Difunctionalization of Olefins by Radicals and Nucleophiles

Inaugural-Dissertation

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Content

ABSRTCAT

Transition metal free, difunctionalization of olefins by radical and nucleophile is presented in this PhD's work. The combination of benzoyl peroxide with strong Brønsted acid HPF_6 allows the difunctionalizationn of alkenes with radicals derived from thioxanthene, xanthene and thiophenols together with nitrile and alcohol nucleophiles. Mechanistic studies suggest the acid promotes the electron transfer step by making BPO as a better electron acceptor.

By using of triarylamine as organo-redox catalyst under transition metal and acid free in difunctionalization of alkenes was further studied. BPO with catalytic amount of triarylamine, alkenes can be difunctionalized by a wide range of alkyl radical, generated from $C(sp^3)$-H or halogenated hydrocarbon, nucleophiles, including nitriles, acetic acid, alcohols and fluoride. Moreover, the oxidative Ritter reaction of allylic or benzylic C-H bonds can be also achieved under this reaction system.

Abstrakt

In dieser Doktorarbeit wird übergangsmetallfreie, radikal- und nukleophil vermittelte Difunktionalisierung von Olefinen vorgestellt. Die Kombination von Benzoylperoxid mit starker Brønsted-Säure HPF_6 ermöglicht die Difunktionalisierung von Alkenen mit Radikalen aus Thioxanthen, Xanthen und Thiophenolen zusammen mit Nitril- und Alkoholnukleophilen. Mechanistische Studien legen nahe, dass die Säure den Elektronentransferschritt fördert, indem BPO als besseren Elektronenakzeptor fungiert.

Die Verwendung von Triarylamin als Organo-Redox-Katalysator unter übergangsmetallfreier und säurefreier Difunktionalisierung von Alkenen wurde weiter untersucht. BPO mit katalytischer Menge Triarylamin, kann Alkene difunktionalisieren, durch einen weiten Bereich von Alkylradikalen, die aus $C(sp^3)$-H oder halogeniertem Kohlenwasserstoff, Nucleophilen, einschließlich Nitrilen, Essigsäure, Alkoholen und Fluorid erzeugt werden. Darüber hinaus kann unter diesem Reaktionssystem auch die oxidative Ritter-Reaktion von allylischen oder benzylischen CH-Bindungen erreicht werden.

LIST OF ABBREVIATIONS

Ac	Acetyl
ad	adamantyl
AIBN	2,2'-azo *bis*-isobutyronitrile
Alk	alkyl
aq.	aqueous
Ar	aryl
ATRA	Atom transfer radical addition
ATRP	Atom transfer radical polymerization
BTH	2,6-di-*tert*-butylphenol
Bn	benzyl
BPO	benzoyl peroxide
Bu	butyl
Bz	benzoyl
Calcd	calculated
CAN	cerium ammonium nitrate
cat.	catalyst
conv.	conversion
Cy	cyclohexyl
d	doubles
DABCO	1,4-Diazabicyclo[2.2.2]octane

DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
DDQ	2,3-Dichlor-5,6-dicyano-*p*-benzochinon
DMF	dimethylformamide
DMSO	dimethylsulfoxide
DMSO-d_6	hexadeuterodimethylsulfoxid
dr	diasteromeric ratio
DTBP	di-*tert*-butyl peroxide
EDG	electron donation group
EI	electron impact
ee	enantiomeric excess
equiv	equivalent
Et	ethyl
ESI	electrospray ionization
EWG	electron withdrawing group
GC	gas chromatography
GC-MS	gas chromatography with mass detection
h	hour(s)
HAT	hydrogen atom transfer
HOMO	highest occupied molecular orbital

HRMS	high resolution mass spectrometry
HPF_6	Hexafluorophosphoric acid
*i*Pr	isopropyl
IR	infrared spectroscopy
LG	leaving group
Lit.	literature
LUMO	lowest unoccupied molecular orbital
m	*meta*
m	multiplet
M	metal
*m*CPBA	3-Chloroperoxybenzoic acid
Me	methyl
MeO	methoxyl
Mestityl	mesityl(2,4,6-trimetylphenyl)
MS	mass spectrometry
Ms	methylsulfonyl
MW	molecular weight
m/*z*	atomic mass units per charge
n.d.	not determind
NHC	*N*-heterocyclic carbene
NHPI	*N*-hydrothalimide

NMR	nuclear magnetic resonance spectroscopy
N.R.	no reaction
Nu-H/Nu	nucleophile
o	ortho
OAc	acetyl
P	product
p	*para*
Ph	phenyl
Pr	propyl
Py	pyridine
quint	quintet
r.t.	room temperature
s	singlet
SET	single electron transfer
SOMO	single occupied molecular orbital
t	*tert*, *tertiary*
t	triplet
TBPB	*tert*-Butyl peroxybenzoate
TBHP	*tert*-Butyl hydroperoxide
^{t}Bu	tertiary butyl
TEA	triethylamine

TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
Tol	toluene
TsOH	*para*-toluene sulfonic acid
TMS	trimethylsilyl
wt	weight

ACKNOWLEDGEMENTS

All of these works described in this thesis have been conducted from October 2018 to August 2021 at Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr under the guidance of PD. Dr. Klußmann Martin. Of course, my journey to work as a PhD candidate would not have been possible without the generous financial support from Chinese Scholarship Council.

Apart from that, I would like to express my deep gratitude to PD. Dr. Klußmann Martin for giving me this wonderful chance to work in this amazing institute as a PhD candidate. PD. Dr. Klußmann Martin is always so nice, who is incredibly patient to teach me a lot. I truly appreciated our communication and discussion. I also appreciate the freedom to try, design and perform my own project. I also want to thank Prof. Dr. Benjamin List for his unconditional support to our group, and for the supervising me during the last year of my PhD. I also want to thank Prof. Dr. Hans-Günther Schmalz, who is the second supervisor during my PhD, for his enthusiastic helps to me.

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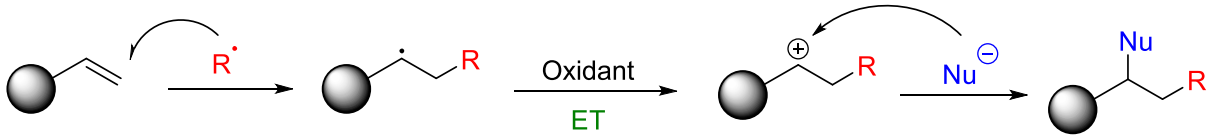
I want to thank my wife dear Weihong Yan. I know I can never thank you enough for the years we've spent together as husband and wife.

And finally, I want to thank my parents, brothers and sisters in law, who have always supported me in the following of my dreams. Besides, I am so happy to have nephews and niece who bring me a lot of fun. I am also indebted to all my friends, their insistence, kindness, and bravery always inspire me to carry on a wonderful and unique life.

OBJECTIVES OF THIS PhD's WORK

The radical difunctionalization of olefins is the major topic of my PhD thesis. The goal of my PhD thesis is to find a method, which can be suitable for different radicals and nucleophiles under one simple and easy handle reaction condition.



Goal of my PhD thesis

The major works in this thesis are two parts, which were already published during my PhD with PD. Dr. Klußmann Martin, see the blow for references:

Chapter 1: Liu, S.; Klussmann, M., *Chem. Commun*., **2020**, *56*, 1557—1560.

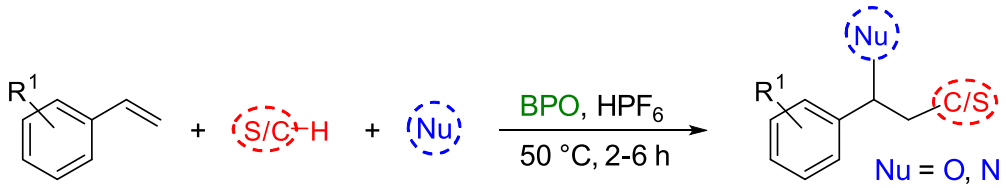
Chapter 2: Liu, S.; Klussmann, M., *Org. Chem. Front*., **2021**, DOI: 10.1039/D1QO00259G.

Chapter 1: Acid promoted radical-chain difunctionalization of styrenes

The first project of this dissertation is dealing with a reaction based on metal free, Brønsted acid promoted radical-chain difunctionalization of styrenes with stabilized radicals and (N,O)-nucleophiles.

Typical method for difunctionliaztion of olefins by radical and nucleophile needs an electron transfer step after the radical addition, which could form a carbocation from carbon centered radical. Followed by trapping with nucleophiles to produce the desired products.

Our group had previously reported the activation of TBHP by strong acid, besides, we noticed Bao and co-workers' work on copper-catalyzed difunctionalization of alkenes using benzoyl peroxide (BPO) as oxidant, and HPF_6 as additive. However, in their report, the role of acid was not clear, and the method could only use acetonitrile as radical precursor and nucleophile.

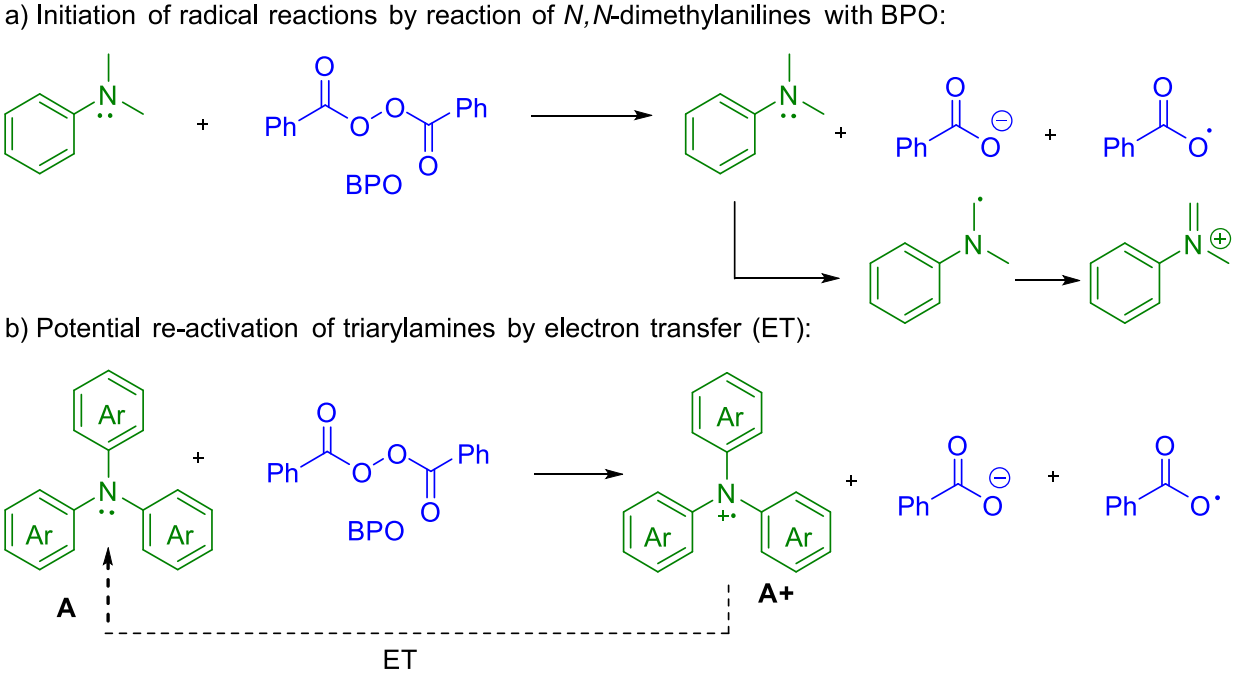


Acid promoted radical-chain difunctionalization of styrenes

The combination of BPO with HPF_6, a novel method for the difunctionalization of olefins with radicals derived from thioxanthene, xanthene and thiophenols together with nitrile and alcohol nucleophiles was developed. Mechanistic studies showed that the strong Brønsted acid plays a key role in electron transfer step, which could make the BPO as a good electron acceptor.

Chapter 2: Organo-redox-catalysis for the difunctionalization of alkenes and oxidative Ritter reactions

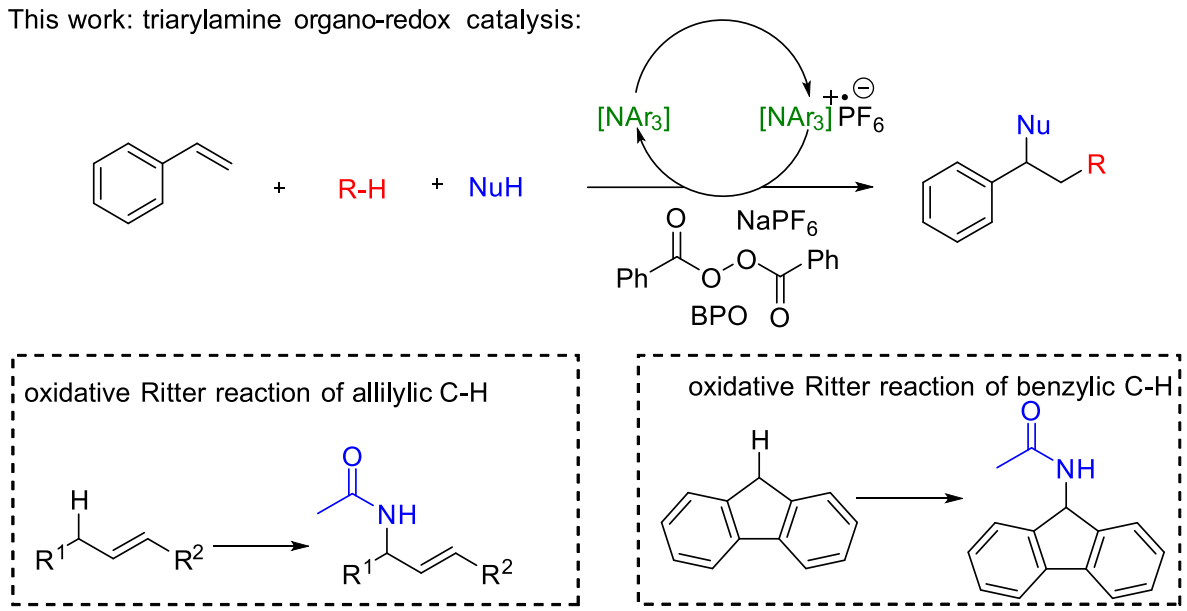
The second project of this dissertation is dealing with difunctionalization of alkenes by radicals and nucleophiles catalyzed by an organo-redox triarylamine catalyst.



Activation of BPO with *N*, *N*-dimethylaniline and triarylamines

Typical method for activation of peroxides needs transition metal. However, an organo-redox catalyst catalyzed oxidative radical and nucleophile difunctionalization of alkenes is lack of studies. *N*,*N*-Dialkylanilines are well known initiators for peroxides, especially BPO. The reaction is irreversible. In contrast, we assumed that triarylamines could react as catalysis, which could form a radical cation salt by ET.

Here, we show that triarylamines can be used as organic redox-catalysts in oxidative radical and nucleophile difunctionalization of alkenes and oxidative Ritter-reactions. Alkyl radicals, generated from plain and halogenated hydrocarbons, and nucleophiles, including nitriles, acetic acid, alcohols and fluoride were successfully used into oxidative difunctionalization of alkenes. The oxidative allylic and benzylic C-H bonds Ritter reaction could also achieve. Mechanistic studies suggest that the triarylamines are catalysts and not initiators.

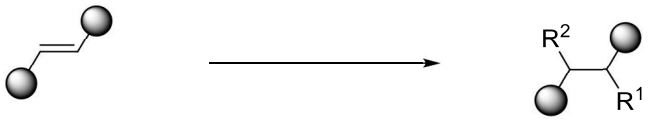


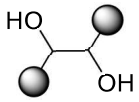
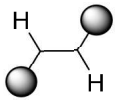
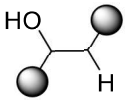
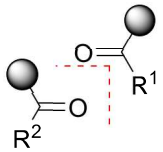
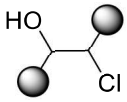
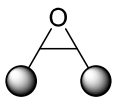
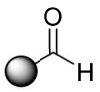
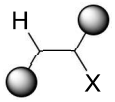
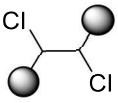
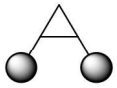
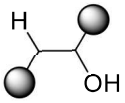
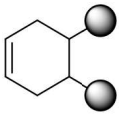
Organo-redox-catalysis for the difunctionalization of alkenes and oxidative Ritter reactions

INTRODUCTION AND BACKGROUND

INTRODUCTION

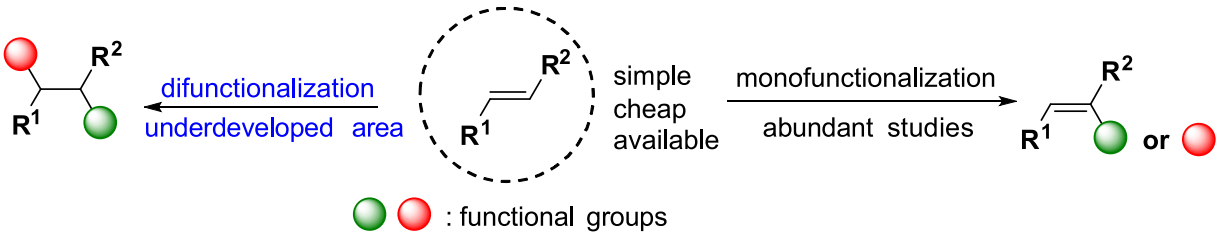
Olefins are readily available and valuable building blocks in natural products, materials and pharmaceuticals. Therefore, many olefins have a tremendous demand in industry, such as ethylene (with a worldwide production over 191.54 million tons in 2019),[1] propene (with a worldwide production around 120 million tons in 2018),[2] and styrene (4.8 million tons in 2020).[3] Structurally, olefins contain at least one π bond, which can be either a good electrophiles or nucleophiles. The conversion of versatile and readily available olefins into more structurally complex molecules has been a long-standing research topic in modern organic synthesis methodology for chemists.[4] Some famous reactions based on the functionalization of olefins have been well developed, such as the Sharpless dihydroxylation,[5] Ozonolysis,[6] Diels-Alder reaction,[7] Wacker oxidation,[8] hydrogenation,[9] holohydrins.[10]



Dihydroxylation	Hydrogenation	Hydration	Ozonolysis
OsO_4	Pd/C, H_2	H_2O, H_2SO_4	e.g. O_3, then Zn, H^+
			
Holohydration	**Epoxidation**	**Wacker oxidation**	**Alkyl halides**
e.g. Cl_2, H_2O	RCO_3H (*m*CPBA)	$PdCl_2$, CuCl, O_2, H_2O	HX
			
Vicinal Dihalides	**Cyclopropanesation**	**Hydroboration**	**Diels-Alder reaction**
e.g. Cl_2, CCl_4	Zn-Cu; CH_2I_2	BH_3 then H_2O_2, Base	conjugated diene
			

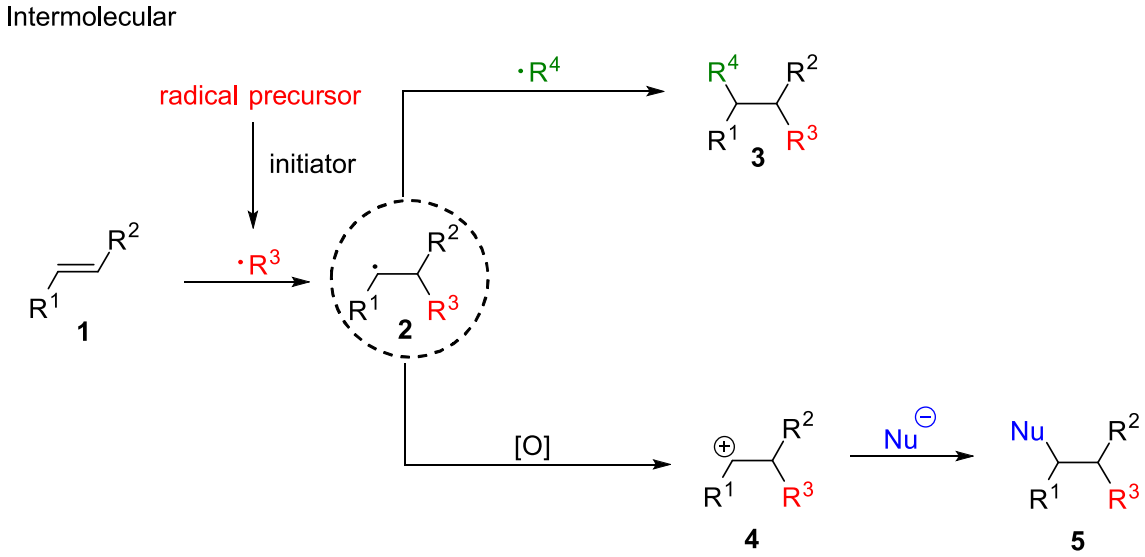
Scheme 1-1. Selected examples of olefin functionalization

The functionalization of olefins is one the most powerful methods for the construction C-C or C-X bonds. However, in comparison with the abundant studies on the monofunctionalization of olefins, the difunctionalization of olefins remains an underdeveloped area.[11] The classical difunctionalization of olefins requires two functional groups incorporate onto a carbon-carbon double bond, in one step, with high efficiency, which is a challenging but fascinating concept for the formation of unconventional bonds by designing simple processes.[12]



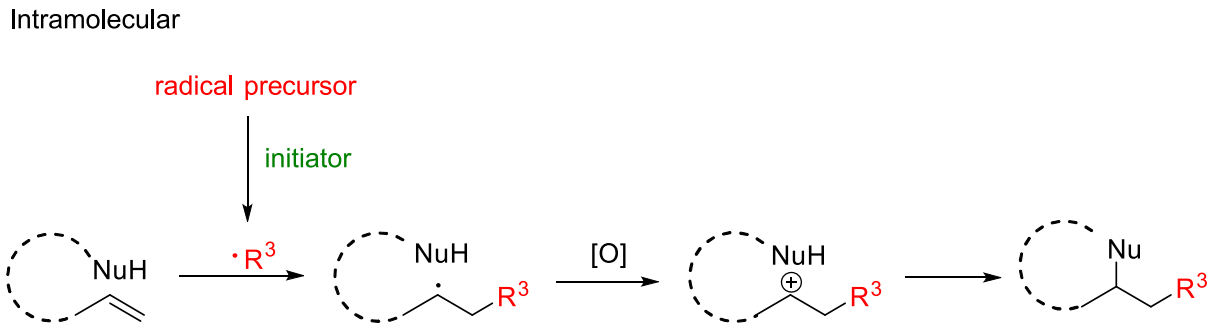
Scheme 1-2. Monofunctionalization and difunctionalization of alkenes

An interesting method amongst those is radical difunctionalization of olefins (Scheme 1-3).[13] This method enables olefin functionalizing, which is initiated by a radical addition to the carbon-carbon double bond, forming a new C-centered radical intermediate of type **2**. This intermediate radical **2** can either combine with another radical donor to give the product **3** or be further oxidized to a carbocation **4**. The carbocation **4** can be attacked by nucleophile to give the product **5**.



Scheme 1-3. Typical intermolecular radical-mediated difunctionalization of olefins

The difunctionalization of olefins by radicals and nucleophiles is extremely interesting for chemists in the field of radical chemistry. This protocol allows difuntionalization of olefins with a wide variety of reagents in high chemo- and regioselectivity, which enables radicals and nucleophiles to react complementarily.[12] Certainly, the intramolecular radical difunctionalization of olefins can provide a new approach for synthesis of cyclic compound. (Scheme 1-4)



Scheme 1-4. Typical intramolecular pathway for difunctionlization of olefins by radical and nucleophile

Over the past decade, the radical difunctionalization of olefins has made remarkable progress due to the development of transition metal catalysts, organo-catalysts, photo- or electro chemistry and other technologies. Although some interesting synthetic methods have been developed towards this goal, there is as of yet no method with a truly broad substrate scope of both radicals and nucleophiles, which has spurred our efforts for further research.[14]

In the following chapters, an overview of difunctionalization of olefins by radicals and nucleophiles is given. Radicals that are either carbon- or heteroatom-centered or a wide range of nucleophiles are described, as well as, some interesting methods such as atom- or group transfer radical additions. This thesis does not aim to be a comprehensive presentation of all the known literature but instead highlights the typical cases and some recent examples that best demonstrate the current state of affairs.

BACKGROUND

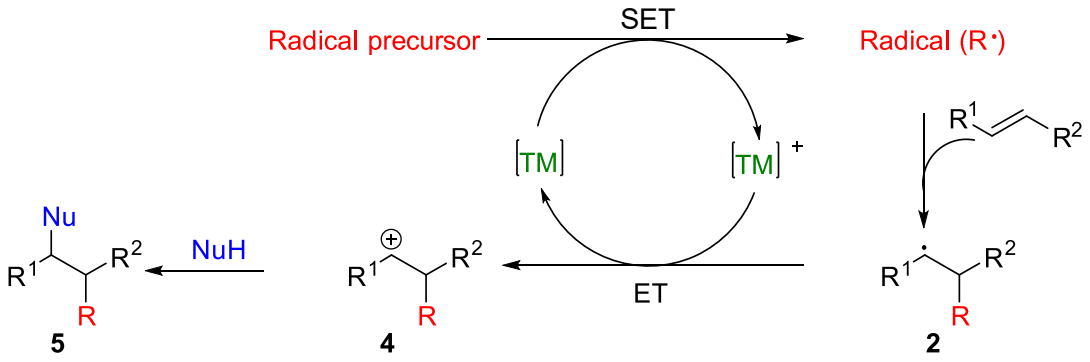
Metal-catalyzed radical difunctionalization of olefins

Introduction

Recently, transition metal-catalyzed radical difunctionalization of olefins has progressed remarkably. In this section, the historical developments and typical reports in the particular area is highlighted. Due to the tremendous development of novel methods. There have been a number of excellent reviews written on this subject.[12,13,15]

Overview of different transition metal catalysts

Typically, the initial radicals could be generated by transition metal catalyst through single electron transfer (SET) with some radical precursors, such as peroxides. The addition of initial radicals to carbon-carbon double bonds, mostly styrene derivatives are used in the transformation to form a stabilized benzylic radical **2**. Oxidation by the transition metal intermediate regenerates the catalyst and gives the benzylic carbocation **4**, which is then attacked by the nucleophile to provide the final product **5**.

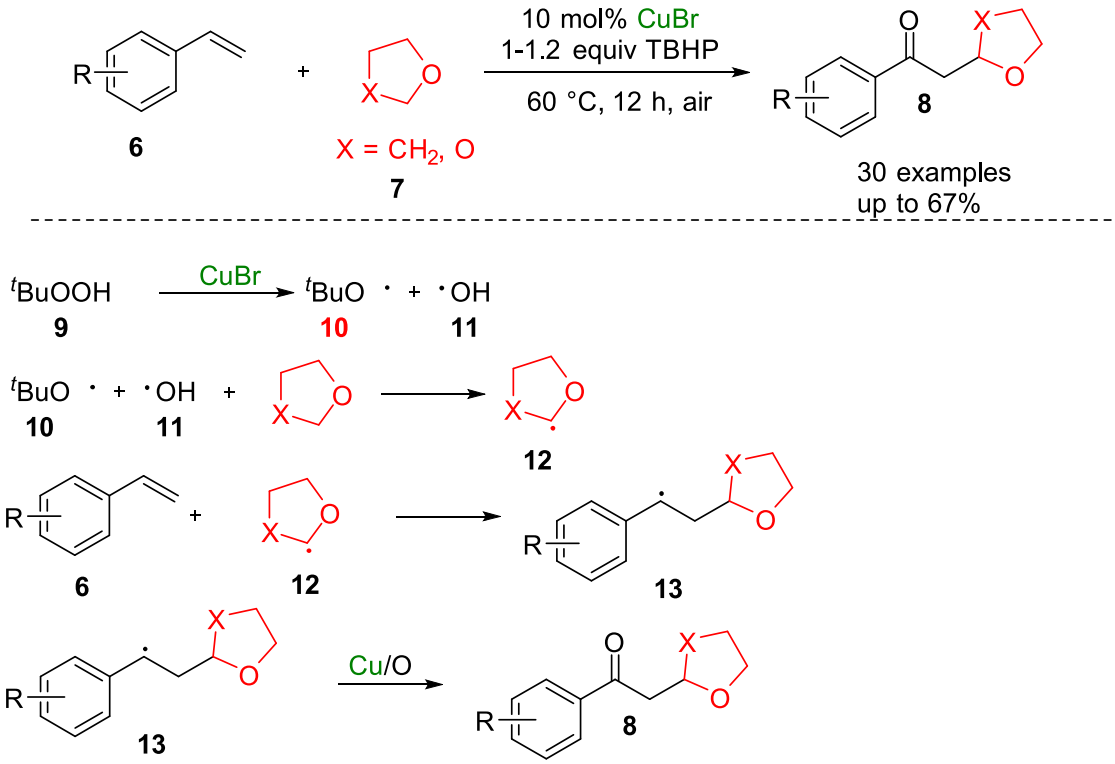


Scheme 2-1. Transition metal catalyzed radical difunctionalization of olefins.

Based on this concept, chemists have developed many protocols for the addition of carbon- or heteroatom-centered radicals with nucleophiles into carbon-carbon double bond by using transition metal catalysts over the past decade.[12,16]

Transition metal-catalyzed oxidative difunctionalization of olefins

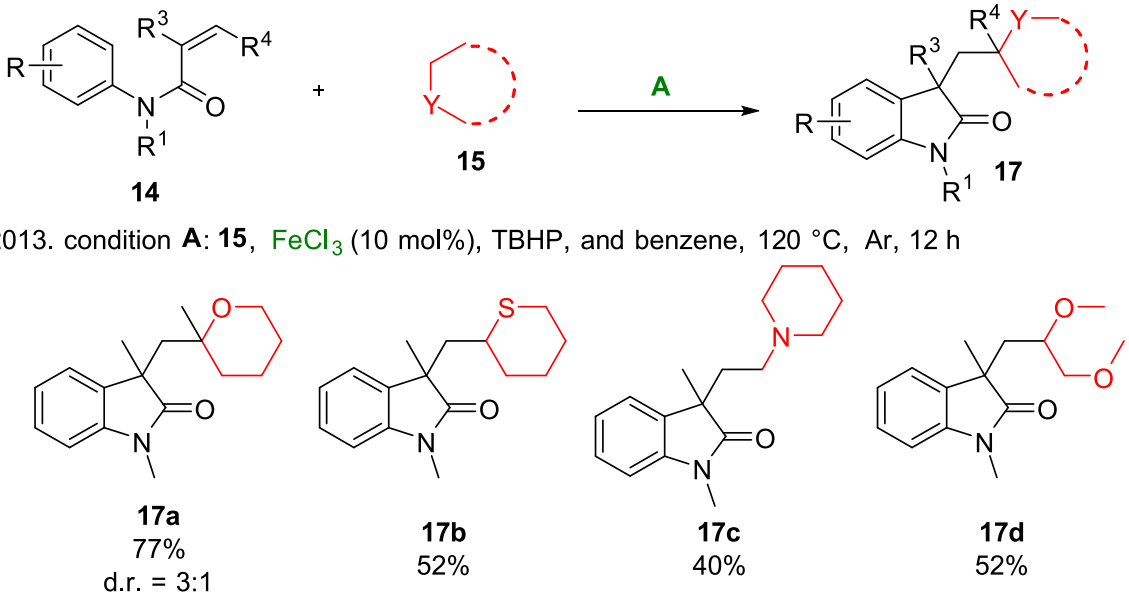
In 2009, Zhang and co-workers firstly reported a copper-catalyzed difunctionalization reaction of vinylarenes with cyclic ethers in the presence of *tert*-butyl hydroperoxide (TBHP) (Scheme 2-2).[17] With the combination of CuBr and TBHP, *tert*-butyoxyl radical **10** and hydroxyl radical **11** were generated, which can then engage with cyclic ethers **7** in a hydrogen atom transfer (HAT) step, forming a new carbon centered radical **12**. The addition of **12** to alkenes could deliver the benzylic radical intermediate **13**, which reacted with the oxidant to give the final product **8**. To the best of our knowledge, this is the first example of a transition metal catalyzed oxidative difunctionalization of olefins with unactivated radical precursors. However, this method showed low reactivity and suffered from a limited substrate scope.



Scheme 2-2. Copper-catalyzed difunctionalization of vinylarenes with cyclic ethers.

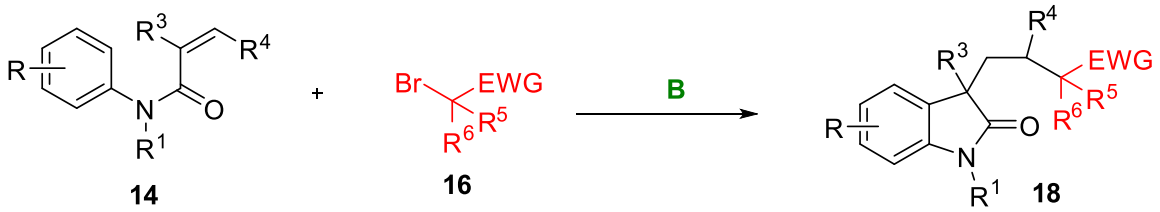
Of particular interest for the further development of difunctionalization of vinylarenes with cyclic ethers, in 2010 and 2012, the group of Wang and Park developed metal-nanoparticles as catalysts,[18,19] which could catalyze the reaction more efficiently leading to higher yields of the desired products.

In 2013, Li and co-workers reported an iron-catalyzed oxidative 1,2-alkylarylation of activated alkenes.[20] With the combination of the iron catalyst and a peroxide source, cyclic ethers can be efficient radical precursors. A cascade radical reaction through radical cycloaddition, single electron transfer, oxidation and deprotonation to give the desired products was achieved. However, this reaction needs an organic base, DBU, as a ligand, and moreover the high temperature limited the application in other fields.

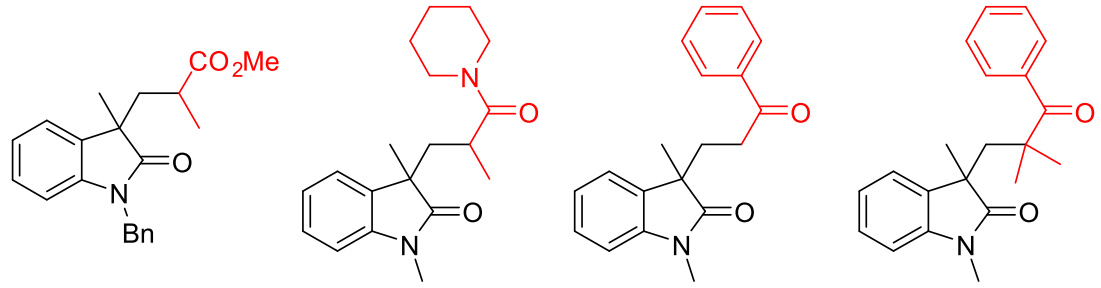


Scheme 2-3a. Transition metal-catalyzed 1,2-alkylarylation of activated alkenes

In 2014, the same group developed a palladium-catalyed Heck-type insertion reaction (Scheme 2-3b).[21] the reaction, which required a Ag_2CO_3 additive, was proposed to proceed via a radical pathway, with a key bromine atom transfer step.



2014. Condition **B**: **16**, [$PdCl_2$ (5 mol%), dppe (10 mol%), Ag_2CO_3, and toluene, 100°C for 24 h.



18a
66%
d.r. = 3:1

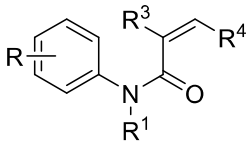
18b
55%
d.r. = 1.5:1

18c
61%

18d
62%

Scheme 2-3b. Palladium-catalyed Heck-type insertion reaction 1,2-alkylarylation of activated alkenes

Based on this model reaction, different radical precursors have been developed by many research groups, such as nitriles,[22] alkyl halides,[23] isocyanides,[24] hydrazinecarboxamides,[25] alkyne halide,[26] ketones,[27] AIBN,[28] as well as other transition metal catalysts.



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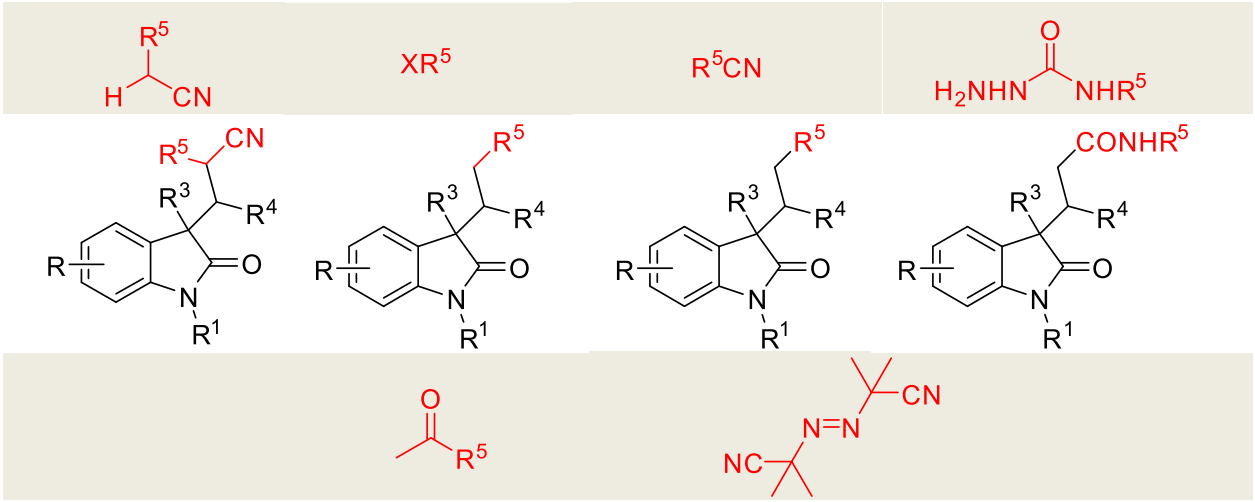
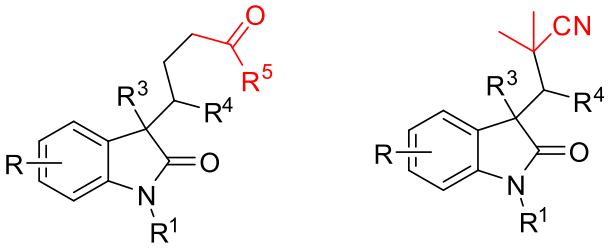
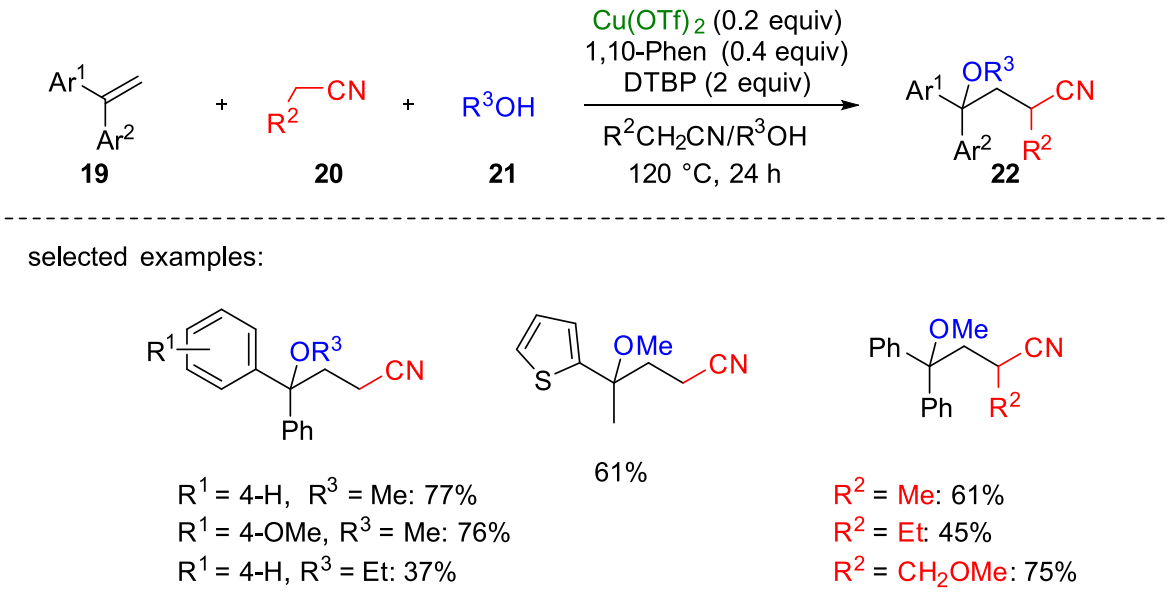




Scheme 2-4. Summary of radical precursors for functionalizing oxindol-derived structures

In 2014, Nevado and co-workers reported a radical-mediated arylphosphonylation and arylazidation of activated alkenes.[29] Different α-aryl-β-azido and α-aryl-β-phosphonyl amides could be formed with excellent yields and highly regioselectivies. One year later, the same group used the same concept to achieve a stereo-selective synthesis of highly functionalized indanes and dibenzocycloheptadienes.[30]

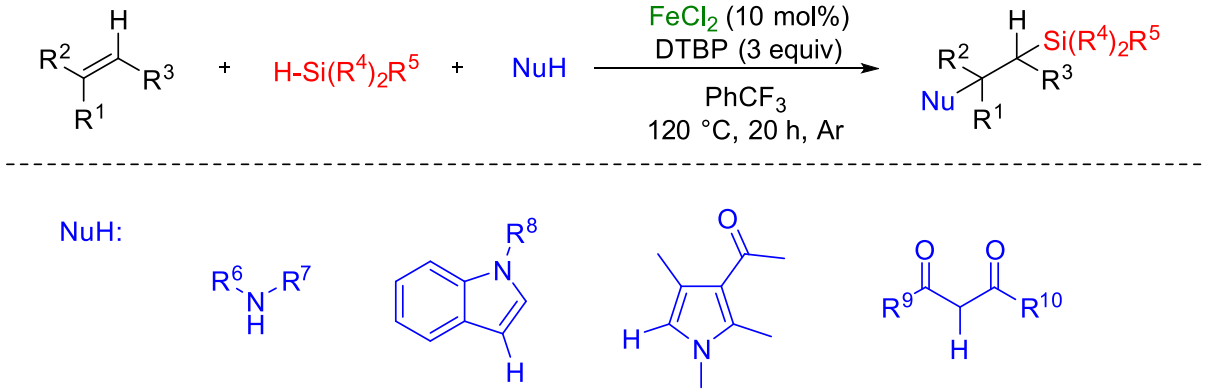
In 2015, Zhu and co-worker reported a copper-catalyzed intermolecular carboetherification of alkenes using nitriles and alcohols (Scheme 2-5).[31] This reaction not only provides a simple method for the construction of a Csp^3-Csp^3 and a Csp^3-O bond in one-step, but also an efficient way for oxidative difunctionlization of olefins by radicals and nucleophiles.



Scheme 2-5. Copper-catalyzed the alkoxycyanomethylation of alkenes.

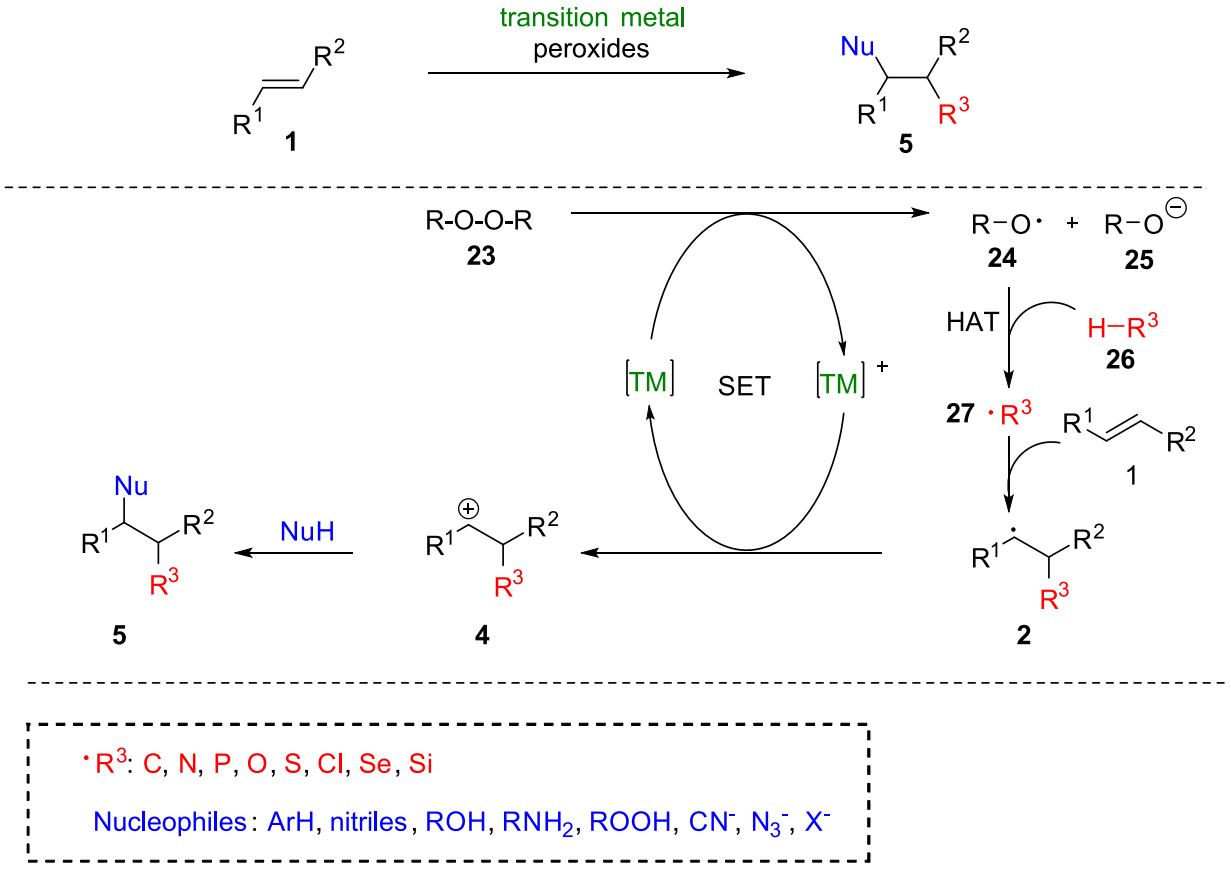
A similar method was reported by Lei's group in the same year.[32] In 2017, Zhu's group developed a three-component carboazidation of alkenes,[33] which used NaN_3 instead of alcohols as the nucleophile. In the same year, groups of Li and Luo reported an iron-catalyzed intermolecular 1,2-difunctionalization of olefins with silanes and nucleophiles.[34] This protocol enables silanes as radical precursors, with nucleophiles, such as amines, amides, indoles, pyrroles, and 1,3-dicarbonyls, which provides a powerful method for the synthesis of silicon-containing alkane derivatives (Scheme 2-6).

The common concept for these reactions are analogous to those presented above. Peroxides **23** can undergo homolytic cleavage of the O-O bond in the presence of transition a transition metal catalyst, generating a hydroxy-complex of higher oxidation state and an alkoxy radical **24**. **24** can then abstract a hydrogen atom from **26** through HAT to generate a new radical **27**. Addition of **27** to olefins forms a new C-centered radical **2**, which is then oxidized to give a carbocation **4** and regenerate the catalyst. **4** can then be attacked by nucleophiles to form the final products **5**. This concept is a so called oxidative difunctionalization of olefins by radicals and nucleophiles.



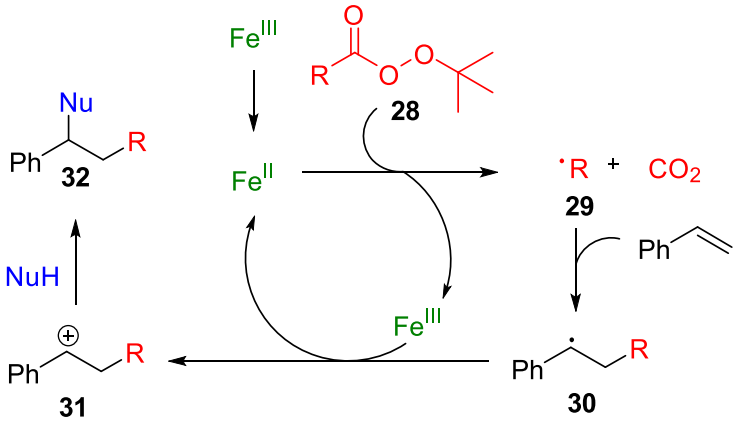
Scheme 2-6. Iron-catalyzed intermolecular 1,2-difunctionalization of olefins with silanes and nucleophiles

With the development of transition metal-catalyzed oxidative difunctionalization of olefins, various radicals have been used, such as C-centered radicals,[35] N-centered radicals,[36,37] P-centered radicals,[38] S-centered radicals[39,40] and others[12,13,15] as well as nucleophiles (Scheme 2-7).



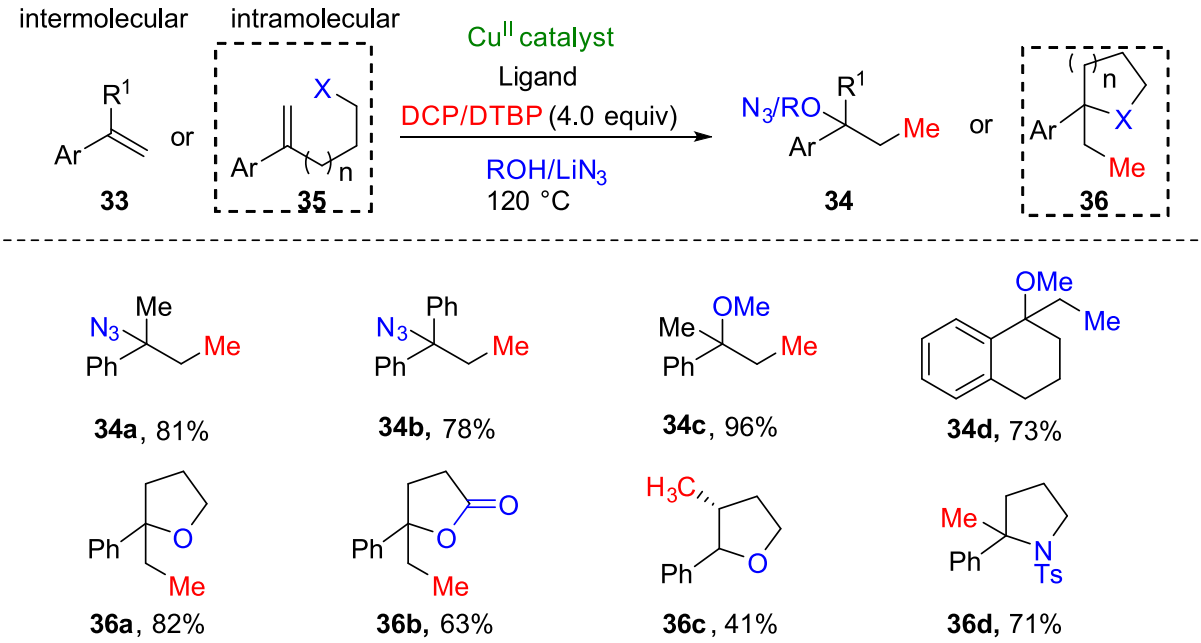
Scheme 2-7. Transition metal-catalyzed difunctionalization of alkenes by radical and nucleophile

In general, peroxides are widely used for radical difunctionalization of olefins, not only because they are good oxidants but also ideal radical precursors.[41] In 2017, Bao and co-workers reported an oxy-alkylation of alkenes with peroxides.[42] In the presence of iron catalyst, several lauroyl peroxides **28** could react with alkenes. A radical-polar crossover mechanism was proposed. An alkyl radical **29** was formed by losing CO_2 in the presence of the iron catalyst with peroxide **28**. Then the alkyl radical **29** reacts with styrene to form a benzylic radical **30**, which is oxidized by iron(III) to give a carbocation **31** and iron(II). The carbocation **31** was then attacked by a nucleophile to deliver the desired product **32** (Scheme 2-8). The same group also developed a carboamination of alkenes through a Ritter reaction in the same year.[43] By using this method, primary, secondary, and tertiary alkyl radicals, and aryl radicals can be easily generated from peroxides, which provides a powerful protocol in difunctionalization of alkenes, to generate the molecules that are otherwise difficult to access.



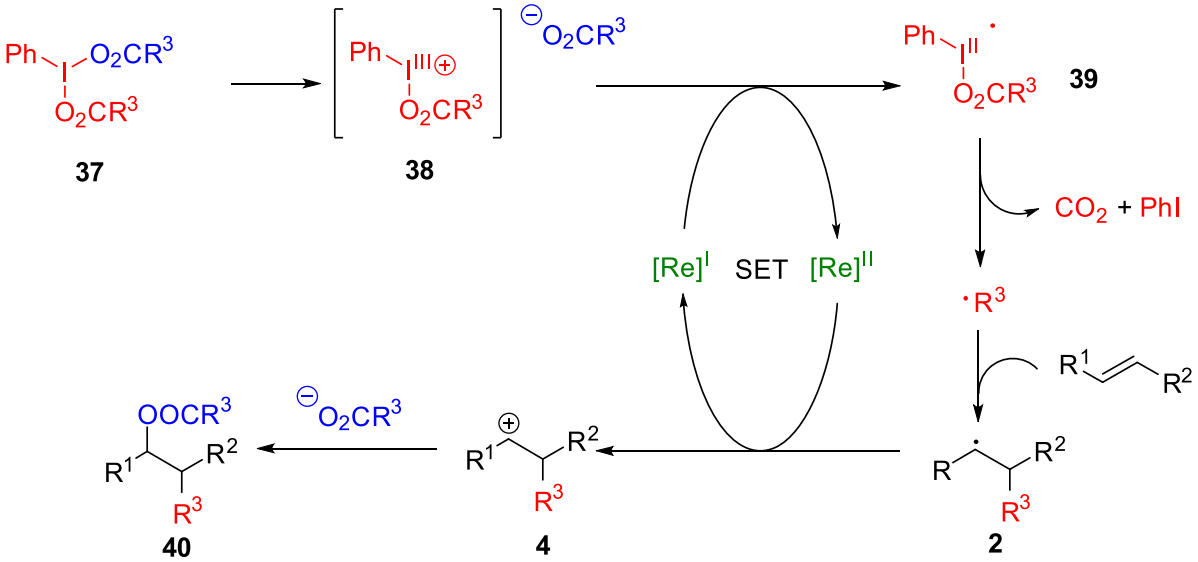
Scheme 2-8. Oxy-alkyation of alkenes with peroxides

In 2018, Zhu and co-workers reported a copper-catalyzed methylative difunctionalization of alkenes.[44] By using dicumyl peroxide or di-*tert*-butyl peroxide (DTBP) as methyl sources, the difunctionalization of alkenes with different nucleophiles, such as alcohols, carboxylic acids, and sulfonamides was achieved. This protocol allows methylated ethers, azides, tetrahydrofurans, tetrahydropyrans, γ-lactones, and pyrrolidines with concurrent generation of a quaternary carbon in good to excellent yields (Scheme 2-9). In 2020, two more nucleophiles $TMSN_3$[45] and $ArB(OH)_2$[46] were applied under similar reaction conditions by Bao's group.



Scheme 2-9. Methylative difunctionalization of alkenes

The group of Wang reported a rhenium-catalyzed alkene oxyalkylation with hypervalent iodine reagents via decarboxylation in 2013.[47] It is the first time that hypervalent iodine reagents **37** have been used as alkylation and oxygenation sources in alkene difunctionalizations. The method showed a wide substrate scope with excellent regioselectivities (Scheme 2-10). Later, an iron-catalyzed acyloxyalkylation of styrenes using hypervalent iodine reagents was reported by Kuninobu's group in 2017.[48] Compared with the previous report, the scope of hypervalent iodine reagents with various functional groups was expanded. This protocol proceeded in a moderate to good yields and could also performed on gram scale.



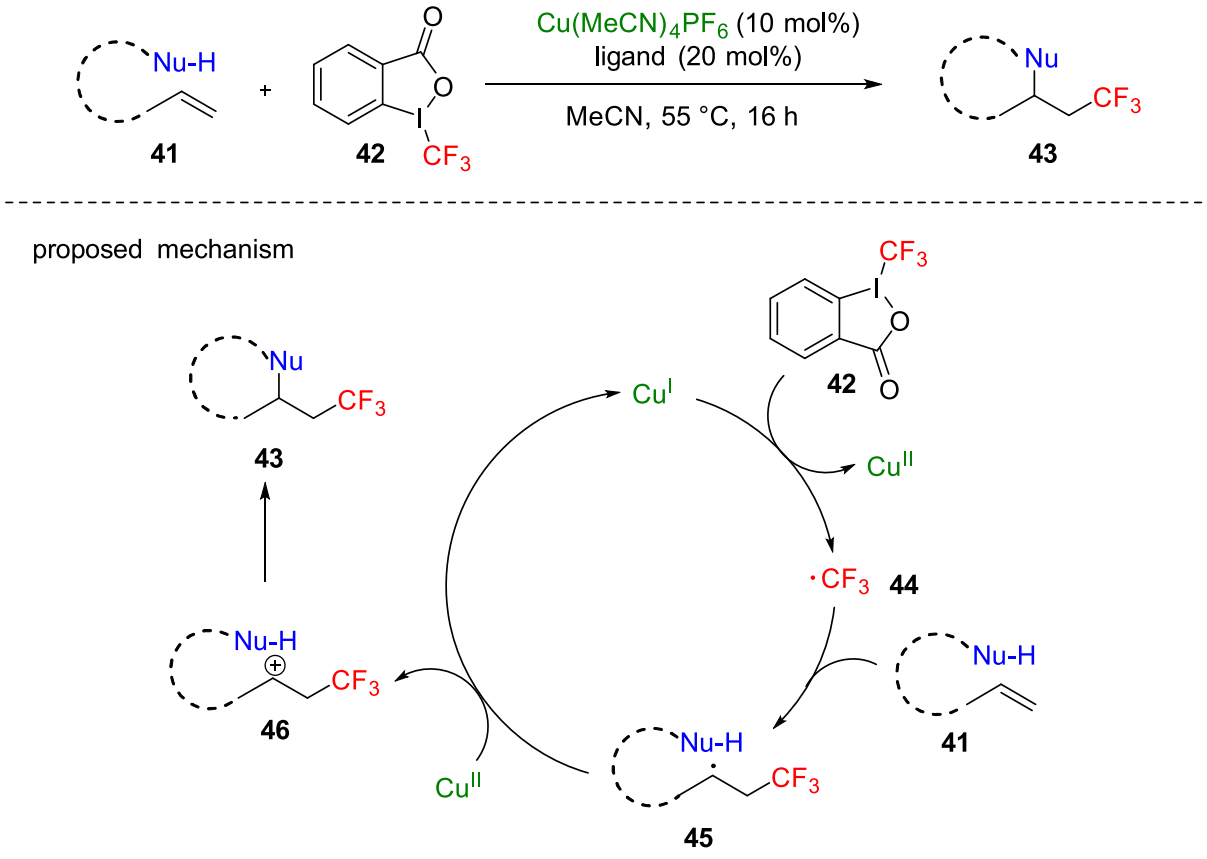
Scheme 2-10. Rhenium-catalyzed alkene oxyalkylation with hypervalent iodine reagents.

In a short summary, the use of transition metals to catalyze oxidative difunctionalization of olefins by radical and nucleophile has been investigated by many chemists. Iron and copper catalysts are frequently used for initiating the radical precursors and electron transfer step. A wide range of radicals and nucleophiles have been added across alkenes, which provide a general approach for the preparation of functionalized compounds. However, most of these methods need high temperatures, prolonged reaction times, and a large excess of the peroxide. Thus, the development of a redox-neutral method under mild reaction conditions with a board substrate

scope will enable the rapid construction of molecular complexity in a green and sustainable manner.

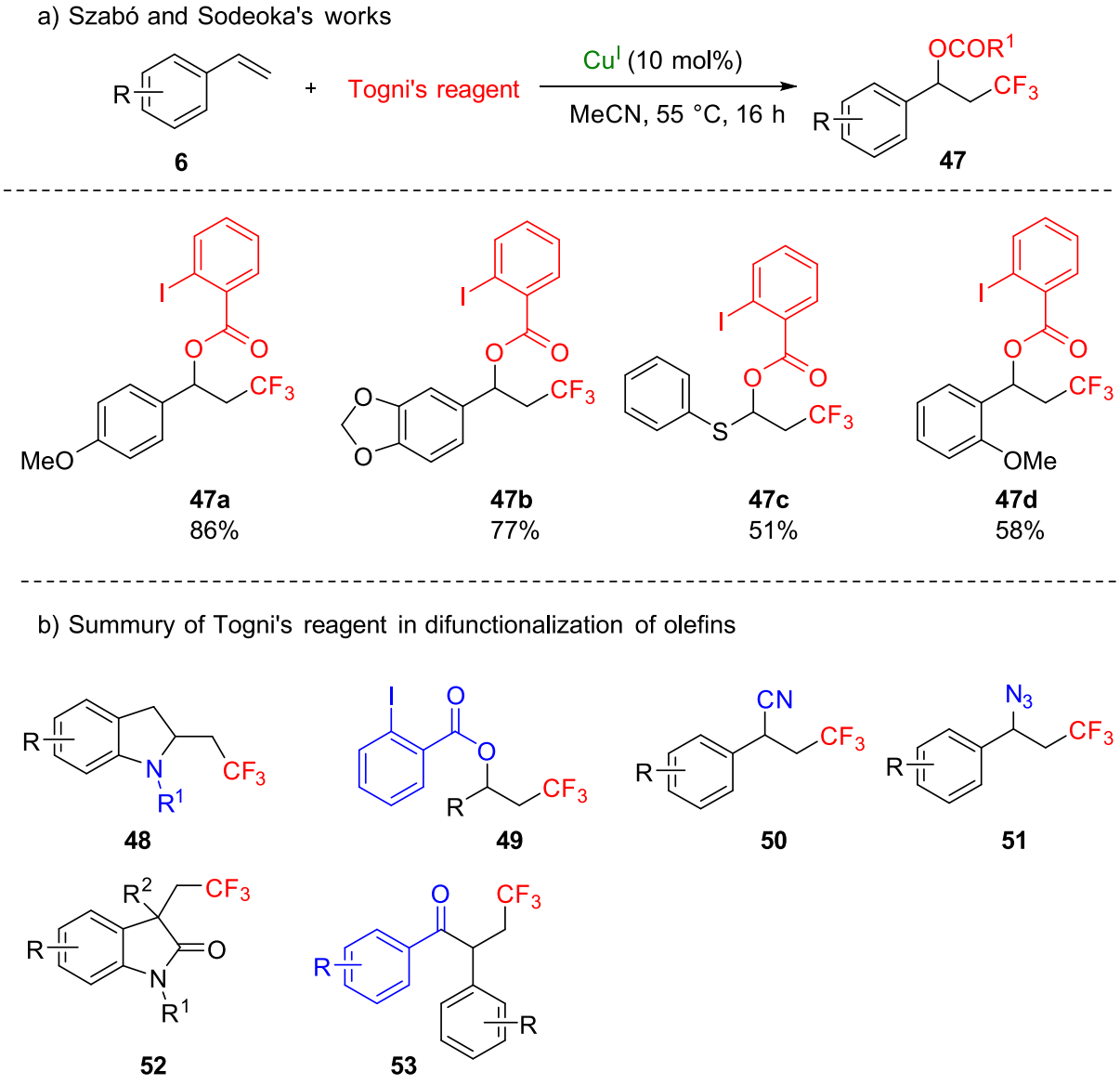
Transition metal-catalyzed trifluoromethylation of olefins

Another approach relies on trifluoromethylation of olefins with CF_3 radical has been well studied, in this section, we aim to make a short summary in order to show the achievements in this area. In 2012, Buchwald and Zhu reported transition metal-catalyzed trifluoromethylation of olefins.[49] This method provides a mild, versatile and convenient way for oxytrifluoromethylation of unactivated alkenes. Nucleophiles, such as carboxylic acids, alcohols, and phenols are all suitable for this reaction. Mechanistic studies suggest that the Togni's reagent **42** is reduced by the copper catalyst to generate the CF_3 radical **44**, followed by radical addition and single electron transfer to give carbocation intermediate **46** and regenerate the copper catalyst. Subsequent trapping of **46** with the nucleophile leads to the desired products **43**. One year later, the same group used chiral ligands to enable an asymmetric process that delivers similar products with good enantioselective (Scheme 2-11).[50]



Scheme 2-11. Oxytrifluoromethylation of unactivated alkenes by CF_3 radical.

In the same year, the groups of Szabó and Sodeoka both reported a copper-catalyzed three-component trifluoromethylation of alkenes.[51,52] Their approaches proceed with high regio- and stereoselectivity, and also a significant breakthroughs as they utilised Umemoto's reagent[53] and Togni's reagent respectively (Scheme 2-11a).[54]



Scheme 2-12. CF_3 radicals in transition metal-catalyzed difunctionalization of olefins.

With the development of transition metal-catalyzed trifluoromethylation of olefins with CF_3 radicals, there have been a number of developed methods. To summarize, these includes oxytrifluoromethylation, aminotrifluoromethylation **48**,[55] allylic trifluoromethylation **49**,[56] cyanotrifluoromethylation **50**,[57,58] carbotrifluoromethylazidation **52**,[59,60] and trifluoromethylation rearrangement **53** (Scheme 2-11b).[61,62]

Most of the methods facilitate convenient trifluoromethylation of olefins under mild reaction conditions with high chemo- or regioselectivties. Owing to the widespread use of olefin trifluoromethylation, this area has now became an increasingly hot topic for the difunctionalization of olefins.[63]

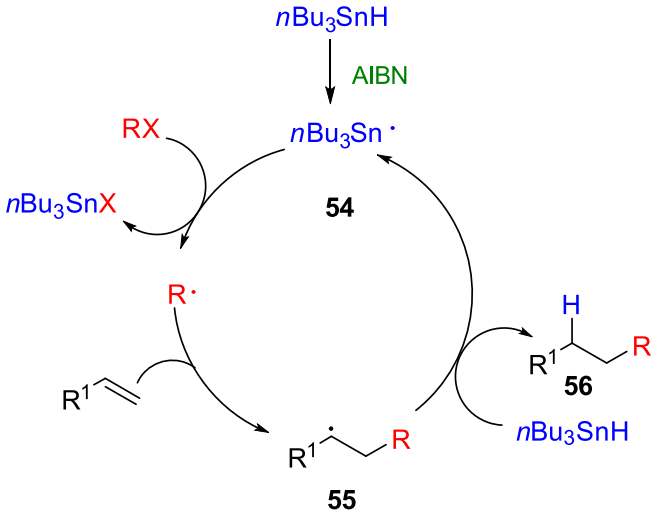
Metal-free radical difunctionalization of olefins

Introduction

With the development of difunctionalization of olefins, a common drawback to these methods is the use of precious or toxic transition metal catalysts. Finding more environmentally friendly and inexpensive oxidants without needing metal catalysts is extremely important for synthetic chemists. In this section, the advancements of radical mediates olefin difunctionalization under metal-free conditions is summarized. Again, a number of the important literatures and reviews were written on the subject.

Overview of metal-free radical chain-difunctionalization of olefins

Almost every radical chain reaction need an initiator. Thus, the radical difunctionalization of olefins that proceed through a radical chain mechanism, can be divided by the respective initiator.

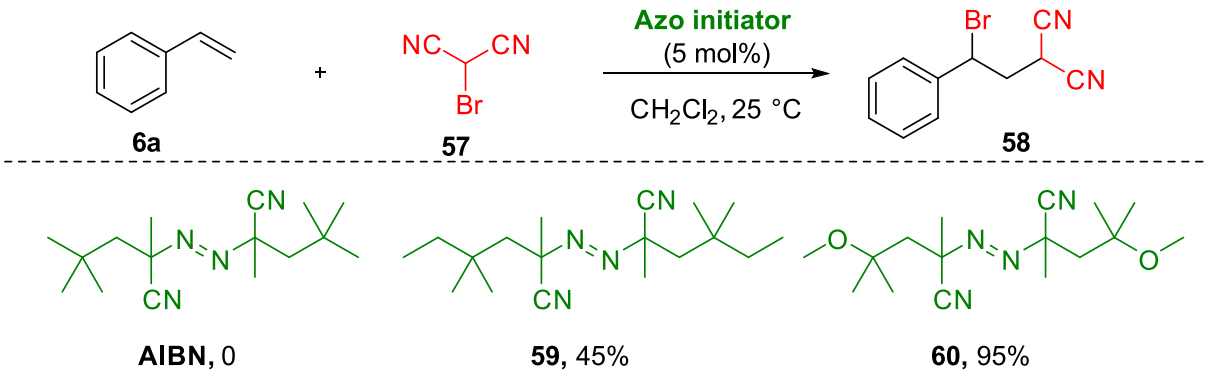


Scheme 2-13. Azo initiators with Tin hydride reagents for radical chain reactions

Azo initiators, such as azobisisobutyronitrile (AIBN) are well known radical initiators.[64,65] In the early developments, most radical chain difunctionalization of olefins relied on tin hydride reagents combined with AIBN, typically tributyltin hydride.[66,67] The decomposition of azo compounds leads to the formation of nitrogen and two radicals that undergo hydrogen atom

transfer from nBu$_3$SnH, and delivery the tributyltin radical **54**, which then facilitates the atom-transfer difunctionalization of olefin. However, most tin hydride reagents are toxic, and the tin byproducts generated are difficult to remove completely, which limites the application in an industrial setting.

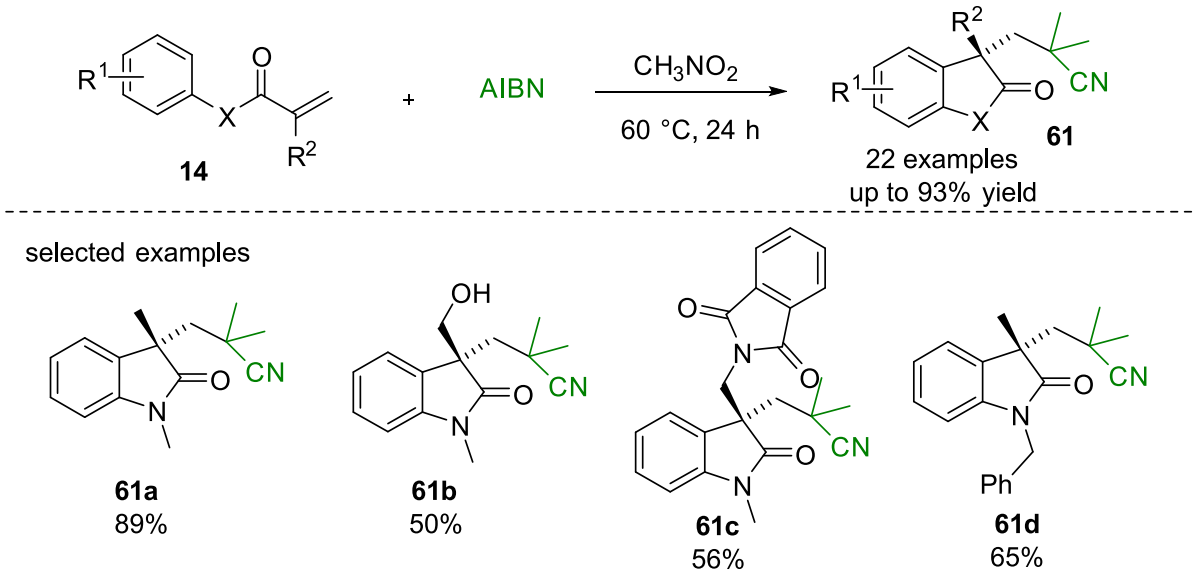
Azo initiators are widely used for enabling atom-transfer radical addition reactions (ATRA).[68-72] Kita and co-workers reported atom-transfer radical addition reactions with bromomalononitrile in 1998.[73] Using catalytic quantities of an azo initiator, the desired product was formed under mild reaction conditions (Scheme 2-14).



Scheme 2-14. Azo initiators in atom-transfer radical addition reactions with bromomalononitrile

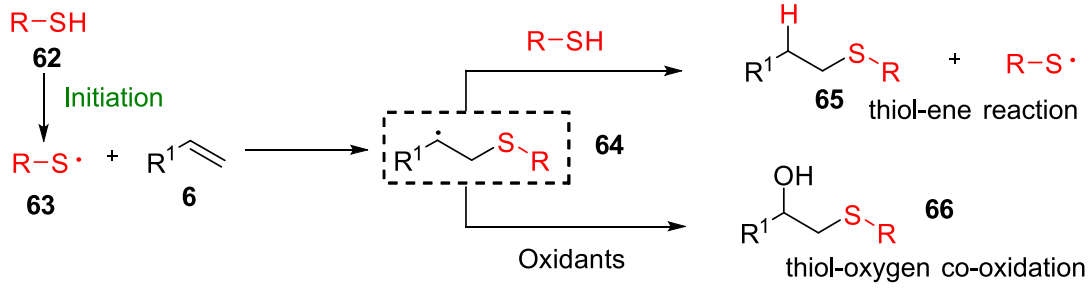
Moreover, azo initiators can also be donors of cyano or cyano-containing functional groups. The incorporation of cyano or cyano-containing functional groups into organic structures is a hot research topic in organic synthesis.

In 2015, Guo and co-workers developed a simple and metal-free direct cyanoisopropylation/arylation of *N*-arylacrylamides or *N*-alkyl-*N*-(arylsulfonyl)acrylamides with AIBN (Scheme 2-15).[74]



Scheme 2-15. Metal-free cyanoisopropylation/arylation of alkenes

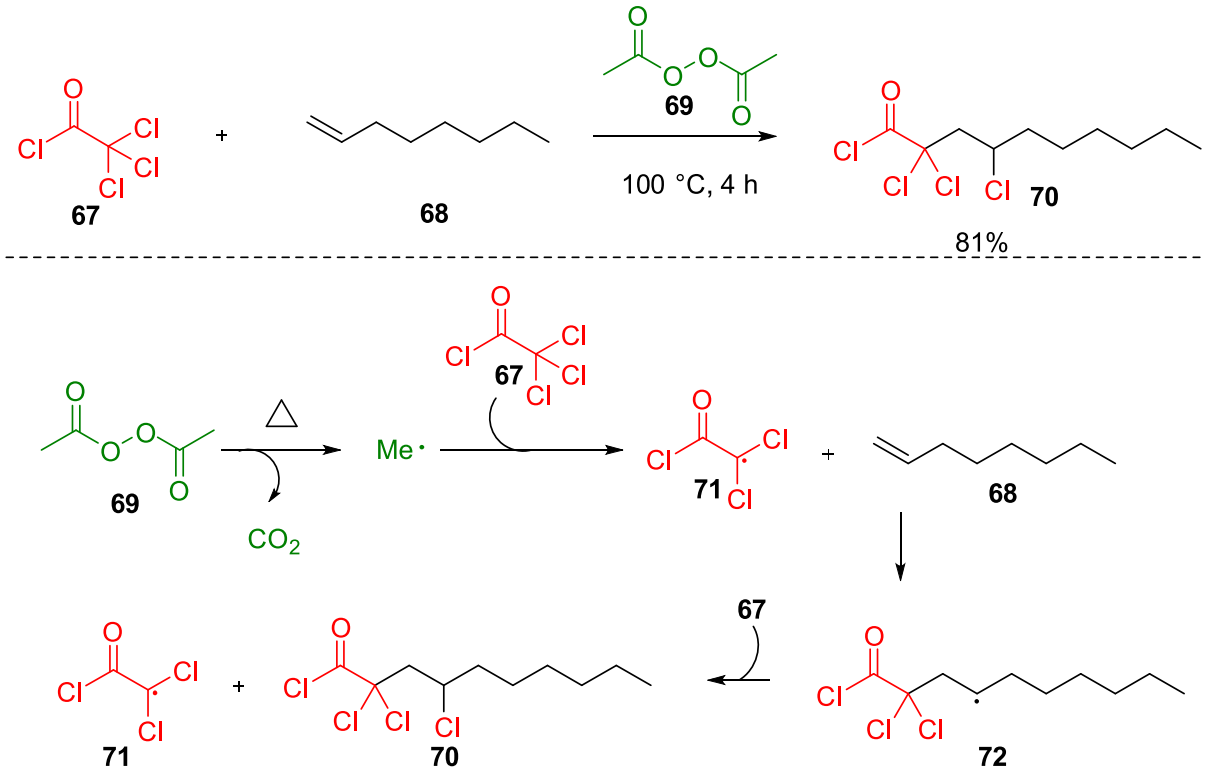
Together with azo initiators, peroxides are important thermal initiators.[75] The peroxides are easily decomposed into oxyl radicals because of the week O-O bond. A notable example is the thiol-ene reaction that was reported by Theodor in 1905.[76] Using either light, heat or peroxide initiators, the thiyl radicals **63** were generated through HAT, which then added to the carbon-carbon double bond to form a new carbon centered radical **64**, followed by hydrogen atom transfer from thiol **62**. The thiol ene product **65** and another thiyl radical **63** were formed, which can subsequently participate in multiple propagation steps. Similarly, thiol-oxygen co-oxidation of olefins was first reported by Kharasch and co-workers in 1951,[77] as well as the radical difunctionalization reaction, both of which require UV irradiation or excess peroxides for initiating. These two type of radical difunctionalization reactions gained prominence in the late 1990s and early 2000s for their feasibility and wide range of applications (Scheme 2-16).[78] [79]



Scheme 2-16. Typical thiol-ene reaction and thiol-oxygen co-oxidation of olefins

The formation of carbon-centered radicals often requires homolytic cleavage of a carbon-halogen bond or carbon-hydrogen bond in the presence of radical initiators. However, both of these two approaches need higher temperature, which always sufficient in producing useless by-products or polymerization.[80] Thus, appropriate temperature is significant.

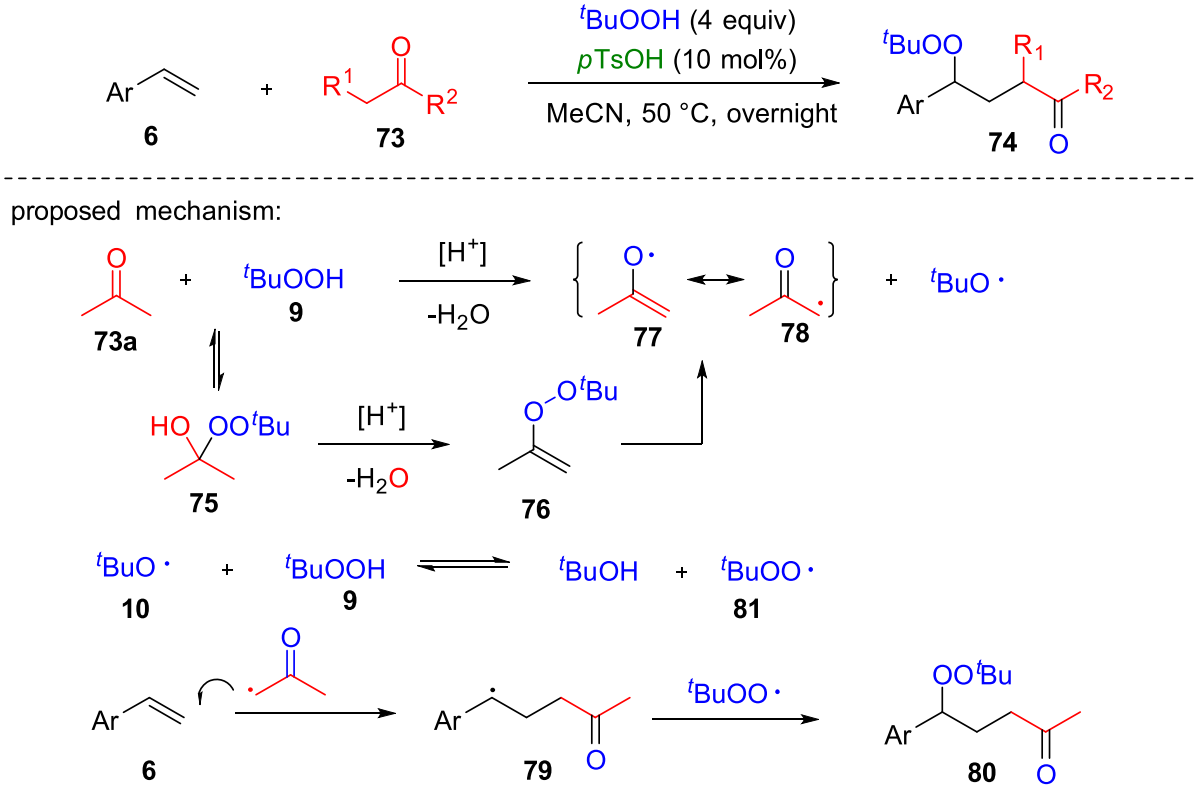
In 1945, Kharasch and co-workers reported an atom transfer radical addition, which has become known as the Kharasch reaction.[81,82] In the presence of radical initiators, carbon tetrachloride adds to olefins, to give the product in good yields. At 100 °C, peroxide **69** undergoes homolytic cleavage of the O-O bond, and after losing CO_2, forms a methyl radical, which can engage in the halogen atom transfer from **67** to generate a new radical **71**. **71** then adds to olefins to give a new C-centered radical **72**, which is trapped by an additional equivalent of **67** and generates the desired product **70** (Scheme 2-17).



Scheme 2-17. Kharasch addition of trichloracetylchloride to 1-octene

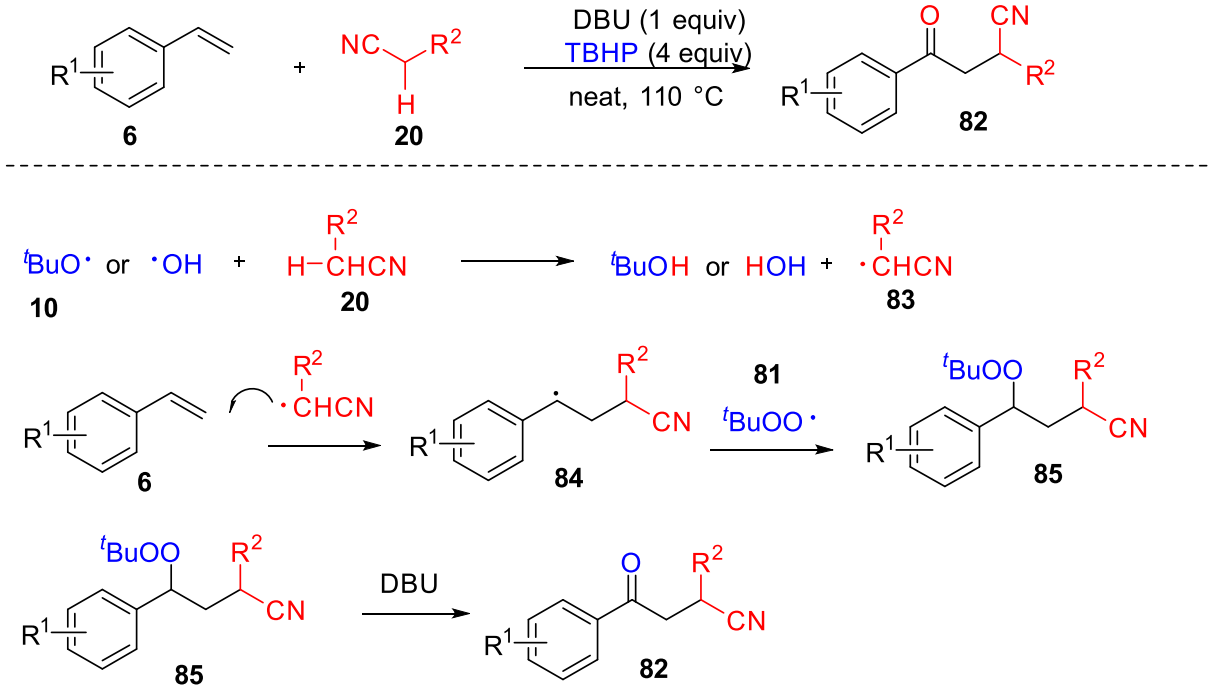
Although the majority of examples require photoredox or transition metal catalysts, there are a few published reports under transition metal free conditions.[83-85] The major problem is that an atom transfer radical polymerization (ATRP) reaction is much more favored than atom transfer radical addition reactions (ATRA). So far, transition metal-free processes are underdeveloped in the area of olefin difunctionalization.[86,87]

In 2014, Klussmann and co-workers reported an acid-catalyzed oxidative radical addition of ketones to olefins.[88] The resulting *γ*-peroxyketones can be further transformed into various useful products, such as 1,4-diketones, homoaldol products, and alkyl ketones. This protocol offers a valuable method for the addition of simple ketones to olefins under metal-free conditions. A radical chain mechanism was more favored in this reaction. In the presence of a strong Brønsted acid, TBHP reacts with ketone to form **75** and subsequently alkenylperoxide **76**. **76** can undergo facile homolytic bond cleavage, delivering the resonance-stabilized ketone radical **77** and a *tert*-butoxyl radical **78**. In the presence of ^{t}BuOOH, a fast equilibrium exists between **77** and the tertbutylperoxyl radical **78**, favoring the latter.[89] Addition of **78** to the carbon-carbon double bond generates **79**, which reacts with the peroxy radical **81** to give the final product **74** (Scheme 2-18).



Scheme 2-18. Oxidative radical addition of ketones to olefins

In 2016, Xing and co-workers reported a metal-free, difunctionalization of terminal vinylarenes with C(sp^3)–H bonds alpha to nitriles for the synthesis of γ-ketonitriles **82** (Scheme 2-19).[90] A similar mechanism to Klußmann's work was proposed.[88] The highly activated *tert*-butoxyl radical **10** or the hydroxyl radical abstracts the *α*-H atom from the nitrile **20** to generate a primary alkyl radical **83**. Addition of the primary alkyl radical **83** to the carbon-carbon double bond forms a new benzylic radical **84**. **85** is then formed after radical-radical coupling between the benzylic radical **84** and tBuOO·. Finally, **85** is converted to the desired product **82** in the presence of DBU (Scheme 2-16). A similar method was also reported by the groups of Li and Duan with aldehydes[91] or alcohols[92] as hydrogen donors.

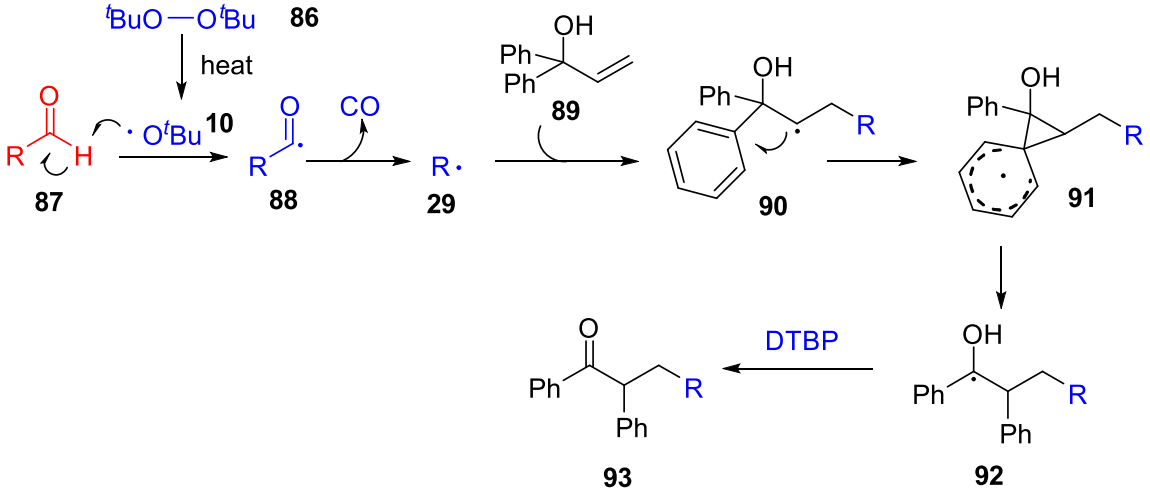


Scheme 2-19. Difunctionalization of terminal vinylarenes with alkyl nitriles

Additionally, other TBHP-involved radical difunctionalization of alkenes have been developed recently.[93-96] In 2015, Wang and co-workers reported the difunctionalization of alkenes with I_2O_5

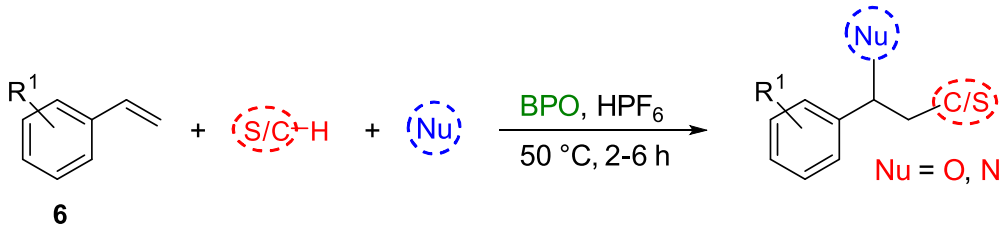
and P(O)–H compounds to synthesize *β*-iodophosphates, using TBHP as the radical initiator and oxidant.[97]

In 2017, Yu's group developed a metal-free 1,2-alkylarylation of allylic alcohols with aliphatic aldehydes.[98] Di-*tert*-butyl peroxide (DTBP) **86** was used as the initiator and oxidant in this reaction. DTBP was decomposed at 100 °C to form two *tert*-butoxyl radicals **10**, followed by hydrogen atom transfer and decarbonylation to give the alkyl radical **29**. The alkyl radical **29** then undergoes intermolecular radical addition to the diaryl allylic alcohol **89** to give a new radical intermediate **90**. After radical addition, neophyl rearrangement and oxidation generates the final product **93** (Scheme 2-20). Similar reactions with different peroxides have also been published.[99,100,101,102]



Scheme 2-20. 1,2-alkylarylation of allylic alcohols with aliphatic aldehydes

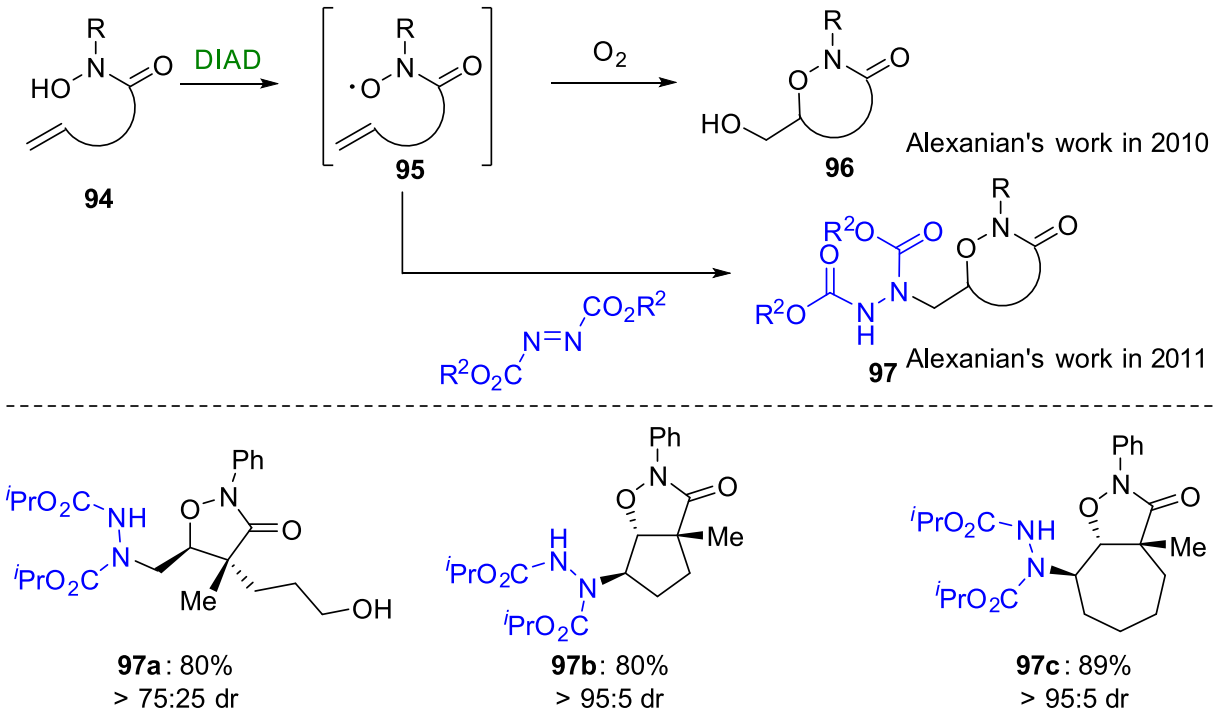
In 2020, Klußmann and Liu reported an acid-promoted radical-chain difunctionalization of styrenes with stabilized radicals and (N,O)-nucleophiles (Scheme 2-21).[103] The reaction proceeds through sequential addition of a radical and a nucleophile, which is suggested to react by a radical chain mechanism and hence does not requiring a catalyst. An electron transfer step to the benzoyl peroxide (BPO) oxidant is facilitated by protonation with a strong acid. This reaction will find in the chapter one of this thesis for a detailed discussion.



Scheme 2-21. Acid-promoted radical-chain difunctionalization of styrenes

Other oxidants and radical initiators, such as *tert*-butyl peroxybenzoate (TBPB),[104] (diacetoxyiodo)benzene,[105-107] *tert*-butyl nitrite,[108,109] disulfides[110-113] and molecular oxygen[114,115] have been successfully utilized for radical difunctionalization of olefins by other research groups.

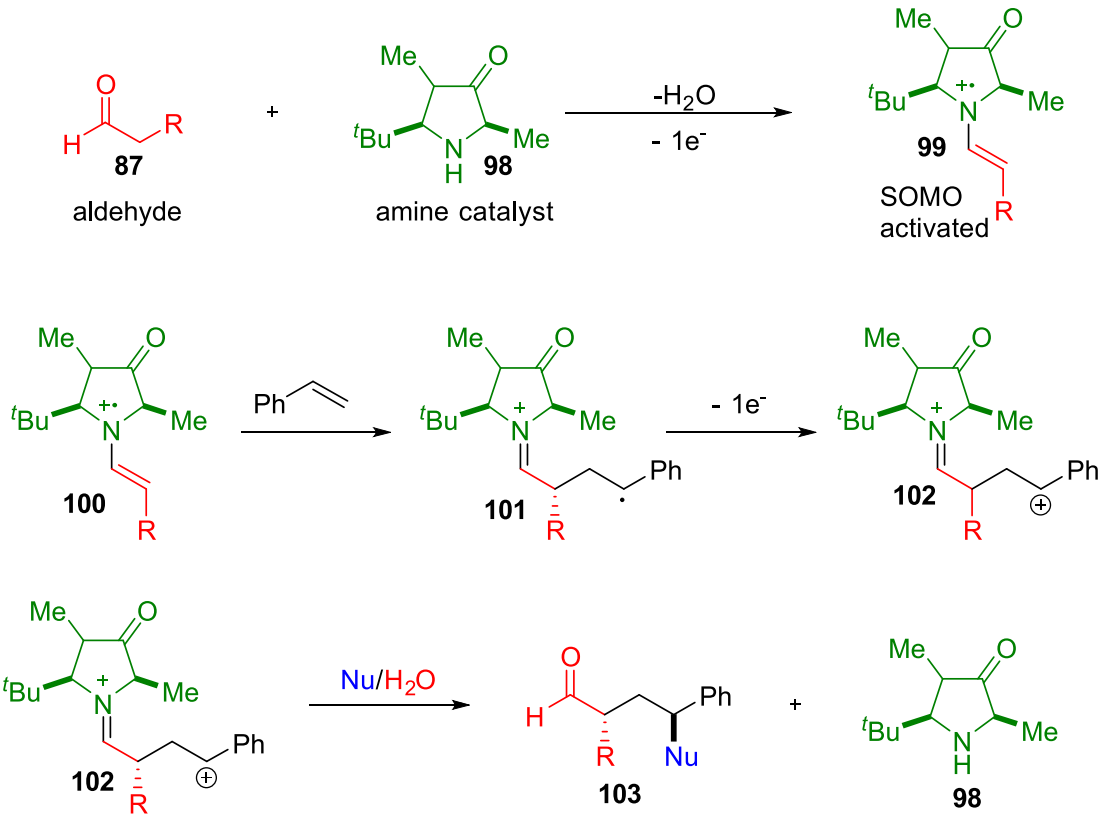
Later, Alexanian and co-workers reported a metal-free, aerobic dioxygenation of alkenes using hydroxamic acids in 2010.[116] By using hydroxamic acids **94**, radical difunctionalization of olefins was achieved for a wide range of unsaturated substrates and affords dioxygenation products with differentiated oxygen atom functionalities. One year later, the same group reported an oxyamination of alkenes with even higher chemo- and regioselectivities (Scheme 2-22).[117]



Scheme 2-22. Oxyalkylation and oxyaminations of alkenes

Overview of organocatalytic radical difunctionalization of olefins

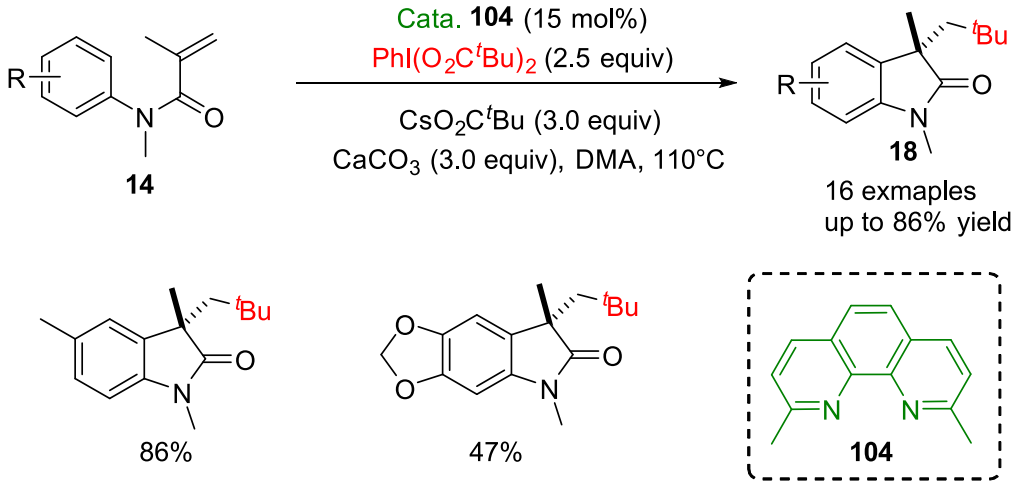
In 2008, Macmillan and co-workers developed a carbo-oxidation of alkenes using an amine organocatalyst.[118] This catalyst **98** was designed and used for what has become known as SOMO catalysis in difunctionalization of olefins for the first time. This protocol allows the enantioselective *α*-homobenzylation of aldehydes using a variety of alkenes (Scheme 2-23). In 2010, the same group used the same catalyst for the enantioselective synthesis of six- and five-membered carbocycles by cycloaddition from simple aldehydes and olefins with high enantioselectivies and high yields.[119] Few years later, the asymmetric synthesis of pyrrolidines was also reported with similarly high selectivities and yields.[120]



Scheme 2-23. SOMO amine catalysis for the difunctionalization of olefins

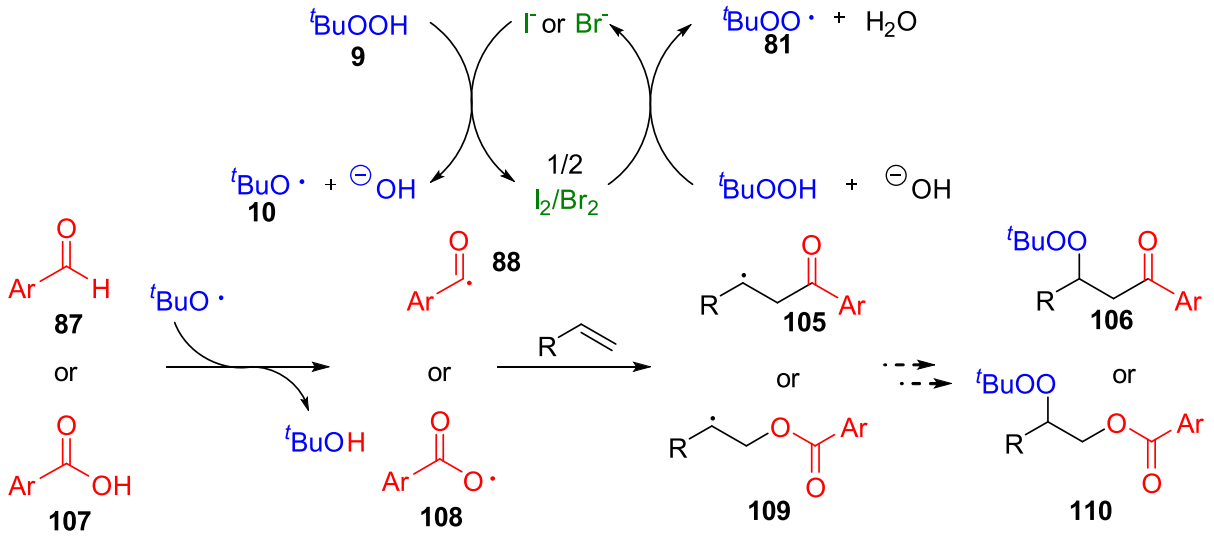
In 2012, Liu and co-workers reported a novel organocatalyzed arylalkylation of activated alkenes.[121] The dinitrogen compounds **104** play an important role, which may react with (diacetoxyiodo)benzene to form *tert*-butyl radical and then the *tert*-butyl radical promotes this

radical cyclization. This reaction provides a highly efficient way to synthesize a variety of oxindoles **18** from simple aryacrylamides **14** (Scheme 2-24).



Scheme 2-24. Organocatalyzed arylalkylation of activated alkenes

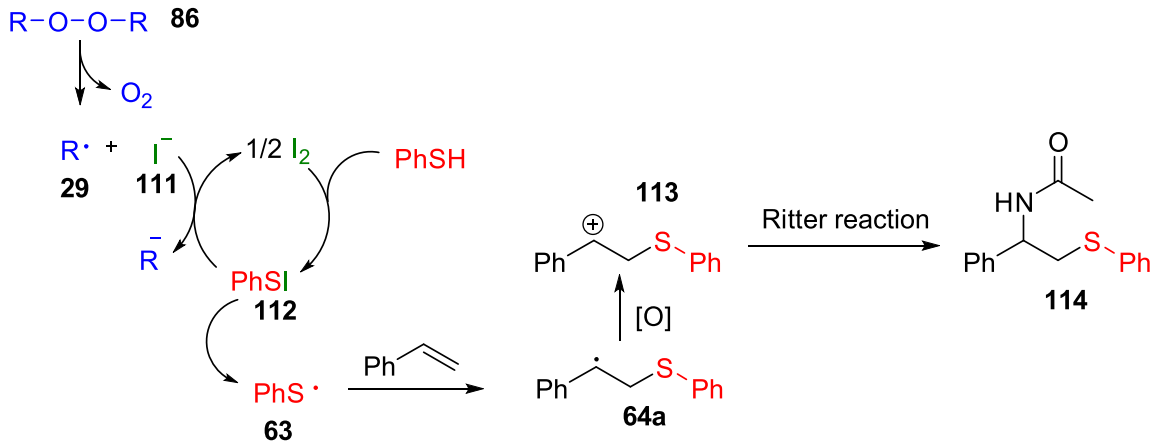
The uses of organic small molecules for catalyzing the difunctionalization of olefins has been further studied since. In 2013, Zhu's group reported a tetra-*n*-butylammonium iodide-catalyzed regioselective difunctionalization of unactivated alkenes.[122] In addition, Wang and co-workers reported a tetra-*n*-butylammonium bromide (nBu$_4$NBr) catalyzed carbonylation–peroxidation of



Scheme 2-25. nBu$_4$NI-TBHP and nBu$_4$NBr-TBHP systems for difunctionaliaztion of olefins

styrene derivatives.[123] Both *n*Bu$_4$NI-TBHP and *n*Bu$_4$NBr-TBHP systems have become widely used for the difunctionlization of olefins because of their high efficiency, lower toxicity and environmental friendliness (Scheme 2-25).[124,125]

In 2015, Mao's group reported a catalytic amount of NaI-catalyzed acetamidosulphenylation of alkenes with nitriles as the nucleophiles.[126] This is the first example where sodium iodide **111** was used as a catalyst for the difunctionalization of alkenes (Scheme 2-26). This protocol is suitable for a wide range of substrates with excellent yields.

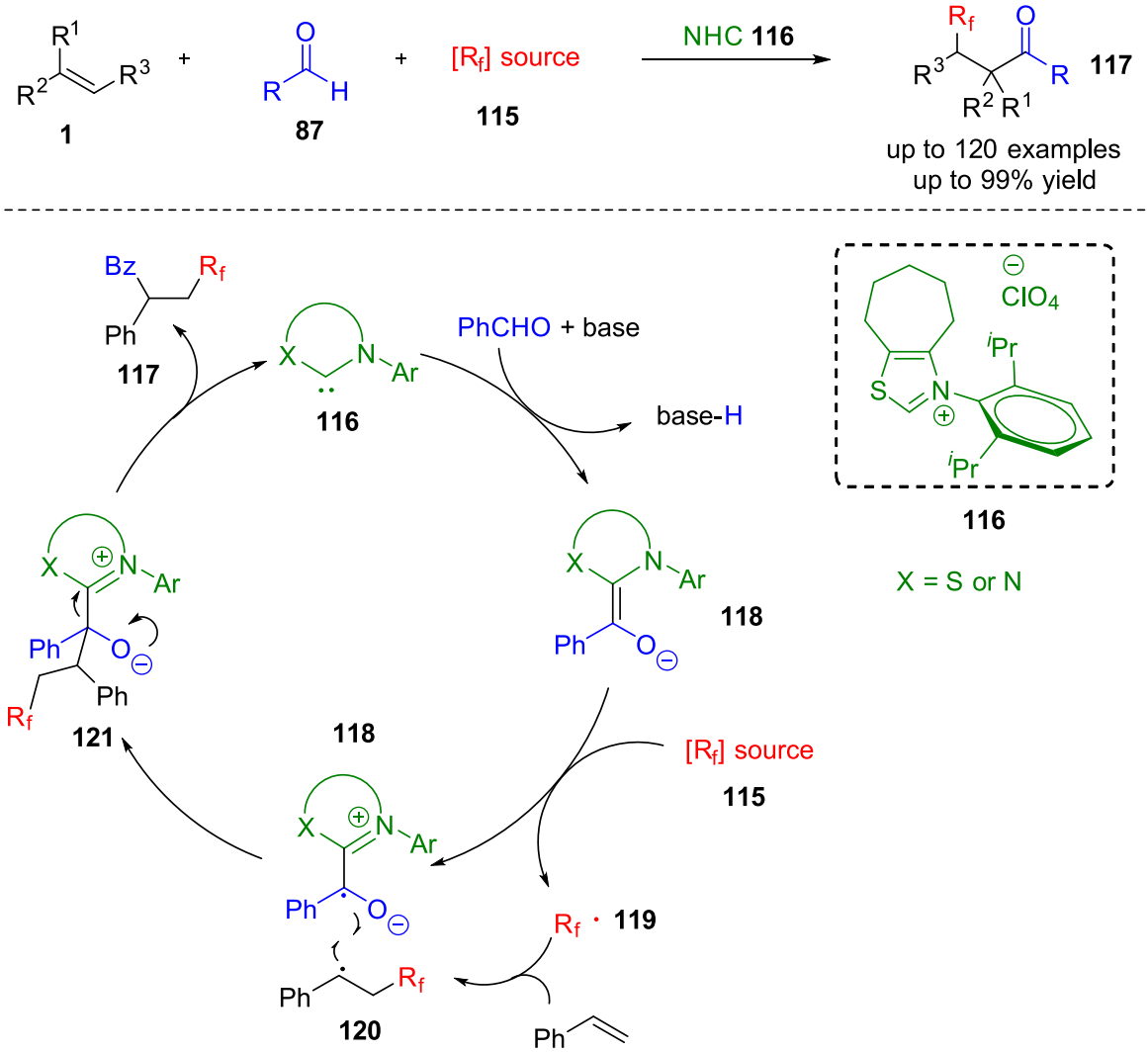


Scheme 2-26. NaI-catalyzed acetamidosulphenylation of alkenes

Recently, a number of additional iodide-catalyzed radical difunctionalizations of olefins have been published by other groups.[125,127,128] However, these reactions are still lacking a truly broad substrate scope, spurring our efforts of further research.

In 2020, Li's group reported the first *N*-heterocyclic carbene (NHC)-catalyzed radical acylfluoroalkylation of olefins.[129] This protocol was shown to be suitable for various difluoroalkyl bromides bearing diverse functionalities, such as sulfonyl, ester, amide, and bromide moieties. Moreover, perfluoroalkylation could also achieved. With this strategy, over 120 examples of fluoroketones were easily accessed from simple feedstock materials. Mechanistic studies suggested that intermediate **118** reduces of the Togni's reagent **115** via single electron transfer to give a fluoroalkyl radical **119** and a persistent ketyl radical. Addition of the fluoroalkyl radical **119** to styrene produces a benzylic radical **120**. Subsequently, a radical–

radical cross-coupling pathway forms intermediate **121**, and the fluoroketone product **117** is delivered by releasing NHC **116** to finish the catalytic cycle (Scheme 2-27).



Scheme 2-27: NHC catalyzed radical acylfluoroalkylation of olefins

During the past decade, organocatalytic radical difunctionalizations of olefins have been explored by many other groups.[130] However, most reported methods are focus on hypervalent iodine reagents or catalyzed by iodide. As can be seen, the use of organocatalysts for radical difunctionalization of olefins are still lacking, which motivates our efforts to develop novel processes.

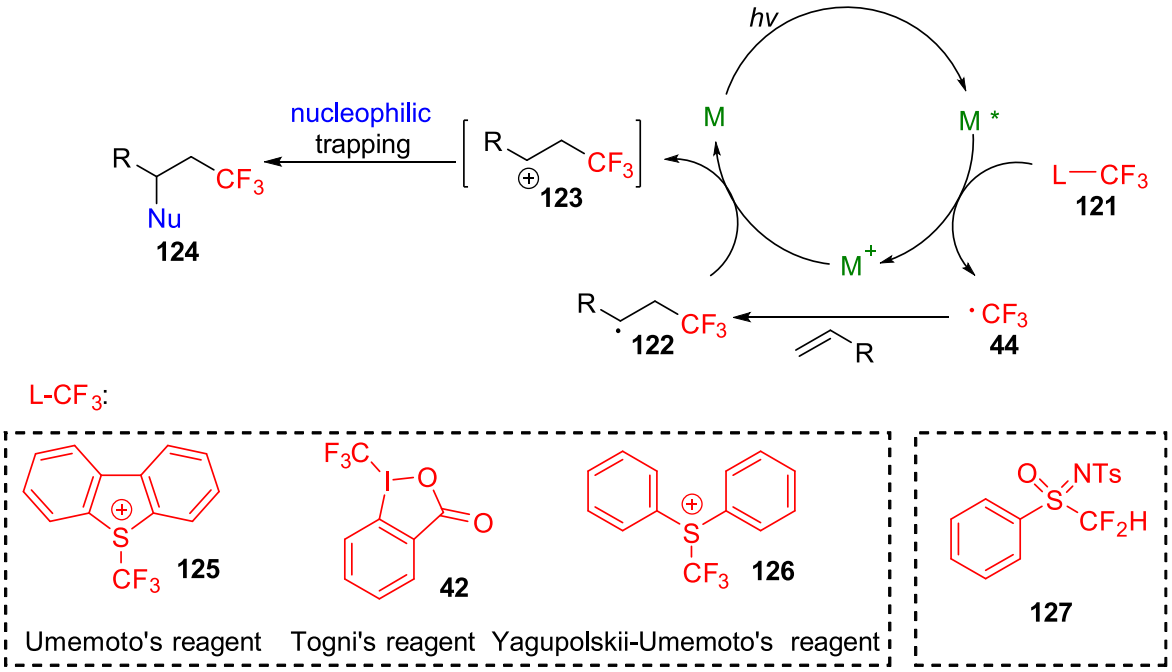
Additional methods for radical difunctionalization of olefins

Introduction

Photo- or electro chemistry has now become a very hot topic in modern organic synthesis. By using photo- or electro chemistry for olefin difunctionalizations, broad substrate scopes and a good tolerance of functional groups has been achieved. In this part, different methods relating to photo or electrochemical conditions will be summarized.

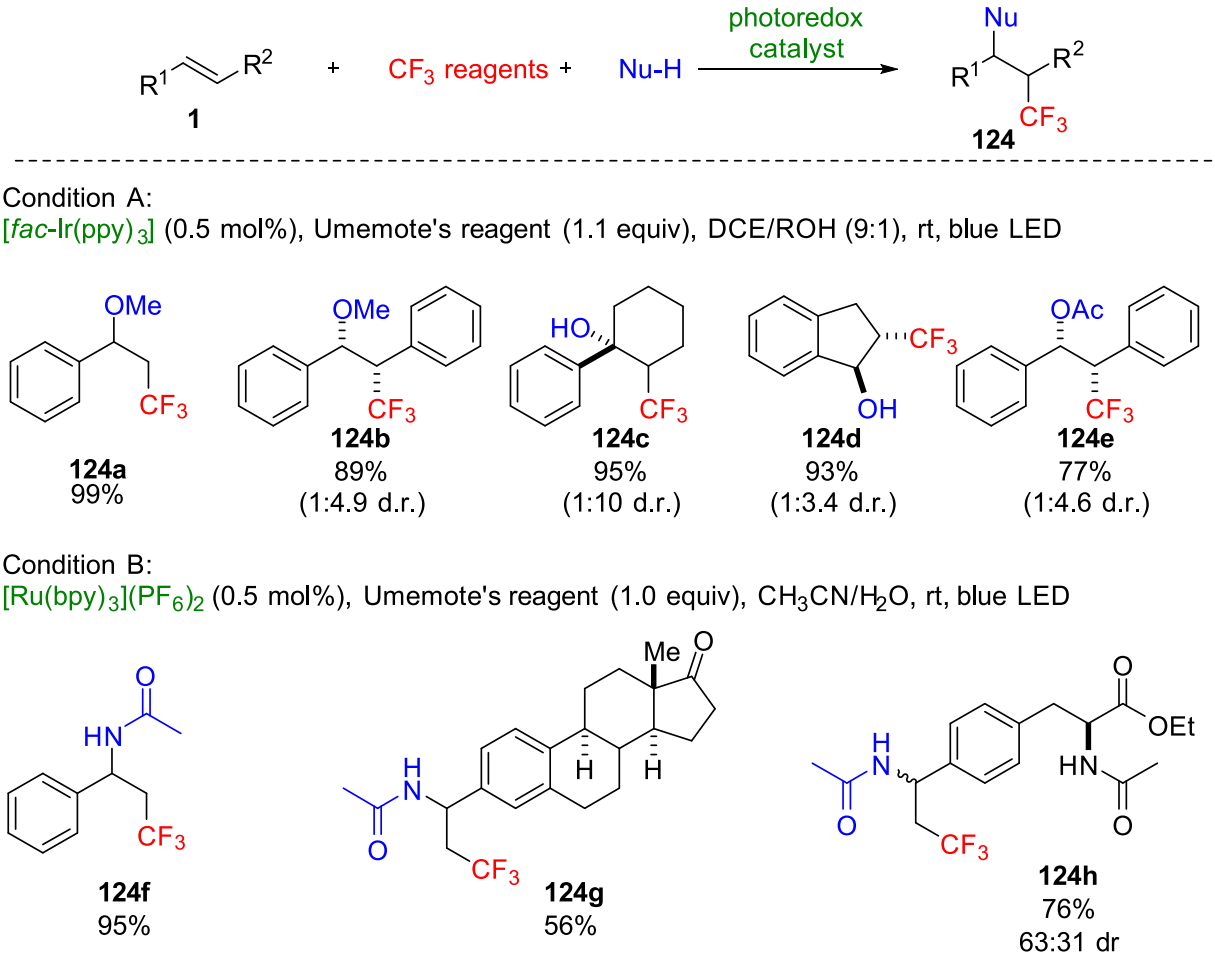
Photochemistry in radical difunctionalization of olefins

In recent years, photoredox catalysis has emerged as an useful tool for radical reactions through visible-light-induced single-electron-transfer (SET) processes.[131] Photoredox-catalyzed difunctionalization of olefins with various radicals and nucleophiles have now been developed. Amongst them, the trifluoromethyl radical (·CF_3) **44** and difluoromethyl radical (·CF_2H) have become widely used for construction of tri- and difluoromethylated skeletons (Scheme 2-28).



Scheme 2-28: Typical mechanism for the photocatalytic difunctionalization of olefins with fluoromethylating reagents

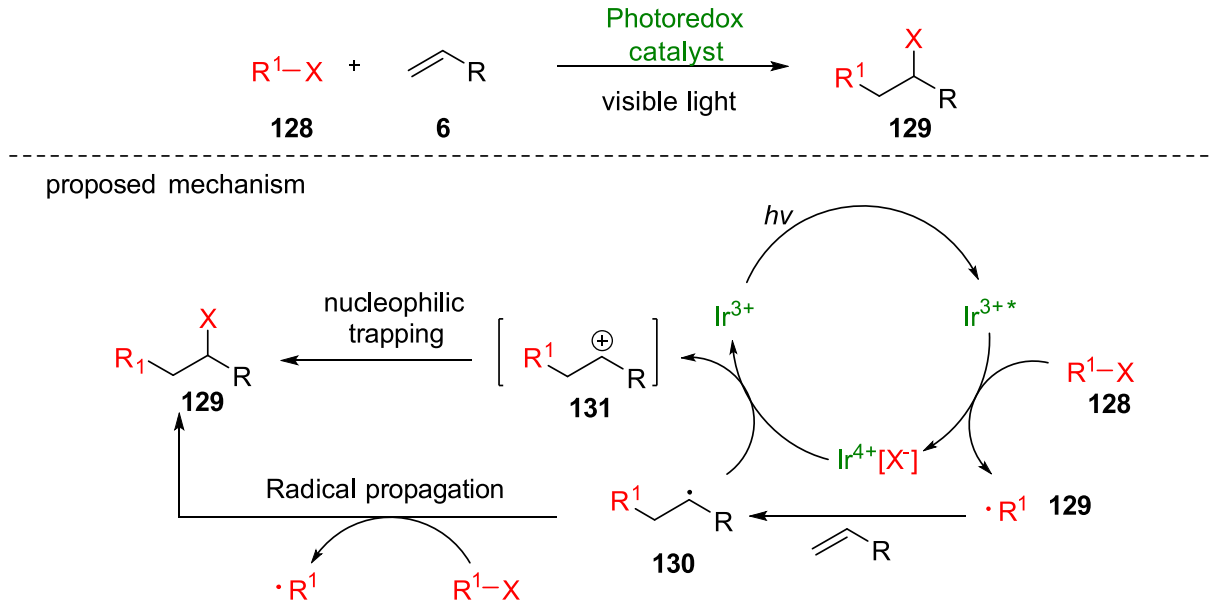
In 2012 and 2013, Akita and co-workers found that CF_3 radicals could be generated by a SET reduction process by the excited Ir[132] or Ru[133] catalyst with Umemoto's reagent **125** and Togni's reagents **42**. Oxytrifluoromethylated and aminotrifluoromethylated products were afforded with broad scope and regioselectivities for both terminal and internal aromatic alkenes. However, aliphatic alkenes did not produce the corresponding products well (Scheme 2-29).



Scheme 2-29: Oxytrifluoromethylation and aminotrifluoromethylation reactions of olefins

The strategy of using photoredox-catalyzed fluoromethylation of carbon−carbon multiple bonds has now been seen as a powerful tool for difunctionalization of olefins by radical and nucleophile. Nucleophiles, such as water, alcohols, carboxylic acids, amides and indole have all been used successfully.[131,134] In addition to these methods, which have utilized CF_3 radical sources, recent advancements have shown that a number of other radical reagents can be used for olefin difunctionalization.

In 2011, Stephenson and co-workers used photocatalytic intermolecular atom transfer radical addition to olefins under mild reaction conditions.[135] This protocol was characterized by excellent yields and broad scope. In the present reaction, the Ir photoredox catalyst $[Ir(dF(CF_3)ppy)_2(dtbbpy)](PF_6)$ was used. Under the visible light irradiation, the Ir^{3+} excited species reduces the haloalkane **128** to afford the alkyl radical **129**. The alkyl radical **129** then adds to the olefin to give a new C-centered radical **130**, which is oxidized via a single electron transfer step to give the Ir^{3+} catalyst in the ground state and the carbocation intermediate **131**. Subsequent nucleophilic trapping by the halide produces the desired product **129**. The author suggested the involvement of a radical propagation pathway was not excluded completely in the present reaction (Scheme 2-30). Later, other groups have also reported methods for sulfonyl cyanation[136] and sulfonyl halogenation[137,138] of olefins through atom transfer radical addition with different photoredox catalysts.

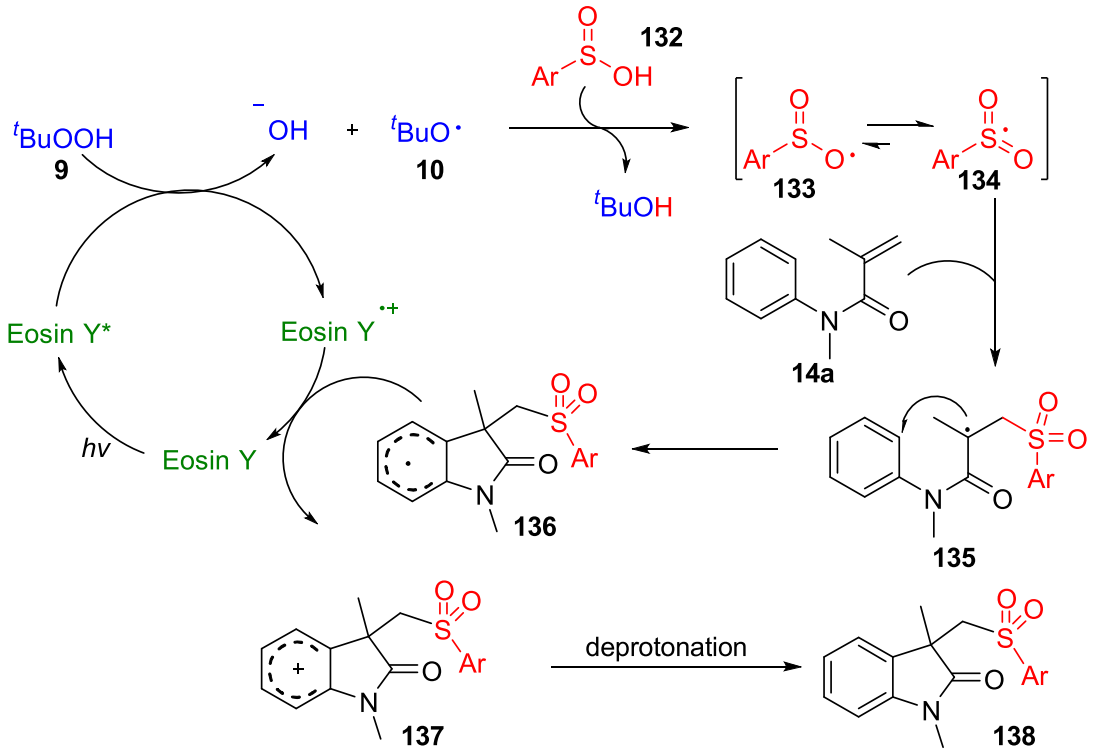


Scheme 2-30: Atom transfer radical addition to olefins enabled by photoredox catalysis

Visible light-mediated photoredox-catalyzed difunctionalization of olefins via an atom transfer radical addition reaction is a versatile and efficient process to facilitate the construction of various structural motifs with many potential applications.[139,140,141]

Another type of photochemistry for olefin difunctionalization reactions is the combination of photoredox-catalysis and peroxides, which can introduce a nucleophile and a radical into styrene involving hydrogen atom transfer.

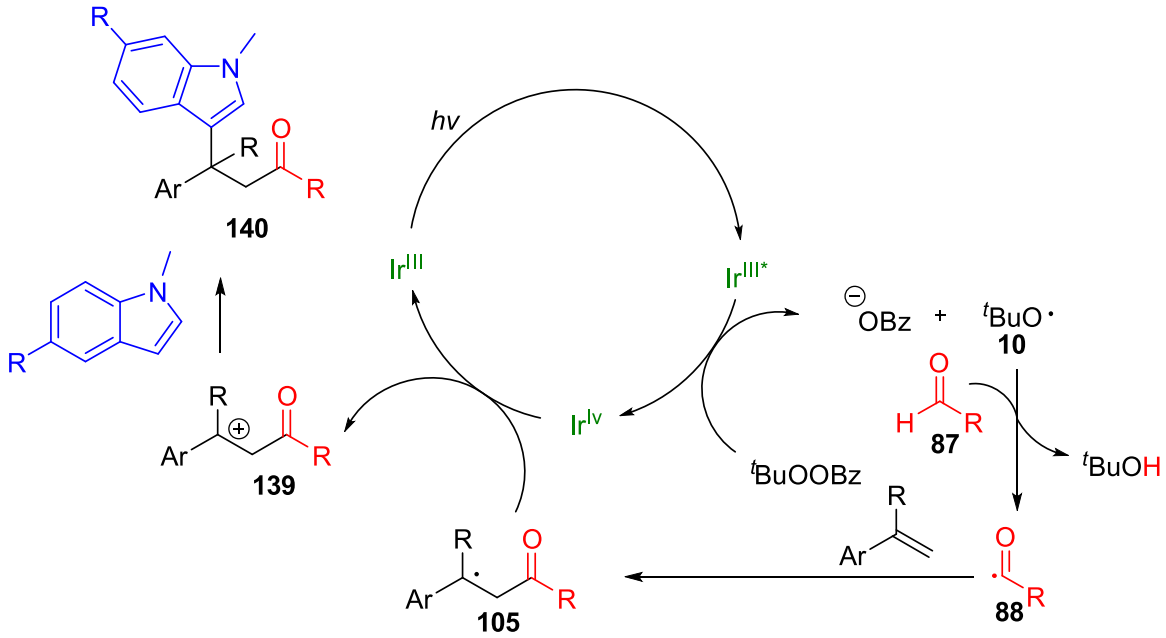
In 2015, Wang and co-workers developed a novel photocatalytic synthesis of sulfonated oxindoles.[142] TBHP **9** can be reduced by the excited Eosin Y catalyst to give a *tert*-butyloxy radical **10**, which abstracts a hydrogen atom from the arylsulfinic acid **132** to generate an oxygen-centered radical **133** that is in resonance with the sulfonyl radical **134**. The addition of the sulfonyl radical **134** to the carbon-carbon double bond affords a new alkyl radical **135**. After intramolecular cyclization, oxidation and deprotonation delivers the final product **138** (Scheme 2-31).



Scheme 2-31: Photocatalytic synthesis of sulfonated oxindoles.

In 2017, Sun and co-workers used the same photocatalytic-peroxide reaction conditions for the synthesis of ester-functionalized pyrido[4,3,2-*gh*]phenanthridine derivatives.[143] In this report, a N-centered radical was formed, which is the key for the construction of the polyheterocycles. Recently, Klußmann and Marcel reported the consecutive addition of acyl radicals and N-

alkylindole nucleophiles to styrenes using photoredox catalysis.[144] Different substituted functional groups on the olefins can be employed, forming quaternary all-carbon centers upon addition of indoles and benzotriazole to the benzylic position. The combination of TBPB and iridium photocatalysis forms the benzoate intermediate and a *tert*-butoxyl radical **10**. The tert-butoxyl radical **10** then abstracts a hydrogen atom from aldehyde **87**, thus giving a new radical **88**, which adds to the styrene derivatives. The benzylic radical **105** is then formed. Subsequently, oxidation by the Ir(IV) species generates carbocation intermediate **139**, which is trapped by the nucleophile to form the final product **140** (Scheme 2-32).

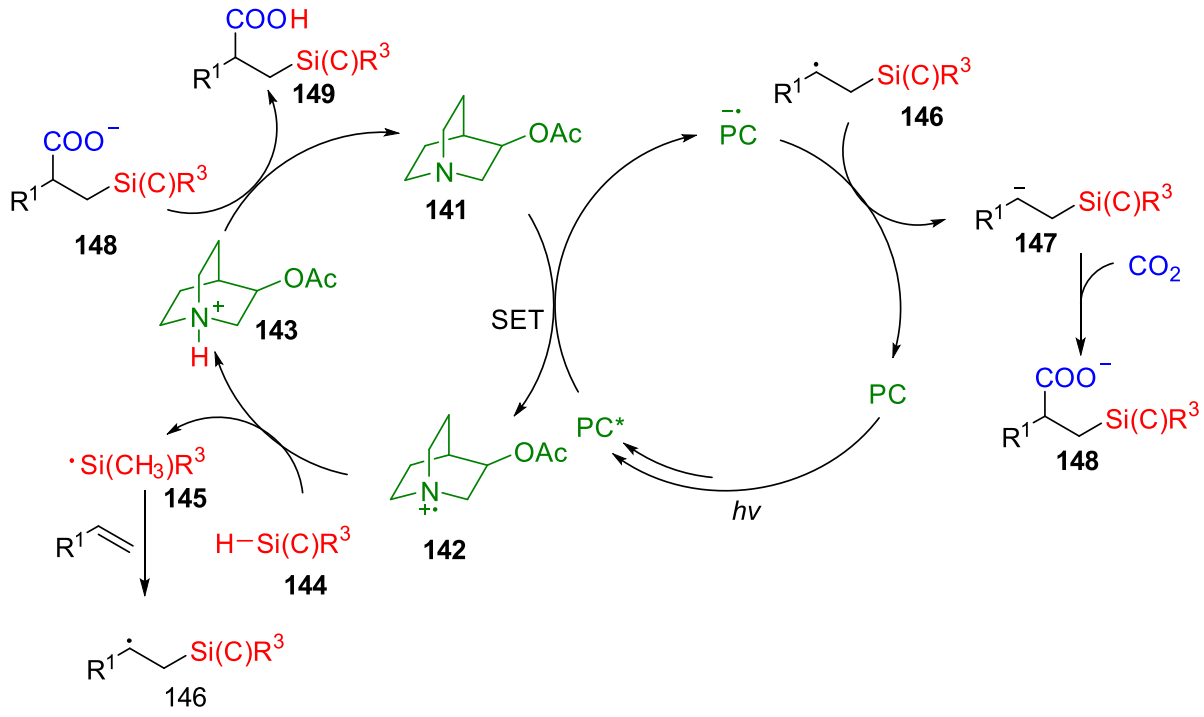


Scheme 2-32: Photoredox catalysis for the difunctionalization of alkenes with aldehydes and indoles

In 2019, Li and co-workers reported an intermolecular dialkylation of alkenes with two distinct C(sp^3)-H bonds using photoredox and iron catalysis.[145] This protocol provides a powerful method for the addition of two vicinal alkyl groups across the carbon-carbon double bond via dual C(sp^3)-H functionalization under mild conditions. The reaction has a broad substrate scopes with respect to the sp^3 carbon-centered radical precursors (such as cycloalkanes, linear alkanes, and 1,4-dioxane) However, the nucleophiles are limited in 1,3-dicarbonyl compounds. The key

charateristic in this method is that the photoredox catalysis can assist in the single-electron oxidation step by regulating the redox potentials of the iron intermediates and the reaction partner.

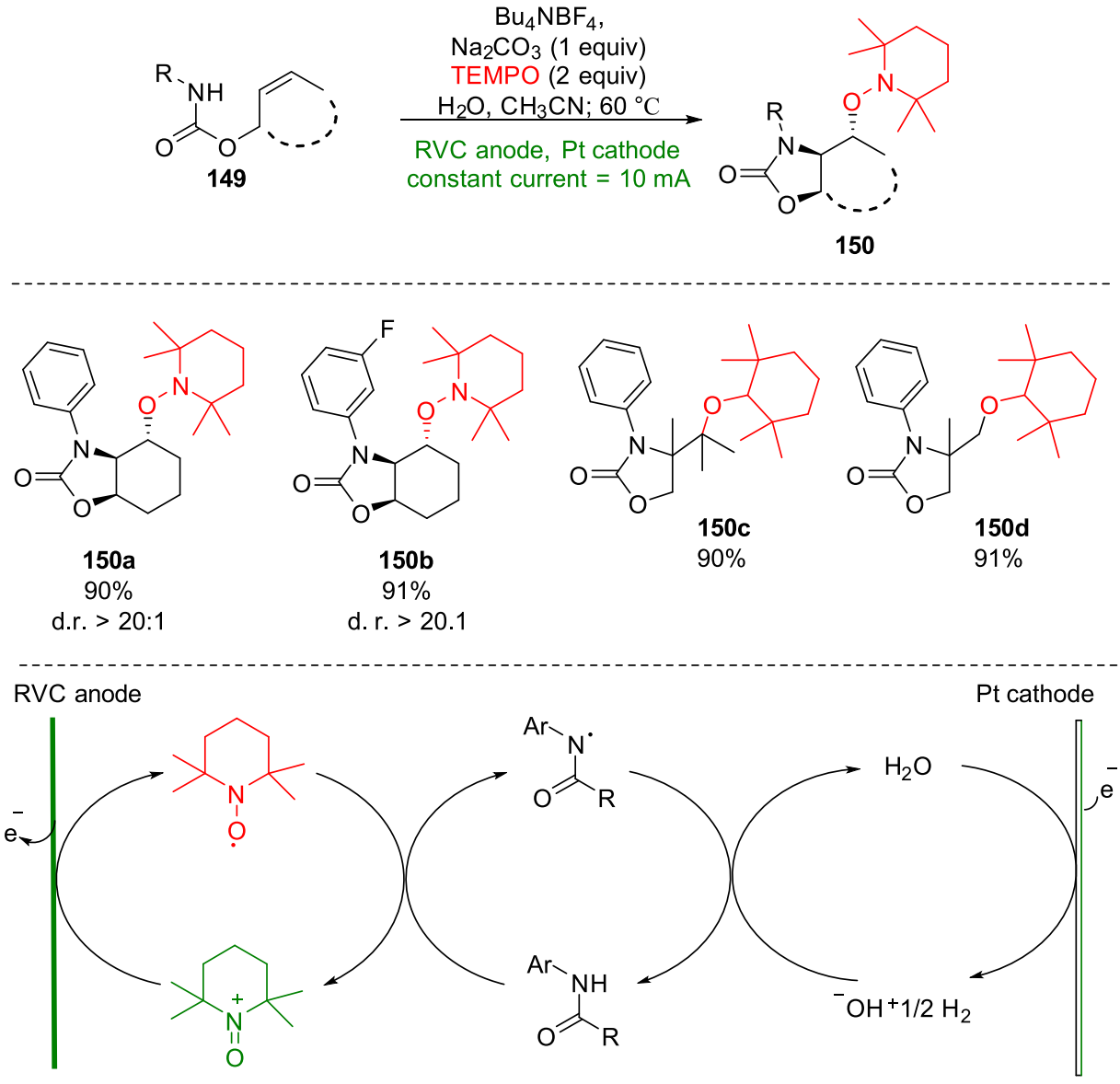
In 2018, Wu and co-workers reported a difunctionalization of alkenes with CO_2 and silanes or C(sp^3)-H partners under photocatalytic conditions (Scheme 2-33).[146] With the combination of photoredox and HAT catalysis, a broad substrate scope under mild reaction conditions was achieved. This protocol provides a new method for the difunctionalization of olefins by using electrophiles rather than nucleophiles, which could lead to a new general olefin difunctionalization platform. Other methods using CO_2 as an electrophiles under photoredox conditions have been reported[147] with P-centered[148] or aryl[149] radicals.



Scheme 2-33: CO_2 and silanes or C(sp^3)-H partners for the difunctionalization of alkenes under photocatalytic conditions

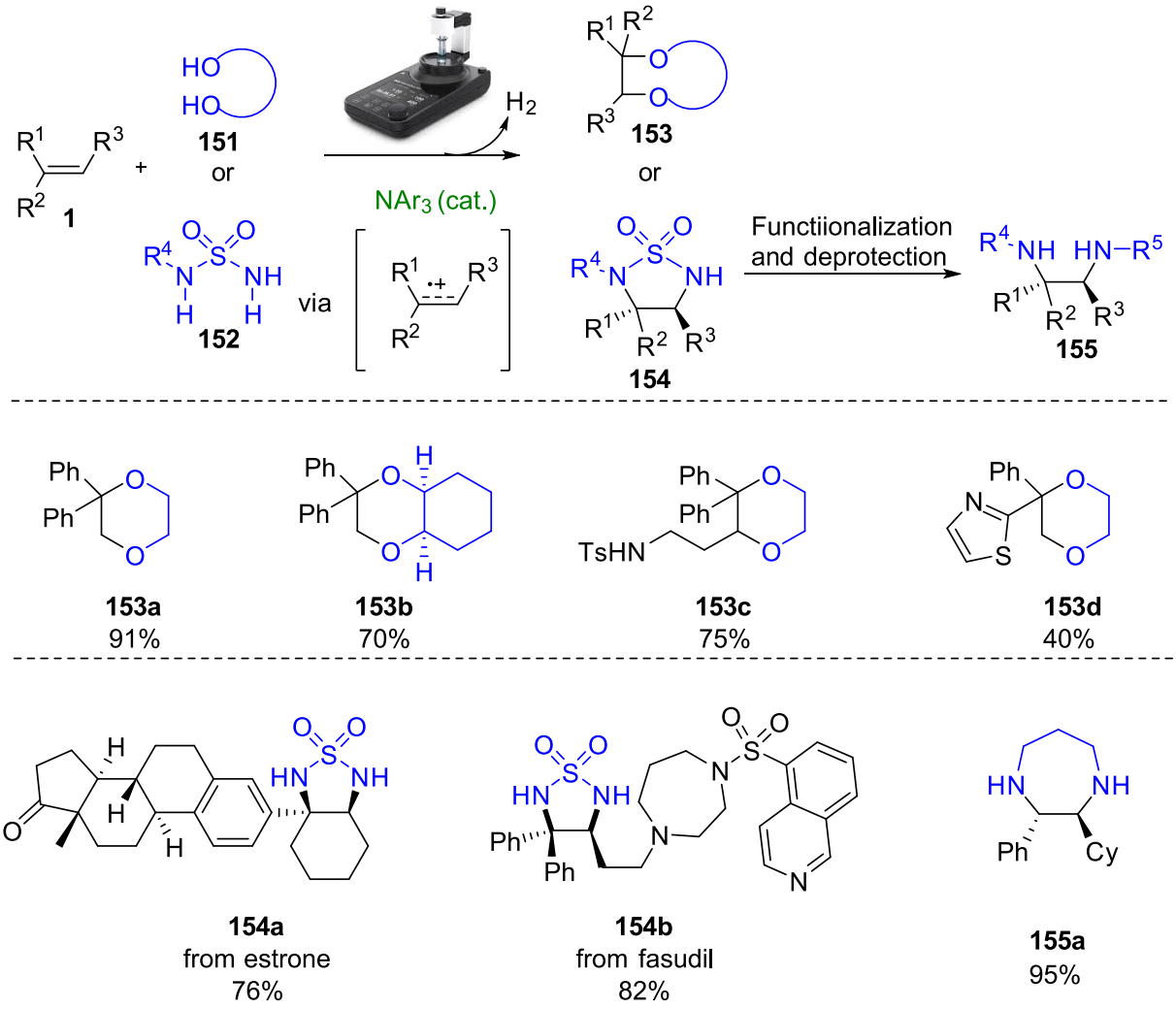
Electrochemical radical difunctionalization of olefins

In 2014, Xu and co-workers developed an electrochemical intramolecular aminooxygenation of unactivated alkenes.[150] This protocol enabled the addition of nitrogen-centered radicals to alkenes, followed by trapping of the cyclized radical intermediates with 2,2,6,6-tetramethylpiperidine-Noxyl radical (TEMPO) to give the desired aminooxygenation products **150** in high yields and regioselectivtites (Scheme 2-34).



Scheme 2-34: Electrochemical intramolecular aminooxygenation of unactivated alkenes

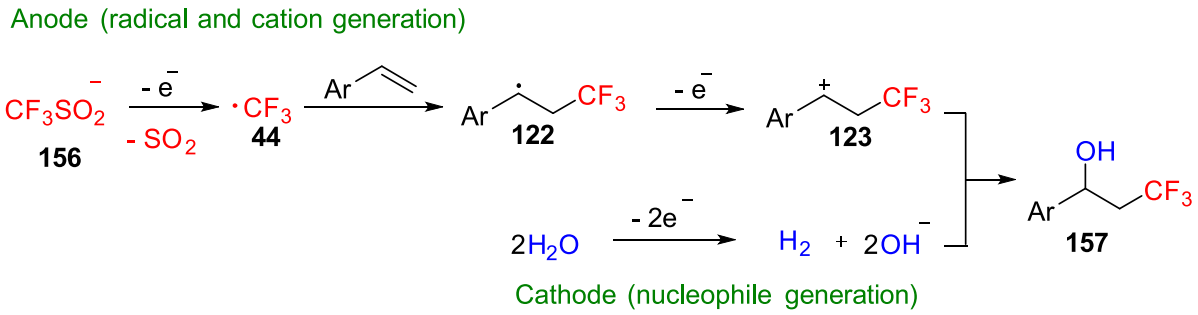
In 2018 and 2019, Xu and co-workers reported the addition of diols[151] or diamines[152] to alkenes under electrocatalytic conditions. These reactions are among the most straightforward and efficient approaches for the preparation of cyclic structures. Additionally, the oxidizing reagent free conditions provide a more green and practical method for chemists to get complex organic molecular (Scheme 2-35).



Scheme 2-35: Difunctionalization of alkenes with diols or diamines under electrocatalytic conditions

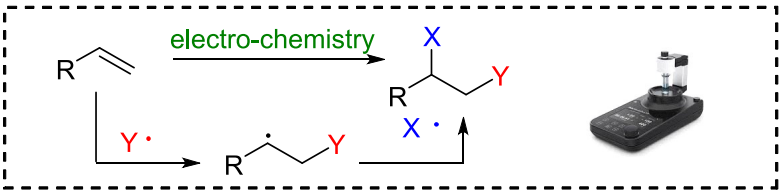
Xu's group has also developed various additional electrochemical difunctionalizations of alkenes. For instance, fluoroalkynylation of aryl alkenes,[153] difluoromethylation of electron-deficient alkenes[154] have been reported.[155]

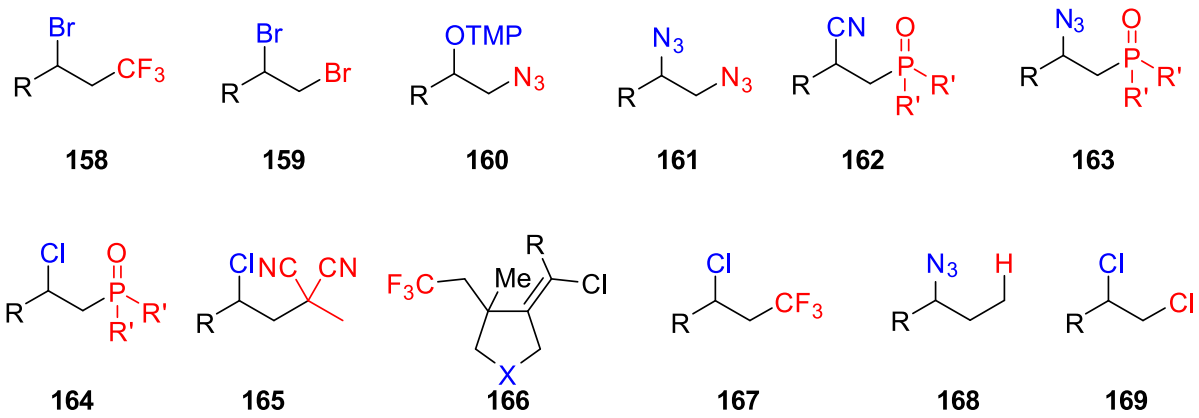
In 2018, the Cantillo group reported a mild, catalyst-free electrochemical oxytrifluoromethylation of alkenes,[156] based on the concept of paired electrolysis of sodium trifluoromethanesulfinate and water in an undivided cell. CF_3 radicals **44** were generated from oxidation of the CF_3SO_2 anion **156** at the anodic site, meanwhile water acts as the oxidant at the cathode as well as the nucleophile to provide the hydroxyl groups for the reaction. The electrochemical method is suitable for substituted terminal and internal alkenes, giving excellent yields for the desired 1-hydroxy-2-trifluoromethyl compounds **157** (Scheme 2-36).



Scheme 2-36: Electrochemical oxytrifluoromethylation of alkenes

Recently, Lin's group is certainly one of the most active in developing electrocatalytic approaches to enable radical difunctionalization of alkenes.[157] In 2017, Lin and co-workers reported an electrochemical manganese-catalyzed diazidation of alkenes.[158] This transformation provides a useful method to access diaminated products. The anodic oxidation of N_3^- furnishes the N_3 radical, which then adds to the alkene in an anti-Markovnikov fashion, forming a C-centered radical. Finally, the C-centered radical is trapped by another equivalent of N_3 radical and completes the desired diazidation. With the development of electrochemistry in radical difunctionalization of olefins, various nucleophiles and radicals have been added to carbon-carbon double bonds successfully (Scheme 2-37).[157]





Scheme 2-37: Summary of difunctionalizations of olefins enabled by electrochemistry

Indeed, electrochemistry has empowered a new area for organic synthesis by avoiding the use of transition metal catalysts and oxidants for the difunctionalization of olefins. Thus, further developments in this field are sure to be disclosed in time.

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CHAPTER 1

Acid promoted radical-chain difunctionalization of styrenes with stabilized radicals and (N,O)-nucleophiles

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Acid promoted radical-chain difunctionalization of styrenes with stabilized radicals and (N,O)-nucleophiles†

Sensheng Liu and Martin Klussmann *

A difunctionalization of alkenes through sequential addition of a radical and a nucleophile has been developed, which is suggested to proceed by a radical chain mechanism not requiring a catalyst. An electron transfer step to the oxidant benzoyl peroxide is facilitated by protonation with a strong acid.

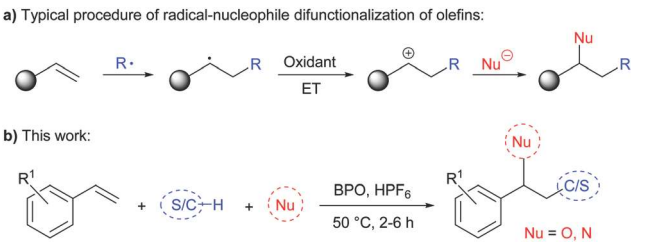
The difunctionalization of alkenes is a powerful transformation in synthetic organic chemistry. Besides transition-metal catalysed methods that proceed *via* organometallic intermediates,[1] such reactions can be efficiently conducted by addition of free radicals.[2] An interesting strategy amongst these is the consecutive addition of a radical and a nucleophile, which requires an electron transfer (ET) step after the radical addition, in order to generate a carbocation that could be trapped by a nucleophile (Scheme 1a).[2a,3] Such reactions would enable functionalizing olefins with a wide variety of reagents in a regioselective manner, given that radical precursors and nucleophiles mostly react complementarily. Although many synthetically interesting methods have been developed towards this goal, there is as of yet no method with a truly broad substrate scope of both radicals and nucleophiles.[4–6] Most of these methods require the presence of a transition metal catalyst or reagent to achieve the desired ET forming the carbocation intermediate, notable exceptions utilize an organic photocatalyst,[7] iodide as catalyst[8] or electrochemistry.[9]

We had previously worked on the activation of *tert*-butyl hydroperoxide by Brønsted acids, most notably in the presence of ketones.[10] We noticed the work by Zhang, Bao and co-workers, who reported a copper-catalysed difunctionalization of alkenes using benzoyl peroxide (BPO) in the presence of HPF_6.[11] Acetonitrile was both radical precursor and nucleophile and the role of the acid was not clear, thus it raised our interest for its combination of a peroxide and acid and its potential to add radicals and nucleophiles to olefins.

Here, we report mechanistic details of the effect of acid on benzoyl peroxide and a method for difunctionalization of styrene derivatives with stabilized C- and S-radicals and N- and O-nucleophiles. The reactions do not require a catalyst but the presence of a strong Brønsted acid, and they operate at only slightly elevated temperature (Scheme 1b).

We found that the combination of BPO with HPF_6 allowed for the addition of thioxanthene (**2a**) and acetonitrile to styrene (**1a**) without any additional catalyst within two hours at 50 °C (Table 1, entry 1). The product's structure (**3a**) suggested that a thioxanthenyl radical was added to styrene and subsequently acetonitrile attacked as a nucleophile in a Ritter reaction.[12] The C-radical of thioxanthene had apparently formed by H-atom transfer (HAT),[13] presumably to a benzoyloxyl radical generated from BPO.

The acid plays a crucial role for the reaction: with lower amounts, the yield drops significantly (entry 2) and without acid, no reaction occurs (entry 3; for further results under changed reaction conditions, see the ESI†). In the presence of other acids, the product was also formed, but apparently the yield is correlated with the acid strength. For example, trifluoroacetic acid gave only 11% of **3a**, while the stronger acids HBF_4 and $HClO_4$ gave 39% and 51% (entries 4–6). In the absence of BPO and with other peroxide oxidants, the product was not formed. Ambient temperature is sufficient for the reaction, but



Scheme 1 Radical-nucleophile addition of olefins. BPO = Benzoyl peroxide.

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† Electronic supplementary information (ESI) available: Including experimental details, NMR spectra, X-ray crystallographic data and a CIF file. CCDC 1957001. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9cc09369a

Table 1 Optimization of the reaction conditions[a]

Entry	Acid	Acid equiv.	Yield[b] (%)
1	HPF_6 (aq., 55%)	1.0	88
2	HPF_6 (aq., 55%)[c]	0.1	20
3	—	—	0
4	CF_3CO_2H[c]	1.0	11
5	HBF_4 (aq., 48%)	1.0	39
6	$HClO_4$ (aq., 70%)	1.0	51
7[d]	HPF_6 (aq., 55%)	1.0	91 (88, 83[e])

[a] **1a** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv.), BPO (0.3 mmol, 1.5 equiv.), Acid (0.2 mmol, 1.0 equiv.) in CH_3CN (2 ml). [b] Yields determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard CH_3NO_2, yield of isolated product in parentheses. [c] With addition of 1.0 equiv. of water. [d] Degassed, under argon. [e] Performed on a larger scale, isolating 1.5 g of **3a**.

the rate is significantly reduced. Performing the reaction under strict exclusion of oxygen increased the yield, and the reaction could also be performed on a larger scale, giving 1.5 g of **3a** with an isolated yield of 83% (entry 7).

The reaction is very likely proceeding *via* a radical mechanism, as the addition of radical inhibitors reduced the yield significantly (see the ESI† for details). The acid apparently does not affect the decomposition of BPO, which has a reported 10 hour half-life temperature of 73 °C.[14] As an NMR experiment revealed, BPO with or without acid did not change when heated in acetonitrile at 50 °C for two hours (Scheme 2a). However, in the presence of thioxanthene, benzoic acid was formed in significant amounts under these conditions, indicating that it accelerates the peroxide decomposition (Scheme 2b).

While the acid does not accelerate the homolytic cleavage of BPO, it does change its redox potential. We studied this effect by cyclic voltammetry (Fig. 1). The reduction of BPO alone was found to occur at −345 mV, which underwent a shift by +470 mV in the presence of 0.66 equiv. of HPF_6, the relative amount used under reaction conditions. Other acids also induced such a shift, but less strong, as is shown here for trifluoroacetic acid (for other acids, see the ESI†). The reduction was thus significantly eased by the strong acid HPF_6, possibly

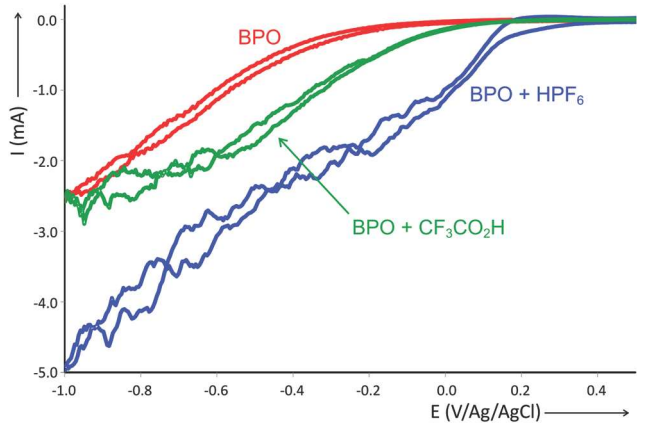
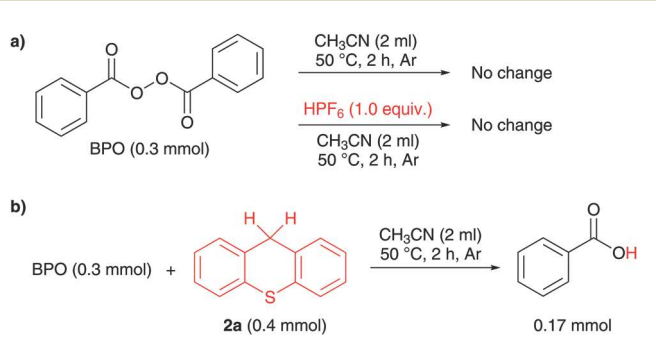


Fig. 1 Cyclic voltammograms showing the effect of acid addition on the reduction potential of BPO. Two platinized Pt wires as a counter and working electrode with a Ag/AgCl electrode as a reference were used. The cyclic voltammetry (CV) was conducted from −1.0 V to 2.0 V with a scan rate of 100 mV s^{-1}. BPO (0.3 mmol), acid (0.2 mmol), tetrabutylammonium hexafluorophosphate (0.1 M) in CH_3CN under Ar.

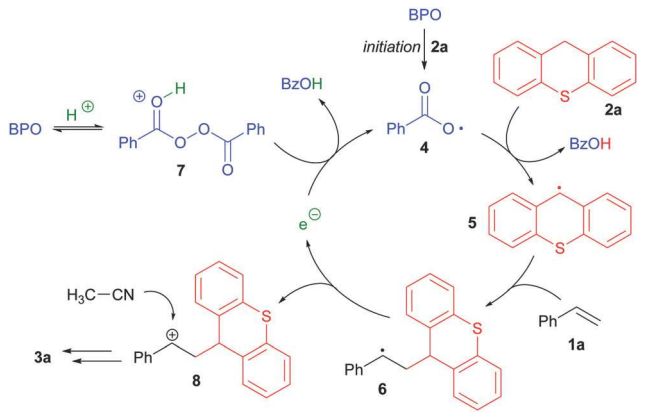
by protonation that turns the now cationic peroxide into a better electron acceptor.

These results indicate a reaction mechanism that relies on electron transfer (ET) steps (Scheme 3). Initiating benzoyloxyl radicals (**4**) are formed from BPO in the presence of thioxanthene, possibly by ET to BPO that is facilitated by protonation. These induce HAT from thioxanthene, generating a new radical (**5**), which then adds to styrene, forming the benzylic radical **6**. This is oxidized by BPO in the presence of HPF_6, most likely by ET to the protonated peroxide (**7**), giving the intermediate carbocation **8**, benzoate and a new benzoyloxyl radical. The cation **8** can react as an electrophile with acetonitrile, generating the product **3a** in the fashion of a Ritter reaction. Thus, the reaction appears to run by a radical chain mechanism and can be seen as a case of "electron-catalysis".[15]

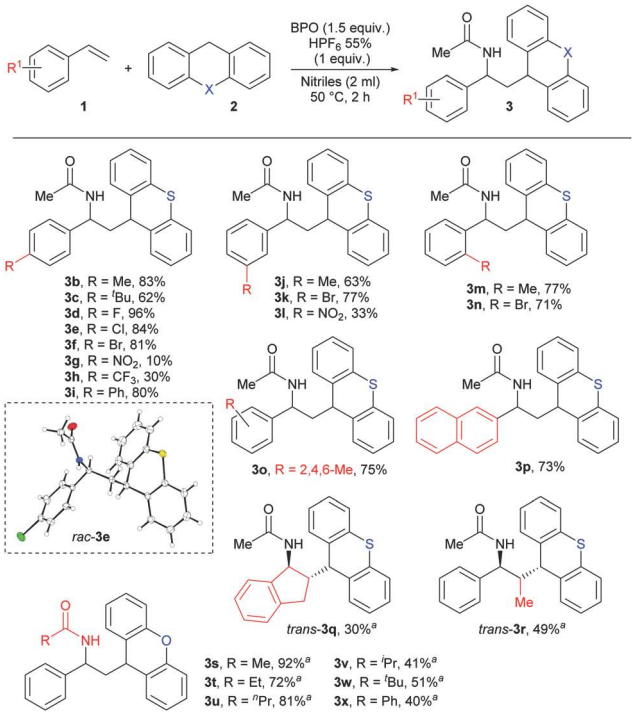
Based on this working model of the reaction's mechanism, other substrates that can initiate such a radical chain by interaction with BPO[16] and that easily form radicals by HAT to a benzoyloxyl radical should also be employable, as well as other olefins and alternative nucleophiles.



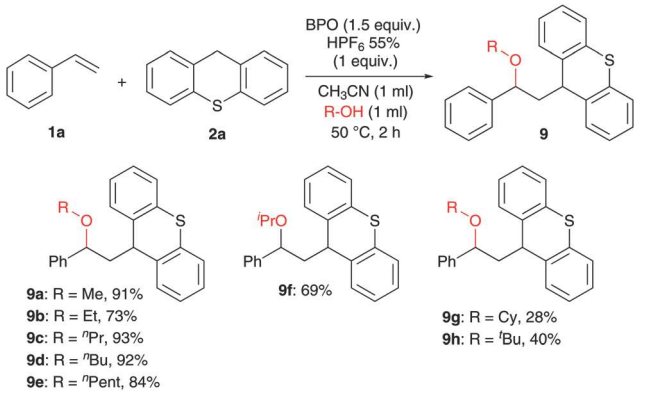
Scheme 2 Experiments pointing to the reaction mechanism.



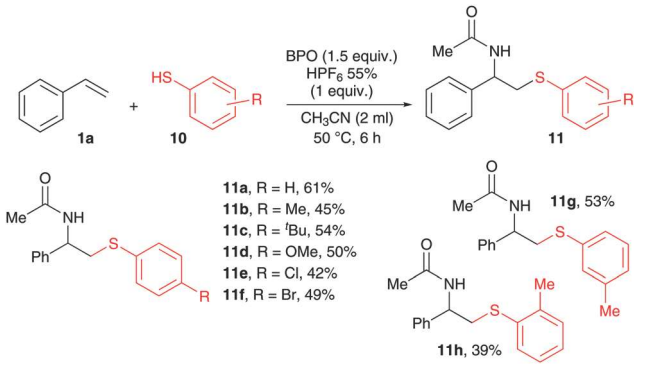
Scheme 3 Potential reaction mechanism, shown exemplary for **1a** and **2a**.



Scheme 4 Substrate scope for the reaction of styrenes and nitriles: **1** (0.2 mmol), **2** (0.4 mmol, 2.0 equiv.), BPO (0.3 mmol, 1.5 equiv.), HPF_6 (0.2 mmol, 1.0 equiv.) and nitriles (2 ml), Ar, isolated yield. [a]Reaction time: 6 hours. ORTEP diagram is drawn with displacement ellipsoids at the 50% probability level.



Scheme 5 Substrate scope for the reaction of alcohol nucleophiles: **1a** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv.), BPO (0.3 mmol, 1.5 equiv.), HPF_6 (0.2 mmol, 1.0 equiv.), alcohols (1 ml) and CH_3CN (1 ml), Ar, isolated yield.



Scheme 6 Substrate scope for thiylation: **1a** (0.2 mmol), **10** (0.4 mmol, 2.0 equiv.), BPO (0.3 mmol, 1.5 equiv.), HPF_6 (0.2 mmol, 1.0 equiv.) and CH_3CN (2 ml), Ar, isolated yield.

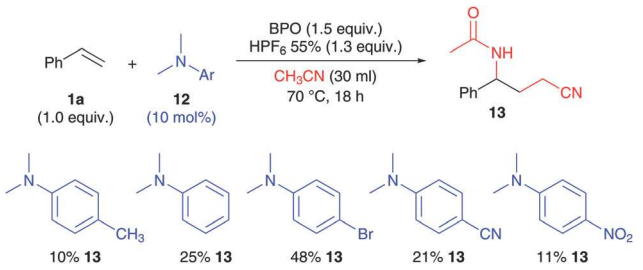
As shown in Scheme 4, styrenes with both weakly electron-donating (Me, ^{t}Bu) and withdrawing (F, Cl, Br) substituents on the aromatic ring, regardless of their positions, afforded the desired products in good yields 62–96% (**3b–3f**, **3j–3k** and **3m–3o**), as did 4-vinylbiphenyl and vinylnaphthalene (**3i**, **3p**). However, styrene bearing the strongly electron-donating methoxy substituent did not give the desired product, and the strongly electron-withdrawing NO_2 and CF_3 substituents led to low yields of **3g**, **3h** and **3l** in 10%, 30% and 33%. Using indene as olefin gave the product **3q** in 30% yield, but it is remarkable for its high trans-selectivity. A diastereomeric ratio of $>21:1$ was determined in the crude reaction mixture, but after purification, we received the pure trans-product **3q**. Similarly, only the trans-product **3r** was isolated from the reaction with *E*-β-methylstyrene. Strangely, other nitriles besides acetonitrile did not lead to the expected products with thioxanthene. However, when we used xanthene as HAT-donor, we could isolate different amide products by performing the reaction in different nitriles as solvent. Aliphatic and aromatic nitriles as well gave the products **3s–3x** with good yields after an extended reaction time of 6 hours. The general structure of these products was confirmed by X-ray crystallography of product **3e**.

Next, the scope with respect to nucleophiles was explored. Although we tried many substrates (see the ESI† for further details), only alcohols were successful, and only with thioxanthene but not with xanthene (Scheme 5). Reactions of styrene with various alcohols produced the expected products in good yields, with primary alcohols in generally higher yields (**9a–9e**, 73–93%) than secondary (**9f–9g**) and tertiary alcohols (**9h**).

Thiophenols (**10**) as HAT-donors with acetonitrile as nucleophile could also be employed successfully in this reaction with styrene (Scheme 6). While alkyl thiols did not react under those conditions, products **11** with various differently substituted thiophenols could be employed. Products of a thiol–ene reaction were not observed. Similar products like **11** had recently been reported, being synthesized by an iodide-catalysed radical reaction[8] or by ionic reactions also utilizing stoichiometric amounts of oxidants.[17]

Substrates not capable of initiating BPO decomposition obviously fail in this reaction. However, addition of extra initiators may overcome this limitation. We found that addition of *N*,*N*-dimethylanilines, well-known initiators for BPO,[18] enable the addition of two molecules of acetonitrile to styrene, furnishing **13** (Scheme 7). Although the yields are not as high as with Cu-catalysts,[11] 48% is reached with the use of 10 mol% of the *p*-bromo aniline. The product yield is obviously linked to the initiation rate and electronic properties of the anilines, as the comparison with more and less electron rich derivatives shows.

In conclusion, a method for the difunctionalization of styrenes with radicals derived from thioxanthene, xanthene



Scheme 7 Investigating dimethylaniline initiators: **1a** (0.5 mmol), BPO (0.75 mmol, 1.5 equiv.), HPF_6 (0.66 mmol, 1.3 equiv.), **12** (0.05 mmol) and CH_3CN (30 ml), isolated yield.

and thiophenols together with nitrile and alcohol nucleophiles was developed. The combination of benzoyl peroxide with HPF_6, a strong Brønsted acid, is a key element of the reaction that does not require transition-metal catalysts, high temperatures or prolonged reaction times. Mechanistic studies suggest that the acid can promote the electron transfer to the peroxide, and that the reaction proceeds by a radical chain that is initiated by interaction of the radical precursor with the peroxide. Addition of an extra radical initiator can overcome this limitation, which suggests a way to extend this synthetic strategy.

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Conflicts of interest

There are no conflicts to declare.

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CHAPTER 2

Organo-redox-catalysis for the difunctionalization of alkenes and oxidative Ritter reactions by C–H functionalization

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Organo-redox-catalysis for the difunctionalization of alkenes and oxidative Ritter reactions by C–H functionalization†

Sensheng Liu and Martin Klussmann *

Transition metals are the dominant catalysts for redox-reactions between peroxides and organic substrates. Here, we show that triarylamines can act as organic redox-catalysts, enabling oxidative difunctionalization reactions of alkenes and oxidative Ritter-reactions. Styrene derivatives can be functionalized with alkyl radicals, generated from plain and halogenated hydrocarbons, and with nucleophiles, including nitriles, acetic acid, alcohols and fluoride. An oxidative Ritter reaction can be conducted between allylic C–H bonds as well as fluorene and acetonitrile. Benzoyl peroxide is the oxidant in both reactions. Mechanistic studies suggest that the triarylamines are catalysts and not initiators, mediating the reaction by electron transfer to the peroxide, forming benzoyloxyl radicals, and from C-radical intermediates, forming carbocations.

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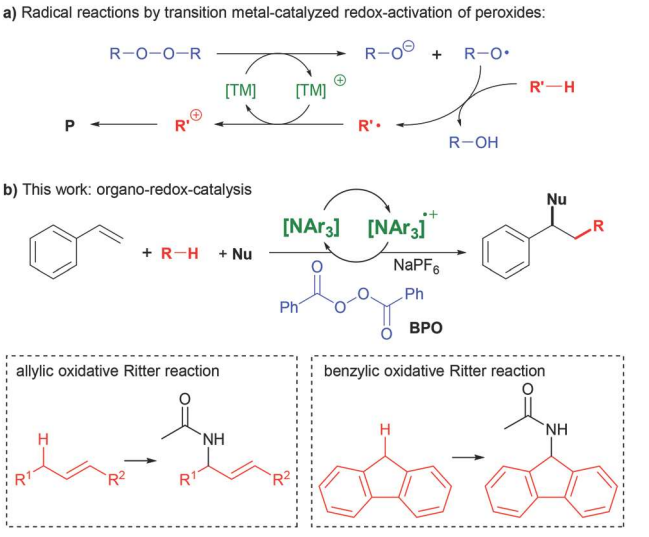
Introduction

The difunctionalization of alkenes is a powerful method for the construction of C–C and C–X bonds.[1–4] A very interesting type amongst those is the successional addition of a radical and a nucleophile.[1,3] This method enables functionalizing olefins with a wide variety of reagents in a selective manner, given that radicals and nucleophiles generally react complementarily. However, these reactions are still lacking a truly broad substrate scope, spurring our efforts of further research.

A widely used strategy for generating radicals from simple substrates is C–H bond cleavage by hydrogen atom transfer (HAT) to oxyl radicals, which are readily generated from peroxides.[5] The subsequent addition of a nucleophile requires an electron transfer (ET) step to convert the radical intermediate into a carbocation. Thus, transition metals are widely used as redox-catalysts in such reactions, as they can mediate peroxide O–O bond cleavage and subsequent ET (Scheme 1a).[1,3,6–9]

Alternative methods for the consecutive addition of radicals and nucleophiles utilize organic photocatalysts,[10,11] hypervalent iodine reagents or iodide as catalyst[12–14] and electrochemistry.[15,16] We are not aware, however, of the use of an organo-redox catalyst independent of irradiation in such reactions. Here, we report the use of triarylamines as catalysts in the activation of peroxides for synthetic radical reactions (Scheme 1b).

Triarylamines can form stable ammoniumyl radical cation salts by ET, and variation of the aryl-substituents allows for fine-tuning of their properties.[17–21] Both the amines and the radical cations are widely applied in electro-optical materials.[18–20,22] The radical cations can be used as stoichiometric single-electron oxidants in chemical reactions,[23] or in substoichiometric amounts as initiators of radical chain



Scheme 1 Activation of peroxides and formation of carbocations by redox-catalysis.

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†Electronic supplementary information (ESI) available: Method development, synthesis, characterization and mechanistic studies. See DOI: 10.1039/d1qo00259g

reactions.[17,24] Both the amines and the radical cations are also utilized as redox-catalysts in electrochemical[25,26] or photochemical reactions,[27,28] as well as in aerobic oxidations.[29,30] Despite this plethora of applications, we are not aware of amine-based redox catalysis in the activation of peroxides, which would open many opportunities for synthetic applications.

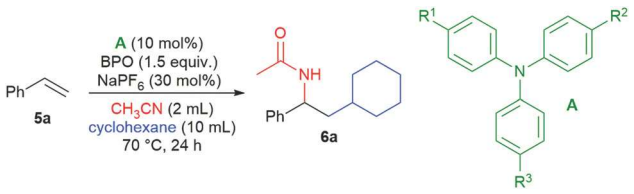
N,*N*-Dialkylanilines like **1** are well-known to generate radicals from diacylperoxides, especially benzoyl peroxide (BPO, Scheme 2a).[31,32] The reaction is irreversible due to the reactivity of the ammoniumyl radical cation **2**, which readily forms a C-radical **3**, an iminium ion **4** and other products derived thereof.[32,33] In contrast, we assumed that triarylamines **A** could be suitable candidates for catalysis, as the stable radical cation salts **A+** could be regenerated by ET (Scheme 2b).

We had previously utilized BPO in the addition of thioxanthene and similarly facile radical precursors together with nucleophiles to styrenes, which was rationalized as a radical-chain reaction.[34] The addition of hexafluorophosphoric acid (HPF_6) was found to modulate the redox potential of BPO, and the addition of *N*,*N*-dimethylanilines as initiators allowed difunctionalization with acetonitrile with moderate success. We kept working on finding a more efficient method for a broad substrate scope that would also avoid the use of a strong acid.

Results and discussion

We found that the addition of cyclohexane and acetonitrile to styrene (**5a**) took place in the presence of catalytic amounts of some triarylamines and $NaPF_6$ as an additive, forming the desired product **6a** in good yields (Table 1, entries 1–3). The most effective amine was 4-iodo-*N*,*N*-diphenylaniline (**A1**), closely followed by tris(4-methylphenyl)amine (**A2**) and tris(4-bromophenyl)amine (**A3**), other amines were much less efficient. Without triarylamine, product **6a** was not formed (entry 4) and the addition of $NaPF_6$ is indispensable (entry 5). A reduction in the product's yield was also seen with other additives and oxidants (see the ESI† for a detailed investigation). The product's structure supported the subsequent addition of a cyclohexyl radical and acetonitrile as a nucleophile in a Ritter reaction.

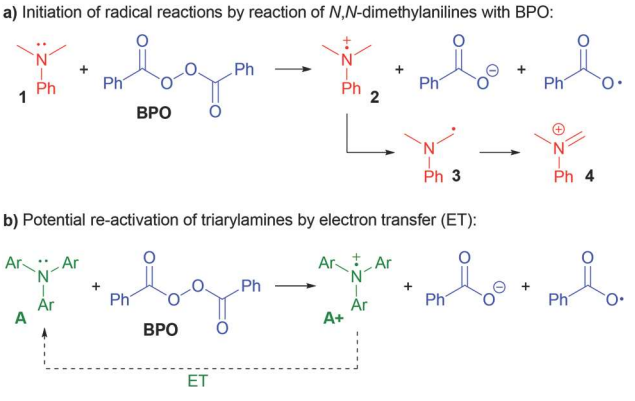
Table 1 Evaluation of catalysts[a]



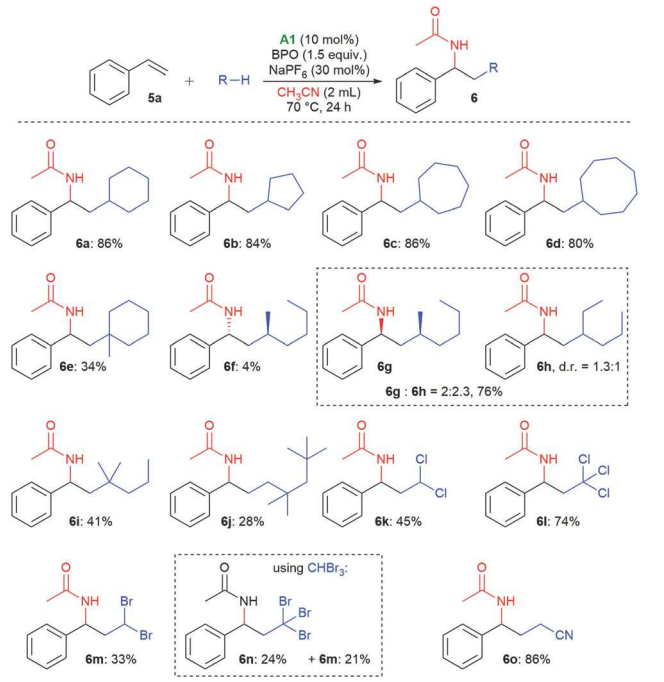
Entry	Catalyst	R^1	R^2	R^3	Additive	Yield[b] (%)
1	**A1**	I	H	H	$NaPF_6$	91 (86)
2	**A2**	Me	Me	Me	$NaPF_6$	58
3	**A3**	Br	Br	Br	$NaPF_6$	86
4	—				$NaPF_6$	0
5	**A1**	I	H	H	—	0

[a] Reaction conditions: **5a** (0.5 mmol), **A** (0.05 mmol, 10 mol%), CH_3CN (2 mL), cyclohexane (10 mL), BPO (0.75 mmol, 1.5 equiv.), additive (0.15 mmol, 0.3 equiv.). [b] Determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-trimethoxybenzene, isolated yield in parentheses.

With these reaction conditions, we investigated the product scope by testing other substrates. Using cyclopentane, cyclohexane, cycloheptane, and cyclooctane as radical precursors with acetonitrile as nucleophile afforded the products **6a–6d** in good yields of 80–86% (Scheme 3). Methylcyclohexane gave a mixture of regioisomers from which we could isolate **6e**, the major one, in 34% yield. With *n*-hexane, a mixture of the iso-



Scheme 2 Activation of BPO with *N*,*N*-dimethylaniline and triarylamines.



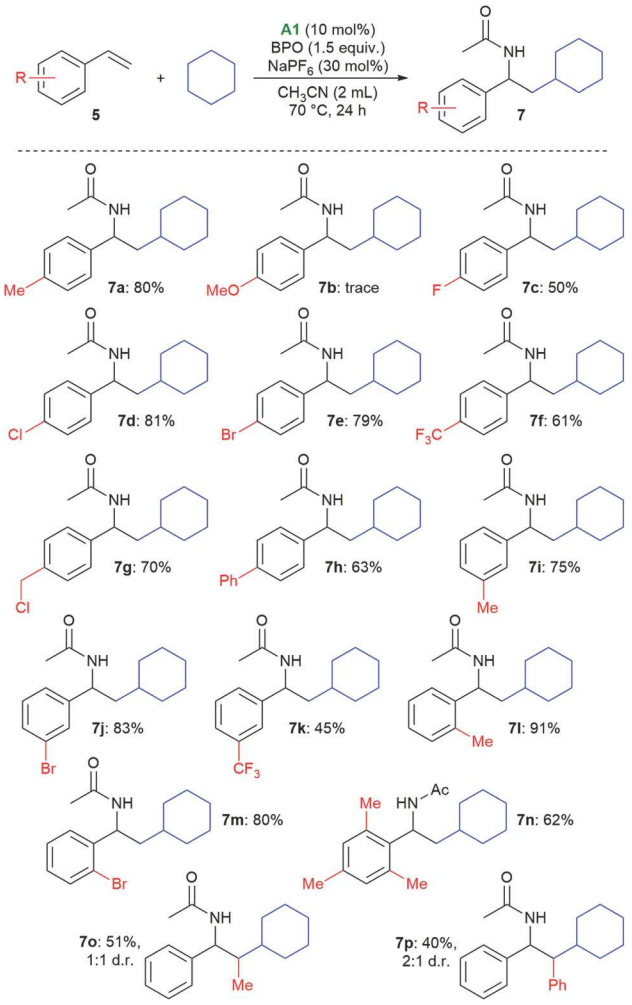
Scheme 3 Scope of radicals.

meric products **6f–6h** was isolated in 80% overall yield, from which we could isolate the isomer **6f** in 4% yield as a pure compound by column chromatography. With 2-methylpentane, the selectivity for the tertiary C–H bond was relatively high, allowing for isolation of the major isomer **6i** in 41% yield. With 2,2,4,4-tetramethylpentane, only isomer **6j** was isolated, apparently because the methylene group is sterically shielded, resulting in HAT from a primary C–H bond. The haloalkanes dichloromethane, chloroform, dibromomethane and bromoform could also be employed successfully in this reaction, producing the products **6k–6m**. When using bromoform, not only **6n** was formed by HAT, but also **6m** by bromine atom transfer.[35,36] When only acetonitrile was used as solvent, **6o** was isolated in 86%.

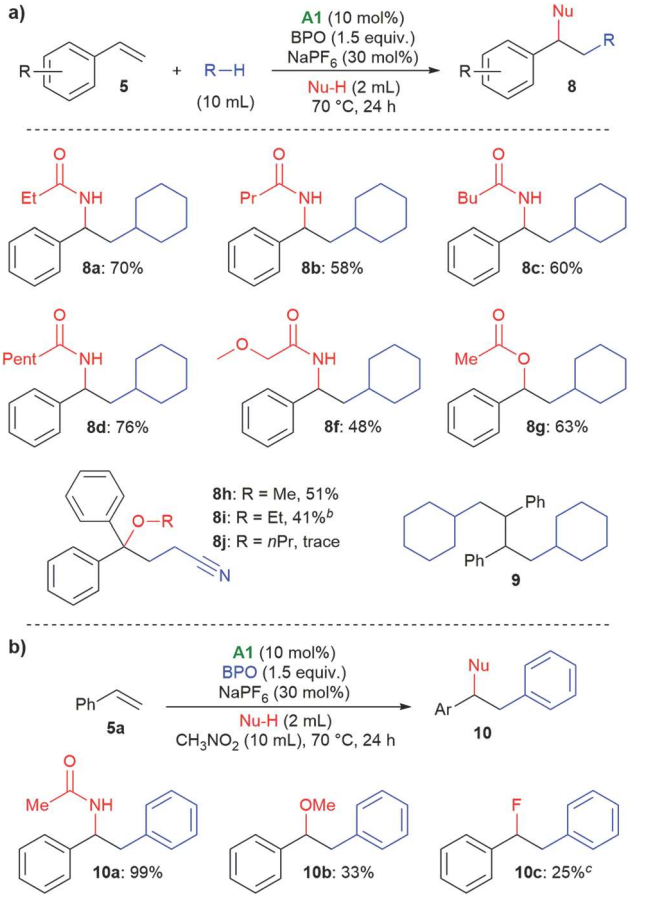
Styrenes with various substituents on the aromatic ring afforded the desired products in generally good yields (Scheme 4). There is no clear electronic substituent effect on the product yields, also substitution in the *ortho* position was not detrimental (**7l–7n**). Only in the case of *p*-methoxystyrene, the desired product was only observed in traces (**7b**). 2-Methylstyrene and stilbene could also be employed, giving the expected products **7o** and **7p** in medium yields and as mixtures of diastereomers.

Next, the scope with respect to nucleophiles was explored. As shown in Scheme 5a, different nitrile solvents and cyclohexane delivered the desired amides **8a–8e** in good yields of 48%–76%. Similarly, when acetic acid was used, the corresponding acetate **8f** was formed in 63% yield. With 1,1-diphenylethylene, difunctionalization with the α-cyanoalkyl radical from acetonitrile and alcohols was possible. With methanol and ethanol, the products **8g** and **8h** were isolated in 51% and 41% yields, respectively, however, long-chain alcohols showed a low reactivity. Very similar tertiary alcohols had recently been synthesized by copper-catalysis at higher temperature.[37] We also isolated the dimer **9** from unsuccessful tests of other nucleophiles, supporting the occurrence of radical intermediate **15**.[38,39] In nitromethane as solvent, phenyl groups were incorporated into the products (**10a–10c**, Scheme 5b). These likely originated from phenyl radicals, formed by decarboxylation of the benzoyloxyl radicals. Acetonitrile and methanol could be used as nucleophiles, and with triethylamine hydrofluoride even fluoride, albeit in low yield (**10c**).

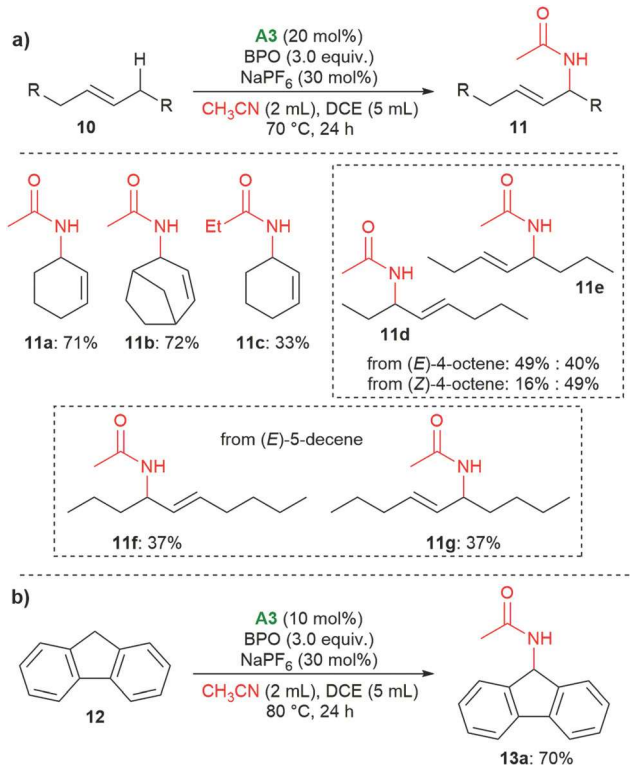
The organo-redox system also proved to catalyze the oxidative Ritter reaction of allylic and benzylic C–H bonds; for



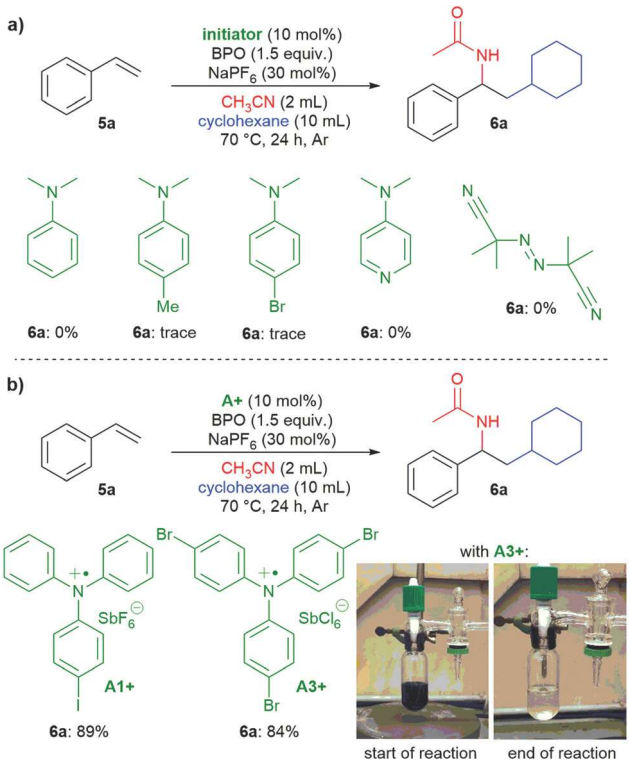
Scheme 4 Substrate scope of substituted styrenes.



Scheme 5 Scope of nucleophiles.



Scheme 6 Amination of allylic and benzylic C–H bond.



Scheme 7 a) Testing *N*,*N*-dimethylanilines and AIBN as initiators; (b) triarylamine radical cation salts act as catalysts.

these reactions, amine **A3** was found to be superior to **A1** (see the ESI† for details). As shown in Scheme 6a, cyclohexene and bicyclo[3.2.1]oct-2-ene delivered the amides **11a** and **11b** in 71% and 72% yield, respectively. When propionitrile was used, the corresponding product **11c** was isolated in 33% yield. With (*E*)-4-octene, **11d** and **11e** were isolated in 89% yield as a mixture of two isomers with a ratio of 1 : 0.8. When (*Z*)-4-octene was used, the same products were isolated with a ratio of 1 : 3. (*E*)-5-Decene gave the *E*-isomers **11f** and **11g** in equimolar amounts. When we used 9*H*-fluorene, the benzylic methylene group was functionalized, providing the amide **13** in 70% yield (Scheme 6b).

Are the triarylamines efficient initiators of a radical chain reaction, reacting irreversibly, or are they catalysts, achieving turnover?[40] As mentioned above, *N*,*N*-dialkylanilines are well-known activators of benzoyl peroxide in radical chain reactions;[31] however, they proved to be inefficient for the reactions presented here (Scheme 7a). Also, the reaction did not proceed when employing the well know radical initiator azobisisobutyronitrile (AIBN), suggesting that a radical chain mechanism is not operating. We used two radical cation salts, [(**A1**+)SbF_6^-] and [(**A3**+)$SbCl_6^-$], in place of the corresponding triarylamines under otherwise unchanged reaction conditions (Scheme 7b). In both cases, comparable yields of **6a** were achieved (89% and 84%, resp.). When **A3**+ was used, its dark blue colour disappeared and 10% of the reduced form **A3** could be isolated, ruling out that the triarylamines are irreversibly consumed and supporting that both the amine and the oxidized radical cation salts are involved in a catalytic reaction.

After completion of the reaction, the system remains active. When we added another batch of BPO and styrene to a reaction mixture forming **6a** that had gone to completion, a further 85% of these added substrates were converted to **6a** after another 30 hours. Also, a third batch of substrates could be converted to product, which further supports that the reaction is catalytic in nature (see the ESI† for details).

We also investigated the system by ^{1}H-NMR at the reaction temperature of 70 °C (Fig. 1). *Ca.* 40% of BPO on its own had

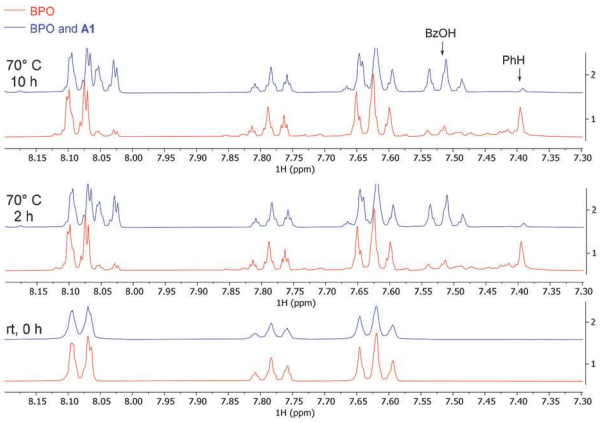
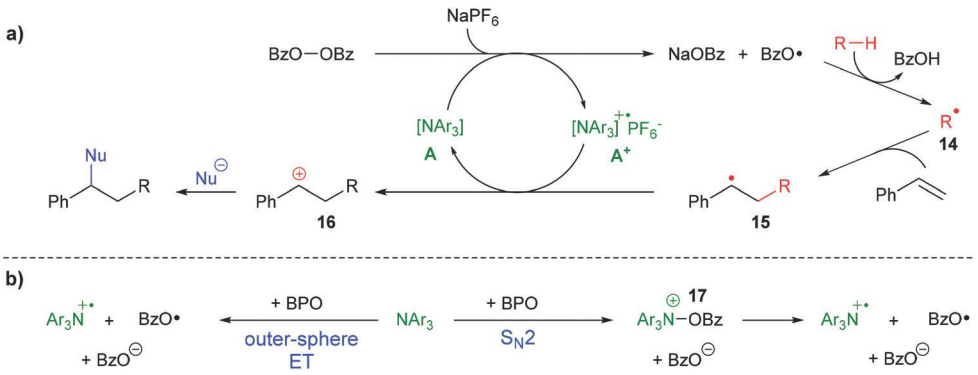


Fig. 1 NMR experiments, comparing thermal and **A1**-induced BPO decomposition (red and blue lines, resp.); conditions: BPO (0.1 mmol), **A1** (10 mol%), CD_3CN (0.5 mL), 70 °C.



Scheme 8 Proposed reaction mechanism: (a) organo-redox-catalysis; (b) effective ET by direct outer-sphere ET or stepwise *via* S_N2 reaction.

decomposed after 10 h, in line with the reported 10 hours half-life temperature of 73 °C (red bottom line).[41] Benzene and benzoic acid were formed in roughly equal amounts, indicating that half of the benzoyloxyl radicals had decarboxylated before they were quenched by HAT. Adding catalytic amounts (10 mol%) of **A1** accelerated the decomposition of BPO during the first 2 hours and resulted in forming predominantly benzoic acid (blue upper line). These results indicate that the amine catalyses the decomposition of BPO by an effective ET reaction (see Scheme 7b below and its discussion for details), forming one molecule each of benzoate – observed as benzoic acid by NMR – and benzoyloxyl radical. The latter can decarboxylate to a phenyl radical and both radicals can react by HAT reactions from the medium to form benzoic acid and benzene, respectively. This explains the appearance of significantly more benzoic acid than benzene, compared to the thermal decomposition of BPO.

During the difunctionalization reaction, a white precipitate formed, which we found to be sodium benzoate, in line with the suggested cleavage of BPO by ET (see the ESI†). All these results enable us to propose a mechanism for the formation of difunctionalization products like **6a** (Scheme 8a) The peroxide bond of BPO is cleaved by an ET reaction from the triarylamine catalyst **A**, forming the radical cation **A+**, a benzoate anion and a benzoyloxyl radical. The presence of $NaPF_6$ likely helps stabilizing the radical cation **A+** in the form of the salt [**A1** +]PF_6^-. The benzoyloxyl radical can engage with cyclohexane or other substrates in a HAT reaction, forming a carbon radical **14**, which then adds to styrene, forming the benzylic radical **15**. Oxidation by the ammoniumyl radical cation **A+** regenerates the triarylamine **A** and forms the carbocation **16**, which is attacked by nucleophiles to provide the final product. To some extent, the benzoyloxyl radicals decarboxylate, generating phenyl radicals which can either participate in HAT reactions, too, or add to styrene, as was shown in Scheme 5b above.

Whether the reaction between the triarylamine **A** and BPO proceeds by an outer-sphere ET, directly forming benzoate and two radicals, or by an S_N2-reaction *via* *N*-benzoyloxylammonium salt **17**, which in a second step decomposes homolytically into the same products (Scheme 8b), is at present unclear. Both pathways have been suggested for reactions between diacylperoxides and amines,[32,42–44] but the combination of BPO with the triarylamines used in this study has not been investigated yet.

Additionally, we studied the redox potentials of several triarylamines and the radical cation **A1+** as well as BPO by cylic voltammetry (see the ESI†). The reduction potential of **A1** was indeed lower than that of BPO, supporting that **A1** can reduce BPO by ET. However, BPO has the higher oxidation potential of the two, suggesting that it is the better electron acceptor. However, we consider these results of separate measurements as not fully conclusive for the interpretation of the mechanism, since they are not in agreement with the aforementioned results supporting catalysis by the amine. Furthermore, they do not take potential interactions in the reaction mixture into account. For example, the addition of $NaPF_6$ is crucial for the reaction to occur, which indicates an ionic interaction that might shift the redox potential of the ammoniumyl radical cation.[34] A species like **17** could be involved as electron acceptor, or the radical cation **A1+** could be transformed into the actual catalyst *in situ* by attack at its free *para*-positions.[21] Thus, we acknowledge that not all details of the present reactions are understood and we are therefore planning more detailed investigations.

Conclusions

In summary, we have established triarylamines as organo-redox catalysts for oxidative C–H functionalization reactions, with *p*-iodophenyl diphenylamine as the catalyst of choice in the newly developed method. By using benzoyl peroxide as oxidant, the difunctionalization of styrenes could be accomplished with radicals generated from hydrocarbons by hydrogen atom transfer and with nucleophiles, including nitriles, alcohols, acetic acid and fluoride. Besides, the amination of allylic and benzylic C–H bonds is also achieved under the same reaction conditions. The method does not require irradiation, electrolysis, transition metals nor significantly elevated temperatures. This application of a relatively simple

amine might pave the way for further developments of organo-redox-catalysts, which may thus become another established class amongst organocatalysts.[45]

Author contributions

S.L. and M.K. conceived the project, M.K. supervised the project, S.L. executed all experiments, S.L. and M.K. composed the manuscript, S.L. composed the ESI.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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EXPERIMENT PART

Electronic Supplementary Material (ESI) for ChemComm.

Acid Promoted Radical-Chain Difunctionalization of Styrenes with Stabilized Radicals and (N,O)-Nucleophiles

Sensheng Liu, and Martin Klussmann*

Contents

General experimental details

Unless otherwise indicated, all reagents and solvents were purchased from commercial distributors and used as received. Solvents (hexanes, ethyl acetate) used for column chromatography were of technical grade and used after distillation in a rotary evaporator.

Benzoyl peroxide (BPO) 75% remainder H_2O and Hexafluorophosphoric acid solution (HPF_6, 55% wt. in H_2O) from Sigma-Aldrich, used directly without further purification.

TLC was used to check the reactions for full conversion and was performed on Macherey-Nagel Polygram Sil G/UV254 thin layer plates. TLC spots were visualized by UV-light irradiation.

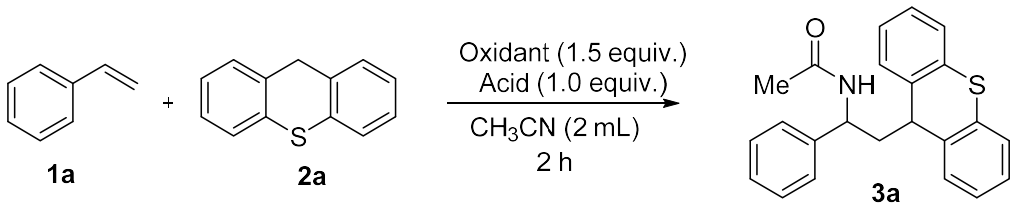
Flash column chromatography was carried out using Merck Silica Gel 60 (40-63 µm). Yields refer to pure isolated compounds.

^{1}H and ^{13}C NMR spectra were measured with Bruker AV 500 spectrometer. All chemical shifts are given in ppm downfield relative to TMS and were referenced to the solvent residual peaks.[1] ^{1}H NMR chemical shifts are designated using the following abbreviations as well as their combinations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. For ^{13}C NMR data the following abbreviations are used: p = primary (CH_3), s = secondary (CH_2), t = tertiary (CH), q = quaternary (C).

High resolution mass spectra were recorded with a Bruker APEX III FTICR-MS or a Finnigan SSQ 7000 quadrupole MS or a Finnigan MAT 95 double focusing sector field MS instrument.

The three electrode system was controlled by using a potentiostat/galvanostat (BioLogic VSP, France). Two platinized Pt wire as a counter and working electrode with a Ag/AgCl electrode as a reference were used. The cyclic voltammetry (CV) was conducted from -1 V to 0.5 V with a scan rate of 100 mV/s.

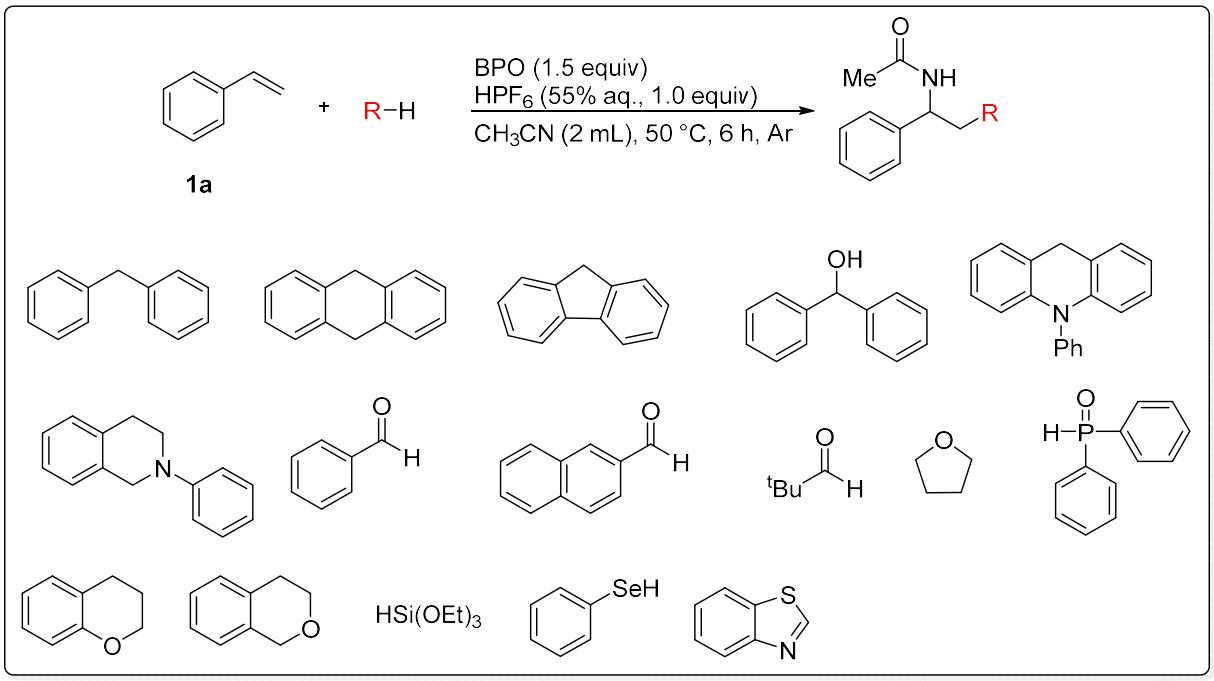
Optimization of reaction conditions[a]



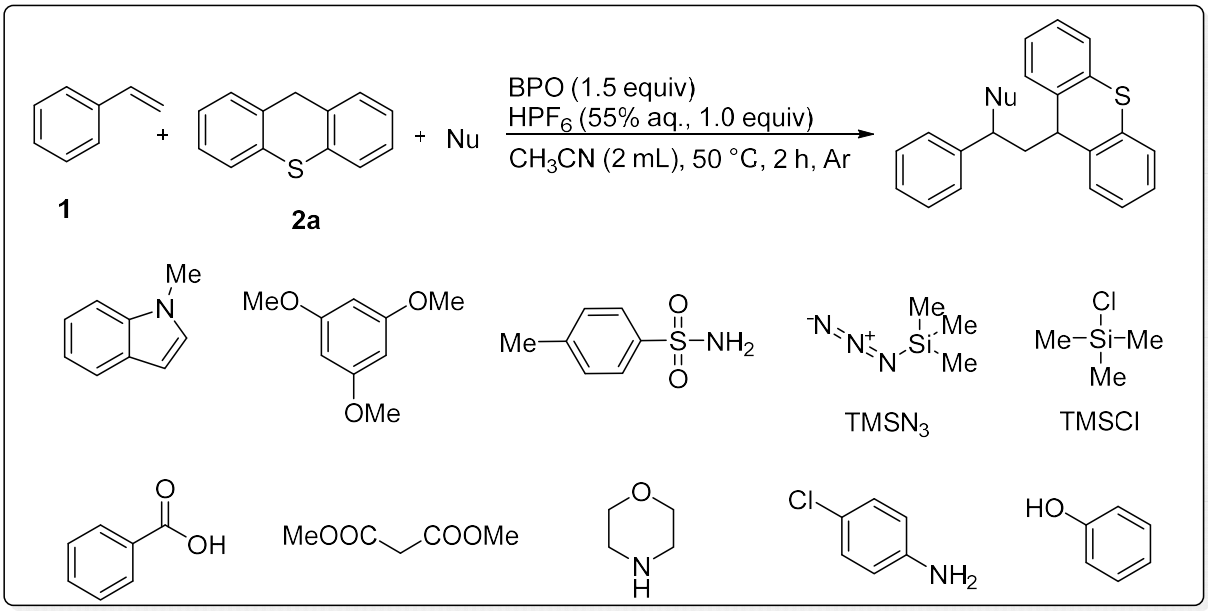
Entry	Oxidant	Equiv.	Acid	Equiv.	Additive	T/°C	Yield (%)[b]
1	BPO	(1.5 equiv.)	HCl (aq., 38%)	1.0	-	50	7
2	BPO	(1.5 equiv.)	CF_3COOH[c]	1.0	-	50	11
3	BPO	(1.5 equiv.)	H_2SO_4 (aq., 55%)	1.0	-	50	25
4	BPO	(1.5 equiv.)	HBF_4 (aq., 48%)	1.0	-	50	39
5	BPO	(1.5 equiv.)	$HClO_4$ (aq., 70%)	1.0	-	50	51
6	BPO	(1.5 equiv.)	TfOH[c]	1.0	-	50	47
7	BPO	(1.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	50	88
8	BPO	(1.5 equiv.)	-	-	$NaPF_6$ (1.0 equiv.)	50	< 5
9	DTBP	(1.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	50	0
10	TBPB	(1.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	50	0
11	TBHP	(1.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	50	0
12	BPO	(1.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	100	35
13	BPO	(1.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	r.t.	25
14	BPO	(1.5 equiv.)	HPF_6 (aq., 55%)	0.5	-	50	16
15	BPO	(1.5 equiv.)	HPF_6 (aq., 55%)	0.1	-	50	20
16	BPO	(1.5 equiv.)	-	-	-	50	0
17	BPO	(1.0 equiv.)	HPF_6 (aq., 55%)	1.0	-	50	40
18	BPO	(0.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	50	18
19	-	-	HPF_6 (aq., 55%)	1.0	-	50	0
20[d]	BPO	(1.5 equiv.)	HPF_6 (aq., 55%)	1.0	-	50	91 (88)

[a] **1a** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv.), Oxidant (0.3 mmol, 1.5 equiv.), Acid (0.2 mmol, 1.0 equiv.) and CH_3CN (2 mL), for 2 hours. [b] Yields were determined by **^{1}H NMR** spectroscopic analysis of the crude reaction mixture relative to the internal standard CH_3NO_2, yield of isolated product in parentheses. [c] H_2O (0.2 mmol, 1.0 equiv.) was added. [d] Degassed, under argon.

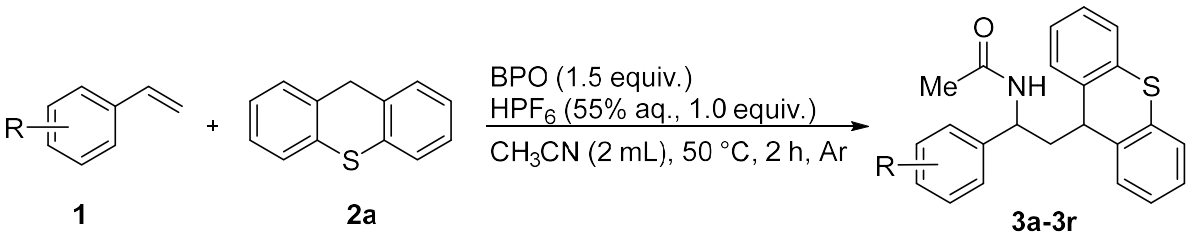
Failed examples for Hydrogen donors



Failed examples for Nucleophiles



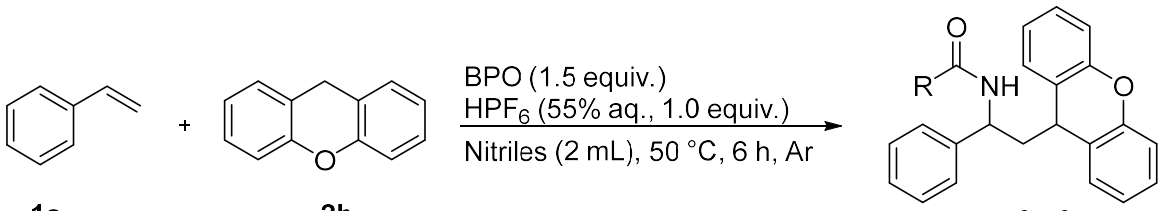
General procedure A: synthesis of *N*-(1-phenyl-2-(9*H*-thioxanthen-9-yl)ethyl)acetamides.



1 **2a** **3a-3r**

Under argon atmosphere, the thioxanthene **2a** (0.4 mmol, 2.0 equiv.), BPO (0.3 mmol, 1.5 equiv.) were added into a 10 mL glass tube. Then CH_3CN (2 mL), alkenes **1** (0.2 mmol), HPF_6 (55% aq., 0.2 mmol, 1.0 equiv.) were added. The reaction mixture was stirred at 50 °C for 2 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 10:1 to 1:1) to give the desired products **3a-3r** (*trans*-**3q** and *trans*-**3r** need 6 h).

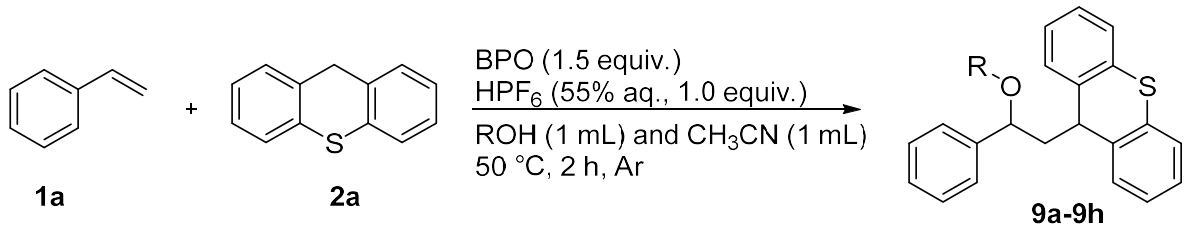
General procedure B: synthesis of *N*-(1-phenyl-2-(9*H*-xanthene-9-yl)ethyl)amides.



1a **2b** **3s-3x**

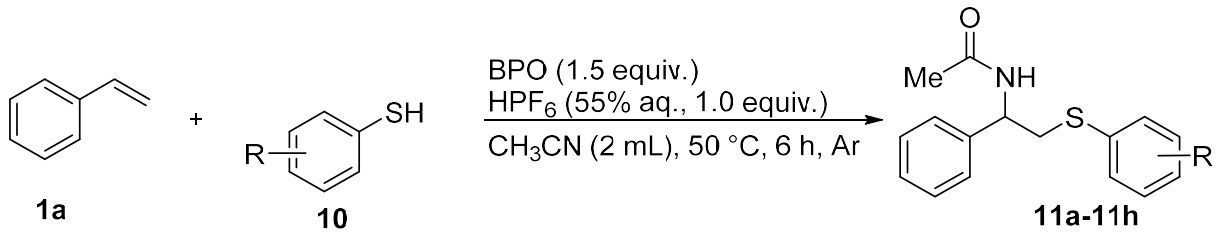
Under argon atmosphere, the xanthene **2b** (0.4 mmol, 2.0 equiv.), BPO (0.3 mmol, 1.5 equiv.) were added into a 10 mL glass tube. Then nitriles (2 mL), styrene **1a** (0.2 mmol), HPF_6 (55% aq., 0.2 mmol, 1.0 equiv.) were added. The reaction mixture was stirred at 50 °C for 6 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 10:1 to 1:1) to give the desired products **3s-3x** .

General procedure C: synthesis of 9-(2-methoxy-2-phenylethyl)-9*H*-thioxanthenes.



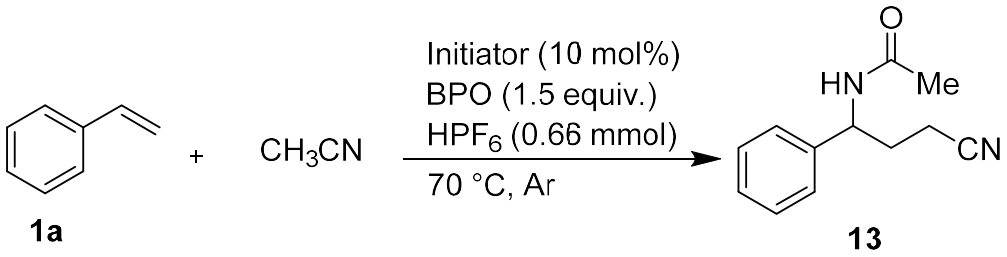
Under argon atmosphere, the thioxanthene **2a** (0.4 mmol, 2.0 equiv), BPO (0.3 mmol, 1.5 equiv) were added into a 10 mL glass tube. Then CH_3CN (1 mL), alcohols (1 mL), styrene **1a** (0.2 mmol), HPF_6 (55% aq., 0.2 mmol, 1.0 equiv) were added. The reaction mixture was stirred at 50 °C for 2 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (100:1) to give the desired products **9a-9h**.

General procedure D: synthesis of 9-(2-methoxy-2-phenylethyl)-9*H*-thioxanthene *N*-(1-phenyl-2-(phenylthio)ethyl)acetamides



Under argon atmosphere, the thiophenols **10** (0.4 mmol, 2.0 equiv.), BPO (0.3 mmol, 1.5 equiv.) were added into a 10 mL glass tube. Then CH_3CN (1 mL), alcohols (1 mL), styrene **1a** (0.2 mmol), HPF_6 (55% aq., 0.2 mmol, 1.0 equiv.) were added. The reaction mixture was stirred at 50 °C for 6 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 10:1 to 2:1) to give the desired products **5a-5h**.

General procedure E: synthesis of *N*-(3-cyano-1-phenylpropyl)acetamide

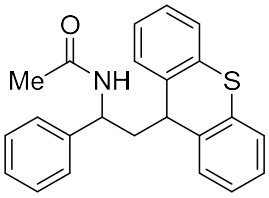


1a **13**

Under argon atmosphere, BPO (0.75 mmol, 1.5 equiv., three portions every 2 hours) were added into a 10 mL glass tube. Then CH_3CN (30 mL), styrene **1a** (0.5 mmol), HPF_6 (55% aq., 0.66 mmol, 1.32 equiv.) and a *N*,*N*-dimethylaniline derivative as initiator (10 mol%, 0.05 mmol) were added. The reaction mixture was stirred at 70 °C for 18 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 10:1 to 1:1) to give the desired products **13**.

Characterization Data

***N*-(1-phenyl-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3a**, unreported product)



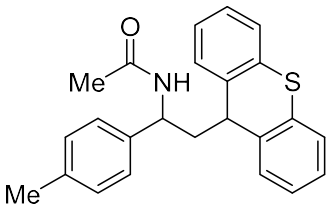
Following the general procedure **A**, white solid (65.3 mg, 91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.32 (m, 2H), 7.24-7.09 (m, 11H), 5.39 (d, J = 12.5 Hz, 1H), 4.85-4.80 (m, 1H), 4.07-4.00 (m, 1H), 2.20-2.09 (m, 2H), 1.80 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.99, 142.05, 137.66, 137.62, 132.53, 132.32, 128.97, 128.71, 128.68, 127.42, 127.23, 127.10, 126.79, 126.77, 126.71, 126.60, 51.63, 46.77, 38.02, 23.46.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{21}NOSNa$ 382.123605; found 382.123850.

***N*-(2-(9*H*-thioxanthen-9-yl)-1-(*p*-tolyl)ethyl)acetamide** (**3b**, unreported product)



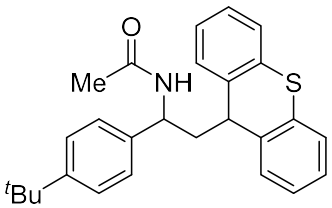
Following the general procedure **A**, white solid (62.0 mg, 83%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.31 (m, 1H), 7.20-7.10 (m, 7H), 7.04 (s, 4H), 5.35 (d, J = 8.5 Hz, 1H), 4.78 (dd, J = 15.5 Hz, 7.5 Hz, 1H), 4.05 (dd, J = 15.0 Hz, 5.0 Hz, 1H), 2.24 (s, 3H), 2.14 (t, J = 7.5 Hz, 2H), 1.79 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.89, 139.04, 137.78, 137.65, 137.12, 132.54, 132.35, 129.39, 128.93, 128.72, 127.23, 127.07, 126.67, 126.59, 51.31, 46.69, 37.93, 23.49, 21.06.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{24}H_{23}NOSNa$ 396.139255; found 396.139160.

***N*-(1-(4-(*tert*-butyl)phenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3c**, unreported product)



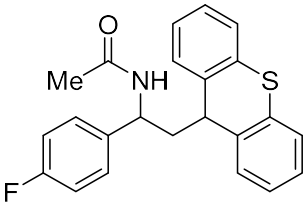
Following the general procedure **A**, white solid (51.4 mg, 62%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (d, J = 8.5 Hz, 1H), 7.49 (dd, J = 6.5 Hz, 4.0 Hz, 1H), 7.44 (d, J = 7.0 Hz, 1H), 7.40 (d, J = 6.5 Hz, 1H), 7.32-7.23 (m, 7H), 7.00 (d, J = 8.0 Hz, 2H), 4.45-4.40 (m, 1H), 4.18 (dd, J = 9.5 Hz, 4.5 Hz, 1H), 2.09-2.04 (m, 1H), 1.92 (s, 3H), 1.85-1.78 (m, 1H), 1.22 (s, 9H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.95, 149.42, 141.14, 138.65, 137.14, 131.87, 131.72, 129.89, 129.13, 127.35, 127.22, 127.18, 127.11, 126.29, 125.48, 50.28, 45.69, 39.13, 34.55, 31.58, 23.26.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{27}H_{29}NOSNa$ 438.186205; found 438.186910.

***N*-(1-(4-fluorophenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3d**, unreported product)



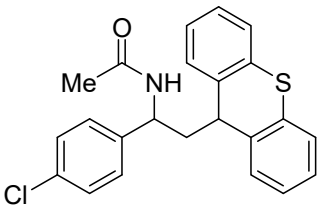
Following the general procedure **A**, white solid (72.4 mg, 96%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7-33 (m, 2H), 7.17-7.09 (m, 8H), 6.90 (t, J = 10.0 Hz, 2H), 5.35 (d, J = 5.0 Hz, 1H), 4.81-4.76 (m, 1H), 4.01 (t, 2H, J = 10.0 Hz, 1H), 2.15-2.11 (m, 2H), 1.80 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.05, 162.92, 160.97, 137.92 (d, J = 3.75 Hz, 1C), 137.46 (d, J = 8.75 Hz, 1C), 133.46, 132.52, 132.29, 130.12, 128.92, 128.66, 128.45, 128.26, 128.19, 127.28, 127.16, 126.86 (d, J = 3.75 Hz, 1C), 126.78, 115.57, 115.40, 51.09, 46.85, 37.92, 23.42.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{20}FNOSNa$ 400.114184; found 400.114170.

***N*-(1-(4-chlorophenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3e**, unreported product)



Following the general procedure **A**, white solid (66.0 mg, 84%).

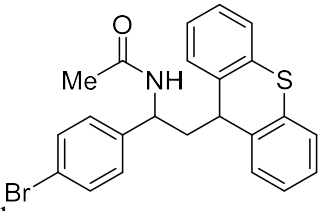
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 (d, J = 5.0 Hz, 1H), 7.55-7.54 (m, 1H), 7.50 (dd, J = 5.0 Hz, 2.5 Hz, 1H), 7.45 (dd, J = 5.0 Hz, 1.5 Hz, 1H), 7.38-7.28 (m, 7H), 7.15 (d, J = 8.5 Hz, 2H), 4.48-4.41 (m, 1H), 4.25 (dd, J = 10.0 Hz, 5.5 Hz, 1H), 2.12-2.08 (m, 1H), 1.98 (s, 3H), 1.92-1.86 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.10, 143.08, 138.40, 136.97, 131.88, 131.73, 131.63, 129.84, 129.20, 128.76, 128.51, 127.42, 127.40, 127.37, 127.30, 127.24, 127.17, 50.24, 45.58, 38.76, 23.20.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{20}ClNOSNa$ 416.084633; found 416.084760.

***N*-(1-(4-bromophenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3f**, unreported product)

Following the general procedure **A**, white solid (70.8 mg, 81%).

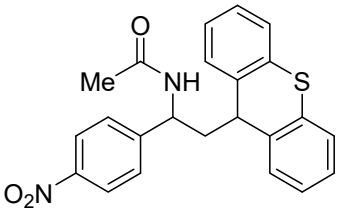


^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 (d, J = 5.0 Hz, 1H), 7.55-7.53 (m, 1H), 7.50 (d, J = 8.5 Hz, 3H), 7.45 (dd, J = 7.5 Hz, 1.0 Hz, 1H), 7.38-7.28 (m, 5H), 7.09 (d, J = 8.5 Hz, 2H), 4.46-4.41 (m, 1H), 4.25 (dd, J = 9.5 Hz, 5.0 Hz, 1H), 2.14-2.08 (m, 1H), 1.97 (s, 3H), 1.92-1.85 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.11, 143.51, 138.39, 136.96, 131.88, 131.73, 131.67, 129.84, 129.20, 128.89, 127.43, 127.41, 127.37, 127.30, 127.24, 127.17, 120.12, 50.31, 45.57, 38.69, 23.20.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{20}BrNOSNa$ 460.034131; found 460.034780.

***N*-(1-(4-nitrophenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3g**, unreported product)



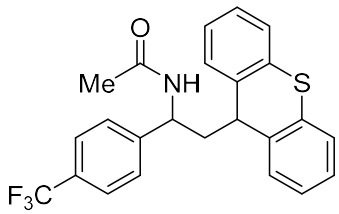
Following the general procedure **A**, light yellow solid (8.0 mg, 10%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.69 (d, J = 8.0 Hz, 1H), 8.81 (d, J = 8.5 Hz, 2H), 7.57-7.55 (m, 1H), 7.50 (t, J = 16.5 Hz, 8.0 Hz, 2H), 7.40-7.30 (m, 7H), 4.56-4.51 (m, 1H), 4.34 (dd, J = 10.0 Hz, 5.0 Hz, 1H), 2.18-2.12 (m, 1H), 2.01 (s, 3H), 1.94-1.88 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.37, 151.87, 146.76, 138.27, 136.67, 131.90, 131.77, 129.89, 129.22, 127.86, 127.53, 127.47, 127.42, 127.36, 127.25, 127.21, 124.12, 50.78, 45.49, 38.33, 23.15.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{20}N_2O_3SNa$ 427.108684; found 427.109200.

***N*-(2-(9*H*-thioxanthen-9-yl)-1-(4-(trifluoromethyl)phenyl)ethyl)acetamide** (**3h**, unreported product)



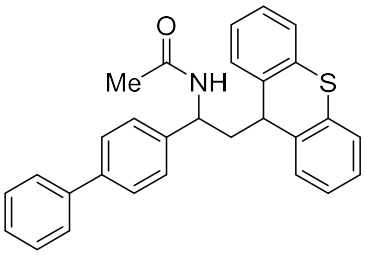
Following the general procedure **A**, white solid (25.6 mg, 30%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.64 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.56-7.55 (m, 1H), 7.50-7.47 (m, 2H), 7.37-7.30 (m, 7H), 4.54-4.50 (m, 1H), 4.31 (dd, J = 10.0 Hz, 5.0 Hz, 1H), 2.18-2.14 (m, 1H), 2.00 (s, 3H), 1.92-1.87 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.27, 148.88, 138.38, 136.79, 131.88, 131.75, 129.89, 129.20, 127.48, 127.44, 127.39, 127.32, 127.23, 127.18, 125.78, 125.74, 125.71, 50.72, 45.55, 38.61, 23.17.

HRMS (ESIneg) (m/z): H^- calculated for $C_{24}H_{20}F_3NOS$ 426.114497; found 426.115170.

***N*-(1-([1,1'-biphenyl]-4-yl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3i**, unreported product)



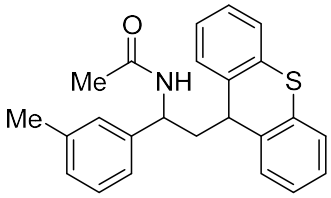
Following the general procedure **A**, white solid (69.6 mg, 80%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 7.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H), 7.51-7.49 (m, 1H), 7.46-7.42 (m, 4H), 7.35-7.24 (m, 6H), 7.71 (d, J = 8.0 Hz, 2H), 4.51-4.46 (m, 1H), 4.23 (dd, J = 10.0 Hz, 5.0 Hz, 1H), 2.15-2.10 (m, 1H), 1.59 (s, 3H), 1.91-1.85 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.06, 143.34, 140.37, 139.11, 138.55, 137.11, 131.89, 131.75, 129.89, 129.34, 129.19, 127.75, 127.40, 127.37, 127.27, 127.23, 127.21, 127.15, 127.01, 50.46, 45.68, 39.01, 23.27.

HRMS (ESIpos+neg) (m/z): M^+ calculated for $C_{29}H_{25}NOSNa$ 458.154905; found 458.154970.

***N*-(2-(9*H*-thioxanthen-9-yl)-1-(*m*-tolyl)ethyl)acetamide** (**3j**, unreported product)



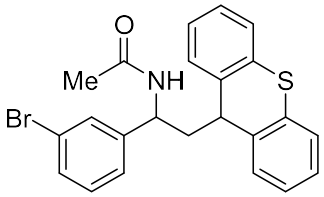
Following the general procedure **A**, white solid (50.0 mg, 63%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.43 (d, J = 8.5 Hz, 1H), 7.50-7.48 (m, 1H), 7.45-7.39 (m, 2H), 7.33-7.23 (m, 5H), 7.14 (t, J = 7.5 Hz 1H), 6.98 (d, J = 7.5 Hz, 1H), 6.88-6.86 (m, 2H), 4.42-4.40 (m, 1H), 4.18 (dd, J = 10.0 Hz, 5.0 Hz, 1H), 2.24 (s, 3H), 2.09-2.03 (m, 1H), 1.93 (s, 3H), 1.85-1.79 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.95, 144.10, 138.62, 137.81, 137.10, 131.86, 131.71, 129.89, 129.17, 128.69, 127.78, 127.37, 127.24, 127.22, 127.19, 127.13, 123.71, 50.58, 45.66, 39.19, 23.28, 21.49.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{24}H_{23}NOSNa$ 396.139256; found 396.139410.

***N*-(1-(3-bromophenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3k**, unreported product)



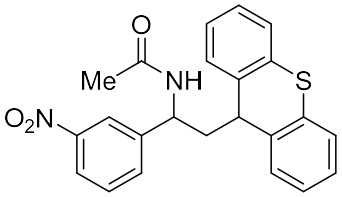
Following the general procedure **A**, white solid (67.3 mg, 77%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (d, J = 8.5 Hz, 1H), 7.55-7.53 (m, 1H), 7.50 (dd, J = 7.5 Hz, 1.0 Hz, 1H), 7.47-7.41 (m, 2H), 7.38-7.25 (m, 7H), 7.10 (d, J = 7.5 Hz, 1H), 4.48-4.39 (m, 1H), 4.28 (dd, J = 9.5 Hz, 5.0 Hz, 1H), 2.14-2.08 (m, 1H), 2.04 (s, 3H), 1.92-1.86 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.17, 146.97, 138.43, 136.86, 131.90, 131.76, 131.06, 130.08, 129.85, 129.22, 129.17, 127.44, 127.42, 127.38, 127.29, 127.22, 127.16, 125.83, 122.12, 50.49, 45.63, 38.80, 23.22.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{20}BrNOSNa$ 460.034131; found 460.033700.

***N*-(1-(3-nitrophenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3l**, unreported product)



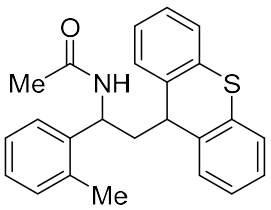
Following the general procedure **A**, light yellow solid (26.6 mg, 33%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.64 (d, J = 8.0 Hz, 1H), 8.05-8.63 (m, 1H), 7.94 (s, 1H), 7.56-7.42 (m, 5H), 7.32-7.25 (m, 5H), 4.56-4.51 (m, 1H), 4.29 (dd, J = 10.0 Hz, 5.5 Hz, 1H), 2.15-2.09 (m, 1H), 1.94 (s, 3H), 1.92-1.88 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.30, 148.30, 146.30, 138.31, 136.75, 133.66, 131.91, 131.79, 130.41, 129.85, 129.22, 127.47, 127.43, 127.40, 127.34, 127.24, 127.19, 122.28, 121.15, 50.61, 45.57, 38.43, 23.18.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{20}N_2O_3SNa$ 427.108684; found 427.109450.

***N*-(2-(9*H*-thioxanthen-9-yl)-1-(*o*-tolyl)ethyl)acetamide** (**3m**, unreported product)



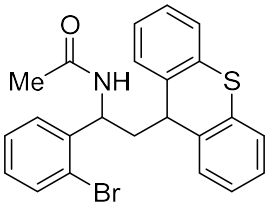
Following the general procedure **A**, white solid (57.4 mg, 77%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (d, J = 8.5 Hz, 1H), 7.50-7.48 (m, 1H), 7.43 (d, J = 7.0 Hz, 1H), 7.42 (d, J = 5.0 Hz, 1H), 7.34-7.29 (m, 4H), 7.26-7.20 (m, 2H), 7.10 (t, J = 7.5 Hz, 1H), 7.04-7.00 (m, 1H), 6.97 (d, J = 10.0 Hz, 1H), 4.71-4.67 (m, 1H), 4.25 (dd, J = 11.0 Hz, 3.5 Hz, 1H), 2.20-1.97 (m, 4H), 1.70 (s, 3H), 1.62-1.56 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.11, 142.90, 138.74, 136.57, 134.12, 131.74, 131.66, 130.39, 130.28, 129.04, 127.50, 127.41, 127.24, 127.15, 127.07, 127.00, 126.69, 126.45, 125.22, 46.93, 45.82, 38.62, 23.26, 18.01.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{24}H_{23}NOSNa$ 396.139255; found 396.139960.

***N*-(1-(2-bromophenyl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3n**, unreported product)



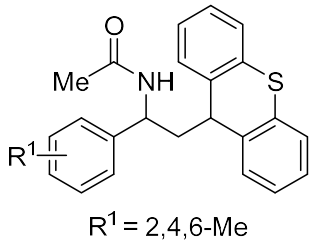
Following the general procedure **A**, white solid (62.0 mg, 71%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.69 (d, J = 7.5 Hz, 1H), 7.48-7.45 (m, 2H), 7.41-7.39 (m, 2H), 7.34-7.28 (m, 6H), 7.25-7.21 (m, 1H), 7.08 (td, J = 15.0 Hz, 7.5 Hz, 2.5 Hz, 1H), 4.81-4.76 (m, 1H), 4.31 (dd, J = 11.5 Hz, 4.0 Hz, 1H), 2.22-2.16 (m, 1H), 2.02 (s, 3H), 1.49-1.43 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.17, 146.97, 138.43, 136.86, 131.90, 131.76, 131.06, 130.08, 129.85, 129.22, 129.17, 127.44, 127.42, 127.38, 127.29, 127.22, 127.16, 125.83, 122.12, 50.49, 45.63, 38.80, 23.22.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{20}BrNOSNa$ 460.034131; found 460.034720.

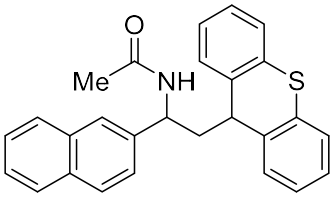
***N*-(1-mesityl-2-(9H-thioxanthen-9-yl)ethyl)acetamide** (**3o**, unreported product)



Following the general procedure **A**, white solid (61.5 mg, 75%).

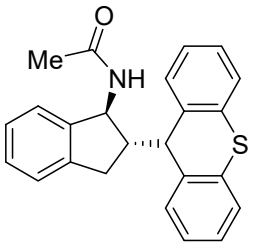
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (d, J = 8.5 Hz, 1H), 7.50-7.48 (m, 1H), 7.44 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.40 (dd, J = 10.0 Hz, 5.0 Hz, 1H), 7.33-7.24 (m, 7H), 7.00 (d, J = 8.5 Hz, 2H), 4.45-4.42 (m, 1H), 4.18 (dd, J = 9.5 Hz, 4.5 Hz, 1H), 2.10-2.04 (m, 1H), 1.92 (s, 3H), 1.84-1.78 (m, 1H), 1.22 (s, 9H).
^{13}C NMR (125 MHz, DMSO-d_6) δ 168.93, 149.43, 141.14, 138.65, 137.14, 131.86, 131.72, 129.89, 129.13, 127.36, 127.22, 127.19, 127.12, 126.26, 125.49, 50.27, 45.68, 39.13, 34.56, 31.58, 23.26.
HRMS (ESIpos) (m/z): M^+ calculated for $C_{26}H_{27}NOSNa$.170555; found 424.170840424.

***N*-(1-(naphthalen-2-yl)-2-(9*H*-thioxanthen-9-yl)ethyl)acetamide** (**3p**, unreported product)



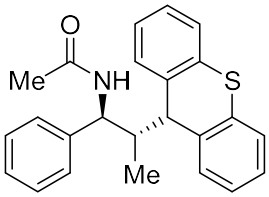
Following the general procedure **A**, white solid (59.7 mg, 73%).
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.62 (d, J = 8.5 Hz, 1H), 7.91-7.86 (m, 3H), 7.57-7.48 (m, 6H), 7.38-7.29 (m, 6H), 4.69-4.64 (m, 1H), 4.30 (dd, J = 9.5 Hz, 5.0 Hz, 1H), 2.28-2.21 (m, 1H), 2.04-1.98 (m, 4H).
^{13}C NMR (125 MHz, DMSO-d_6) δ 169.12, 141.52, 138.57, 137.11, 133.26, 132.48, 131.91, 131.77, 129.92, 129.25, 128.51, 128.11, 127.86, 127.42, 127.39, 127.28, 127.23, 127.19, 126.58, 126.12, 125.25, 124.93, 50.83, 45.66, 38.83, 23.30.
HRMS (ESIpos) (m/z): M^+ calculated for $C_{27}H_{23}NOSNa$ 432.139255; found 432.139730.

***trans*-*N*-(2-(9*H*-thioxanthen-9-yl)-2,3-dihydro-1*H*-inden-1-yl)acetamide** (*trans*-**3q**, unreported product)



Following the general procedure **A** (reaction time for 6 hours), white solid (22.2 mg, 30%).
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.69 (d, J = 9.0 Hz, 1H), 7.59 (dd, J = 7.5 Hz, 2.0 Hz, 1H), 7.52 (dd, J = 6.5 Hz, 1.5 Hz, 1H), 7.50-7.48 (m, 1H), 7.44 (dd, J = 7.0 Hz, 2.0 Hz, 1H), 7.37-7.31 (m, 2H), 7.30-7.24 (m, 2H), 7.16-7.12 (m, 3H), 7.00-7.98 (m, 1H), 5.33 (t, J = 9.0 Hz, 1H), 4.45 (d, J = 9.0 Hz, 1H), 2.93-2.86 (m, 1H), 2.79-2.74 (m, 1H), 2.39-2.34 (m, 1H), 1.56 (s, 3H).
^{13}C NMR (125 MHz, DMSO-d_6) δ 168.90, 144.77, 140.73, 137.22, 132.48, 131.97, 130.30, 129.83, 127.59, 127.24, 127.13, 126.95, 126.91, 126.84, 124.53, 123.78, 57.29, 51.70, 47.42, 35.39, 22.76.
HRMS (ESIpos) (m/z): M^+ calculated for $C_{24}H_{21}NOSNa$ 394.123605; found 394.124240.

***trans*-*N*-(1-phenyl-2-(9*H*-thioxanthen-9-yl)propyl)acetamide** (*trans*-**3r**, unreported product)



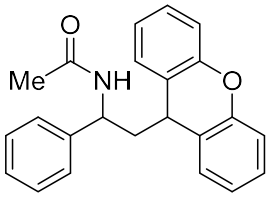
Following the general procedure **A** (reaction time for 6 hours), white solid (36.5 mg, 49%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.09 (d, J = 8.5 Hz, 1H), 7.57-7.55 (m, 1H), 7.48 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.37-7.35 (m, 2H), 7.31-7.21 (m, 6H), 7.12 (t, J = 7.5 Hz, 1H), 7.09-6.87 (m, 2H), 4.58 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 4.07 (d, J = 10.0 Hz, 1H), 2.41-2.37 (m, 1H), 2.11 (s, 3H), 0.44 (d, J = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.90, 143.46, 137.71, 137.67, 132.47, 130.56, 128.49, 127.62, 127.46, 127.23, 127.10, 126.97, 126.78, 126.60, 126.12, 53.48, 51.76, 37.80, 23.23, 12.08.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{24}H_{23}NOSNa$ 396.1392563; found 96.139390.

***N*-(1-phenyl-2-(9*H*-xanthen-9-yl)ethyl)acetamide** (**3s**, unreported product)



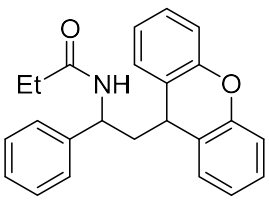
Following the general procedure **B**, white solid (63.1 mg, 92%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 7.5 Hz, 1H), 7.20-7.10 (m, 8H), 7.08-6.99 (m, 4H), 5.40 (d, J = 8.5 Hz, 1H), 4.95-4.90 (m, 1H), 3.98 (dd, J = 7.0 Hz, 5.5 Hz, 1H), 2.13-2.05 (m, 2H), 1.79 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.06, 152.39, 152.29, 142.25, 128.68, 128.66, 128.21, 127.90, 127.34, 126.41, 125.25, 124.98, 123.50, 123.44, 116.78, 116.62, 50.82, 46.67, 36.86, 23.40.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{23}H_{21}NO_2Na$ 366.146448; found 366.146620.

***N*-(1-phenyl-2-(9*H*-xanthen-9-yl)ethyl)propionamide** (**3t**, unreported product)



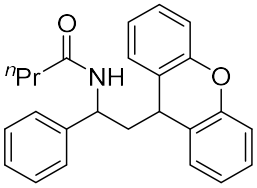
Following the general procedure **B**, white solid (51.4 mg, 72%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.21-7.09 (m, 8H), 7.06-6.99 (m, 4H), 5.35 (d, J = 8.0 Hz, 1H), 4.98-4.93 (m, 1H), 3.96 (t, J = 6.5 Hz, 1H), 2.11-1.97 (m, 4H), 1.01 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.74, 152.38, 152.27, 142.28, 133.60, 130.16, 128.68, 128.46, 128.20, 127.88, 127.33, 126.43, 125.32, 125.08, 123.50, 123.42, 116.77, 116.60, 50.66, 46.76, 36.85, 29.67, 9.63.

HRMS (ESIpos+neg) (m/z): $[M+H]^+$ calculated for $C_{24}H_{24}NO_2Na$ 358.180154; found 358.179870.

***N*-(1-phenyl-2-(9*H*-xanthen-9-yl)ethyl)butyramide** (**3u**, unreported product)



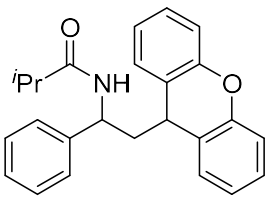
Following the general procedure **B**, white solid (60.1 mg, 81%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 8.5 Hz, 1H), 7.40 (dd, J = 7.5 Hz, 6.0 Hz, 1H), 7.35-7.29 (m, 5H), 7.23-7.16 (m, 7H), 4.90-4.80 (m, 1H), 4.07 (dd, J = 9.5 Hz, 4.0 Hz, 1H), 2.27-2.18 (m, 2H), 2.07-2.04 (m, 1H), 1.85-1.70 (m, 1H), 1.66-1.60 (m, 2H), 0.94 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 171.97, 152.09, 152.03, 144.08, 129.60, 129.05, 128.75, 128.46, 128.23, 127.11, 126.55, 125.13, 124.05, 123.79, 116.81, 116.53, 49.82, 47.98, 37.95, 36.25, 19.27, 14.15.

HRMS (ESIpos+neg) (m/z): $[M+H]^+$ calculated for $C_{25}H_{26}NO_2$ 372.195804; found 372.195770.

***N*-(1-phenyl-2-(9*H*-xanthen-9-yl)ethyl)*iso*-butyramide** (**3v**, unreported product)



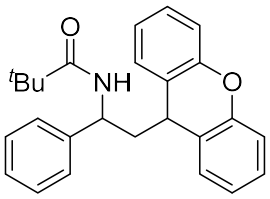
Following the general procedure **B**, white solid (30.4 mg, 41%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 (d, J = 8.5 Hz, 1H), 7.40 (dd, J = 7.5 Hz, 2.0 Hz, 1H), 7.32-7.26 (m, 1H), 7.25-7.23 (m, 4H), 7.17-7.10 (m, 7H), 4.81-4.76 (m, 1H), 4.01 (dd, J = 9.5 Hz, 4.0 Hz, 1H), 2.06-2.00 (m, 1H), 1.99-1.74 (m, 1H), 1.12 (d, J = 6.5 Hz, 3H), 1.01 (d, J = 6.5 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 175.97, 152.09, 152.03, 144.12, 129.59, 129.06, 128.78, 128.47, 128.24, 127.09, 126.56, 126.48, 125.14, 124.05, 123.81, 116.81, 116.54, 49.64, 48.06, 36.29, 34.58, 20.30, 19.87.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{25}H_{25}NO_2Na$ 394.177747; found 394.177150.

***N*-(1-phenyl-2-(9*H*-xanthen-9-yl)ethyl)pivalamide** (**3w**, unreported product)



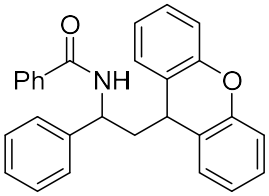
Following the general procedure **B**, white solid (39.2 mg, 51%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.01 (d, J = 7.5 Hz, 1H), 7.46 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 7.37-7.34 (m, 1H), 7.33-7.28 (m, 4H), 7.22-7.16 (m, 7H), 4.91-4.88 (m, 1H), 4.02 (dd, J = 10.0 Hz, 4.0 Hz, 1H), 2.27-2.21 (m, 1H), 1.85-1.80 (m, 1H), 1.24 (s, 9H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 177.34, 152.09, 152.03, 144.34, 129.60, 129.20, 128.69, 128.44, 128.22, 126.98, 126.61, 126.46, 125.21, 123.99, 123.80, 116.83, 116.50, 49.87, 47.73, 38.65, 36.42, 27.90.

HRMS (ESIpos+neg) (m/z): $[M+H]^+$ calculated for $C_{26}H_{27}NO_2$ 386.211454; found 386.210940.

***N*-(1-phenyl-2-(9*H*-xanthen-9-yl)ethyl)benzamide** (**3x**, unreported product)



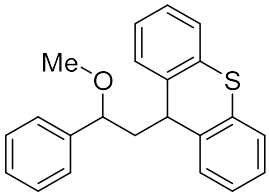
Following the general procedure **B**, white solid (32.4 mg, 40%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.94 (d, J = 8.5 Hz, 1H), 7.90-7.88 (m, 2H), 7.56-7.39 (m, 5H), 7.2-7.20 (m, 7H), 7.17-7.11 (m, 4H), 5.04-5.00 (m, 1H), 4.12 (dd, J = 9.5 Hz, 4.5 Hz, 1H), 2.36-2.30 (m, 1H), 1.90-1.85 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 166.46, 152.14, 152.01, 144.05, 134.99, 131.71, 129.60, 129.21, 128.79, 128.71, 128.67, 128.65, 128.44, 128.24, 127.89, 127.82, 127.21, 126.75, 126.50, 126.44, 125.16, 123.99, 123.82, 116.82, 116.53, 50.76, 47.34, 36.49.

HRMS (ESIpos+neg) (m/z): $[M+Na]^+$ calculated for $C_{28}H_{23}NO_2Na$ 428.162098; found 428.162020.

9-(2-methoxy-2-phenylethyl)-9*H*-thioxanthene (**9a**, unreported product)



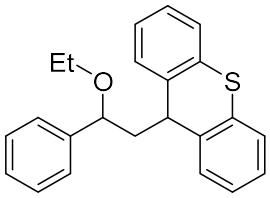
Following the general procedure **C**, white solid (58.6 mg, 91%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.43 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.41-7.34 (m, 7H), 7.28-7.23 (m, 2H), 7.11-7.10 (m, 2H), 4.43 (dd, J = 10.5 Hz, 5.5 Hz, 1H), 4.07 (dd, J = 10.5 Hz, 3.5 Hz, 1H), 3.08 (s, 3H), 2.01-1.95 (m, 1H), 1.81-1.76 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 141.85, 138.77, 137.04, 131.89, 129.90, 129.01, 128.94, 128.07, 127.50, 127.44, 127.19, 127.11, 126.80, 80.67, 56.17, 45.29, 40.80.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{22}H_{20}OSNa$ 355.112707; found 355.112750.

9-(2-ethoxy-2-phenylethyl)-9*H*-thioxanthene (**9b**, unreported product)



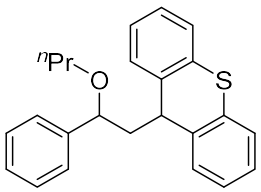
Following the general procedure **C**, colorless oil (50.5 mg, 73%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.43 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.40-7.22 (m, 9H), 7.11-7.10 (m, 2H), 4.43 (dd, J = 10.5 Hz, 5.5 Hz, 1H), 3.76 (dd, J = 10.0 Hz, 3.0 Hz, 1H), 3.21-3.13 (m, 2H), 2.00-1.95 (m, 1H), 1.80-1.75 (m, 1H), 1.16 (t, J = 6.5 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 142.57, 138.84, 137.13, 131.95, 131.93, 129.87, 128.99, 128.89, 127.91, 127.50, 127.47, 127.40, 127.20, 127.14, 127.07, 126.61, 79.01, 63.73, 45.44, 40.91, 15.79.

HRMS (EI) (m/z): calculated for $C_{23}H_{22}OS$ 346.139138; found 346.139318.

9-(2-phenyl-2-propoxyethyl)-9*H*-thioxanthene (**9c**, unreported product)



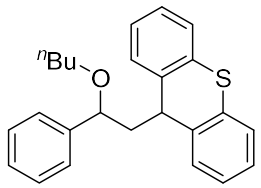
Following the general procedure **C**, colorless oil (67.0 mg, 93%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.52-7.50 (m, 1H), 7.44 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.40 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.36-7.34 (m, 2H), 7.32-7.27 (m, 4H), 7.25-7.21 (m, 2H), 7.11-7.09 (m, 2H), 4.43 (dd, J = 10.5 Hz, 4.5 Hz, 1H), 3.76 (dd, J = 10.0 Hz, 3.0 Hz, 1H), 3.10 (t, J = 6.5 Hz, 2H), 2.01-1.95 (m, 1H), 1.81-1.75 (m, 1H), 1.60-1.53 (m, 2H), 0.93 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 142.58, 138.85, 137.14, 131.93, 131.90, 129.83, 128.99, 128.89, 127.92, 127.53, 127.50, 127.42, 127.21, 127.16, 127.09, 126.64, 79.10, 70.03, 45.45, 41.03, 23.20, 11.31.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{24}H_{24}OSNa$ 383.144007; found 383.144320.

9-(2-butoxy-2-phenylethyl)-9*H*-thioxanthene (**9d**, unreported product)



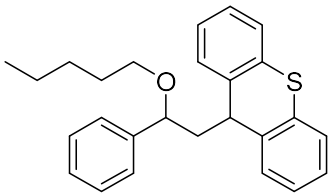
Following the general procedure **C**, Colorless oil (68.8 mg, 92%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.35 (m, 1H), 7.28-7.26 (m, 3H), 7.18-7.05 (m, 9H), 4.41 (dd, J = 11.0 Hz, 4.5 Hz, 1H), 3.70 (dd, J = 10.5 Hz, 3.0 Hz, 1H), 3.21-3.17 (m, 1H), 3.12-3.07 (m, 1H), 2.14-2.09 (m, 1H), 1.80-1.74 (m, 1H), 1.59-1.52 (m, 2H); 1.43-1.36 (m, 2H), 0.89 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.71, 138.98, 137.10, 132.56, 132.39, 129.60, 128.51, 128.25, 127.28, 127.20, 126.83, 126.68, 126.60, 126.46, 126.38, 126.15, 79.21, 68.32, 45.71, 40.82, 32.33, 19.71, 14.08.

HRMS (EI) (m/z): calculated for $C_{25}H_{26}OS$ 374.170438; found 374.170248.

9-(2-(pentyloxy)-2-phenylethyl)-9*H*-thioxanthene (**9e**, unreported product)



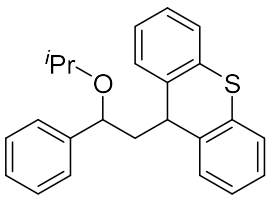
Following the general procedure **C**, Colorless oil (65.1 mg, 84%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.57-7.55 (m, 1H), 7.48 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.44 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.40-7.31 (m, 6H), 7.30-7.25 (m, 2H), 7.16-7.14 (m, 2H), 4.46 (dd, J = 10.5 Hz, 5.5 Hz, 1H), 3.80 (dd, J = 10.0 Hz, 3.5 Hz, 1H), 3.17 (t, J = 6.5 Hz, 2H), 2.05-2.00 (m, 1H), 1.86-1.80 (m, 1H), 1.61-1.57 (m, 2H), 1.42-1.31 (m, 5H), 0.94 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 142.58, 138.83, 137.16, 133.70, 131.96, 131.91, 129.78, 129.51, 129.22, 128.97, 128.88, 127.92, 127.53, 127.49, 127.42, 127.21, 127.16, 127.05, 126.64, 79.13, 68.31, 45.46, 41.01, 29.58, 28.45, 22.43, 14.38.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{26}H_{28}OSNa$ 411.175307; found 411.175940.

9-(2-isopropoxy-2-phenylethyl)-9*H*-thioxanthene (**9f**, unreported product)



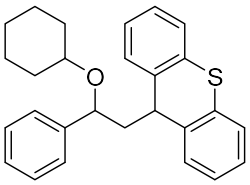
Following the general procedure **C**, colorless oil (49.6 mg, 69%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.55 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.47 (dd, J = 7.5 Hz, 1.0 Hz, 1H), 7.44-7.41 (m, 2H), 7.39-7.25 (m, 7H), 7.14-7.16 (m, 2H), 4.40 (dd, J = 10.0 Hz, 5.0 Hz, 1H), 4.05 (dd, J = 9.5 Hz, 3.0 Hz, 1H), 3.41-3.39 (m, 1H), 2.06-2.00 (m, 1H), 1.82-1.77 (m, 1H), 1.16 (d, J = 6.0 Hz, 3H), 1.05 (d, J = 6.0 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 143.36, 139.06, 137.37, 131.99, 131.95, 130.00, 128.93, 128.85, 127.85, 127.57, 127.49, 127.39, 127.24, 127.11, 126.98, 126.71, 76.05, 68.55, 45.40, 41.36, 23.91, 21.66.

HRMS (EI) (m/z): calculated for $C_{24}H_{24}OS$ 360.154787; found 360.154395.

9-(2-(cyclohexyloxy)-2-phenylethyl)-9*H*-thioxanthene (**9g**, unreported product)



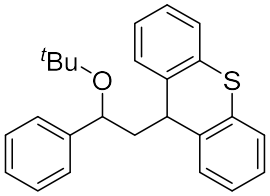
Following the general procedure **C**, colorless oil (22.4 mg, 28%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.50 (dd, J = 7.0 Hz, 1.0 Hz, 1H), 7.43 (dd, J = 7.5 Hz, 1.5 Hz, 1H), 7.39-7.34 (m, 2H), 7.33-7.24 (m, 5H), 7.23-7.20 (m, 2H), 7.12-7.10 (m, 2H), 4.35 (dd, J = 10.0 Hz, 4.5 Hz, 1H), 4.09 (dd, J = 9.5 Hz, 3.0 Hz, 1H), 3.08-3.04 (m, 1H), 2.01-1.95 (m, 1H), 1.90-1-87 (m, 1H), 1.78-1.71 (m, 2H), 1.61-1.56 (m, 2H), 1.45-1.42 (m, 1H), 1.35-1.30 (m, 1H), 1.25-1.03 (m, 4H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 143.59, 139.11, 137.51, 132.00, 131.93, 129.82, 129.51, 129.17, 128.88, 128.84, 127.81, 127.60, 127.51, 127.37, 127.24, 127.12, 127.03, 126.64, 75.93, 74.77, 45.44, 41.62, 33.72, 31.79, 25.78, 24.28, 24.19.

HRMS (EI) (m/z): calculated for $C_{27}H_{28}OS$ 400.186088; found 400.185978.

9-(2-(tert-butoxy)-2-phenylethyl)-9*H*-thioxanthene (**9h**, unreported product)



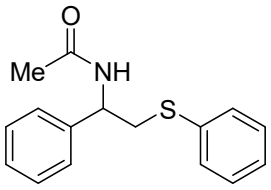
Following the general procedure **C**, colorless oil (30.0 mg, 40%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.42-7.37 (m, 2H), 7.24-7.14 (m, 11H), 4.19 (dd, J = 7.0 Hz, 5.5 Hz, 1H), 3.99 (dd, J = 7.5 Hz, 6.0 Hz, 1H), 1.92-1.82 (m, 2H), 0.92 (s, 9H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 145.65, 138.95, 138.57, 132.18, 132.13, 129.06, 128.93, 128.72, 127.54, 127.48, 127.36, 127.32, 127.20, 127.16, 127.11, 126.86, 74.35, 72.08, 45.23, 42.29, 29.13.

HRMS (EI) (m/z): calculated for $C_{25}H_{26}OS$ 374.170438; found 374.170366.

***N*-(1-phenyl-2-(phenylsulfinyl)ethyl)acetamide** (**11a**, CAS: 98289-63-5)



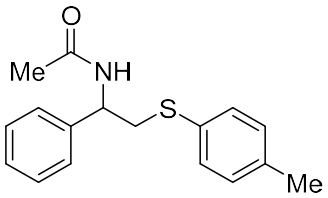
Following the general procedure **D**, light yellow oil (35.0 mg, 61%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.46 (d, J = 8.0 Hz, 1H), 7.37-7.31 (m, 8H), 7.28-7.25 (m, 1H), 7.22-7.19 (m, 1H), 4.94 (dd, J = 15.5 Hz, 7.5 Hz, 1H), 3.27 (d, J = 7.0 Hz, 2H), 1.85 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.09, 142.24, 136.41, 129.71, 129.53, 129.02, 128.81, 128.74, 127.69, 127.23, 126.25, 52.34, 38.90, 23.10.

HRMS (ESIpos) (m/z): $[M-H]^-$ calculated for $C_{16}H_{17}NOS$ 270.095811; found 270.095880.

***N*-(1-phenyl-2-(*p*-tolylthio)ethyl)acetamide** (**11b**, CAS: 1820957-34-3)



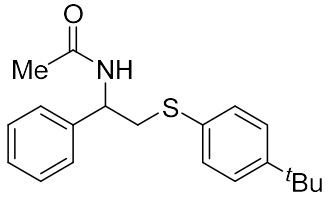
Following the general procedure **D**, colorless oil (25.6 mg, 45%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.44 (d, J = 8.5 Hz, 1H), 7.49-7.25 (m, 7H), 7.14 (d, J = 8.0 Hz, 1H), 4.90 (dd, J = 15.0 Hz, 7.5 Hz, 1H), 3.32 (d, J = 7.5 Hz, 2H), 2.82 (s, 3H), 1.85 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.09, 142.36, 135.98, 133.31, 132.54, 130.18, 129.65, 129.02, 128.79, 127.63, 127.19, 52.32, 39.00, 23.11, 21.01.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{17}H_{19}NOSNa$ 308.107956; found 308.107750.

***N*-(2-((4-(tert-butyl)phenyl)thio)-1-phenylethyl)acetamide** (**11c**, unreported product)



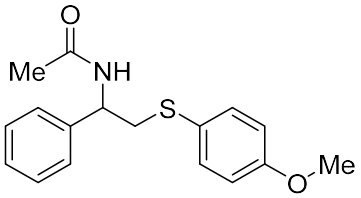
Following the general procedure **D**, colorless oil (35.1 mg, 54%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-7.18 (m, 9H), 5.87 (d, J = 7.5 Hz, 1H), (m, 7H), 5.13 (dd, J = 13.5 Hz, 6.0 Hz, 1H), 3.31-3.21 (m, 2H), 1.87 (s, 3H), 1.22 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.53, 149.96, 140.35, 131.85, 130.14, 130.11, 128.72, 128.42, 127.79, 126.58, 126.17, 53.06, 40.24, 34.50, 31.25, 23.28.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{20}H_{25}OSNa$ 350.154905; found 350.154770.

***N*-(2-((4-methoxyphenyl)thio)-1-phenylethyl)acetamide** (**11d**, CAS: 141248-72-8)



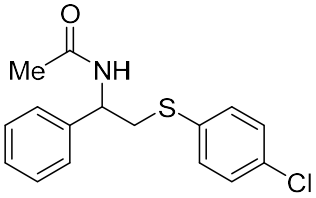
Following the general procedure **D**, colorless oil (30.1 mg, 50%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.22 (m, 4H), 7.20-7.15 (m, 3H), 5.93 (d, J = 8.0 Hz, 1H), 5.02 (dd, J = 13.5 Hz, 7.0 Hz, 1H), 3.71 (s, 3H), 3.19-3.11 (s, 3H), 1.90 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.50, 159.25, 140.51, 133.64, 128.71, 127.74, 126.56, 125.42, 114.77, 55.35, 52.95, 41.81, 23.33.

HRMS (ESIpos) (m/z): [M] calculated for $C_{17}H_{19}NO_2S$ 301.113110; found 301.113101.

***N*-(2-((4-chlorophenyl)thio)-1-phenylethyl)acetamide** (**11e**, CAS: 1883670-31-2)

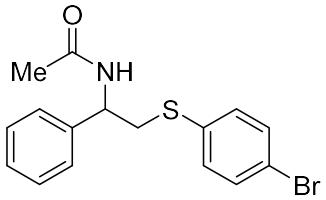


Following the general procedure **D**, colorless oil (24.7 mg, 42%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (d, J = 7.5 Hz, 1H), 7.37 (s, 4H), 7.35-7.31 (m, 4H), 7.28-7.25 (m, 4H), 7.28-7.25 (m, 1H), 4.95-4.91 (m, 1H), 3.30-3.24 (m, 2H), 1.84 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.12, 142.06, 130.89, 130.47, 129.40, 128.82, 127.74, 127.25, 52.20, 38.93, 23.08.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{16}H_{16}ClNOSNa$ 328.053333; found 328.052790.



***N*-(2-((4-bromophenyl)thio)-1-phenylethyl)acetamide** (**11f**, CAS: 1883670-32-3)

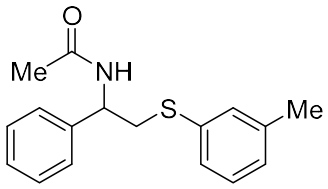
Following the general procedure **D**, colorless oil (34.3 mg, 49%).

^{1}H NMR ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.34 (m, 2H), 7.28-7.25 (m, 2H), 7.27-7.22 (m, 1H), 7.19-7.17 (m, 2H), 7.16-7.14 (m, 2H), 5.80 (d, J = 7.5 Hz, 1H), 5.09 (dd, J = 14.0 Hz, 7.0 Hz, 1H), 3.37 (dd, J = 13.5 Hz, 6.5 Hz, 1H), 3.20 (dd, J = 13.5 Hz, 6.5 Hz, 1H), 1.92 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.50, 139.80, 132.06, 131.19, 128.88, 128.09, 126.70, 120.36, 52.94, 39.45, 23.34.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{16}H_{16}BrNOSNa$ 372.002830; found 372.002510.

***N*-(1-phenyl-2-(*m*-tolylthio)ethyl)acetamide** (**11g**, CAS: 1883670-29-8)



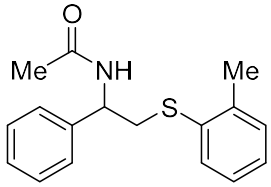
Following the general procedure **D**, colorless oil (30.2 mg, 53%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (d, J = 8.0 Hz, 1H), 7.34-7.31 (m, 4H), 7.27-7.25 (m, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.16-7.13 (m, 2H), 7.01-7.00 (m, 1H), 4.96-4.93 (m, 1H), 3.26 (d, J = 7.5 Hz, 2H), 2.28 (s, 3H), 1.85 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.10, 142.25, 138.84, 136.19, 129.71, 129.43, 129.12, 129.02, 128.80, 127.69, 127.24, 126.98, 125.70, 52.40, 38.82, 23.09, 21.35.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{17}H_{19}NOSNa$ 308.107955; found 308.107310.

***N*-(1-phenyl-2-(o-tolylthio)ethyl)acetamide** (**11h**, CAS: 1820957-37-6)



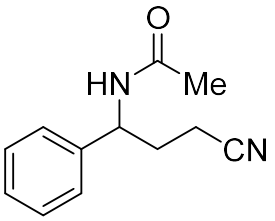
Following the general procedure **D**, colorless oil (20.1 mg, 39%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.47 (d, J = 8.0 Hz, 1H), 7.39-7.37 (m, 1H), 7.36-7.31 (m, 4H), 7.28-7.25 (m, 1H), 7.16-7.13 (m, 1H), 7.21-7.18 (m, 2H), 7.13-7.10 (m, 1H), 4.94 (dd, J = 15.5 Hz, 7.5 Hz, 1H), 3.26 (d, J = 1.0 Hz, 2H), 2.25 (s, 3H), 1.86 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.09, 142.30, 136.98, 135.60, 130.46, 128.81, 128.01, 127.70, 127.21, 127.13, 126.04, 52.32, 38.55, 23.10, 20.41.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{17}H_{19}NOSNa$ 308.107955; found 308.107620.

***N*-(3-cyano-1-phenylpropyl)acetamide** (**13**, CAS: 2127514-83-2)



Following the general procedure **E**, using *p*-bromo-*N*,*N*-dimethylaniline as initiator; isolated as a white solid (48.5 mg, 48%).

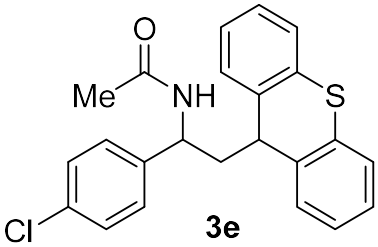
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 2H), 7.32-7.30 (m, 1H), 7.27-7.26 (m, 2H), 5.90 (d, J = 8.0 Hz, 1H), 5.04 (dd, J = 15.5 Hz, 8.0 Hz, 1H), 2.37-2.31 (m, 2H), 2.27-2.22 (m, 1H), 2.15-2.10 (m, 1H), 1.99 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.85, 139.83, 129.21, 128.34, 126.55, 119.26, 52.90, 31.66, 23.37, 14.54.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{12}H_{14}N_2O$ 202.110063; found 202.109890.

X-ray study

Single crystals of **3e** were crystallized from CH_3CN.



3e

Table 1. Crystal data and structure refinement.

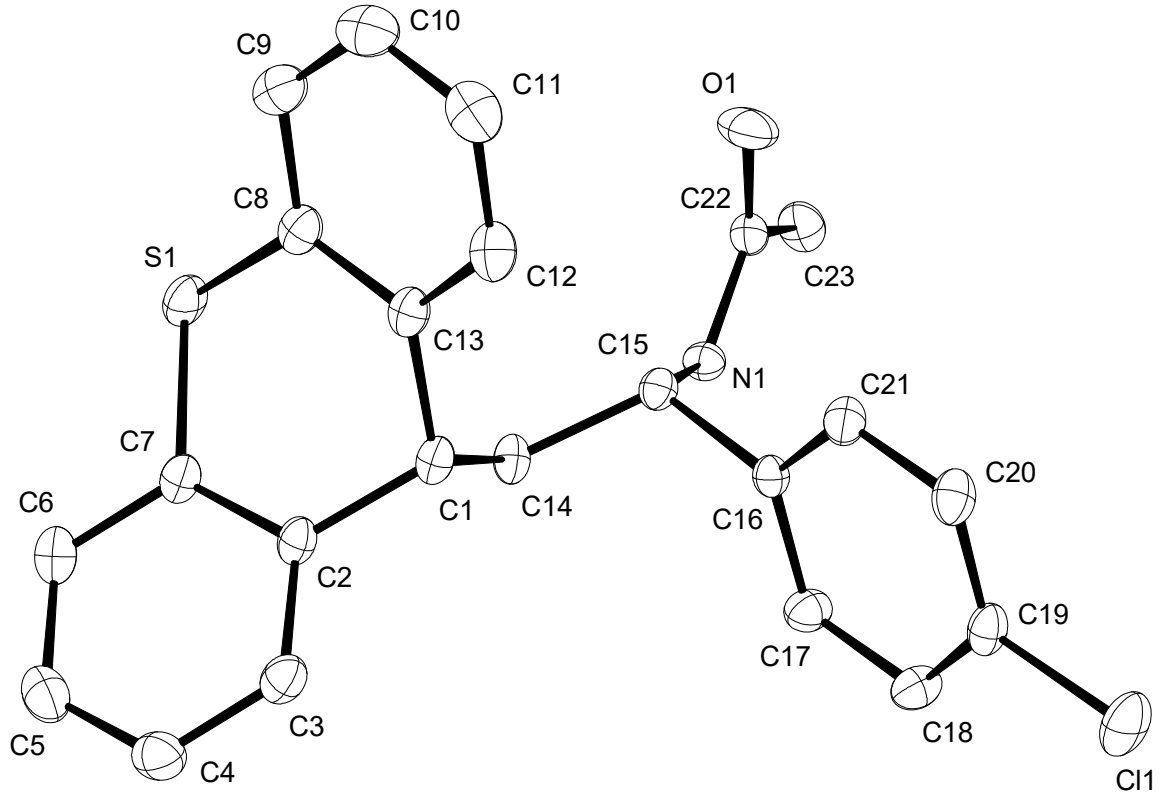
Identification code	CCDC 1957001	
Empirical formula	$C_{23}H_{20}ClNOS$	
Color	colourless	
Formula weight	393.91 g·mol^{-1}	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	MONOCLINIC	
Space group	**$P2_1/n$, (no. 14)**	
Unit cell dimensions	a = 13.3178(19) Å	α= 90°.
	b = 9.6266(14) Å	β= 106.661(5)°.
	c = 15.545(2) Å	γ= 90°.
Volume	1909.2(5) Å^3	
Z	4	
Density (calculated)	1.370 Mg · m^{-3}	
Absorption coefficient	0.322 mm^{-1}	
F(000)	824 e	

Crystal size	0.128 x 0.100 x 0.040 mm^3	
θ range for data collection	2.381 to 31.679°.	
Index ranges	$-19 \leq h \leq 19$, $-14 \leq k \leq 14$, $-22 \leq l \leq 22$	
Reflections collected	53315	
Independent reflections	6405 [R_{int} = 0.0286]	
Reflections with I>2σ(I)	5548	
Completeness to θ = 25.242°	99.9 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.99 and 0.96	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6405 / 0 / 257	
Goodness-of-fit on F^2	1.035	
Final R indices [I>2σ(I)]	R_1 = 0.0343	wR^2 = 0.0889
R indices (all data)	R_1 = 0.0413	wR^2 = 0.0930
Largest diff. peak and hole	0.5 and -0.3 e · $Å^{-3}$	

Table 2. Bond lengths [Å] and angles [°].

Cl(1)-C(19)	1.7418(10)	S(1)-C(7)	1.7638(11)
S(1)-C(8)	1.7666(11)	O(1)-C(22)	1.2366(13)
N(1)-C(15)	1.4632(13)	N(1)-C(22)	1.3377(13)
C(1)-C(2)	1.5095(14)	C(1)-C(13)	1.5111(14)
C(1)-C(14)	1.5479(14)	C(2)-C(3)	1.3946(15)
C(2)-C(7)	1.3983(13)	C(3)-C(4)	1.3911(16)
C(4)-C(5)	1.3894(17)	C(5)-C(6)	1.3869(17)
C(6)-C(7)	1.3965(15)	C(8)-C(9)	1.3941(16)
C(8)-C(13)	1.4003(14)	C(9)-C(10)	1.3849(18)
C(10)-C(11)	1.3900(19)	C(11)-C(12)	1.3878(17)
C(12)-C(13)	1.3959(15)	C(14)-C(15)	1.5312(13)
C(15)-C(16)	1.5184(13)	C(16)-C(17)	1.3978(13)
C(16)-C(21)	1.3905(14)	C(17)-C(18)	1.3893(14)
C(18)-C(19)	1.3837(15)	C(19)-C(20)	1.3793(16)
C(20)-C(21)	1.3931(15)	C(22)-C(23)	1.5063(15)
C(7)-S(1)-C(8)	100.13(5)	C(22)-N(1)-C(15)	122.68(8)
C(2)-C(1)-C(13)	111.05(8)	C(2)-C(1)-C(14)	108.92(8)
C(13)-C(1)-C(14)	111.19(8)	C(3)-C(2)-C(1)	121.46(9)
C(3)-C(2)-C(7)	118.43(9)	C(7)-C(2)-C(1)	120.08(9)
C(4)-C(3)-C(2)	121.16(10)	C(5)-C(4)-C(3)	119.71(11)
C(6)-C(5)-C(4)	120.06(10)	C(5)-C(6)-C(7)	119.98(10)
C(2)-C(7)-S(1)	121.05(8)	C(6)-C(7)-S(1)	118.34(8)
C(6)-C(7)-C(2)	120.60(10)	C(9)-C(8)-S(1)	118.34(8)
C(9)-C(8)-C(13)	120.77(10)	C(13)-C(8)-S(1)	120.89(8)
C(10)-C(9)-C(8)	120.06(11)	C(9)-C(10)-C(11)	119.95(11)
C(12)-C(11)-C(10)	119.76(11)	C(11)-C(12)-C(13)	121.35(10)
C(8)-C(13)-C(1)	120.18(9)	C(12)-C(13)-C(1)	121.76(9)
C(12)-C(13)-C(8)	118.05(10)	C(15)-C(14)-C(1)	113.85(8)
N(1)-C(15)-C(14)	108.99(8)	N(1)-C(15)-C(16)	109.44(7)
C(16)-C(15)-C(14)	113.53(8)	C(17)-C(16)-C(15)	120.63(8)
C(21)-C(16)-C(15)	120.59(9)	C(21)-C(16)-C(17)	118.68(9)

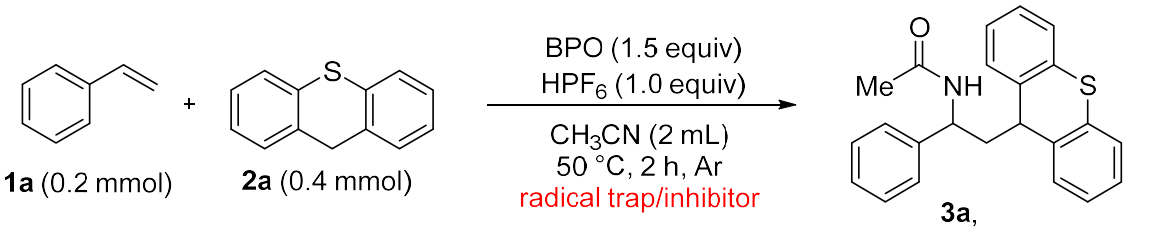
C(18)-C(17)-C(16)	121.00(9)	C(19)-C(18)-C(17)	118.73(10)
C(18)-C(19)-Cl(1)	119.27(8)	C(20)-C(19)-Cl(1)	118.97(8)
C(20)-C(19)-C(18)	121.75(9)	C(19)-C(20)-C(21)	118.89(10)
C(16)-C(21)-C(20)	120.94(10)	O(1)-C(22)-N(1)	123.02(10)
O(1)-C(22)-C(23)	121.39(9)	N(1)-C(22)-C(23)	115.59(9)



ORTEP diagram of the X-ray structure of **3e**. Displacement ellipsoids are drawn at the 50% probability level.

Mechanistic studies:

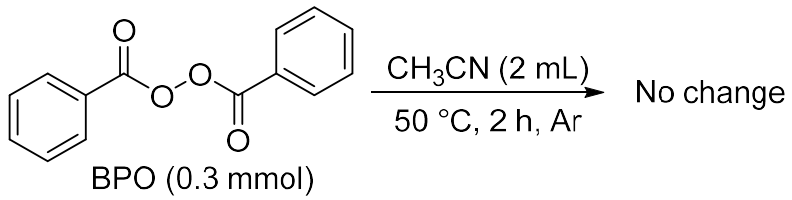
Radical trapping experiment:

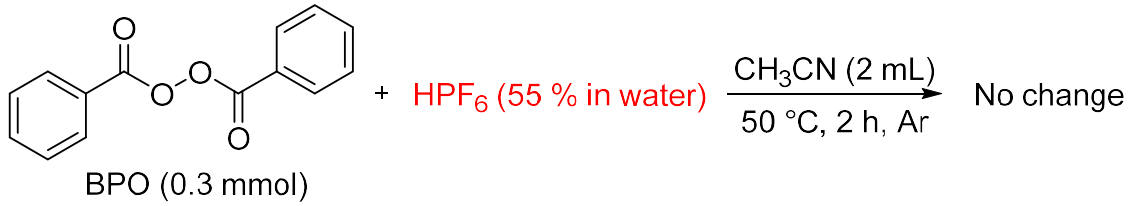


Under the optimization reaction condition, TEMPO or 2,4,6-tri-*tert*-butylphenol (3.0 equiv.) were added. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. Yields were determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture relative to the internal standard CH_3NO_2. TEMPO and 2,4,6-tri-*tert*-butylphenol reduced the yield significantly, which proves that this reaction might go through the radical procedure.

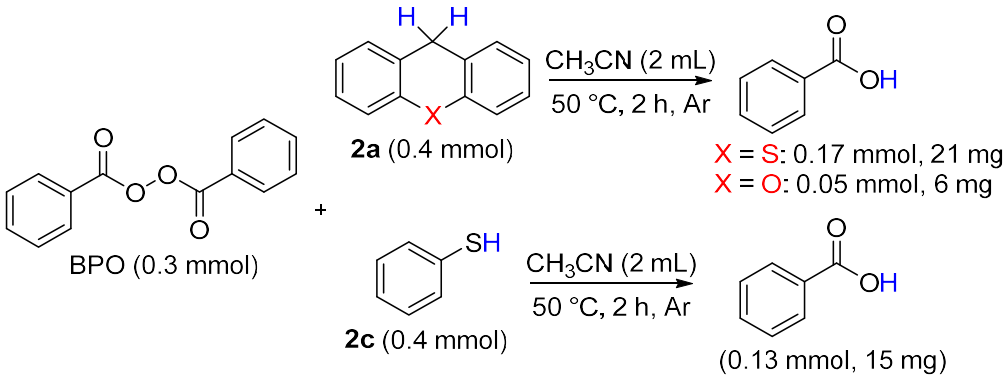
Investigation of the initiation step:

These experiments were performed in a Schlenk tube under Ar and analyze directly without any workup. Yields were determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture relative to the internal standard CH_3NO_2.

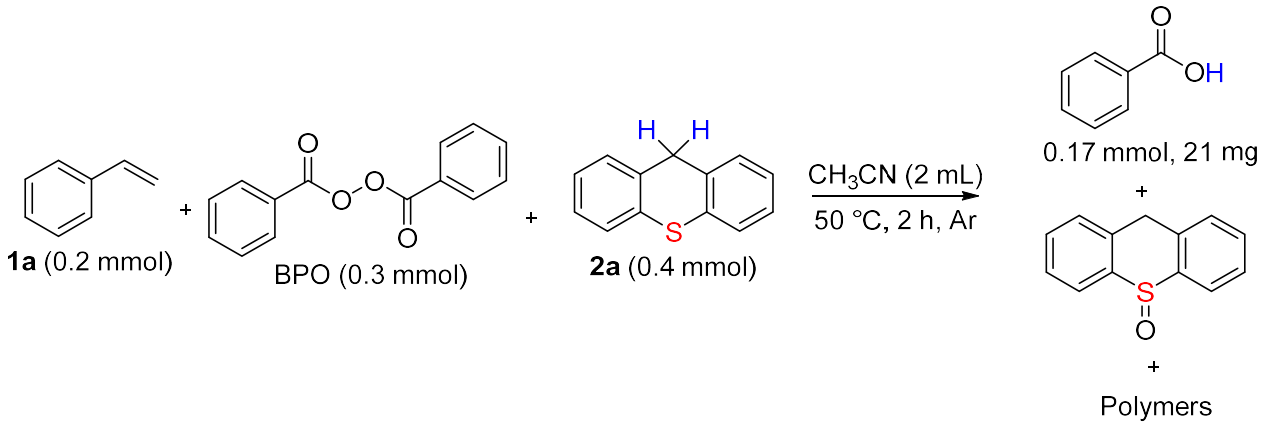




BPO with or without acid in acetonitrile at 50 °C for 2 h did not change, this acid apparently does not affect the decomposition of BPO.

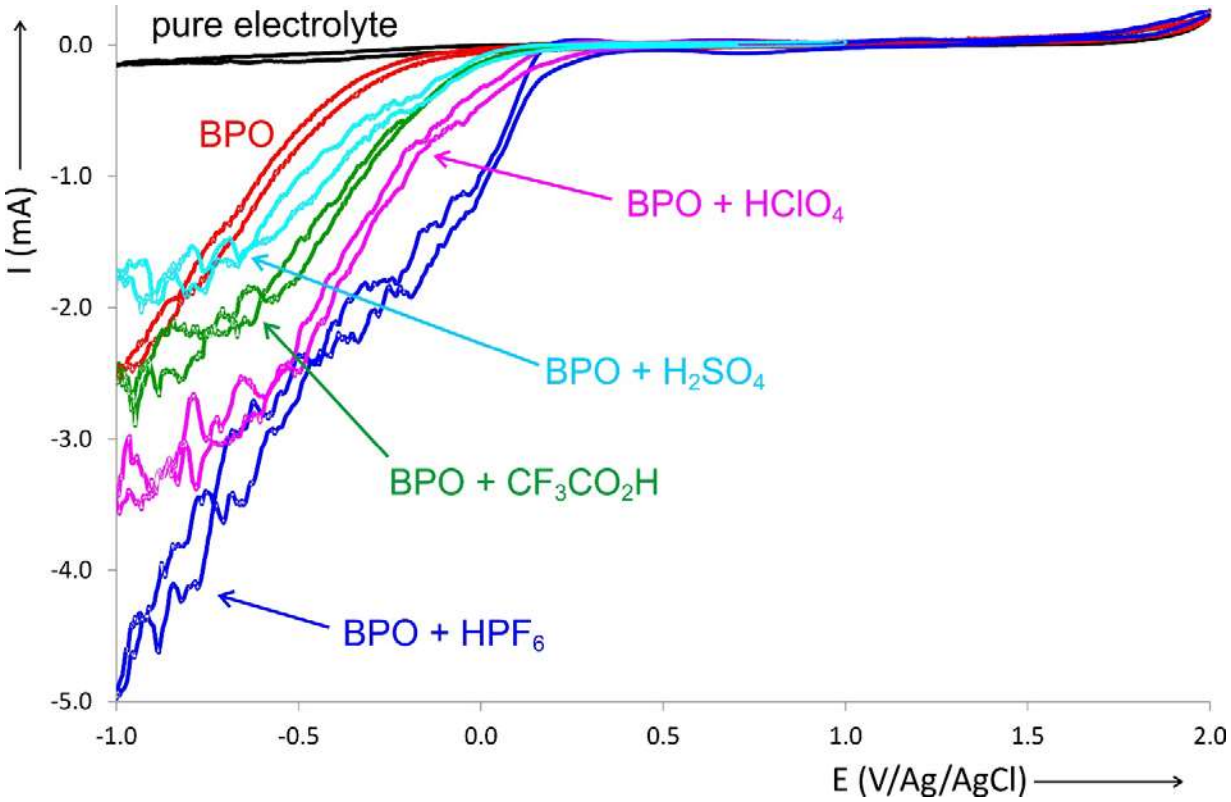


In the presence of thioxanthene, xanthene or thiolphenols, benzoic acid was formed in significant amounts under these conditions, indicating that thioxanthene, xanthene and thiolphenols can accelerate the peroxide decomposition.



In the absence of acid, the product was not formed, indicating that the electron transfer (ET) steps are facilitated by the effect of acid.

Cyclic Voltammetry of BPO in the presence of different acids



Cyclic voltammograms showing the effect of acid addition on the reduction potential of BPO. Two platinized Pt wires as a counter and working electrode with a Ag/AgCl electrode as a reference were used. The cyclic voltammetry (CV) was conducted from -1.0 V to 2.0 V with a scan rate of 100 mV/s. BPO (0.3 mmol), acid (0.2 mmol), tBu_4NPF_6 (0.1 M) in CH_3CN, under a stream of Ar.

The BPO can be reduced at -345 mV. With the addition of the HPF_6, the reduction process becomes much easier. The reduction potential of the BPO is shifted by around 470 mV, which means the acid addition is favorable for the BPO reduction. Other acid like H_2SO_4, $HClO_4$ and CF_3COOH induce a smaller shift. Apparently, the shift in the reduction potential of BPO is connected with the pKa of the acid.

Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Organo-Redox-Catalysis for the difunctionalization of alkenes and oxidative Ritter reactions by C-H functionalization

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Contents

Supplementary Methods

General Information

Unless otherwise indicated, all reagents and solvents were purchased from commercial distributors and used as received. Solvents (hexanes, ethyl acetate) used for column chromatography were of technical grade and used after distillation in a rotary evaporator.

TLC was used to check the reactions for full conversion and was performed on Macherey-Nagel Polygram Sil G/UV254 thin layer plates. TLC spots were visualized by UV-light irradiation or used of Phosphomolybdic acid hydrate after heated.

Flash column chromatography was carried out using Merck Silica Gel 60 (40-63 µm). Yields refer to pure isolated compounds.

^{1}H and ^{13}C NMR spectra were measured with Bruker AV 300 spectrometer, Bruker AV 500 spectrometer, Bruker AV 600 spectrometer. All chemical shifts are given in ppm downfield relative to TMS and were referenced to the solvent residual peaks.[1] ^{1}H NMR chemical shifts are designated using the following abbreviations as well as their combinations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. For ^{13}C NMR data the following abbreviations are used: p = primary (CH_3), s = secondary (CH_2), t = tertiary (CH), q = quaternary (C).

High resolution mass spectra were recorded with a Bruker APEX III FTICR-MS or a Finnigan SSQ 7000 quadrupole MS or a Finnigan MAT 95 double focusing sector field MS instrument.

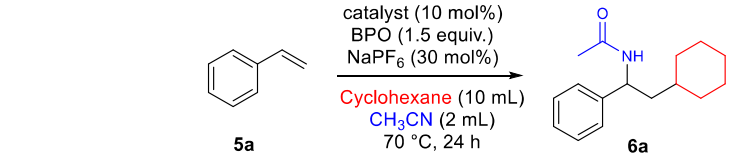
Cyclic Voltammetry (CV) were measured with the BAS Epsilon potentiostat.

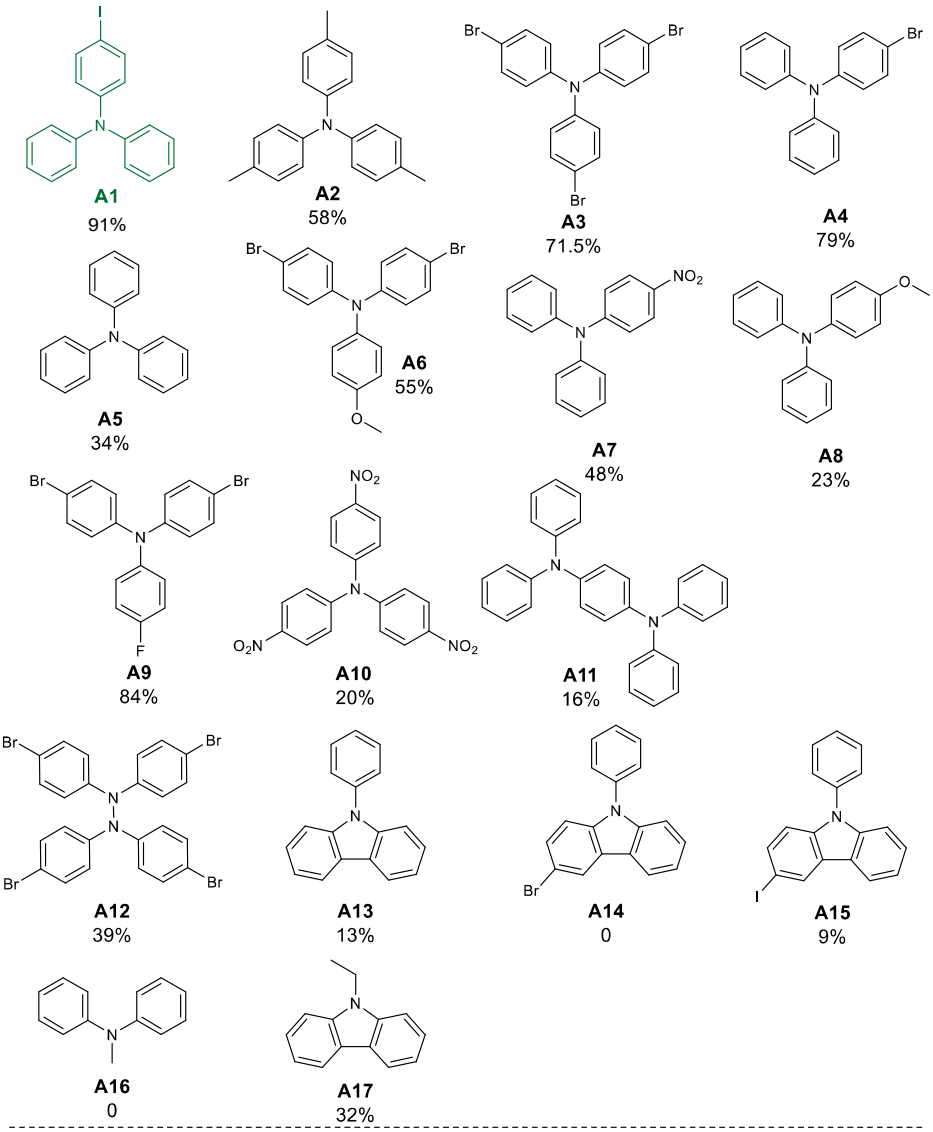
Benzoyl peroxide (BPO, 75% in H_2O) and Sodium hexafluorophosphate ($NaPF_6$) was purchased from Sigma-Aldrich and used directly without further purification.

Tris(4-bromophenyl)ammoniumyl hexachloroantimonate (TBPA·+) was purchased from Sigma-Aldrich and used directly without further purification.

Optimization of reaction conditions

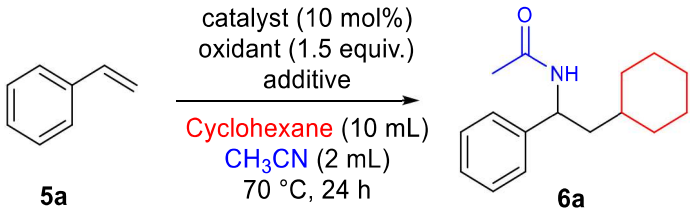
Table S1: Optimization of amine catalysts[a]





[a] 1a (0.5 mmol, 57 µL), BPO (0.75 mmol, 1.5 equiv.), catalyst (10 mol%), $NaPF_6$ (0.15 mmol), cyclohexane (10 mL), CH_3CN (2 mL), 70 °C, 24 h. Yields were determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-Trimethoxybenzene.

Table S2: Optimization of other reaction conditions



5a **6a**

Entry	Catalyst	Oxidant	Additive	Yield (%)
1	**A1**	BPO	NaOTf (30 mol%)	8.4
2	**A1**	BPO	$NaBF_4$ (30 mol%)	47
3	**A1**	BPO	$^tBu_4NPF_6$ (30 mol%)	0
4	**A1**	BPO	NaOBz (30 mol%)	0
5	**A1**	BPO	$NaSbF_6$ (30 mol%)	16
6	**A1**	BPO	$NaPF_6$ (30 mol%)	91(87) [b]
7	**A1**	BPO	$NaPF_6$ (50 mol%)	88
8	**A1**	BPO	$NaPF_6$ (10 mol%)	63
9	**A1**	BPO	$NaPF_6$ (5 mol%)	50
10	**A1** (5 mol%)	BPO	$NaPF_6$ (30 mol%)	66
11	**A1** (2.5 mol%)	BPO	$NaPF_6$ (30 mol%)	26
12	**A1** (1.0 mol%)	BPO	$NaPF_6$ (30 mol%)	23
13	**A1** (0.5 mol%)	BPO	$NaPF_6$ (30 mol%)	8
14[c]	**A1**	BPO	$NaPF_6$ (30 mol%)	89
15[d]	**A1**	BPO	$NaPF_6$ (30 mol%)	2
16	**A1**	TBHP	$NaPF_6$ (30 mol%)	0
17	**A1**	TBPB	$NaPF_6$ (30 mol%)	<10
18	**A1**	DTBP	$NaPF_6$ (30 mol%)	<10
19[e]	**A1**	DTBP	$NaPF_6$ (30 mol%)	32
20	-	BPO	$NaPF_6$ (30 mol%)	0
21	**A1**	-	$NaPF_6$ (30 mol%)	0
22	**A1**	BPO	-	0

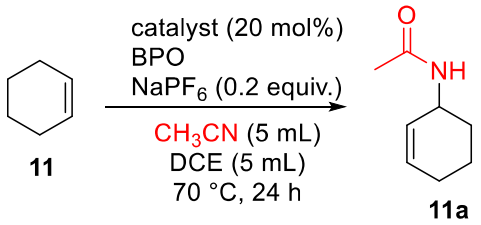
[a] 1a (0.5 mmol, 57 µL), BPO (0.75 mmol, 1.5 equiv.), catalyst (10 mol%), additive, cyclohexane (10 mL), CH_3CN (2 mL), 70 °C, 24 h. Yields were determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-Trimethoxybenzene. [b] Isolated yield. [c] 90 °C. [d] 50 °C. [e] 100 °C.

Additive effect: additive is required (compare entries 1-6) and the $NaPF_6$ is important for good yields of product **6a**. However, others such as $NaBF_4$, $NaSbF_6$ and NaOTf give low yield of **6a**, NaOBz and $^tBu_4NPF_6$ give no desired products. The concentration of additive seems to be less important, compare entries 6-9.

Catalyst loading: The lower concentration of catalyst, the lower yields were got.

Oxidants: BPO is the best oxidant in this reaction.

Table S3: Optimization of allylic C-H Ritter reaction

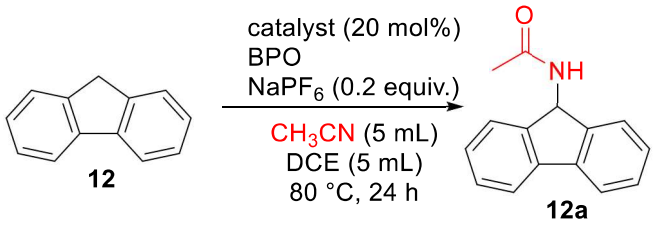


11 **11a**

Entry	Catalyst	Oxidant	Solvent	Yield (%)
1	**A1**	BPO (1.5 equiv.)	CH_3CN (10 mL)	20
2	**A1**	BPO (2.0 equiv.)	CH_3CN (10 mL)	25
3	**A2**	BPO (2.0 equiv.)	CH_3CN (10 mL)	36
4	**A3**	BPO (2.0 equiv.)	CH_3CN (10 mL)	37
5	**A3**	BPO (2.0 equiv.)	CH_3CN (5 mL) + CH_3NO_2 (5 mL)	0
6	**A3**	BPO (2.0 equiv.)	CH_3CN (5 mL) + THF (5 mL)	0
7	**A3**	BPO (2.0 equiv.)	CH_3CN (5 mL) + DCE (5 mL)	71
8[b]	**A3**	BPO (2.0 equiv.)	CH_3CN (5 mL) + DCE (5 mL)	0
9	**-**	BPO (2.0 equiv.)	CH_3CN (5 mL) + DCE (5 mL)	0

[a] **11** (0.5 mmol), BPO, catalyst (20 mol%), $NaPF_6$ (20 mol%), solvent, 70 °C, 24 h. Yields were determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-Trimethoxybenzene. [b] no $NaPF_6$.

Table S4: Optimization of benzylic C-H Ritter reaction

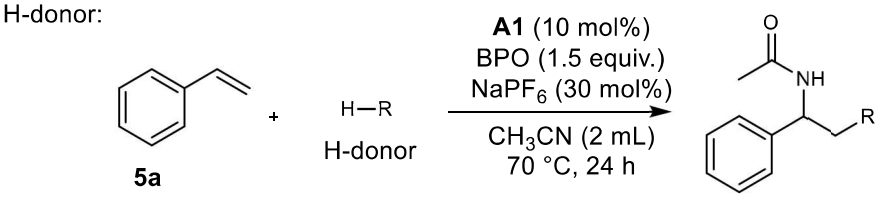


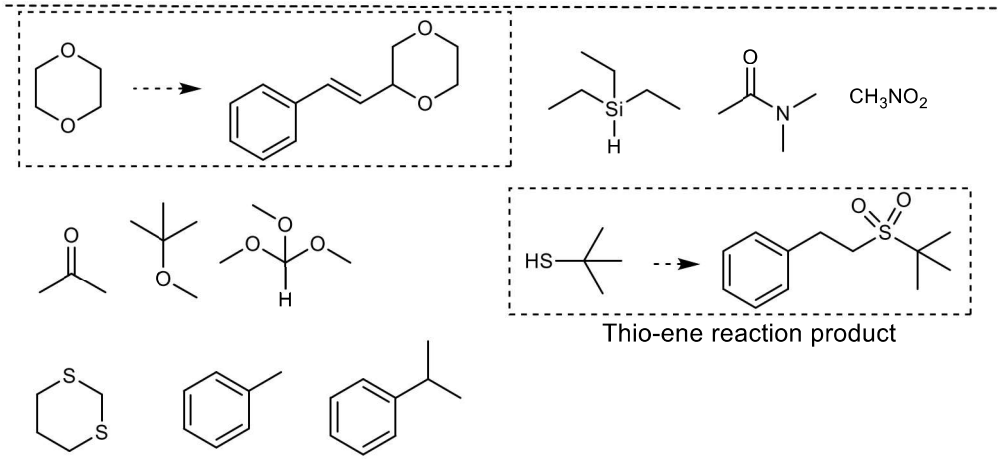
Entry	Catalyst	Oxidant	Tem/ ℃	Yield (%)
1	**A3**	BPO (2.0 equiv.)	70	32
2	**A3**	BPO (3.0 equiv.)	70	43
3	**A3**	BPO (3.0 equiv.)	80	70
4	**A3**	BPO (3.0 equiv.)	100	60
5	**A1**	BPO (2.0 equiv.)	80	41
6	**A2**	BPO (2.0 equiv.)	80	15
7[b]	**A3**	BPO (2.0 equiv.)	80	0
8	**-**	BPO (2.0 equiv.)	80	0

[a] **12** (0.5 mmol), BPO, catalyst (20 mol%), $NaPF_6$ (20 mol%), DCE (5 mL), CH_3CN (5 mL), 80 ℃, 24 h. Yields were determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-Trimethoxybenzene. [b] no $NaPF_6$.

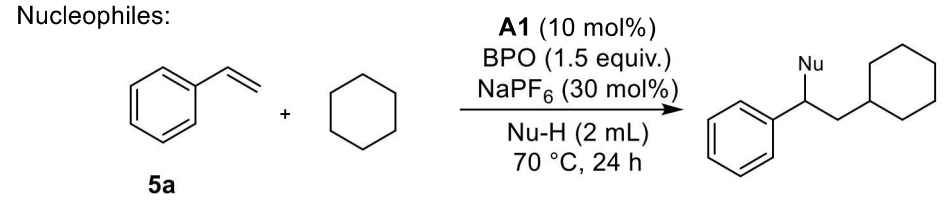
Failed examples:

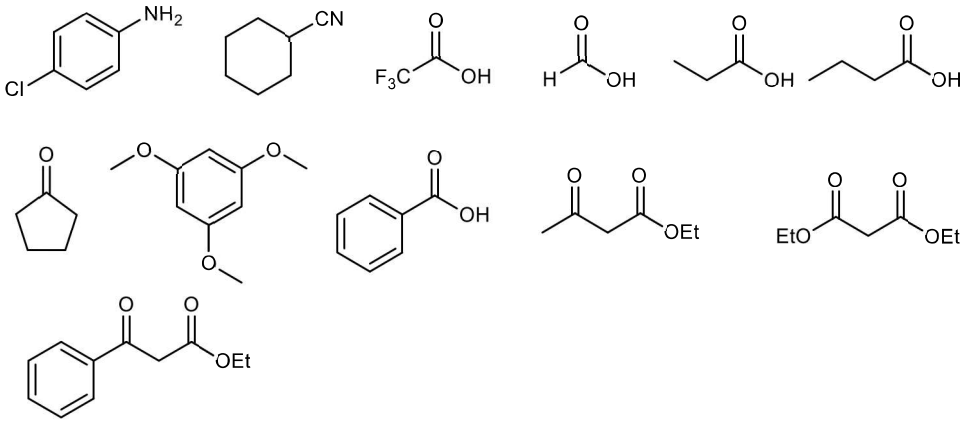
H-donor:





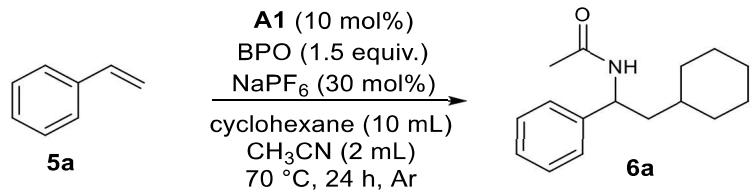
Nucleophiles:





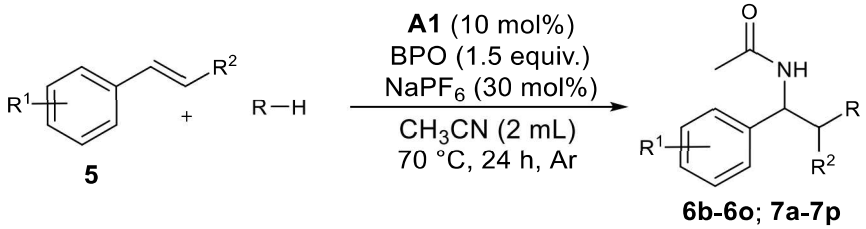
Reaction procedures

Procedure A: synthesis of *N*-(2-cyclohexyl-1-phenylethyl)acetamide.



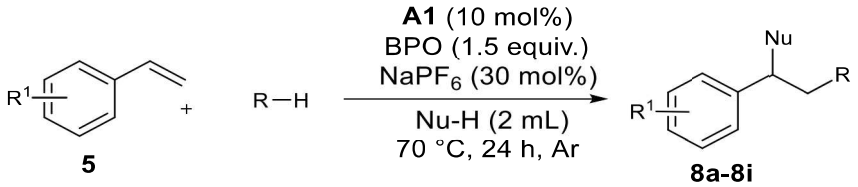
Under argon atmosphere, the styrene **5a** (0.5 mmol, 57 μL), catalyst **A1** (10 mol%, 0.05 mmol, 18.5 mg), cyclohexane (10 mL), CH_3CN (2 mL), BPO (0.75 mmol, 1.5 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 10:1 to 1:1) to give the desired products **6a**.

General procedure B: synthesis of *N*-(1-phenylalkyl)acetamides.



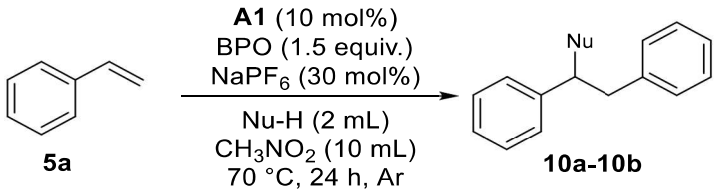
Under argon atmosphere, the styrenes **5** (0.5 mmol), catalyst **A1** (10 mol%, 0.05 mmol, 18.5 mg), R-H (10 mL), CH_3CN (2 mL), BPO (0.75 mmol, 1.5 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 10:1 to 1:1) to give the desired products **6b**-**6o** and **7a**-**7p**.

General procedure C: synthesis of radicals and nucleophiles addition.



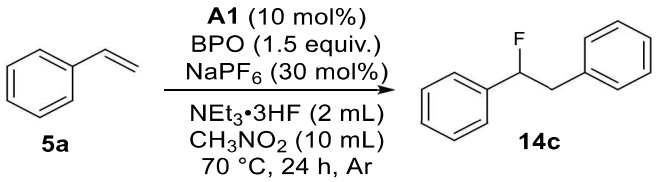
Under argon atmosphere, the styrenes **5** (0.5 mmol), catalyst **A1** (10 mol%, 0.05 mmol, 18.5 mg), nucleophiles (2 mL), R-H (10 mL), BPO (0.75 mmol, 1.5 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 50:1 to 10:1) to give the desired products **8a**-**8i**.

General procedure D: synthesis of phenyl radicals and nucleophiles addition.



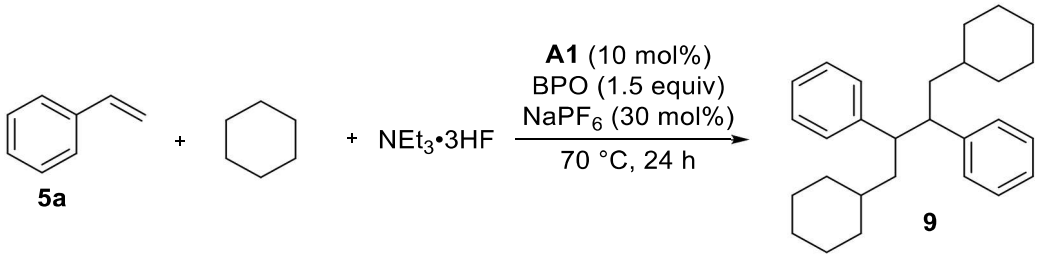
Under argon atmosphere, the styrene **5a** (0.5 mmol, 57 μL), catalyst **A1** (10 mol%, 0.05 mmol, 18.5 mg), nucleophiles (2 mL), CH_3NO_2 (10 mL), BPO (0.75 mmol, 1.5 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 50:1 to 10:1) to give the desired products **10a** and **10b**.

Synthesis of (1-fluoroethane-1,2-diyl)dibenzene.



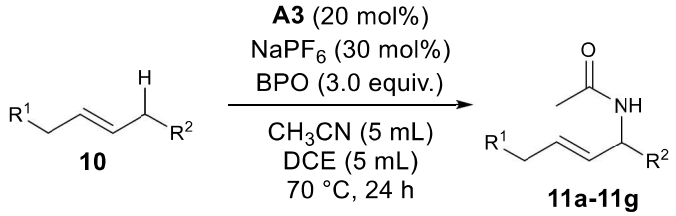
Under argon atmosphere, the styrene **5a** (0.5 mmol, 57 μL), catalyst **A1** (10 mol%, 0.05 mmol, 18.5 mg), $NEt_3{\cdot}3HF$ (2 mL), CH_3NO_2 (10 mL), BPO (0.75 mmol, 1.5 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 500:1 to 100:1) to give the desired product **14c** in the yield of 26 %.

Synthesis of (1,4-dicyclohexylbutane-2,3-diyl)dibenzene.



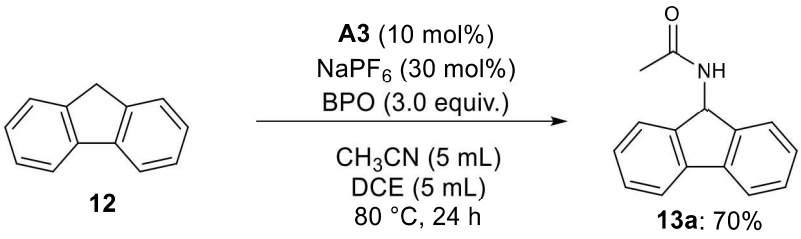
Under argon atmosphere, the styrene **5a** (0.5 mmol), catalyst **A1** (10 mol%, 0.05 mmol, 18.5 mg), NEt_3·3HF (2 mL), cyclohexane (10 mL), BPO (0.75 mmol, 1.5 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 500:1 to 100:1), not giving the desired fluoride but the dimer **9** in the yield of 31%.

General procedure E: oxidative Ritter reaction of allylic C-H bond.



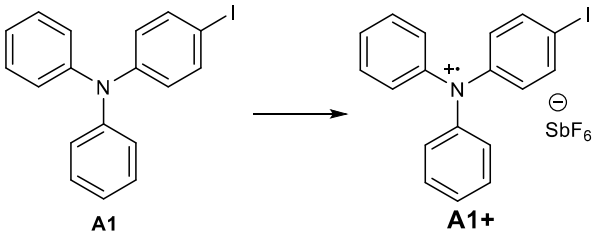
Under argon atmosphere, the olefins **10** (0.5 mmol), catalyst **A3** (20 mol%, 0.05 mmol, 24.1 mg), CH_3CN (5 mL), DCE (5 mL), BPO (1.5 mmol, 3.0 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 50:1 to 10:1) to give the desired products **11a**-**11g**. By using (Z)-decene as starting material, (*E*)-**11d** and (*E*)-**11c** were isolated.

Oxidative Ritter reaction of *N*-(9*H*-fluoren-9-yl)acetamide.



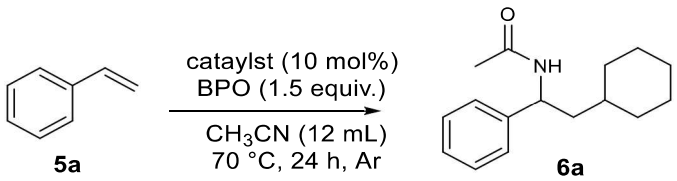
Under argon atmosphere, the 9*H*-fluorene **12** (0.5 mmol, 83 mg), catalyst **A3** (20 mol%, 0.05 mmol, 24.1 mg), CH_3CN (5 mL), DCE (5 mL), BPO (1.5 mmol, 3.0 equiv.) and $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 80 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. The residue was further purified by silica gel column with *iso*-hexane/ethyl acetate (from 50:1 to 10:1) to give the desired product **13a**.

Synthesis of triarylamine radical cation salt A1+ [2]

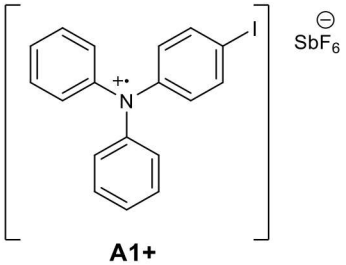


A1+. To a solution of **A1** (185 mg, 0:5 mmol, 1.0 equiv.) in dry CH_2Cl_2 (5 mL) under Ar atmosphere was added $AgSbF_6$ (180.4 mg, 0.525 mmol, 1.05 equiv.) at room temperature. The slightly yellowish reaction mixture immediately turned dark blue and the reaction was stirred for about one minute. After removal of insoluble contents by filtration, product **A1+** was obtained by precipitation from CH_2Cl_2/hexanes as a deep blue powder (275.7 mg, 91%). HRMS (ESI, DCM/CH_3CN, positive mode) m/z for $C_{18}H_{14}NI\bullet$+(M+) calcd. 371.0165, found 371.0163; for SbF_6^-(M^-) calcd. 234.8949, found 234.8949. In the ^1H NMR, only a very broad signal around 8.5ppm -6.5 ppm could be observed, and no signal in the ^{13}C NMR. No signals from the starting material (**A1**) could be seen, suggesting that the product is the pure ammoniumyl radical cation, free of the closed-shell starting material.

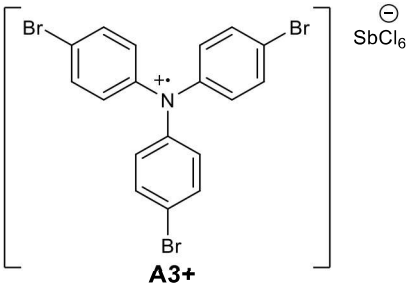
Synthesis of *N*-(3-cyano-1-phenylpropyl)acetamide catalyzed by triarylamine radical cation salts.



Under argon atmosphere, the styrene **5a** (0.5 mmol, 57 µL), catalyst (10 mol%, 0.05 mmol), CH_3CN (12 mL), BPO (0.75 mmol, 1.5 equiv.), $NaPF_6$ (0.15 mmol, 30 mol%) were added into a 25 mL glass tube. The reaction mixture was stirred at 70 °C for 24 h under Ar atmospheres. After the reaction was fully completed, the mixture was cooled to room temperature and concentrated under reduced pressure to give a crude product. 1,3,5-Trimethoxybenzene (10 mg) added as internal standard for NMR, yields base on the NMR yield.



A1+
6a in 89%



A3+
6a in 84%

Cyclic voltammograms

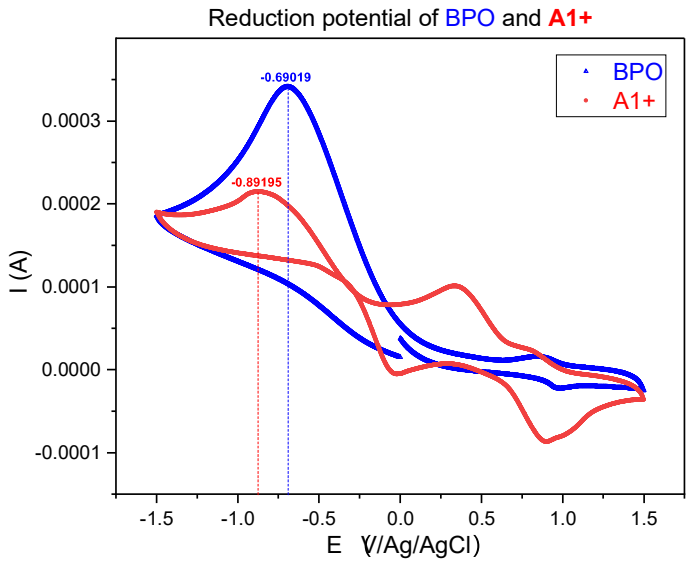


Figure 1. Cyclic voltammograms shows the reduction potential of **A1**+ and BPO. Two platinized Pt and Carbon wires as a counter and working electrode with a Ag/AgCl electrode as a reference were used. The cyclic voltammetry (CV) was conducted from -1.5 V to 1.5 V with a scan rate of 200 mV/s $^{-}$1. **A1**+ (0.03 mmol) or BPO (0.03 mmol) in 3 mL in CH_3CN of $LiClO_4$ (0.1 M) under Ar.

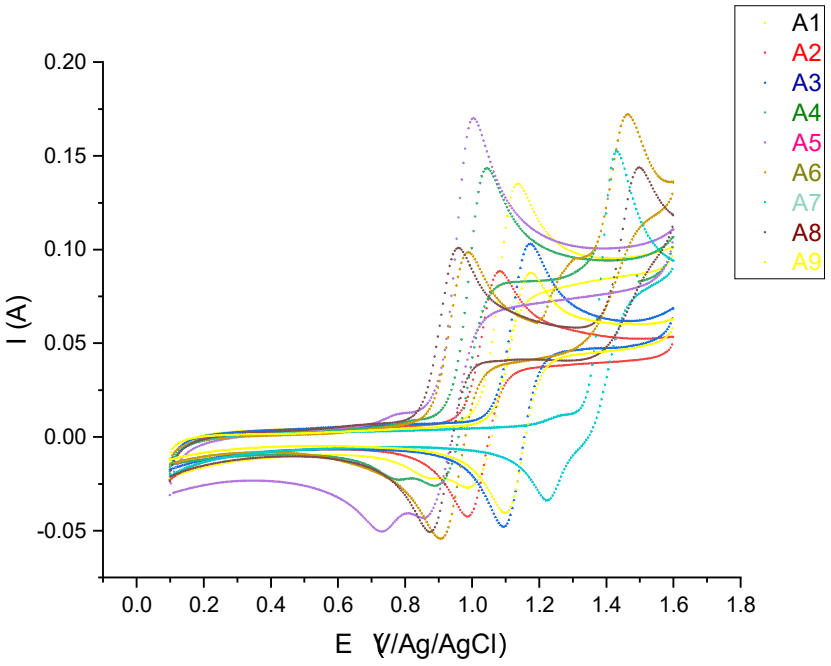
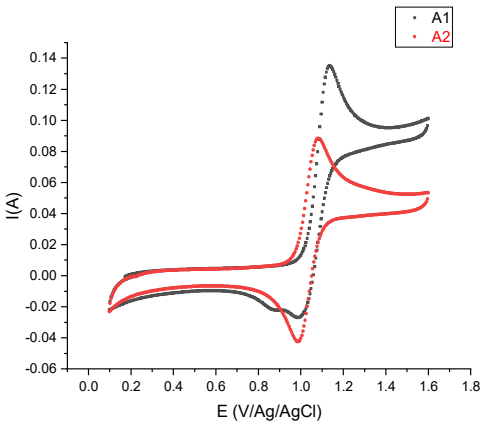
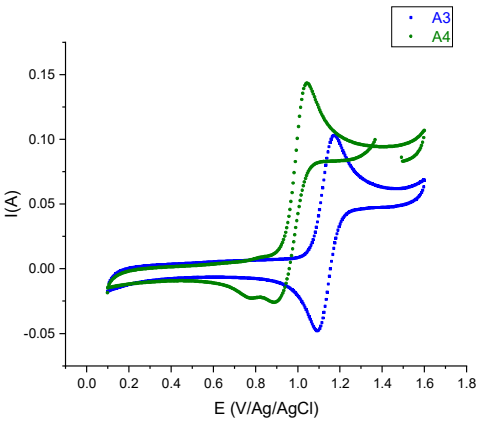
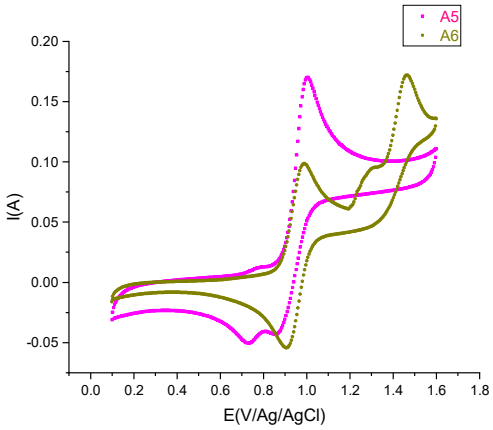
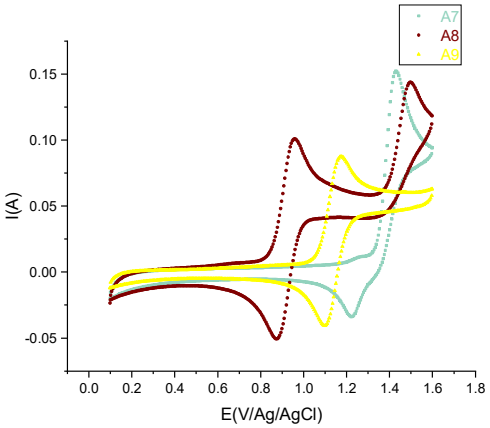


Figure 2. Cyclic voltammogram showing the structure-function relationship on the reduction and oxidation potential of amine catalysts. Two platinized Pt wires as a counter and working electrode with a Ag/AgCl electrode as a reference were used. The cyclic voltammetry (CV) was conducted from 0 V to 1.5 V with a scan rate of 100 mVs^{-1}. Triarylamine (0.2 mmol), tetrabutylammonium hexafluorophosphate (0.1 M) in CH_3CN under Ar.


A1
A2
I(A)
E (V/Ag/AgCl)


A3
A4
I(A)
E (V/Ag/AgCl)


A5
A6
I(A)
E(V/Ag/AgCl)


A7
A8
A9
I(A)
E(V/Ag/AgCl)

Mechanistic study

NMR study of BPO and catalyst in CD3CN at 70 ℃.

In an NMR tube, BPO (0.1 mmol) was added to CD_3CN (0.5 mL) and a first ^{1}H-NMR spectrum was measured as a control. The NMR tube was then heated at 70 ℃ in an oil-bath and ^{1}H-NMR spectra were measured after 2 h and 10 h, respectively, each time by removing the NMR tube from the oil-bath and measuring the spectra at ambient temperature. See the red line in the scheme below.

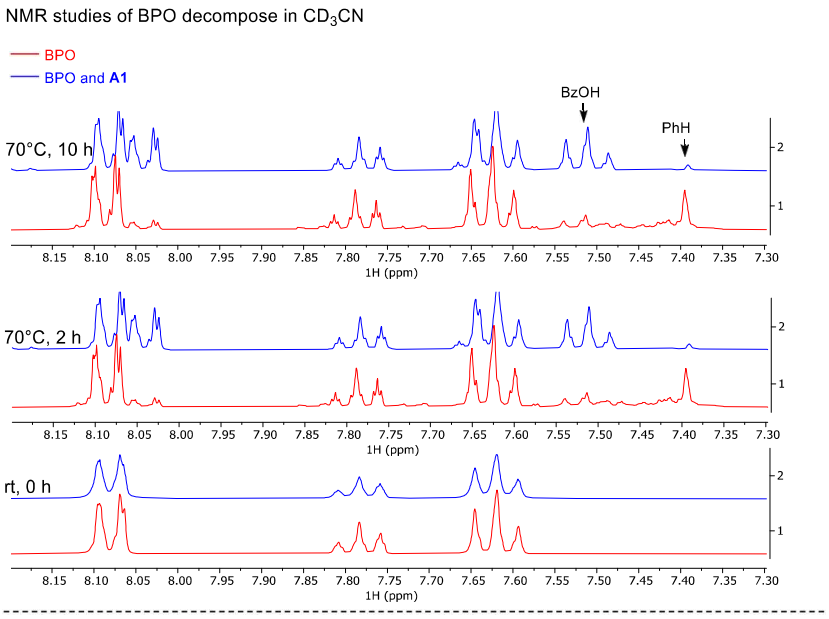


Table S5: Relative amounts of BPO, BzOH, and PhH for each experiment after 2 h and 10 h

A: BPO only; B: BPO + **A1**.

Reaction	BPO (mmol)					BzOH (mmol)					PhH (mmol)				
	0 h	0.5 h	1 h	2 h	10 h	0 h	0.5 h	1 h	2 h	10 h	0 h	0.5 h	1h	2 h	10 h
A	0.1	0.097	0.087	0.073	0.039	0	0.005	0.017	0.025	0.081	0	0.003	0.021	0.023	0.076
B	0.1	0.088	0.079	0.063	0.041	0	0.0027	0.05	0.079	0.132	0	0.001	0.003	0.01	0.012

BPO (0.1 mmol), catalyst (10 mol%) in 0.5 mL CD3CN.

Amount of BPO, BzOH, and PhH.

NMR yields based on the integration of BPO.

Table S6: % conversion of BPO, BzOH, and PhH for each experiment after 2 h and 10 h

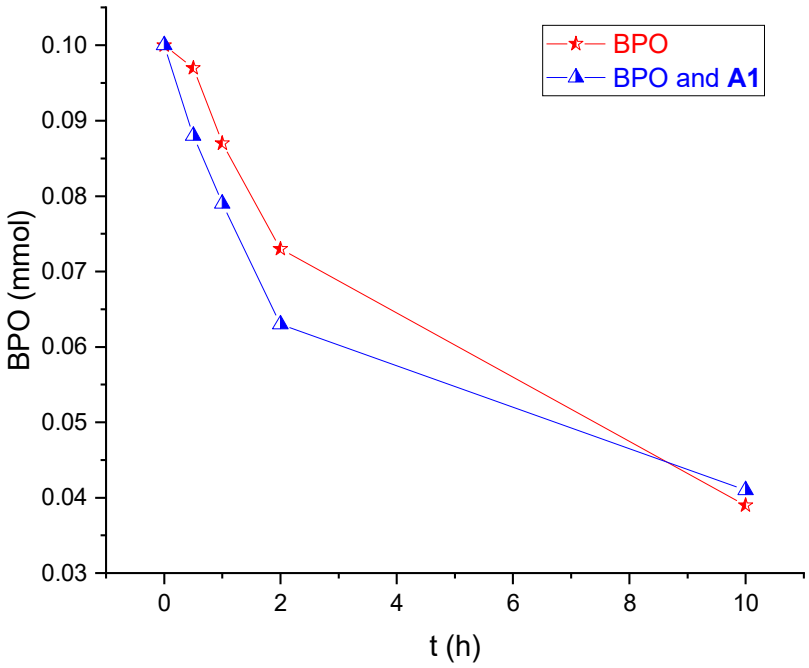
A: BPO only; B: BPO + **A1**.

Reaction	BPO					BzOH					PhH				
	0 h	0.5 h	1 h	2 h	10 h	0 h	0.5 h	1 h	2 h	10 h	0 h	0.5 h	1h	2 h	10 h
A	1	3%	13%	27%	60%	0	2.5%	8.5%	12.5%	40.5%	0	1.5%	10.5%	11.5%	38%
B	1	12%	21%	37%	59%	0	1.35%	25%	39.5%	66%	0	0.5%	1.5%	5%	6%

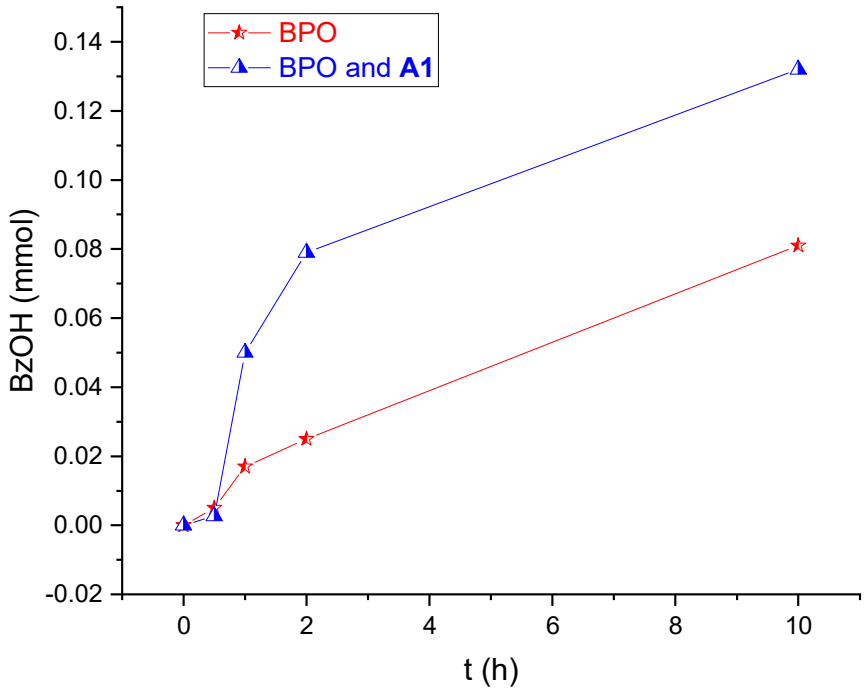
BPO (0.1 mmol), catalyst (10 mol%) in 0.5 mL CD3CN.

Amount of BPO, BzOH, and PhH.

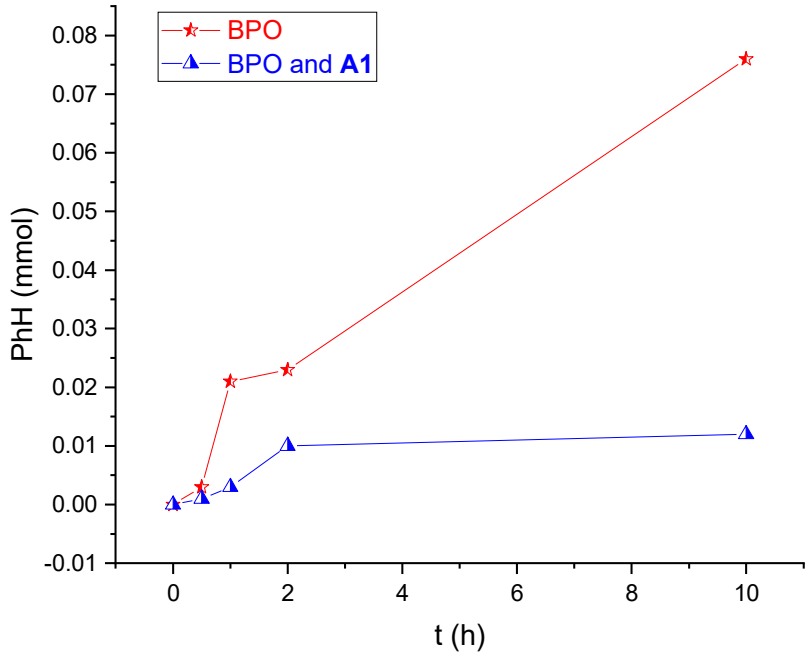
% conversion based on the integration of BPO.



Amount of BPO in different time

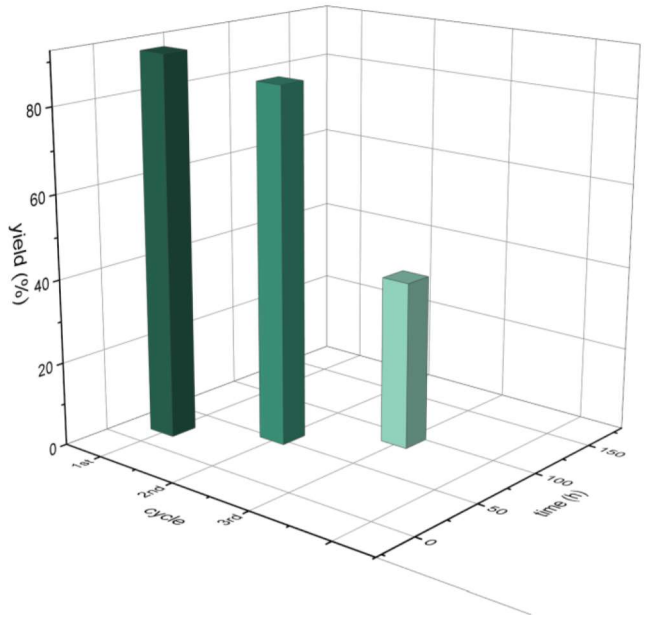


Amount of BzOH in different time



Amount of PhH in different time

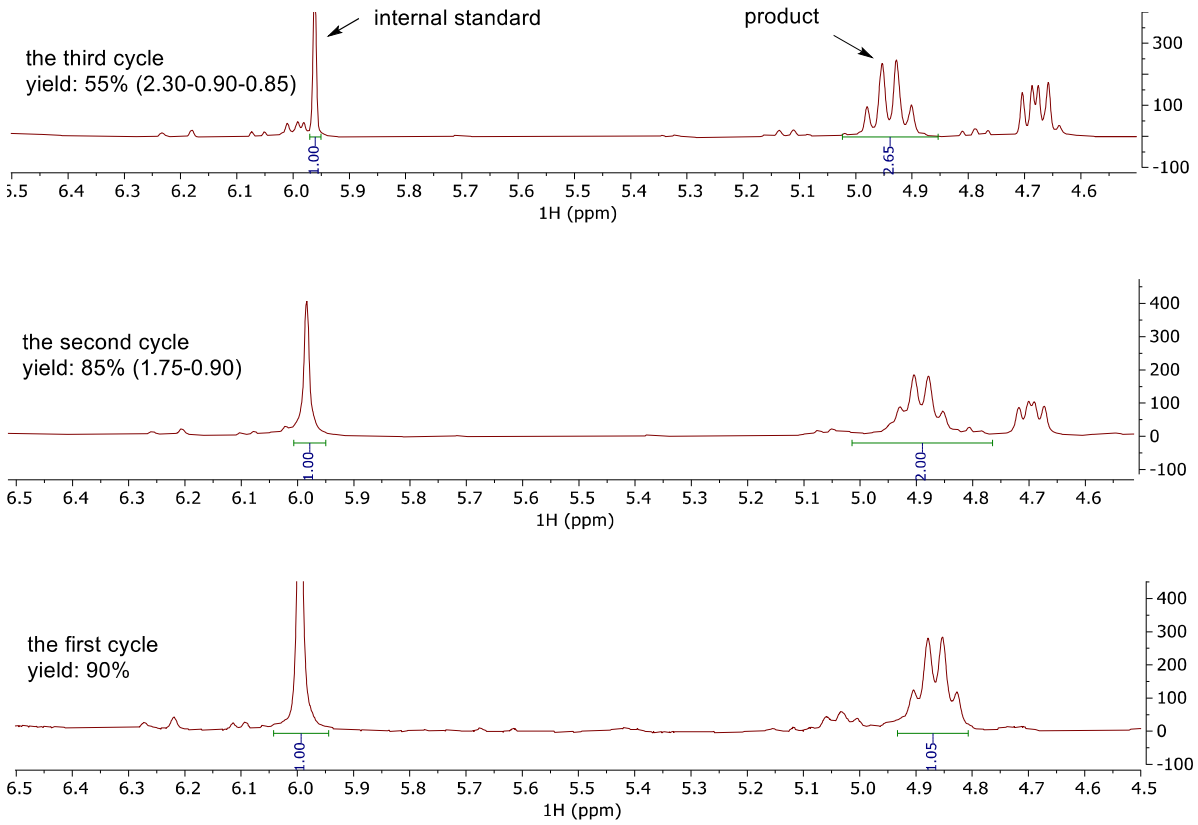
Details of the repetitive cycles experiment



a) The 1st cycle: **1a** (0.5 mmol), **A1** (10 mol%), BPO (1.5 equiv.), $NaPF_6$ (30 mo%), cyclohexane (10 mL), CH_3CN (2 mL), 70 ℃, 24 h. Yield: 90%. Determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-trimethoxybenzene.

b) The 2nd cycle: **1a** (0.5 mmol), **A1** (10 mol%), BPO (1.5 equiv.), $NaPF_6$ (30 mo%), cyclohexane (10 mL), CH_3CN (2 mL), 70 ℃, after 24 h, **1a** (0.5 mmol) and BPO (1.5 equiv.) were added again, keep the reaction at 70 ℃ for another 30 h. Yield: 85%. Determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-trimethoxybenzene.

c) The 3rd cycle: **1a** (0.5 mmol), **A1** (10 mol%), BPO (1.5 equiv.), $NaPF_6$ (30 mo%), cyclohexane (10 mL), CH_3CN (2 mL), 70 ℃, after 24 h, **1a** (0.5 mmol) and BPO (1.5 equiv.) were added again, after 30 h at 70 ℃, added **1a** (0.5 mmol) and BPO (1.5 equiv.) again, keep the reaction at 70 ℃ for another 38 h. Yield: 55%. Determined by ^1H NMR spectroscopic analysis of the crude reaction mixture relative to internal standard 1,3,5-trimethoxybenzene.

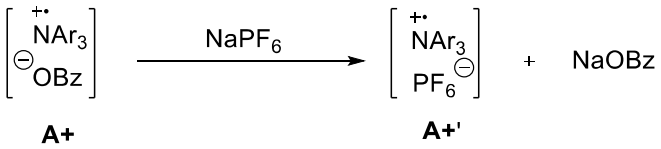


^{1}H NMR yield for repetitive cycle experiments

Anions exchange between PF_6^- and OBz^-

White participate can be isolated after the reaction cooled down. Washed the white participate three time with acetonitrile, acetone, and dichloromethane. Analyzing it by HRMS. From MS and HRMS spectral, only OBz- can be detected. Which means a little amount of NaOBz was formed. Besides, NaOBz is insoluble but $NaPF_6$ is soluble in cyclohexane and acetonitrile.

Triarylamine catalysts react with BPO to form intermediate radical cation **A+**, which under goes anion exchange to give more stable radical cation **A+**'. and NaOBz. This is the reason why the additive $NaPF_6$ is indispensable in this reaction system.



A+ **A+'**

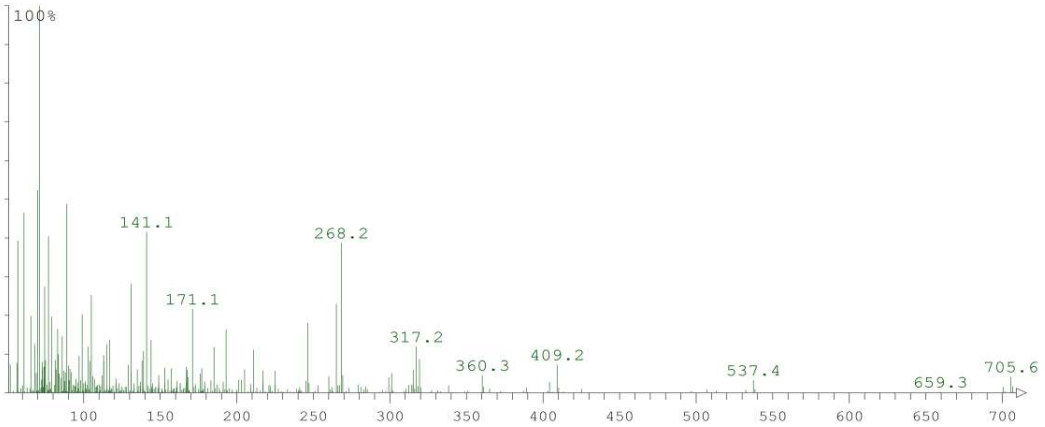
NaOBz

```
electrospray ionisation pos. ions

Characteristic Ions:
57, 61, 71, 89, 141, 171, 268, 409,
537 et. al. possible

m/z 23= [Na]   - out of measurement range
```

Datum:	29.10.2020
Analyse:	150185a-00
Sigel:	LJB-LA-785-01 KMA: Liu, Sensheng
Methode:	ESI pos+neg
Lösungsmittel:	CH3OH+CH2Cl2
Spektrometer:	Exactive
Auswerter:	Marcus, Tel:2243

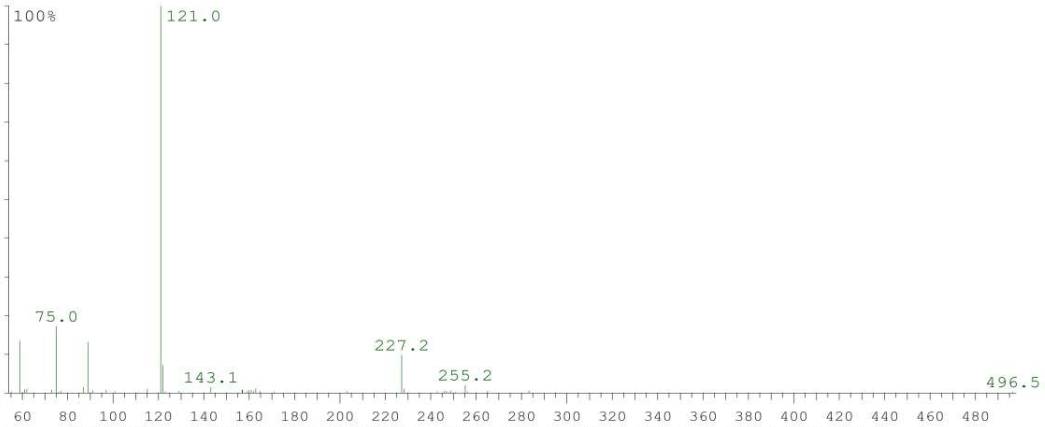


R3: 54(1:59) m(51-57) 233 7% 150185a-00 * LJB-LA-785-01/ESIneg/CH2Cl2+CH3OH/Exactive/

```
electrospray ionization neg. ions

Characteristic Ions:
59
75
89
121 = [C7H5O2]- = [144 - Na] possible
227
255 et. al. possible

Other measurements will follow (HRMS)
```



R3: 19(0:42) m(5-25) 1384 53% 150185a-00 * LJB-LA-785-01/ESIneg/CH2Cl2+CH3OH/Exactive/

*** Angegebene Mol.-Gewichte u. Massenzahlen basieren auf dem häufigsten Isotop der Elemente ***

MassLib

Mass to be matched (m/z): 121.029550 Charge: -1

Mass Tolerance: ±0.005550
Restriction of atom numbers:
C H O
1-100 1-100 1-10
Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C7 H5 O2	-0.37	121.029505

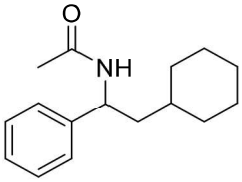
Datum:	29.10.2020
Analyse:	150185b-00
Sigel:	LJB-LA-785-01
	KMA: Liu, Sensheng
Method:	HR-MS
Ionis. :	ESIneg
solvent :	CH2Cl2 + CH3OH
Spectrometer:	Exactive
Auswerter:	Marcus, Tel:2243

--- possible element composition----

suggestion:
121 = [C7H5O2]-

Characterization Data

N-(2-cyclohexyl-1-phenylethyl)acetamide (**6a**, CAS: 2400221-26-1)



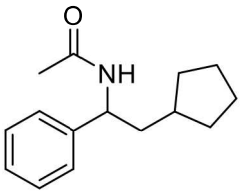
Following the **general procedure A**, white solid (105.5 mg, 86%)

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.27 (d, J = 8.6 Hz, 1H), 7.39–7.30 (m, 4H), 7.28–7.22 (m, 1H), 4.92 (td, J = 9.2, 5.8 Hz, 1H), 1.88 (s, 3H), 1.84–1.59 (m, 6H), 1.50 (ddd, J = 13.8, 8.1, 5.8 Hz, 1H), 1.35–1.13 (m, 4H), 0.98–0.94 (m, 2H);

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.73, 144.98, 128.66, 126.95, 126.75, 50.17, 44.66, 34.39, 33.51, 32.54, 26.56, 26.23, 26.09, 23.13.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{23}NO$ 245.1774; found 245.1774.

N-(2-cyclopentyl-1-phenylethyl)acetamide (**6b**, unreported product)



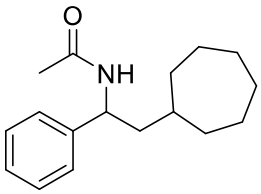
Following the **general procedure B**, white solid (97.0 mg, 84%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.29 (d, J = 8.6 Hz, 1H), 7.43–7.32 (m, 4H), 7.30–7.22 (m, 1H), 4.83 (td, J = 8.5, 6.0 Hz, 1H), 1.88 (s, 3H), 1.75 (ddq, J = 16.3, 11.4, 5.7 Hz, 4H), 1.62–1.57 (m, 3H), 1.55–1.43 (m, 2H), 1.24–1.09 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.71, 144.76, 128.65, 126.99, 126.84, 52.28, 43.39, 37.14, 32.62, 32.53, 25.19, 25.04, 23.16.

HRMS (ESIpos) (m/z): calculated for $C_{15}H_{21}NO$ 231.1617; found 231.1617.

N-(2-cycloheptyl-1-phenylethyl)acetamide (**6c**, unreported product)



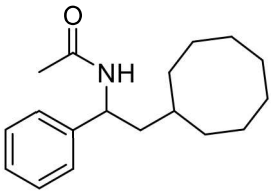
Following **the general procedure B**, white solid (111.6 mg, 86%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.28 (d, J = 8.6 Hz, 1H), 7.41–7.29 (m, 4H), 7.29–7.24 (m, 1H), 4.89 (td, J = 9.1, 5.6 Hz, 1H), 1.88 (s, 3H), 1.73–1.69 (m, 2H), 1.67–1.35 (m, 11H), 1.29–1.18 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.75, 144.94, 128.67, 126.95, 126.77, 50.75, 45.25, 35.73, 34.79, 33.67, 28.56, 28.53, 26.20, 26.08, 23.13.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO$ 259.1930; found 259.1930.

N-(2-cyclooctyl-1-phenylethyl)acetamide (**6d**, unreported product)



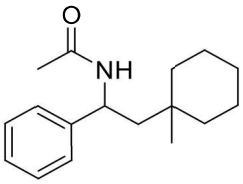
Following **the general procedure B**, white solid (107.5 mg, 80%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.24 (d, J = 8.6 Hz, 1H), 7.35–7.25 (m, 4H), 7.23–7.18 (m, 1H), 4.85 (td, J = 9.0, 4.9 Hz, 1H), 1.83 (s, 3H), 1.66–1.17 (m, 17H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.74, 144.94, 128.67, 126.96, 126.78, 50.69, 45.13, 33.61, 32.67, 31.03, 27.42, 27.19, 26.29, 25.31, 25.16, 23.12.

HRMS (ESIpos) (m/z): calculated for $C_{18}H_{27}NO$ 273.2087; found 273.2087.

N-(2-(1-methylcyclohexyl)-1-phenylethyl)acetamide (**6e**, major product from the reaction with methylcyclohexane, unreported product)



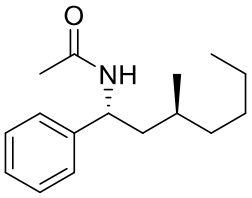
Following **the general procedure B**, white solid (44.0 mg, 34%).

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.25 (d, J = 8.8 Hz, 1H), 7.31–7.24 (m, 4H), 7.20–7.16 (m, 1H), 4.93 (td, J = 9.0, 3.5 Hz, 1H), 1.78 (s, 3H), 1.74 (dd, J = 14.4, 9.1 Hz, 1H), 1.48 (dd, J = 14.4, 3.5 Hz, 1H), 1.46–1.17 (m, 10H), 0.89 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.16, 146.39, 128.71, 126.80, 126.64, 49.17, 49.08, 38.11, 38.03, 33.32, 26.39, 25.56, 23.23, 21.99, 21.94.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO$ 259.1930; found 259.1930.

N-((1*R*, 3*S*)-3-methyl-1-phenylheptyl)acetamide (**6f**, unreported product)



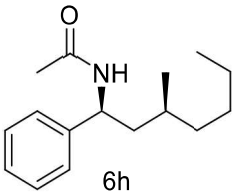
Following **the general procedure B**, colorless oil (5 mg , 4.1%).

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.23 (d, J = 8.8 Hz, 1H), 7.33–7.27 (m, 2H), 7.29–7.24 (m, 2H), 7.20 (tt, J = 7.2, 1.5 Hz, 1H), 4.83 (q, J = 8.80, 8.5, 7.0 Hz, 1H), 1.80 (s, 3H), 1.71–1.55 (m, 1H), 1.50–1.43 (m, 1H), 1.38–1.88 (m, 8H), 0.86–0.82 (m, 5H).

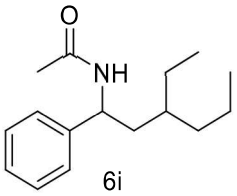
^{13}C NMR (151 MHz, DMSO-d_6) δ 168.06, 144.05, 128.14, 126.50, 126.38, 50.33, 43.66, 35.20, 28.95, 28.18, 22.58, 22.21, 19.56, 13.87.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{25}NO$ 247.1930; found 247.1931.

N-((1*S*,3*S*)-3-methyl-1-phenylheptyl)acetamide (**6g**, unreported product); *N*-(3-ethyl-1-phenylhexyl)acetamide (**6h**, unreported product)



6h



6i

6g and **6h** are a mixture (**6g**:**6h** = 2:2.3) as determined by **^{1}H NMR**.

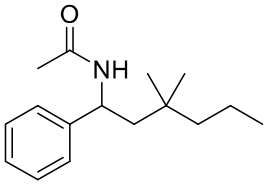
Following **the general procedure B**, colorless oil (94.0 mg, 76%).

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.20 (dd, J = 8.7, 3.7 Hz, 1H), 7.32–7.23 (m, 4H), 7.19 (ddt, J = 8.7, 5.4, 1.6 Hz,1H), 4.89–4.78 (m, 1H), 1.83–1.78 (m, 2H), 1.66 (ddd, J = 13.3, 10.5, 4.4 Hz, 0.37H), 1.56 (dp, J = 14.0, 4.3Hz, 0.43H), 1.47 (dtd, J = 13.6, 6.3, 3.7 Hz, 0.38H), 1.41 (d, J = 5.5 Hz, 0.16H), 1.34–1.25 (m, 1H), 1.29–1.15 (m, 7H), 1.14–1.07 (m, 0.3H), 0.91–0.82 (m, 3H), 0.82–0.77 (m, 1H), 0.75 (t, J = 7.2Hz, 1H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 168.83, 168.73, 168.69, 145.12, 144.86, 144.81, 128.66, 126.92, 126.74, 50.73, 50.67, 50.53, 44.54, 41.02, 40.99, 36.90, 35.37, 35.09, 35.02, 34.63, 29.68, 29.02, 25.88, 24.93, 23.10, 22.89, 19.51, 19.47, 19.21, 14.83, 14.72, 14.46, 10.87, 10.41.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{25}NO$ 247.1930; found 247.1929 and 247.1930.

N-(3,3-dimethyl-1-phenylhexyl)acetamide (**6i**, Major product from the reaction with *iso*-hexane, unreported product)



Following **the general procedure B**, colorless oil (50.6 mg, 41%)

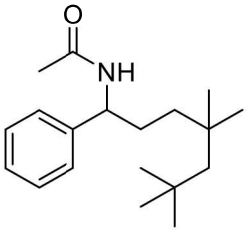
^{1}H NMR (600 MHz, DMSO-d_6) δ 8.23 (d, J = 8.6 Hz, 1H), 7.36–7.21 (m, 3H), 7.17 (ddt, J = 7.2, 5.3, 1.4 Hz, 1H), 4.89 (td, J = 9.1, 4.1 Hz, 1H), 1.78 (s, 3H), 1.72–1.65 (m, 1H), 1.45 (dd, J = 14.3, 3.6 Hz, 1H), 1.22–1.08 (m, 4H), 0.86–0.79 (m, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 168.18, 146.24, 128.69, 126.81, 126.64, 49.60, 48.53, 44.83, 33.46, 27.91, 27.89, 23.21, 17.18, 15.33.

^{15}N NMR (61 MHz, DMSO-d_6) δ -247.5.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{25}NO$ 247.1930; found 247.1930.

N-(4,4,6,6-tetramethyl-1-phenylheptyl)acetamide (**6j**, unreported product)



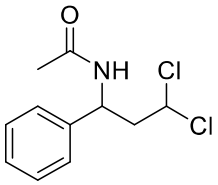
Following **the general procedure B**, colorless oil (40.4 mg, 28%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.28 (d, J = 8.6 Hz, 1H), 7.40–7.30 (m, 4H), 7.27 (t, J = 7.0 Hz, 1H), 4.72 (q, J = 8.1 Hz, 1H), 1.88 (s, 3H), 1.73–1.57 (m, 2H), 1.34 (ddd, J = 13.4, 11.4, 5.5 Hz, 1H), 1.26–1.10 (m, 3H), 1.02–0.84 (m, 15H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 186.76, 144.47, 128.62, 127.02, 126.93, 53.98, 53.75, 41.33, 34.65, 32.46, 32.28, 31.74, 29.42, 29.27, 23.14.

HRMS (ESIpos) (m/z): calculated for $C_{19}H_{31}NO$ 289.2400; found 289.2401.

N-(3,3-dichloro-1-phenylpropyl)acetamide (**6k**, unreported product)



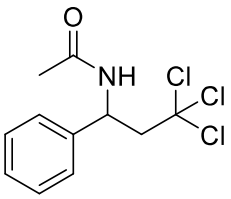
Following **the general procedure B**, white solid (53.9 mg, 45%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (d, J = 8.5 Hz, 1H), 7.40–7.30 (m, 4H), 7.29–7.25 (m, 1H), 6.07 (dd, J = 8.6, 4.5 Hz, 1H), 5.02 (ddd, J = 10.0, 8.4, 4.7 Hz, 1H), 2.68–2.62 (m, 1H), 2.49–2.44 (m, 1H), 1.86 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d6) δ 169.15, 142.44, 129.01, 127.71, 126.83, 72.30, 50.55, 49.79, 23.20.

HRMS (ESIpos) (m/z): $[M+H]^+$ calculated for $C_{11}H_{13}Cl_2NO$ 246.0446; found 246.0447.

N-(3,3,3-trichloro-1-phenylpropyl)acetamide (**6l**, unreported product)



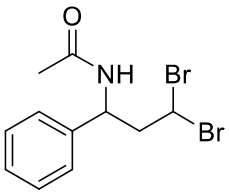
Following **the general procedure B**, white solid (102.8 mg, 74%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (d, J = 8.6 Hz, 1H), 7.40–7.33 (m, 4H), 7.29–7.26 (m, 1H), 5.35 (td, J = 8.4, 3.4 Hz, 1H), 3.34 (dd, J = 15.2, 3.4 Hz, 1H), 3.09 (dd, J = 15.2, 3.4 Hz, 1H), 1.86 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.66, 142.75, 129.05, 127.76, 126.99, 98.40, 59.51, 51.02, 23.25.

HRMS (ESIpos) (m/z): calculated for $C_{11}H_{12}Cl_3NO$ 278.9978; found 278.9977.

N-(3,3-dibromo-1-phenylpropyl)acetamide (**6m**, unreported product)



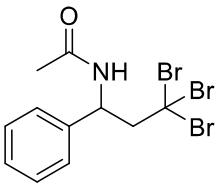
Following **the general procedure B**, colorless oil (54.7 mg, 33%).

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.36 (d, J = 8.4 Hz, 1H), 7.35–7.28 (m, 2H), 7.28–7.22 (m, 2H), 5.87 (dd, J = 9.0, 4.7 Hz, 1H), 4.94 (ddd, J = 9.7, 8.3, 4.8 Hz, 1H), 2.79 (ddd, J = 14.6, 9.8, 4.7 Hz, 1H), 2.63 (ddd, J = 14.6, 9.0, 4.8 Hz, 1H), 1.82 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.13, 142.31, 128.99, 127.67, 126.79, 52.09, 51.55, 44.73, 23.17.

HRMS (ESIpos) (m/z): $[M+Na]^+$ calculated for $C_{11}H_{13}Br_2NONa$ 355.9256; found 355.9253.

N-(3,3,3-tribromo-1-phenylpropyl)acetamide (**6n**, unreported product)



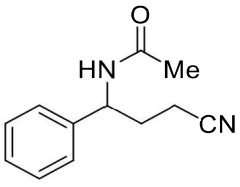
Following **the general procedure B**, colorless oil (49.2 mg, 24%) (Mixed with 21% of **6p**).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.68 (d, J = 8.4 Hz, 1H), 7.46–7.39 (m, 3H), 7.38–7.29 (m, 2H), 5.29 (ddd, J = 9.7, 8.3, 4.8 Hz, 1H), 3.71 (dd, J = 15.4, 8.1 Hz, 1H), 3.36 (d, J = 2.8 Hz, 1H), 1.92 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 186.61, 142.60, 128.52, 127.14, 126.34, 63.81, 53.44, 38.59, 23.37.

HRMS (ESIpos) (m/z): $[M+Na]^+$ calculated for $C_{11}H_{12}Br_3NONa$ 433.8361; found 433.8359.

N-(3-cyano-1-phenylpropyl)acetamide (**6o**, CAS: 2127514-83-2)



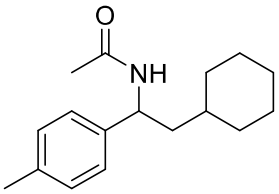
Following **the general procedure B**, white solid (86.8 mg, 86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 2H), 7.32-7.30 (m, 1H), 7.27-7.26 (m, 2H), 5.90 (d, *J* = 8.0 Hz, 1H), 5.04 (dd, *J* = 15.5 Hz, 8.0 Hz, 1H), 2.37-2.31 (m, 2H), 2.27-2.22 (m, 1H), 2.15-2.10 (m, 1H), 1.99 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.85, 139.83, 129.21, 128.34, 126.55, 119.26, 52.90, 31.66, 23.37, 14.54.

HRMS (ESIpos) (m/z): M^+ calculated for $C_{12}H_{14}N2O$ 202.1100; found 202.1098.

N-(2-cyclohexyl-1-(*p*-tolyl)ethyl)acetamide (**7a**, unreported product)



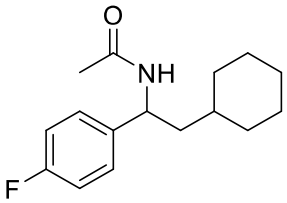
Following **the general procedure B**, colorless oil (103.6 mg, 80%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (d, J = 8.6 Hz, 1H), 7.20–7.07 (m, 4H), 4.82 (td, *J* = 9.0, 6.1 Hz, 1H), 2.27 (s, 3H), 1.81 (s, 3H), 1.77–1.49 (m, 6H), 1.43 (ddd, *J* = 13.8, 7.9, 6.1 Hz, 1H), 1.26–1.06 (m, 4H), 0.97–0.81 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.61, 141.89, 135.93, 129.20, 126.70, 49.85, 44.62, 34.37, 33.44, 32.63, 26.56, 26.22, 26.10, 23.14, 21.09.

HRMS (ESIpos) (m/z): $[M+Na]^+$ calculated for $C_{11}H_{13}Br_2NONa$ 333.9436; found 333.9434.

N-(2-cyclohexyl-1-(4-fluorophenyl)ethyl)acetamide (**7c**, unreported product)



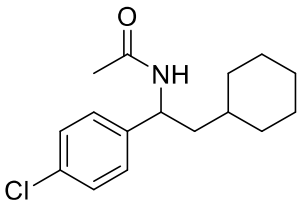
Following **the general procedure B**, colorless oil (65.7 mg, 50%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.28 (d, J = 8.5 Hz, 1H), 7.49–7.30 (m, 2H), 7.18 (t, *J* = 8.9 Hz, 2H), 4.91 (td, *J* = 9.1, 5.9 Hz, 1H), 1.88 (s, 3H), 1.84–1.55 (m, 6H), 1.49 (ddd, *J* = 13.8, 8.1, 5.9 Hz, 1H), 1.3 –1.11 (m, 4H), 1.02–0.88 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.76, 141.14 (d, *J* = 3.75 Hz, 1C), 128.65 (d, *J* = 6.25 Hz, 1C), 115.44, 115.27, 49.55, 44.53, 34.37, 33.44, 32.52, 26.55, 26.22, 26.07, 23.12.

HRMS (ESIpos) (m/z): calculated for $C_{12}H_{22}FNO$ 263.1679; found 263.1681.

N-(1-(4-chlorophenyl)-2-cyclohexylethyl)acetamide (**7d**, unreported product)



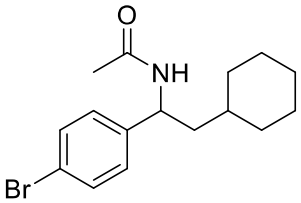
Following **the general procedure B**, colorless oil (113.0 mg, 81%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (d, J = 8.4 Hz, 1H), 7.56–7.11 (m, 4H), 4.90 (td, J = 9.1, 5.9 Hz, 1H), 1.88 (s, 3H), 1.84 –1.55 (m, 6H), 1.48 (ddd, J = 13.8, 8.1, 5.9 Hz, 1H), 1.32–1.12 (m, 4H), 1.04–0.85 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.85, 144.01, 131.46, 128.67, 128.63, 49.68, 44.33, 34.35, 33.44, 32.49, 26.54, 26.21, 26.06, 23.10.

HRMS (ESIpos) (m/z): $[M+Na]^+$ calculated for $C_{16}H_{22}ClNONa$ 302.1282; found 302.1278.

N-(1-(4-bromophenyl)-2-cyclohexylethyl)acetamide (**7e**, unreported product)



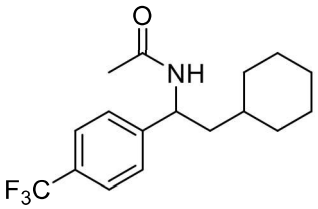
Following **the general procedure B**, colorless oil (127.6 mg, 79%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 4.88 (td, J = 9.1, 5.9 Hz, 1H), 1.88 (s, 3H), 1.82–1.57 (m, 6H), 1.48 (ddd, J = 13.8, 8.1, 5.9 Hz, 1H), 1.36–1.06 (m, 4H), 1.03–0.81 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.86, 144.45, 131.55, 129.07, 119.93, 49.75, 44.28, 34.34, 33.44, 32.49, 26.53, 26.20, 26.06, 23.09.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{22}BrNO$ 323.0879; found 323.0883.

N-(2-cyclohexyl-1-(4-(trifluoromethyl)phenyl)ethyl)acetamide (**7f**, unreported product)



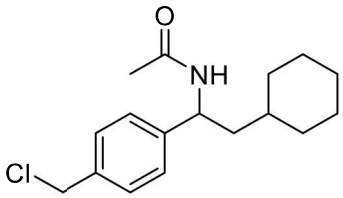
Following **the general procedure B**, colorless oil (95.5 mg, 61%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 (d, J = 8.2 Hz, 1H), 7.68 (d, J = 8.1 Hz, 2H), 7.49 (d, J = 8.0 Hz, 2H), 4.92 (td, J = 9.2, 5.6 Hz, 1H), 1.84 (s, 3H), 1.78–1.54 (m, 6H), 1.45 (ddd, J = 13.8, 8.3, 5.6 Hz, 1H), 1.31–1.08 (m, 4H), 0.99–0.78 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.05, 127.57, 127.54, 125.63 (q, J = 30, 15 Hz, 1C), 50.11, 44.22, 34.33, 33.50, 32.28, 26.53, 26.20, 26.03, 23.06.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{22}F_3NO$ 312.1580; found 312.1584.

N-(1-(4-(chloromethyl)phenyl)-2-cyclohexylethyl)acetamide (**7g**, unreported product)



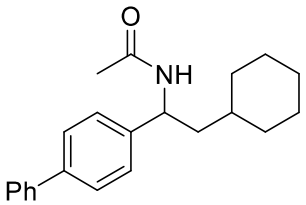
Following **the general procedure B**, colorless oil (102.5 mg, 70%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.29 (d, J = 8.5 Hz, 1H), 7.42 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 4.91 (td, J = 9.1, 6.0 Hz, 1H), 4.79 (s, 2H), 1.88 (s, 3H), 1.82–1.59 (m, 6H), 1.50 (ddd, J = 13.8, 8.1, 5.9 Hz, 1H), 1.35–1.14 (m, 4H), 1.04–0.89 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.82, 145.25, 136.30, 129.29, 127.06, 49.97, 46.53, 44.45, 34.36, 33.47, 32.52, 26.55, 26.21, 26.07, 23.11.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{24}ClNO$ 293.1540; found 293.1542.

N-(1-([1,1'-biphenyl]-4-yl)-2-cyclohexylethyl)acetamide (**7h**, unreported product)



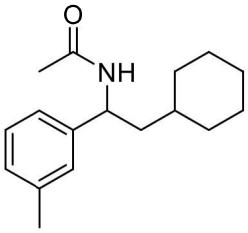
Following **the general procedure B**, white solid (101.1 mg, 63%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.32 (d, J = 8.5 Hz, 1H), 7.78–7.61 (m, 3H), 7.52 (t, J = 7.7 Hz, 2H), 7.42 (dd, J = 7.9, 2.7 Hz, 3H), 4.96 (td, J = 9.1, 5.9 Hz, 1H), 1.90 (s, 3H), 1.84–1.62 (m, 6H), 1.55 (ddd, J = 13.8, 8.1, 5.9 Hz, 1H), 1.38–1.12 (m, 4H), 1.06–0.91 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.80, 144.24, 140.50, 138.95, 129.37, 127.73, 127.39, 127.06, 49.92, 44.51, 34.40, 33.51, 32.56, 26.57, 26.23, 26.09, 23.16.

HRMS (ESIpos) (m/z): $[M+Na]^+$ calculated for $C_{22}H_{27}NONa$ 344.1984; found 344.1987.

N-(2-cyclohexyl-1-(*m*-tolyl)ethyl)acetamide (**7i**, unreported product)



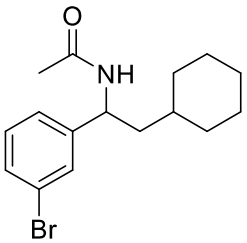
Following **the general procedure B**, colorless oil (97.1 mg, 75%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.23 (d, J = 8.6 Hz, 1H), 7.24 (d, J = 7.6 Hz, 1H), 7.18–6.77 (m, 3H), 4.88 (td, J = 9.2, 5.7 Hz, 1H), 2.34 (s, 3H), 1.87 (s, 3H), 1.82–1.57 (m, 6H), 1.48 (ddd, J = 13.8, 8.2, 5.7 Hz, 1H), 1.32–1.14 (m, 4H), 1.04–0.86 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.69, 144.95, 137.66, 128.57, 127.59, 127.38, 123.84, 50.09, 44.69, 34.39, 33.54, 32.51, 26.57, 26.23, 26.09, 23.15, 21.57.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO$ 259.1930; found 259.1930.

N-(1-(3-bromophenyl)-2-cyclohexylethyl)acetamide (**7j**, unreported product)



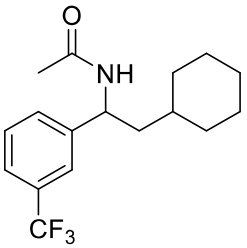
Following **the general procedure B**, colorless oil (133.8 mg, 83%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.33 (d, J = 8.5 Hz, 1H), 7.52 (d, J = 1.3 Hz, 1H), 7.46 (ddd, J = 5.7, 3.6, 2.0 Hz, 1H), 7.36–7.30 (m, 2H), 5.15–4.60 (m, 1H), 1.89 (s, 3H), 1.82–1.59 (m, 6H), 1.48 (ddd, J = 13.7, 8.3, 5.5 Hz, 1H), 1.33–1.13 (m, 4H), 1.06–0.88 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.96, 147.97, 130.94, 129.90, 129.41, 126.00, 122.11, 49.89, 44.40, 34.38, 33.51, 32.37, 26.54, 26.22, 26.05, 23.10.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{22}BrNO$ 323.0879; found 323.0881.

N-(2-cyclohexyl-1-(3-(trifluoromethyl)phenyl)ethyl)acetamide (**7k**, unreported product)



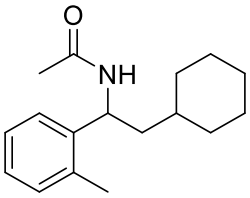
Following **the general procedure B**, colorless oil (70.4 mg, 45%).

1H NMR (500 MHz, DMSO-d_6) δ 8.41 (d, J = 8.4 Hz, 1H), 7.72–7.57 (m, 4H), 5.00 (ddd, J = 10.1, 8.3, 5.4 Hz, 1H), 1.90 (s, 3H), 1.82–1.62 (m, 6H), 1.50 (ddd, J = 13.8, 8.5, 5.4 Hz, 1H), 1.37–1.13 (m, 4H), 1.05–0.89 (m, 2H).

13C NMR (125 MHz, DMSO-d_6) δ 169.07, 146.63, 131.05, 129.82, 123.82 (d, J = 4.25 Hz, 1C), 123.09 (q, J = 364, 17 Hz, 1C), 50.02, 44.40, 34.41, 33.54, 32.31, 26.53, 26.22, 26.05, 23.08.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{22}F_3NO$ 313.1647; found 313.1649.

N-(2-cyclohexyl-1-(o-tolyl)ethyl)acetamide (**7l**, unreported product)



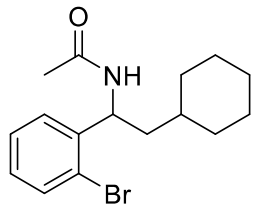
Following **the general procedure B**, colorless oil (117.8 mg, 91%).

1H NMR (500 MHz, DMSO-d_6) δ 8.30 (d, J = 8.4 Hz, 1H), 7.40–7.31 (m, 1H), 7.21 (td, J = 8.0, 3.0 Hz, 1H), 7.19–7.11 (m, 2H), 5.15 (ddd, J = 10.4, 8.2, 3.7 Hz, 1H), 2.36 (s, 3H), 1.87 (s, 3H), 1.75–1.49 (m, 5H), 1.46–1.34 (m, 2H), 1.26–1.16 (m, 3H), 1.03–0.96 (m, 2H).

13C NMR (125 MHz, DMSO-d_6) δ 168.73, 143.57, 134.54, 130.38, 126.67, 126.50, 125.75, 46.29, 44.07, 34.56, 33.92, 32.25, 26.56, 26.27, 26.08, 23.08, 19.18.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO$ 259.1930; found 259.1931.

N-(1-(2-bromophenyl)-2-cyclohexylethyl)acetamide (**7m**, unreported product)



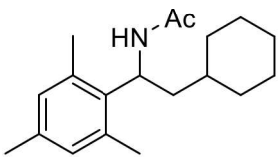
Following **the general procedure B**, colorless oil (129.2 mg, 80%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (d, J = 8.3 Hz, 1H), 7.60 (dd, J = 8.0, 1.2 Hz, 1H), 7.49–7.38 (m, 2H), 7.21 (ddd, J = 8.0, 7.0, 2.0 Hz, 1H), 5.66–5.04 (m, 1H), 1.92–1.90 (m, 4H), 1.78–1.61 (m, 4H), 1.53–1.41 (m, 3H), 1.31–1.16 (m, 3H), 1.00 (t, J = 6.9 Hz, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 169.06, 144.45, 132.90, 128.93, 128.44, 127.71, 122.38, 49.87, 43.68, 34.58, 34.01, 31.90, 26.54, 26.25, 26.02, 23.06.

HRMS (ESIpos) (m/z): $[M+Na]^+$ calculated for $C_{16}H_{22}BrNONa$ 346.0777; found 346.0776.

N-(2-cyclohexyl-1-mesitylethyl)acetamide (**7n**, unreported product)



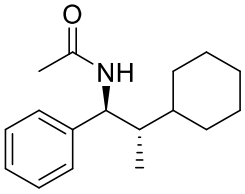
Following **the general procedure B**, white solid (88.9 mg, 62%).

1H NMR (500 MHz, DMSO-d_6) δ 8.11 (d, J = 7.1 Hz, 1H), 6.77 (s, 2H), 5.21 (ddd, J = 11.2, 7.1, 4.4 Hz, 1H), 2.38 (s, 6H), 2.21 (s, 3H), 1.95–1.88 (m, 1H), 1.86 (s, 3H), 1.83–1.62 (m, 6H), 1.46–1.12 (m, 5H), 1.08–0.84 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.88, 137.59, 135.63, 135.09, 47.06, 40.91, 34.52, 34.06, 32.13, 26.58, 26.30, 26.10, 22.80, 21.00, 20.73.

HRMS (ESIpos) (m/z): calculated for $C_{19}H_{29}NO$ 287.2243; found 287.2242.

N-((1*S*, 2*S*)-1,2-diphenylpropyl)acetamide (1*S*, 2*S*-**7o**, unreported product)



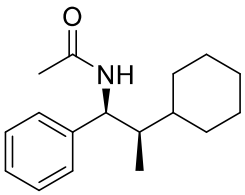
Following **the general procedure B**, colorless oil (33.0 mg, 25.5 %).

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.26 (d, J = 9.2 Hz, 1H), 7.31–7.27 (m, 2H), 7.26–7.23 (m, 2H), 7.22–7.18 (m, 1H), 4.59 (dd, J = 10.6, 9.2 Hz, 1H), 1.79 (s, 3H), 1.77–1.54 (m, 5H), 1.47 (d, J = 12.4 Hz, 1H), 1.33–1.06 (m, 5H), 0.91 (td, J = 12.4, 8.9 Hz, 1H), 0.45 (d, J = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 168.41, 144.04, 128.52, 127.85, 127.01, 55.58, 42.81, 38.38, 32.10, 27.15, 26.80, 26.78, 26.11, 23.11, 12.53.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO$ 259.1930; found 259.1931.

N-((1*S*, 2*R*)-2-cyclohexyl-1-phenylpropyl)acetamide (1*S*, 2*R*-**7o**, unreported product)



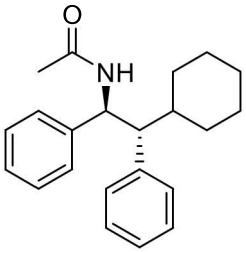
Following **the general procedure B**, colorless oil (33.0 mg, 25.5 %)

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.07 (d, J = 9.2 Hz, 1H), 7.33–7.28 (m, 2H), 7.25–7.16 (m, 3H), 4.88 (dd, J = 9.3, 7.6 Hz, 1H), 1.85 (s, 3H), 1.73–1.59 (m, 4H), 1.57–1.49 (m, 2H), 1.15–0.86 (m, 5H), 0.77 (d, J = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 168.96, 143.90, 128.56, 127.21, 126.86, 54.87, 43.59, 39.13, 31.61, 27.99, 26.73, 26.59, 26.50, 23.11, 11.77.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO$ 259.1930; found 259.1931.

N-((1*S*, 2*R*)-2-cyclohexyl-1,2-diphenylethyl)acetamide (1*S*, 2*R*-**7p**, unreported product, minor component)



Following **the general procedure B**, colorless oil (21.3 mg, 13.3%).

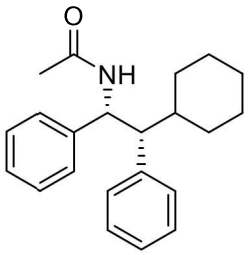
^{1}H NMR (600 MHz, DMSO-d_6) δ 8.35 (d, *J* = 9.3 Hz, 1H), 7.36–6.96 (m, 10H), 5.38 (dd, *J* = 9.3 Hz, 11.7 Hz, 1H), 3.02 (dd, *J* = 3.9 Hz, 11.7 Hz, 1H), 1.91-1.81 (m, 5H), 1.67–1.32 (m, 2H), 1.58–1.50 (m, 2H), 1.24–1.22 (m, 1H), 1.11–1.08 (m, 1H), 0.95–0.58 (m, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 168.47, 143.51, 139.61, 130.28, 128.16, 128.10, 127.75, 126.62, 126.30, 55.85, 53.16, 39.00, 32.60, 27.35, 26.91, 26.75, 26.59, 23.18.

HRMS (ESIpos) (m/z): $[M+H]^+$ calculated for $C_{22}H_{27}NO$ 322.2165; found 322.2165.

N-((*1S*, 2*S*)-2-cyclohexyl-1,2-diphenylethyl)acetamide (1*S*, 2*S*-**7p**, unreported product, major component)

Following **the general procedure B**, colorless oil (42.6 mg, 26.7%).

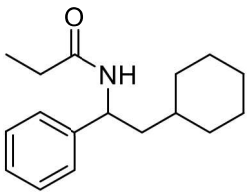


^{1}H NMR (600 MHz, DMSO-d_6) δ 7.94 (d, *J* = 9.3 Hz, 1H), 7.36–6.96 (m, 10H), 5.37 (dd, *J* = 9.3 Hz, 10.9 Hz, 1H), 2.91 (dd, *J* = 4.3 Hz, 10.9 Hz, 1H), 1.75-1.71 (m, 1H), 1.58–1.47 (m, 6H), 1.43–1.42 (m, 1H), 1.14–1.11 (m, 1H), 0.95–0.58 (m, 5H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 168.21, 143.61, 139.73, 129.92, 128.67, 127.75, 127.68, 127.27, 126.62, 126.54, 56.73, 53.23, 38.61, 32.67, 27.64, 26.59, 26.38, 26.37, 22.96.

HRMS (ESIpos) (m/z): $[M+H]^+$ calculated for $C_{22}H_{27}NO$ 322.2165; found 322.2165.

N-(2-cyclohexyl-1-phenylethyl)propionamide (**8a**, unreported product)



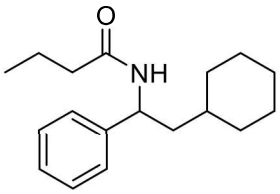
Following **the general procedure C**, white solid (90.6 mg, 70%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13 (d, J = 8.6 Hz, 1H), 7.51–7.24 (m, 4H), 7.23–7.17 (m, 1H), 4.88 (td, J = 9.2, 5.8 Hz, 1H), 2.10 (m, 2H), 1.77 – 1.54 (m, 6H), 1.45 (m, 1H), 1.29–1.07 (m, 4H), 0.98 (t, J = 7.6 Hz, 3H), 0.94–0.80 (m, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 172.53, 145.09, 128.66, 126.91, 126.71, 50.00, 44.66, 34.47, 33.53, 32.47, 29.04, 26.56, 26.26, 26.13, 10.57.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO$ 259.1930; found 259.1933.

N-(2-cyclohexyl-1-phenylethyl)butyramide (**8b**, unreported product)



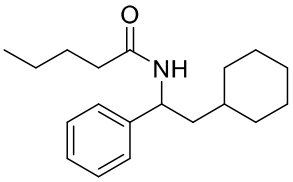
Following **the general procedure C**, white solid (79.1 mg, 58%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (d, J = 8.7 Hz, 1H), 7.35–7.24 (m, 4H), 7.23–7.17 (m, 1H), 4.89 (td, J = 9.5, 5.4 Hz, 1H), 2.09–2.05 (m, 2H), 1.66–1.43 (m, 9H), 1.24–1.11 (m, 4H), 0.94–0.81 (m, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 171.64, 145.16 128.64, 126.90, 126.69, 49.91, 44.61, 37.85, 34.49, 33.63, 32.31, 26.55, 26.32, 26.13, 19.29, 13.95.

HRMS (ESIpos) (m/z): calculated for $C_{18}H_{27}NO$ 273.2087; found 273.2088.

N-(2-cyclohexyl-1-phenylethyl)pentanamide (**8c**, unreported product)



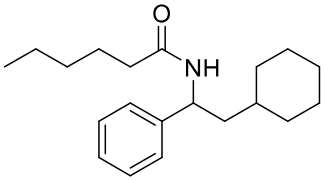
Following **the general procedure C**, white solid (86.1 mg, 60%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (d, J = 8.6 Hz, 1H), 7.34–7.24 (m, 4H), 7.23–7.18 (m, 1H), 4.89 (td, J = 9.5, 5.4 Hz, 1H), 2.19–2.02 (m, 2H), 1.74 (d, J = 12.8 Hz, 1H), 1.69–1.37 (m, 8H), 1.28–1.22 (m, 3H), 1.15–1.09 (m, 3H), 1.04–0.86 (m, 2H), 0.85 (t, J = 7.4 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 171.77, 145.16, 128.64, 126.89, 126.67, 49.90, 44.63, 35.60, 34.49, 33.65, 32.31, 28.01, 26.56, 26.13, 22.11, 14.16.

HRMS (ESIpos) (m/z): calculated for $C_{19}H_{29}NO$ 287.2243; found 287.2242.

N-(2-cyclohexyl-1-phenylethyl)hexanamide (**8d**, unreported product)



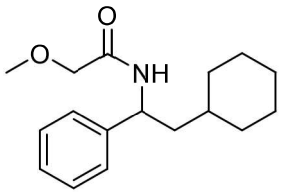
Following **the general procedure C**, white solid (114.4 mg, 76%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (d, J = 8.6 Hz, 1H), 7.32–7.25 (m, 4H), 7.23–7.17 (m, 1H), 4.89 (td, J = 9.6, 5.3 Hz, 1H), 2.15–2.03 (m, 2H), 1.75 (d, J = 13.0 Hz, 1H), 1.71–1.35 (m, 8H), 1.37–1.05 (m, 8H), 1.00–0.88 (m, 1H), 0.85 (t, J = 7.2 Hz, 4H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 171.78, 145.18, 128.62, 126.89, 126.67, 49.87, 44.64, 35.83, 34.49, 33.68, 32.28, 31.21, 26.56, 26.35, 26.14, 25.56, 22.32, 14.37.

HRMS (ESIpos) (m/z): calculated for $C_{20}H_{31}NO$ 301.2400; found 301.2400.

N-(2-cyclohexyl-1-phenylethyl)-2-methoxyacetamide (**8f**, unreported product)



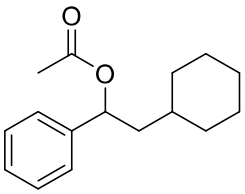
Following **the general procedure C**, white solid (61.7 mg, 48%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.14 (d, J = 8.8 Hz, 1H), 7.31 (d, J = 6.7 Hz, 4H), 7.25–7.18 (m, 1H), 4.95 (td, J = 9.4, 5.7 Hz, 1H), 3.81 (d, J = 3.8 Hz, 2H), 3.30 (s, 3H), 1.78–1.37 (m, 7H), 1.29–1.06 (m, 4H), 0.98–0.83 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.67, 144.63, 128.67, 127.07, 126.93, 71.99, 58.95, 49.85, 43.92, 34.44, 33.50, 32.40, 26.56, 26.25, 26.10.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{25}NO_2$ 275.1879; found 275.1879.

2-cyclohexyl-1-phenylethyl acetate (**8g**, CAS: 2366999-88-2)



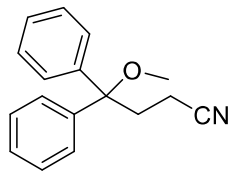
Following **the general procedure C**, colorless oil (77.5 mg, 63%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.46–7.30 (m, 5H), 5.80 (dd, J = 8.8, 5.6 Hz, 1H), 2.09 (s, 3H), 1.83 (ddd, J = 14.4, 8.8, 6.1 Hz, 1H), 1.78–1.57 (m, 6H), 1.31–1.14 (m, 4H), 1.03–0.96 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 170.23, 141.58, 128.88, 128.16, 126.67, 73.61, 43.94, 34.08, 33.33, 32.75, 26.45, 26.11, 26.01, 21.41.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{22}O_2$ 246.1614; found 246.1616.

4-methoxy-4,4-diphenylbutanenitrile (**8h**, CAS: 1653998-30-1)



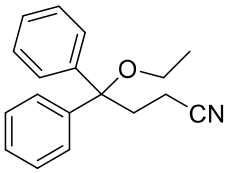
Following **the procedure C**, pale yellow solid (64.3 mg, 51%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.29 (m, 8H), 7.25–7.21 (m, 2H), 3.05 (s, 3H), 2.79–2.62 (m, 2H), 2.25–2.03 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.40, 128.32, 127.38, 126.76, 120.10, 81.46, 50.37, 31.34, 11.52.

HRMS (ESIpos) (m/z): calculated for $C_{17}H_{17}NO$ 252.1382; found 252.1381.

4-ethoxy-4,4-diphenylbutanenitrile (**8i**, CAS: 1808942-62-2)



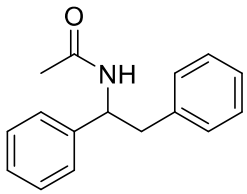
Following **the procedure C**, yellow oil (54.5 mg, 41%) .

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.28 (m, 8H), 7.25–7.21 (m, 2H), 3.15 (q, *J* = 6.9 Hz, 2H), 2.73–2.66 (m, 2H), 2.17–2.10 (m, 2H), 1.21 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.89, 128.27, 127.27, 126.64, 120.18, 81.01, 57.84, 32.02, 15.36, 11.59.

HRMS (ESIpos) (m/z): calculated for $C_{18}H_{20}NO$ 266.1539; found 266.1544.

N-(1,2-diphenylethyl)acetamide (**10a**, CAS: 21511-90-0)



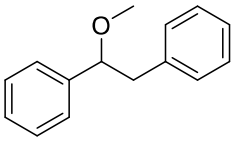
Following **the general procedure D**, white solid (118.3 mg, 99%).

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (d, *J* = 8.7 Hz, 1H), 7.41–7.34 (m, 4H), 7.33–7.20 (m, 6H), 5.08 (td, *J* = 8.6, 6.6 Hz, 1H), 3.07–2.87 (m, 2H), 1.82 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.73, 143.89, 139.19, 129.52, 128.61, 128.46, 127.17, 127.04, 126.53, 54.50, 42.75, 23.08.

HRMS (ESIpos) (m/z): calculated for $C_{16}H_{17}NO$ 240.1382; found 240.1386.

(1-methoxyethane-1,2-diyl)dibenzene (**10b**, CAS: 27820-29-7)



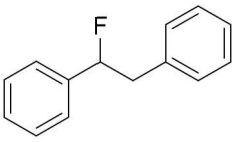
Following **the general procedure D**, colorless oil (33 mg, 31%) .

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (ddd, *J* = 8.8, 6.4, 0.9 Hz, 2H), 7.29–7.25 (m, 3H), 7.23 (dd, *J* = 7.9, 6.5 Hz, 2H), 7.20–7.10 (m, 3H), 4.40 (dd, *J* = 7.9, 5.7 Hz, 1H), 3.07 (s, 3H), 3.02 (dd, *J* = 13.8, 7.9 Hz, 1H), 2.85 (dd, *J* = 13.8, 5.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.01, 138.90, 129.78, 128.68, 128.39, 127.96, 127.19, 126.43, 84.32. 5650. 44.17.

HRMS (ESIpos) (m/z): $[M+Na]^+$ calculated for $C_{15}H_{16}ONa$ 235.1093; found 235.1094.

(1-fluoroethane-1,2-diyl)dibenzene (**10c**, CAS: 74185-77-6)



Colorless solid (26.0 mg, 25%)

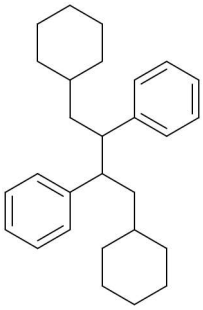
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.21 (m, 8H), 7.20–7.15 (m, 2H), 5.61 (ddd, *J* = 47.4, 8.1, 4.8 Hz, 1H), 3.27 (ddd, *J* = 17.5, 14.3, 8.1 Hz, 1H), 3.11 (ddd, *J* = 28.6, 14.3, 4.8 Hz, 1H).

^{19}F NMR (471 MHz, $CDCl_3$) δ -153.64 – -193.14 (m).

^{13}C NMR (125 MHz, $CDCl_3$) δ 129.53, 128.40, 128.38, 128.36, 126.70, 125.70, 125.65, 94.90 (d, *J* = 172.5 Hz, 1C), 43.96 (d, *J* = 23.8 Hz, 1C).

HRMS (ESIpos) (m/z): calculated for $C_{14}H_{13}F$ 200.0995; found 200.0995.

(1,4-dicyclohexylbutane-2,3-diyl)dibenzene (**9**, CAS: 644985-99-9)



Colorless solid (48.6 mg, 31%)

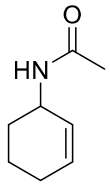
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, J = 7.5 Hz, 4H), 7.23–7.17 (m, 2H), 7.16–7.10 (m, 4H), 2.79–2.72 (m, 2H), 1.70 (d, J = 12.4 Hz, 2H), 1.52–1.39 (m, 7H), 1.31 (dtd, J = 12.9, 10.7, 10.1, 3.1 Hz, 4H), 1.08–1.03 (m, 2H), 0.98–0.93 (m, 5H), 0.76–0.66 (m, 4H), 0.51 (qd, J = 11.8, 3.7 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 145.02, 128.36, 128.12, 125.82, 49.37, 42.33, 34.58, 34.49, 31.69, 26.57, 26.16, 25.94.

HRMS (ESIpos) (m/z): calculated for $C_{28}H_{38}$ 374.2968; found 374.2964.

N-(cyclohex-2-en-1-yl)acetamide (**11a**, CAS: 39819-72-2)

Following **the general procedure E**, colorless solid (49.6 mg, 70%)

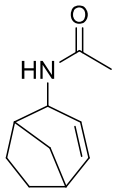


^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81–5.85 (m, 1H), 5.53–5.48(m, 1H), 4.45–4.39 (m, 1H), 1.96–1.90 (m, 2H), 1.90 (s, 3H), 1.89–1.79 (m, 1H), 1.61–1.53 (m, 2H), 1.49–1.40 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 169.16, 130.94, 127.64, 44.68, 29.43, 24.79, 23.51, 19.69.

HRMS (ESIpos) (m/z): calculated for $C_8H_{13}NO$ 140.1069; found 140.1068.

N-(bicyclo[3.2.1]oct-3-en-2-yl)acetamide (**11b**, CAS: 1823085-93-3)



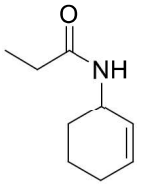
Following **the general procedure E**, colorless solid (59.4 mg, 72%)

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.05–5.99 (m, 1H), 5.47 (s, 1H), 5.27–5.22 (m, 1H), 4.06–4.02 (m, 1H), 2.42–2.33 (m, 2H), 1.90 (s, 3H), 1.83–1.81 (m, 1H), 1.60–1.53 (m, 2H), 1.44–1.22 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.64, 138.76, 123.26, 52.31, 38.50, 35.41, 32.19, 31.52, 26.63, 23.52.

HRMS (ESIpos) (m/z): calculated for $C_{10}H_{15}NO$ 165.1148; found 165.1149.

N-(cyclohex-2-en-1-yl)propionamide (**11c**, CAS: 95973-99-2)



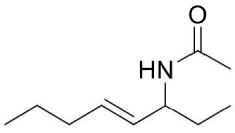
Following **the general procedure E**, colorless solid (25.2 mg, 33%)

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.81 (d, J = 8.0 Hz, 1H), 5.83–5.81 (m, 1H), 5.57–5.49 (m, 1H), 4.30–4.27 (m, 1H), 2.11 (q, J = 7.5, 3.5 Hz, 2H), 2.02–1.99 (m, 2H), 1.80–1.1.76 (m, 2H), 1.60–1.56 (m, 1H), 1.48–1.44 (m, 1H), 1.03 (t, J = 7.5 Hz, 1H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 172.57, 129.56, 129.35, 44.26, 29.48, 28.87, 24.86, 20.18, 10.45.

HRMS (ESIpos) (m/z): calculated for $C_9H_{15}NO$ 153.1148; found 153.1149.

(*E*)-*N*-(oct-4-en-3-yl)acetamide (**11d**, CAS: 2308508-60-1)



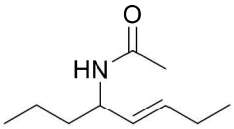
Following **the general procedure E**, colorless solid (41.4 mg, 49%)

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.78 (d, J = 10.8 Hz, 1H), 5.55–5.49 (m, 1H), 5.39–5.35 (m, 1H), 4.17–4.11 (m, 1H), 2.03–1.99 (m, 2H), 1.86 (s, 3H), 1.46–1.37 (m, 4H), 0.91 (t, J = 9.0 Hz, 3H), 0.86 (t, J = 9.0 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.61, 131.58, 130.09, 51.99, 34.19, 28.21, 23.17, 22.38, 13.94, 10.86.

HRMS (ESIpos) (m/z): calculated for $C_{10}H_{19}NO$ 169.1461; found 169.1461.

(*E*)-*N*-(oct-5-en-4-yl)acetamide (**11e**, CAS: 2308508-61-2)



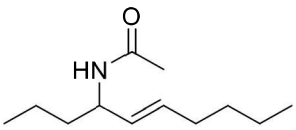
Following **the general procedure E**, colorless solid (33.8 mg, 40%)

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.77 (d, J = 10.2 Hz, 1H), 5.59–5.54 (m, 1H), 5.39–5.34 (m, 1H), 4.26–4.21 (m, 1H), 2.07–2.01 (m, 2H), 1.85 (s, 3H), 1.44–1.40 (m, 2H), 1.32–1.27 (m, 2H), 0.99 (t, J = 9.0 Hz, 3H), 0.90 (t, J = 8.4 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 168.52, 131.54, 130.70, 50.04, 37.48, 25.11, 23.17, 19.18, 14.19, 13.99.

HRMS (ESIpos) (m/z): calculated for $C_{10}H_{19}NO$ 169.1461; found 169.1461.

(*E*)-*N*-(dec-5-en-4-yl)acetamide (**11f**, unreported product)



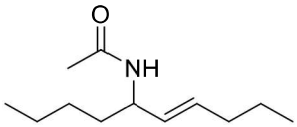
Following **the general procedure E**, colorless solid (36.4 mg, 37%)

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.71 (d, J = 6.0 Hz, 1H), 5.46–5.41 (m, 1H), 5.32–5.27 (m, 1H), 4.18–4.11 (m, 1H), 1.95–1.91 (m, 2H), 1.78 (s, 3H), 1.38–1.30 (m, 2H), 1.28–1.18 (m, 5H), 0.86–0.82 (m, 7H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 167.98, 131.17, 129.46, 49.56, 36.92, 31.18, 30.85, 22.62, 21.84, 18.61, 13.70, 13.64.

HRMS (ESIpos) (m/z): calculated for $C_{12}H_{23}NO$ 197.3172; found 197.3171.

(*E*)-*N*-(dec-6-en-5-yl)acetamide (**11g**, CAS: 131317-75-4)



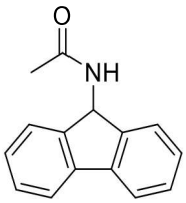
Following **the general procedure E**, colorless solid (36.4 mg, 37%)

^{1}H NMR (600 MHz, DMSO-d6) δ 7.71 (d, J = 6.0 Hz, 1H), 5.46–5.41 (m, 1H), 5.32–5.27 (m, 1H), 4.18–4.11 (m, 1H), 1.95–1.91 (m, 2H), 1.78 (s, 3H), 1.38–1.30 (m, 2H), 1.28–1.18 (m, 5H), 0.86–0.82 (m, 7H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 167.98, 131.40, 129.30, 49.87, 34.45, 33.62, 27.65, 22.62, 21.82, 21.48, 13.86, 13.38.

HRMS (ESIpos) (m/z): calculated for $C_{12}H_{23}NO$ 197.3172; found 197.3171.

N-(9*H*-fluoren-9-yl)acetamide (**13a**, CAS: 5424-77-1)



Colorless solid (78.1 mg, 70%)

^{1}H NMR (300 MHz, DMSO-d_6) δ 8.50 (d, J = 8.4 Hz, 1H), 7.92–7.89 (m, 2 H), 7.57–7.47 (m, 2H), 7.46–7.45 (m, 2H), 7.41–7.36 (m, 2H), 6.07 (d, J = 8.4 Hz, 1H), 2.0 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6) δ 170.07, 144.86, 139.95, 128.28, 127.54, 124.82, 120.05, 54.02, 22.53.

HRMS (ESIpos) (m/z): calculated for $C_{15}H_{13}NO$ 223.0989; found 223.0997.

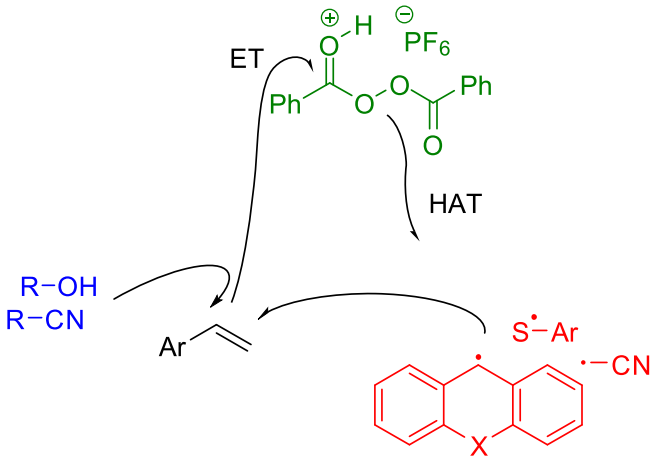
SUMMARY

Based on the importance and attractiveness of oxidative difunctionlization of alkenes in terms of atom efficiency and potential for greener chemistry, many efforts are now dedicated to the improvement of metal free, high efficiency, and environmental benign methods. This thesis is mainly dedicated to this task.

Acid Promoted Radical-Chain Difunctionalization of Styrenes with Stabilized Radicals and (N,O)-Nucleophiles

Base on previous reports, a novel metal free, acid promoted difunctionalization of alkenes was developed. This protocol provides a powerful method for difunctionlization of alkenes with different radicals and nucleophiles under transition metal free conditions.

Under the optimal reaction conditions, oxidative difunctionalization of alkenes with thioxanthene, xanthene and thiophenols radicals via hydrogen atom transfer, nitrile and alcohols as nucleophiles were successfully added to the carbon-carbon double bonds. Mechanistic studies including CV measurement, NMR calculations supported a radical chain mechanism, the acid does not accelerate the decomposition of BPO, but it changes the oxidation and reduction potential of BPO, which makes the BPO as a better electron acceptor.

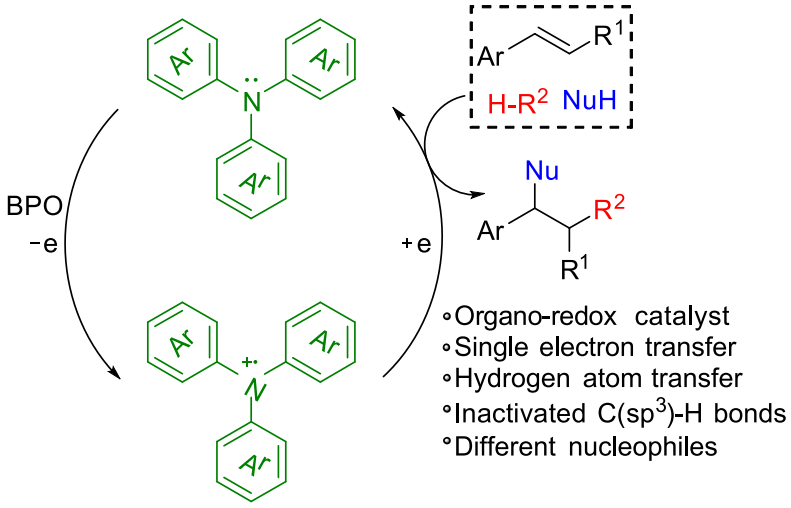


Acid promoted difunctionalization of alkenes

Organo-Redox-Catalysis for the difunctionalization of alkenes and oxidative Ritter reactions

We reported an organo-redox catalyst triaylamine in oxidative difunctionalization of alkenes. The triarylamine could be reduced into a radical cation salts by BPO, which turns into a good single electron oxidant. Oxidative difunctionalization of alkenes with a wide range of radicals, generated from C(sp^3)-H Hydrocarbon via hydrogen atom transfer, nitriles, alcohols, acetic acid and fluoride could be used as nucleophiles. Besides, this method could also be used into oxidative Ritter reaction of allylic and benzylic C-H bonds.

Mechanistic studies support the triarylamine is catalyst rather than radical initiator. The transformation does not need high temperature, irradiation, electrolysis, transition metals. This application of triarylamine might pave the way for further developments of organo-redox-catalysts, which may thus become another established class amongst organocatalysts.



Organo-Redox-Catalysis for the difunctionalization of alkenes and oxidative Ritter reactions

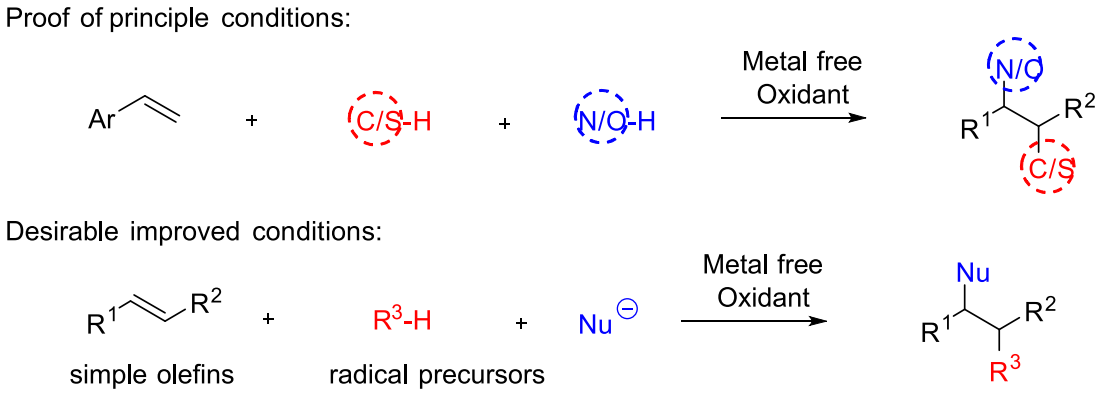
OUTLOOK

Acid promoted difunctionalization of alkenes

Tolerance of Substrate scope

Continuation of the search for other oxidants under mild reaction conditions to apply to radical and nucleophile difunctionalization of alkenes is expected to provide a valuable method.

In our initial exploration, we focused on peroxides as oxidants, especially BPO. However, peroxides are strong oxidants and very dangerous due to its explosion. Besides, BPO can react with other nucleophiles easily, which limited the scope of other nucleophiles. Moreover, the substrate scope of radicals is extremely correlated with the peroxides. Thus, find other reaction conditions suit for oxidative radical and nucleophile difunctionalization of olefins under transition metal free conditions are significate progress for chemists.



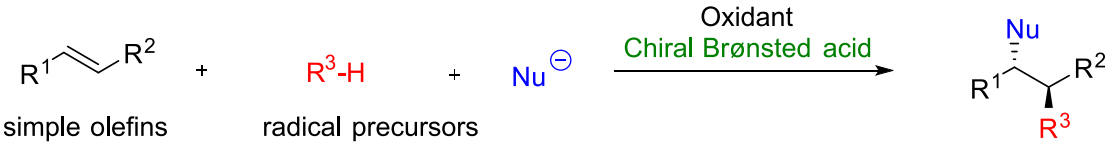
radical precursors. C-centered, N-centered, O-centered, P-centered, Si-centered...
Nu: amine, indole, acid...

Outlook for substrate scope

Another continuation of search is the olefins. Most reported methods are based on styrene and its derivatives. However, simple olefins are less reported due to its lower reactivity. Oxidative radical difunctionalization of simple olefins is more challengeable, spurring our effort for further studies.

Chiral Brønsted acid catalysis approach

One particularly attractive feature of the conditions discussed in this work in the use of the strong Brønsted acid. The products contain two chiral center, by using of chiral Brønsted acid instead of HPF_6, might provide an approach to access enantioenriched radical and nucleophile difunctionalizd products.



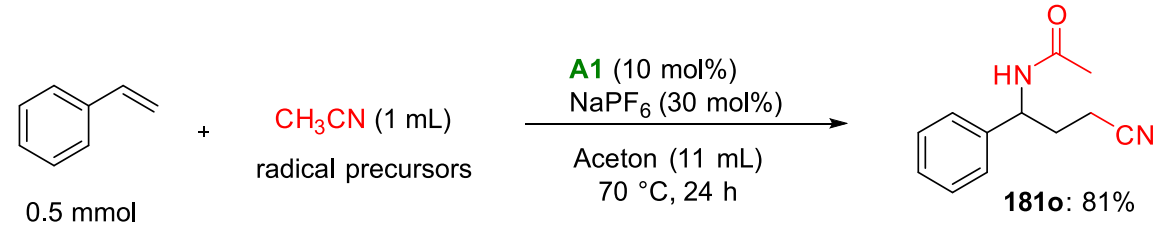
radical precursors. C-centered, N-centered, O-centered, P-centered, Si-centered...
Nu: amine, indole, acid...

Asymmetric synthesis of oxidative radical and nucleophile mediated difunctionalization of olefins

Organo-Redox-Catalysis for the difunctionalization of alkenes and oxidative Ritter reactions

Tolerance of Substrate scope

In this part, radical precursors, such as cyclohexane, chloroform or acetonitrile need to be used not only as hydrogen donor sources, but also as solvents. This limitation restricts the substrate scope of radical precursors. Find a method for dealing with this limitation is significant problem for chemists. We did initially researches about it. By using acetone as solvent, we can reduce the use of acetonitrile into 1 mL, giving the product **181o** in 81% yield. This result indicated that there is possibility to reduce the amount of the hydrogen donor source.



R^3-H, radical precursors. C-centered, N-centered, O-centered, P-centered, Si-centered...

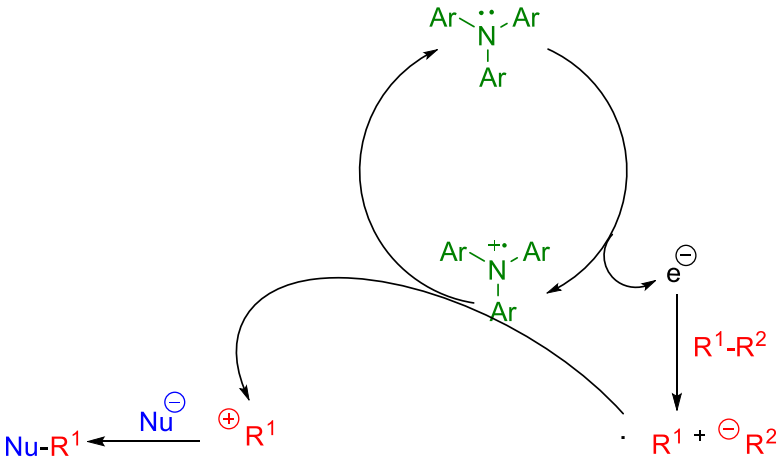
The proposed method for substrate scope of radical precursors

Other organic redox reactions catalyzed by triarylamine

In this thesis, the triarylamine showed a good ability in the using of organic redox reactions. So far, we could only achieve oxidative radical and nucleophile mediated difunctionalization of alkenes and Ritter reaction of allylic and benzylic C-H bond. In our report, triarylamine should react with BPO in the first step to form the radical cation, a strong one-electron oxidant, which can regenerate the triarylamine by electron transfer and deliver the carbocation. Thus, finding more combination system of oxidant and triarylamine may open a new area of organic-redox catalysts in organic synthesis methodology.

There are several literatures reported the triarylamine as catalyst under electro-chemistry conditions.[124-125] The combination of electrochemistry and redox catalysis using an organic catalyst allows the electro synthesis to proceed under transition metal- and oxidizing reagent free

conditions, which providing an efficient and straightforward access to difunctionalization of olefins with a broad substrate scope and other functional groups.



Use of triarylamine in other organic redox reactions

APPENDIX

Erklärung

„Hiermit versichere ich an Eides statt, dass ich die vorliegende Dissertation selbstständig und ohne die Benutzung anderer als der angegebenen Hilfsmittel und Literatur angefertigt habe. Alle Stellen, die wörtlich oder sinngemäß aus veröffentlichten und nicht veröffentlichten Werken dem Wortlaut oder dem Sinn nach entnommen wurden, sind als solche kenntlich gemacht. Ich versichere an Eides statt, dass diese Dissertation noch keiner anderen Fakultät oder Universität zur Prüfung vorgelegen hat; dass sie - abgesehen von unten angegebenen Teilpublikationen und eingebundenen Artikeln und Manuskripten - noch nicht veröffentlicht worden ist sowie, dass ich eine Veröffentlichung der Dissertation vor Abschluss der Promotion nicht ohne Genehmigung des Promotionsausschusses vornehmen werde. Die Bestimmungen dieser Ordnung sind mir bekannt. Darüber hinaus erkläre ich hiermit, dass ich die Ordnung zur Sicherung guter wissenschaftlicher Praxis und zum Umgang mit wissenschaftlichem Fehlverhalten der Universität zu Köln gelesen und sie bei der Durchführung der Dissertation zugrundeliegenden Arbeiten und der schriftlich verfassten Dissertation beachtet habe und verpflichte mich hiermit, die dort genannten Vorgaben bei allen wissenschaftlichen Tätigkeiten zu beachten und umzusetzen. Ich versichere, dass die eingereichte elektronische Fassung der eingereichten Druckfassung vollständig entspricht.

Mülheim an der Ruhr, June 2021.

Lebenslauf

Sensheng Liu

Geboren am 07. Oktober 1991
In Ningxia, China
Staatsangehörigkeit: Chinese

Akademischer Werdegang

10/2018–10/2021	**Promotion** am Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr unter der Anleitung Von PD. Dr. Martin Klußmann, Prof. Dr. Benjamin List und Prof. Dr. Hans-Günther Schmalz zum Thema: *Difunctionalization of Olefins by Radicals and Nucleophiles.*
09/2015–06/2018	**Master** der Chemie, Sanxia University in Hubei (China) unter der Anleitung Von Prof. Dr. Haifeng Zhou zum Thema: *Asymmetric Synthesis of Chiral Secondary Alcohols Catalyzed by Chiral Diamine Ruthenium Complexes.*
09/2014–06/2018	**Licence** der Chemie und Biologisch, Sanxia University in Hubei (China) unter der Anleitung Von Prof. Dr. Haifeng Zhou zum Thema: *Iron-Catalyzed Green Synthesis of 2-Alkenylazaarenes.*

Schlbilding

Statement

Herein, I declare that:

The dissertation has been accepted by the *Faculty of Mathematics and Natural Sciences* of the University of Cologne and the disputation took place in 22-07-2021.