2 mg, 0.12 mmol)[102] in 71% yield (41 mg; 97:3 dr at phosphorus). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.75 – 7.64 (m, 2H), 7.52 – 7.44 (m, 1H), 7.41 – 7.33 (m, 4H), 7.29 – 7.24 (m, 1H), 7.23 – 7.17 (m, 2H), 4.56 – 4.47 (m, 1H), 2.28 – 2.11 (m, 2H), 1.74 – 1.62 (m, 2H), 1.50 – 1.38 (m, 2H), 1.17 (q, *J* = 11.7 Hz, 1H), 1.06 (qd, *J* = 13.1, 3.2 Hz, 1H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.84 – 0.80 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 135.6 (d, *J* = 4.4 Hz), 133.4 (d, *J* = 149.4 Hz), 132.4 (d, *J* = 3.0 Hz), 131.6 (d, *J* = 10.7 Hz), 129.2 (d, *J* = 2.2 Hz), 128.9 (d, *J* = 2.6 Hz), 128.3 (d, *J* = 15.2 Hz), 126.9 (d, *J* = 4.9 Hz), 80.0 (d, *J* = 8.2 Hz), 48.9 (d, *J* = 7.1 Hz), 43.6, 34.2, 31.8, 25.8, 23.1, 22.1, 21.4, 16.2. **^{31}P NMR** (203 MHz, $CDCl_3$): δ 39.9. **FT-IR** (ATR): 2921, 1456, 1439, 1233, 1117, 975, 690 cm^{-1}. **HRMS** (ESI): *m/z* 389.1691($[M+H]^+$, $C_{22}H_{30}O_2PS^+$ calcd. 389.1699).

The NMR spectra (^{1}H, ^{31}P) of the title compound contain two sets of signals in 97:3 ratio, corresponding exactly to the dr of the starting material, indicating that no epimerization has occurred, demonstrating the stability of the stereocenters (both at carbons and at phosphorus) under the reaction conditions.



***S*-Phenyl diphenylphosphinothioate** (**97a**): The title compound was prepared according to the General procedure C from triethylammonium diphenylphosphinothioate and diphenyliodonium tetrafluoroborate **87b**[102] in 31% yield (38 mg). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.92 – 7.77 (m, 4H), 7.55 – 7.37 (m, 8H), 7.27 – 7.14 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 135.5 (d, *J* = 3.8 Hz), 137.7 (d, *J* = 106.8 Hz), 132.5 (d, *J* = 2.8 Hz), 131.8 (d, *J* = 10.1 Hz), 129.3, 129.1 (d, *J* =

1.7 Hz), 128.7 (d, *J* = 13.2 Hz), 126.3 (d, *J* = 5.0 Hz). **^{31}P NMR** (203 MHz, $CDCl_3$): δ 41.5. **FT-IR** (ATR): 1438, 1192, 1097, 740, 691 cm^{-1}. **HRMS** (ESI): *m/z* 311.0654($[M+H]^+$, $C_{18}H_{16}OPS^+$ calcd. 311.0654). **Mp.**: 90-92 °C.

Computational Details for Chapter 5 (Paper III)

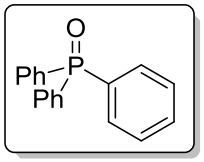
The calculations were carried out with Gaussian 16 software package[389] using B3LYP functional,[390–394] including the D3 dispersion correction with the BJ dumping.[395,396] Geometries were optimized with SMD solvation model (in 1,4-dioxane),[397] using Def2-SVP basis set,[398] including a pseudopotential for iodine.[399,400] For each stationary point a thorough conformational analysis was performed in order to locate the conformer with the lowest energy. This was done by identifying key rotatable bonds and manually building possible starting geometries for optimizations.

The identified lowest energy stationary points were then characterized by frequency calculations to confirm their character as minima (no imaginary frequencies) or transition states (a single imaginary frequency). The final free energies were obtained from single-point calculations on the optimized geometries with a larger Def2-QZVP basis set[398] (with SMD solvation) and were corrected for the thermodynamic effects using the quasi-harmonic approximation[401] (100 cm^{-1} cut-off) as implemented in GoodVibes program.[402]

Table S1. Energies and energy corrections of stationary points (in atomic units)

Stationary point	B3LYP-D3BJ/ Def2-SVP (1,4-dioxane) optimization	B3LYP-D3BJ/ Def2-QZVP (1,4-dioxane) single-point	Thermal correction to Gibbs free energy at 100 °C
92b	-1602.975209	-1602.704331	0.270878
87b	-1184.879847	-1184.739631	0.140216
93a	-1659.474866	-1659.245371	0.229495
3O	-1659.474889	-1659.245270	0.229619
INT-O	-2188.728742	-2190.397469	0.308658
INT-S	-2188.728478	-2190.398980	0.307500
Me_3N-BF_4	-599.130961	-599.022880	0.108081
PhI	-529.299466	-529.246901	0.052565
Ph_2I·	-760.724504	-760.597933	0.126571
$(PhO)_2P(O)S$·	-1427.913790	-1427.770084	0.143706
TS1-O	-2188.691159	-2188.385911	0.305248
TS1-S	-2188.692471	-2188.388697	0.303774
TS2-O	-2188.694516	-2188.388631	0.305885
TS2-S	-2188.697204	-2188.392661	0.304543

Experimental procedure for Chapter 6



Triphenylphosphine oxide (**100a**); Figure 6.5: Experiment was carried out under a nitrogen atmosphere in a glove box. A 20 mL vial was charged with diphenylphosphine (78.4 mg, 0.40 mmol) and diaryliodonium trifluoromethanesulfonate (258.1 mg, 0.60 mmol). Anhydrous MeCN (8 mL) was added via syringe, followed by *t*-BuOK (33.7 mg, 0.60 mmol), and the reaction mixture was stirred at RT for 2 hours. Then, *t*-BuOOH (70% in water) (274 μl, 2.0 mmol) was added to the reaction mixture and stirred for additional 15 minutes. The solvent was evaporated under reduced pressure. Dichloromethane (2 mL) was added to the residue, followed by a small amount of silica. The solvent was evaporated under reduced pressure, the solid residue was applied on the top of silica column, and the product was purified by column chromatography in 93% yield (103 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 – 7.57 (m, 6H), 7.56 – 7.46 (m, 3H), 7.45 – 7.30 (m, 6H). **^{31}P NMR** (162 MHz, $CDCl_3$): δ 29.2.

References

(1) Langmuir, I. *J. Am. Chem. Soc.* **1919**, *41* (6), 868–934.
(2) Musher, J. I. *Angew. Chem. Int. Ed. Engl.* **1969**, *8* (1), 54–68.
(3) Pauling, Linus. *J. Am. Chem. Soc.* **1931**, *53* (4), 1367–1400.
(4) Pimentel, G. C. *J. Chem. Phys.* **1951**, *19* (4), 446–448.
(5) Hach, R. J.; Rundle, R. E. *J. Am. Chem. Soc.* **1951**, *73* (9), 4321–4324.
(6) Magnusson, E. *J. Am. Chem. Soc.* **1990**, *112* (22), 7940–7951.
(7) Courtois, B. *Ann. Chim.* **1813**, *88*, 304–310.
(8) Gay-Lussac, J. L. *Ann. Chim.* **1814**, *91*, 5–160.
(9) *Hypervalent Iodine in Organic Synthesis*; Elsevier, 1997.
(10) *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; de Meijere, A., Kessler, H., Ley, S. V., Thiem, J., Vögtle, F., Houk, K. N., Lehn, J.-M., Schreiber, S. L., Trost, B. M., Yamamoto, H., Series Eds.; Topics in Current Chemistry; Springer Berlin Heidelberg: Berlin, Heidelberg, 2003; Vol. 224.
(11) Zhdankin, V. V. *Hypervalent Iodine Chemistry: Preparation, Structure and Synthetic Applications of Polyvalent Iodine Compounds*; John Wiley & Sons Ltd: Chichester, UK, 2013.
(12) *Hypervalent Iodine Chemistry*; Springer Berlin Heidelberg: New York, NY, 2016.
(13) Richardson, R. D.; Wirth, T. *Angew. Chem. Int. Ed.* **2006**, *45* (27), 4402–4404.
(14) Dohi, T.; Kita, Y. *Chem. Commun.* **2009**, No. 16, 2073.
(15) Yusubov, M. S.; Zhdankin, V. V. *Resour.-Effic. Technol.* **2015**, *1* (1), 49–67.
(16) Elsherbini, M.; Wirth, T. *Chem. - Eur. J.* **2018**, *24* (51), 13399–13407.
(17) Elsherbini, M.; Winterson, B.; Alharbi, H.; Folgueiras-Amador, A. A.; Génot, C.; Wirth, T. *Angew. Chem. Int. Ed.* **2019**, *58* (29), 9811–9815.
(18) Amey, R. L.; Martin, J. C. *J. Org. Chem.* **1979**, *44* (11), 1779–1784.
(19) Yoshimura, A.; Yusubov, M. S.; Zhdankin, V. V. *Org. Biomol. Chem.* **2016**, *14* (21), 4771–4781.
(20) Ochiai, M. Reactivities, Properties and Structures. In *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; de Meijere, A., Kessler, H., Ley, S. V., Thiem, J., Vögtle, F., Houk, K. N., Lehn, J.-M., Schreiber, S. L., Trost, B. M., Yamamoto, H., Series Eds.; Topics in Current Chemistry; Springer Berlin Heidelberg: Berlin, Heidelberg, 2003; Vol. 224, pp 5–68.
(21) Kajigaeshi, S.; Kakinami†, T.; Moriwaki, M.; Tanaka, T.; Fujisaki, S. *Tetrahedron Lett.* **1988**, *29* (45), 5783–5786.
(22) Edwards, A. J. *J. Chem. Soc. Dalton Trans.* **1978**, No. 12, 1723.
(23) Koser, G. F.; Wettach, R. H.; Smith, C. S. *J. Org. Chem.* **1980**, *45* (8), 1543–1544.
(24) Boelke, A.; Caspers, L. D.; Nachtsheim, B. J. *Org. Lett.* **2017**, *19* (19), 5344–5347.
(25) Ray, D. G.; Koser, G. F. *J. Am. Chem. Soc.* **1990**, *112* (14), 5672–5673.
(26) Malmgren, J.; Santoro, S.; Jalalian, N.; Himo, F.; Olofsson, B. *Chem. - Eur. J.* **2013**, *19* (31), 10334–10342.
(27) Çelik, M.; Alp, C.; Coşkun, B.; Gültekin, M. S.; Balci, M. *Tetrahedron Lett.* **2006**, *47* (22), 3659–3663.
(28) Ghosh, M. K.; Rzymkowski, J.; Kalek, M. *Chem. – Eur. J.* **2019**, *25* (41), 9619–9623.

(29) Rajkiewicz, A. A.; Wojciechowska, N.; Kalek, M. *ACS Catal.* **2020**, *10* (1), 831–841.
(30) Reich, H. J.; Peake, S. L. *J. Am. Chem. Soc.* **1978**, *100* (15), 4888–4889.
(31) Kitamura, T.; Yamane, M.; Inoue, K.; Todaka, M.; Fukatsu, N.; Meng, Z.; Fujiwara, Y. *J. Am. Chem. Soc.* **1999**, *121* (50), 11674–11679.
(32) Braddock, D. C.; Cansell, G.; Hermitage, S. A.; White, A. J. P. *Chem. Commun.* **2006**, No. 13, 1442.
(33) Petko, F.; Świeży, A.; Ortyl, J. *Polym. Chem.* **2021**, *12* (32), 4593–4612.
(34) Genovino, J.; Lian, Y.; Zhang, Y.; Hope, T. O.; Juneau, A.; Gagné, Y.; Ingle, G.; Frenette, M. *Org. Lett.* **2018**, *20* (11), 3229–3232.
(35) Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Oka, S. *J. Am. Chem. Soc.* **1994**, *116* (9), 3684–3691.
(36) Takaya, T.; Enyo, H.; Imoto, E. *Bull. Chem. Soc. Jpn.* **1968**, *41* (4), 1032–1032.
(37) Tohma, H.; Takizawa, S.; Maegawa, T.; Kita, Y. *Angew. Chem.* **2000**, *112* (7), 1362–1364.
(38) Kida, M.; Sueda, T.; Goto, S.; Okuyama, T.; Ochiai, M. *Chem. Commun.* **1996**, No. 16, 1933.
(39) De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. *J. Org. Chem.* **1997**, *62* (20), 6974–6977.
(40) Karade, N. N.; Tiwari, G. B.; Huple, D. B. *Synlett* **2005**, No. 13, 2039–2042.
(41) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113* (19), 7277–7287.
(42) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35* (43), 8019–8022.
(43) Kong, W.; Feige, P.; de Haro, T.; Nevado, C. *Angew. Chem. Int. Ed.* **2013**, *52* (9), 2469–2473.
(44) Muñiz, K. *Acc. Chem. Res.* **2018**, *51* (6), 1507–1519.
(45) Fujita, M.; Mori, K.; Shimogaki, M.; Sugimura, T. *Org. Lett.* **2012**, *14* (5), 1294–1297.
(46) Molnár, I. G.; Gilmour, R. *J. Am. Chem. Soc.* **2016**, *138* (15), 5004–5007.
(47) Flores, A.; Cots, E.; Bergès, J.; Muñiz, K. *Adv. Synth. Catal.* **2019**, *361* (1), 2–25.
(48) Pouységu, L.; Deffieux, D.; Quideau, S. *Tetrahedron* **2010**, *66* (13), 2235–2261.
(49) Zheng, H.; Sang, Y.; Houk, K. N.; Xue, X.-S.; Cheng, J.-P. *J. Am. Chem. Soc.* **2019**, *141* (40), 16046–16056.
(50) Harned, A. M. *Org. Biomol. Chem.* **2018**, *16* (13), 2324–2329.
(51) Tang, T.; Harned, A. M. *Org. Biomol. Chem.* **2018**, *16* (37), 8249–8252.
(52) Kraszewski, K.; Tomczyk, I.; Drabinska, A.; Bienkowski, K.; Solarska, R.; Kalek, M. *Chem. – Eur. J.* **2020**, *26* (50), 11584–11592.
(53) Juneau, A.; Lepage, I.; Sabbah, S. G.; Winter, A. H.; Frenette, M. *J. Org. Chem.* **2022**, *87* (21), 14274–14283.
(54) Pelter, A.; Elgendy, S. M. A. *J. Chem. Soc. Perkin 1* **1993**, No. 16, 1891.
(55) Ley, S. V.; Thomas, A. W.; Finch, H. *J. Chem. Soc. Perkin 1* **1999**, No. 6, 669–672.
(56) Ficht, S.; Mülbaier, M.; Giannis, A. *Tetrahedron* **2001**, *57* (23), 4863–4866.
(57) Dohi, T.; Nakae, T.; Takenaga, N.; Uchiyama, T.; Fukushima, K.; Fujioka, H.; Kita, Y. *Synthesis* **2012**, *44* (08), 1183–1189.
(58) McKillop, A.; McLaren, L.; Taylor, R. J. K. *J. Chem. Soc. Perkin 1* **1994**, No. 15, 2047.
(59) Fleck, A. E.; Hobart, J. A.; Morrow, G. W. *Synth. Commun.* **1992**, *22* (1), 179–187.
(60) Canesi, S.; Bouchu, D.; Ciufolini, M. A. *Org. Lett.* **2005**, *7* (2), 175–177.

(61) Sabot, C.; Commare, B.; Duceppe, M.-A.; Nahi, S.; Guérard, K.; Canesi, S. *Synlett* **2008**, *2008* (20), 3226–3230.
(62) Karam, O.; Jacquesy, J.-C.; Jouannetaud, M.-P. *Tetrahedron Lett.* **1994**, *35* (16), 2541–2544.
(63) Karam, O.; Martin, A.; Jouannetaud, M.-P.; Jacquesy, J.-C. *Tetrahedron Lett.* **1999**, *40* (22), 4183–4186.
(64) Karam, O.; Martin-Mingot, A.; Jouannetaud, M.-P.; Jacquesy, J.-C.; Cousson, A. *Tetrahedron* **2004**, *60* (31), 6629–6638.
(65) Kita, Y.; Tohma, H.; Kikuchi, K.; Inagaki, M.; Yakura, T. *J. Org. Chem.* **1991**, *56* (1), 435–438.
(66) Singh, F. V.; Kole, P. B.; Mangaonkar, S. R.; Shetgaonkar, S. E. *Beilstein J. Org. Chem.* **2018**, *14*, 1778–1805.
(67) Wipf, P.; Kim, Y. *J. Org. Chem.* **1993**, *58* (7), 1649–1650.
(68) Ye, Y.; Zhang, L.; Fan, R. *Org. Lett.* **2012**, *14* (8), 2114–2117.
(69) Braun, N. A.; Ciufolini, M. A.; Peters, K.; Peter, E.-M. *Tetrahedron Lett.* **1998**, *39* (26), 4667–4670.
(70) Braun, N. A.; Ousmer, M.; Bray, J. D.; Bouchu, D.; Peters, K.; Peters, E.-M.; Ciufolini, M. A. *J. Org. Chem.* **2000**, *65* (14), 4397–4408.
(71) Canesi, S.; Belmont, P.; Bouchu, D.; Rousset, L.; Ciufolini, M. A. *Tetrahedron Lett.* **2002**, *43* (29), 5193–5195.
(72) Liang, H.; Ciufolini, M. A. *Tetrahedron* **2010**, *66* (31), 5884–5892.
(73) Liang, H.; Ciufolini, M. A. *Chem. - Eur. J.* **2010**, *16* (44), 13262–13270.
(74) Kita, Y.; Yakura, T.; Tohma, H.; Kikuchi, K.; Tamura, Y. *Tetrahedron Lett.* **1989**, *30* (9), 1119–1120.
(75) Kita, Y.; Tohma, H.; Inagaki, M.; Hatanaka, K.; Kikuchi, K.; Yakura, T. *Tetrahedron Lett.* **1991**, *32* (18), 2035–2038.
(76) Kita, Y.; Tohma, H.; Inagaki, M.; Hatanaka, K.; Yakura, T. *J. Am. Chem. Soc.* **1992**, *114* (6), 2175–2180.
(77) Hempel, C.; Weckenmann, N. M.; Maichle-Moessmer, C.; Nachtsheim, B. J. A *Org. Biomol. Chem.* **2012**, *10* (47), 9325.
(78) Liang, J.; Chen, J.; Du, F.; Zeng, X.; Li, L.; Zhang, H. *Org. Lett.* **2009**, *11* (13), 2820–2823.
(79) Zheng, C.; Wang, L.; Li, J.; Wang, L.; Wang, D. Z. *Org. Lett.* **2013**, *15* (16), 4046–4049.
(80) Dohi, T.; Uchiyama, T.; Yamashita, D.; Washimi, N.; Kita, Y. *Tetrahedron Lett.* **2011**, *52* (17), 2212–2215.
(81) Dohi, T.; Maruyama, A.; Yoshimura, M.; Morimoto, K.; Tohma, H.; Kita, Y. *Angew. Chem. Int. Ed.* **2005**, *44* (38), 6193–6196.
(82) Dohi, T.; Maruyama, A.; Takenaga, N.; Senami, K.; Minamitsuji, Y.; Fujioka, H.; Caemmerer, S. B.; Kita, Y. *Angew. Chem. Int. Ed.* **2008**, *47* (20), 3787–3790.
(83) Uyanik, M.; Yasui, T.; Ishihara, K. *Angew. Chem. Int. Ed.* **2010**, *49* (12), 2175–2177.
(84) Uyanik, M.; Yasui, T.; Ishihara, K. *Angew. Chem.* **2013**, *125* (35), 9385–9388. https://doi.org/10.1002/ange.201303559.
(85) Yusubov, M. S.; Maskaev, A. V.; Zhdankin, V. V. Iodonium Salts in Organic Synthesis. *Arkivoc* **2011**, *2011* (1), 370–409.
(86) Yoshimura, A.; Zhdankin, V. V. *Chem. Rev.* **2016**, *116* (5), 3328–3435.

(87) Olofsson, B. In *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; Topics in Current Chemistry; Springer International Publishing: Cham, 2015; Vol. 373, pp 135–166.
(88) Früh, N.; Charpentier, J.; Togni, A. Iodanes as Trifluoromethylation Reagents. In *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; Topics in Current Chemistry; Springer International Publishing: Cham, 2015; Vol. 373, pp 167–186.
(89) Hari, D. P.; Nicolai, S.; Waser, J. Alkynylations and Vinylations. In *PATAI'S Chemistry of Functional Groups*; Rappoport, Z., Ed.; John Wiley & Sons, Ltd: Chichester, UK, 2018; pp 1–58.
(90) Simonet-Davin, R.; Waser, J. *Synthesis* **2022**, a-1966-4974.
(91) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem. Int. Ed.* **2007**, *46* (5), 754–757.
(92) Waser, J. Alkynylation with Hypervalent Iodine Reagents. In *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; Topics in Current Chemistry; Springer International Publishing: Cham, 2015; Vol. 373, pp 187–222.
(93) Chen, C. C.; Waser, J. *Chem Commun* **2014**, *50* (85), 12923–12926.
(94) Chen, C. C.; Waser, J. *Org. Lett.* **2015**, *17* (3), 736–739.
(95) Stridfeldt, E.; Seemann, A.; Bouma, M. J.; Dey, C.; Ertan, A.; Olofsson, B. *Chem. - Eur. J.* **2016**, *22* (45), 16066–16070.
(96) Hartmann, C.; Meyer, V. *Berichte Dtsch. Chem. Ges.* **1894**, *27* (1), 426–432.
(97) Alcock, N. W.; Countryman, R. M. *J. Chem. Soc. Dalton Trans.* **1977**, No. 3, 217.
(98) Ledwith, A.; Al-Kass, S.; Sherrington, D. C.; Bonner, P. *Polymer* **1981**, *22* (2), 143–145.
(99) Beringer, F. M.; Drexler, M.; Gindler, E. M.; Lumpkin, C. C. *J. Am. Chem. Soc.* **1953**, *75* (11), 2705–2708.
(100) Bielawski, M.; Zhu, M.; Olofsson, B. *Adv. Synth. Catal.* **2007**, *349* (17–18), 2610–2618.
(101) Bielawski, M.; Olofsson, B. *Chem. Commun.* **2007**, No. 24, 2521.
(102) Bielawski, M.; Aili, D.; Olofsson, B. *J. Org. Chem.* **2008**, *73* (12), 4602–4607.
(103) Zhu, M.; Jalalian, N.; Olofsson, B. *Synlett* **2008**, *2008* (04), 592–596.
(104) Bielawski, M.; Olofsson., B. Efficient One-Pot Synthesis of Bis(4- *Tert* -Butylphenyl) Iodonium Triflate. In *Organic Syntheses*; John Wiley & Sons, Inc., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2009; pp 308–314.
(105) Hossain, Md. D.; Ikegami, Y.; Kitamura, T. *J. Org. Chem.* **2006**, *71* (26), 9903–9905.
(106) Hossain, Md. D.; Kitamura, T. *Bull. Chem. Soc. Jpn.* **2007**, *80* (11), 2213–2219.
(107) Merritt, E.; Malmgren, J.; Klinke, F.; Olofsson, B. *Synlett* **2009**, *2009* (14), 2277–2280.
(108) Dohi, T.; Yamaoka, N.; Itani, I.; Kita, Y. O *Aust. J. Chem.* **2011**, *64* (5), 529.
(109) Postnikov, P. S.; Guselnikova, O. A.; Yusubov, M. S.; Yoshimura, A.; Nemykin, V. N.; Zhdankin, V. V. *J. Org. Chem.* **2015**, *80* (11), 5783–5788.
(110) Dohi, T.; Ito, M.; Yamaoka, N.; Morimoto, K.; Fujioka, H.; Kita, Y. *Angew. Chem.* **2010**, *122* (19), 3406–3409.
(111) Ozanne-Beaudenon, A.; Quideau, S. *Angew. Chem.* **2005**, *117* (43), 7227–7231.
(112) Satkar, Y.; Wrobel, K.; Trujillo-González, D. E.; Ortiz-Alvarado, R.; Jiménez-Halla, J. O. C.; Solorio-Alvarado, C. R. *Front. Chem.* **2020**, *8*, 563470.
(113) Castro, S.; Fernández, J. J.; Vicente, R.; Fañanás, F. J.; Rodríguez, F. *Chem. Commun.* **2012**, *48* (72), 9089.
(114) Wen, J.; Zhang, R.-Y.; Chen, S.-Y.; Zhang, J.; Yu, X.-Q. D*J. Org. Chem.* **2012**, *77* (1), 766–771.

(115) Ackermann, L.; Dell'Acqua, M.; Fenner, S.; Vicente, R.; Sandmann, R. *Org. Lett.* **2011**, *13* (9), 2358–2360.
(116) Zhu, Y.; Bauer, M.; Ploog, J.; Ackermann, L. *Chem. - Eur. J.* **2014**, *20* (41), 13099–13102.
(117) Zhou, X.; Wu, Q.; Yu, Y.; Yu, C.; Hao, E.; Wei, Y.; Mu, X.; Jiao, L. *Org. Lett.* **2016**, *18* (4), 736–739.
(118) Chen, K.; Koser, G. F. *J. Org. Chem.* **1991**, *56* (20), 5764–5767.
(119) Oh, C. H.; Kim, J. S.; Jung, H. H. *J. Org. Chem.* **1999**, *64* (4), 1338–1340.
(120) Aggarwal, V. K.; Olofsson, B. *Angew. Chem. Int. Ed.* **2005**, *44* (34), 5516–5519.
(121) Wang, D.; Ge, B.; Li, L.; Shan, J.; Ding, Y. *J. Org. Chem.* **2014**, *79* (18), 8607–8613.
(122) Monastyrskyi, A.; Namelikonda, N. K.; Manetsch, R. *J. Org. Chem.* **2015**, *80* (5), 2513–2520.
(123) Zhang, Y.; Han, J.; Liu, Z.-J. *Synlett* **2015**, *26* (18), 2593–2597.
(124) Mao, S.; Geng, X.; Yang, Y.; Qian, X.; Wu, S.; Han, J.; Wang, L. *RSC Adv.* **2015**, *5* (46), 36390–36393.
(125) Chan, L.; McNally, A.; Toh, Q. Y.; Mendoza, A.; Gaunt, M. J. *Chem. Sci.* **2015**, *6* (2), 1277–1281.
(126) Qian, X.; Han, J.; Wang, L. *Adv. Synth. Catal.* **2016**, *358* (6), 940–946.
(127) Dey, C.; Lindstedt, E.; Olofsson, B. *Org. Lett.* **2015**, *17* (18), 4554–4557.
(128) An, Y.; Zhang, X.-M.; Li, Z.-Y.; Xiong, W.-H.; Yu, R.-D.; Zhang, F.-M. *Chem. Commun.* **2019**, *55* (1), 119–122.
(129) Zaheer, M. K.; Gupta, E.; Kant, R.; Mohanan, K. *Chem. Commun.* **2020**, *56* (1), 153–156.
(130) Toh, Q. Y.; McNally, A.; Vera, S.; Erdmann, N.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135* (10), 3772–3775.
(131) Beringer, F. M.; Brierley, A.; Drexler, M.; Gindler, E. M.; Lumpkin, C. C. *J. Am. Chem. Soc.* **1953**, *75* (11), 2708–2712.
(132) Beringer, F. M.; Gindler, E. M. *J. Am. Chem. Soc.* **1955**, *77* (12), 3203–3207.
(133) Crowder, J. R.; Glover, E. E.; Grundon, M. F.; Kaempfen, H. X. 870. *J. Chem. Soc. Resumed* **1963**, 4578.
(134) Jalalian, N.; Ishikawa, E. E.; Silva, L. F.; Olofsson, B. *Org. Lett.* **2011**, *13* (6), 1552–1555.
(135) Jalalian, N.; Petersen, T. B.; Olofsson, B. *Chem. - Eur. J.* **2012**, *18* (44), 14140–14149.
(136) Kakinuma, Y.; Moriyama, K.; Togo, H. *Synthesis* **2012**, *45* (02), 183–188.
(137) Lindstedt, E.; Ghosh, R.; Olofsson, B. *Org. Lett.* **2013**, *15* (23), 6070–6073.
(138) Kervefors, G.; Becker, A.; Dey, C.; Olofsson, B. *Beilstein J. Org. Chem.* **2018**, *14*, 1491–1497.
(139) Lubinkowski, J. J.; Knapczyk, J. W.; Calderon, J. L.; Petit, L. R.; McEwen, W. E. *J. Org. Chem.* **1975**, *40* (21), 3010–3015.
(140) Fujita, M.; Mishima, E.; Okuyama, T. *J. Phys. Org. Chem.* **2007**, *20* (4), 241–244.
(141) Ghosh, R.; Lindstedt, E.; Jalalian, N.; Olofsson, B. *ChemistryOpen* **2014**, *3* (2), 54–57.
(142) Sundalam, S. K.; Stuart, D. R. *J. Org. Chem.* **2015**, *80* (12), 6456–6466.
(143) Lindstedt, E.; Stridfeldt, E.; Olofsson, B.. *Org. Lett.* **2016**, *18* (17), 4234–4237.
(144) Tolnai, G. L.; Nilsson, U. J.; Olofsson, B. *Angew. Chem. Int. Ed.* **2016**, *55* (37), 11226–11230.

(145) Ghosh, R.; Olofsson, B. *Org. Lett.* **2014**, *16* (6), 1830–1832.
(146) Ghosh, R.; Stridfeldt, E.; Olofsson, B. *Chem. - Eur. J.* **2014**, n/a-n/a.
(147) Reitti, M.; Gurubrahamam, R.; Walther, M.; Lindstedt, E.; Olofsson, B. *Org. Lett.* **2018**, *20* (7), 1785–1788.
(148) Petersen, T. B.; Khan, R.; Olofsson, B. *Org. Lett.* **2011**, *13* (13), 3462–3465.
(149) Xiong, B.; Feng, X.; Zhu, L.; Chen, T.; Zhou, Y.; Au, C.-T.; Yin, S.-F. *ACS Catal.* **2015**, *5* (2), 537–543.
(150) Lubinkowski, J. J.; Gomez, M.; Calderon, J. L.; McEwen, W. E. *J. Org. Chem.* **1978**, *43* (12), 2432–2435.
(151) Li, J.; Liu, L. *RSC Adv.* **2012**, *2* (28), 10485.
(152) Carroll, M. A.; Wood, R. A. *Tetrahedron* **2007**, *63* (46), 11349–11354.
(153) Pang, X.; Lou, Z.; Li, M.; Wen, L.; Chen, C. *Eur. J. Org. Chem.* **2015**, *2015* (15), 3361–3369.
(154) Purkait, N.; Kervefors, G.; Linde, E.; Olofsson, B. *Angew. Chem.* **2018**, *130* (35), 11597–11601.
(155) Kervefors, G.; Kersting, L.; Olofsson, B. *Chem. – Eur. J.* **2021**, *27* (18), 5790–5795.
(156) Landge, K. P.; Jang, K. S.; Lee, S. Y.; Chi, D. Y. *J. Org. Chem.* **2012**, *77* (13), 5705–5713.
(157) Yang, Y.; Wu, X.; Han, J.; Mao, S.; Qian, X.; Wang, L. *Eur. J. Org. Chem.* **2014**, *2014* (31), 6854–6857.
(158) Li, P.; Cheng, G.; Zhang, H.; Xu, X.; Gao, J.; Cui, X. *J. Org. Chem.* **2014**, *79* (17), 8156–8162.
(159) Tinnis, F.; Stridfeldt, E.; Lundberg, H.; Adolfsson, H.; Olofsson, B. *Org. Lett.* **2015**, *17* (11), 2688–2691.
(160) Wang, M.; Huang, Z. *Org. Biomol. Chem.* **2016**, *14* (43), 10185–10188.
(161) Villo, P.; Kervefors, G.; Olofsson, B. *Chem. Commun.* **2018**, *54* (64), 8810–8813.
(162) Gonda, Z.; Novák, Z. *Chem. - Eur. J.* **2015**, *21* (47), 16801–16806.
(163) Guo, F.; Wang, L.; Wang, P.; Yu, J.; Han, J. *Asian J. Org. Chem.* **2012**, *1* (3), 218–221.
(164) Riedmüller, S.; Nachtsheim, B. *Synlett* **2015**, *26* (05), 651–655.
(165) Bugaenko, D. I.; Yurovskaya, M. A.; Karchava, A. V. *Org. Lett.* **2018**, *20* (20), 6389–6393.
(166) Sandin, R. B.; Christiansen, R. G.; Brown, R. K.; Kirkwood, S. *J. Am. Chem. Soc.* **1947**, *69* (6), 1550–1550.
(167) Crivello, J. V.; Lam, J. H. W. *Synth. Commun.* **1979**, *9* (3), 151–156.
(168) Chen, Z.; Jin, Y.; Stang, P. J. *J. Org. Chem.* **1987**, *52* (18), 4117–4118.
(169) Chen, Z.-C.; Jin, Y.-Y.; Yang, R.-Y. *Synthesis* **1988**, *1988* (09), 723–724.
(170) You, J.-Z.; Chen, Z.-C. *Synthesis* **1992**, *1992* (06), 521–522.
(171) Du-Dong, L.; Da-wei, C.; Zhen-Chu, C. *Synth. Commun.* **1992**, *22* (20), 2903–2908.
(172) Xia, M.; Chen, Z.-C. *Synth. Commun.* **1997**, *27* (8), 1309–1313.
(173) Huang, X.; Zhu, Q.; Xu, Y. *Synth. Commun.* **2001**, *31* (18), 2823–2828.
(174) Wagner, A. M.; Sanford, M. S. *J. Org. Chem.* **2014**, *79* (5), 2263–2267.
(175) Racicot, L.; Kasahara, T.; Ciufolini, M. A. *Org. Lett.* **2014**, *16* (24), 6382–6385.
(176) Umierski, N.; Manolikakes, G. *Org. Lett.* **2013**, *15* (1), 188–191.
(177) Umierski, N.; Manolikakes, G. *Org. Lett.* **2013**, *15* (19), 4972–4975.
(178) Margraf, N.; Manolikakes, G. *J. Org. Chem.* **2015**, *80* (5), 2582–2600.

(179) Deeming, A. S.; Russell, C. J.; Hennessy, A. J.; Willis, M. C. *Org. Lett.* **2014**, *16* (1), 150–153.
(180) Gong, B.; Zhu, H.; Yang, L.; Wang, H.; Fan, Q.; Xie, Z.; Le, Z. *Org. Biomol. Chem.* **2022**, *20* (17), 3501–3505.
(181) Liu, Z.-D.; Chen, Z.-C. *Synthesis* **1993**, *1993* (04), 373–374.
(182) Lecroq, W.; Bazille, P.; Morlet-Savary, F.; Breugst, M.; Lalevée, J.; Gaumont, A.-C.; Lakhdar, S. *Org. Lett.* **2018**, *20* (14), 4164–4167.
(183) Bugaenko, D. I.; Volkov, A. A.; Livantsov, M. V.; Yurovskaya, M. A.; Karchava, A. V. *Chem. – Eur. J.* **2019**, *25* (54), 12502–12506.
(184) Miralles, N.; Romero, R. M.; Fernández, E.; Muñiz, K. *Chem. Commun.* **2015**, *51* (74), 14068–14071.
(185) Der Puy, M. V. *J. Fluor. Chem.* **1982**, *21* (3), 385–392.
(186) *Positron Emission Tomography: Basic Sciences*; Bailey, D. L., Townsend, D. W., Valk, P. E., Maisey, M. N., Eds.; Springer London: London, 2005.
(187) Pike, V. W.; Aigbirhio, F. I. *J Chem Soc Chem Commun* **1995**, No. 21, 2215–2216.
(188) Cai, L.; Lu, S.; Pike, V. W. *Eur. J. Org. Chem.* **2008**, *2008* (17), 2843–2843.
(189) Yusubov, M. S.; Svitich, D. Yu.; Larkina, M. S.; Zhdankin, V. V. *Arkivoc* **2013**, *2013* (1), 364–395.
(190) Edwards, R.; Wirth, T. *J. Label. Compd. Radiopharm.* **2015**, *58* (5), 183–187.
(191) Wang, B.; Qin, L.; Neumann, K. D.; Uppaluri, S.; Cerny, R. L.; DiMagno, S. G. *Org. Lett.* **2010**, *12* (15), 3352–3355.
(192) Carroll, M. A.; Nairne, J.; Smith, G.; Widdowson, D. A. *J. Fluor. Chem.* **2007**, *128* (2), 127–132.
(193) Yamada, Y.; Okawara, M. *Bull. Chem. Soc. Jpn.* **1972**, *45* (6), 1860–1863.
(194) Yamada, Y.; Kashima, K.; Okawara, M. *Bull. Chem. Soc. Jpn.* **1974**, *47* (12), 3179–3180.
(195) Lancer, K. M.; Wiegand, G. H. *J. Org. Chem.* **1976**, *41* (21), 3360–3364.
(196) Hu, B.; Miller, W. H.; Neumann, K. D.; Linstad, E. J.; DiMagno, S. G. *Chem. - Eur. J.* **2015**, *21* (17), 6394–6398.
(197) Zheng, Z.; Zhang-Negrerie, D.; Du, Y.; Zhao, K. *Sci. China Chem.* **2014**, *57* (2), 189–214.
(198) Kumar, D.; Arun, V.; Pilania, M.; Kumar, N. M. In *Green Synthetic Approaches for Biologically Relevant Heterocycles*; Elsevier, 2015; pp 353–376.
(199) Wirth, T. *Angew. Chem. Int. Ed.* **2005**, *44* (24), 3656–3665.
(200) Merritt, E.; Olofsson, B. *Angew. Chem. Int. Ed.* **2009**, *48* (48), 9052–9070.
(201) Tellitu, I.; Domínguez, E. *Synlett* **2012**, *23* (15), 2165–2175.
(202) Samanta, R.; Matcha, K.; Antonchick, A. P. *Eur. J. Org. Chem.* **2013**, *2013* (26), 5769–5804.
(203) *PATAI'S Chemistry of Functional Groups*, 1st ed.; Rappoport, Z., Ed.; Wiley, 2009.
(204) Taguchi, H.; Sankawa, U.; Shibata, S. *Chem. Pharm. Bull. (Tokyo)* **1969**, *17* (10), 2054–2060.
(205) Li, D. B.; Woithe, K.; Geib, N.; Abou-Hadeed, K.; Zerbe, K.; Robinson, J. A. Chapter 19 In Vitro Studies of Phenol Coupling Enzymes Involved in Vancomycin Biosynthesis. In *Methods in Enzymology*; Elsevier, 2009; Vol. 458, pp 487–509.

(206) Kawaguchi, M.; Ohshiro, T.; Toyoda, M.; Ohte, S.; Inokoshi, J.; Fujii, I.; Tomoda, H. *Angew. Chem. Int. Ed.* **2018**, *57* (18), 5115–5119.
(207) Pal, T.; Pal, A. Oxidative Phenol Coupling: *Curr. Sci.* **1996**, *71* (2), 106–108.
(208) Rahman, A.-. *Studies in Natural Products Chemistry. Volume 20*; Elsevier: Amsterdam, 1997.
(209) Bringmann, G.; Gulder, T.; Gulder, T. A. M.; Breuning, M. *Chem. Rev.* **2011**, *111* (2), 563–639.
(210) Musso, H. *Angew. Chem. Int. Ed. Engl.* **1963**, *2* (12), 723–735.
(211) Mori, K.; Takahashi, M.; Yamamura, S.; Nishiyama, S. *Tetrahedron* **2001**, *57* (26), 5527–5532.
(212) Malkowsky, I. M.; Rommel, C. E.; Fröhlich, R.; Griesbach, U.; Pütter, H.; Waldvogel, S. R. *Chem. - Eur. J.* **2006**, *12* (28), 7482–7488.
(213) Malkowsky, I. M.; Rommel, C. E.; Wedeking, K.; Fröhlich, R.; Bergander, K.; Nieger, M.; Quaiser, C.; Griesbach, U.; Pütter, H.; Waldvogel, S. R. *Eur. J. Org. Chem.* **2006**, *2006* (1), 241–245.
(214) Tzeng, S.-C.; Liu, Y.-C. *J. Mol. Catal. B Enzym.* **2004**, *32* (1–2), 7–13.
(215) Hawranik, D. J.; Anderson, K. S.; Simmonds, R.; Sorensen, John. L. *Bioorg. Med. Chem. Lett.* **2009**, *19* (9), 2383–2385.
(216) Navarra, C.; Goodwin, C.; Burton, S.; Danieli, B.; Riva, S. *J. Mol. Catal. B Enzym.* **2010**, *65* (1–4), 52–57.
(217) Kametani, T.; Ogasawara, K. *Chem. Pharm. Bull. (Tokyo)* **1968**, *16* (6), 1138–1139.
(218) Tobinaga, S.; Kotani, E. *J. Am. Chem. Soc.* **1972**, *94* (1), 309–310.
(219) Kametani, T.; Kozuka, A.; Fukumoto, K. *J. Chem. Soc. C Org.* **1971**, 1021.
(220) M. Scrowston, R.; M Cave, J.; M Scrowston, R.; D. Kennewell, P.; Westwood, R. A *HETEROCYCLES* **1994**, *37* (2), 1083.
(221) Tanaka, K.; Gotoh, H. *Tetrahedron* **2019**, *75* (29), 3875–3885.
(222) Lee, Y. E.; Cao, T.; Torruellas, C.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2014**, *136* (19), 6782–6785.
(223) Czollner, L.; Frantsits, W.; Küenburg, B.; Hedenig, U.; Fröhlich, J.; Jordis, U. *Tetrahedron Lett.* **1998**, *39* (15), 2087–2088.
(224) Krikorian, D.; Tarpanov, V.; Parushev, S.; Mechkarova, P. *Synth. Commun.* **2000**, *30* (16), 2833–2846.
(225) Hemetsberger, M.; Treu, M.; Jordis, U.; Mereiter, K.; Hametner, C.; Frohlich, J. *Monatshefte Fur ChemieChemical Mon.* **2004**, *135* (10), 1275–1287.
(226) Lewin, A. H.; Szewczyk, J.; Wilson, J. W.; Carroll, F. I. *Tetrahedron* **2005**, *61* (30), 7144–7152.
(227) Knesl, P.; Yousefi, B. H.; Mereiter, K.; Jordis, U. *Tetrahedron Lett.* **2006**, *47* (32), 5701–5703.
(228) Node, M.; Kodama, S.; Hamashima, Y.; Katoh, T.; Nishide, K.; Kajimoto, T. *Chem. Pharm. Bull. (Tokyo)* **2006**, *54* (12), 1662–1679.
(229) Holton, R. A.; Sibi, M. P.; Murphy, W. S. *J. Am. Chem. Soc.* **1988**, *110* (1), 314–316.
(230) Pelish, H. E.; Westwood, N. J.; Feng, Y.; Kirchhausen, T.; Shair, M. D. *J. Am. Chem. Soc.* **2001**, *123* (27), 6740–6741.
(231) Gao, F.; Carr, J. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2012**, *51* (27), 6613–6617.

(232) Kil'met'ev, A. S.; Shul'ts, E. E.; Shakirov, M. M.; Rybalova, T. V.; Tolstikov, G. A. *J. Org. Chem.* **2013**, *49* (6), 872–885.
(233) Kita, Y.; Dohi, T. *Chem. Rec.* **2015**, *15* (5), 886–906.
(234) Morimoto, K.; Sakamoto, K.; Ohshika, T.; Dohi, T.; Kita, Y. *Angew. Chem. Int. Ed.* **2016**, *55* (11), 3652–3656.
(235) Waters, W. A. *J. Chem. Soc. B Phys. Org.* **1971**, 2026.
(236) Moss, G. P. *Pure Appl. Chem.* **1999**, *71* (3), 531–558.
(237) Baeyer, A. *Berichte Dtsch. Chem. Ges.* **1900**, *33* (3), 3771–3775.
(238) Smith, L. K.; Baxendale, I. R. *Org. Biomol. Chem.* **2015**, *13* (39), 9907–9933.
(239) Undheim, K. *Synthesis* **2014**, *46* (15), 1957–2006.
(240) Kotha, S.; Panguluri, N. R.; Ali, R. *Eur. J. Org. Chem.* **2017**, *2017* (36), 5316–5342.
(241) Bajracharya, G. B. *J. Nepal Chem. Soc.* **2013**, *28*, 1–23.
(242) Ding, K.; Han, Z.; Wang, Z. *Chem. - Asian J.* **2009**, *4* (1), 32–41.
(243) Xie, J.-H.; Zhou, Q.-L. *Acc. Chem. Res.* **2008**, *41* (5), 581–593.
(244) Liang, H.; Ciufolini, M. A. *Angew. Chem. Int. Ed.* **2011**, *50* (50), 11849–11851.
(245) Parra, A.; Reboredo, S. *Chem. – Eur. J.* **2013**, *19* (51), 17244–17260.
(246) Kainz, Q. M.; Matier, C. D.; Bartoszewicz, A.; Zultanski, S. L.; Peters, J. C.; Fu, G. C. *Science* **2016**, *351* (6274), 681–684.
(247) List, B. *Acc. Chem. Res.* **2004**, *37* (8), 548–557.
(248) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107* (12), 5471–5569.
(249) Pihko, P. M.; Majander, I.; Erkkilä, A. Enamine Catalysis. In *Asymmetric Organocatalysis*; List, B., Ed.; Topics in Current Chemistry; Springer Berlin Heidelberg: Berlin, Heidelberg, 2010; Vol. 291, pp 145–200.
(250) Koposov, A. Y.; Netzel, B. C.; Yusubov, M. S.; Nemykin, V. N.; Nazarenko, A. Y.; Zhdankin, V. V. *Eur. J. Org. Chem.* **2007**, *2007* (27), 4475–4478.
(251) Lee, S.; MacMillan, D. W. C. *Tetrahedron* **2006**, *62* (49), 11413–11424.
(252) Prinsep, M. R.; Rahman, A. U. *Studies in Natural Products Chemistry*; Elsevier Amsterdam, The Netherlands, 2003.
(253) Tatsuta, T.; Hosono, M.; Rotinsulu, H.; Wewengkang, D. S.; Sumilat, D. A.; Namikoshi, M.; Yamazaki, H. *J. Nat. Prod.* **2017**, *80* (2), 499–502.
(254) Dumas, J.; Brittelli, D.; Chen, J.; Dixon, B.; Hatoum-Mokdad, H.; König, G.; Sibley, R.; Witowsky, J.; Wong, S. *Bioorg. Med. Chem. Lett.* **1999**, *9* (17), 2531–2536.
(255) Hamada, M.; Kiuchi, M.; Adachi, K. *Synthesis* **2007**, *2007* (13), 1927–1929.
(256) Raghavan, S.; Krishnaiah, V.; Sridhar, B. *J. Org. Chem.* **2010**, *75* (2), 498–501.
(257) Chen, G.; Højer, A.-M.; Areberg, J.; Nomikos, G. *Clin. Pharmacokinet.* **2018**, *57* (6), 673–686.
(258) Sugahara, T.; Murakami, K.; Yorimitsu, H.; Osuka, A. *Angew. Chem.* **2014**, *126* (35), 9483–9487.
(259) Otsuka, S.; Yorimitsu, H.; Osuka, A. *Chem. - Eur. J.* **2015**, *21* (42), 14703–14707.
(260) Rentner, J.; Kljajic, M.; Offner, L.; Breinbauer, R. *Tetrahedron* **2014**, *70* (47), 8983–9027.
(261) Lian, Z.; Bhawal, B. N.; Yu, P.; Morandi, B. *Science* **2017**, *356* (6342), 1059–1063.
(262) Delcaillau, T.; Woenckhaus-Alvarez, A.; Morandi, B. *Org. Lett.* **2021**, *23* (18), 7018–7022.

(263) Rahate, A. S.; Nemade, K. R.; Waghuley, S. A. *Rev. Chem. Eng.* **2013**, *29* (6).
(264) Boyd, D. A. *Angew. Chem. Int. Ed.* **2016**, *55* (50), 15486–15502.
(265) Li, X.; Ma, W.; Li, H.; Zhang, Q.; Liu, H. *Coord. Chem. Rev.* **2020**, *408*, 213191.
(266) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev.* **2011**, *111* (3), 1596–1636.
(267) Lee, C.-F.; Liu, Y.-C.; Badsara, S. S. *Chem. - Asian J.* **2014**, *9* (3), 706–722.
(268) Shen, C.; Zhang, P.; Sun, Q.; Bai, S.; Hor, T. S. A.; Liu, X. *Chem. Soc. Rev.* **2015**, *44* (1), 291–314.
(269) Fernández-Rodríguez, M. A.; Shen, Q.; Hartwig, J. F. *Chem. - Eur. J.* **2006**, *12* (30), 7782–7796.
(270) Wong, Y.-C.; Jayanth, T. T.; Cheng, C.-H. *Org. Lett.* **2006**, *8* (24), 5613–5616.
(271) Zhang, Y.; Ngeow, K. C.; Ying, J. Y. *Org. Lett.* **2007**, *9* (18), 3495–3498.
(272) Sperotto, E.; van Klink, G. P. M.; de Vries, J. G.; van Koten, G. *J. Org. Chem.* **2008**, *73* (14), 5625–5628.
(273) Correa, A.; Carril, M.; Bolm, C. *Angew. Chem.* **2008**, *120* (15), 2922–2925.
(274) Reddy, V. P.; Swapna, K.; Kumar, A. V.; Rao, K. R. *J. Org. Chem.* **2009**, *74* (8), 3189–3191.
(275) Jean, M.; Renault, J.; van de Weghe, P.; Asao, N. *Tetrahedron Lett.* **2010**, *51* (2), 378–381.
(276) Sayah, M.; Organ, M. G. *Chem. - Eur. J.* **2011**, *17* (42), 11719–11722.
(277) Uyeda, C.; Tan, Y.; Fu, G. C.; Peters, J. C. *J. Am. Chem. Soc.* **2013**, *135* (25), 9548–9552.
(278) Joyce, L. L.; Batey, R. A. *Org. Lett.* **2009**, *11* (13), 2792–2795.
(279) Xu, H.-J.; Zhao, Y.-Q.; Feng, T.; Feng, Y.-S. *J. Org. Chem.* **2012**, *77* (6), 2878–2884.
(280) Ajiki, K.; Hirano, M.; Tanaka, K. *Org. Lett.* **2005**, *7* (19), 4193–4195.
(281) Arisawa, M.; Suzuki, T.; Ishikawa, T.; Yamaguchi, M. *J. Am. Chem. Soc.* **2008**, *130* (37), 12214–12215.
(282) Zou, L.-H.; Reball, J.; Mottweiler, J.; Bolm, C. *Chem. Commun.* **2012**, *48* (92), 11307.
(283) Chauhan, P.; Mahajan, S.; Enders, D. *Chem. Rev.* **2014**, *114* (18), 8807–8864.
(284) Hostier, T.; Ferey, V.; Ricci, G.; Gomez Pardo, D.; Cossy, J. *Org. Lett.* **2015**, *17* (15), 3898–3901.
(285) Liu, B.; Lim, C.-H.; Miyake, G. M. *J. Am. Chem. Soc.* **2017**, *139* (39), 13616–13619.
(286) Chatterjee, N.; Goswami, A. *Eur. J. Org. Chem.* **2017**, *2017* (21), 3023–3032.
(287) Ghosh, M.; Rajkiewicz, A.; Kalek, M. *Synthesis* **2019**, *51* (02), 359–370.
(288) Budhwan, R.; Yadav, S.; Murarka, S. *Org. Biomol. Chem.* **2019**, *17* (26), 6326–6341.
(289) Namboothiri, I. N. N.; Budhwan, R.; Garg, G.; Murarka, S. *Targets Heterocycl. Syst.* **2020**, *23*, 27.
(290) Wang, F.-Y.; Chen, Z.-C.; Zheng, Q.-G. *J. Chem. Res.* **2004**, *2004* (2), 127–128.
(291) Zhang, B.; Kang, Y.; Yang, L.; Chen, X. A *ChemistrySelect* **2016**, *1* (8), 1529–1532.
(292) Wang, L.; Chen, Z.-C. *Synth. Commun.* **2001**, *31* (8), 1227–1232.
(293) Movassagh, B.; Mossadegh, A. *Phosphorus Sulfur Silicon Relat. Elem.* **2005**, *180* (10), 2275–2278.
(294) Olofsson, B. Arylation with Diaryliodonium Salts. In *Hypervalent Iodine Chemistry*; Wirth, T., Ed.; Topics in Current Chemistry; Springer International Publishing: Cham, 2015; Vol. 373, pp 135–166.
(295) Bátori, S.; Messmer, A. *J. Heterocycl. Chem.* **1988**, *25* (2), 437–444.

(296) Parida, S. K.; Jaiswal, S.; Singh, P.; Murarka, S. *Org. Lett.* **2021**, *23* (16), 6401–6406.
(297) Azam, M. A. *Sci. Pharm.* **2012**, *80* (4), 789–823.
(298) Huchet, Q. A.; Kuhn, B.; Wagner, B.; Kratochwil, N. A.; Fischer, H.; Kansy, M.; Zimmerli, D.; Carreira, E. M.; Müller, K. *J. Med. Chem.* **2015**, *58* (22), 9041–9060.
(299) Gillis, E. P.; Eastman, K. J.; Hill, M. D.; Donnelly, D. J.; Meanwell, N. A. *J. Med. Chem.* **2015**, *58* (21), 8315–8359.
(300) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Aceña, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. *Chem. Rev.* **2016**, *116* (2), 422–518.
(301) Norrby, P.-O.; Petersen, T. B.; Bielawski, M.; Olofsson, B. *Chem. - Eur. J.* **2010**, *16* (28), 8251–8254.
(302) Stridfeldt, E.; Lindstedt, E.; Reitti, M.; Blid, J.; Norrby, P.-O.; Olofsson, B. *Chem. - Eur. J.* **2017**, *23* (53), 13249–13258.
(303) Frei, R.; Wodrich, M. D.; Hari, D. P.; Borin, P.-A.; Chauvier, C.; Waser, J. *J. Am. Chem. Soc.* **2014**, *136* (47), 16563–16573.
(304) Wodrich, M. D.; Caramenti, P.; Waser, J. *Org. Lett.* **2016**, *18* (1), 60–63.
(305) Wing, K. D.; Glickman, A. H.; Casida, J. E. *Pestic. Biochem. Physiol.* **1984**, *21* (1), 22–30.
(306) Matolcsy, G.; NÃ¡dasy, M.; Andriska, V. *Pesticide Chemistry*; Elsevier Science: Amsterdam, 2014.
(307) Li, N.-S.; Frederiksen, J. K.; Piccirilli, J. A. *Acc. Chem. Res.* **2011**, *44* (12), 1257–1269.
(308) Eckstein, F. *Nucleic Acid Ther.* **2014**, *24* (6), 374–387.
(309) Qiu, Y.; Worch, J. C.; Chirdon, D. N.; Kaur, A.; Maurer, A. B.; Amsterdam, S.; Collins, C. R.; Pintauer, T.; Yaron, D.; Bernhard, S.; Noonan, K. J. T. *Chem. – Eur. J.* **2014**, *20* (25), 7746–7751.
(310) Shapiro, N. D.; Rauniyar, V.; Hamilton, G. L.; Wu, J.; Toste, F. D. *Nature* **2011**, *470* (7333), 245–249.
(311) Robertson, F. J.; Wu, J. *J. Am. Chem. Soc.* **2012**, *134* (5), 2775–2780.
(312) Murdock, L. L.; Hopkins, T. L. *J. Agric. Food Chem.* **1968**, *16* (6), 954–958.
(313) Lee, A.; Metcalf, R. L. *Pestic. Biochem. Physiol.* **1973**, *2* (4), 408–417.
(314) Lee, A.-H.; Metcalf, R. L.; Booth, G. M. *Ann. Entomol. Soc. Am.* **1973**, *66* (2), 333–343.
(315) Kazuo, H.; Katsuki, S.; Mitsuo, H.; Masaru, N.; Kenji, T.; Masaaki, Y. JP 48018461 B 19730606, 1973.
(316) Yasuhiko, M.; Yasuyuki, K.; Harumi, T.; Takashi, Y. JP 51033200 A 19760322, 1976.
(317) Reddy, E. P.; Reddy, M. V. R.; Bell, S. C. WO 2005089269 A2 20050929, 2005.
(318) Sekine, Mitsuo.; Hata, Tsujiaki. *J. Am. Chem. Soc.* **1986**, *108* (15), 4581–4586.
(319) Hotoda, H.; Koizumi, M.; Koga, R.; Kaneko, M.; Momota, K.; Ohmine, T.; Furukawa, H.; Agatsuma, T.; Nishigaki, T.; Sone, J.; Tsutsumi, S.; Kosaka, T.; Abe, K.; Kimura, S.; Shimada, K. *J. Med. Chem.* **1998**, *41* (19), 3655–3663.
(320) Seio, K.; Wada, T.; Sakamoto, K.; Yokoyama, S.; Sekine, M. *J. Org. Chem.* **1998**, *63* (5), 1429–1443.
(321) Ohuchi, S.; Ayukawa, H.; Hata, T. *Chem. Lett.* **1992**, *21* (8), 1501–1504.
(322) Fukuoka, M.; Shuto, S.; Minakawa, N.; Ueno, Y.; Matsuda, A. *Tetrahedron Lett.* **1999**, *40* (29), 5361–5364.
(323) Fukuoka, M.; Shuto, S.; Minakawa, N.; Ueno, Y.; Matsuda, A. *J. Org. Chem.* **2000**, *65* (17), 5238–5248.

(324) Huang, L.-J.; Zhao, Y.-Y.; Yuan, L.; Min, J.-M.; Zhang, L.-H. *J. Med. Chem.* **2002**, *45* (24), 5340–5352.
(325) Nishiyama, Y.; Hazama, Y.; Yoshida, S.; Hosoya, T. *Org. Lett.* **2017**, *19* (14), 3899–3902.
(326) Masson, S.; Saint-Clair, J.-F.; Saquet, M. *Synthesis* **1993**, *1993* (05), 485–486.
(327) Han, L.-B.; Tanaka, M. *Chem. Lett.* **1999**, *28* (9), 863–864.
(328) Jones, D. J.; O'Leary, E. M.; O'Sullivan, T. P. *Tetrahedron Lett.* **2018**, *59* (49), 4279–4292.
(329) Zhu, Y.; Chen, T.; Li, S.; Shimada, S.; Han, L.-B. *J. Am. Chem. Soc.* **2016**, *138* (18), 5825–5828.
(330) Song, S.; Zhang, Y.; Yeerlan, A.; Zhu, B.; Liu, J.; Jiao, N. *Angew. Chem. Int. Ed.* **2017**, *56* (9), 2487–2491.
(331) Huang, H.; Denne, J.; Yang, C.; Wang, H.; Kang, J. Y. *Angew. Chem. Int. Ed.* **2018**, *57* (22), 6624–6628.
(332) Shen, J.; Li, Q.-W.; Zhang, X.-Y.; Wang, X.; Li, G.-Z.; Li, W.-Z.; Yang, S.-D.; Yang, B. *Org. Lett.* **2021**, *23* (5), 1541–1547.
(333) Bai, J.; Cui, X.; Wang, H.; Wu, Y. *Chem Commun* **2014**, *50* (64), 8860–8863.
(334) Liu, Y.-C.; Lee, C.-F. *Green Chem* **2014**, *16* (1), 357–364.
(335) Wang, D.; Zhao, J.; Xu, W.; Shao, C.; Shi, Z.; Li, L.; Zhang, X. *Org. Biomol. Chem.* **2017**, *15* (3), 545–549.
(336) Choudhary, R.; Singh, P.; Bai, R.; Sharma, M. C.; Badsara, S. S.. *Org. Biomol. Chem.* **2019**, *17* (45), 9757–9765.
(337) Shen, B.-R.; Annamalai, P.; Wang, S.-F.; Bai, R.; Lee, C.-F. *J. Org. Chem.* **2022**, *87* (14), 8858–8870.
(338) Wang, W.-M.; Liu, L.-J.; Yao, L.; Meng, F.-J.; Sun, Y.-M.; Zhao, C.-Q.; Xu, Q.; Han, L.-B. *J. Org. Chem.* **2016**, *81* (17), 8121–8121.
(339) Knouse, K. W.; deGruyter, J. N.; Schmidt, M. A.; Zheng, B.; Vantourout, J. C.; Kingston, C.; Mercer, S. E.; Mcdonald, I. M.; Olson, R. E.; Zhu, Y.; Hang, C.; Zhu, J.; Yuan, C.; Wang, Q.; Park, P.; Eastgate, M. D.; Baran, P. S. *Science* **2018**, *361* (6408), 1234–1238.
(340) Featherston, A. L.; Kwon, Y.; Pompeo, M. M.; Engl, O. D.; Leahy, D. K.; Miller, S. J. *Science* **2021**, *371* (6530), 702–707.
(341) Knouse, K. W.; Flood, D. T.; Vantourout, J. C.; Schmidt, M. A.; Mcdonald, I. M.; Eastgate, M. D.; Baran, P. S. *ACS Cent. Sci.* **2021**, *7* (9), 1473–1485.
(342) Huang, Y.; Knouse, K. W.; Qiu, S.; Hao, W.; Padial, N. M.; Vantourout, J. C.; Zheng, B.; Mercer, S. E.; Lopez-Ogalla, J.; Narayan, R.; Olson, R. E.; Blackmond, D. G.; Eastgate, M. D.; Schmidt, M. A.; McDonald, I. M.; Baran, P. S. *Science* **2021**, *373* (6560), 1265–1270.
(343) Xu, J.; Zhang, L.; Li, X.; Gao, Y.; Tang, G.; Zhao, Y. *Org. Lett.* **2016**, *18* (6), 1266–1269.
(344) Shi, S.; Chen, J.; Zhuo, S.; Wu, Z.; Fang, M.; Tang, G.; Zhao, Y. *Adv. Synth. Catal.* **2019**, *361* (13), 3210–3216.
(345) Kovács, S.; Bayarmagnai, B.; Aillerie, A.; Gooßen, L. J. *Adv. Synth. Catal.* **2018**, *360* (10), 1913–1918.
(346) Zhang, L.; Zhang, P.; Li, X.; Xu, J.; Tang, G.; Zhao, Y.. *J. Org. Chem.* **2016**, *81* (13), 5588–5594.

(347) Wang, L.; Yang, S.; Chen, L.; Yuan, S.; Chen, Q.; He, M.-Y.; Zhang, Z.-H. *Catal. Sci. Technol.* **2017**, *7* (11), 2356–2361.
(348) Chen, X.; Pu, M.; Cheng, H.; Sperger, T.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2019**, *58* (33), 11395–11399.
(349) Sarkar, S.; Wojciechowska, N.; Rajkiewicz, A. A.; Kalek, M. *Eur. J. Org. Chem.* **2022**, *2022* (2).
(350) Dang, Q.; Liu, Y.; Cashion, D. K.; Kasibhatla, S. R.; Jiang, T.; Taplin, F.; Jacintho, J. D.; Li, H.; Sun, Z.; Fan, Y.; DaRe, J.; Tian, F.; Li, W.; Gibson, T.; Lemus, R.; van Poelje, P. D.; Potter, S. C.; Erion, M. D. *J. Med. Chem.* **2011**, *54* (1), 153–165.
(351) Eto, M. *Biosci. Biotechnol. Biochem.* **1997**, *61* (1), 1–11.
(352) Chou, H.-H.; Cheng, C.-H. *Adv. Mater.* **2010**, *22* (22), 2468–2471.
(353) Hsu, F.-M.; Chien, C.-H.; Shu, C.-F.; Lai, C.-H.; Hsieh, C.-C.; Wang, K.-W.; Chou, P.-T. *Adv. Funct. Mater.* **2009**, *19* (17), 2834–2843.
(354) Iaroshenko, V. *Organophosphorus Chemistry: From Molecules to Applications*; Wiley-VCH: Weinheim, 2019.
(355) Guo, H.; Fan, Y. C.; Sun, Z.; Wu, Y.; Kwon, O. *Chem. Rev.* **2018**, *118* (20), 10049–10293.
(356) Albrecht, Å.; Albrecht, A.; Krawczyk, H.; JÃ¸rgensen, K. *Chem. - Eur. J.* **2010**, *16* (1), 28–48.
(357) Demchuk, O. M.; Jasiński, R. *Phosphorus Sulfur Silicon Relat. Elem.* **2016**, *191* (2), 245–253.
(358) Heiss, T. K.; Dorn, R. S.; Prescher, J. A. *Chem. Rev.* **2021**, *121* (12), 6802–6849.
(359) Zhou, T.; Chen, Z.-C. *Synth. Commun.* **2001**, *31* (21), 3289–3294.
(360) Xu, J.; Zhang, P.; Gao, Y.; Chen, Y.; Tang, G.; Zhao, Y. *J. Org. Chem.* **2013**, *78* (16), 8176–8183.
(361) Beaud, R.; Phipps, R. J.; Gaunt, M. J. *J. Am. Chem. Soc.* **2016**, *138* (40), 13183–13186.
(362) Hanamoto, T.; Kiguchi, Y.; Shindo, K.; Matsuoka, M.; Kondo, M. *Chem. Commun.* **1999**, No. 2, 151–152.
(363) Fearnley, A. F.; An, J.; Jackson, M.; Lindovska, P.; Denton, R. M. *Chem. Commun.* **2016**, *52* (28), 4987–4990.
(364) Gasnot, J.; Botella, C.; Comesse, S.; Lakhdar, S.; Alayrac, C.; Gaumont, A.-C.; Dalla, V.; Taillier, C. *Synlett* **2020**, *31* (09), 883–888.
(365) Sarkar, S.; Kalek, M. *Org. Lett.* **2023**, acs.orglett.2c04310.
(366) Wauters, I.; Debrouwer, W.; Stevens, C. V. *Beilstein J. Org. Chem.* **2014**, *10*, 1064–1096.
(367) Zhou, Y.; Liu, C.; Shen, Z.; Dai, B.; Chen, J. *J. Organomet. Chem.* **2021**, *949*, 121932.
(368) Screttas, C.; Isbell, A. F. *J. Org. Chem.* **1962**, *27* (7), 2573–2577.
(369) Kanchana, U. S.; Diana, E. J.; Mathew, T. V.; Anilkumar, G. *ChemistrySelect* **2021**, *6* (7), 1579–1588.
(370) Stadler, A.; Kappe, C. O. *Org. Lett.* **2002**, *4* (20), 3541–3543.
(371) Gelman, D.; Jiang, L.; Buchwald, S. L. *Org. Lett.* **2003**, *5* (13), 2315–2318.
(372) Allen, D. V.; Venkataraman, D. *J. Org. Chem.* **2003**, *68* (11), 4590–4593.
(373) Sun, M.; Zang, Y.-S.; Hou, L.-K.; Chen, X.-X.; Sun, W.; Yang, S.-D. *Eur. J. Org. Chem.* **2014**, *2014* (30), 6796–6801.
(374) Yu, R.; Chen, X.; Martin, S. F.; Wang, Z. *Org. Lett.* **2017**, *19* (7), 1808–1811.

(375) Chen, X.; Wu, H.; Yu, R.; Zhu, H.; Wang, Z. *J. Org. Chem.* **2021**, *86* (13), 8987–8996.
(376) Tunney, S. E.; Stille, J. K. *J. Org. Chem.* **1987**, *52* (5), 748–753.
(377) Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112* (13), 5244–5252.
(378) Lipshutz, B. H.; Buzard, D. J.; Yun, C. S. *Tetrahedron Lett.* **1999**, *40* (2), 201–204.
(379) Arockiam, P. B.; Lennert, U.; Graf, C.; Rothfelder, R.; Scott, D. J.; Fischer, T. G.; Zeitler, K.; Wolf, R. *Chem. – Eur. J.* **2020**, *26* (69), 16374–16382.
(380) Bugaenko, D. I.; Karchava, A. V. *Adv. Synth. Catal.* **2022**, *364* (13), 2248–2253.
(381) Saltzman, H.; Sharefkin. *Org. Synth.* **1963**, *43*, 60.
(382) Verga, D.; Percivalle, C.; Doria, F.; Porta, A.; Freccero, M. *J. Org. Chem.* **2011**, *76* (7), 2319–2323.
(383) Takuwa, A.; Iwamoto, H.; Soga, O.; Maruyama, K. *J. Chem. Soc. Perkin 1* **1986**, 1627.
(384) Yan, C.-S.; Peng, Y.; Xu, X.-B.; Wang, Y.-W. *Chem. - Eur. J.* **2012**, *18* (19), 6039–6048.
(385) Hurd, C. D.; Yarnall, W. A. *J. Am. Chem. Soc.* **1937**, *59* (9), 1686–1690.
(386) Bering, L.; Jeyakumar, K.; Antonchick, A. P. *Org. Lett.* **2018**, *20* (13), 3911–3914.
(387) Hong, X.; Tan, Q.; Liu, B.; Xu, B. *Angew. Chem.* **2017**, *129* (14), 4019–4023.
(388) Kuriyama, M.; Hamaguchi, N.; Onomura, O. *Chem. - Eur. J.* **2012**, *18* (6), 1591–1594.
(389) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16 Rev. A.03, 2016.
(390) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37* (2), 785–789.
(391) Becke, A. D. *Phys. Rev. A* **1988**, *38* (6), 3098–3100.
(392) Becke, A. D. *J. Chem. Phys.* **1992**, *96* (3), 2155–2160.
(393) Becke, A. D. *J. Chem. Phys.* **1992**, *97* (12), 9173–9177.
(394) Becke, A. D. *J. Chem. Phys.* **1993**, *98* (7), 5648–5652.
(395) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. *J. Chem. Phys.* **2010**, *132* (15), 154104.
(396) Grimme, S.; Ehrlich, S.; Goerigk, L. *J. Comput. Chem.* **2011**, *32* (7), 1456–1465.
(397) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113* (18), 6378–6396.
(398) Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7* (18), 3297.
(399) Peterson, K. A.; Figgen, D.; Goll, E.; Stoll, H.; Dolg, M. *J. Chem. Phys.* **2003**, *119* (21), 11113–11123.
(400) Pritchard, B. P.; Altarawy, D.; Didier, B.; Gibson, T. D.; Windus, T. L. *J. Chem. Inf. Model.* **2019**, *59* (11), 4814–4820.

(401) Grimme, S. *Chem. - Eur. J.* **2012**, *18* (32), 9955–9964.
(402) Paton, R. Bobbypaton/Goodvibes: Goodvibes V2.0.1, 2017.
(403) Gao, H.; Xu, Q.-L.; Keene, C.; Kürti, L. Scalable, *Chem. - Eur. J.* **2014**, n/a-n/a.

Appendix B (Contribution Reports)

Contribution report for the doctoral thesis of Sudeep Sarkar

Sudeep Sarkar

My contribution to the publications listed below:

"Synthesis of Pummerer's Ketone and Its Analogs by Iodosobenzene-Promoted Oxidative Phenolic Coupling"
Sarkar, S.; Ghosh, M. K.; Kalek, M. *Tetrahedron Lett.* **2020**, *61* (43), 152459.

I conducted approximately half of the experimental work, including: ~30% of the optimization of the reaction conditions, ~90% of the assessing the scope and limitations, 100% of the characterization of the products. I wrote the first draft of the manuscript and the supporting information.

"Synthesis of Aryl Sulfides by Metal-Free Arylation of Thiols with Diaryliodonium Salts under Basic Conditions"
Sarkar, S.; Wojciechowska, N.; Rajkiewicz, A. A.; Kalek, M. *Eur. J. Org. Chem.* **2022**, *2022* (2), e202101408.

I conducted approximately half of the experimental work, including: ~30% of the optimization of the reaction conditions, ~50% of the assessing the scope and limitations, 90% of the characterization of the products. I wrote the first draft of the manuscript and the supporting information.

"Metal-free *S*-arylation of Phosphorothioate Diesters and Related Compounds with Diaryliodonium Salts"
Sarkar, S.; Kalek, M. *Org. Lett.* **2023**, *25 (4)*, 671–675

I participated in the planning of the research, conducted all the experimental work, and wrote the first draft of the manuscript and the supporting information.

Date

23/02/2023

Signature

UNIVERSITY OF WARSAW | CeNT CENTRE OF NEW TECHNOLOGIES

Dr. hab. Marcin Kalek
University of Warsaw, Centre of New Technologies
Banacha 2C, 02-097 Warsaw, Poland

TEL.: +48 225543730, **FAX:** +48 225540801
E-MAIL: m.kalek@cent.uw.edu.pl, **http:**//kalekgroup.pl

Warsaw, 20-02-2023

Contribution report for the doctoral thesis of Sudeep Sarkar

Sarkar, S.; Ghosh, M. K.; Kalek, M.
„Synthesis of Pummerer's Ketone and Its Analogs by Iodosobenzene-Promoted Oxidative Phenolic Coupling"
Tetrahedron Lett. **2020**, *61 (43)*, 152459
I proposed the subject of the research, participated in the planning of the experiments, and I oversaw the ongoing work. I edited the manuscript and the supporting information.

Sarkar, S.; Wojciechowska, N.; Rajkiewicz, A. A.; Kalek, M.
„Synthesis of Aryl Sulfides by Metal-Free Arylation of Thiols with Diaryliodonium Salts under Basic Conditions"
Eur. J. Org. Chem. ***2022***, *e202101408*
I participated in the planning of the experiments, performed the computational studies, and I oversaw the ongoing work. I edited the manuscript and the supporting information.

Sarkar, S.; Kalek, M.
„Metal-free S-arylation of Phosphorothioate Diesters and Related Compounds with Diaryliodonium Salts"
Org. Lett. **2023**, *25 (4)*, 671-675
I proposed the subject of the research, participated in the planning of the experiments, performed the computational studies, and I oversaw the ongoing work. I edited the manuscript and the supporting information.

Sincerly Yours

Marcin Kalek

Contribution report for the doctoral thesis of Sudeep Sarkar

Dr. Manoj Kumar Ghosh

My contribution to the publications listed below:

"Synthesis of Pummerer's Ketone and Its Analogs by Iodosobenzene-Promoted Oxidative Phenolic Coupling"
Sarkar, S.; Ghosh, M. K.; Kalek, M. *Tetrahedron Lett.* **2020**, *61* (43), 152459.

I participated in the planning of the research and I conducted approximately half of the experimental work (optimization of the reaction conditions, exploration of the scope and limitations).

Date 23.02.2023 Signature

UNIVERSITY OF WARSAW

Faculty of Chemistry

Faculty of Chemistry
University of Warsaw

Contribution report for the doctoral thesis of Sudeep Sarkar

Dr. Adam A. Rajkiewicz

My contribution to the publications listed below:

"Synthesis of Aryl Sulfides by Metal-Free Arylation of Thiols with Diaryliodonium Salts under Basic Conditions."
Sarkar, S.; Wojciechowska, N.; Rajkiewicz, A. A.; Kalek, M. *Eur. J. Org. Chem.* **2022**, *2022* (2), e202101408.

I proposed the project and performed a preliminary optimization of the reaction conditions.

22-02-2023

Date

Adam Rajkiewicz

Signature

ul. Ludwika Pasteura 1, 02-093 Warsaw, Poland
phone.: 22 55 26211 (Dean's Office), 22 55 26230 (Administration)
e-mail: dziekan@chem.uw.edu.pl, chemia@chem.uw.edu.pl, www.chem.uw.edu.pl

Contribution report for the doctoral thesis of Sudeep Sarkar

Natalia Wojciechowska

My contribution to the publications listed below:

"Synthesis of Aryl Sulfides by Metal-Free Arylation of Thiols with Diaryliodonium Salts under Basic Conditions."
Sarkar, S.; Wojciechowska, N.; Rajkiewicz, A. A.; Kalek, M. *Eur. J. Org. Chem.* **2022**, *2022* (2), e202101408.

I participated in the optimization of the reaction conditions and the exploration of its scope and limitations

Date

22.02.2023r

Signature

Natalia Wojciechowska