Asymmetric Catalysis with Octahedral Chiral-at-Metal Iridium and Rhodium Complexes

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Publications


Abstract

This thesis details the applications of a class of chiral-at-metal iridium(III) and rhodium(III) complexes for asymmetric catalysis.

A rhodium-based asymmetric catalyst $\Delta$-RhO is introduced which derives its optical activity from octahedral centrochirality. Besides serving as the exclusive source of chirality, the rhodium center functions as a Lewis acid to activate $\alpha,\beta$-unsaturated 2-acyl imidazoles by two point binding and thereby catalyzes the asymmetric Michael addition of CH-acidic $\beta$-dicarbonyl compounds, for which the rhodium catalyst is found to be superior to its iridium congener (chapter 3.1). Due to its straightforward proline-mediated synthesis, high catalytic activity, and tolerance towards moisture and air, this chiral-at-rhodium complex has been used as chiral Lewis acid catalyst for many other asymmetric transformations in the Meggers group.

The chiral-at-metal complexes $\Delta$-IrO and $\Delta$-IrS are investigated as highly efficient dual function photoredox/chiral Lewis acid catalysts in asymmetric photoactivated reactions. A simple chiral iridium complex $\Delta$-IrO is capable of catalyzing the visible light activated $\alpha$-aminoalkylation of 2-acyl-1-phenyl imidazoles, thereby serving as a “2-in-1” catalyst by combining photoinduced oxidation with asymmetric alkylation (chapter 3.2). Moreover, its derivative $\Delta$-IrS is successfully utilized to the catalytic enantio- and diastereoselective redox coupling of trifluoromethyl ketones with tertiary amines to form 1,2-diamino alcohols (chapter 3.3). This single catalyst strategy provides new avenues for the synthesis of non-racemic molecules.

An alternative strategy of merging the chiral Lewis acid $\Delta$-RhS with photoredox catalyst $\text{fac-[Ir(ppy)$_3$]}]$ is well applied to the asymmetric photoredox-mediated C(sp$^3$)-H functionalization. This synthetic strategy exploits a radical translocation ($1,5$-hydrogen transfer) from an oxygen-centered to a carbon-centered radical with a subsequent stereocontrolled radical addition, affording C-C bond formation products with high enantioselectivities (up to 97% ee). Notably, the previously developed dual function catalyst $\Delta$-IrS is not applicable for this asymmetric transformation (chapter 3.4).
Zusammenfassung

In der vorliegenden Dissertation wird die Anwendung neuer Iridium(III)- und Rhodium(III)-Komplexe mit metallzentrierter Chiralität in der asymmetrischen Katalyse erläutert.


Weitere Untersuchungen hinsichtlich der Eignung von Δ-IrO und Δ-IrS als bifunktionelle Photoredox/LEWIS-Säure Katalysatoren in asymmetrischen, durch Licht aktivierte Reaktionen, wurden in den folgenden Projekten durchgeführt. Der einfach gehaltene chirale Iridium(III)-Komplex Δ-IrO ist in der Lage, die durch sichtbares Licht aktivierte α-Aminoalkylierung von 2-Acyl-1-phenylimidazol zu katalysieren. Dabei fungiert Δ-IrO als "2-in-1"-Katalysator durch die Kombination von photoinduzierter Oxidation und asymmetrischer Alkylierung (Kapitel 3.2). Des Weiteren wurde das Derivat Δ-IrS erfolgreich für die enantio- und diastereoselektive Redox-Kupplung von Trifluormethylketonen mit tertiären Aminen zur Synthese von 1,2-Diaminoalkoholen eingesetzt (Kapitel 3.3). Die gezeigte Strategie, einen einzelnen multifunktionellen Katalysator zu verwenden, ebnet neue Wege zur Synthese nicht-racemischer Verbindungen.

Als alternative konnte der chirale LEWIS-Säure-Katalysator Δ-RhS mit dem Photoredox-Katalysator fac-[Ir(ppy)3] in der asymmetrischen, photoredox-vermittelten C(sp3)-H Funktionalisierung eingesetzt werden. In dieser Strategie wird eine 1,5-Wasserstoff-Verschiebung genutzt, um ein Sauerstoffradikal in ein Kohlenstoffradikal zu überführen, welches unter katalysatorkontrollierter C-C-Bindungsknüpfung
Produkte mit hohem Enantiomerenüberschuss erzeugt (bis zu 97% ee). Beachtenswert ist, dass der analoge bifunktionelle Iridiumkomplex Δ-IrS nicht für diese Reaktion geeignet ist (Kapitel 3.4).
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Chapter 1: Theoretical Part

1.1 Introduction

Asymmetric catalysis is a fundamental methodology in modern chemistry and is particularly important in the field of pharmaceuticals, as the different enantiomers or diastereomers of a molecule often have different biological activity.\(^1\) Thalidomide is a striking example that illustrates the difference in which the \((R)\)-enantiomer acts as a sedative in contrast to deformities caused by the \((S)\)-enantiomer (Figure 1).\(^2\) Therefore, the asymmetric synthesis of enantiomerically pure compounds is under intense scrutiny.

![Figure 1 Structures of \((R)\)-thalidomide and \((S)\)-thalidomide.](image)

Photocatalysis has seen growing interest not only in the reactions of small molecules such as \(\text{H}_2\text{O}\) (water splitting)\(^3\) and \(\text{CO}_2\) (forming solar fuels)\(^4\), but also in organic synthesis.\(^5\) Particularly, the recent progress in this area has been promoted by using visible light as a driving force, providing a number of otherwise unachievable modes of molecular transformations.\(^6\)

Combining these two aspects, visible light induced asymmetric photocatalysis is appreciated as a powerful tool to achieve high efficiency and selectivity in asymmetric synthesis.\(^7\) Whereas asymmetric catalysis is considered as an economic strategy to obtain enantiopure compounds, visible light can assist in generating highly reactive intermediates under mild conditions and at the same time providing an environmentally friendly and sustainable source of energy for activating chemical reactions.

This chapter will be divided into two parts: 1) summarize some typical examples of asymmetric catalysis with octahedral chiral only-at-metal complexes; 2) discuss two systems of visible light
activated asymmetric catalysis, namely dual catalyst systems based on the combined use of photoredox with chiral catalyst or single chiral catalyst systems.

1.2 Asymmetric Catalysis with Octahedral Chiral only-at-Metal Complexes

A crucial role in asymmetric catalysis is the development of efficient chiral catalysts. Octahedral chiral only-at-metal complexes are an emerging class of catalysts for catalytic asymmetric synthesis of non-racemic compounds. For the developed octahedral chiral only-at-metal complexes, the central transition metal always serves as a structural anchorpoint and provides metal centrochirality, catalysis is mediated through the ligand sphere, thereby merging organocatalysis with transition metal catalysis.

1.2.1 Octahedral Chiral only-at-Metal Ruthenium(II) and Cobalt(III) Complexes for Asymmetric Catalysis

In 2003, the Fontecave group reported asymmetric oxidation of sulfide with an octahedral ruthenium(II) complex Λ-Ru1 in which the ruthenium ion is coordinated by two 2,9-dimethyl-1,10-phenanthroline ligands and two labile acetonitrile molecules (Figure 2). Despite the low enantioselectivity obtained (18% ee), this study reveals the first experimental validation of the concept that an octahedral chiral only-at-metal complex has the potential to catalyze enantioselective oxidations. Later, they reported asymmetric transfer hydrogenation with a dinuclear ruthenium catalyst Λ-Ru2, in which the Λ-[Ru(2,2'-bipyridine)2(2,2'-bipyrimidine)]2+ moiety serves as a chiral bidentate ligand for a second, catalytically active ruthenium complex. The low enantioselective (26% ee) can be rationalized by the large distance between the chiral and catalytic centers.

![Figure 2 Asymmetric catalysis by octahedral chiral-at-metal ruthenium(II) complexes.](image-url)
In 2008, Gladysz and co-workers demonstrated asymmetric conjugate addition with a simple octahedral chiral-at-metal Werner complex. As shown in Figure 3, the enantiopure chiral-at-metal cobalt(III) complex \( \Delta \text{-Co} \) is capable of catalyzing the Michael addition of dimethyl malonate to cyclopentenone in \( \text{CH}_2\text{Cl}_2 \) to afford the adduct in 78% yield, albeit with a low enantioselectivity of just 33\% \text{ee}. The chirality induction in this reaction relies on the stereogenic octahedral cobalt center and N-H bonds (H-bonding donors).

\[
\text{Figure 3 Asymmetric Michael addition by a chiral-at-metal Werner complex.}
\]

1.2.2 Octahedral Chiral only-at-Metal Iridium(III) Complexes for Asymmetric Catalysis

For the past several years, the Meggers group has successfully designed and synthesized a series of octahedral chiral-at-metal iridium(III) complexes for asymmetric catalysis.

In 2013, the Meggers group reported a chiral-at-metal iridium(III) complex \( \Lambda \text{-Ir1} \) for the highly efficient catalytic asymmetric transfer hydrogenation of \( \beta,\beta \)-disubstituted nitroalkenes (Figure 4). The design of the substitutionally inert biscyclometalated iridium complex \( \Lambda \text{-Ir1} \) was inspired by the non-covalent organocatalyst thiourea. While the pyrazole moiety acts as a double H-bonding donor for the nitroalkene, a hydroxy group serves as a H-bonding acceptor for the Hantzsch ester (Figure 5). Notably, although the iridium complex relies only on the formation of three hydrogen bonds, it exceeds the performance of most organocatalysts with respect to enantioselectivities (up to 99\% \text{ee}) and catalyst loadings (down to 0.1 mol\%). This work is of great significance as it reveals the potential of octahedral metal complexes as chiral scaffolds for the design of high-performance asymmetric catalysts.
Chapter 1: Theoretical Part

Figure 4 Asymmetric transfer hydrogenation catalyzed by a chiral-metal iridium(III) complex.

![Asymmetric transfer hydrogenation catalyzed by a chiral-metal iridium(III) complex.](image)

Figure 5 Proposed transition state of Λ-Ir1 in asymmetric transfer hydrogenation.

![Proposed transition state](image)

This non-covalent metal-templated complex was further applied to a more challenging transformation, namely enantioselective Friedel-Crafts alkylation of indoles to β,β-disubstituted nitroolefins. By using 1 mol% of Λ-Ir2, all-carbon quaternary centers can be created in high enantioselectivities of up to 98% ee (Figure 6). Since the iridium catalyst functions completely as a H-bonding catalyst, the high reactivity and enantioselectivity of Λ-Ir2 are superior to the performance of Λ-Ir1 (70% ee with 5 mol% catalyst loading) which can be rationalized by the H-bonding affinity of the carboxamide (-CONEt2, Λ-Ir2) over the hydroxyl group (-OH, Λ-Ir1) in combination with the preferred conformation of the amide group, thereby placing the amide oxygen in an ideal position for H-bonding with the indole nucleophile. Notably, tested thiourea organocatalysts only provided very low enantioselectivities for this challenging formation.14

Figure 6 Asymmetric Friedel-Crafts alkylation catalyzed by a chiral-at-metal iridium(III) complex.

![Asymmetric Friedel-Crafts alkylation catalyzed by a chiral-at-metal iridium(III) complex.](image)
Inert octahedral metal complexes are general, powerful templates for the efficient design of bifunctional catalysts. The developed octahedral 3-aminopyrazolato iridium(III) complexes $\Lambda$-Ir$^3$ and $\Lambda$-Ir$^4$ as chiral Brønsted base catalysts are suitable for highly effective asymmetric sulfa-Michael addition and aza-Henry reactions, permitting catalyst loadings down to 0.02 and 0.25 mol%, respectively (Figure 7). The observed high reactivity and stereoselectivity can be rationalized by the bifunctional mode of action in which the iridium catalyst, after the initial proton transfer, controls a ternary complex through defined H-bonding interactions (Figure 8).\textsuperscript{15}

![Figure 7](image1.png) Asymmetric sulfa-Michael and aza-Henry reactions catalyzed by chiral Brønsted base catalysts.

![Figure 8](image2.png) Proposed ternary complex for the asymmetric sulfa-Michael addition catalyzed by $\Lambda$-Ir$^3$.

Asymmetric enamine/H-bonding dual activation catalyst is presented as another successful example for the power for a metal-templated design of “organocatalyst” (Figure 9). An octahedral chiral-atom metal complex $\Lambda$-Ir$^5$ catalyzes the enantioselective $\alpha$-amination of aldehydes with high enantioselectivities of up to 97% ee and catalyst loadings down to 0.1 mol%. Mechanistically, this highly efficient chiral iridium complex can be rationalized by a dual activation catalysis which converts the aldehyde into a nucleophilic enamine, while at the same time activating the azodicarboxylate electrophile through H-bonding with one OH-group (Figure 10).\textsuperscript{16} Notably, $\Lambda$-Ir$^5$ constitutes one of the most efficient catalysts for the enantioselective $\alpha$-amination of aldehydes to date.
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Figure 9: Asymmetric catalysis by enamine/H-bonding dual activation chiral-at-metal Iridium(III) catalyst.

Figure 10: Proposed enamine/H-bonding mechanism model of the asymmetric α-amination catalyzed by iridium complex Λ-Ir5.

Having demonstrated several remarkable asymmetric transformations directed by the ligand sphere of the stereogenic iridium center, the Meggers group further modified the metal-templated system to Lewis acid catalysts. In 2014, the Meggers group introduced a substitutionally labile chiral-at-metal iridium(III) complex Λ-IrO. As shown in Figure 11, the catalytic activity investigation demonstrated that the chiral complex Λ-IrO can effectively catalyze the enantioselective Friedel-Crafts addition of indoles to α,β-unsaturated 2-acyl imidazoles with high yields (75-99%) and excellent enantioselectivities (90-98% ee) at low catalyst loadings (0.25-2 mol%).

Figure 11: Asymmetric Friedel-Crafts reaction by a simple chiral-at-metal Lewis acid catalyst.

The iridium complex Λ-IrO serves as a chiral Lewis acid by activating α,β-unsaturated 2-acyl imidazoles through bidentate N,O-coordination. Despite its substitutional lability, the metal-centered chirality is maintained throughout the catalysis. A proposed model for the asymmetric induction in the
course of the indole addition by using Λ-IrO as catalyst is shown in Figure 12 and demonstrates that Re face of the alkene is sterically shielded effectively by one tert-butyl group, and the Si face is leaving open for the approach of nucleophile. This novel class of reactive chiral-at-metal complexes has been proven to be of high value for a variety of asymmetric transformations in the Meggers group.\textsuperscript{18}

**Figure 12** Proposed reaction model of enantioselective Friedel-Crafts addition with Λ-IrO.
1.3 Asymmetric Photocatalysis Activated by Visible Light

In homogeneous photocatalysis, photoredox catalysis employs small quantities of a light-sensitive compound (photocatalyst) that, when excited by light, can mediate the transfer of electron or energy between chemical compounds.\(^\text{18}\) Desired features of common photocatalysts are as follows: 1) photostability; 2) long excited-state lifetime; 3) strong absorption in the visible region; 4) high reduction or oxidation potential to achieve electron transfer to substrates. Alongside organic dyes and inorganic semiconductors, the most widely-applied and effective photocatalysts are coordinatively saturated transition-metal-pyridyl complexes which are outlined in Figure 13.\(^\text{19}\)

![Figure 13](image)

The common classic transition metal photocatalysts (\textit{vs.} SCE).

1.3.1 Dual Catalyst Systems in Asymmetric Photoredox Catalysis

The combination of visible light redox catalysts with chiral catalysts has enabled a number of highly enantioselective photoinduced reactions. The following section summarized some representative catalytic asymmetric transformations utilizing dual photoredox organocatalysis or transition-metal catalysis.

1) Dual photoredox organocatalysis: covalent interactions

In 2008, MacMillan’s group reported the first example of the combination of visible light induced photoredox catalysis and asymmetric organocatalysis.\(^\text{20}\) Accordingly, the reaction of aldehydes with bromo diethylmalonates or phenacyl bromides in the presence of [Ru(bpy)\(_3\)]Cl\(_2\), chiral imidazolidinone and 15 W compact fluorescent lamp (CFL) afforded \(\alpha\)-alkylation products with highly enantioselectivities of up to 99\% \textit{ee} (Figure 14). The generality of this dual photoredox organocatalytic protocol was demonstrated by further investigating the enantioselective \(\alpha\)-trifluoromethylation\(^\text{21}\) and \(\alpha\)-benzylolation of aldehydes.\(^\text{22}\)
A mechanism for this transformation combining an enamine catalytic cycle and a photoredox catalytic cycle is shown in Figure 14. It is generally accepted that a photoredox catalytic cycle results in the reductive, heterolytic cleavage of the benzyl bromide or phenacyl bromide to afford electron deficient carbon radical which rapidly added to the electron rich double bond of chiral intermediate enamine in a stereocontrolled fashion. The generated α-aminoalkyl radical is oxidized to iminium ion via single electron transfer (SET). The iminium ion intermediate is further hydrolyzed to form the α-alkylation product, and thereby regenerate the amine catalyst for a new catalytic cycle. It is most likely that product-forming step would be chain-propagating reduction of the alkyl electrophile substrates by the intermediate α-amino radical.\textsuperscript{23}

![Figure 14 Enantioselective α-functionalization of aldehydes via dual photoredox enamine catalysis.]

Following MacMillan’s initial work, several other research groups have merged enamine catalysis with photocatalysis. For example, Zeiter, König, and Pericàs revealed that transition metal photocatalysts could be replaced by organic dyes and inorganic semiconductors in this asymmetric photoredox enamine catalysis system.\textsuperscript{24} Luo and co-workers extended this strategy and applied to the enantioselective α-alkylation of β-ketocarbonyls by merging photoredox catalysis with chiral primary amine catalysis (Figure 15).\textsuperscript{25} The reactions enable the creation of all-carbon stereocenters with excellent enantioselectivities (up to 99% ee) and a broad substrate scope (28 examples). The author proposed that
the high asymmetric induction can be rationalized by a hydrogen bond in the transition state between the protonated tertiary amine (N-H as hydrogen bond donor) of the intermediate enamine and the intermediate phenacyl radical (C=O as hydrogen bond accepter).

Figure 15 Asymmetric α-photoalkylation of β-ketocarbonyls with a combination of chiral primary amine and photoredox catalyst.

Recently, Melchiorre and co-workers reported an excellent work about the enantioselective radical conjugate addition to β,β-disubstituted cyclic enones driven by UV light (365 nm) or visible light. The outlined visible light activated iminium dual catalysis platform enables challenging quaternary carbon stereocenters to be constructed in a highly enantioselective manner (Figure 16). The critical to their success is the design of a chiral organic catalyst, containing a redox-active carbazole moiety, which drives the formation of iminium ion intermediates and the stereoselective trapping of photogenerated carbon-centred radicals. The key step in the catalytic transformation is the rapid intramolecular electron transfer between the electron-rich carbazole and the α-iminyl radical cation, thereby forging the corresponding enamine and avoiding the undesired β-scission event.

Figure 16 Asymmetric radical conjugate addition by photoredox iminium dual catalysis.
In 2012, the Rovis group identified a productive dual catalysis mode which enables the catalytic asymmetric α-acylation of tertiary amines.\textsuperscript{27} Through the powerful combination of chiral N-heterocyclic carbene (NHC) catalyst and photoredox catalyst [Ru(bpy)\textsubscript{3}]Cl\textsubscript{2}, the α-acylation products could be produced in high yields (up to 94\% yield) with high enantioselectivities (up to 92\% ee). Mechanistically, single-electron oxidation of a tertiary amine followed by hydrogen atom abstraction results in the formation of iminium ion. Meanwhile, interaction of a chiral NHC catalyst with an aldehyde generates the nucleophilic Breslow-type complex. The chiral Breslow intermediate intercepts the newly formed iminium ion, thereby forming the non-racemic α-amino ketone product. The stoichiometric amount of oxidant \textit{m}-dinitrobenzene (\textit{m}-DNB) are needed for this asymmetric transformation (Figure 17).

![Asymmetric α-acylation of tertiary amines by photoredox carbene dual catalysis.](image)

**Figure 17** Asymmetric α-acylation of tertiary amines by photoredox carbene dual catalysis.

2) Dual photoredox organocatalysis: noncovalent interactions

In 2013, the Knowles group reported a photoinduced proton-coupled electron transfer (PCET) protocol for the asymmetric reductive coupling of ketones and hydrazones.\textsuperscript{28} Accordingly, the exposure of \textit{ε}-hydrazino arylketones to blue light in the presence of [Ir(ppy)\textsubscript{2}(dtbbpy)]PF\textsubscript{6}, the chiral phosphoric acid, and Hantzsch ester (HE) provided the \textit{syn} 1,2-amino alcohols with 45-96\% yield and 77-95\% ee (Figure 18). Mechanistically, photoactivated [Ir\textsuperscript{III}]\textsuperscript{*} accepts an electron from Hantzsch ester to generate [Ir\textsuperscript{III}]\textsuperscript{−}. The phosphoric acid forms a H-bonding with the aryl ketone, followed by an electron transfer...
from the $\text{[Ir}^{III}]^- \text{to the aryl ketone in concert with proton transfer from the Brønsted acid to the oxygen of the formed ketyl radical. The enantioselective radical cyclization is based on the H-bonding between the chiral phosphate anion and the OH-group of the ketyl. Hantzsch ester acts as a terminal reduction agent in the catalytic cycle.}

### Figure 18
Enantioselective aza-pinacol cyclizations by a chiral phosphoric acid catalyst and a photoredox catalyst.

In 2014, Stephenson and Jacobsen reported a sequential two-step asymmetric Mukaiyama Mannich reaction. With the employment of a chiral thiourea H-bonding catalyst combined with a photoredox catalyst $\text{[Ru(bpy)}_3\text{Cl}_2$ under the irradiation of blue LEDs, single-electron oxidation of $N$-aryl tetrahydroisoquinolines followed by nucleophilic addition with silyl enol ethers afforded $\alpha$-alkylated products in 11-72% yields and 42-99% $ee$ (Figure 19). In the first step, 1-chlorinated products are generated from 1,2,3,4-tetrahydroisoquinolines by photooxidation with stoichiometric oxidant carbon tetrachloride. In the second step, the addition of the chiral thiourea results in the formation of an intermediate contact ion pair (a H-bonded chloride anion and the iminium ion), which enantioselectively reacts with the silyl enol ether to provide the non-racemic compounds with moderate to high enantioselectivities.
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Figure 19 Asymmetric $\alpha$-acylation of tertiary amines by photoredox hydrogen bonding dual catalysis.

Recently, the Ooi group developed a redox neutral, highly enantioselective $\alpha$-coupling of $N$-arylaminomethanes with $N$-sulfonyl imines under visible light irradiation. By using chiral arylaminophosphonium ion and iridium complex $[\text{Ir}(ppy)_{2}(\text{Me}_{2}\text{Phen})]\text{BAR}$ ($\text{Ar} = 3,5-(\text{CF}_{3})_{2}\text{C}_{6}\text{H}_{3}$) as co-catalyst, the coupling products were achieved with 60-90% yields and 85-98% ee. In their proposed mechanism (Figure 20), photoexcited iridium catalyst is reductively quenched by $N$-arylamine. The thereby generated $[\text{Ir}^{II}]$ serves as a strong reducing agent and transfers a single electron to imine under formation of a prochiral radical anion. The chiral aminophosphonium ion (H-bonding donor) undergoes counterion exchange with the prochiral radical anion to form a chiral ion pair, thereby reacting with deprotonated $\alpha$-aminoalkyl radical to afford the coupling product. The critical success factor is that chiral ion controls the enantiofacial approach of the oxidatively generated $\alpha$-aminoalkyl radical.

Figure 20 Enantioselective radical coupling reaction with chiral arylaminophosphonium ion catalyst and iridium photoredox catalyst.
3) Dual photoredox transition-metal catalysis: Lewis acid catalyst

In 2014, the Yoon group developed a dual catalysis strategy in asymmetric [2+2] photocycloadditions of α,β-unsaturated ketones to the corresponding cyclobutanes.\(^{31}\) Employing 1 mol% of \([\text{Ru(bpy)}_3]\)Cl\(_2\) and 10 mol% Eu(OTf)\(_3\) with 20 mol% of dipeptide-derived chiral ligand led to form the 1,2-trans-cycloadducts with high enantioselectivities of up to 97% ee. Interestingly, by simply switching to saturated dipeptide ligand, the 1,2-cis-cycloadducts were generated as the major products (Figure 21). Mechanistically, the crucial step is the single-electron reduction of a chiral Lewis acid coordinated aryl enone to generated radical anion. The intermediate radical anion can react with another Michael acceptor to form a chiral Lewis acid mediated radical which subsequently undergoes intermolecular cyclization.

In this protocol, the requirement of the Lewis acid catalyst for both reactivity and stereoselectivity prevents undesired background reaction. And recently, the author extended this strategy for the asymmetric [3+2] photocycloaddition of aryl cyclopropyl ketones, which enables the enantiocontrolled construction of densely substituted cyclopentane structures not synthetically accessible using other catalytic methods.\(^{32}\)

![Figure 21](image_url)

**Figure 21** Enantioselective [2+2] photocycloadditions with a photoredox catalyst and a stereocontrolling Lewis acid.

The principle of cooperative Lewis acid-photoredox catalysis was further applied to the asymmetric Giese addition of photogenerated α-amino radicals to Michael acceptors by Yoon’s group.\(^{33}\) Chiral pybox ligand and relay auxiliary are two key points for achieving the radical addition products with high
levels of enantiocontrol (up to 96% ee). Notably, the Lewis acid here is not directly involved in the photoinduced electron transfer step. Rather, the chiral Lewis acids control the rate and selectivity of a step independent of the photoredox process itself (Figure 22).

![Figure 22 Enantioselective radical addition with cooperative Lewis acid-photoredox catalysis.](image)

4) Dual photoredox transition-metal catalysis: Nickel catalyst

In 2016, MacMillan and Fu performed an elegant work of the enantioselective decarboxylative C(sp^3)-C(sp^2) cross-coupling reaction of α-amino acids with aryl halides by interfacing photoredox and nickel catalysis.\(^3\)\(^4\) This method is very practical and useful because non-racemic benzylic amine products can be formed by using low-cost α-amino acids as radical precursors (Figure 23). Mechanistically, photocatalyst-mediated oxidation and decarboxylation of an α-amino acid produce a prochiral α-amino radical. Meanwhile, activation of an aryl halide via oxidative addition lead to a chiral Ni(II)-aryl complex, which intercept the newly generated α-amino radical. The resulting diorganonickel(III) adduct then undergoes reductive elimination to achieve the C-C bond formation. The presence of a chiral ligand induces enantioselectivity and the last reductive elimination of diorganonickel(III) intermediate is proposed as the stereocontrol step.

![Figure 23 Enantioselective C(sp^3)-C(sp^2) cross-coupling reaction by interfacing photoredox and nickel catalysis.](image)
1.3.2 Single Catalyst Systems in Asymmetric Photoredox Catalysis

1) Organocatalysis with electron donor-acceptor (EDA) complex

Melchiorre’s group demonstrated that the synthetic potential of chiral enamines is not limited to the ground-state domain (enamines as nucleophiles or SOMO activation), but can be further expanded by exploiting their photochemical activity. In 2013, Melchiorre and co-workers reported visible light induced asymmetric α-alkylation of aldehydes with electron deficient benzyl bromides and phenacyl bromides in the presence of the chiral secondary amine (Figure 24, pathway a). Although the compounds used in the reaction system do not contain any photoactive unit, they guide the photoactivation of the substrate by inducing the in-situ formed chiral electron donor-acceptor (EDA) complex. The EDA complex is able to absorb visible light and triggers a single electron transfer (SET) from the enamine to the organobromide substrate. In addition, quantum yield measurements established that a radical chain propagation mechanism is operative.

Interestingly, the recent mechanistic studies from the Melchiorre group show another radical initiation pathway (Figure 24, pathway b) that the chiral enamine can directly reach an electronically excited state upon light absorption and then act as an effective photoinitiator to induce carbon-centered radical formation by reduction of the bromomalonate through SET process.

Figure 24 Visible light induced asymmetric α-alkylation of aldehydes via radical initiation step and chain process.
2) Organocatalysis with hydrogen bonding catalyst

The Bach group recently reported an organocatalyst for enantioselective intramolecular [2+2]-photocycloaddition reactions induced by visible light.\textsuperscript{36} By using the enantiopure thioxanthone as single catalyst, the intramolecular cycloaddition products were achieved with good yields (79-95\%) and high enantioselectivities (87-94\% ee).

With respect to the organocatalyst, it is based on a 1,5,7-trimethyl-3-azabicyclo[3.3.1]nonan-2-one scaffold connected to a thioxanthone chromophore \textit{via} an oxazole moiety. The mechanistic model assumes the binding of the 4-substituted chinolones to the catalyst through a double H-bonding as depicted in Figure 25. The thioxanthone not only serves as the light-absorbing molecule and transfers the energy to the chinolone, but also provides the asymmetric induction by allowing the attack of the double bond only from one prochiral face, thereby affording the cycloaddition product in an enantioselective fashion. The author mentioned that the enantiopure thioxanthone catalyst can be recovered in high yields after the reaction which demonstrate that visible light induced catalyst decomposition is not severe.

\textbf{Figure 25} Photoinduced asymmetric [2+2] intramolecular cycloaddition \textit{via} energy transfer process.
3) Metal catalysis: chiral-at-metal iridium(III) complex

In 2014, the Meggers group reported a highly efficient chiral-at-metal iridium Λ-IrS for the visible light induced enantioselective α-alkylation of 2-acyl imidazoles. As shown in Figure 26, under visible light irradiation, 2 mol% of iridium catalyst Λ-IrS is able to catalyze the reaction between 2-aryl imidazoles and electron deficient benzyl bromides in high yields (up to 100% yield) and with high enantioselectivities (up to 99% ee).

Mechanistically, the catalysis is initiated by the coordination of 2-acyl imidazole to the iridium catalyst, followed by deprotonation to form the iridium enolate complex. The subsequent addition of the reductively generated electrophilic carbon radical to form the ketyl radical intermediate. Oxidation of the ketyl radical to the carbonyl group by single electron transfer (SET) provides the iridium-coordinated product, which is subsequently released. The SET process either regenerates the iridium photoredox catalyst or leads to the reduction of another organobromide substrate, thereby initiating a chain process. Proposed key intermediate is the iridium enolate complex, which not only provides the crucial asymmetric induction but also serves as the in-situ generated active photoredox catalyst.

**Figure 26** Enantioselective α-alkylation of 2-acyl imidazoles with a single chiral-at-metal iridium catalyst. PC = photoredox catalyst.
4) Metal catalysis: chiral copper(I) complex

Very recently, the Fu group described a copper-based chiral catalyst derived from commercially available components can achieve asymmetric C-N cross-coupling reactions of racemic tertiary alkyl chlorides with high enantioselectivities of up to 99% ee (Figure 27). In this method, an in-situ formed chiral copper(I) complex in which copper cation is coordinated with two chiral phosphine ligands and one monoanionic carbazolide is responsible for the photocatalysis and the enantioselective C-N bond construction.

Mechanistically, the first step is the binding of the nucleophile to copper to form a copper-nucleophile complex. Irradiation of the copper-nucleophile complex leads to an excited-state copper adduct which then engages in electron transfer with the alkyl halide to generate an alkyl radical. Then, C-N bond formation between the nucleophile and the alkyl radical occurs through an inner sphere pathway involving a copper-nucleophile complex. This work is of great significance because it stands at a previously unexplored intersection of asymmetric synthesis, catalysis with earth-abundant metals, visible light induced processes, and cross-coupling reactions of alkyl electrophiles, each of them represents an important current theme in organic synthesis.

![Figure 27 Enantioselective C-N cross-coupling with an in-situ chiral copper catalyst.](image-url)
1.4 Conclusions

Octahedral chiral-at-metal complexes have developed not only because of their importance in fundamental stereochemistry but also because of their application as asymmetric catalysts in organic synthesis.

In above examples of asymmetric catalysis, several inert octahedral transition-metal complexes are presented as chiral templates, in which the transition metal serves as a structural center, whereas catalytic transformation is mediated through the organic ligand sphere. Among them, chiral-at-metal iridium complexes developed by the Meggers group exhibited impressive properties, achieving high enantioselectivities with low catalyst loadings. Remarkably, a chiral Lewis acid iridium catalyst should be of high practical value since it provides an excellent substrate scope for the highly enantioselective Friedel-Crafts addition of indoles to α,β-unsaturated 2-acyl imidazoles at low catalyst loadings. This high performance indicates the value of a direct chirality transfer from the chiral metal center to the coordinated substrate.

Under irradiation with visible light, highly enantioselective transformations could be achieved by merging photocatalyst with chiral catalyst or using a single catalyst. A variety of reaction types are developed via photoinduced electron transfer or energy transfer processes. The highly reactive intermediates, directed asymmetric induction and the tolerance of the reaction conditions to a wide range of functional groups enable the application of these reactions to the synthesis of various enantiopure compounds. The encouraging work from the Meggers group, a single chiral-at-metal iridium complex catalyzed the visible light activated asymmetric α-alkylation, provide new opportunities to realize different kinds of enantioselective photoredox catalysis with single chiral-at-metal complexes.

References

Chapter 1: Theoretical Part


Chapter 1: Theoretical Part


Chapter 2: Aim of the Work

1) Synthesis and catalytic activity of chiral rhodium Lewis acid catalyst

The inert octahedral chiral-at-iridium complexes provide ideal environments to induce asymmetry. However, efforts to exploit highly desirable features of chiral-at-rhodium complexes have met with great challenges, mainly due to limited methods to synthesize enantiopure rhodium complexes.\(^1\)

The Meggers group has recently introduced a substitutionally labile yet configurational stable chiral-at-metal iridium Lewis acid catalyst. The iridium center serves as a dual function of activating a substrate through bidentate coordination and at the same time provides the asymmetric induction.\(^2\) In this work, we wish to accomplish the first isostructural synthesis of chiral-at-metal rhodium(III) complex, and subsequently, we would like to search for different reactions for the comparison of the catalytic properties of the homologous chiral iridium and rhodium Lewis acid catalysts. Stability and the potential racemization of such rhodium complex should be considered.

2) Development of visible light induced asymmetric photoredox catalysis with chiral-at-metal complexes

General solutions for interfacing visible light induced photoredox chemistry and asymmetric catalysis with single catalysts are highly desirable. The Meggers group has recently reported a single chiral-at-metal iridium complex catalyzed the visible light induced asymmetric α-alkylation of 2-acyl imidazoles.\(^3\) Several useful information can be obtained: 1) the chiral-at-metal iridium complex can serve as “2-in-1” catalyst by combining photoinduced reduction with asymmetric alkylation; 2) the chiral catalyst can not be dissociated or racemized under visible light irradiation; 3) highly effective asymmetric induction can be mediated by the propeller-like C\(_2\)-symmetrical ligand sphere. All these informations potentially provide opportunities for reaction design by having a closer control over the entire reaction path.

The aim of this research part is the development of new and efficient visible light mediated asymmetric reactions with newly developed chiral-at-metal iridium or rhodium complexes. For instance, the activation of α-C(sp\(^3\))-H bond of tertiary amines represents an important organic synthesis process. Although oxidation of amines into iminium ions or α-aminoalkyl radicals \(\text{via}\) photoinduced electron
transfer has been extensively studied, only a few asymmetric methodologies are available. Whether the oxidation potentials of such chiral-at-metal iridium complexes are positive for activing $\alpha$-C(sp$^3$)-H bonds need further investigation.

References


Chapter 3: Results and Discussion

3.1 Asymmetric Lewis Acid Catalysis Directed by Octahedral Rhodium Centrochirality

3.1.1 Catalyst Design

Chiral Lewis acid catalysts play a significant role in asymmetric catalysis because many reactions are amenable to Lewis acid activation. Recently, the Meggers group has developed a chiral-at-metal iridium(III) complex (Δ-IrO) as a novel type of chiral Lewis acid catalyst in which the metal center is cyclometalated by two achiral bidentate ligands in a propeller type fashion and thereby provides the sole source of chirality. Herein, we wish to synthesize an octahydral chiral-at-metal rhodium(III) complex. The designed structure of Δ-RhO, like its congener Δ-IrO, consists of two cyclometalating benzoazoles and two coordinated acetonitrile ligands. We hope the rhodium center can also serve as the source of centrochirality and Lewis acidity in the catalytic asymmetric reactions (Figure 28).

![Figure 28 Catalyst design for the chiral-at-metal rhodium complex.](image)

3.1.2 Catalyst Synthesis

The study was started by developing a synthesis of the complex Δ-RhO. The methodology was developed by the Meggers group. Accordingly, RhCl₃ hydrate was reacted with tert-butyl-2-phenylbenzoazole (1) in a mixture of 2-ethoxyethanol and water under reflux to provide the rhodium dimer complex rac-2 (Scheme 1). The subsequent reaction with D-proline afforded the prolinato-rhodium complexes Δ-(R)-3 and Λ-(R)-3 as a mixture of diastereomers, and Δ-(R)-3 is isolable in a straightforward fashion in a yield of 40% with high purity by just washing the mixture of diastereomers.
with CH$_2$Cl$_2$/Et$_2$O. Exposure of $\Delta$-(R)-3 to NH$_4$PF$_6$ in acetonitrile at 50 °C for 12 h resulted in a substitution of D-proline by two acetonitrile ligands under complete retention of configuration to afford $\Delta$-RhO in a yield of 90%. Notably, $\Delta$-RhO is air stable, moisture tolerant and can be purified by standard flash silica gel chromatography. The mirror-imaged complex $\Lambda$-RhO is accessible in an analogous fashion by using the chiral auxiliary L-proline instead.

Scheme 1 Proline-mediated synthesis of the enantiomerically pure rhodium(III) complexes $\Lambda$-RhO and $\Delta$-RhO.

It is worth noting that the prolinato-rhodium complexes $\Delta$-(R)-3 and $\Lambda$-(R)-3 can not be separated by chromatography due to a limited stability of the complexes. The isolation of $\Delta$-(R)-3 or its enantiomer $\Lambda$-(S)-3 is based on the different solubilities of the diastereomers in solutions. Whereas $\Lambda$-(R)-3 is very soluble in a mixture of CH$_2$Cl$_2$/Et$_2$O, its diastereomer $\Delta$-(R)-3 is insoluble. Thus, $\Delta$-(R)-3 could be obtained by washing with CH$_2$Cl$_2$/Et$_2$O (for details, see experimental part). The structure of $\Delta$-(R)-3 is demonstrated by single crystal X-ray crystallography (Figure 29). Notably, other tested auxiliaries did not provide rhodium auxiliary complexes with distinct solubilities and were not stable enough for a resolution via silica gel chromatography. Chiral proline here serves as a cheap and readily available powerful chiral auxiliary for the synthesis of enantiopure rhodium complexes. This method provides opportunity for the large-scale synthesis of enantiomerically pure transition metal complexes.
Chapter 3: Results and Discussion

Figure 29 Crystal structure of $\Delta$-$(R)$-$3$. Hydrogen atoms are omitted for clarity. ORTEP drawing with 50% probability thermal ellipsoids.

Thus, following this convenient proline-mediated synthesis, $\Lambda$- and $\Delta$-$\text{RhO}$ can be obtained in a non-racemic fashion as verified by CD-spectroscopy (Figure 30). HPLC on a chiral stationary phase demonstrates that the chiral-at-rhodium complexes are virtually enantiopure (Figure 31). Furthermore, time dependent stability tests by $^1$H NMR and HPLC confirm that the relative and absolute metal-centered configuration is completely retained in solution over many days (for details, see experimental part).

Figure 30 CD spectra (0.2 mM in CH$_3$OH) of $\Lambda$- and $\Delta$-$\text{RhO}$. 
Chapter 3: Results and Discussion

Figure 31 Chiral HPLC traces demonstrating the enantiopurity of synthesized $\Lambda$- and $\Delta$-RhO. HPLC conditions: Daicel Chiralpak IB (250 × 4.6 mm), flow rate = 0.6 mL/min, 0.1% aq. TFA with MeCN as eluent (30% to 41% in 60 min).

A structure of $\Delta$-RhO was obtained by single crystal X-ray diffraction and verifies the $\Delta$-configuration at the rhodium center (Figure 32, left). As expected, affected by the lanthanide contraction, the period 5 transition metal complex $\Delta$-RhO and its period 6 congener $\Delta$-IrO (Figure 32, right) possess almost identical structures. For example, the lengths of the bonds between the transition metals and the cyclometalating benzoxazoles differ just in the range of 0.009 and 0.022 Å. However, the bonds to the coordinated acetonitrile ligands are notably longer in $\Delta$-RhO compared to $\Delta$-IrO by 0.041–0.043 Å, thereby indicating more exchange labile acetonitrile ligands in $\Delta$-RhO.

Figure 32 Crystal structures of $\Delta$-RhO (left) and $\Delta$-IrO (right). The hexafluorophosphate counteranion and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): N1-Rh1 = 2.056(2), N20-Rh1 = 2.044(2), N39-Rh1 = 2.142(3), N42-Rh1 = 2.155(3); N1-Ir1 = 2.054(9), N20-Ir1 = 2.044(6), N39-Ir1 = 2.111(6), N42-Ir1 = 2.100(9).
3.1.3 Catalytic Reactions

With the novel Lewis acid catalyst $\Delta$-RhO in hand, we next searched for different reactions for the comparison of the homologous catalysts $\Delta$-IrO and $\Delta$-RhO. Preliminary works of the following asymmetric conjugate additions by using $\Delta$-IrO as catalyst were explored by Haohua Huo (a former Ph.D. student in the Meggers group).

1) Asymmetric Friedel-Crafts alkylation

First reaction is the enantioselective Friedel-Crafts addition of indoles to $\alpha,\beta$-unsaturated 2-acyl imidazoles which is effectively catalyzed by $\Delta$-IrO. As shown in Figure 33, although 1 mol% $\Delta$-RhO catalyzes the addition of indole to $\alpha,\beta$-unsaturated 2-acyl imidazole 4a affording the Friedel-Crafts product (R)-5a with 94% yield and respectable 95% ee after 40 h, reaction time, yield, and enantioselectivity can not quite match the performance of the homolog $\Delta$-IrO (96% yield and 96% ee after 20 h).

![Figure 33 Asymmetric Friedel-Crafts alkylation catalyzed by $\Delta$-IrO and $\Delta$-RhO.](image)

2) Asymmetric addition of malononitrile

Next, the Michael addition of 2-acyl imidazoles 4a with malononitrile was investigated. As shown in Table 1, the addition of malononitrile to 4a catalyzed by 1 mol% $\Delta$-RhO in THF at room temperature afforded the adduct (R)-5b with a significantly higher ee value of 88% (entry 2) compared to 70% using $\Delta$-IrO (entry 1). After a brief survey of reaction conditions (entries 3-8), THF (0.5 M) and malononitrile (1.2 eq.) are favorable to get a high enantioselectivity of 92% ee (entry 8). It is worth noting that the rhodium catalyst is tolerant towards moisture and air, and the presence of 1 mol% H$_2$O and air atmosphere did neither affect the yield nor the enantioselectivity (entries 9 and 10). Upon the best conditions (entry 8), the addition of malononitrile to substrate 4b catalyzed by $\Delta$-RhO afforded the product (R)-5c with 91% yield and 95% ee after 28 h, reaction time, yield, and enantioselectivity are superior to the performance of the homolog $\Delta$-IrO (entries 11 and 12).
Table 1 Asymmetric addition of malononitrile.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst\textsuperscript{b}</th>
<th>substrate</th>
<th>solvent\textsuperscript{c}</th>
<th>malononitrile</th>
<th>t (h)</th>
<th>yield (%)\textsuperscript{d}</th>
<th>ee(%)\textsuperscript{e}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\Delta-\text{IrO})</td>
<td>4a</td>
<td>THF (1 M)</td>
<td>3.0 eq.</td>
<td>16</td>
<td>99</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>THF (1 M)</td>
<td>3.0 eq.</td>
<td>16</td>
<td>98</td>
<td>88</td>
</tr>
<tr>
<td>3</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>DCM (1 M)</td>
<td>3.0 eq.</td>
<td>16</td>
<td>96</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>MeOH (1 M)</td>
<td>3.0 eq.</td>
<td>16</td>
<td>97</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>THF (0.5 M)</td>
<td>3.0 eq.</td>
<td>16</td>
<td>97</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>THF (0.25 M)</td>
<td>3.0 eq.</td>
<td>16</td>
<td>97</td>
<td>91</td>
</tr>
<tr>
<td>7</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>THF (0.5 M)</td>
<td>2.0 eq.</td>
<td>16</td>
<td>96</td>
<td>91</td>
</tr>
<tr>
<td>8</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>THF (0.5 M)</td>
<td>1.2 eq.</td>
<td>16</td>
<td>96</td>
<td>92</td>
</tr>
<tr>
<td>9\textsuperscript{f}</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>THF (0.5 M)</td>
<td>1.2 eq.</td>
<td>16</td>
<td>96</td>
<td>92</td>
</tr>
<tr>
<td>10\textsuperscript{g}</td>
<td>(\Delta-\text{RhO})</td>
<td>4a</td>
<td>THF (0.5 M)</td>
<td>1.2 eq.</td>
<td>16</td>
<td>96</td>
<td>92</td>
</tr>
<tr>
<td>11</td>
<td>(\Delta-\text{RhO})</td>
<td>4b</td>
<td>THF (0.5 M)</td>
<td>1.2 eq.</td>
<td>28</td>
<td>91</td>
<td>95</td>
</tr>
<tr>
<td>12</td>
<td>(\Delta-\text{IrO})</td>
<td>4b</td>
<td>THF (0.5 M)</td>
<td>1.2 eq.</td>
<td>96</td>
<td>40</td>
<td>88</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction conditions: 2-acyl imidazole 4a or 4b (0.20 mmol), malononitrile (0.24 mmol or 0.40 mmol or 0.60 mmol) in solvent with catalyst \(\Delta-\text{IrO}\) or \(\Delta-\text{RhO}\) (1 mol%) under nitrogen atmosphere at room temperature. \textsuperscript{b} Catalyst loadings in brackets given in mol%. \textsuperscript{c} Concentration of solvents are given in brackets. \textsuperscript{d} Isolated yields. \textsuperscript{e} Enantioselectivities were determined by HPLC analysis. \textsuperscript{f} under air. \textsuperscript{g} with 1% H\textsubscript{2}O.

3) Asymmetric addition of Meldrum’s acid

Meldrum’s acid is widely used as a nucleophile in organic synthesis due to its adequate acidity (\(pK_a = 4.83\)).\textsuperscript{6} As shown in Table 2, by using \(\Delta-\text{RhO}\) (1 mol%) as catalyst, the Michael addition of Meldrum’s acid with 2-acyl imidazole 4a provided the expected product (\(R\))-5d with 85% ee compared to just 68% ee with \(\Delta-\text{IrO}\) (entries 1 and 2). The enantioselectivity for the \(\Delta-\text{RhO}\) catalyzed reaction can be further improved significantly by either reducing the temperature to 5 ºC (entry 4, 94% ee) or increasing the catalyst loading to 2 mol% (entry 5, 95% ee), as both ways can inhibit the background reaction efficiently (entry 3).
Chapter 3: Results and Discussion

Table 2 Asymmetric addition of Meldrum’s acid.

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst$^b$</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>yield (%)$^c$</th>
<th>ee (%)$^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Δ-IrO (1 mol%)</td>
<td>25</td>
<td>16</td>
<td>99</td>
<td>68</td>
</tr>
<tr>
<td>2</td>
<td>Δ-RhO (1 mol%)</td>
<td>25</td>
<td>16</td>
<td>99</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>none</td>
<td>25</td>
<td>16</td>
<td>8.5</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>Δ-RhO (1 mol%)</td>
<td>5</td>
<td>16</td>
<td>97</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>Δ-RhO (2 mol%)</td>
<td>25</td>
<td>6</td>
<td>96</td>
<td>95</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 2-acyl imidazole $4a$ (0.20 mmol), Meldrum’s acid (0.60 mmol) in THF (0.2 mL) with catalyst Δ-IrO or Δ-RhO under nitrogen atmosphere at room temperature. $^b$ Catalyst loadings in brackets given in mol%. $^c$ Isolated yields. $^d$ Enantioselectivities were determined by HPLC analysis. n.d. = not determined.

4) Asymmetric addition of β-ketoesters

Interestingly, Δ-RhO (1 mol%) is even capable of catalyzing the formation of an all-carbon quaternary stereocenter (Table 3). The reaction of tert-butyl 2-oxocyclopentane-1-carboxylate with acyl imidazole $4a$ yields $5e$ with 99% ee and 4:1 dr (entry 1). Under the same conditions, Δ-IrO displays inferior performance with 97% ee and 3:1 dr and a low yield of just 41%. Δ-RhO (1 mol%) also catalyzes the addition of 2,3-dihydro-1-oxo-1H-indene-2-carboxylic acid tert-butyl ester to acyl imidazole $4a$ providing the adduct $5f$ in 92% yield with 96% ee and 14:1 dr. Δ-IrO performs similar for this transformation although the catalysis rate is somewhat sluggish and requires an elongated reaction time (72 h) for a complete conversion (entry 2).
Table 3 Asymmetric addition of β-ketoesters.

<table>
<thead>
<tr>
<th>entry</th>
<th>β-ketoester</th>
<th>product</th>
<th>catalyst\textsuperscript{b}</th>
<th>t (h)</th>
<th>yield (%)\textsuperscript{c}</th>
<th>ee (%)\textsuperscript{d}</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>(\text{4a} (1.0 \text{ eq.}))</td>
<td>(\text{β-ketoesters} (2.0 \text{ eq.}))</td>
<td>(\Delta-\text{IrO} (1 \text{ mol%}))</td>
<td>96</td>
<td>41</td>
<td>97 (3:1 \text{ dr})</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(\Delta-\text{RhO} (1 \text{ mol%}))</td>
<td>48</td>
<td>83</td>
<td>99 (4:1 \text{ dr})</td>
</tr>
<tr>
<td>2</td>
<td>(\text{5f} )</td>
<td>(\text{5e-5f} )</td>
<td>(\Delta-\text{IrO} (1 \text{ mol%}))</td>
<td>72</td>
<td>89</td>
<td>97 (10:1 \text{ dr})</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(\Delta-\text{RhO} (1 \text{ mol%}))</td>
<td>20</td>
<td>92</td>
<td>96 (14:1 \text{ dr})</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction conditions: 2-acyl imidazole \textit{4a} (0.20 mmol), β-ketoester (0.40 mmol) in THF (0.4 mL) with catalyst \(\Delta-\text{IrO}\) or \(\Delta-\text{RhO}\) under nitrogen atmosphere at room temperature. \textsuperscript{b}Catalyst loadings in brackets given in mol%. \textsuperscript{c}Isolated yields. \textsuperscript{d}Enantioselectivities were determined by HPLC analysis; diastereoselectivities were determined by \(^1\text{H}\) NMR analysis of the crude products.

5) Asymmetric cascade reactions

Asymmetric cascade sequences provide an ecologically and economically desirable approach to organic synthesis.\textsuperscript{7} Taking into account that the asymmetric additions of \(\alpha,\beta\)-unsaturated 2-acyl imidazoles are efficiently catalyzed by the iridium and rhodium complexes, and this class of catalysts exhibits impressive catalytic activity in the asymmetric \(\alpha\)-amination of 2-acyl imidazoles through enolate activation mode (Liang-A. Chen’s work, a former Ph.D. student in the Meggers group)\textsuperscript{8}, we were wondering if the cascade reaction could be realized which combine two intermolecular and stereoselective steps involving a Michael addition/amination pathway (Figure 34).

Figure 34 Reaction design of the asymmetric cascade reaction.
The asymmetric cascade strategy was first examined by the mixture of α,β-unsaturated 2-acyl imidazole 4a, malononitrile and diethyl azodicarboxylate in isopropanol with rac-IrO as catalyst, to our disappointment, only Michael addition product 5b was observed (Table 4, entry 1). Encouragingly, by using rac-RhO (2 mol%) as catalyst (entry 2), the desired product 6 was provided with 40% yield (mixture of two diastereoisomers). After a brief screen of solvents, a high yield of 82% and diastereoselectivity of 4:1 dr can be achieved (entry 4). The enantioselectivity of the major diastereoisomer was observed as 92% ee when Δ-RhO was used as chiral catalyst (entry 5).

Table 4 Asymmetric cascade reaction.⁶

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent ²</th>
<th>catalyst (2 mol%)</th>
<th>yield (%) ³</th>
<th>ee (%) ⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>iPrOH (2 M)</td>
<td>rac-IrO</td>
<td>0</td>
<td>n.d.</td>
</tr>
<tr>
<td>2</td>
<td>iPrOH (2 M)</td>
<td>rac-RhO</td>
<td>40</td>
<td>n.d.</td>
</tr>
<tr>
<td>3</td>
<td>CH₂Cl₂ (1 M)</td>
<td>rac-RhO</td>
<td>48</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>THF (1 M)</td>
<td>rac-RhO</td>
<td>83</td>
<td>n.d.</td>
</tr>
<tr>
<td>5</td>
<td>THF (1 M)</td>
<td>Δ-RhO</td>
<td>82</td>
<td>92 (dr 4:1)⁵</td>
</tr>
</tbody>
</table>

⁶ Reaction conditions: 2-acyl imidazole 4a (0.2 mmol), malononitrile (0.24 mmol) and (E)-dibenzyl diazene-1,2-dicarboxylate (0.4 mmol) in solvent with catalyst Δ-IrO or Δ-RhO under nitrogen atmosphere at room temperature. ² Concentration of solvents are given in brackets. ³ Isolated yields. ⁴ Enantioselectivities were determined by HPLC analysis. ⁵ Diastereoselectivity was determined by the isolated yield of each isomer. n.d. = not determined.

The above described alkene alkylation and amination processes afford straightforward access to the product 6 which have two adjacent stereogenic centers with high enantioselectivity. However, the substrate scope of this catalytic tandem reaction is narrow. For example, only the Michael addition product (step 1) was afforded when replacing malononitrile to indole or switching diethyl azodicarboxylate to imine electrophile (Scheme 2). It is probably because either the intermediate enolate complexes are difficult to generate or the in-situ formed enolate complexes could not efficiently attack to other electron deficient double bonds.
Some limitations for asymmetric cascade reaction.

3.1.4 Mechanistic Investigations

1) Proposed mechanism and reaction model

A plausible mechanism of asymmetric conjugate additions is outlined in Figure 34. $\Delta$-RhO, analogous to $\Delta$-IrO, apparently serves as a chiral Lewis acid which coordinates in a bidentate fashion to the $\alpha,\beta$-unsaturated 2-acyl imidazole, forming intermediate rhodium complex I. The activated double bond in complex I could be attacked by the nucleophile, thereby forging the intermediate enolate complex II. After protonation, the rhodium coordinated product III is subsequently released the product upon coordination to a new substrate molecule, thereby starting a new catalytic cycle.

In the stereocontrol model, $\Delta$-RhO coordinates in two-point fashion to the $\alpha,\beta$-unsaturated acyl imidazole, thereby shielding Si prochiral face of the alkene and raising its electrophilicity, so that an asymmetric induction is provided in the course of the addition of the deprotonated carbon nucleophiles to the prochiral $\beta$-carbon (Figure 35). $^1$H NMR spectra recorded in CD$_2$Cl$_2$ at room temperature after the addition of substrate 4a to catalyst $\Delta$-RhO support the fast bidentate coordination of 4a to the rhodium complex (see experimental part). The mode of reaction is also supported by a crystal structure of RhO-I, which was obtained upon mixing of the racemic rhodium catalyst with an $\alpha,\beta$-unsaturated 2-acyl imidazole substrate 4b at room temperature, confirming the anticipated two-point coordination of the acyl imidazole to the rhodium center upon replacement of the two labile acetonitrile ligands (Figure 36).
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Figure 35 Proposed mechanism for Δ-RhO catalyzed asymmetric additions and reaction model for the asymmetric induction in the transition state in which one face of the alkene is shielded by the C2-symmetrical ligand sphere.

Figure 36 Crystal structure of substrate-coordinated rhodium intermediate complex RhO-I. Hydrogen atoms and the hexafluorophosphate counteranion are omitted for clarity. ORTEP drawing with 50% probability thermal ellipsoids.

2) The acetonitrile exchange experiments

It is quite intriguing that the congeners Δ-RhO and Δ-IrO differ in their catalytic performance despite their isostructural nature, with the iridium catalyst being superior for the asymmetric Friedel-Crafts reaction, whereas the rhodium congener providing higher turnover frequencies and, in most cases, higher enantioselectivities for the shown Michael additions of β-dicarbonyl compounds. 1H NMR experiments of Δ-RhO/Δ-IrO with bipyridine reveal that the acetonitrile exchange rates are much faster in Δ-RhO compared to Δ-IrO which is consistent with longer coordinative bonds of the metal-coordinated acetonitrile ligands in Δ-RhO compared to Δ-IrO (Figure 37).
The acetonitrile exchange experiments of \( \Delta-\text{RhO} \) and \( \Delta-\text{IrO} \) in the presence of bipyridine.

It is therefore plausible that the superior catalytic activity of the more coordinatively labile \( \Delta-\text{RhO} \) over the more inert \( \Delta-\text{IrO} \) for the Michael additions with \( \beta \)-dicarbonyl compounds is due to substrate coordination and/or release being the rate limiting steps in the catalytic cycle, while it is the nucleophile addition step for the Friedel-Crafts reaction in which the aromaticity of the pyrrole ring is lost temporarily in the course of the addition. The observed higher turnover frequencies for the rhodium-catalyzed Michael additions may also contribute to the observed higher enantioselectivities since a higher turnover frequency suppresses the undesired, uncatalyzed background reaction.\(^{10}\)
3.1.5 Conclusions

In conclusion, the first example of an asymmetric catalyst which derives both its optical activity and Lewis acidity from an octahedral rhodium stereocenter was developed. This novel, configurationally surprisingly stable chiral Lewis acid is conceptually very simple, as it just contains achiral mono- and bidentate ligands, and it can be accessed conveniently in an enantiomerically pure fashion through a proline-mediated synthesis. Interestingly, although isostructural to its iridium congener, the two homologs differ significantly in their catalytic Lewis acid activity, with the rhodium complex demonstrating advantages as catalyst for the Michael addition of CH-acidic β-dicarbonyl compounds to α,β-unsaturated 2-acyl imidazoles and the cascade reaction of α,β-unsaturated 2-acyl imidazole with malononitrile and diethyl azodicarboxylate. The superiority of the rhodium catalyst over its iridium congener can in large parts be attributed to a significantly higher lability of the two accessible rhodium coordination sites which allow higher turnover frequencies and turnover numbers.
References


3.2 Merger of Visible Light Induced Oxidation and Enantioselective Alkylation with Chiral Iridium Catalyst

3.2.1 Reaction design

The development of methods for fundamental functionalizations, as well as protocols for the construction of chiral molecules is an ongoing challenge. Recently, the Meggers group reported for the first time that a single chiral-at-metal complex Δ-IrS can serve as an effective catalyst for the visible light induced enantioselective α-alkylation of 2-acyl imidazoles with electron deficient benzyl bromides and phenacyl bromides under reductive activation.\(^1\) We were wondering whether this class of chiral iridium catalysts could also be capable of catalyzing asymmetric photoredox processes which instead proceed through oxidative chemistry. As shown in Figure 38, the designed reaction of the electrophilic iminium ion with the nucleophilic iridium enolate complex might produce a non-racemic compound. We hypothesized the intermediate iridium enolate complex could provide the crucial asymmetric induction as well as serve as the active photocatalytic species.

![Reaction design diagram](image)

**Figure 38** Reaction design for photoactivated asymmetric catalysis with chiral iridium(III) Lewis acids.
3.2.2 Initial Experiments and Reaction Optimization

The initial experiments were inspired by Stephenson and co-workers, who utilized the oxidation of N-phenyl tetrahydroisoquinolines with bromotrichloromethane (BrCCl₃) to generate the iminium ion under photoredox conditions.² This study was started by investigating the reaction of 2-acyl imidazole 7a'' with dimethylaniline (Eₐox ≈ +0.78 V vs. SCE)³ and carbon tetrabromide (CBr₄) under visible light irradiation. In the presence of the previously developed dual function photoredox/chiral Lewis acid catalyst Δ-IrO (3 mol%), the expected C-C bond formation product 8 was obtained in 34% yield after irradiation of 16 h (Figure 39). However, racemization was observed in the course of the reaction. The enantioselectivity of product 8 was dropped dramatically from 96% to 0% ee during the reaction time from 1 h to 16 h. Control experiment in the absence of iridium catalyst showed that about 10% of rac-8 was observed after 16 h of the reaction. As the product 8 is stable in the solution, the observed racemization phenomenon might be explained by the reversibility of this Mannich reaction.⁴

![Figure 39 Asymmetric photoactivated α-aminoalkylation of 2-acyl imidazole7a'' with dimethylaniline.](image)

To get non-racemic product under mild conditions, we next used α-silylamines (Eₐox ≈ +0.44 V vs. NHE) as precursors. The silyl group in α-silylamines not only serves as a redox handle to facilitate a single electron oxidation, but also results in a subsequent rapid cleavage of the C-Si bond under release of α-aminoalkyl radicals, which then be involved in iminium chemistry after further oxidation.⁴ Thus, the reaction of 2-acyl imidazole 7a'' and N,N-diphenyl-N-(trimethylsilyl)methylamine 9a was carried out in the presence of the enantiomerically pure iridium complex Δ-IrO (2 mol%), while exposed to air (Scheme 3). Encouragingly, irradiation with visible light in form of a standard 12 W energy saving household lamp for 20 h afforded the expected product 10a'' in 34% yield and 91% ee. However, the reaction is not straightforward and the intermediate α-aminoalkyl radical can either form a dimer 11 via homocoupling or be oxidized to form amide 12 in the presence of oxygen.² The isolated side products, on the other hand, provide good evidence in support of a radical pathway of the reaction.

⁴
Scheme 3 Asymmetric photoactivated α-aminoalkylation of 2-acyl imidazole 7a'' with α-silylamine 9a.

Improved results were obtained after the modification of the 2-acyl imidazole substrate (Table 5). Accordingly, replacing the N-methyl imidazole moiety (7a'') with N-isopropyl imidazole (7a') provided the aminoalkylation product 10a' with an increased yield of 48% and 90% ee after 20 h of irradiation (entries 1 and 2). However, the best results were obtained with the N-phenyl imidazole substrate 7a, giving 92% yield and 97% ee after just 6.5 h of photolysis (entry 3). Notably, excess α-silylamine 9a is crucial for high yield of the product (entries 4 and 5). Control experiments in the absence of catalyst (no reaction) or performed in the dark (very sluggish and incomplete reaction after an elongated reaction time of 48 h) reveal that it is the combination out of chiral iridium complex Λ-IrO and visible light that is required for an efficient reaction (entries 6 and 7). It is also worth noting that the catalyst Λ-IrS,¹ which was found superior for the reported asymmetric photo-reductive C-C bond formation, turned out to be inferior for the here investigated photo-oxidative activation (entry 8 compared to entry 3).
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Table 5 Optimization of the enantioselective photoactivated α-aminoalkylation of 2-acyl imidazoles. 

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>catalyst</th>
<th>hv</th>
<th>ratio of 7 and 9a</th>
<th>t (h)</th>
<th>yield (%) (e)</th>
<th>ee (%) (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1c</td>
<td>7a''</td>
<td>Δ-IrO</td>
<td>yes</td>
<td>1:3</td>
<td>20</td>
<td>34</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>7a'</td>
<td>Δ-IrO</td>
<td>yes</td>
<td>1:3</td>
<td>20</td>
<td>48</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>7a</td>
<td>Δ-IrO</td>
<td>yes</td>
<td>1:3</td>
<td>6.5</td>
<td>92</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>7a</td>
<td>Δ-IrO</td>
<td>yes</td>
<td>1:2</td>
<td>20</td>
<td>71</td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>7a</td>
<td>Δ-IrO</td>
<td>yes</td>
<td>2:1</td>
<td>20</td>
<td>49</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>7a</td>
<td>none</td>
<td>yes</td>
<td>1:3</td>
<td>20</td>
<td>0</td>
<td>n.d.</td>
</tr>
<tr>
<td>7</td>
<td>7a</td>
<td>Δ-IrO</td>
<td>no</td>
<td>1:3</td>
<td>48</td>
<td>18</td>
<td>94</td>
</tr>
<tr>
<td>8</td>
<td>7a</td>
<td>Δ-IrS</td>
<td>yes</td>
<td>1:3</td>
<td>20</td>
<td>51</td>
<td>97</td>
</tr>
</tbody>
</table>

\(a\) Reaction conditions: Reactions performed in CH₂Cl₂ (0.5 mL) with 2-acyl imidazole (0.2 or 0.4 mmol) and α-silylamine 9a (0.2 or 0.4 or 0.6 mmol) in the presence of catalyst (2 mol% or none) at room temperature under an atmosphere of air. \(b\) 12 W white light energy saving lamp. \(c\) Isolated yield. \(d\) Determined by chiral HPLC analysis. \(e\) Shown for comparison. n.d. = not determined.

3.2.3 Substrate Scope

After the optimized conditions were identified, the scope of the asymmetric photoinduced α-aminoalkylation with catalyst Δ-IrO was then tested. Figure 40 shows that the reaction of a variety of 2-acyl imidazoles with \(N,N\)-diaryl-\(N\)-(trimethylsilyl)methylamines in the presence of Δ-IrO (2-4 mol%) and under air while illuminating with visible light provided the expected alkylation products in 61-93% yields and with excellent enantioselectivities of 90-98% ee. The 2-acyl-\(N\)-phenyl imidazole substrates tolerate steric (products 10b and 10c), electron donating (product 10d) and electron accepting (product 10e) substituents in the phenyl moiety, and it can be replaced by the heteroaromatic thiophene (product 10f). Furthermore, a 2-propionic imidazole (product 10g) as well as a 2-butyric imidazole (product 10h) were aminoalkylated in the α-position of the carbonyl group with high enantioselectivities, although an increased catalyst loading of 4 mol% and more active silymethylamine are required to achieve
satisfactory results. With respect to silymethylamines, different substituents are tolerated in the phenyl groups (10i-k), and one phenyl can be replaced by a naphthyl group (10l).

![Chemical structures and yields](image)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Time</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10a</td>
<td>6.5 h</td>
<td>92%</td>
<td>97%</td>
</tr>
<tr>
<td>10b</td>
<td>16 h</td>
<td>82%</td>
<td>96%</td>
</tr>
<tr>
<td>10c</td>
<td>20 h</td>
<td>77%</td>
<td>96%</td>
</tr>
<tr>
<td>10d</td>
<td>20 h</td>
<td>61%</td>
<td>90%</td>
</tr>
<tr>
<td>10e</td>
<td>16 h</td>
<td>70%</td>
<td>98%</td>
</tr>
<tr>
<td>10f</td>
<td>20 h</td>
<td>62%</td>
<td>94%</td>
</tr>
<tr>
<td>10g</td>
<td>7 h</td>
<td>93%</td>
<td>96%</td>
</tr>
<tr>
<td>10h</td>
<td>16 h</td>
<td>65%</td>
<td>96%</td>
</tr>
<tr>
<td>10i</td>
<td>4 h</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td>10j</td>
<td>20 h</td>
<td>65%</td>
<td>95%</td>
</tr>
<tr>
<td>10k</td>
<td>4 h</td>
<td>89%</td>
<td>91%</td>
</tr>
<tr>
<td>10l</td>
<td>16 h</td>
<td>63%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Figure 40 Substrate scope of the asymmetric photoinduced α-aminoalkylation. a Catalyst loading of 4 mol%.

Unfortunately, the application of this α-aminoalkylation technology to other substrates did not succeed (Figure 41). The α-silyl and the two aryl groups are required for this transformation. When one aryl group was replaced by aliphatic group (methyl, isopropyl or n-butyl group), both the yields and enantioselectivities dropped dramatically. Without α-silyl group or one aryl group was replaced by electron-withdrawing group (-COOMe), the expected product was not observed under the standard conditions. However, with additional 1.2 equivalent of oxidant CBr₄, the C-C bond formation product was obtained, albeit in a low yield. These results support that the α-silyl and two aryl groups are crucial
for reducing the oxidation potential of amines.\textsuperscript{4}

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Substrate</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me\textsubscript{3}Si(\text{-})N(_{\text{Me}})Ph</td>
<td>N(_{\text{Me}})Ph</td>
<td>Me\textsubscript{3}Si(\text{-})N(_{\text{Me}})Ph</td>
<td>not observed</td>
</tr>
<tr>
<td></td>
<td>20 h, 54% yield, 45% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me\textsubscript{3}Si(\text{-})N(_{\text{iPr}})Ph</td>
<td>N(_{\text{iPr}})Ph</td>
<td>Me\textsubscript{3}Si(\text{-})N(_{\text{CO}_2}\text{Me})Ph</td>
<td>not observed</td>
</tr>
<tr>
<td></td>
<td>20 h, 27% yield, 15% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me\textsubscript{3}Si(\text{-})N(_{\text{nBu}})Ph</td>
<td>N(_{\text{nBu}})Ph</td>
<td>Me\textsubscript{3}Si(\text{-})N(_{\text{CO}_2}\text{Me})Ph</td>
<td>16 h, 25% yield, n.d. ee</td>
</tr>
<tr>
<td></td>
<td>20 h, 17% yield, n.d. ee</td>
<td>(+ C\textsubscript{Br}_4 1.2 eq.)</td>
<td></td>
</tr>
</tbody>
</table>

\textbf{Figure 41} Some limitations of the substrate scope with respect to silymethylamines. n.d. = not determined.
3.2.4 Plausible Mechanism

A plausible mechanism in which photoredox catalysis intertwines with asymmetric catalysis is outlined in Figure 42. Herein, the catalytic cycle is initiated upon coordination of the 2-acyl imidazole substrate 7 to the iridium complex $\Delta$-IrO in a bidentate fashion under release of the two labile monodentate acetonitrile ligands to provide the substrate coordinated intermediate A. The subsequent reversible deprotonation in $\alpha$-position of the carbonyl group affords the nucleophilic iridium enolate intermediate B. Meanwhile, an electrophilic iminium ion is generated by an iridium-photoinduced oxidation of the $\alpha$-silylamine 9 with oxygen serving as the terminal oxidant according to the generally accepted photoredox catalysis cycle. The reaction of the iminium ion with the iridium enolate complex B occurs in a stereocontrolled fashion dictated by the metal-centered chirality and provides the iridium coordinated product C, which is subsequently released the product 10 upon coordination to a new substrate molecule 7, thereby initiating a new catalytic cycle. A series of investigations have been executed to verify the proposed mechanism in the following section.

![Figure 42](image_url) Plausible mechanism for the photoinduced asymmetric catalysis. PC = iridium photoredox catalyst, most likely intermediates A and C. [O] = oxidant in form of molecular oxygen and superoxide anion.
Chapter 3: Results and Discussion

3.2.5 Mechanistic Investigations

1) Crystal structure analysis

The catalytic cycle was firstly investigated by verifying the involvement of the proposed iridium intermediate A and enolate intermediate B. Accordingly, upon reaction of an excess substrate 7a with racemic $\Delta/\Lambda$-IrO we could isolate the proposed intermediate A and subsequent deprotonation generated intermediate enolate B ($Ar = Ph$). A crystal structure of enolate intermediate B is shown in Figure 43 and reveals that a $\Lambda$-configuration at the iridium center shields the $Si$-face of the $\alpha$-enolate carbon and directs the addition of the electrophile to the $Re$-face, thereby being consistent with the observed $S$-configuration of the alkylation product when using the catalyst with $\Lambda$-configuration at the metal.

![Crystal structure of the proposed complex B (left) and proposed model for the asymmetric photoinduced $\alpha$-aminoalkylation (right).](image)

2) Evaluating the Catalytic Activities of Complexes A and B

It is safe to assume that at the beginning of the reaction, due to the bidentate nature of the 2-acyl imidazole substrate and a high substrate/catalyst ratio of 50, all iridium catalyst will be captured by the imidazole substrate, while an equilibrium may exist between the cationic intermediate A and the deprotonated enolate intermediate B. The involvement of the enolate complex B as a photoredox catalyst in this reaction was excluded based on a simple experiment which is outlined in Figure 44. The replacement of $\Delta$-IrO with the enolate complex B showed that it was not capable of catalyzing the photoinduced reaction at all, whereas on the other hand the cationic intermediate A displayed almost the same catalytic activity compared to $\Delta$-IrO. Thus, the substrate-coordinated intermediate A must be the
active photoredox catalyst at the beginning of the reaction, probably complemented later by the related product-coordinated intermediate C.

![Chemical reaction](image)

**Figure 44** Evaluating the catalytic activities of complexes A and B.

### 3) Control experiments

**Enolate chemistry**

The involvement of an enolate complex B in the catalytic cycle is further supported by a reaction of 7a with the electrophile dibenzyl diazodicarboxylate catalyzed by \( \Delta\text{-IrO} \) which afforded the \( \alpha \)-amination product 13 in 87% yield and 89% ee, apparently through the intermediate formation of a nucleophilic iridium enolate complex (Scheme 4). Thus, \( \Delta\text{-IrO} \) is capable of catalyzing enolate chemistry as has been recently also demonstrated for a related iridium and rhodium complex and the observed enantioselective C-C bond formation can be explained with the stereoselective reaction between the chiral iridium enolate B and an intermediate iminium ion.

![Scheme 4](image)

**Scheme 4** The control experiment with dibenzyl diazodicarboxylate.

**Iminium chemistry**

The formation of the electrophile through chemical oxidation—replacing the photoinduced oxidation—also provides the desired C-C bond formation product in an enantioselective fashion as shown for the oxidant \( t\text{BuOOH} \) (Scheme 5). The oxidative formation of the iminium ion intermediate starting from the oxidation of \( \alpha \)-silylamine along the pathway of photoinduced single electron oxidation with a photoredox catalyst, followed by rapid desilylation, and further oxidation by air is well established and consistent with the observation that the absence of air completely suppresses the formation of the desired product.
Scheme 5 The control experiments with tBuOOH in the dark or without air.

4) The replacement of iridium catalyst $\Delta$-IrO with a dual catalyst system

Next, the requirement for a photoredox process was verified. We thereby exploited the circumstance that, in contrast to biscyclometalated iridium complexes which are well established photoredox catalyst, there are few cases for the analogous rhodium complex $\Delta$-RhO. The replacement of iridium in catalyst $\Delta$-IrO with rhodium $\Delta$-RhO therefore allows us to dissect the catalytic and photoredox activity of $\Delta$-IrO. Accordingly, the reaction of imidazole 7a with amine 9a in the presence of $\Delta$-RhO (2 mol%) under irradiation with visible light provided the C-C bond formation product 10a only in very low yield (6% after an elongated reaction time, compare entries 1 and 2 of Table 6). Revealingly, when combined $\Delta$-RhO with the established photoredox catalyst $[\text{Ir}(ppy)_2(\text{dtbbpy})]PF_6$ (1.0 mol%) or $[\text{Ru(bpy)}_3]\text{Cl}_2\cdot6\text{H}_2\text{O}$ (0.5 mol%), the reaction provided the product 10a with good conversions and high enantioselectivities. Consistent with our proposed mechanism, neither the Lewis acid catalyst $\Delta$-IrO (entry 2) nor photocatalyst (entries 3 and 4) alone are capable of catalyzing the asymmetric photoreaction, apparently because asymmetric enolate catalysis and photoinduced amine oxidation have to proceed hand in hand, which can be achieved with a dual catalyst system (entries 5 and 6) or even more efficiently with the single catalyst $\Delta$-IrO. It is also worth noting that the weaker photooxidant but highly efficient singlet oxygen sensitizer meso-tetraphenylpropyhrin (TPP) provides only a reduced yield of 30% after an elongated reaction time (entry 7), thereby supporting the notion that singlet oxygen does not have a major contribution to the observed oxidation of the $\alpha$-silylamines in this reaction scheme.
Table 6 Single versus dual catalysis for the photoactivated α-aminoalkylation of 2-acyl imidazoles.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>( t ) (h)</th>
<th>conv. (%)\textsuperscript{b}</th>
<th>ee (%)\textsuperscript{c}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{d}</td>
<td>( \Delta\text{-IrO} ) (2.0 mol%)</td>
<td>6.5</td>
<td>quant.</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>( \Delta\text{-RhO} ) (2.0 mol%)</td>
<td>16</td>
<td>6</td>
<td>n.d.</td>
</tr>
<tr>
<td>3</td>
<td>[Ir(ppy)(_2)(dtbbpy)]PF(_6) (1.0 mol%)</td>
<td>16</td>
<td>0</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>[Ru(bpy)(_3)]Cl(_2)6H(_2)O (0.5 mol%)</td>
<td>16</td>
<td>0</td>
<td>n.d.</td>
</tr>
<tr>
<td>5</td>
<td>( \Delta\text{-RhO} ) (2.0 mol%) + [Ir(ppy)(_2)(dtbbpy)]PF(_6) (1.0 mol%)</td>
<td>24</td>
<td>84</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>( \Delta\text{-RhO} ) (2.0 mol%) + [Ru(bpy)(_3)]Cl(_2)6H(_2)O (0.5 mol%)</td>
<td>24</td>
<td>72</td>
<td>94</td>
</tr>
<tr>
<td>7</td>
<td>( \Delta\text{-RhO} ) (2.0 mol%) + TPP(^e) (0.5 mol%)</td>
<td>24</td>
<td>30</td>
<td>90</td>
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</tbody>
</table>

\textsuperscript{a} Reaction conditions: Reactions performed in CH\(_2\)Cl\(_2\) (0.5 mL) with 2-acyl imidazole 7a (0.2 mmol) and α-silylamine 9a (0.6 mmol) at room temperature under an atmosphere of air while illuminating with a 12 W white light energy saving lamp. \textsuperscript{b} Determined by \(^1\)H NMR. \textsuperscript{c} Determined by chiral HPLC analysis; \textsuperscript{d} Shown for comparison. \textsuperscript{e} meso-Tetraphenylporphyrin. n.d. = not determined.

5) UV/Vis-absorption spectra

The absorbance spectra of the substrate 7a coordinated iridium complex A (Ar = Ph) and catalyst rac-\text{-IrO} were measured in solution of CH\(_2\)Cl\(_2\). As shown in Figure 45, the intermediate A absorbs visible light with a longer wavelength absorbance band in the visible region (\( \lambda_{\text{max,abs}} = 398 \) nm) compared to catalyst rac-\text{-IrO} (\( \lambda_{\text{max,abs}} = 375 \) nm).

![UV/Vis-absorbance spectra](image)

**Figure 45** UV/Vis-absorbance spectra of intermediate complex A and racemic catalyst \( \Delta/\Lambda\text{-IrO} \). Measured as solution in CH\(_2\)Cl\(_2\). a.u. = absorbance units.
6) Luminescence quenching experiments

In order to further verify the potential photoredox catalyst involving in the photoredox cycle, rac-IrO and intermediate A and [Ir(ppy)2(dtbbpy)]PF6 were selected to perform the luminescence quenching experiments with quencher 9a (Figure 46). Notably, [Ir(ppy)2(dtbbpy)]PF6 is a photoredox catalyst that has been used for the photo-oxidative cleavage of C-Si bond. The iridium complex A photoluminescence (λ_{max,em} = 516 and 552 nm) is efficiently quenched by the α-silylamine 9a in a dose dependent fashion as shown with a Stern-Volmer plot compared to catalyst rac-IrO and [Ir(ppy)2(dtbbpy)]PF6, which can be explained by a quenching of the excited state of A through electron transfer from the electron donor 9a.

Figure 46 Stern-Volmer plots. I_0 and I = luminescence intensities in the absence and presence of the indicated concentrations of the α-silylamine 9a, respectively. All experiments were performed in CH_2Cl_2.

7) Cyclic voltammetry measurements

The cyclic voltammetry was tested by Philipp Röse, a graduate student in Prof. Hilt group (Department of Chemistry, University of Marburg). From the DPV in combination with the emission spectrum (Figure 47), the excited state reduction potential (E^*_{red} = E_{red} + E_00) of complex A (Ar = Ph) can be estimated according to the Rehm-Weller approximation, with the E_00 transition energy calculated from the luminescence peak (λ_{max,em} = 516 nm, 2.403 eV) and E_{red} from DPV measurements (−0.98 V vs. Ag/AgCl): E^*_{red} = +1.4 V vs. Ag/AgCl in THF.
Figure 47 Cyclic voltammograms (CV) and differential pulse voltammograms (DPV) of the complex A and the reference iridium complex [Ir(ppy)₂(dtbbpy)]PF₆ in THF containing 0.1 M nBu₄NBF₄.

3.2.6 Conclusions

In conclusion, a visible light activated asymmetric aerobic α-aminoalkylation of 2-acyl imidazoles has been developed. From the perspective of the catalyst, it is intriguing that the metal center is capable of serving multiple functions at the same time: it constitutes the exclusive center of chirality, the catalytically active Lewis acid center, and additionally functions as the key component of the photoredox catalyst that is formed in situ. From the perspective of the catalytic reaction, the photo-oxidative activation and net oxidation of the here featured asymmetric catalysis complements our previous work on a redox neutral reaction in which the photoactivation occurred in a reductive fashion. It is fascinating that the metal-centered configuration (the exclusive source of chirality in the catalyst) retains throughout the catalysis, considering the oxidative conditions and the exposure to light. This conceptionally simple reaction scheme may provide new avenues for the green synthesis of non-racemic molecules.


9. The involvement of H$_2$O$_2$ in this process can be excluded since a reaction in the presence of H$_2$O$_2$ as an oxidant afforded the desired product only in low yields and with low enantiomeric excess (13% conversion after 16 h with 47% ee).


3.3 Asymmetric Radical-Radical Cross-Coupling through Visible Light Activated Iridium Catalysis

3.3.1 Reaction Design

A single chiral-at-metal iridium complex Δ-IrO has been proven to be very efficient dual function catalyst in visible light induced enantioselective α-aminoalkylation of 2-acyl imidazoles with silymethylamines (chapter 3.2).\(^1\) Despite its novelty, one may criticize that it is not atom economical reaction as a trimethylsilyl (TMS) group is released during the formation of α-aminoalkylation product. In this case, commercially available or easily prepared tertiary amines are more favorable as reducing agents in photoredox chemistry. Compared with the well established iminium ion, the application of α-aminoalkyl radical to asymmetric coupling reaction or nucleophilic addition under photoredox conditions still remains challenging (Figure 48).\(^2\)

![Figure 48](image)

**Figure 48** Two possible pathways for α-C(sp\(^3\))-H bond functionalization of tertiary amines by photoredox catalysis.

On the other hand, the enantioselective radical-radical cross-coupling reaction, which is used as a powerful tool for asymmetric transformations, still remains in its infancy when compared with other highly developed reactions.\(^3\) Normally, in order to control the selective bond formation, a persistent radical and a transient radical should be engaged in the radical-radical cross-coupling reaction according to the persistent radical effect.\(^4\) Therefore, we envisioned that it is possible to transfer the reactive ketyl radical to a persistent one by stabilizing it through coordination to the chiral iridium Lewis acid catalyst after protonation. Then, once a transient carbon-centered radical is added, a selective radical-radical cross-coupling reaction could be achieved. Herein, we designed a catalytic and asymmetric process that closely interlocks a visible light activated single electron transfer between two substrates with the stereocontrolled radical-radical cross-coupling of an intermediate radical pair, namely the
enantioselective redox coupling of ketones with tertiary amines to 1,2-diaminoalcohols (Figure 49). A big challenge is whether the α-amino radical and ketyl radical could be simultaneously generated in a single photoredox catalytic cycle.

![Figure 49 Linking (photoinduced) single electron transfer between a donor substrate and an acceptor substrate to asymmetric radical-radical recombination with a single iridium catalyst.](image)

### 3.3.2 Initial Experiments and Reaction Optimization

The study was started by investigating the reaction of 2-acetyl imidazole 14a' with tertiary amine 15a under photoredox conditions (Table 7). In the presence of the previously developed dual function photoredox/chiral Lewis acid catalyst Δ-IrO\(^{1}\) (3 mol%) under irradiation with a 23 W compact fluorescent lamp (CFL), the desired product 16a' was not observed (entry 1). Encouragingly, using instead the more electron-deficient trifluoroacetyl imidazole 14a provided the coupling product 16a with 69% yield and 95% ee (entry 2). Replacing the solvent CH\(_2\)Cl\(_2\) with CHCl\(_3\) improved the yield to 75%, albeit under the cost of slightly reduced enantioselectivity (entry 3). The reaction is very sensitive to solvent effect and other tested solvents did not provide satisfactory results (entries 4-6). With the catalyst Δ-IrS instead of Δ-IrO, yields and enantioselectivities could be further enhanced (entries 7 and 8). In CHCl\(_3\), 82% yield and excellent 98.6% ee were observed. Effects of N-substitutions on the 2-acyl imidazoles were also investigated (entries 9-11) and the best results were still obtained with the N-phenyl imidazole substrate 14a. Control experiments in the absence of the catalyst or in the dark demonstrate that this reaction crucially depends on the presence of the iridium catalyst and light, otherwise no traces of product were monitored (entries 12 and 13). It is also worth noting that no C-C coupling product is formed when using the common photoredox catalyst [Ru(bpy)\(_3\)]Cl\(_2\)-6H\(_2\)O or [Ir(ppy)\(_2\)(dtbbpy)]PF\(_6\) or a dual catalyst system combining [Ir(ppy)\(_2\)(dtbbpy)]PF\(_6\) and Δ-RhO (entries 14-16).\(^5\)
**Table 7** Initial experiments and optimization of the visible light induced asymmetric C-C bond formation.$^a$

![Chemical structure](image)

$^a$ Reaction conditions: 2-acyl imidazoles 14 (0.2 mmol), amine 15a (0.6 mmol), and catalyst (entries 1-13, 16: 3.0 mol%, entry 14: 0.5 mol%, entry 15: 1.0 mol%) in the indicated solvent (0.4 mL) irradiated for 22 h under an atmosphere of nitrogen at room temperature. $^b$ Light source: 23 W compact fluorescent lamp (CFL) at a distance of approximately 5 cm from the Schlenk tube. $^c$ Isolated yields. $^d$ Determined by HPLC on chiral stationary phase. n.d. = not determined.
3.3.3 Substrate Scope

Having identified the optimal conditions for this visible light activated asymmetric aminoalkylation of trifluoromethyl ketones, the scope of the amine partner was first examined (Figure 50). The reactions between 2-trifluoroacetyl imidazole 14a and various N-methyldiarylamines (15a-h) provided the respective 1,2-aminoalcohols (16a-h) in satisfactory yields (60-82%) and with high enantioselectivities (91-98% ee). Crystal structure of 16g was obtained to determine the absolute configuration of the products. However, the two aryl groups, which reduce the oxidation potential of amines, are required for obtaining satisfactory results. When one aryl group was replaced by heterocyclic group (-Py) or aliphatic group (-Me), the C-C bond formation products were obtained with very low yields (Figure 51). It is noteworthy that we found empirically that certain reactions provide better results under white light irradiation (CFL), whereas others prefer blue light (blue LEDs).

![Chemical Structures](image)

**Figure 50** Substrate scope with respect to N-methyldiarylamines.
Cyclic tertiary amines are relatively simple to synthesize and have been successfully utilized in the α-amino radical chemistry to generate α-heteroaryl amines by MacMillan and other research groups.\(^6\)

Herein, the reaction of substrate 14a with 2-phenylisoindoline was investigated. However, the expected α-aminoalkylation product was not observed. Encouragingly, by using a more reactive N-phenyl tetrahydroisoquinoline as radical precursor, the C-C bond formation product 18a was obtained with diastereoselectivity of 3:1 \(\text{dr}\) and enantioselectivity of 72% \(\text{ee}\) (the major diastereoisomer), and at a catalyst loading of 5 mol%, even 8:1 \(\text{dr}\) and 94% \(\text{ee}\) were reached (Figure 52).

Thus, the substrate scope with respect to N-aryl tetrahydroisoquinolines was tested by using 5 mol% \(\Lambda\text{-IrS}\) (Figure 53). As expected, a series of C-C bond formation products (18a-f) were obtained with good diastereoselectivities (4:1 to 10:1 \(\text{dr}\)) and high enantioselectivities (94-98% \(\text{ee}\)) (Figure 53).

Notably, a bromine (Br) substituent promoted the product excellent yield and enantioselectivity. However, a \(p\)-methoxyphenyl (PMP) substituent, which serves as a well-established protecting group for the nitrogen atom,\(^7\) can not be used here because of the limited stability of the product.
Figure 53 2-Aryl-1,2,3,4-tetrahydroisoquinolines as amine substrates for enantio- and diastereoselective reactions. Relative configurations are assigned based on a crystal structure of 18a. n.d. = not determined.

Another interesting aspect to investigate with this aminoalkylation chemistry would be to extend the imidazole moiety to other coordination groups. Herein, 2-acyl pyridines were chosen due to the prevalence of pyridines and piperidines in bioactive compounds. The reaction of 2-trifluoroacetyl pyridine with amine 15a in the presence of catalyst Λ-IrS (3 mol%) under irradiation with a 24 W blue LEDs afforded the coupling product 20a with 74% yield and 93% ee. Steric effect of the pyridine substrates in this asymmetric aminoalkylation was then investigated. By using pyridine substrate with methyl substitute group at 4 and 5-position, the C-C bond coupling products 20b and 20c were afforded with moderate yields and good enantioselectivities, while 3-position substituted pyridine substrate was failed to convert to the desired product 20d efficiently. Further investigation of other coordination groups, such as thiazole and ester, did not give any satisfactory results (Figure 54).

Figure 54 Asymmetric C-C bond cross coupling with other coordination groups.
3.3.4 Plausible Mechanism

A plausible mechanism is shown in Figure 55. The catalytic process starts with the photoactivation of the iridium-coordinated trifluoromethyl ketone I to its excited state II (step 1), which induces a single electron transfer from a tertiary amine, thereby generating an amino radical cation in addition to a reduced iridium complex which can be described as an iridium-coordinated ketyl radical III (step 2). This is followed by a proton transfer (step 3) and a radical-radical cross-coupling between the electron-rich α-amino radical and the electron-deficient ketyl IV (step 4) which is stereochemically controlled by the chiral iridium complex V. Finally, the product is replaced by a new substrate (step 5). Several investigations have been executed to verify the proposed mechanism in the following section.

Figure 55 Putative mechanism for the visible light activated catalytic asymmetric process.
3.3.5 Mechanistic Investigations

1) Substrate-coordinated iridium complex IrS-I

To start with, the iridium intermediate complex IrS-I was synthesized by reacting of substrate 14a with Δ/Λ-IrS in toluene/CHCl₃ at 50 ºC overnight. The freshly prepared complex IrS-I catalyzed the photoinduced C-C bond coupling reaction with an almost identical efficiency compared to Λ-IrS (Figure 56). In addition, the absorbance spectra of racemic Δ/Λ-IrS and intermediate complex IrS-I were measured in solution of CHCl₃ (0.2 mM). As shown in Figure 57, compared to Δ/Λ-IrS, the complex IrS-I displays a bathochromically shifted long wavelength absorbance maximum with an additional shoulder at around 600 nm. With the efficient catalytic reactivity and good absorption property, complex IrS-I is most likely the active photoredox catalyst in the catalytic cycle mentioned above.

![Figure 56](image1.png)

**Figure 56** Evaluation of the catalytic activity of intermediate complex IrS-I.

![Figure 57](image2.png)

**Figure 57** UV/Vis-absorbance spectra of Δ/Λ-IrS and intermediate complex IrS-I. Measured in solution of CHCl₃ (0.2 mM). a.u. = absorbance units.
2) Control experiments

*Control experiment in the presence of air*

The reaction was performed in a 10 mL test tube under an atmosphere of air (air balloon), no C-C coupling product was formed (detected by crude $^1$H NMR of the mixture after 22 h of irradiation), being consistent with the presence of intermediate radicals which react with oxygen in a diffusion controlled fashion.

![Scheme 6 Control experiment in the presence of air.](image)

*Control experiment in the dark with chemical initiator*

Can the reaction be chemically initiated, potentially with a chemical one-electron oxidant? If so, a reaction conducted in the dark but in the presence of the iridium complex as a Lewis acid might be able to determine whether there is turnover (a chain) or not.$^9$ Thus, the reaction was performed in the dark in the presence of catalyst $\Delta/\Lambda$-IrS and one-electron oxidant, like Cp$_2$FePF$_6$, (BrC$_6$H$_4$)$_3$NSbCl$_6$ and Ce(NH$_4$)$_2$(NO$_3$)$_6$. However, no C-C bond coupling product 16a was detected by $^1$H NMR after stirring at room temperature for 22 h. It provides good evidence that no chain process exists in the catalytic cycle (Figure 58).

![Figure 58 Control experiment in the dark with chemical initiators.](image)
3) Trapping experiments

**Trapping experiments of α-aminomethyl radical**

Trapping experiments of electron-rich α-aminomethyl radicals have been well established. In the presence of dibenzyl azodicarboxylate, a hydrazone C-N coupling product is formed in high yield which can be traced back to a reaction of the proposed intermediate (nucleophilic) α-aminomethyl radical with the (electrophilic) N=N double bond, followed by reduction and protonation. Likewise, in the presence of EWG-alkene acrylonitrile or methyl acrylate, the addition/cyclization product 22a or 22b together with 16a are afforded, which again provide good evidence to demonstrate the existence of α-aminomethyl radical (Figure 59).

![Reaction Scheme]

**Figure 59** Trapping experiments of α-aminomethyl radical.

**Trapping experiment of ketyl radical**

Pinacol coupling product was not observed from the model reaction which probably because the resulting stabilized ketyl radical III is a persistent radical that possesses relatively little propensity towards homodimerization. To capture the ketyl radical, electron rich alkene, ethene-1,1-diyldibenzene, was used under the modified reaction conditions. Unfortunately, only the aminoalkylation product 16a was observed (Scheme 7). Since the evidence of ketyl radical is limited, radical addition pathway which electron-rich α-aminomethyl radical adds to the iridium-coordinated electron-deficient C=O double bond could not be completely excluded.
Chapter 3: Results and Discussion

**Scheme 7** Trapping experiment of ketyl radical in the presence of ethene-1,1-diyldibenzene.

4) Quantum yield

The quantum yield was measured by standard ferrioxalate actinometry. The relevant data was collected and calculated by Xiaodong Shen (a former Ph.D. student in the Meggers group). The moles of products formed were determined by crude $^1$H NMR. The quantum yield of the model reaction $14a + 15a \rightarrow 16a$ with ferrioxalate actinometry was determined to be 0.09. A quantum yield of $\leq 1$ in agreement with the expected closed catalytic cycle. According to the control experiments in the presence of chemical one-electron oxidants and quantum yield, it is safety to say that no chain process is possible with one photon being required for each C-C bond formation event.\(^{12}\)

5) Stereochemistry model

The photogenerated $\alpha$-amino radical interacts with the persistent ketyl radical within the chiral environment of the iridium complex, which provides impressively high enantioselectivity. The observed absolute configuration of the C-C bond coupling reaction, providing $S$-configuration at the carbon next to the OH group when using $\Lambda$-IrS, is consistent with this mechanistic picture in which the prochiral $Si$-face of the iridium-coordinated ketyl is effectively shielded by one tert-butyl group of the propeller-type ligand sphere, providing an excellent stereochemical control of the radical process (Figure 60).

![Figure 60](image.png)  
**Figure 60** Model for the asymmetric induction in the course of the radical-radical recombination shown for selected substrates.
3.3.6 Conclusions

In conclusion, a unique catalytic asymmetric process in which a visible light driven single electron transfer reaction between a donor substrate and a catalyst-bound acceptor substrate is followed by a stereocontrolled radical-radical recombination was introduced. Using a chiral iridium complex as dual chiral Lewis acid/photoredox catalyst, 1,2-aminoalcohols are synthesized from trifluoromethylketones and tertiary amines with high enantioselectivities of up to 99\% ee. Such non-racemic CF$_3$-containing compounds might be useful building blocks for the synthesis of bioactive compounds.$^{17}$ It is also worth noting that this mild method follows the spirit of sustainable chemistry, not only because the activation energy is provided by visible light as an abundant light source, but also since in the course of the C-C bond formation with the implementation of one or two new stereocenters, no waste products are generated, thereby constituting a perfect atom economy.
References


3.4 Catalytic Asymmetric C(sp\(^3\))-H Functionalization under Photoredox Conditions by Radical Translocation and Stereocontrolled Alkene Addition

### 3.4.1 Reaction Design

In chapter 3.3, we developed a catalytic asymmetric C(sp\(^3\))-H functionalization protocol that allows tertiary amines to undergo α-aminoalkylation of trifluoromethyl ketones to achieve 1,2-diamino alcohols (through radical-radical cross-coupling). Besides the functional group at its α-position, there are many other powerful strategies that have been emerged for the functionalization of C(sp\(^3\))-H bonds.\(^1\)

Recently, Chen and co-workers introduced a visible light induced release of alkoxyl radicals from N-alkoxyphthalimides and applied it to the selective C(sp\(^3\))-H functionalization by exploiting an 1,5-hydrogen atom transfer (1,5-HAT).\(^2\) Radical translocation\(^3\) has been used extensively for the functionalization of remote C(sp\(^3\))-H bonds, but to our knowledge the combination with a catalytic asymmetric C-C bond formation remains elusive. Therefore, we envisioned to merge this photoredox-mediated C-H functionalization with asymmetric catalysis as shown in Figure 61 by trapping the intermediate (electron rich) carbon-centered radical in a stereocontrolled fashion with an acceptor-substituted alkene catalyzed by a chiral Lewis acid. Challenges include the compatibility of the individual steps with respect to the reactivity of the radical intermediates and the kinetics of the individual steps, as well as the ability to control the relative and absolute stereochemistry of the radical reaction in a catalytic fashion.

**Figure 61** Reaction design of photoredox-mediated C-H functionalization with asymmetric catalysis.
3.4.2 Initial Experiments and Reaction Optimization

This study was started by investigating the reaction of α,β-unsaturated acyl imidazole 24a' with N-alkoxyphthalimide 25a and Hantzsch ester (HE) under photoredox conditions. In the presence of the previously developed dual function photoredox/chiral Lewis acid catalyst Δ-IrS₄ (3 mol%), to our disappointment, the desired product 26a' was not achieved. Encouragingly, when α,β-unsaturated acyl pyrazole 24a was used as a Michael acceptor instead, the C-C bond formation product 26a was obtained in 85% yield after irradiation of 20 h. However, no enantioselectivity was observed (Figure 62).

![Figure 62](initial-experiments-two-different-michael-acceptors.png)

Thus, the optimization began with the reaction of α,β-unsaturated acyl pyrazole 24a and N-alkoxyphthalimide 25a under photoredox conditions (Table 8). When the dual catalyst system of a chiral Lewis acid Δ-RhO₅ (3 mol%) in combination with a photoredox catalyst fac-[Ir(ppy)_3] (1 mol%) was applied to this system, the reaction proceeded in 60% yield and 18% ee (entry 1). The enantioselectivity was improved to 79% ee when Δ-RhS₆ (3 mol%) was used as the chiral Lewis acid (entry 2). At a catalyst loading of 8 mol%, even 92% ee was reached (entry 5). Other photoredox catalysts, such as [Ir(ppy)₂(dtbbpy)]PF₆ and [Ru(bpy)₃](PF₆)₂, were inferior to fac-[Ir(ppy)₃] (entries 3 and 4). The reaction is sensitive to solvent effects (entries 6 and 7) and the light source, as blue LEDs provided a somewhat lower enantioselectivity (entry 8). Control experiments verified that both visible light and Hantzsch ester are essential for product formation (entries 9 and 10). In the absence of the chiral Lewis acid Δ-RhS, product 26a was still formed (75% yield), albeit as a racemic mixture (entry 11). It is worth noting that in the absence of the additional photoredox catalyst fac-[Ir(ppy)₃] (entry 12) or both fac-[Ir(ppy)₃] and Δ-RhS (entry 13), the product 26a was still generated but with significantly reduced efficiency. UV/Vis-absorbance spectra of the individual substrates and Hantzsch ester suggest that this should be due to the direct photoexcitation of the Hantzsch ester.⁷
Table 8 Reaction development.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>photoredox catalyst</th>
<th>(h) (^b)</th>
<th>solvent</th>
<th>(t) (h)</th>
<th>yield (%) (^c)</th>
<th>ee(%) (^d)</th>
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<td>(\Delta\text{-RhO}) (3.0)</td>
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<td>CFL</td>
<td>THF</td>
<td>20</td>
<td>60</td>
<td>18</td>
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<tr>
<td>2</td>
<td>(\Delta\text{-RhS}) (3.0)</td>
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<td>CFL</td>
<td>THF</td>
<td>20</td>
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<td>THF</td>
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<td>60</td>
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<td>blue LEDs</td>
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</table>

\(^a\)Reaction conditions: 2-Acyl pyrazole 24a (0.4 mmol), N-alkoxyphthalimide 25a (0.2 mmol), Hantzsch ester (none or 0.3 mmol) with chiral Lewis acid catalyst (none or 3 or 8 mol%) and photoredox catalyst (none or 1 mol%) in solvent (1.0 mL) at room temperature for 20-40 h under an atmosphere of nitrogen.  
\(^b\) 23 W compact fluorescent lamp (CFL) or 6 W blue LEDs.  
\(^c\) Isolated yield.  
\(^d\) Enantiomeric excess determined by HPLC on chiral stationary phase.  
\(^e\) Control experiment without Hantzsch ester. n.a. = not applicable, n.d. = not determined.

It is worth noting that compared to N-alkoxyphthalimide 25a (n = 1), N-alkoxyphthalimide 25a\(^\prime\) (n=0) and 25a\(^\prime\prime\) (n=2) were not suitable for the reaction (Figure 63). The results are in agreement with Curran’s work\(^8\) and can be rationalized by the possible transition state involved in the HAT process. It is currently accepted that the ideal arrangement of the three atoms involved in the transition state of intramolecular HAT is linear (low energetic cost). The six-membered transition structure can readily accommodate a C-H-O angle close to 180°. Thus, 1,5-HAT is a more favorable process compare to 1,4-HAT or 1,6-HAT.
3.4.3 Substrate Scope

After the optimized conditions were established, we next tested the substrate scope of the asymmetric photoinduced C(sp³)-H functionalization. Figure 64 shows that the reaction of a variety of 2-acyl pyrazoles 24a-j with N-alkoxyphthalimide 25a in the presence of Λ-RhS, fac-[Ir(ppy)_3] and Hantzsch ester while illuminating with visible light provided the expected C-C bond formation products 26a-j in 51-80% yields and 82-97% ee. The reaction was tolerant of aliphatic substituents, regardless of acyclic and cyclic paraffins (26a-f). Notably, ethoxy- and benzyloxy-substituted 24g and 24h are favorable here, affording the corresponding products 26g and 26h in good yields and high stereoselectivities, respectively. The electronic effects have a significant influence upon substituents on the aromatic moieties, and with electron-donating substituents, the radical addition products (26i and 26j) were obtained in moderate yields and good enantioselectivities. As for the aromatic moiety with no substituent or electron-withdrawing substituent, the undesired reductive homocoupling of alkene was the main process.⁹
To further expand the scope, a wide range of tertiary N-alkoxyphthalimides were applied to the reaction, affording the adducts in 54-85% yields and with 86-97% ee (26m-26u). Secondary N-alkoxyphthalimide with aromatic substitutes were also suitable for the reaction and afforded the corresponding products (26v and 26w) with diastereoselectivities of up to 3:1 and enantioselectivities of up to 97% ee (Figure 65). The effort to improve the diastereoselectivity by changing reaction temperature or catalyst loadings of $\Delta$-RhS was not succeeded. In addition, this $\alpha$-heteroatom activation is not limited by oxygen, $\alpha$-sulfur activated C-H bonds also work well under the standard condition (Figure 66), while $\alpha$-nitrogen activated C-H bonds could not give satisfactory results. For unactivated C-H bonds, low yields may be rationalized by high reactivity of the intermediate alkoxyl radical or carbon-centered radical and once generated, it was rapidly trapped by Hantzsch ester, thereby forming alcohol as a side product.
Figure 65 Substrate scope with respect to N-alkoxyphthalimides. Crystal structure of 26t was obtained to determine the absolute configuration of the products.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Substrate</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Substrate" /></td>
<td><img src="image2" alt="Product" /></td>
<td>38 h, 49% yield, 86% ee</td>
<td>45 h, 72% yield, 92% ee</td>
</tr>
<tr>
<td><img src="image3" alt="Substrate" /></td>
<td><img src="image4" alt="Product" /></td>
<td>not observed</td>
<td>not observed</td>
</tr>
<tr>
<td><img src="image5" alt="Substrate" /></td>
<td><img src="image6" alt="Product" /></td>
<td>&lt; 5% yield</td>
<td>20 h, 18% yield (24 W blue LEDs)</td>
</tr>
</tbody>
</table>

Figure 66 Limitation with respect to N-alkoxyphthalimides.
The formation of quaternary carbon stereocenters in a catalytic enantioselective fashion is promising and challenging. Unfortunately, the reactions of several 2-acyl pyrazoles with N-alkoxyphthalimide $25\text{a}$ for the construction of quaternary carbon stereocenters were not succeeded under standard conditions (Figure 67). Comparing to Melchiorre’s recent work, we thought that the chiral Lewic acid catalyst $\Delta$-RhS might not efficiently activate 2-acyl pyrazoles with two substituted groups in $\beta$-position due to its crowded coordination atmosphere.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
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<tbody>
<tr>
<td><img src="image1" alt="" /></td>
<td>not observed</td>
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<tr>
<td><img src="image2" alt="" /></td>
<td>not observed</td>
</tr>
<tr>
<td><img src="image3" alt="" /></td>
<td>not observed</td>
</tr>
<tr>
<td><img src="image4" alt="" /></td>
<td>not observed</td>
</tr>
</tbody>
</table>

**Figure 67** Some limitations for the construction of quaternary carbon stereocenters.

It is noteworthy to mention that N-acyl pyrazole is a very useful precursor for the conversion into other functionality. As shown in Figure 68, the aminolysis of product $26\text{s}$ underwent smoothly to yield $27$ without compromise any of enantiopurity, while the treatment of $26\text{s}$ with NaBH$_4$ afforded diol $28$ without detectable racemization.$^{11}$

**Figure 68** Exemplary transformations starting with one N-acyl pyrazole.
3.4.4 Plausible Mechanism

A plausible mechanism is shown in Figure 69 and starts with the photoactivation of $\text{fac-}[\text{Ir(ppy)}_3]$, whose excited state $[\text{Ir(ppy)}_3]^*$ is reductively quenched by the Hantzsch ester. Thereby generated $\text{fac-}[\text{Ir(ppy)}_3]^{-}$ serves as a strong reducing agent and transfers a single electron to $N$-alkoxyphthalimide (redox handle) under formation of an $N$-alkoxyphthalimide radical anion, which is subsequently protonated by the oxidized Hantzsch ester (radical cation), and then undergoes a homolytic N-O bond cleavage under formation of an alkoxy radical. The alkoxy radical engages in an intramolecular 1,5-hydrogen atom transfer (HAT) to yield a carbon-centered radical, which adds to $N,O$-rhodium-coordinated 2-acyl pyrazole substrate ($\text{RhS-I}$), thereby generating the secondary radical intermediate ($\text{RhS-II}$). This radical intermediate is further trapped by the Hantzsch ester radical to provide rhodium-bound product ($\text{RhS-III}$). The observed high enantioselectivity in this new process demonstrates that the chiral Lewis acid $\Delta$-$\text{RhS}$ strongly accelerates the radical addition so that it is capable of outcompeting the prevailing racemic background reaction.

![Figure 69 Proposed mechanism which is consistent with the observed product formation and the mechanistic experiments.](image-url)
3.4.5 Mechanistic Investigations

1) Crystal structure analysis of the proposed rhodium intermediate RhS-I

The catalytic cycle was first investigated by verifying the involvement of the proposed rhodium intermediate RhS-I. Accordingly, upon reaction of an excess substrate 24a with racemic A/Δ-RhS we could isolate the proposed intermediate RhS-I. A crystal structure of intermediate RhS-I is shown in Figure 70 (left). The stereocontrol model reveals that a Δ-configuration at the rhodium center shields the Re-face of the carbon in β-position and directs the addition of the electron-rich radical to the Si-face, thereby being consistent with the observed R-configuration of the alkylation product when using the catalyst with Δ-configuration at the metal (Figure 70, right).

![Crystal structure of intermediate RhS-I](image)

Figure 70 Crystal structure of proposed intermediate RhS-I (left, hydrogen atoms and the hexafluorophosphate counteranion are omitted for clarity) and stereochemical model (right).

2) Isolation of byproducts and a side product

Isolation of byproducts

The expected byproducts diethyl 2,6-dimethylpyridine-3,5-dicarboxylate (29) and isoindoline-1,3-dione (30) could be isolated under the standard conditions. Accordingly, compound 29 was generated by oxidation of Hantzsch ester, while compound 30 was formed by reduction of N-alkoxyphthalimide 25a.

![Scheme 8 Isolation of byproducts 29 and 30](image)
**Isolation of a side product**

2-((1-Tosylazetidin-3-yl)oxy)ethanol 31 was isolated as a side product with 15% yield in the relatively sluggish conversion reaction Scheme 9. This further supports our proposed mechanism and can be explained by a competing undesired reduction of the initial oxygen- or carbon-centered radicals.

![Scheme 9](image)

**Scheme 9** Isolation of a side product 31.

**3) Control reactions**

The presence of air or the radical inhibitor BHT (5 eq.) results in a reduced yield and enantioselectivity of the C-C bond formation product 26a, which provides evidence for a radical pathway (Scheme 10). The intermediate carbon-centered radical serving as a relatively stabilized radical that could not be trapped efficiently by oxygen or BHT. These results are in agreement with Haohua Huo’s work and may explain why the product 26a was still formed with about 45% yield.

![Scheme 10](image)

**Scheme 10** Probing radical pathway in the presence of air or BHT.

**4) Trapping experiments**

The proposed intermediate carbon-centered radical was verified by trapping experiments with competing electron deficient alkenes (Scheme 11). For example, when 2 equivalents of ((2-phenylallyl)sulfonyl)benzene 32 were added to the reaction under standard conditions, the C(sp³)-H allylation adduct 33 was isolated with 18% yield. N-arylacrylamides are currently magic reagents for trapping carbon radicals by sequential intermolecular addition of radicals followed by intramolecular cyclization. When 2 equivalents of N-methyl-N-phenylmethacrylamide 34 were added to the reaction
under modified conditions, the addition/cyclization product 35 was isolated as a yield of 18%.

Scheme 11 Trapping experiments in the presence of alkene 32 or 34.

5) UV/Vis-absorption spectra

The absorption spectra of the possible metal photoredox catalysts of the reaction were measured in THF. As shown in Figure 71, not only fac-[Ir(ppy)$_3$] ($\lambda_{\text{max}} = 370$ nm) but also the Lewis acid catalyst RhS ($\lambda_{\text{max}} = 395$ nm) and the intermediate RhS-I ($\lambda_{\text{max}} = 390$ nm) have absorption in the visible region.

![Absorption Spectra Graph](image)

**Figure 71** UV/Vis-absorption spectra of the used photoredox catalyst, the Lewis acid catalyst RhS and intermediate RhS-I. Measured as solutions in THF (0.2 mM). a.u. = absorbance units.

The absorption spectra of the substrate 25a and Hantzsch ester were measured in THF as well. As shown in Figure 72, substrate 25a does not absorb in the visible part of the spectrum, while the Hantzsch ester exhibits an absorption band in the near UV, with a maximum at about 350 nm. Notably, the absorbance of the mixture of 25a and Hantzsch ester is the same as that of Hantzsch ester in the visible light region. The absorption spectrum of Hantzsch ester and control experiment (Table 8, entry 13)
support that the Hantzsch ester can also be photoexcited and reduce the \( N \)-alkoxyphthalimide in the absence of \( \text{fac-}[\text{Ir(ppy)}_3] \) and \( \text{RhS} \), but it is not the major pathway of the \( N \)-alkoxyphthalimide reduction.

![UV/Vis-absorption spectra of substrate 25a and Hantzsch ester](image)

**Figure 72** UV/Vis-absorption spectra of substrate 25a and Hantzsch ester. Measured as solutions in THF (2 mM). a.u. = absorbance units.

6) Luminescence quenching experiments

*Quenching experiments with fac-\([\text{Ir(ppy)}_3]\) in the absence of intermediate RhS-I*

Stern-Volmer plots (Figure 73) illustrate that the luminescence emission of \( \text{fac-}[\text{Ir(ppy)}_3] \) is quenched efficiently by the Hantzsch ester, in contrast to the substrates 2-acyl pyrazole 24a or \( N \)-alkoxyphthalimide 25a, which supports the proposed catalytic mechanism in which electron transfer from Hantzsch ester to the excited state \( \text{fac-}[\text{Ir(ppy)}_3]^+ \) occurs and is at the center of the redox process. This observation is also in agreement with recent studies by Chen.²

![Stern-Volmer plots](image)

**Figure 73** Stern-Volmer plots. \( I_0 \) and \( I \) are respective luminescence intensities in the absence and presence of the indicated concentrations of the corresponding quencher.
Quenching experiments with fac-[Ir(ppy)₃] in the presence of intermediate RhS-I

When the quenching experiments were performed in the presence of intermediate RhS-I, a decreased luminescence of fac-[Ir(ppy)₃] was observed. Despite the lower luminescence intensity of the iridium sensitizer, the quenching of the photoexcited state of fac-[Ir(ppy)₃] by Hantzsch ester can be observed which is demonstrated by the emission intensity of the mixture solution of fac-[Ir(ppy)₃] and intermediate RhS-I and Hantzsch ester (Figure 74).

Figure 74 Emission spectra of the photoactive species. The photoactive species were measured as solutions in THF (0.2 mM). a.u. = arbitrary unit.

7) Quantum yield measurement

The quantum yield was measured by standard ferrioxalate actinometry. The moles of product formed was measured by GC analysis using dodecane as internal standard (for details, see experimental part). The quantum yield of the model reaction 24a + 25a \( \rightarrow \) 26a with ferrioxalate actinometry was determined to be 0.05 which is consistent with the proposed absence of a chain process.¹⁵
3.4.6 Conclusions

In summary, this work shows how C(sp³)-H bond functionalization through radical translocation can be merged with a catalytic asymmetric C-C bond formation by combining visible light activated photoredox catalysis with chiral Lewis acid catalysis. By using dual catalysis strategy, radical addition products were achieved with enantioselectivities of up to 97% ee, and with some diastereoselectivity (3:1 dr). We believe that this method is practically valuable since it makes use of the functionalization of unactivated C(sp³)-H bonds, at the same time introduces two stereocenters, and employs simple activating groups, namely N-alkoxyphthalimides as known redox-active radical precursors, as well as N-acyl pyrazoles as Lewis-acid-activatable functional groups.

References


Chapter 3: Results and Discussion

7 For photoinduced electron transfer by direct excitation of Hantzsch ester with visible light, see also:
Chapter 4: Summary and Outlook

4.1 Summary

In this thesis, a class of octahedral chiral-at-metal complexes $\text{IrO(S)}$ and $\text{RhO(S)}$ have been successfully applied to asymmetric reactions (Figure 75). Accordingly, rhodium complexes $\Delta\text{-RhO}$ and $\Delta\text{-RhS}$ have been demonstrated as very efficient chiral Lewis acid catalysts in asymmetric Michael additions and visible light induced asymmetric Giese radical addition, respectively. Iridium complexes $\Delta\text{-IrO}$ and $\Lambda\text{-IrS}$ have been proven to be capable of serving as dual chiral Lewis acid/photoredox catalysts in visible light activated asymmetric $\alpha$-aminoalkylation and radical-radical cross-coupling reaction, respectively. These novel octahedral chiral-at-metal iridium and rhodium complexes provide new opportunities for the efficient and economical synthesis of highly enantioenriched molecules.

Figure 75 An overview for the thesis.
1) Asymmetric Lewis acid catalysis directed by octahedral rhodium centrochirality

Figure 76 Enantiomers of a substitutionally labile yet configurationally stable chiral-at-metal rhodium(III) Lewis acids $\Lambda$-RhO and $\Delta$-RhO.

A rhodium-based asymmetric catalyst which derives its optical activity from octahedral centrochirality was introduced (Figure 76). The chiral Lewis acid complexes $\Lambda$-RhO and $\Delta$-RhO were synthesized according to chiral proline-mediated strategy developed by the Meggers group. Accordingly, the reaction of dimer rac-2 with D-proline afforded the prolinato-rhodium complexes $\Delta$-(R)-3 and $\Lambda$-(R)-3 as a mixture of diastereomers, and $\Delta$-(R)-3 is isolable in a straightforward fashion with high purity by just washing the mixture of diastereomers with CH$_2$Cl$_2$/Et$_2$O. The virtually enantiopure $\Delta$-RhO was yielded after stereospecific substitution of D-proline by two acetonitrile ligands. The mirror-imaged complex $\Lambda$-RhO is accessible in an analogous fashion by using the chiral auxiliary L-proline instead (Figure 77).

Figure 77 Synthesis of the enantiomerically pure Lewis acid complexes $\Lambda$-RhO and $\Delta$-RhO.

Besides providing the exclusive source of chirality, the rhodium center serves as a Lewis acid by activating 2-acyl imidazoles through two-point-binding and enabling a very effective asymmetric induction mediated by the propeller-like C$_2$-symmetrical ligand sphere. Applications of asymmetric
Michael additions as well as asymmetric cascade reaction are disclosed, for which the rhodium catalyst is found to be overall superior to its iridium congener (Figure 78). By virtue of its straightforward proline-mediated synthesis, high catalytic activity, and tolerance towards moisture and air, this novel class of chiral-at-rhodium catalysts has been proven to be of widespread use for a variety of asymmetric transformations in the Meggers group.

![Catalytic asymmetric conjugate additions and cascade reaction catalyzed by Δ-IrO and Δ-RhO.](image)

**Figure 78** Catalytic asymmetric conjugate additions and cascade reaction catalyzed by Δ-IrO and Δ-RhO.
2) Merger of visible light induced oxidation and enantioselective alkylation with chiral iridium catalyst

A visible light activated asymmetric α-aminoalkylation of 2-acyl imidazoles catalyzed by a single chiral iridium complex was developed. In the presence of a conventional household lamp and under an atmosphere of air, the oxidative coupling of 2-acyl-N-phenyl imidazoles with α-silylamines provide aminoalkylated products in 61-93% yields with high enantioselectivities (90-98% ee). Mechanistically, the catalytic cycle is started by the formation of the substrate coordinated intermediate A. The subsequent deprotonation in α-position of the carbonyl group affords the nucleophilic iridium enolate intermediate B. The reaction of the enolate complex B with the newly formed iminium ion (generated by an iridium-photocatalyzed oxidation of the α-silylamine with oxygen serving as the terminal oxidant) occurs in a stereocontrolled fashion dictated by the metal-centered chirality and provides the iridium coordinated product C. The intermediate C subsequently released the product upon coordination to a new substrate, thereby initiating a new catalytic cycle (Figure 79). This conceptionally simple reaction scheme may provide new avenues for the green synthesis of chiral molecules.

![Figure 79: Visible light activated asymmetric α-aminoalkylation of 2-acyl imidazoles with a chiral iridium complex Δ-IrO. PC = photoredox catalyst.](image-url)
3) Asymmetric radical-radical cross-coupling through visible light activated iridium catalysis

A catalytic process of asymmetric radical-radical cross-coupling through visible light activated iridium catalysis was introduced. Combining single electron transfer between a donor substrate and a catalyst-activated acceptor substrate with a stereocontrolled radical-radical recombination enables the catalytic enantio- and diastereoselective synthesis of 1,2-aminoalcohols from trifluoromethyl ketones and tertiary amines. With a dual function chiral iridium complex acting as both a Lewis acid and a photoredox catalyst, enantioselectivities of up to 99% ee and where applicable, with diastereoselectivities of up to 10:1 dr were achieved (Figure 80). A quantum yield of <1 supports the proposed catalytic cycle in which at least one photon is needed for each asymmetric C–C bond formation mediated by single electron transfer. It is also worth noting that this mild method follows the spirit of sustainable chemistry, not only because the activation energy is provided by visible light as an abundant light source, but also since in the course of the C-C bond formation with the implementation of one or two new stereocenters, no waste products are generated, thereby constituting a perfect atom economy.

Figure 80 Visible light activated asymmetric radical-radical cross-coupling with a chiral iridium complex Λ-IrS.
4) Catalytic asymmetric C(sp$^3$)-H functionalization under photoredox conditions by radical translocation and stereocontrolled alkene addition

How photoredox-mediated C(sp$^3$)-H activation through radical translocation can be combined with asymmetric catalysis was demonstrated. Upon irradiation with visible light, α,β-unsaturated N-acyl pyrazoles react with N-alkoxyphthalimides in the presence of a rhodium-based chiral Lewis acid catalyst $\Delta$-RhS and the photoredox catalyst $fac$-[Ir(ppy)$_3$] to provide C-C bond-formation products with high enantioselectivities (up to 97% ee) and, where applicable, with some diastereoselectivities (3:1 dr). Mechanistically, the synthetic strategy exploits a radical translocation (1,5-hydrogen transfer) from an oxygen-centered to a carbon-centered radical with a subsequent stereocontrolled radical alkene addition. It is worth noting that N-acyl pyrazole is a very useful precursor for the conversion into other carbonyl functionality as shown for the representative conversion into a diol and an amide (Figure 81).

Figure 81 Visible light activated asymmetric C(sp$^3$)-H functionalization with a chiral Lewis acid $\Delta$-RhS and a photoredox catalyst $fac$-[Ir(ppy)$_3$].
4.2 Outlook

The work described in this thesis contributes to the development of new catalysts and synthetic strategies. Further investigations can be focus on the following aspects:

1) Nowadays, one of the most challenging projects in organic synthetic methodology is visible light induced asymmetric C(sp³)-H functionalization. Radical translocation is an old but very useful strategy which has been discussed in chapter 3.4. However, the complexity certainly limits the practical application. The simultaneous use of iridium and rhodium complexes and the stoichiometric amount of the Hantzsch ester required make the reaction less attractive for large scale synthesis. Very recently, the Knowles group and the Rovis group simultaneously reported symmetric photoredox catalyzed C-C bond formation by directed cleavage of traditionally non-reactive C(sp³)-H bonds (through intramolecular 1,5-HAT) and their subsequent addition to readily available alkenes, no waste products are generated. These results suggest that enantioselectivity photoredox catalyzed C-C bond formation products can be formed by combining our chiral rhodium Lewis acid catalysts with the newly developed C(sp³)-H functionalization approaches.

2) Although high enantioselectivities could be achieved by using chiral-at-metal complexes in chapter 3.2-3.4, the substrates limitation is obvious and such imidazole or pyrazole coordination group is always required which makes the products less usable. How to make the products more general and practical? Maybe iridium-templated Brønsted acid or co-catalysts of the combination of rhodium-templated Brønsted acid with photocatalysis would give opportunities to activate carbonyl substrates, thereby reacting with intermediates in a stereocontrolled fashion under photoredox conditions.

3) In recent years, ruthenium(II), iridium(III) and platinum(II) complexes with cyclometalated arylpyridines and related ligands have become the most studied systems because they display highly tunable emission energies and can reach very high quantum yields. The González-Herrero group recently developed a variety of platinum(IV) complexes with cyclometalated arylpyridines which exhibit impressively luminescence properties. However, the application of these platinum(IV) complexes in photoredox catalysis is rarely. Next work may focus on the synthesis of a platinum(IV) Lewis acid catalyst which contains two achiral bidentate ligands and two labile acetonitriles, and thereby investigates its catalytic properties in asymmetric photoredox catalysis.
Chapter 5: Experimental Part

5.1 Materials and Methods

All reactions were carried out under an atmosphere of nitrogen with magnetic stirring. The catalysis reactions were performed using standard Schlenk glassware techniques.

Solvents and Reagents

Solvents were distilled under nitrogen from calcium hydride (CHCl₃, CH₂Cl₂, CH₃CN and DMF), magnesium turnings/iodine (MeOH) or sodium/benzophenone (Et₂O, THF and toluene). HPLC grade solvents, such as 2-methoxyethanol, ethanol and 1,4-dioxane used directly without further drying. All reagents were purchased from Acros, Alfa Aesar, Sigma Aldrich, TCI, ChemPur and Fluorochem and used without further purification.

Chromatographic Methods

The course of the reactions and the column chromatographic elution were monitored by thin layer chromatography (TLC) [Macherey-Nagel (ALUGRAM®Xtra Sil G/UV254)]. Flash column chromatography was performed with silica gel from Merck (particle size 0.040-0.063 mm).

Nuclear Magnetic Resonance Spectroscopy (NMR)

¹H NMR, proton decoupled ¹³C NMR, and proton coupled ¹⁹F NMR spectra were recorded on Bruker Avance 300 system (¹H NMR: 300 MHz, ¹³C NMR: 75 MHz, ¹⁹F NMR: 282 MHz) spectrometers at ambient temperature. Chemical shifts are given in ppm on the δ scale, and were determined after calibration to the residual signals of the solvents, which were used as an internal standard. NMR standards were used are as follows: ¹H NMR spectroscopy: δ = 7.26 ppm (CDCl₃), δ = 5.32 ppm (CD₂Cl₂), δ = 2.50 ppm (DMSO-d₆), δ = 3.31 ppm (CD₃OD); ¹³C-NMR spectroscopy: δ = 77.0 ppm (CDCl₃), δ = 53.8 ppm (CD₂Cl₂), δ = 118.26, 1.32 ppm (CD₃CN), δ = 206.26, δ = 39.52 ppm (DMSO-d₆), δ = 49.0 ppm (CD₃OD). ¹⁹F NMR spectroscopy: δ = 0 ppm (CFCl₃). The characteristic signals were specified from the low field to high field with the chemical shifts (δ in ppm). ¹H NMR spectra peak
multiplicities indicated as singlet (s), doublet (d), doublet of doublet (dd), doublet of doublet of doublet (ddd), triplet (t), doublet of triplet (dt), quartet (q), multiplet (m). The coupling constant $J$ indicated in hertz (Hz).

**High-Performance Liquid Chromatography (HPLC)**

Chiral HPLC was performed with an Agilent 1200 Series or Agilent 1260 Series HPLC System. All the HPLC conditions were detailed in the individual procedures. The type of the columns, mobile phase and the flow rate were specified in the individual procedures.

**Infrared Spectroscopy (IR)**

IR measurements were recorded on a Bruker Alpha-P FT-IR spectrometer. The absorption bands were indicated a wave numbers $\nu$ (cm$^{-1}$). All substances were measured as films or solids.

**Mass Spectrometry (MS)**

High-resolution mass spectra were recorded on a Bruker En Apex Ultra 7.0 TFT-MS instrument using ESI or APCI or FD technique. Ionic masses are given in units of m/z for the isotopes with the highest natural abundance.

**Circular Dichroism Spectroscopy (CD)**

CD spectra were recorded on a JASCO J-810 CD spectropolarimeter. The parameters we used as follows: from 600 nm to 200 nm; data pitch (0.5 nm); band with (1 nm); response (1 second); sensitivity (standard); scanning speed (50 nm/min); accumulation (5 times). The concentration of the compounds for the measurements was 0.2 mM. The formula for converting $\theta$ to $\varepsilon$ is shown as below.

$$\Delta \varepsilon = \frac{\theta [m \text{deg}]}{32980 \times c (mol / L) \times L (cm)}$$

$C$ = concentration of the sample; $L$ = thickness of the measurement vessel

**Crystal Structure Analysis**

Crystal X-ray measurements and the crystal structure analysis were carried out by Dr. Klaus Harms (Chemistry Department, Philipps University of Marburg). X-ray data were collected with a Bruker 3
circuit D8 Quest diffractometer with MoKα radiation (microfocus tube with multilayer optics) and Photon 100 CMOS detector. Scaling and absorption correction was performed by using the SADABS\textsuperscript{1} software package of Bruker. Structures were solved using direct methods in SHELXS\textsuperscript{2} and refined using the full matrix least squares procedure in SHELXL-2013\textsuperscript{3} or SHELXL-2014\textsuperscript{4}. The Flack parameter is a factor used to estimate the absolute configuration of the compounds.\textsuperscript{5} The hydrogen atoms were placed in calculated positions and refined as riding on their respective C atom, and Uiso(H) was set at 1.2 Ueq(Csp\textsuperscript{2}) and 1.5 Ueq(Csp\textsuperscript{3}). Disorder of PF\textsubscript{6} ions, solvent molecules or methylene groups was refined using restraints for both the geometry and the anisotropic displacement factors.

**UV/Vis Analysis Spectroscopy**

UV/Vis measurements were taken on a Spectra Max M5 microplate reader in a 10.0 mm quartz cuvette.

**Optical Rotation Polarimeter**

Optical rotations were measured on a Krüss P8000-T or Perkin-Elmer 241 polarimeter with [α]\textsubscript{D}\textsuperscript{20} or [α]\textsubscript{D}\textsuperscript{25} values reported in degrees with concentrations reported in g/100 mL.
5.2 Asymmetric Lewis Acid Catalysis Directed by Octahedral Rhodium Centrochirality

5.2.1 Synthesis of the Rhodium Catalysts $\Lambda$-RhO and $\Delta$-RhO

1) Synthesis of benzoxazole ligands

$5$-tert-Butyl-2-phenylbenzo[$d$]oxazole (1)

\[
\begin{align*}
\text{C} & \quad \text{N} \\
\text{C} & \quad \text{N} \\
\text{C} & \quad \text{N} \\
\text{C} & \quad \text{N}
\end{align*}
\]

The compound 1 was synthesized following a published procedure with slight modifications.\(^6\) A solution of 2-amino-4-tert-butylphenol (0.825 g, 5.0 mmol) and benzaldehyde (0.5 mL, 5.0 mmol) in m-xylene (16.0 mL) was stirred at 120 °C for 30 min. 4-Methoxy-TEMPO (46.5 mg, 5 mol%) was added to the mixture and the reaction was stirred at this temperature for further 8 h under an oxygen atmosphere. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:20) to obtain the product 1 (1.152 g, 4.6 mmol, yield: 92%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.29–8.22 (m, 2H), 7.81 (d, \(J = 1.8\) Hz, 1H), 7.56–7.48 (m, 4H), 7.42 (dd, \(J = 8.6, 1.9\) Hz, 1H), 1.40 (s, 9H).

All spectroscopic data are in agreement with the literature.\(^7\)

2) Precursor rhodium complex $\text{rac-}2$

\[
\begin{align*}
\text{C} & \quad \text{N} \\
\text{C} & \quad \text{N} \\
\text{C} & \quad \text{N} \\
\text{C} & \quad \text{N}
\end{align*}
\]

The new complex $\text{rac-}2$ was synthesized according to a route reported by Mesmaeker for rhodium(III) \(\mu\)-chloro-bridged dimers with related cyclometalated ligands.\(^8\) Accordingly, 5-tert-butyl-2-phenylbenzo[$d$]oxazole 1 (1.030 g, 4.1 mmol) was added to RhCl\(_3\)•3H\(_2\)O (526.6 mg, 2.0 mmol) in a mixture of 2-ethoxyethanol and water (3:1, 92.0 mL). The reaction mixture was heated at 120 °C for 24 h under an atmosphere of nitrogen. The resulting precipitate was collected by centrifugation, washed with methanol and dried to obtain the product $\text{rac-}2$ (792.4 mg, 0.62 mmol, yield: 62%) as a pale yellow
solid.

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 8.38 (t, $J = 1.2$ Hz, 4H), 7.58 (dd, $J = 7.6$, 1.3 Hz, 4H), 7.31–7.20 (m, 8H), 6.97 (td, $J = 7.4$, 0.9 Hz, 4H), 6.77 (td, $J = 7.6$, 1.5 Hz, 4H), 6.12 (d, $J = 7.9$ Hz, 4H), 1.22 (s, 36H).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 170.4 (4C), 164.8 (4C), 164.4 (4C), 149.0 (4C), 148.0 (4C), 139.6 (4C), 133.6 (4C), 125.5 (4C), 124.1 (4C), 123.1 (4C), 115.8 (4C), 110.5 (4C), 35.4 (4C), 31.8 (12C).

IR (film): $\nu$ (cm$^{-1}$) 3055, 2957, 2870, 1589, 1526, 1441, 1373, 1271, 1196, 1120, 1075, 1027, 929, 892, 808, 727, 702, 647, 448.

HRMS (ESI, $m/z$) calcd for C$_{68}$H$_{64}$Rh$_{3}$N$_{4}$O$_{4}$Cl $[M-Cl]^+$: 1241.2721, found: 1241.2709.

3) Rhodium auxiliary complexes $\Lambda$-(S)-3 and $\Delta$-(R)-3

The new rhodium auxiliary complexes $\Lambda$-(S)-3 and $\Delta$-(R)-3 were synthesized according to a reported method$^9$ with some modifications. To a solution of NaOMe (16.2 mg, 0.30 mmol) in methanol (16.0 mL), L-proline (34.5 mg, 0.30 mmol) or D-proline (34.5 mg, 0.30 mmol) was added in one portion. The mixture was stirred for 10 min, to which a suspension of rhodium dimer (201.3 mg, 0.15 mmol) was added. The mixture was stirred and heated at 50 °C for 12 h. After the mixture cooled to room temperature, CH$_2$Cl$_2$ (16.0 mL) was added. The reaction mixture was stirred for a further 12 h to give a clear, yellow solution. The solvent was removed in vacuo and the mixture of two diastereoisomers was washed by dichloromethane/diethyl ether (1:6, v/v) until the filtrate was almost colorless. The residual insoluble solid was dried and collected as $\Lambda$-(S)-3 (77.4 mg, 36%) or $\Delta$-(R)-3 (86.1 mg, 40%). The absolute configurations of the obtained $\Lambda$-(S)/$\Delta$-(R) configured rhodium(III) complexes were assigned by an X-ray crystal structure of $\Delta$-(R)-3. CD spectroscopy confirmed that they are enantiomers.

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 8.17 (d, $J = 1.8$ Hz, 1H), 7.84–7.79 (m, 2H), 7.73 (d, $J = 15.2$, 8.8 Hz, 2H), 7.63 (td, $J = 9.0$, 1.8 Hz, 2H), 7.36 (d, $J = 1.6$ Hz, 1H), 7.10–7.07 (m, 2H), 6.95 (td, $J = 7.5$, 1.5 Hz, 2H), 6.76 (d, $J = 7.7$ Hz, 1H), 6.49 (d, $J = 7.7$ Hz, 1H), 4.34–4.17 (m, 2H), 2.80–2.67 (m, 1H), 2.30–2.13 (m, 2H), 2.07–1.94 (m, 1H), 1.68–1.53 (m, 2H), 1.45 (d, $J = 7.6$ Hz, 18H).


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\(^{13}\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 180.5, 172.7, 172.6, 171.5, 171.4, 167.4, 167.0, 166.1, 165.7, 151.4, 150.6, 149.09, 149.06, 138.9, 138.3, 135.4, 134.4, 131.7, 131.3, 131.2, 131.0, 126.3, 126.0, 124.3, 124.2, 123.5, 123.1, 115.7, 112.2, 111.5, 111.1, 64.3, 49.7, 35.8, 35.6, 32.0, 31.9, 30.4, 27.3.

IR (film): \(\nu\) (cm\(^{-1}\)) 3146, 3056, 2958, 1591, 1524, 1445, 1373, 1270, 1191, 1122, 1077, 1033, 928, 814, 773, 648, 550, 449.

\(\Lambda\)-(S)-3:

HRMS (ESI, \(m/z\)) calcd for C\(_{39}\)H\(_{41}\)Rh\(_3\)N\(_3\)O\(_4\) [M+H]\(^+\): 718.2147, found: 718.2133.

CD (MeOH): \(\lambda\), nm (\(\Delta\varepsilon\), M \(\cdot\) cm\(^{-1}\)) 394 (−18), 353 (+26), 295 (−23), 253 (+15), 233 (−4), 216 (+35), 203 (−53).

\(\Delta\)-(R)-3:

HRMS (ESI, \(m/z\)) calcd for C\(_{39}\)H\(_{40}\)Rh\(_3\)N\(_3\)O\(_4\)Na [M+Na]\(^+\): 740.1966, found: 740.1930.

CD (MeOH): \(\lambda\), nm (\(\Delta\varepsilon\), M \(\cdot\) cm\(^{-1}\)) 394 (+9), 353 (−12), 295 (+14), 253 (−6), 233 (+4), 216 (−15), 203 (+30).

4) Synthesis of non-racemic rhodium catalysts

A suspension of the rhodium auxiliary complex \(\Lambda\)-(S)-3 (71.7 mg, 0.10 mmol) or \(\Delta\)-(R)-3 (71.7 mg, 0.10 mmol) and NH\(_4\)PF\(_6\) (163.0 mg, 1.00 mmol) in acetonitrile (20.0 mL) was heated at 50 \(^\circ\)C for 12 h under nitrogen in the dark. The reaction mixture was concentrated to dryness and subjected to flash silica gel chromatography (100% CH\(_2\)Cl\(_2\) to CH\(_2\)Cl\(_2\)/CH\(_3\)CN = 15:1) to give the enantiopure catalyst \(\Lambda\)-RhO (72.2 mg, 0.09 mmol, 87%) or \(\Delta\)-RhO (74.7 mg, 0.09 mmol, 90%) as a pale yellow solid. The absolute configurations of the obtained \(\Lambda\)- and \(\Delta\)-configured rhodium(III) complexes were verified by CD spectroscopy and confirmed by an X-ray crystal structure of \(\Delta\)-RhO. The enantiomeric purity was
verified by HPLC analysis with a chiral stationary phase.

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 7.88 (d, $J = 1.6$ Hz, 2H), 7.80–7.74 (m, 6H), 7.09 (td, $J = 7.5$, 0.9 Hz, 2H), 6.94 (td, $J = 7.6$, 1.5 Hz, 2H), 6.40 (d, $J = 7.8$ Hz, 2H), 2.31 (s, 6H), 1.46 (s, 18H).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 171.5, 160.2, 159.8, 151.2, 148.9, 138.2, 133.5, 132.4, 130.6, 126.3, 125.3, 124.6, 122.0, 113.4, 112.0, 35.7, 31.9, 3.7.

IR (film): $\nu$ (cm$^{-1}$) 2957, 1593, 1528, 1446, 1381, 1274, 1193, 1126, 1081, 1033, 931, 835, 730, 649, 555, 449.

$\Delta$-RhO:

HRMS (ESI, m/z) calcd for C$_{38}$H$_{38}$RhN$_4$O$_2$ [M–PF$_6$]$^+$: 685.2044, found: 685.2036.

CD (MeOH): $\lambda$, nm ($\Delta\varepsilon$, M$^{-1}$cm$^{-1}$) 390 (−33), 350 (+69), 295 (−61), 242 (+36), 228 (+3), 218 (+16), 204 (−30).

$\Delta$-RhO:

HRMS (ESI, m/z) calcd for C$_{38}$H$_{38}$RhN$_4$O$_2$ [M–PF$_6$]$^+$: 685.2044, found: 685.2026.

CD (MeOH): $\lambda$, nm ($\Delta\varepsilon$, M$^{-1}$cm$^{-1}$) 390 (+34), 350 (−70), 295 (+61), 242 (−36), 228 (−14), 218 (−24), 204 (+34).

5.2.2 Catalytic Reactions with $\Delta$-IrO and $\Delta$-RhO

1) **General procedure for asymmetric Michael additions.** To a solution of catalyst $\Delta$-IrO$^{10}$ (1 mol%) or $\Delta$-RhO (1 or 2 mol%) in distilled, anhydrous THF was added the acylimidazole 4a or 4b (0.20 mmol) in a Schlenk tube. After being stirred at room temperature for 20 min, the corresponding nucleophile was added at room temperature or 5 °C. The reaction was stirred at the indicated temperature for the indicated time (monitored by TLC) under nitrogen atmosphere. Afterwards, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:2 to 2:1) to afford the products 5a-f. The $dr$ values were determined by $^1$H NMR analysis of the crude products, and the $ee$ values were determined by chiral HPLC chromatography using a Chiralpak IC or AD-H column.
(R)-3-(1H-Indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (5a)

\[
\begin{align*}
\text{Starting from 4a (30.2 mg, 0.2 mmol) and 1H-indole (58.6 mg, 0.5 mmol) according to the general procedure to give 5a as a white solid (catalyzed by } \Delta\text{-IrO: 51.9 mg, yield: 97%, ee: 96%; catalyzed by } \Delta\text{-RhO: 50.2 mg, yield: 94%, ee: 95%). Enantiomeric excess established by HPLC analysis using a Chiralpak IC column (HPLC: IC, 254 nm, hexane/isopropanol = 85:15, flow rate 0.5 mL/min, 40 °C, t_r (major) = 22.4 min, t_r (minor) = 25.9 min); [\alpha]_D^{20} = +13.8° (c 0.5, CH}_2Cl_2 for 95% ee of 5a ([\alpha]_D^{20} = −14.5° (c 2.7, CH}_2Cl_2) for 96% ee of product with S-configuration).}
\end{align*}
\]

\(^1\text{H NMR (300 MHz, CDCl}_3\) \(\delta\) 8.41 (br s, 1H), 7.67 (d, \(J = 7.8\) Hz, 1H), 7.34–7.28 (m, 1H), 7.22–7.05 (m, 3H), 7.01–6.95 (m, 2H), 7.01–6.95 (m, 2H), 3.93 (s, 3H), 3.66–3.34 (m, 2H), 1.40 (d, \(J = 6.9\) Hz, 3H).

\(^13\text{C NMR (75 MHz, CDCl}_3\) \(\delta\) 192.4, 143.4, 136.5, 128.9, 127.0, 126.7, 121.9, 121.5, 120.3, 119.3, 119.1, 111.2, 46.8, 36.2, 27.2, 21.8.

All spectroscopic data were in agreement with the literature.

(R)-2-(4-(1-Methyl-1H-imidazol-2-yl)-4-oxobutan-2-yl)malononitrile (5b)

\[
\begin{align*}
\text{Starting from 4a (30.2 mg, 0.2 mmol) and malononitrile (15.8 mg, 0.24 mmol) according to the general procedure to give 5b as a colorless oil (catalyzed by } \Delta\text{-IrO: 41.5 mg, yield: 96%, ee: 89%; catalyzed by } \Delta\text{-RhO: 41.5 mg, yield: 96%, ee: 92%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 1.0 mL/min, 25 °C, t_r (major) = 22.8 min, t_r (minor) = 24.1 min); [\alpha]_D^{20} = −33.2° (c 0.4, CH}_2Cl_2) for 92% ee of 5b.}
\end{align*}
\]

\(^1\text{H NMR (300 MHz, CDCl}_3\) \(\delta\) 7.15 (s, 1H), 7.08 (s, 1H), 4.37 (d, \(J = 4.9\) Hz, 1H), 3.99 (s, 3H), 3.47 (dd, \(J = 18.0, 5.3\) Hz, 1H), 3.28 (dd, \(J = 18.0, 8.2\) Hz, 1H), 2.89–2.71 (m, 1H), 1.36 (d, \(J = 6.9\) Hz, 3H).

\(^13\text{C NMR (75 MHz, CDCl}_3\) \(\delta\) 189.6, 142.4, 129.8, 127.9, 112.5, 111.5, 41.6, 36.2, 31.9, 28.2, 17.3.

All spectroscopic data were in agreement with the literature.
(R)-2-(3-(1-Isopropyl-1H-imidazol-2-yl)-3-oxo-1-phenylpropyl)malononitrile (5c)

Starting from 4b (45.8 mg, 0.2 mmol) and malononitrile (15.8 mg, 0.24 mmol) according to the general procedure to give 5c as a colorless oil (catalyzed by \( \Delta -\text{IrO} \): 24.7 mg, yield: 40%, ee: 88%; catalyzed by \( \Delta -\text{RhO} \): 55.8 mg, yield: 91%, ee: 95%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column (HPLC: AD-H, 254 nm, hexane/isopropanol = 70:30, flow rate 0.8 mL/min, 25 °C, \( t_{r} \) (minor) = 13.0 min, \( t_{r} \) (major) = 23.6 min); \([\alpha]_{D}^{20} = -0.4^\circ (c 0.8, \text{CH}_{2}\text{Cl}_2)\) for 95% ee of 5c.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.46–7.35 (m, 5H), 7.30 (d, \( J = 0.9 \) Hz, 1H), 7.19 (d, \( J = 0.8 \) Hz, 1H), 5.42 (dt, \( J = 13.4, 6.7 \) Hz, 1H), 4.53–4.45 (m, 1H), 4.03–3.88 (m, 2H), 3.87–3.72 (m, 1H), 1.41 (dd, \( J = 8.6, 6.7 \) Hz, 6H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 188.7, 141.5, 136.5, 130.2, 129.2, 129.0, 128.2, 122.1, 112.0, 111.7, 49.5, 41.7, 41.2, 29.3, 23.55, 23.52.

IR (film): \( \nu (\text{cm}^{-1}) \) 3034, 2983, 2909, 2254, 1670, 1497, 1465, 1454, 1395, 1371, 1254, 1199, 1162, 1087, 971, 914, 772, 731, 700, 671, 646, 591, 548, 488, 407.

HRMS (ESI, \( m/z \)) calcd for C\(_{18}\)H\(_{18}\)N\(_4\)O\(_4\)Na \([\text{M}+\text{Na}]^+\): 329.1373, found: 329.1369.

(R)-2,2-Dimethyl-5-(4-(1-methyl-1H-imidazol-2-yl)-4-oxobutan-2-yl)-1,3-dioxane-4,6-dione (5d)

Starting from 4a (30.2 mg, 0.2 mmol) and 2,2-dimethyl-1,3-dioxane-4,6-dione (86.5 mg, 0.6 mmol) according to the general procedure to give 5d as a white solid (catalyzed by \( \Delta -\text{IrO} \): 58.3 mg, yield: 99%, ee: 68%; catalyzed by \( \Delta -\text{RhO} \): 58.3 mg, yield: 99%, ee: 85%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.8 mL/min, 40 °C, \( t_{r} \) (major) = 24.9 min, \( t_{r} \) (minor) = 26.6 min); \([\alpha]_{D}^{20} = -3.3^\circ (c 0.8, \text{CH}_{2}\text{Cl}_2)\) for 95% ee of 5d (catalyzed by \( \Delta -\text{RhO} \) (2 mol%) at room temperature).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.13 (d, \( J = 0.9 \) Hz, 1H), 7.03 (s, 1H), 4.22–4.16 (m, 1H), 3.98 (s, 3H), 3.56 (dd, \( J = 7.2, 5.0 \) Hz, 2H), 3.24–3.10 (m, 1H), 1.77 (d, \( J = 5.8 \) Hz, 6H), 1.21 (d, \( J = 7.0 \) Hz, 3H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 192.3, 165.2, 164.7, 142.9, 129.2, 127.2, 104.7, 49.3, 41.9, 36.2, 28.9.
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28.4, 26.9, 17.3.

IR (film): ν (cm⁻¹) 3136, 2928, 2883, 1780, 1739, 1667, 1459, 1408, 1298, 1200, 1151, 1086, 1053, 991, 958, 914, 871, 787, 698, 670, 634, 596, 544, 496, 426.


(R)-tert-Butyl 1-((R)-4-(1-methyl-1H-imidazol-2-yl)-4-oxobutan-2-yl)-2-oxocyclopentanecarboxylate (5e)

Starting from 4a (30.2 mg, 0.2 mmol) and tert-butyl 2-oxocyclopentanecarboxylate (73.7 mg, 0.4 mmol) according to the general procedure to give 5e (major product) as a colorless oil (catalyzed by Δ-IrO: 27.4 mg, yield: 41%, ee: 97%, dr: 3:1; catalyzed by Δ-RhO: 55.5 mg, yield: 83%, ee: 99%, dr: 4:1).

The dr was determined by ¹H NMR and the enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column (HPLC: AD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 0.5 mL/min, 40 °C, tᵣ (minor) = 26.4 min, tᵣ (major) = 29.5 min); [α]D²⁰ = +13.1° (c 1.4, CH₂Cl₂) for 99% ee of 5e.

¹H NMR (300 MHz, CDCl₃) δ 7.08 (d, J = 0.8 Hz, 1H), 6.99 (s, 1H), 3.96 (s, 3H), 3.22 (dd, J = 16.6, 10.3 Hz, 1H), 3.08–2.97 (m, 1H), 2.74 (dd, J = 16.6, 2.6 Hz, 1H), 2.50–2.30 (m, 2H), 2.21–2.06 (m, 1H), 2.01–1.85 (m, 3H), 1.42 (s, 9H), 0.94 (d, J = 6.7 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 214.5, 191.2, 169.2, 143.2, 128.9, 127.0, 82.0, 65.8, 41.7, 38.6, 36.2, 32.4, 29.4, 27.9, 19.4, 16.4.

IR (film): ν (cm⁻¹) 3112, 2970, 2868, 1743, 1715, 1673, 1462, 1405, 1368, 1283, 1246, 1151, 1125, 1005, 979, 914, 834, 775, 695, 589, 549, 434.

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(R)-tert-Butyl 2-((R)-4-(1-methyl-1H-imidazol-2-yl)-4-oxobutan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5f)

Starting from 4a (30.2 mg, 0.2 mmol) and tert-butyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (92.9 mg, 0.4 mmol) according to the general procedure to give 5f (major product) as a colorless oil (catalyzed by $\Delta$-IrO: 68.1 mg, yield: 89%, ee: 97%, dr: 10:1; catalyzed by $\Delta$-RhO: 70.4 mg, yield: 92%, ee: 96%, dr: 14:1). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, t_r (major) = 84.2 min, t_r (minor) = 168.0 min); $[\alpha]_D^{20} = -96.9^\circ$ (c 0.7, CH$_2$Cl$_2$) for 97% ee of 5f. The dr value was determined by $^1$H NMR as shown below (Figure 82).

**Figure 82** $^1$H NMR of the crude product 5f and its diastereomer 5f'. Calculated $dr = 1:10$.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.74 (d, $J = 7.6$ Hz, 1H), 7.65–7.56 (m, 1H), 7.50 (d, $J = 7.7$ Hz, 1H), 7.45–7.31 (m, 1H), 7.13 (d, $J = 0.9$ Hz, 1H), 7.03 (s, 1H), 4.01 (s, 3H), 3.69 (d, $J = 17.5$ Hz, 1H), 3.51–
3.39 (m, 1H), 3.32–3.18 (m, 2H), 3.09 (dd, J = 16.3, 2.8 Hz, 1H), 1.36 (s, 9H), 0.76 (d, J = 6.7 Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 202.4, 191.2, 169.3, 154.1, 143.3, 136.0, 135.2, 128.9, 127.6, 127.0, 126.3, 124.6, 82.1, 65.9, 42.4, 36.3, 33.1, 33.0, 27.8, 15.2.

IR (film): $\nu$ (cm$^{-1}$) 2969, 2930, 1705, 1673, 1604, 1464, 1406, 1369, 1332, 1252, 1213, 1146, 1092, 986, 913, 844, 769, 743, 694, 651, 590, 517, 466.

HRMS (ESI, m/z) calcd for C$_{22}$H$_{27}$N$_2$O$_4$ [M+H]$^+$: 383.1965, found: 383.1962.

2) Procedure for asymmetric cascade reaction.

To a solution of catalyst $\Delta$-RhO (3.2 mg, 2 mol%) in distilled, anhydrous THF (0.2 mL) was added the acylimidazole 4a (30.2 mg, 0.20 mmol) in a Schlenk tube. After being stirred at room temperature for 20 min, malononitrile (15.9 mg, 0.24 mmol) and ($E$)-dibenzyl diazene-1,2-dicarboxylate (119.3 mg, 0.40 mmol) were added. The reaction was stirred at room temperature for 16 h under nitrogen atmosphere. Afterwards, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:4 to 1:2) to afford the diastereomeric mixture of 6 as a white solid (84.3 mg, yield: 82%, ee of the major diastereoisomer: 92%, dr: 4:1 (after purified by flash chromatography)). The ee values were determined by HPLC analysis using a Chiralpak AD-H column (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C. Major diastereoisomer $t_r$ (minor) = 80.5 min, $t_r$ (major) = 117.4 min; $[\alpha]_D^{20} = -30.5^\circ$ (c 1.0, CH$_2$Cl$_2$, 92% ee).

**Dibenzyl 1-(2S,3S)-4,4-dicyano-3-methyl-1-(1-methyl-1H-imidazol-2-yl)-1-oxobutan-2-yl)hydrazine-1,2-dicarboxylate (6)**

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.25–6.72 (m, 12H), 5.22–4.60 (m, 6H), 3.77 (s, 3H), 3.10–2.95 (m, 1H), 1.29 (s, 3H). (major diastereoisomer)

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 155.7, 141.3, 135.4, 135.3, 128.8, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0,
127.9, 113.3, 111.7, 69.1, 68.3, 53.5, 36.2, 35.4, 26.9. (major diastereoisomer)

IR (film): $v$ (cm$^{-1}$) 3260, 2958, 2925, 2254, 1726, 1677, 1454, 1396, 1241, 1207, 1156, 1079, 1040, 986, 959, 918, 852, 795, 740, 697, 641, 567, 506, 475, 403.

HRMS (ESI, $m/z$) calcd for C$_{27}$H$_{26}$N$_6$O$_5$Na [M+Na]$^+$: 537.1856, found: 537.1848.

### 5.2.3 Investigation of the Stability of Rhodium Catalyst $\Delta$-/Δ-RhO

1) Catalyst stability investigated by $^1$H NMR

The rhodium complex $\Delta$-RhO (5.0 mg) was dissolved in CD$_2$Cl$_2$ and kept in the NMR tube at room temperature under reduced light. $^1$H NMR spectra were recorded after 2, 4, 6 and 8 days (Figure 83).

**Figure 83** $^1$H NMR of $\Delta$-RhO recorded in CD$_2$Cl$_2$ over 8 days.
2) Catalyst stability investigated by chiral HPLC

Enantiopure pure rhodium complex Λ-RhO (2.0 mg) was dissolved in CH₂Cl₂ (1.0 mL, HPLC grade) and kept in a brown glass vial at room temperature. The HPLC spectra were collected after 2-8 days. HPLC conditions: Daicel Chiralpak IB (250 × 4.6 mm) HPLC column, the column temperature was 25 °C and UV-absorption was measured at 254 nm. Solvent A = 0.1% TFA, solvent B = MeCN with a linear gradient of 30% to 41% B in 60 min at a flow rate = 0.6 mL/min.

![HPLC traces](image)

**Figure 84** HPLC traces of the freshly prepared Λ-RhO in CH₂Cl₂ (>99% ee) and after 2-8 days in CH₂Cl₂ (>99% ee).
5.2.4 Investigation of the Proposed Catalyst-Coordinated Substrate Intermediate

To a solution of $\Delta$-RhO (10.0 mg, 0.012 mmol) in CD$_2$Cl$_2$ (0.70 mL) at room temperature was added substrate 4a (9.5 mg, 0.063 mmol). The mixture was stirred at room temperature for 20 min and then analyzed by $^1$H NMR spectroscopy. The $^1$H NMR analysis is consistent with a fast bidentate coordination of 4a to $\Delta$-RhO under release of the coordinated acetonitrile ligands.

![Proposed structure]

Figure 85 $^1$H NMR spectra of substrate 4a, catalyst $\Delta$-RhO, and a mixture of 4a and $\Delta$-RhO.
5.2.5 The Acetonitrile Exchange Rates: Δ-RhO vs. Δ-IrO

To a solution of Δ-RhO (5.0 mg, 0.006 mmol) or Δ-IrO (5.5 mg, 0.006 mmol) in CD$_2$Cl$_2$ (3 mL) at room temperature was added bipyridine (1.64 mg, 0.0105 mmol). The $^1$H NMR spectra were collected after the indicated time. The conversion was calculated by area integration ratio of two different tert-butyl groups, which reveal that the acetonitrile exchange rates are faster in Δ-RhO compared to Δ-IrO.

![Diagram showing the exchange of acetonitrile in Rh and Ir complexes](image)

Figure 86 $^1$H NMR spectra of Δ-RhO and the mixture of Δ-RhO and bipyridine in CD$_2$Cl$_2$. 
Figure 87 $^1$H NMR spectra of the mixture of $\Delta$-IrO and bipyridine in CD$_2$Cl$_2$. 
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5.2.6 Single Crystal X-Ray Diffraction

Crystals of Δ-(R)-3 and Δ-RhO were obtained by slow diffusion from a solution of the compounds in CH₂Cl₂ layered with Et₂O at room temperature for several weeks. Crystals of 5d, racemic 5f and 6 were obtained by slow diffusion from a solution of the compounds in CH₂Cl₂ layered with hexane at 5 °C for several days. Single crystals suitable for X-ray diffraction of the substrate coordinated rhodium catalyst (here denoted as RhO-I) were obtained by reacting 4b (0.06 mmol) with Δ/Λ-RhO (0.06 mmol) overnight at room temperature in CH₂Cl₂ (2.0 mL). After the slow addition of hexane (5.0 mL), crystals were collected after several days (70% yield).

Crystal data and details of the structure determination are presented in Appendices 6.7. In the packing of RhO-I there are holes present that contain diffuse electron density that may belong to heavily disordered solvent molecules. This was taken into account using the “squeeze” procedure in the PLATON program system. The determination of the absolute configuration of the light atom structure 5d by means of refining the “Flack parameter” was not possible. The absolute configurations of compounds Δ-(R)-3 and Δ-RhO have been determined.
5.3 Merger of Visible Light Induced Oxidation and Enantioselective Alkylation with Chiral Iridium Catalyst

5.3.1 Synthesis of Substrates

1) Synthesis of 2-acyl imidazoles

2-Acyl imidazoles 7a', 7a'' and Weinreb amides were synthesized following our recently published procedures.12 2-Acyl imidazoles 7a-h were synthesized following the route shown below.

General procedure for the preparation of the 2-acyl imidazoles. All 2-acyl imidazoles were synthesized according to reported procedures with some modifications.13 To a solution of N-phenylimidazole (1.1 eq.) in THF (0.4 M) at −78 °C was added n-BuLi (1.1 eq.) dropwise. The reaction was stirred at −78 °C for 30 min, then stirred at room temperature for 30 min. The corresponding Weinreb amides (1.0 eq.) was added to the flask after the reaction was cooled back down to −78 °C. The reaction was allowed to slowly warm to room temperature and stirred overnight. The reaction was quenched with AcOH (6.0 eq.) and extracted with EtOAc. The organic layer was washed with aqueous saturated NaHCO₃ and brine. The combined organic layers were dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:3) to provide the 2-acyl imidazoles 7a-h.

2-Phenyl-1-(1-phenyl-1H-imidazol-2-yl)ethanone (7a)

Following the general procedure, N-methoxy-N-methyl-2-phenylacetamide (1.797 g, 10.0 mmol) was converted to 2-acyl imidazole 7a (1.709 g, 6.5 mmol, yield: 65%) as a white solid.

1H NMR (300 MHz, CDCl₃) δ 7.46–7.37 (m, 3H), 7.34–7.20 (m, 8H), 7.19 (d, J = 1.0 Hz, 1H), 4.45 (s, 2H).
All spectroscopic data are in agreement with the literature.\(^{13}\)

**1-(1-Phenyl-1\(H\)-imidazol-2-yl)-2-meta-tolylethanone (7b)**

Following the general procedure, \(N\)-methoxy-\(N\)-methyl-2-(\(m\)-tolyl)acetamide (1.544 g, 8.0 mmol) was converted to 2-acyl imidazole 7b (1.186 g, 4.3 mmol, yield: 54\%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.45–7.38 (m, 3H), 7.33 (d, \(J = 1.0\) Hz, 1H), 7.25–7.20 (m, 2H), 7.20–7.09 (m, 4H), 7.07–7.01 (m, 1H), 4.42 (s, 2H), 2.32 (s, 3H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 188.5, 142.8, 138.3, 138.0, 134.2, 130.7, 129.6, 128.9, 128.6, 128.3, 127.5, 127.3, 126.9, 125.8, 45.5, 21.3.

IR (film): \(v\) (cm\(^{-1}\)) 3125, 3109, 1681, 1597, 1500, 1448, 1393, 1245, 1209, 1176, 1160, 1094, 963, 913, 894, 880, 842, 798, 767, 652, 543.

HRMS (ESI, \(m/z\)) calcd for C\(_{18}\)H\(_{17}\)N\(_2\)O [M+H]: 277.1333, found: 277.1335.

**1-(1-Phenyl-1\(H\)-imidazol-2-yl)-2-ortho-tolylethanone (7c)**

Following the general procedure, \(N\)-methoxy-\(N\)-methyl-2-(\(o\)-tolyl)acetamide (1.544 g, 8.0 mmol) was converted to 2-acyl imidazole 7c (1.450 g, 5.3 mmol, yield: 66\%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.44–7.38 (m, 3H), 7.33 (d, \(J = 1.0\) Hz, 1H), 7.29–7.22 (m, 2H), 7.22–7.19 (m, 2H), 7.17–7.10 (m, 3H), 4.53 (s, 2H), 2.29 (s, 3H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 188.4, 142.9, 138.2, 137.1, 133.1, 130.8, 130.2, 129.5, 128.9, 128.7, 127.3, 127.1, 125.87, 125.85, 43.5, 19.8.

IR (film): \(v\) (cm\(^{-1}\)) 3104, 2936, 2911, 1691, 1594, 1490, 1407, 1393, 1340, 1326, 1208, 1189, 1142, 1076, 964, 942, 868, 806, 773, 738, 706, 693, 607, 556.

HRMS (ESI, \(m/z\)) calcd for C\(_{18}\)H\(_{17}\)N\(_2\)O [M+H]: 277.1335, found: 277.1333.
Chapter 5: Experimental Part

2-(4-Methoxyphenyl)-1-(1-phenyl-1H-imidazol-2-yl)ethanone (7d)

Following the general procedure, N-methoxy-2-(4-methoxyphenyl)-N-methylacetamide (1.674 g, 8.0 mmol) was converted to 2-acyl imidazole 7d (1.682 g, 5.8 mmol, yield: 72%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.48–7.41 (m, 3H), 7.35 (d, J = 1.0 Hz, 1H), 7.31–7.23 (m, 4H), 7.22 (d, J = 1.0 Hz, 1H), 6.92–6.87 (m, 1H), 6.87–6.84 (m, 1H), 6.80 (s, 2H), 3.80 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 188.7, 158.5, 142.7, 138.3, 130.9, 129.6, 128.9, 128.6, 127.3, 126.4, 125.8, 113.9, 55.2, 44.7.

IR (film): ν (cm$^{-1}$) 3129, 2949, 2828, 1668, 1602, 1505, 1450, 1393, 1345, 1302, 1244, 1170, 1141, 1032, 967, 910, 853, 823, 791, 763, 689, 610, 584, 520.

HRMS (ESI, m/z) calcd for C$_{18}$H$_{17}$N$_2$O$_2$ [M+H]$^+$: 293.1285, found: 293.1283.

2-(4-Chlorophenyl)-1-(1-phenyl-1H-imidazol-2-yl)ethanone (7e)

Following the general procedure, 2-(4-chlorophenyl)-N-methoxy-N-methylacetamide (1.764 g, 8.3 mmol) was converted to 2-acyl imidazole 7e (1.536 g, 5.2 mmol, yield: 63%) as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.47–7.40 (m, 3H), 7.33 (d, J = 1.0 Hz, 1H), 7.28–7.18 (m, 7H), 4.43 (s, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 187.9, 142.5, 138.2, 132.8, 132.7, 131.3, 129.8, 129.0, 128.8, 128.5, 127.6, 125.8, 44.8.

IR (film): ν (cm$^{-1}$) 3012, 1682, 1594, 1492, 1446, 1397, 1307, 1148, 1092, 1041, 965, 862, 805, 764, 689, 659, 578, 547.

HRMS (ESI, m/z) calcd for C$_{17}$H$_{14}$ClN$_2$O [M+H]$^+$: 297.0789, found: 297.0788.
1-(1-Phenyl-1H-imidazol-2-yl)-2-(thiophen-3-yl)ethanone (7f)

Following the general procedure, N-methoxy-N-methyl-2-(thiophen-3-yl)acetamide (1.482 g, 8.0 mmol) was converted to 2-acyl imidazole 7f (1.256 g, 4.7 mmol, yield: 59%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.46–7.40 (m, 3H), 7.32 (d, \(J = 1.0\) Hz, 1H), 7.28–7.22 (m, 3H), 7.21–7.16 (m, 2H), 7.06 (dd, \(J = 4.9, 1.3\) Hz, 1H), 4.50 (s, 2H).

\(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 187.8, 142.6, 138.2, 133.9, 129.7, 129.0, 128.9, 128.7, 127.4, 125.8, 125.3, 123.2, 40.1.

IR (film): \(\nu\) (cm\(^{-1}\)) 3122, 3094, 1698, 1593, 1490, 1407, 1387, 1317, 1295, 1149, 1038, 969, 880, 823, 805, 763, 696, 669, 610, 589.

HRMS (ESI, \(m/z\)) calcd for C\(_{15}\)H\(_{13}\)N\(_2\)O [M+H]^+: 269.0743, found: 269.0743.

1-(1-Phenyl-1H-imidazol-2-yl)propan-1-one (7g)

Following the general procedure, N-methoxy-N-methylpropionamide (874 mg, 7.5 mmol) was converted to 2-acyl imidazole 7g (1.071 g, 5.3 mmol, yield: 71%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.48–7.41 (m, 3H), 7.31–7.23 (m, 3H), 7.16 (d, \(J = 1.0\) Hz, 1H), 3.17 (q, \(J = 7.3\) Hz, 2H), 1.13 (t, \(J = 7.3\) Hz, 3H).

\(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 192.0, 142.9, 138.5, 129.3, 128.9, 128.7, 126.8, 125.9, 32.4, 7.8.

IR (film): \(\nu\) (cm\(^{-1}\)) 3123, 2972, 1686, 1593, 1491, 1450, 1407, 1346, 1215, 1149, 1034, 976, 936, 879, 801, 769, 693, 608, 565.

HRMS (ESI, \(m/z\)) calcd for C\(_{12}\)H\(_{13}\)N\(_2\)O [M+H]^+: 201.1022, found: 201.1023.

1-(1-Phenyl-1H-imidazol-2-yl)butan-1-one (7h)
Following the general procedure, N-methoxy-N-methylbutyramide (1.495 g, 11.4 mmol) was converted to 2-acyl imidazole 7h (1.305 g, 6.1 mmol, yield: 54%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.51–7.43 (m, 3H), 7.32–7.25 (m, 3H), 7.18 (d, $J = 1.0$ Hz, 1H), 3.14 (t, $J = 7.2$ Hz, 2H), 1.82–1.60 (m, 2H), 0.98 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 191.5, 143.1, 138.5, 129.3, 128.9, 128.7, 126.9, 125.9, 41.1, 17.4, 13.7.

IR (film): $\nu$ (cm$^{-1}$) 3095, 2966, 2930, 2877, 1683, 1594, 1449, 1339, 1328, 1265, 1112, 1072, 961, 914, 891, 814, 796, 691, 542.

HRMS (ESI, $m/z$) calcld for C$_{13}$H$_{15}$N$_2$O [M+H]$^+$: 215.1179, found: 215.1180.

2) Synthesis of $\alpha$-silylamines

All $\alpha$-silylamines were synthesized according to reported procedures with some modifications.$^{14}$ To a solution of amines (1.0 eq.) in THF (0.4 M) under nitrogen atmosphere at 0 $^\circ$C was added $n$-BuLi (1.0 eq.) dropwise. The reaction was stirred at 0 $^\circ$C for 30 min, then stirred at room temperature for further 1 h. (Iodomethyl)trimethylsilane (1.5 eq.) was added slowly to the flask after the reaction was cooled back down to 0 $^\circ$C, and the resulting solution was stirred at room temperature ($9a$-$b$) or 60 $^\circ$C ($9c$-$e$) overnight. Afterwards, the reaction was quenched with water and extracted with $n$-hexane. The combined organic layers were dried (Na$_2$SO$_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (100% $n$-hexane) to produce $9a$-$e$. The new synthesized $\alpha$-silylamines were stored at $-20$ $^\circ$C under nitrogen atmosphere.

$N$-Phenyl-$N$-((trimethylsilyl)methyl)aniline ($9a$)

$\begin{array}{c}
\begin{array}{c}
\text{Si} \\
\text{N}
\end{array} \\
\begin{array}{c}
\text{Ph}
\end{array}
\end{array}$

Following the general procedure, diphenylamine (1.690 g, 10.0 mmol) was converted to $\alpha$-silylamine $9a$ (1.788 g, 7.0 mmol, yield: 70%) as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.33–7.23 (m, 4H), 7.06–7.00 (m, 4H), 6.98–6.92 (m, 2H), 3.34 (s, 2H), $-0.01$ (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 149.6, 129.1, 121.1, 120.9, 43.7, $-1.3$. 

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All spectroscopic data are in agreement with the literature.\textsuperscript{14}

4-Methyl-\(N\)-\(p\)-tolyl-\(N\)-((trimethylsilyl)methyl)aniline (9b)

\[
\text{\begin{tikzpicture}
  \node[anchor=base,inner sep=0] (image) at (0,0) {
    \includegraphics[width=0.5\textwidth]{image.png}
  };
\end{tikzpicture}}
\]

Following the general procedure, di-\(p\)-tolylamine (1.479 g, 7.5 mmol) was converted to \(\alpha\)-silylamine 9b (1.381 g, 4.9 mmol, yield: 65\%) as a pale yellow oil.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.04 (d, \(J = 8.3\) Hz, 4H), 6.86 (d, \(J = 8.4\) Hz, 4H), 3.23 (s, 2H), 2.29 (s, 6H), \(-0.05\) (s, 9H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 147.4, 130.6, 129.6, 121.1, 44.2, 20.6, \(-1.3\).

All spectroscopic data were in agreement with the literature.\textsuperscript{14}

4-Methoxy-\(N\)-phenyl-\(N\)-((trimethylsilyl)methyl)aniline (9c)

\[
\text{\begin{tikzpicture}
  \node[anchor=base,inner sep=0] (image) at (0,0) {
    \includegraphics[width=0.5\textwidth]{image.png}
  };
\end{tikzpicture}}
\]

Following the general procedure, 4-methoxy-\(N\)-phenylaniline (1.374 g, 6.9 mmol) was converted to \(\alpha\)-silylamine 9c (0.925 g, 3.2 mmol, yield: 47\%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.26–7.05 (m, 4H), 6.98–6.68 (m, 5H), 3.87 (s, 3H), 3.27 (s, 2H), 0.00 (s, 9H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 156.5, 150.9, 142.1, 128.7, 127.6, 117.5, 115.7, 114.7, 55.5, 43.9, \(-1.38\).

IR (film): \(\nu\) (cm\(^{-1}\)) 3036, 2950, 2833, 1595, 1574, 1494, 1463, 1341, 1296, 1237, 1179, 1130, 1088, 868, 832, 790, 692, 555, 516.

HRMS (ESI, \(m/z\)) calcd for C\(_{17}\)H\(_{24}\)NO\(_2\)Si [M+H]\(^+\): 286.1622, found: 286.1624.
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4-Chloro-N-phenyl-N-((trimethylsilyl)methyl)aniline (9d)

Following the general procedure, 4-chloro-N-phenylaniline (0.713 g, 3.5 mmol) was converted to α-silylamine 9d (0.639 g, 2.2 mmol, yield: 63%) as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.36–7.27 (m, 2H), 7.23–7.17 (m, 2H), 7.09–6.98 (m, 3H), 6.93–6.85 (m, 2H), 3.31 (s, 2H), 0.00 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 149.1, 148.3, 129.3, 128.9, 124.9, 122.4, 122.2, 120.8, 43.9, −1.3.

IR (film): $\nu$ (cm$^{-1}$) 2952, 1585, 1487, 1429, 1354, 1248, 1188, 1095, 901, 839, 815, 746, 697, 627, 510.

HRMS (ESI, $m/z$) calcd for C$_{16}$H$_{21}$ClN$_2$Si [M+H]$^+$: 290.1126, found: 290.1129.

N-Phenyl-N-((trimethylsilyl)methyl)naphthalen-2-amine (9e)

Following the general procedure, N-phenynaphthalen-2-amine (2.192 g, 10.0 mmol) was converted to α-silylamine 9e (1.832 g, 6.0 mmol, yield: 60%) as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.75–7.61 (m, 3H), 7.44–7.36 (m, 1H), 7.33–7.24 (m, 4H), 7.17 (dd, $J = 8.9, 2.4$ Hz, 1H), 7.10–7.05 (m, 2H), 7.03–6.95 (m, 1H), 3.44 (s, 2H), 0.00 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 149.6, 147.0, 134.7, 129.2, 128.9, 128.4, 127.5, 126.6, 126.2, 123.4, 122.1, 121.8, 114.9, 44.2, −1.2.

All spectroscopic data are in agreement with the literature.$^{14}$
5.3.2 Iridium-Catalyzed Photoredox Reactions

1) Reaction of 2-acyl imidazoles with N,N-diaryl-N-(trimethylsilyl)methylamines

General catalysis procedure. To a solution of catalyst Λ- or Δ-IrO (2 mol% or 4 mol%) in distilled, anhydrous CH$_2$Cl$_2$ (0.50 mL, 0.4 M) in a 10 mL test tube, was added the 2-acyl imidazole (0.20 mmol). After being stirred at room temperature for 20 min, the α-silylamine (0.60 mmol) was added. The tube was positioned approximately 2 cm away from a 12 W white light energy saving lamp. The reaction was stirred at room temperature for the indicated time (monitored by TLC) under an atmosphere of air (air balloon). Afterwards, the solvent was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/n-hexane = 1:20) to afford the non-racemic product. The enantiomeric excess was determined by chiral HPLC analysis. The absolute configuration of the product (R)-10e was determined by X-ray crystallography and used to assign the configuration of all other compounds. Racemic samples were obtained by carrying out the analogous reactions with the racemic catalyst rac-IrO.

(S)-3-(Diphenylamino)-1-(1-methyl-1H-imidazol-2-yl)-2-phenylpropan-1-one (10a'')

Using Λ-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7a'' (40.0 mg, 0.20 mmol) and α-silylamine 9a (153.2 mg, 0.60 mmol) according to the general procedure to give 10a'' as a pale yellow oil (25.9 mg, 0.068 mmol, yield: 34%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 91% (HPLC: AD-H, 254 nm, hexane/isopropanol = 85:15, flow rate 0.5 mL/min, 25 °C, t$_r$ (minor) = 13.2 min, t$_r$ (major) = 13.9 min).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ 7.45–7.38 (m, 2H), 7.34–7.25 (m, 3H), 7.24–7.20 (m, 3H), 7.19–7.16 (m, 1H), 7.05 (d, $J = 0.9$ Hz, 1H), 7.00–6.97 (m, 1H), 6.97–6.90 (m, 2H), 6.90–6.84 (m, 4H), 5.66 (dd, $J = 8.8$, 4.9 Hz, 1H), 4.73–4.62 (dd, $J = 14.5$, 8.7 Hz, 1H), 4.02 (dd, $J = 14.5$, 4.9 Hz, 1H), 3.80 (s, 3H).
\( ^{13} \text{C NMR (75 MHz, CD}_2\text{Cl}_2 \) \delta 191.4, 148.5, 143.5, 138.3, 129.6, 129.5, 129.1, 129.0, 127.9, 127.6, 121.9, 121.8, 55.8, 51.8, 36.3. \\
IR (film): \( \nu (\text{cm}^{-1}) \) 3059, 2923, 2853, 1668, 1587, 1491, 1453, 1364, 1288, 1207, 1185, 1154, 1029, 990, 950, 909, 862, 772, 745, 693, 630, 506. \\
HRMS (ESI, \( m/z \) calcd for C\(_{25}\)H\(_{24}\)N\(_3\)O [M+H]\(^+\): 382.1914, found: 382.1916. \\

\( (S)-3-\text{(Diphenylamo)-1-(1-isopropyl-1H-imidazol-2-yl)-2-phenylpropan-1-one (10a')} \)

Using \( \Delta \text{IrO} \) (2 mol\%) as catalyst, starting from 2-acyl imidazole \( 7a' \) (45.7 mg, 0.20 mmol) and \( \alpha \)-silylamine \( 9a \) (153.2 mg, 0.60 mmol) according to the general procedure to give \( 10a' \) as a pale yellow oil (39.3 mg, 0.096 mmol, yield: 48\%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, \( ee = 90\% \) (HPLC: AD-H, 254 nm, hexane/isopropanol = 85:15, flow rate 0.5 mL/min, 25 °C, \( t_r \) (major) = 10.0 min, \( t_r \) (minor) = 10.8 min).

\( ^{1} \text{H NMR (300 MHz, CD}_2\text{Cl}_2 \) \( \delta 7.45-7.38 \) (m, 3H), 7.33–7.26 (m, 3H), 7.24–7.17 (m, 5H), 7.09 (d, \( J = 0.8 \) Hz, 1H), 6.97–6.86 (m, 5H), 5.72 (dd, \( J = 8.8, 4.9 \) Hz, 1H), 5.36–5.26 (m, 1H), 4.68 (dd, \( J = 14.5, 8.8 \) Hz, 1H), 4.00 (dd, \( J = 14.5, 4.9 \) Hz, 1H), 1.34 (d, \( J = 6.7 \) Hz, 3H), 1.30 (d, \( J = 6.7 \) Hz, 3H).

\( ^{13} \text{C NMR (75 MHz, CD}_2\text{Cl}_2 \) \( \delta 191.4, 161.9, 148.5, 138.5, 130.0, 129.5, 129.1, 129.0, 127.5, 127.3, 127.2, 126.7, 125.5, 122.1, 121.9, 121.8, 55.9, 52.3, 49.7, 23.6, 23.5. \\
IR (film): \( \nu (\text{cm}^{-1}) \) 3060, 3030, 2979, 2931, 2870, 1687, 1670, 1589, 1492, 1392, 1298, 1254, 1194, 1029, 990, 947, 910, 862, 846, 745, 720, 695, 647, 577, 543. \\
HRMS (ESI, \( m/z \) calcd for C\(_{27}\)H\(_{27}\)N\(_3\)ONa [M+Na]\(^+\): 432.2046, found: 432.2052.

\( (R)-3-\text{(Diphenylamo)-2-phenyl-1-(1-phenyl-1H-imidazol-2-yl)propan-1-one (10a)} \)

Using \( \Delta \text{IrO} \) (2 mol\%) as catalyst, starting from 2-acyl imidazole \( 7a \) (52.4 mg, 0.20 mmol) and \( \alpha \)-silylamine \( 9a \) (153.2 mg, 0.60 mmol) according to the general procedure to give \( 10a \) as a pale yellow oil (79.7 mg, 0.184 mmol, yield: 92\%). Enantiomeric excess established by HPLC analysis using a
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Chiralpak AD-H column, $ee = 97\%$ (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, $t_r$ (major) = 20.8 min, $t_r$ (minor) = 24.4 min). $[\alpha]_D^{20} = +76.4^\circ$ (c 0.6, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ 7.47–7.36 (m, 5H), 7.34–7.27 (m, 3H), 7.26–7.19 (m, 5H), 7.14 (d, $J = 0.9$ Hz, 1H), 7.10–7.03 (m, 2H), 7.00–6.93 (m, 2H), 6.93–6.86 (m, 4H), 5.68 (dd, $J = 8.7$, 5.0 Hz, 1H), 4.62 (dd, $J = 14.6$, 8.7 Hz, 1H), 3.97 (dd, $J = 14.6$, 5.0 Hz, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 189.7, 161.6, 147.9, 142.7, 138.2, 137.4, 129.8, 129.6, 129.1, 128.7, 128.6, 128.5, 127.2, 127.0, 126.8, 126.0, 125.7, 125.0, 121.5, 121.4, 55.3, 51.7.

IR (film): ν (cm$^{-1}$) 3059, 2924, 2854, 1681, 1588, 1490, 1398, 1339, 1304, 1266, 1247, 1150, 1095, 990, 908, 862, 744, 665, 621.

HRMS (ESI, m/z) calcd for C$_{30}$H$_{25}$N$_3$ONa [M+Na]$^+$: 466.1890, found: 466.1893.

(R)-3-(Diphenlamino)-1-(1-phenyl-1H-imidazol-2-yl)-2-m-tolylpropan-1-one (10b)

![Chemical Structure](image)

Using $\Delta$-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7b (55.3 mg, 0.20 mmol) and $\alpha$-silylamine 9a (153.2 mg, 0.60 mmol) according to the general procedure to give 10b as a pale yellow oil (75.0 mg, 0.164 mmol, yield: 82%). Enantiomeric excess established by HPLC analysis using a Chiralpak O-H column, $ee = 96\%$ (HPLC: OD-H, 254 nm, hexane/isopropanol = 99:1, flow rate 0.5 mL/min, 25 °C, $t_r$ (major) = 23.5 min, $t_r$ (minor) = 25.9 min). $[\alpha]_D^{20} = +82.7^\circ$ (c 0.6, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ 7.47–7.39 (m, 4H), 7.34–7.30 (m, 1H), 7.29–7.23 (m, 3H), 7.22–7.18 (m, 5H), 7.14 (d, $J = 1.0$ Hz, 1H), 7.10–7.05 (m, 2H), 7.01–6.94 (m, 2H), 6.94–6.90 (m, 3H), 5.66 (dd, $J = 8.9$, 4.8 Hz, 1H), 4.62 (dd, $J = 14.5$, 8.9 Hz, 1H), 3.97 (dd, $J = 14.5$, 4.9 Hz, 1H), 2.32 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 190.0, 161.9, 148.5, 143.4, 138.9, 137.8, 130.1, 130.0, 129.8, 129.5, 129.1, 128.9, 128.8, 128.4, 127.9, 127.3, 127.2, 126.7, 126.2, 125.5, 121.9, 121.8, 55.7, 52.0, 21.5.

IR (film): ν (cm$^{-1}$) 3035, 2920, 1682, 1590, 1491, 1448, 1399, 1305, 1261, 1147, 1067, 1031, 943, 905, 865, 750, 693, 578, 547.

HRMS (ESI, m/z) calcd for C$_{31}$H$_{27}$N$_3$ONa [M+Na]$^+$: 480.2046, found: 480.2049.
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(R)-3-(Diphenylamino)-1-(1-phenyl-1H-imidazol-2-yl)-2-o-tolylpropan-1-one (10c)

Using Δ-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7c (55.3 mg, 0.20 mmol) and α-silylamine 9a (153.2 mg, 0.60 mmol) according to the general procedure to give 10c as a pale yellow oil (70.5 mg, 0.154 mmol, yield: 77%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 96% (HPLC: AD-H, 254 nm, hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, t_r (minor) = 16.7 min, t_r (major) = 17.3 min). [α]_D^{20} = +144.9° (c 0.8, CH₂Cl₂).

^1H NMR (300 MHz, CDCl₃) δ 7.45–7.36 (m, 3H), 7.33–7.28 (m, 1H), 7.25–7.15 (m, 6H), 7.14–7.08 (m, 2H), 7.08–7.03 (m, 3H), 6.98–6.93 (m, 2H), 6.92–6.86 (m, 4H), 5.94 (dd, J = 7.9, 5.6 Hz, 1H), 4.66 (dd, J = 14.6, 7.9 Hz, 1H), 3.93 (dd, J = 14.6, 5.6 Hz, 1H), 2.52 (s, 3H).

^13C NMR (75 MHz, CDCl₃) δ 190.4, 148.1, 143.2, 138.3, 137.8, 135.9, 130.7, 129.8, 129.1, 128.8, 128.5, 127.6, 127.13, 127.10, 126.0, 125.7, 121.5, 121.4, 55.6, 47.5, 20.0.

IR (film): ν (cm⁻¹) 3059, 2924, 1679, 1587, 1490, 1399, 1308, 1271, 1218, 1149, 1072, 991, 869, 731, 658, 648.

HRMS (ESI, m/z) calcd for C₃₁H₂₇N₃ONa [M+Na]+: 480.2046, found: 480.2052.

(R)-3-(Diphenylamino)-2-(4-methoxyphenyl)-1-(1-phenyl-1H-imidazol-2-yl)propan-1-one (10d)

Using Δ-IrO (4 mol%) as catalyst, starting from 2-acyl imidazole 7d (58.5 mg, 0.20 mmol) and α-silylamine 9a (153.2 mg, 0.60 mmol) according to the general procedure to give 10d as a pale yellow oil (57.8 mg, 0.122 mmol, yield: 61%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 90% (HPLC: AD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 0.5 mL/min, 25 °C, t_r (major) = 24.4 min, t_r (minor) = 28.7 min). [α]_D^{20} = +88.2° (c 0.6, CH₂Cl₂).
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$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 7.45–7.37 (m, 3H), 7.31–7.23 (m, 4H), 7.23–7.18 (m, 4H), 7.13 (d, $J = 1.0$ Hz, 1H), 7.08–7.03 (m, 2H), 6.99–6.93 (m, 2H), 6.92–6.87 (m, 3H), 6.86–6.82 (m, 2H), 5.60 (dd, $J = 8.7$, 5.1 Hz, 1H), 4.56 (dd, $J = 14.5$, 8.7 Hz, 1H), 3.93 (dd, $J = 14.5$, 5.1 Hz, 1H), 3.76 (s, 3H).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 190.2, 159.4, 148.5, 143.3, 138.8, 130.2, 130.1, 130.0, 129.8, 129.6, 129.5, 129.4, 129.1, 128.9, 127.8, 126.2, 122.0, 121.9, 121.8, 114.4, 55.62, 55.1.

IR (film): $\nu$ (cm$^{-1}$) 3062, 2931, 2835, 1679, 1587, 1443, 1398, 1244, 1094, 973, 908, 864, 829, 747, 728, 689, 531.


**(R)-2-(4-Chlorophenyl)-3-(diphenylamino)-1-(1-phenyl-1H-imidazol-2-yl)propan-1-one (10e)**

Using Δ-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7e (59.3 mg, 0.20 mmol) and α-silylamine 9a (153.2 mg, 0.60 mmol) according to the general procedure to give 10e as a white solid (66.9 mg, 0.140 mmol, yield: 70%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, $ee = 98\%$ (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, $t_\text{R}$ (major) = 21.7 min, $t_\text{R}$ (minor) = 27.3 min). [$\alpha$]$_D^{20} = +118.0^\circ$ (c 0.8, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.32–7.18 (m, 5H), 7.14–7.04 (m, 7H), 6.97 (d, $J = 0.8$ Hz, 1H), 6.94–6.87 (m, 2H), 6.86–6.81 (m, 2H), 6.80–6.74 (m, 4H), 5.59 (dd, $J = 8.1$, 5.7 Hz, 1H), 4.49 (dd, $J = 14.6$, 8.1 Hz, 1H), 3.88 (dd, $J = 14.6$, 5.6 Hz, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 189.3, 147.8, 142.5, 138.1, 135.9, 133.2, 130.2, 129.9, 129.1, 128.8, 128.7, 128.6, 127.4, 125.7, 121.6, 121.4, 55.2, 51.1.

IR (film): $\nu$ (cm$^{-1}$) 3034, 2910, 1673, 1587, 1455, 1396, 1269, 1185, 1105, 1034, 992, 938, 859, 830, 746, 731, 690, 645, 617, 589, 558, 526.

HRMS (ESI, m/z) calcd for C$_{36}$H$_{34}$ClN$_3$ONa [M+Na]$^+$: 500.1500, found: 500.1506.
Using Δ-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7f (53.7 mg, 0.20 mmol) and α-silylamine 9a (153.2 mg, 0.60 mmol) according to the general procedure to give 10f as a pale yellow oil (55.7 mg, 0.124 mmol, yield: 62%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 94% (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, t\(_r\) (major) = 25.9 min, t\(_r\) (minor) = 38.1 min). [\(\alpha\)]\(_D\)\(^{20}\) = +54.5° (c 0.5, CH\(_2\)Cl\(_2\)).

\(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 7.46–7.39 (m, 3 H), 7.29–7.25 (m, 2 H), 7.25–7.19 (m, 5 H), 7.17 (d, \(J = 1.0\) Hz, 1 H), 7.13–7.06 (m, 3 H), 7.01–6.95 (m, 2 H), 6.94–6.89 (m, 4 H), 5.87 (dd, \(J = 8.7, 5.3\) Hz, 1 H), 4.58 (dd, \(J = 14.5, 8.7\) Hz, 1 H), 3.99 (dd, \(J = 14.5, 5.3\) Hz, 1 H).

\(^13\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 189.7, 148.4, 143.2, 138.7, 138.0, 130.2, 129.5, 129.1, 128.9, 128.0, 126.2, 126.0, 123.2, 122.0, 121.7, 55.6, 47.5.

IR (film): \(\nu\) (cm\(^{-1}\)) 3059, 2922, 1681, 1587, 1490, 1445, 1364, 1341, 1244, 1188, 1148, 1095, 907, 859, 841, 747, 690, 654, 575, 547.

HRMS (ESI, \(m/z\)) calcd for C\(_{28}\)H\(_{23}\)N\(_3\)O\(_{2}\)S Na [M+Na]+: 472.1454, found: 472.1457.

Using Δ-IrO (4 mol%) as catalyst, starting from 2-acyl imidazole 7g (40.0 mg, 0.20 mmol) and α-silylamine 9b (170.0 mg, 0.60 mmol) according to the general procedure to give 10g as a pale yellow oil (76.2 mg, 0.186 mmol, yield: 93%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 96% (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, t\(_r\) (major) = 21.7 min, t\(_r\) (minor) = 29.3 min). [\(\alpha\)]\(_D\)\(^{20}\) = −108.2° (c 0.8, CH\(_2\)Cl\(_2\)).

\(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 7.45–7.40 (m, 2 H), 7.25–7.16 (m, 3 H), 7.14–7.08 (m, 2 H), 7.07–7.00 (m, 4 H), 6.89–6.81 (m, 4 H), 4.53–4.31 (m, 1 H), 4.15 (dd, \(J = 14.4, 8.0\) Hz, 1 H), 3.66 (dd, \(J = 14.4, 6.0\) Hz, 1 H), 2.30 (s, 6 H), 1.20 (d, \(J = 7.0\) Hz, 3 H).
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**13C NMR** (75 MHz, CD$_2$Cl$_2$) $\delta$ 194.3, 161.9, 146.6, 143.3, 139.0, 131.1, 130.5, 130.0, 129.9, 129.1, 128.8, 127.7, 126.4, 126.3, 125.3, 121.6, 56.2, 41.2, 20.7, 15.7.

**IR (film):** $\nu$ (cm$^{-1}$) 3052, 2922, 1679, 1606, 1596, 1505, 1492, 1444, 1366, 1263, 1225, 1074, 949, 910, 810, 758, 727, 691, 664, 578, 539.

**HRMS (ESI, m/z) calcd for C$_{27}$H$_{27}$N$_3$ONa [M+Na]$^+$: 432.2046, found: 432.2049.

**(R)-2-((Di-p-tolylamino)methyl)-1-(1-phenyl-1H-imidazol-2-yl)butan-1-one (10h)**

![Chemical structure of 10h](image)

Using $\Delta$-IrO (4 mol%) as catalyst, starting from 2-acyl imidazole **7h** (42.9 mg, 0.20 mmol) and $\alpha$-silylamine 9b (170.0 mg, 0.60 mmol) according to the general procedure to give **10h** as a pale yellow oil (55.0 mg, 0.130 mmol, yield: 65%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 96% (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, $t_c$ (major) = 18.5 min, $t_c$ (minor) = 22.9 min). $[\alpha]_{D}^{20} = -84.4^\circ$ (c 0.7, CH$_2$Cl$_2$).

**H NMR** (300 MHz, CD$_2$Cl$_2$) $\delta$ 7.45–7.38 (m, 2H), 7.24–7.15 (m, 3H), 7.10–7.00 (m, 6H), 6.85–6.76 (m, 4H), 4.45–4.29 (m, 1H), 3.73 (dd, $J = 14.4, 5.1$ Hz, 1H), 3.73 (dd, $J = 14.4, 8.8$ Hz, 1H), 2.30 (s, 6H), 1.86–1.56 (m, 2H), 0.91 (t, $J = 7.5$ Hz, 3H).

**13C NMR** (75 MHz, CD$_2$Cl$_2$) $\delta$ 194.4, 161.9, 146.6, 144.1, 139.0, 131.0, 130.5, 130.0, 129.9, 129.0, 128.7, 127.6, 126.4, 126.3, 125.3, 121.6, 55.3, 47.9, 24.3, 20.7, 11.9.

**IR (film):** $\nu$ (cm$^{-1}$) 3027, 2962, 2860, 1676, 1607, 1569, 1506, 1456, 1367, 1277, 1187, 1074, 952, 812, 760, 726, 708, 692, 665, 556.

**HRMS (ESI, m/z) calcd for C$_{28}$H$_{29}$N$_3$ONa [M+Na]$^+$: 446.2203, found: 446.2208.

**(R)-3-((4-Methoxyphenyl)(phenyl)amino)-2-phenyl-1-(1-phenyl-1H-imidazol-2-yl)propan-1-one (10i)**

![Chemical structure of 10i](image)
Using Δ-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7a (52.4 mg, 0.20 mmol) and α-silylamine 9c (171.3 mg, 0.60 mmol) according to the general procedure to give 10i as a pale yellow oil (85.2 mg, 0.180 mmol, yield: 90%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 95% (HPLC: AD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 0.5 mL/min, 25 °C, t₁ (major) = 22.6 min, t₂ (minor) = 25.4 min). [α]D20° = +31.3° (c 0.6, CH2Cl2).

1H NMR (300 MHz, CD2Cl2) δ 7.48–7.38 (m, 5H), 7.35–7.26 (m, 3H), 7.22 (d, J = 1.0 Hz, 1H), 7.21–7.13 (m, 3H), 7.11–7.06 (m, 2H), 6.95–6.88 (m, 2H), 6.79–6.71 (m, 3H), 5.68 (dd, J = 8.8, 4.8 Hz, 1H), 4.57 (dd, J = 14.4, 8.8 Hz, 1H), 3.92 (dd, J = 14.4, 4.8 Hz, 1H), 3.81 (s, 3H).

13C NMR (75 MHz, CD2Cl2) δ 190.0, 157.1, 149.5, 143.4, 140.9, 138.9, 138.1, 130.1, 129.3, 129.2, 129.1, 129.0, 128.9, 127.94, 127.91, 127.7, 126.2, 118.9, 116.7, 115.0, 55.9, 55.9, 52.2.

IR (film): ν (cm⁻¹) 3059, 3031, 2931, 2835, 1734, 1681, 1595, 1506, 1492, 1453, 1398, 1371, 1340, 1307, 1273, 1180, 1072, 965, 869, 760, 692.


(R)-3-((4-Chlorophenyl)(phenyl)amino)-2-phenyl-1-(1-phenyl-1H-imidazol-2-yl)propan-1-one (10j)

Using Δ-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7a (52.4 mg, 0.20 mmol) and α-silylamine 9d (174.0 mg, 0.60 mmol) according to the general procedure to give 10j as a pale yellow oil (62.1 mg, 0.130 mmol, yield: 65%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 95% (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, t₁ (major) = 17.6 min, t₂ (minor) = 19.5 min). [α]D20° = +54.3° (c 0.8, CH2Cl2).

1H NMR (300 MHz, CDCl3) δ 7.46–7.38 (m, 5H), 7.33–7.24 (m, 5H), 7.22–7.17 (m, 2H), 7.16–7.14 (m, 2H), 7.10–7.05 (m, 2H), 7.05–6.98 (m, 1H), 6.96–6.90 (m, 2H), 6.87–6.80 (m, 2H), 5.69 (dd, J = 8.6, 5.1 Hz, 1H), 4.61 (dd, J = 14.6, 8.7 Hz, 1H), 3.96 (dd, J = 14.6, 5.1 Hz, 1H).

13C NMR (75 MHz, CD2Cl2) δ 189.8, 148.0, 147.3, 143.2, 138.8, 137.8, 130.2, 129.7, 129.4, 129.2, 129.14, 129.12, 129.0, 128.0, 127.8, 127.7, 126.2, 122.8, 122.6, 122.3, 55.7, 52.0.
IR (film): $\nu$ (cm$^{-1}$) 3065, 2929, 1682, 1488, 1454, 1399, 1218, 1181, 1133, 1030, 938, 909, 865, 830, 759, 692, 541.

HRMS (ESI, $m/z$) calcd for C$_{30}$H$_{24}$ClN$_3$ONa [M+Na]$^+$: 500.1500, found: 500.1504.

(R)-3-(Di-p-tolylamino)-2-phenyl-1-(1-phenyl-1H-imidazol-2-yl)propan-1-one (10k)

Using $\Delta$-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7a (52.4 mg, 0.20 mmol) and $\alpha$-silylamine 9b (170.0 mg, 0.60 mmol) according to the general procedure to give 10k as a pale yellow oil (84.0 mg, 0.178 mmol, yield: 89%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 91% (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, $t_1$ (major) = 22.6 min, $t_2$ (minor) = 25.3 min). [$\alpha$]$_D^{20}$ = +54.5° (c 0.8, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 7.46–7.36 (m, 5H), 7.35–7.24 (m, 3H), 7.23–7.17 (m, 2H), 7.13 (d, $J$ = 1.0 Hz, 1H), 7.08–7.04 (m, 3H), 7.03–7.00 (m, 2H), 6.81–6.74 (m, 4H), 5.65 (dd, $J$ = 8.9, 4.7 Hz, 1H), 4.56 (dd, $J$ = 14.4, 8.9 Hz, 1H), 3.90 (dd, $J$ = 14.4, 4.7 Hz, 1H), 2.30 (s, 6H).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 190.0, 161.9, 146.3, 143.3, 138.8, 138.1, 131.3, 130.5, 130.1, 130.03, 130.00, 129.10, 129.09, 129.00, 128.9, 127.9, 127.6, 126.4, 126.2, 125.3, 121.6, 55.9, 52.0, 20.7.

IR (film): $\nu$ (cm$^{-1}$) 3027, 2919, 2858, 1681, 1598, 1507, 1445, 1399, 1263, 1247, 1148, 1073, 938, 909, 869, 848, 759, 735, 693, 610, 547.

HRMS (ESI, $m/z$) calcd for C$_{32}$H$_{29}$N$_3$ONa [M+Na]$^+$: 494.2203, found: 494.2206.

(R)-3-(Naphthalen-2-yl(phenyl)amino)-2-phenyl-1-(1-phenyl-1H-imidazol-2-yl)propan-1-one (10l)

Using $\Delta$-IrO (2 mol%) as catalyst, starting from 2-acyl imidazole 7a (52.4 mg, 0.20 mmol) and $\alpha$-silylamine 9e (183.3 mg, 0.60 mmol) according to the general procedure to give 10l as a white solid (62.2 mg, 0.126 mmol, yield: 63%). Enantiomeric excess established by HPLC analysis using a
Chiralpak AD-H column, ee = 97% (HPLC: AD-H, 254 nm, hexane/isopropanol = 97:3, flow rate 0.5 mL/min, 25 °C, t_r (minor) = 34.8 min, t_r (major) = 37.3 min). [α]D^20 = +29.2° (c 0.5, CH2Cl2).

^1H NMR (300 MHz, CD2Cl2) δ 7.77 (d, J = 7.9 Hz, 1H), 7.62 (t, J = 8.9 Hz, 2H), 7.48–7.40 (m, 4H), 7.40–7.30 (m, 7H), 7.28–7.22 (m, 2H), 7.19 (d, J = 0.9 Hz, 1H), 7.10 (td, J = 5.1, 2.4 Hz, 2H), 7.05–6.90 (m, 5H), 5.80 (dd, J = 8.6, 4.9 Hz, 1H), 4.77 (dd, J = 14.6, 8.6 Hz, 1H), 4.09 (dd, J = 14.6, 4.9 Hz, 1H).

^13C NMR (75 MHz, CD2Cl2) δ 189.8, 148.4, 145.8, 143.2, 138.7, 138.1, 135.0, 130.1, 129.9, 129.6, 129.2, 129.10, 129.07, 129.00, 128.8, 128.0, 127.8, 127.7, 127.2, 126.6, 126.1, 124.4, 123.3, 122.2, 122.0, 117.1, 55.9, 51.8.

IR (film): ν (cm⁻¹) 3056, 2924, 2853, 1734, 1681, 1627, 1592, 1491, 1397, 1317, 1303, 1263, 1182, 1147, 1044, 938, 902, 846, 814, 742, 691, 663, 521, 503.

HRMS (ESI, m/z) calcd for C34H27N3ONa [M+Na]^+: 516.2046, found: 516.2050.

5.3.3 Substrate-Coordinated Iridium Complex (Proposed Intermediate A)

1) Synthesis of complex A

![Complex A](image)

The racemic complex A was obtained by reacting substrate 7a (13.0 mg, 0.049 mmol) with racemic Δ/A-IrO (40.0 mg, 0.043 mmol) at room temperature overnight in CH2Cl2 (1.0 mL). After the slow addition of hexane (5.0 mL), crystals were collected after several days (32.2 mg, yield: 68%).

^1H NMR (300 MHz, CD2Cl2) δ 7.90–7.80 (m, 2H), 7.78–7.71 (m, 3H), 7.70–7.68 (m, 1H), 7.67–7.47 (m, 4H), 7.28 (t, J = 1.8 Hz, 2H), 7.22–7.07 (m, 3H), 7.05–6.96 (m, 3H), 6.95–6.93 (m, 1H), 6.69 (t, J = 7.8 Hz, 2H), 6.62 (d, J = 7.7 Hz, 2H), 6.12–6.07 (m, 2H), 6.06–6.04 (m, 1H), 4.15 (d, J = 14.7 Hz, 1H), 3.98 (d, J = 14.7 Hz, 1H), 1.36 (s, 9H), 1.13 (s, 9H).

^13C NMR (75 MHz, CD2Cl2) δ 197.0, 178.9, 176.8, 151.3, 151.2, 148.9, 148.8, 147.3, 145.8, 137.6, 137.5, 135.9, 134.8, 134.4, 133.7, 133.3, 133.1, 133.0, 132.9, 132.8, 132.5, 131.2, 130.6, 130.2, 129.3,
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129.1, 128.5, 128.3, 126.9, 126.5, 124.8, 124.6, 124.0, 123.6, 112.4, 112.3, 111.5, 111.0, 45.4, 35.5, 35.4, 31.8, 31.7.

2) Absorption and emission spectra of complex A
UV/Vis-absorbance and photoluminescence (λ<sub>ex</sub> = 390 nm) spectra of complex A were performed in CH<sub>2</sub>Cl<sub>2</sub> at a concentration of 0.1 mM using a Spectra Max M5 microplate reader with a 10 mm quartz cuvette.

3) Stern-volmer-plot with complex A
Performed in CH<sub>2</sub>Cl<sub>2</sub> at a concentration of 0.1 mM of complex A (volume of 1.0 mL) and different concentrations of amine 9a. Emission intensities were recorded with a Spectra Max M5 microplate reader in a 10 mm quartz cuvette with a cap upon excitation at 390 nm. A concentrated stock solution (100 mM in CH<sub>2</sub>Cl<sub>2</sub>) of amine 9a was titrated in 5.0 µL steps. After the additions, the solutions were shaken once in a while over a period of 5 min and thereafter the emission quenching measured.

4) Cyclovoltammetry with complex A
Cyclic voltammetry was carried out on a BAS C3 Cell Strand and a BAS 100 series Electrochemical Analyzer using a platinum disk working electrode (2.0 mm diameter) and a platinum wire counter electrode (0.5 mm diameter) at room temperature in THF containing Bu<sub>4</sub>NBF<sub>4</sub> (0.1 M). Potentials were referred to a saturated Ag/AgCl reference electrode. Before each experiment, the surface of the working electrode was polished followed by thorough rinsing with distilled water. The solution was purged with nitrogen before each measurement.
5.3.4 Synthesis of the Proposed Intermediate Iridium Enolate Complex B

To a solution of racemic catalyst $\Delta$/A-IrO (40.0 mg, 0.043 mmol) in CH$_2$Cl$_2$ (1.5 mL) was added 2-acyl imidazole 7a (33.8 mg, 0.129 mmol). The reaction mixture was concentrated after around 16 h. The residue was purified by flash chromatography on silica gel (CH$_2$Cl$_2$/EtOAc = 50:1) to afford the enolate complex B as a red solid (34.9 mg, 0.036 mmol, yield: 85%).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 7.86 (d, $J$ = 1.5 Hz, 1H), 7.78–7.69 (m, 2H), 7.61 (dt, $J$ = 4.5, 2.2 Hz, 1H), 7.56–7.49 (m, 4H), 7.48–7.38 (m, 4H), 7.37–7.32 (m, 2H), 7.05–6.97 (m, 4H), 6.94 (dd, $J$ = 7.5, 1.1 Hz, 1H), 6.88 (dd, $J$ = 7.5, 1.5 Hz, 1H), 6.85–6.73 (m, 3H), 6.71–6.65 (m, 3H), 4.75 (s, 1H), 1.26 (s, 9H), 0.95 (s, 9H).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 179.1, 178.1, 155.5, 155.4, 153.3, 150.8, 150.0, 149.0, 148.8, 148.1, 139.9, 139.0, 138.9, 138.4, 134.1, 131.7, 131.6, 131.02, 131.01, 129.9, 127.9, 127.5, 127.4, 126.8, 126.1, 126.0, 124.8, 123.5, 123.1, 122.6, 121.3, 120.9, 115.6, 112.7, 111.3, 110.3, 103.9, 35.5, 35.2, 32.0, 31.4.

5.3.5 Control Reactions

1) Evaluating the catalytic activities of complexes A and B

Using complex A (2 mol%) as catalyst, starting from 2-acyl imidazole 7a (52.4 mg, 0.20 mmol) and $\alpha$-silylamine 9a (153.2 mg, 0.60 mmol) according to the general procedure of synthesizing 10a-1 to give 10a (92% yield, 7.5 h). When use complex B (2 mol%) as catalyst instead, the product 10a could not be observed.

2) Trapping experiment with dibenzyl diazodicarboxylate

To a solution of catalyst $\Delta$-IrO (2 mol%) in anhydrous CH$_2$Cl$_2$ (0.50 mL, 0.4 M) was added the 2-acyl imidazole 7a (52.4 mg, 0.2 mmol) in a 10 mL test tube. After being stirred at room temperature for 20
min, dibenzyl diazodicarboxylate (298.3 mg, 1.0 mmol) was added. The reaction was stirred at room temperature for 7 h under air atmosphere. Afterwards, the solvent was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:2) to afford the product 13 (97.5 mg, 0.174 mmol, yield: 87%) as a white oil. Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 89% (HPLC: AD-H, 254 nm, hexane/isopropanol = 60:40, flow rate 1.0 mL/min, 40 °C, t (minor) = 9.0 min, t (major) = 15.8 min).

1H NMR (300 MHz, CD2Cl2) δ 7.55–7.45 (m, 3H), 7.43–7.36 (m, 2H), 7.35–7.24 (m, 12H), 7.23–7.18 (m, 3H), 7.13–6.97 (m, 3H), 5.28–4.30 (m, 5H).

13C NMR (75 MHz, CD2Cl2) δ 171.2, 138.4, 136.4, 133.2, 130.9, 130.8, 130.6, 129.4, 129.2, 129.0, 128.8, 128.7, 128.4, 128.04, 128.02, 127.9, 126.2, 120.4, 68.6, 67.3, 60.6.

IR (film): ν (cm⁻¹) 3300, 3029, 2953, 1691, 1594, 1492, 1448, 1397, 1338, 1213, 1117, 1051, 969, 912, 844, 740, 693, 647, 591, 547.


3) Dark reaction with the oxidant tBuOOH

To a solution of catalyst ∆-IrO (5 mol%) in anhydrous CH2Cl2 (0.50 mL, 0.4 M) was added the 2-acyl imidazole 7a (52.4 mg, 0.2 mmol) in a 10 mL test tube. After being stirred at room temperature for 20 min, 9a (153.2 mg, 0.60 mmol) and tert-butyl hydroperoxide (36.0 mg, 0.40 mmol) were added. The reaction was stirred at room temperature for 24 h in the dark under air atmosphere. Afterwards, the resulting reaction mixture was purified to afford the product 10a (54.0 mg, 0.121 mmol, yield: 61%, ee: 97%).

5.3.6 Single-Crystal X-Ray Diffraction Studies

Single crystals of the intermediate iridium enolate complex B suitable for X-ray diffraction were obtained after several days from a solution of the compound in CH2Cl2 layered with n-hexane. Crystals of 10e were obtained from a solution of the compound in methanol at 5 °C after several days. Crystal data and details of the structure determination are presented in Appendices 6.7. The absolute configuration was determined.
5.4 Asymmetric Radical-Radical Cross-Coupling through Visible Light Activated Iridium Catalysis

5.4.1 Synthesis of Substrates

1) Synthesis of 2-acyl imidazoles

2-AcyI imidazoles 14a, 14b'-d' were synthesized according to a reported procedure with some modifications. To a solution of the corresponding 1-substituted-1H-imidazole (1.0 eq.) in toluene (0.1 M) at −20 °C was added trifluoroacetic anhydride (1.2 eq.) dropwise. After that, triethylamine (1.2 eq.) was added dropwise to the flask. The reaction was allowed to slowly warm to room temperature and stirred overnight. Removal of the solvent in vacuo and the residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:3) to provide the 2-acyl imidazole 14a, 14b'-d'.

2,2,2-Trifluoro-1-(1-phenyl-1H-imidazol-2-yl)ethanone (14a)

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{Ph} & \quad \text{CF}_3
\end{align*}
\]

Following the general procedure, 1-phenyl-1H-imidazole (1.440 g, 10.0 mmol) was converted to 2-acyl imidazole 14a (1.801 g, 7.5 mmol, yield: 75%) as a white solid.

\(^{1}\text{H NMR} (300 \text{ MHz, CDCl}_3) \delta 7.56–7.47 (m, 4 \text{H}), 7.39–7.35 (m, 1 \text{H}), 7.34–7.28 (m, 2 \text{H}).

\(^{13}\text{C NMR} (75 \text{ MHz, CDCl}_3) \delta 169.8 \text{ (q, } J = 36.7 \text{ Hz), 137.9, 137.0, 132.3, 129.6, 129.3, 129.2, 125.7, 116.3 \text{ (q, } J = 288.5 \text{ Hz).}

\(^{19}\text{F NMR} (282 \text{ MHz, CDCl}_3) \delta -73.40 \text{ (s, 3F).}

IR (film): \nu (\text{cm}^{-1}) 3255, 3095, 2918, 2357, 1769, 1704, 1595, 1498, 1408, 1312, 1269, 1188, 1135, 1063, 1006, 906, 819, 757, 691, 649, 528.

2,2,2-Trifluoro-1-(1-methyl-1H-imidazol-2-yl)ethanone (14b')

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{Me} & \quad \text{CF}_3
\end{align*}
\]
Following the general procedure, 1-methyl-1H-imidazole (0.821 g, 10.0 mmol) was converted to 2-acyl imidazole 14b' (1.478, 8.3 mmol, yield: 83%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.37 (d, \(J = 0.9\) Hz, 1H), 7.23 (d, \(J = 0.9\) Hz, 1H), 4.07 (s, 3H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 170.2 (q, \(J = 35.3\) Hz), 137.8, 131.7, 129.5, 116.2 (q, \(J = 288.7\) Hz), 36.3.

All spectroscopic data were in agreement with the literature.\(^{15}\)

**2,2,2-Trifluoro-1-(1-(4-fluorophenyl)-1H-imidazol-2-yl)ethanone (14c')**

Following the general procedure, 1-(4-fluorophenyl)-1H-imidazole (1.622 g, 10.0 mmol) was converted to 2-acyl imidazole 14c' (2.065 g, 8.0 mmol, yield: 80%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.53 (d, \(J = 0.9\) Hz, 1H), 7.37 (d, \(J = 0.9\) Hz, 1H), 7.35–7.27 (m, 2H), 7.26–7.17 (m, 2H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 169.6 (q, \(J = 36.5\) Hz), 164.5, 161.2, 137.8, 132.9, 132.8, 132.2, 129.3, 127.6, 127.5, 116.4, 116.2 (q, \(J = 288.5\) Hz), 116.1.

\(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) −73.45 (s, 3F), −111.49 (s, 1F).

IR (film): \(\nu\) (cm\(^{-1}\)) 3102, 1711, 1604, 1509, 1458, 1408, 1350, 1194, 1140, 898, 815, 740, 682, 633, 528.

**2,2,2-Trifluoro-1-(1-(4-methoxyphenyl)-1H-imidazol-2-yl)ethanone (14d')**

Following the general procedure, 1-(4-methoxyphenyl)-1H-imidazole (1.742 g, 10.0 mmol) was converted to 2-acyl imidazole 14d' (0.811 g, 3.0 mmol, yield: 30%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.47 (d, \(J = 0.9\) Hz, 1H), 7.33 (d, \(J = 0.9\) Hz, 1H), 7.25–7.18 (m, 2H), 7.01–6.94 (m, 2H), 3.87 (s, 3H).
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$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 169.6 (q, $J = 36.0$ Hz), 160.2, 137.8, 132.0, 129.6, 129.5, 126.8, 118.2 (q, $J = 288.8$ Hz), 114.9, 55.5.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –73.37 (s, 3F).

IR (film): $\nu$ (cm$^{-1}$) 3208, 3154, 2942, 2841, 1699, 1605, 1510, 1456, 1355, 1252, 1134, 1073, 933, 828, 777, 633, 538.

2) Synthesis of tertiary amines

2-Aryl-1,2,3,4-tetrahydroisoquinolines 17a-e were synthesized according to a reported procedure without any further change.$^{16}$ All N-methyldiarylamines were synthesized according to a reported procedure with some modifications.$^{17}$ To a solution of the corresponding diarylamines (1.0 eq.) in THF (0.4 M) under nitrogen atmosphere at 0 °C was added n-BuLi (1.1 eq.) dropwise. The reaction was stirred at 0 °C for 30 min, then stirred at room temperature for an additional 1 h. Methyl iodide (1.5 eq.) was added slowly to the flask after the reaction was cooled back down to 0 °C, and the resulting solution was stirred at room temperature overnight. Afterwards, the reaction was quenched with water and extracted with CH$_2$Cl$_2$. The combined organic layers were dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:100) to produce 15a-h.

$N,N$-Dimethyl-$N$-(p-tolyl)aniline (15a)

![N,N-Dimethyl-N-(p-tolyl)aniline](image)

Following the general procedure, di(p-tolyl)amine (3.946 g, 20.0 mmol) was converted to amine 15a (3.676 g, 17.4 mmol, yield: 87%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.14–7.06 (m, 4H), 6.98–6.86 (m, 4H), 3.29 (s, 3H), 2.33 (s, 6H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 147.1, 130.4, 129.7, 120.4, 40.4, 20.6.

All spectroscopic data were in agreement with the literature.$^{18}$
N-Methyl-N-phenylaniline (15b)

Following the general procedure, diphenylamine (1.692 g, 10.0 mmol) was converted to amine 15b (1.557 g, 8.5 mmol, yield: 85%) as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.37–7.26 (m, 4H), 7.11–7.04 (m, 4H), 7.00 (ddt, $J$ = 8.4, 7.5, 1.1 Hz, 2H), 3.37 (s, 3H).

13C NMR (75 MHz, CDCl$_3$) $\delta$ 149.1, 129.2, 121.3, 120.5, 40.2.

All spectroscopic data were in agreement with the literature.$^{17}$

N,4-Dimethyl-N-phenylaniline (15c)

Following the general procedure, 4-methyl-N-phenylaniline (1.410 g, 7.7 mmol) was converted to amine 15c (1.184 g, 6.0 mmol, yield: 78%) as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.32–7.25 (m, 2H), 7.20–7.14 (m, 2H), 7.08–7.04 (m, 2H), 7.01–6.95 (m, 2H), 6.94–6.87 (m, 1H), 3.34 (s, 3H), 2.38 (s, 3H)

13C NMR (75 MHz, CDCl$_3$) $\delta$ 149.4, 146.6, 132.0, 129.9, 129.0, 122.5, 119.8, 118.3, 40.3, 20.7.

All spectroscopic data were in agreement with the literature.$^{18}$

4-Chloro-N-methyl-N-(p-tolyl)aniline (15d)
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Following the general procedure, 4-chloro-N-(p-tolyl)aniline (0.860 g, 3.9 mmol) was converted to amine 15d (0.730 g, 3.1 mmol, yield: 80%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.20–7.08 (m, 4H), 7.00 (d, $J = 8.4$ Hz, 2H), 6.81 (d, $J = 9.0$ Hz, 2H), 3.26 (s, 3H), 2.34 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 148.0, 146.2, 132.9, 130.1, 128.8, 124.2, 123.2, 118.6, 40.4, 20.8.

IR (film): $\nu$ (cm$^{-1}$) 3026, 2917, 2814, 1706, 1589, 1507, 1498, 1411, 1333, 1251, 1068, 937, 868, 748, 716, 641, 607, 546.

HRMS (FD, m/z) calcd for C$_{14}$H$_{14}$ClN: 231.08148, found: 231.08143.

4-Methoxy-N-methyl-N-(p-tolyl)aniline (15e)

Following the general procedure, 4-methoxy-N-(p-tolyl)aniline (1.826 g, 8.5 mmol) was converted to amine 15e (1.642 g, 7.2 mmol, yield: 85%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.08–6.97 (m, 4H), 6.91–6.84 (m, 2H), 6.81–6.75 (m, 2H), 3.81 (s, 3H), 3.25 (s, 3H), 2.29 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 155.5, 147.6, 142.9, 129.5, 128.6, 124.5, 117.5, 114.7, 55.5, 40.7, 20.4.

IR (film): $\nu$ (cm$^{-1}$) 2906, 2824, 1606, 1501, 1331, 1236, 1179, 1113, 1029, 870, 816, 763, 716, 650, 552.

HRMS (FD, m/z) calcd for C$_{15}$H$_{17}$N: 227.13101, found: 227.13108.

4-(tert-Butyl)-N-(4-(tert-butyl)phenyl)-N-methylaniline (15f)

Following the general procedure, bis(4-(tert-butyl)phenyl)amine (2.814 g, 10.0 mmol) was converted to amine 15f (2.393 g, 8.1 mmol, yield: 81%) as a white solid.
1H NMR (300 MHz, CDCl₃) δ 7.35–7.22 (m, 4H), 7.02–6.90 (m, 4H), 3.30 (s, 3H), 1.33 (s, 18H).

13C NMR (75 MHz, CDCl₃) δ 146.6, 143.8, 125.9, 119.8, 40.2, 34.1, 31.5.

IR (film): ν (cm⁻¹) 3032, 2952, 2868, 1604, 1565, 1340, 1252, 1194, 1073, 874, 820, 766, 556.

HRMS (FD, m/z) calcd for C₂₁H₂₉N: 295.23000, found: 295.23011.

4-Chloro-N-(4-chlorophenyl)-N-methylaniline (15g)

Following the general procedure, bis(4-chlorophenyl)amine (1.520 g, 6.4 mmol) was converted to amine 15g (1.290 g, 5.1 mmol, yield: 80%) as a white solid.

1H NMR (300 MHz, CDCl₃) δ 7.33–7.17 (m, 4H), 7.00–6.86 (m, 4H), 3.29 (s, 3H).

13C NMR (75 MHz, CDCl₃) δ 147.3, 129.2, 126.6, 121.7, 40.4.

IR (film): ν (cm⁻¹) 3082, 2894, 1580, 1481, 1328, 1246, 1176, 999, 815, 757, 673, 579.

HRMS (ESI, m/z) calcd for C₁₃H₁₂Cl₂N [M+H]^+: 252.0341, found: 252.0341.

N-Methyl-N-(p-tolyl)naphthalen-2-amine (15h)

Following the general procedure, N-(p-tolyl)naphthalen-2-amine (1.353 g, 5.8 mmol) was converted to amine 15h (1.112 g, 4.5 mmol, yield: 77%) as a white solid.

1H NMR (300 MHz, CDCl₃) δ 7.65–7.57 (m, 2H), 7.56–7.51 (m, 1H), 7.34–7.26 (m, 1H), 7.20–7.15 (m, 1H), 7.14–7.11 (m, 1H), 7.08–7.01 (m, 3H), 7.00–6.94 (m, 2H), 3.31 (s, 3H), 2.26 (s, 3H).

13C NMR (75 MHz, CDCl₃) δ 147.0, 146.7, 134.8, 132.5, 130.0, 128.5, 128.3, 127.5, 126.5, 126.2, 123.2, 123.1, 120.7, 112.1, 40.7, 20.8.

IR (film): ν (cm⁻¹) 3020, 2907, 1607, 1496, 1369, 1275, 1121, 946, 820, 776, 646, 555.
HRMS (FD, m/z) calcd for C_{18}H_{17}N: 247.13610, found: 247.13579.

5.4.2 Iridium-Catalyzed Photoredox Reactions

1) Reactions of 2-acyl imidazoles with $N$-methyldiarylamines

**General catalysis procedure.** A dried 10 mL Schlenk tube was charged with the catalyst $\Lambda$-IrS\textsuperscript{12} (3 mol%), 2-acyl imidazoles 14a, 14b'-d' (0.20 mmol, 1.0 eq.) and the corresponding amine 15a-h (0.60 mmol, 3.0 eq.). The tube was purged with nitrogen and CHCl\textsubscript{3} (0.4 mL) was added via syringe. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm from a 23 W CFL or approximately 8 cm from a 24 W blue LEDs. The reaction was stirred at room temperature for the indicated time (monitored by TLC) under nitrogen atmosphere. Afterwards, the mixture was diluted with CH\textsubscript{2}Cl\textsubscript{2} (4 mL). The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:20 to 1:10) to afford the products 16a-h. Racemic samples were obtained by carrying out the reactions with rac-IrS. The enantiomeric excess was determined by chiral HPLC analysis.

(S)-3-(Di-p-tolylamino)-1,1,1-trifluoro-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16a)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and amine 15a (126.8 mg, 0.60 mmol) according to the general procedure to give 16a as a colorless oil (74.0 mg, 0.164 mmol, yield: 82%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 99\% (HPLC:...
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**AD-H**, 254 nm, hexane/isopropanol = 95:5, flow rate 0.5 mL/min, 25 °C, t\(_r\) (minor) = 14.7 min, t\(_r\) (major) = 20.0 min. [\(\alpha\)]\(_{D}^{20}\) = –63.9° (c 0.7, CH\(_2\)Cl\(_2\)).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.41–7.27 (m, 3H), 7.07 (d, \(J = 1.2\) Hz, 1H), 7.05–6.98 (m, 4H), 6.94–6.86 (m, 2H), 6.78 (d, \(J = 1.3\) Hz, 1H), 6.75–6.66 (m, 4H), 4.86 (d, \(J = 15.1\) Hz, 1H), 4.27 (d, \(J = 15.1\) Hz, 1H), 4.14 (s, 1H), 2.28 (s, 6H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 146.2, 142.7, 139.0, 132.4, 129.8, 128.5, 128.3, 127.4, 126.9, 124.7, 122.0, 74.8 (q, \(J = 28.5\) Hz), 58.1, 20.5.

\(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) –78.00 (s, 3F).

IR (film): \(\nu\) (cm\(^{-1}\)) 3336, 3029, 2922, 2864, 1684, 1607, 1505, 1360, 1161, 1052, 983, 811, 761, 738, 693, 643, 570, 530.

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\((S)-3-(Di-p-tolylamino)-1,1,1-trifluoro-2-(1-methyl-1H-imidazol-2-yl)propan-2-ol (16b')\)

Starting from 2-acyl imidazole 14b' (35.6 mg, 0.20 mmol) and amine 15a (126.8 mg, 0.60 mmol) according to the general procedure to give 16b' as a white solid (30.8 mg, 0.079 mmol, yield: 40%).

Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, \(ee = 98\%\) (HPLC: AD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 0.5 mL/min, 25 °C, t\(_r\) (minor) = 18.9 min, t\(_r\) (major) = 23.9 min). [\(\alpha\)]\(_{D}^{20}\) = –145.0° (c 0.3, CH\(_2\)Cl\(_2\)).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.04–6.98 (m, 4H), 6.94 (d, \(J = 1.1\) Hz, 1H), 6.79–6.73 (m, 4H), 6.71 (d, \(J = 1.1\) Hz, 1H), 5.10 (s, 1H), 4.81 (d, \(J = 15.5\) Hz, 1H), 4.50 (d, \(J = 15.5\) Hz, 1H), 3.56 (s, 3H), 2.28 (s, 6H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 146.6, 141.9, 132.4, 129.9, 126.9, 126.3, 124.3, 122.0, 74.4 (q, \(J = 29.2\) Hz), 57.1, 34.9, 20.6.

\(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \(\delta\) –78.86 (s, 3F).

IR (film): \(\nu\) (cm\(^{-1}\)) 3359, 3112, 2933, 2851, 1654, 1581, 1453, 1336, 1208, 1154, 1029, 950, 910, 862, 745, 693, 663, 586.
(S)-3-(Di-p-tolylamino)-1,1,1-trifluoro-2-(1-(4-fluorophenyl)-1H-imidazol-2-yl)propan-2-ol (16c')

Starting from 2-acyl imidazole 14c' (51.6 mg, 0.20 mmol) and amine 15a (126.8 mg, 0.60 mmol) according to the general procedure to give 16c' as a colorless oil (62.1 mg, 0.132 mmol, yield: 66%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 90% (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, t_r (minor) = 12.9 min, t_r (major) = 17.0 min). [α]_D^{20} = –51.4° (c 0.6, CH_2Cl_2).

^1H NMR (300 MHz, CDCl_3) δ 7.08 (d, J = 1.2 Hz, 1H), 7.05–6.99 (m, 4H), 6.99–6.93 (m, 2H), 6.88–6.81 (m, 2H), 6.76 (d, J = 1.2 Hz, 1H), 6.75–6.69 (m, 4H), 4.88 (d, J = 15.1 Hz, 1H), 4.25 (d, J = 15.1 Hz, 1H), 4.19 (s, 1H), 2.28 (s, 6H).

^13C NMR (75 MHz, CDCl_3) δ 163.9, 160.6, 146.2, 142.9, 135.0, 132.6, 129.8, 128.6, 128.5, 127.7, 126.3, 125.9, 125.3, 124.7, 122.5, 122.0, 115.8, 115.5, 115.3, 115.0, 74.6 (q, J = 28.5 Hz), 58.1, 20.6.

^19F NMR (282 MHz, CDCl_3) δ –73.05 (s, 1F), –79.01 (s, 3F).

IR (film): ν (cm⁻¹) 3305, 3121, 3025, 2923, 1612, 1504, 1445, 1356, 1213, 1152, 959, 823, 769, 707, 628, 523.

(S)-3-(Di-p-tolylamino)-1,1,1-trifluoro-2-(1-(4-methoxyphenyl)-1H-imidazol-2-yl)propan-2-ol (16d')

134
Starting from 2-acyl imidazole 14d' (54.0 mg, 0.20 mmol) and amine 15a (126.8 mg, 0.60 mmol) according to the general procedure to give 16d' as a white solid (64.5 mg, 0.134 mmol, yield: 67%).

Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 92% (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 ºC, t_r (minor) = 11.7 min, t_r (major) = 18.1 min). [α]_D^20 = -73.2º (c 0.6, CH₂Cl₂).

1H NMR (300 MHz, CDCl₃) δ 7.00–6.87 (m, 5H), 6.77–6.52 (m, 9H), 4.70 (d, J = 15.1 Hz, 1H), 4.28–4.12 (m, 2H), 3.72 (s, 3H), 2.19 (s, 6H).

13C NMR (75 MHz, CDCl₃) δ 159.5, 146.3, 142.9, 132.3, 131.6, 129.8, 128.0, 127.2, 125.1, 122.0, 113.4, 74.9 (q, J = 28.5 Hz), 57.9, 55.4, 20.6.

19F NMR (282 MHz, CDCl₃) δ −78.85 (s, 3F).

IR (film): ν (cm⁻¹) 3344, 3020, 2925, 1610, 1508, 1455, 1365, 1247, 1164, 1114, 1038, 980, 887, 813, 743, 628, 568, 515.

(S)-3-(Diphenylamino)-1,1,1-trifluoro-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16b)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and amine 15b (109.9 mg, 0.60 mmol) according to the general procedure to give 16b as a pale yellow oil (50.8 mg, 0.12 mmol, yield: 60%).

Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 98% (HPLC: AD-H, 254 nm, hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 ºC, t_r (major) = 20.4 min, t_r (minor) = 33.0 min). [α]_D^20 = −67.6º (c 0.3, CH₂Cl₂).

1H NMR (300 MHz, CDCl₃) δ 7.47–7.40 (m, 1H), 7.37–7.27 (m, 2H), 7.26–7.22 (m, 1H), 7.21–7.16 (m, 3H), 7.04 (d, J = 1.2 Hz, 1H), 6.98 (ddt, J = 8.5, 6.9, 1.2 Hz, 2H), 6.89–6.79 (m, 6H), 6.74 (d, J = 1.2 Hz, 1H), 4.89 (d, J = 15.2 Hz, 1H), 4.31 (d, J = 15.2 Hz, 1H), 4.06 (s, 1H).

13C NMR (75 MHz, CDCl₃) δ 148.3, 142.5, 138.9, 129.3, 128.9, 128.64, 128.57, 128.4, 127.4, 126.9, 125.8, 125.2, 124.9, 124.3 (q, J = 284.2 Hz), 123.0, 122.1, 75.1 (q, J = 28.5 Hz), 57.7.

19F NMR (282 MHz, CDCl₃) δ −78.50 (s, 3F).
IR (film): $\nu$ (cm$^{-1}$) 3335, 3059, 2923, 1592, 1493, 1452, 1365, 1307, 1258, 1162, 970, 917, 835, 752, 688, 589, 500.

HRMS (ESI, m/z) calcd for C$_{24}$H$_{20}$F$_3$N$_3$ONa [M+Na]$^+$: 446.1462, found: 446.1453.

(S)-1,1,1-Trifluoro-3-(phenyl(p-tolyl)amino)-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16c)

\[
\text{HO} \quad \text{CF}_3 \\
\text{N} \quad \text{Ph} \quad \text{Me}
\]

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and amine 15c (118.4 mg, 0.60 mmol) according to the general procedure to give 16c as a colorless oil (52.5 mg, 0.12 mmol, yield: 60%).

Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, $ee = 96\%$ (HPLC: AD-H, 254 nm, hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, $t_r$ (major) = 23.5 min, $t_r$ (minor) = 27.6 min). $[\alpha]_D^{20} = -78.3^\circ$ (c 0.3, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.42–7.25 (m, 3H), 7.23–7.14 (m, 2H), 7.10–7.01 (m, 3H), 6.98–6.85 (m, 3H), 6.83–6.70 (m, 5H), 4.87 (d, $J = 15.1$ Hz, 1H), 4.31 (d, $J = 15.1$ Hz, 1H), 4.12 (s, 1H), 2.30 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 149.0, 145.6, 142.6, 139.0, 133.5, 130.0, 129.1, 128.6, 128.4, 127.4, 126.9, 124.9, 124.3 (q, $J = 284.2$ Hz), 123.7, 121.9, 120.4, 75.0 (q, $J = 28.5$ Hz), 57.9, 20.7.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –78.58 (s, 3F).

IR (film): $\nu$ (cm$^{-1}$) 3330, 3034, 2924, 1594, 1498, 1454, 1364, 1258, 1166, 1117, 1050, 980, 884, 821, 754, 690, 591.

HRMS (ESI, m/z) calcd for C$_{25}$H$_{22}$F$_3$N$_3$ONa [M+Na]$^+$: 460.1618, found: 460.1609.

(S)-3-((4-Chlorophenyl)(p-tolyl)amino)-1,1,1-trifluoro-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16d)

\[
\text{HO} \quad \text{CF}_3 \\
\text{N} \quad \text{Ph} \quad \text{Me}
\]
Starting from 2-acyl imidazole **14a** (48.0 mg, 0.20 mmol) and amine **15d** (139.0 mg, 0.60 mmol) according to the general procedure to give **16d** as a pale yellow oil (75.5 mg, 0.16 mmol, yield: 80%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 94% (HPLC: AD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 0.5 mL/min, 25 °C, t<sub>r</sub> (minor) = 15.0 min, t<sub>r</sub> (major) = 16.7 min). [α]<sub>D</sub><sup>20</sup> = −95.4° (c 0.7, CH<sub>2</sub>Cl<sub>2</sub>).

**1H NMR (300 MHz, CDCl<sub>3</sub>)** δ 7.43–7.28 (m, 3H), 7.15–7.11 (m, 1H), 7.10–7.06 (m, 4H), 6.92–6.85 (m, 2H), 6.81 (d, J = 1.2 Hz, 1H), 6.79–6.73 (m, 2H), 6.72–6.65 (m, 2H), 4.71 (d, J = 15.2 Hz, 1H), 4.28 (d, J = 15.2 Hz, 1H), 4.22 (s, 1H), 2.32 (s, 3H).

**13C NMR (75 MHz, CDCl<sub>3</sub>)** δ 147.9, 145.1, 142.4, 138.6, 134.4, 130.2, 128.9, 128.8, 128.5, 127.3, 126.9, 126.3, 125.2, 124.6, 124.2 (q, J = 284.2 Hz), 120.5, 75.3 (q, J = 28.5 Hz), 57.5, 20.7.

**19F NMR (282 MHz, CDCl<sub>3</sub>)** δ −78.26 (s, 3F).

IR (film): ν (cm<sup>−1</sup>) 3300, 3050, 2928, 1686, 1594, 1491, 1366, 1257, 1166, 1122, 921, 809, 758, 697, 625, 530.

HRMS (ESI, m/z) calcd for C<sub>25</sub>H<sub>21</sub>ClF<sub>3</sub>N<sub>3</sub>ONa [M+Na]<sup>+</sup>: 494.1228, found: 494.1221.

**1,1,1-Trifluoro-3-((4-methoxyphenyl)(p-tolyl)amino)-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16e)**

![Chemical structure of 16e](image)

Starting from 2-acyl imidazole **14a** (48.0 mg, 0.20 mmol) and amine **15e** (136.4 mg, 0.60 mmol) according to the general procedure to give **16e** as a pale yellow oil (66.4 mg, 0.142 mmol, yield: 71%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 97% (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, t<sub>r</sub> (minor) = 14.1 min, t<sub>r</sub> (major) = 15.5 min). [α]<sub>D</sub><sup>20</sup> = −55.0° (c 0.5, CH<sub>2</sub>Cl<sub>2</sub>).

**1H NMR (300 MHz, CDCl<sub>3</sub>)** δ 7.42–7.27 (m, 3H), 7.08 (d, J = 1.2 Hz, 1H), 7.02–6.90 (m, 4H), 6.87–6.76 (m, 5H), 6.68–6.60 (m, 2H), 4.83 (d, J = 15.0 Hz, 1H), 4.44 (br s, 1H), 4.24 (d, J = 15.0 Hz, 1H), 3.78 (s, 3H), 2.25 (s, 3H).
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$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 156.5, 147.3, 142.7, 141.1, 138.9, 131.0, 129.6, 128.6, 128.4, 127.3, 126.9, 125.9, 124.8, 124.3 (q, $J = 284.2$ Hz), 119.4, 114.7, 74.8 (q, $J = 28.5$ Hz), 58.3, 55.5, 20.4.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –78.63 (s, 3F).

IR (film): $\nu$ (cm$^{-1}$) 3313, 3117, 2928, 2842, 1676, 1605, 1503, 1454, 1359, 1241, 1165, 1035, 886, 814, 757, 693, 643, 576.

HRMS (ESI, $m/z$) calcd for C$_{26}$H$_{24}$F$_3$N$_3$O$_2$Na $[M+Na]^+$: 490.1724, found: 490.1715.

(S)-3-(Bis(4-(tert-butyl)phenyl)amino)-1,1,1-trifluoro-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16f)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and amine 15f (177.3 mg, 0.60 mmol) according to the general procedure to give 16f as a white solid (80.3 mg, 0.15 mmol, yield: 75%). Enantiomeric excess established by HPLC analysis using a Chiralpak IC column, $ee = 95\%$ (HPLC: IC, 254 nm, hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, $t_m$ (minor) = 8.7 min, $t_M$ (major) = 9.4 min). $[\alpha]_D^{20} = -69.4^\circ$ (c 0.8, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.40–7.18 (m, 7H), 7.05 (d, $J = 1.2$ Hz, 1H), 6.86–6.78 (m, 6H), 6.73 (d, $J = 1.2$ Hz, 1H), 4.91 (d, $J = 15.0$ Hz, 1H), 4.29 (d, $J = 15.0$ Hz, 1H), 4.12 (s, 1H), 1.31 (s, 18H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 145.8, 145.6, 142.7, 139.0, 128.5, 128.3, 127.5, 127.3, 126.8, 126.1, 124.6, 124.3 (q, $J = 283.5$ Hz), 121.6, 74.9 (q, $J = 28.5$ Hz), 58.0, 34.2, 31.4.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –78.65 (s, 3F).

IR (film): $\nu$ (cm$^{-1}$) 3304, 3043, 2956, 1601, 1503, 1366, 1168, 1117, 979, 827, 755, 696, 629, 555.

HRMS (ESI, $m/z$) calcd for C$_{32}$H$_{37}$F$_3$N$_3$O $[M+H]^+$: 536.2894, found: 536.2892.
(S)-3-(Bis(4-chlorophenyl)amino)-1,1,1-trifluoro-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16g)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and amine 15g (151.3 mg, 0.60 mmol) according to the general procedure to give 16g as a white solid (62.0 mg, 0.126 mmol, yield: 63%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 91% (HPLC: AD-H, 254 nm, hexane/isopropanol = 99:1, flow rate 0.5 mL/min, 25 °C, t_r (major) = 33.6 min, t_r (minor) = 36.2 min). [α]_D^20 = −105.0° (c 0.5, CH_2Cl_2).

^1H NMR (300 MHz, CDCl_3) δ 7.49–7.43 (m, 1H), 7.42–7.38 (m, 1H), 7.36–7.31 (m, 1H), 7.22–7.18 (m, 2H), 7.17–7.13 (m, 2H), 7.07 (d, J = 1.3 Hz, 1H), 6.95–6.90 (m, 2H), 6.83 (d, J = 1.2 Hz, 1H), 6.78–6.72 (m, 4H), 4.68 (d, J = 15.3 Hz, 1H), 4.27 (d, J = 15.3 Hz, 1H), 4.09 (s, 1H).

^13C NMR (75 MHz, CDCl_3) δ 146.7, 142.1, 138.3, 129.4, 129.0, 128.9, 128.7, 128.6, 128.4, 127.3, 126.9, 126.8, 125.8, 125.5, 125.2, 124.1 (q, J = 285.0 Hz), 123.3, 75.6 (q, J = 28.5 Hz), 57.2.

^19F NMR (282 MHz, CDCl_3) δ −78.10 (s, 3F).


HRMS (ESI, m/z) calcd for C_{24}H_{19}Cl_2F_3N_3O [M+H]^+: 492.0852, 494.0822, found: 492.0855, 494.0824.

(S)-1,1,1-Trifluoro-3-(naphthalen-2-yl(p-tolyl)amino)-2-(1-phenyl-1H-imidazol-2-yl)propan-2-ol (16h)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and amine 15h (148.4 mg, 0.60 mmol) according to the general procedure to give 16h as a white solid (59.5 mg, 0.122 mmol, yield: 61%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 95% (HPLC:
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AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, t, (minor) = 15.3 min, t, (major) = 23.2 min). [α]D20 = -67.0° (c 0.3, CH2Cl2).

1H NMR (300 MHz, CDCl3) δ 7.62 (d, J = 7.9 Hz, 1H), 7.55 (d, J = 8.9 Hz, 1H), 7.48 (d, J = 8.1 Hz, 1H), 7.39–7.29 (m, 1H), 7.28–7.21 (m, 2H), 7.20–7.13 (m, 2H), 7.03–6.90 (m, 5H), 6.79–6.68 (m, 4H), 6.65–6.62 (m, 1H), 4.94 (d, J = 15.1 Hz, 1H), 4.28 (d, J = 15.1 Hz, 1H), 4.00 (s, 1H), 2.23 (s, 3H).

13C NMR (75 MHz, CDCl3) δ 145.9, 145.8, 142.8, 138.9, 134.2, 133.7, 130.1, 129.4, 128.6, 128.5, 128.3, 127.5, 127.4, 127.1, 126.8, 126.4, 124.9, 124.4, 124.3 (q, J = 284.3 Hz), 123.7, 121.6, 116.3, 74.9 (q, J = 29.2 Hz), 57.9, 20.7.

19F NMR (282 MHz, CDCl3) δ –78.86 (s, 3F).

IR (film): ν (cm⁻¹) 3342, 3051, 2924, 1598, 1502, 1458, 1375, 1262, 1164, 1054, 957, 819, 750, 692, 534.


2) Reactions of 2-acyl imidazole 14a with 2-aryl-1,2,3,4-tetrahydroisoquinolines

General catalysis procedure. A dried 10 mL Schlenk tube was charged with the catalyst Λ-IrS (5 mol%), 2-acyl imidazole 14a (0.20 mmol, 1.0 eq.), and the corresponding 2-aryl-1,2,3,4-tetrahydroisoquinolines 17a-e (0.60 mmol, 3.0 eq.). The tube was purged with nitrogen and CHCl3 (0.40 mL) was added via syringe. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 8 cm from 24 W blue LEDs (18a) or approximately 5 cm from a 23 W CFL (18b-e). The reaction was stirred at room temperature for the indicated time (monitored by TLC) under nitrogen atmosphere. Afterwards, the mixture was diluted with CH2Cl2 (4 mL). The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:20 to 1:10) to afford the products 18a-e. Racemic samples were obtained by carrying out the reactions with
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The enantiomeric excess was determined by chiral HPLC analysis and *dr* values were determined by $^1$H NMR analysis of the crude product. Shown below is an example for the calculation of *dr* value (Figure 88).

**(S)-2,2,2-Trifluoro-1-((R)-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(1-phenyl-1H-imidazol-2-yl)ethanol (18a)**

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and 2-aryl-1,2,3,4-tetrahydroisoquinoline 17a (125.6 mg, 0.60 mmol) according to the general procedure to give 18a as a white solid (82.7 mg, 0.184 mmol, yield: 92%, *dr*: 8:1). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, *ee* = 94% (major product) (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, *t*<sub>m</sub> (minor) = 10.7 min, *t*<sub>r</sub> (major) = 17.1 min). \([\alpha]_D^{20} = +15.3^\circ (c 0.5, \text{CH}_2\text{Cl}_2)\). The *dr* value was determined by crude $^1$H NMR as shown below.

![Figure 88](image-url) **Figure 88** $^1$H NMR of the crude product 18a and its diastereomer 18a'. Calculated *dr* = 8:1.
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$^{1}$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.40–7.32 (m, 1H), 7.30–7.22 (m, 1H), 7.19–7.16 (m, 1H), 7.16–7.04 (m, 6H), 7.03–6.97 (m, 3H), 6.85 (d, $J$ = 1.3 Hz, 1H), 6.83–6.76 (m, 1H), 6.65–6.55 (m, 2H), 5.41 (s, 1H), 5.25 (br s, 1H), 3.84 (ddd, $J$ = 13.2, 7.9, 5.6 Hz, 1H), 3.30 (dt, $J$ = 12.4, 6.0 Hz, 1H), 2.88–2.55 (m, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 150.4, 144.7, 138.5, 136.5, 131.6, 129.8–129.6 (m), 129.1, 128.7, 128.3, 128.1, 127.7, 127.5, 126.9, 125.6, 125.5, 124.0 (q, $J$ = 285.8 Hz), 121.0, 118.4, 79.9 (q, $J$ = 27.0 Hz), 63.8, 46.2, 26.0.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –71.23 (s, 3F).

IR (film): $\nu$ (cm$^{-1}$) 3341, 3018, 2974, 2738, 1688, 1593, 1492, 1454, 1385, 1309, 1250, 1162, 1110, 918, 823, 754, 690, 593, 549.

(S)-2,2,2-Trifluoro-1-(1-phenyl-1H-imidazol-2-yl)-1-((R)-2-(p-tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)ethanol (18b)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and 2-aryl-1,2,3,4-tetrahydroisoquinoline 17b (134.0 mg, 0.60 mmol) according to the general procedure to give 18b as a colorless oil (52.8 mg, 0.114 mmol, yield: 57%, $dr$: 4:1 (determined by the isolated yield of each isomer)). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, $ee$ = 97% (major product) (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, $t_r$ (minor) = 10.5 min, $t_r$ (major) = 14.9 min). [$\alpha)_D^{20} = +28.7^\circ$ (c 0.5, CH$_2$Cl$_2$).

$^{1}$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.60–7.51 (m, 1H), 7.46–7.38 (m, 1H), 7.35–7.24 (m, 5H), 7.23–7.14 (m, 3H), 7.07–6.98 (m, 3H), 6.72–6.62 (m, 2H), 5.63 (s, 1H), 5.55 (s, 1H), 3.93 (ddd, $J$ = 13.1, 7.9, 5.5 Hz, 1H), 3.39 (dt, $J$ = 12.4, 5.9 Hz, 1H), 2.95–2.76 (m, 2H), 2.33 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 148.2, 144.9, 138.7, 136.5, 131.6, 130.9, 129.9–129.7 (m), 129.6, 128.6, 128.3, 128.1, 127.6, 127.5, 127.0, 125.6, 125.3, 124.1 (q, $J$ = 285.8 Hz), 119.1, 79.4 (q, $J$ = 27.0 Hz), 64.5, 46.6, 26.0, 20.4.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –70.53 (s, 3F).
IR (film): $\nu$ (cm$^{-1}$) 3279, 3030, 2921, 2732, 1682, 1604, 1504, 1456, 1302, 1165, 1020, 921, 812, 748, 690, 515.

(S)-1-((R)-2-(4-Chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2,2-trifluoro-1-(1-phenyl-1H-imidazol-2-yl)ethanol (18c)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and 2-aryl-1,2,3,4-tetrahydroisoquinoline 17c (146.2 mg, 0.60 mmol) according to the general procedure to give 18c as a white solid (86.7 mg, 0.180 mmol, yield: 90%, $dr$: 8:1). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, $ee = 98\%$ (major product) (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, $t_r$ (minor) = 11.8 min, $t_r$ (major) = 16.3 min). [$\alpha$]$_D^{20} = +11.4^\circ$ (c 0.6, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.45–7.35 (m, 2H), 7.33–7.19 (m, 5H), 7.17–7.12 (m, 2H), 7.11–7.07 (m, 3H), 6.96 (d, $J = 1.3$ Hz, 1H), 6.69–6.58 (m, 2H), 5.38 (s, 1H), 5.09 (s, 1H), 3.96 (ddd, $J = 13.4$, 8.0, 5.8 Hz, 1H), 3.35 (dt, $J = 12.5$, 6.0 Hz, 1H), 2.95–2.60 (m, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 149.0, 144.2, 138.3, 136.4, 131.1, 129.6–129.5 (m), 128.94, 128.89, 128.5, 128.3, 127.9, 127.5, 126.9, 125.7, 125.6, 125.5, 123.9 (q, $J = 285.8$ Hz), 119.2, 80.4 (q, $J = 27.0$ Hz), 63.1, 45.9, 25.8.

$^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –70.53 (s, 3F).

IR (film): $\nu$ (cm$^{-1}$) 3298, 3057, 2921, 1673, 1593, 1488, 1393, 1250, 1166, 1005, 918, 818, 749, 691, 508.
(S)-1-((R)-2-(4-Bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-2,2,2-trifluoro-1-(1-phenyl-1H-imidazol-2-yl)ethanol (18d)

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and 2-aryl-1,2,3,4-tetrahydroisoquinoline 17d (172.9 mg, 0.60 mmol) according to the general procedure to give 18d as a white solid (102.5 mg, 0.194 mmol, yield: 97%, dr: 10:1). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 98% (major product) (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 ℃, tₘ (minor) = 12.4 min, tₘ (major) = 17.4 min). [α]D²⁰ = +9.9° (c 0.6, CH₂Cl₂).

¹H NMR (300 MHz, CDCl₃) δ 7.43–7.33 (m, 2H), 7.31–7.23 (m, 4H), 7.22–7.18 (m, 3H), 7.15–7.07 (m, 3H), 6.96 (d, J = 1.2 Hz, 1H), 6.66–6.48 (m, 2H), 5.38 (s, 1H), 5.02 (s, 1H), 3.96 (ddd, J = 13.4, 8.0, 5.8 Hz, 1H), 3.36 (dt, J = 12.6, 6.0 Hz, 1H), 2.98–2.65 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 149.4, 144.1, 138.3, 136.4, 131.9, 131.1, 129.6–129.5 (m), 128.9, 128.5, 128.3, 128.0, 127.5, 126.8, 125.7, 125.6, 123.9 (q, J = 285.8 Hz), 119.5, 112.8, 80.4 (q, J = 27.0 Hz), 63.0, 45.7, 25.8.

¹⁹F NMR (282 MHz, CDCl₃) δ –70.67 (s, 3F).

IR (film): ν (cm⁻¹) 3352, 3062, 2922, 2856, 1671, 1591, 1490, 1396, 1302, 1254, 1167, 918, 814, 751, 691, 507.

(S)-2,2,2-Trifluoro-1-((R)-2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(1-phenyl-1H-imidazol-2-yl)ethanol (18e)

144
Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol) and 2-aryl-1,2,3,4-tetrahydroisoquinoline 17e (136.4 mg, 0.60 mmol) according to the general procedure to give 18e as a white solid (83.0 mg, 0.178 mmol, yield: 89\%,\ dr: 8:1). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 97\% (major product) (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 0.5 mL/min, 25 °C, t (minor) = 10.7 min, t (major) = 15.3 min). [α]D20 = +17.7° (c 0.8, CH2Cl2).

1H NMR (300 MHz, CDCl3) δ 7.40–7.31 (m, 2H), 7.27–7.14 (m, 5H), 7.13–7.06 (m, 3H), 6.93 (d, J = 1.2 Hz, 1H), 6.89–6.80 (m, 2H), 6.69–6.60 (m, 2H), 5.42 (s, 1H), 5.33 (s, 1H), 3.89 (ddd, J = 12.9, 8.3, 5.5 Hz, 1H), 3.26 (dt, J = 12.3, 5.8 Hz, 1H), 2.92–2.59 (m, 2H).

13C NMR (75 MHz, CDCl3) δ 159.4, 156.2, 147.03, 147.00, 144.5, 138.3, 136.5, 131.1, 129.6–129.4 (m), 128.8, 128.4, 128.3, 127.7, 127.4, 126.6, 125.7, 125.5, 123.9 (q, J = 285.8 Hz), 121.0, 120.9, 115.7, 115.4, 80.9 (q, J = 27.8 Hz), 64.0, 47.2, 25.8.

19F NMR (282 MHz, CDCl3) δ –73.1 (s, 3F), –123.1 (s, 1F).

IR (film): ν (cm⁻¹) 3340, 3039, 2922, 2710, 1682, 1598, 1501, 1385, 1162, 1108, 921, 823, 749, 692, 516.

3) Reactions of 2-acyl pyridines with amine 15a

**General catalysis procedure.** A dried 10 mL Schlenk tube was charged with the catalyst Λ-IrS (3 or 5 mol%), 2-acyl pyridines19 19a-c (0.20 mmol, 1.0 eq.) and amine 15a (0.60 mmol, 3.0 eq.). The tube was purged with nitrogen and CHCl3 (0.4 mL) was added via syringe. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 8 cm from a 24 W blue LEDs. The reaction was stirred at room temperature for the indicated time (monitored by TLC) under nitrogen atmosphere. Afterwards, the mixture was diluted with CH2Cl2 (4 mL). The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:50) to afford the products 20a-c. Racemic samples were obtained by carrying out the reactions with rac-IrS. The enantiomeric excess was determined by chiral HPLC analysis.
(S)-3-(Di-p-tolylamino)-1,1,1-trifluoro-2-(pyridin-2-yl)propan-2-ol (20a)

Starting from 2-acyl pyridine 19a (35.0 mg, 0.20 mmol) and amine 15a (126.6 mg, 0.60 mmol) according to the general procedure to give 20a as a white solid (57.2 mg, 0.148 mmol, yield: 74%).

Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 93% (HPLC: AD-H, 254 nm, hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, t_r (major) = 16.8 min, t_r (minor) = 18.9 min). [α]_D^20 = −266.0° (c 0.3, CH₂Cl₂).

^1H NMR (300 MHz, CDCl₃) δ 8.52–8.43 (m, 1H), 7.43–7.29 (m, 1H), 7.23–7.09 (m, 2H), 6.93–6.84 (m, 4H), 6.72–6.60 (m, 5H), 4.56 (s, 2H), 2.23 (s, 6H).

^13C NMR (75 MHz, CDCl₃) δ 152.5, 146.9, 146.8, 136.3, 131.0, 129.5, 125.1 (q, J = 285 Hz), 123.4, 122.3–122.1 (m), 121.5, 77.4 (q, J = 26.3 Hz), 56.7, 20.5.

^19F NMR (282 MHz, CDCl₃) δ −78.69 (s, 3F).

IR (film): ν (cm⁻¹) 3292, 3023, 2925, 2863, 1605, 1508, 1412, 1367, 1258, 1169, 1052, 988, 916, 857, 815, 769, 708, 661, 572, 520.


(S)-3-(Di-p-tolylamino)-1,1,1-trifluoro-2-(5-methylpyridin-2-yl)propan-2-ol (20b)

Starting from 2-acyl pyridine 19b (37.8 mg, 0.20 mmol) and amine 15a (126.6 mg, 0.60 mmol) according to the general procedure to give 20b as a white solid (52.2 mg, 0.130 mmol, yield: 65%).

Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 90% (HPLC:
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AD-H, 254 nm, hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, \( t_r \) (major) = 15.7 min, \( t_r \) (minor) = 18.0 min).

\(^1\)H NMR (300 MHz, CDCl\(_3\) \( \delta \) 8.18 (dd, \( J = 2.0, 1.1 \) Hz, 1H), 7.05 (dd, \( J = 8.2, 2.1 \) Hz, 1H), 6.98–6.90 (m, 1H), 6.85–6.77 (d, \( J = 8.3 \) Hz, 4H), 6.61–6.54 (m, 4H), 4.44 (s, 2H), 2.20 (s, 3H), 2.15 (s, 6H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\) \( \delta \) 149.7, 147.0, 146.8, 136.9, 133.3, 130.9, 129.4, 121.7, 121.63, 121.58, 56.8, 20.5, 17.9).

(\(S\))-3-(Di-p-tolylamino)-1,1,1-trifluoro-2-(pyridin-2-yl)propan-2-ol (20c)

![Chemical Structure](image)

Starting from 2-acyl pyridine 19c (37.8 mg, 0.20 mmol) and amine 15a (126.6 mg, 0.60 mmol) according to the general procedure to give 20c as a white solid (49.5 mg, 0.124 mmol, yield: 62%).

Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, \( ee = 90\% \) (HPLC: AD-H, 254 nm, hexane/isopropanol = 99:1, flow rate 0.5 mL/min, 25 °C, \( t_r \) (minor) = 12.1 min, \( t_r \) (major) = 18.4 min).

\(^1\)H NMR (300 MHz, CDCl\(_3\) \( \delta \) 8.29 (dd, \( J = 5.1, 0.9 \) Hz, 1H), 6.98–6.93 (m, 1H), 6.92–6.89 (m, 5H), 6.71–6.63 (m, 4H), 4.64–4.45 (m, 2H), 2.23 (s, 6H), 2.05 (s, 3H).

\(^{19}\)F NMR (282 MHz, CDCl\(_3\) \( \delta \) 78.90 (s, 3F).

4) Reaction of 2-acyl imidazole 14a with amine 15a on gram scale

![Chemical Structure](image)

A dried 25 mL Schlenk tube was charged with catalyst \( \Lambda\text{-IrS} \) (5 mol%), 2-acyl imidazole 14a (0.818 g, 3.4 mmol), and amine 15a (2.152 g, 10.2 mmol). The tube was purged with nitrogen and CHCl\(_3\) (6.8 mL) was added via syringe. The reaction mixture was degassed via freeze-pump-thaw for three cycles.
After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 5 cm away from two 23 W CFL. The reaction was stirred at room temperature for 46 h under nitrogen atmosphere. Afterwards, the mixture was diluted with CH₂Cl₂. The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:15) to afford the product 16a (0.915 g, 2.05 mmol, 60% yield with 98% ee) and unreacted starting material 14a was recollected in a yield of 25%.

**Reaction setup:**

5.4.3 Mechanistic Investigations

1) Substrate-coordinated iridium complex IrS-I

![Iridium complex structure](image)

The racemic substrate-coordinated iridium complex was obtained by reacting substrate 14a (12.1 mg, 0.050 mmol) with racemic Δ/Λ-IrS (40.0 mg, 0.042 mmol) at 50 °C overnight in CHCl₃ (5.0 mL). After the slow addition of hexane (5.0 mL), crystals were collected after several days (32.2 mg, yield: 69%).

¹H NMR (300 MHz, CD₂Cl₂) δ 8.12–8.04 (m, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.6 Hz, 1H), 7.83–7.72 (m, 2H), 7.57 (td, J = 8.7, 1.9 Hz, 2H), 7.44–7.25 (m, 5H), 7.12 (d, J = 1.5 Hz, 1H), 7.08–6.95 (m, 2H), 6.94–6.77 (m, 3H), 6.58–6.45 (m, 2H), 6.29 (d, J = 7.6 Hz, 1H), 1.26 (s, 9H), 1.11 (s, 9H).
13C NMR (75 MHz, CD2Cl2) δ 183.1, 178.1, 151.7, 150.8, 149.5, 147.2, 146.2, 143.2, 140.6, 138.2, 136.5, 134.5, 134.3, 130.2, 129.8, 129.5, 128.8, 128.4, 128.2, 127.4, 126.32, 126.29, 125.7, 125.6, 124.8, 124.4, 123.5, 122.5, 122.2, 121.9, 121.7, 117.4, 115.7, 34.83, 34.79, 31.3, 30.6.

2) Control reactions
Performed in analogy to entry 8 of Table 7 (chapter 3.3), but in the presence of air. The reaction was performed in a 10 mL test tube under an atmosphere of air (air balloon). No product 16a could be detected by crude 1H NMR.

3) Trapping experiments with alkenes and a diazodicarboxylate
Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol), amine 15a (21.1 mg, 0.20 mmol) and (E)-dibenzyl diazene-1,2-dicarboxylate (298.3 mg, 1.0 mol) according to the general procedure of synthesizing 16a-h to give 21 (88.2 mg, 0.172 mmol, yield: 86%) and product rac-16a was not observed.

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol), amine 15a (21.1 mg, 0.20 mmol), and ethyl acrylate (0.054 mL, 0.60 mol) according to the general procedure of synthesizing 16a-h to give 22a (30.0 mg, 0.101 mmol, yield: 51%) and rac-16a (24.6 mg, 0.054 mmol, yield: 27%).

Starting from 2-acyl imidazole 14a (48.0 mg, 0.20 mmol), amine 15a (21.1 mg, 0.20 mmol), and acrylonitrile (0.066 mL, 1.0 mol) according to the general procedure of synthesizing 16a-h to give 22b (23.1 mg, 0.088 mmol, yield: 44%) and rac-16a (yield <10%).

Dibenzyl 1-((di-p-tolylamino)methyl)hydrazine-1,2-dicarboxylate (21)

![Dibenzyl 1-((di-p-tolylamino)methyl)hydrazine-1,2-dicarboxylate (21)](image)

1H NMR (300 MHz, CDCl3) δ 7.31–7.10 (m, 11H), 6.98–6.85 (m, 4H), 6.83–6.70 (m, 3H), 5.43–4.72 (m, 6H), 2.17 (s, 6H).
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13C NMR (75 MHz, CDCl₃) δ 155.5, 144.4, 135.6, 131.6, 129.8, 129.3, 128.6, 128.47, 128.45, 128.2, 128.0, 125.7, 121.0, 67.6, 20.6.


Methyl 6-methyl-1-(p-tolyl)-1,2,3,4-tetrahydroquinoline-4-carboxylate (22a)

![Chemical Structure]

1H NMR (300 MHz, CDCl₃) δ 7.20–7.08 (m, 4H), 7.00–6.96 (m, 1H), 6.80 (dd, J = 8.4, 2.2 Hz, 1H), 6.63–6.55 (m, 1H), 3.84 (t, J = 5.2 Hz, 1H), 3.75 (s, 3H), 3.73–3.65 (m, 1H), 3.59–3.50 (m, 1H), 2.39–2.28 (m, 4H), 2.23 (s, 3H), 2.21–2.07 (m, 1H).

13C NMR (75 MHz, CDCl₃) δ 174.7, 145.8, 142.4, 133.8, 130.2, 130.1, 128.5, 127.1, 125.3, 119.9, 116.1, 52.1, 48.2, 42.6, 25.3, 20.9, 20.4.


6-Methyl-1-(p-tolyl)-1,2,3,4-tetrahydroquinoline-4-carbonitrile (22b)

![Chemical Structure]

1H NMR (300 MHz, CDCl₃) δ 7.23–7.16 (m, 2H), 7.14–7.07 (m, 3H), 6.84 (dd, J = 8.5, 2.1 Hz, 1H), 6.56 (d, J = 8.4 Hz, 1H), 4.03 (t, J = 5.9 Hz, 1H), 3.82–3.70 (m, 1H), 3.67–3.53 (m, 1H), 2.42–2.29 (m, 5H), 2.25 (s, 3H).

13C NMR (75 MHz, CDCl₃) δ 144.9, 142.0, 134.6, 130.3, 129.6, 129.4, 127.9, 125.4, 121.2, 116.2, 116.1, 48.4, 29.3, 26.4, 20.9, 20.2.

HRMS (ESI, m/z) calcd for C₁₈H₁₉N₂ [M+H]⁺: 263.1543, found: 263.1543.

4) Trapping experiments with single electron oxidants

A dried 10 mL Schlenk tube was charged with the catalyst ΔΛ-IrS (3 mol%), 2-acyl imidazole 14a (0.20 mmol, 1.0 eq), amine 15a (0.60 mmol, 3.0 eq), and the corresponding single electron oxidant (5 mol% or 1.0 eq). The tube was purged with nitrogen and CHCl₃ (0.40 mL) was added via syringe. The
reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly
degassed, the vial was sealed and positioned in the dark. The reaction was stirred at room temperature
for 22 h under nitrogen atmosphere.

No product 16b could be detected by $^1$H NMR when Cp$_2$FePF$_6$ or (BrC$_6$H$_4$)$_3$NSbCl$_6$ or Ce(NH$_4$)$_2$(NO$_3$)$_6$
(5 mol% or 1.0 eq.) was used as single electron oxidant.

5) Quantum yield measurement

The quantum yield was measured by standard ferrioxalate actinometry. A 150 W Xenon lamp (50%
of light intensity, 420±5 nm bandpass filter high transmittance) was used as the light source. The
measured method was designed according to published procedures with modifications.

The solutions were prepared under the red light (1.1 W red LEDs) and stored in the dark:

**Potassium ferrioxalate solution (0.15 M):** 736.9 mg of potassium ferrioxalate hydrate was dissolved
in 10 mL of 0.05 M H$_2$SO$_4$.

**Buffered solution of phenanthroline:** 50 mg of 1,10-phenanthroline and 11.25 g of sodium acetate
were dissolved in 50 mL of 0.5 M H$_2$SO$_4$.

a) Measurement of light intensity at 420 nm

1 mL of the ferrioxalate solution was added to a quartz cuvette (l = 10 mm). The actinometry solution
was irradiated with 150 W Xenon lamp (50% of light intensity, 420 nm ± 5 nm bandpass filter high
transmittance) for specified time intervals (30s, 60s, 90s, 120s). After irradiation, 175 μL of the
phenanthroline solution was added to the cuvette. The solution was kept in dark for 30 min to make sure
the complete coordination. The absorbance of the actinometry solution was monitored at 510 nm. The
absorbance of a non-irradiated (in dark) sample was also measured at 510 nm.

<table>
<thead>
<tr>
<th>t/s</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔA/a.u.</td>
<td>0.350</td>
<td>0.738</td>
<td>1.108</td>
<td>1.399</td>
</tr>
</tbody>
</table>

The moles of Fe$^{2+}$ formed were determined using Beer’s Law (eq 1):

$$\text{mol Fe}^{2+} = \frac{V \times ΔA(510\ \text{nm})}{l \times ε(510\ \text{nm})} \quad (1)$$

V is the final volume (0.01175 L) after complexation with phenanthroline;
• ΔA (510 nm) is the optical difference in absorbance between the irradiated and non-irradiated solutions;
• l is the path length (1 cm);
• ε(510 nm) is the molar absorptivity of Fe(phen)$_3^{2+}$ (11100 L·mol$^{-1}$·cm$^{-1}$).

The photon flux (defined as the number of photons per second per unit area) can be calculated (eq 2):

$$\text{photon flux} = \frac{d(\text{mol Fe}^{2+})/dt}{\Phi \times f}$$  \hspace{1cm} (2)

$$f = 1 - 10^{-A}$$  \hspace{1cm} (3)

• Φ is the quantum yield for the ferrioxalate actinometer (1.05 for a 0.15 M solution at 412 nm; 1.04 for a 0.15 M solution at 422 nm; 1.03 for a 0.15 M solution at 433 nm);$^{20}$
• f is the fraction of light absorbed which was calculated using eq 3, where A is the absorbance of above ferrioxalate solution at 420 nm (as shown in Figure 90, A > 3, indicating f is > 0.999≈1).

**Figure 89** The moles of Fe$^{2+}$ are plotted as a function of time.

According to the equation, photon flux can be calculated as follows:

$$\text{photon flux} = \frac{1.26 \times 10^{-9}}{1.04 \times 1} = 1.22 \times 10^{-9} \text{einstein} \cdot \text{s}^{-1}$$
Figure 90 Absorbance of the ferrioxalate actinometer solution (0.15 M).

b) Measurement of quantum yield

Model reaction:

A screw-top cuvette (10.0 mm) was charged with the catalyst rac-IrS (3 mol%), 2-acyl imidazole 14a (96.0 mg, 0.40 mmol), amine 15a (253.6 mg, 1.20 mmol), 0.8 mL CHCl$_3$ (0.5 M), and a small magnetic stir bar. The cuvette was degassed with a nitrogen stream for 10 min. After thoroughly degassed, the reaction mixture was stirred and irradiated with 150 W Xenon lamp (50% of light intensity, 420 nm ± 5 nm bandpass filter high transmittance) for 50400 s (14 h). After irradiation, the reaction mixture was passed through a short silica gel column. The yield of product formed was measured by $^1$H NMR with trimethyl(phenyl)silane as internal standard. The quantum yield calculation is then as following:

\[
\Phi = \frac{\text{mole of product formed}}{\text{mole of photon absorbed}} = \frac{0.4 \times 10^{-3} \times 0.014}{1.22 \times 10^{-9} \times 14 \times 3600 \times 1} = 0.09
\]

5.4.4 Single-Crystal X-Ray Diffraction Studies

Crystals of the (S)-16g and (S,R)-18a were obtained from a solution of the compound in CH$_2$Cl$_2$ layered with n-hexane. Crystal data and details of the structure determination are presented in Appendices 6.7. The absolute configuration was determined.
5.5 Catalytic Asymmetric C(sp³)-H Functionalization under Photoredox Conditions by Radical Translocation and Stereocontrolled Alkene Addition

5.5.1 Synthesis of Substrates

α,β-Unsaturated 2-acyl pyrazoles 24a-l, N-alkoxyphthalimides 25i and 25j were synthesized according to published procedures without any further change, while N-alkoxyphthalimides 25a-h, 25k and 25l were synthesized according to the procedure with some modifications.24

General procedure for the synthesis of N-alkoxyphthalimides.

\[
\begin{align*}
\text{alcohol} & \quad + \quad N\text{-hydroxyphthalimide} \\
& \quad \xrightarrow{\text{PPh}_3, \text{DEAD, THF, r.t., overnight}} \\
& \quad \text{N-alkoxyphthalimide} \\
\end{align*}
\]

To a solution of the corresponding alcohol (1.0 eq.), PPh₃ (1.2 eq.) and N-hydroxyphthalimide (1.2 eq.) in THF (0.2 M) was added diisopropyl azodicarboxylate (2.2 M in toluene, 1.2 eq.) over 5 min at room temperature under nitrogen atmosphere. The reaction mixture was stirred overnight at ambient temperature. Afterwards, the reaction was quenched with aqueous saturated NaHCO₃ and extracted with EtOAc. The organic layer was washed with brine. The combined organic layers were dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:10 to 1:5) to produce the N-alkoxyphthalimides 25a-h, 25k and 25l.

2-(2-Methoxyethoxy)isoindoline-1,3-dione (25a)

Following the general procedure, 2-methoxyethanol (0.761 g, 10.0 mmol) was converted to N-alkoxyphthalimide 25a (1.858 g, 8.4 mmol, yield: 84%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl₃) δ 7.83 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 4.39–4.31 (m, 2H), 3.80–3.72 (m, 2H), 3.37 (s, 3H).

\(^13\)C NMR (75 MHz, CDCl₃) δ 163.4, 134.4, 129.0, 123.5, 70.4, 59.1.
All spectroscopic data were in agreement with the literature.24

2-(2-Isopropyloxyethoxy)isoindoline-1,3-dione (25b)

Following the general procedure, 2-isopropyloxyethanol (0.520 g, 5.0 mmol) was converted to N-alkoxyphthalimide 25b (1.122 g, 4.5 mmol, yield: 90%) as a white solid.

1H NMR (300 MHz, CDCl3) δ 7.83 (dd, J = 5.5, 3.1 Hz, 2H), 7.73 (dd, J = 5.5, 3.1 Hz, 2H), 4.40–4.32 (m, 2H), 3.83–3.70 (m, 2H), 3.59 (p, J = 6.1 Hz, 1H), 1.05 (d, J = 6.1 Hz, 6H).

13C NMR (75 MHz, CDCl3) δ 163.5, 134.3, 129.1, 123.4, 72.1, 66.4, 21.8.

IR (film): ν (cm⁻¹) 2969, 2875, 1787, 1726, 1611, 1464, 1417, 1373, 1329, 1283, 1230, 1184, 1127, 1091, 979, 876, 787, 695, 624, 569, 518.


2-(2-(Cyclopentyloxy)ethoxy)isoindoline-1,3-dione (25c)

Following the general procedure, 2-(cyclopentyloxy)ethanol (0.978 g, 5.0 mmol) was converted to N-alkoxyphthalimide 25c (1.211 g, 4.4 mmol, yield: 88%) as a white solid.

1H NMR (300 MHz, CDCl3) δ 7.83 (dd, J = 5.5, 3.1 Hz, 2H), 7.73 (dd, J = 5.5, 3.1 Hz, 2H), 4.42–4.29 (m, 2H), 3.95–3.82 (m, 1H), 3.80–3.69 (m, 2H), 1.73–1.31 (m, 8H).

13C NMR (75 MHz, CDCl3) δ 163.5, 134.3, 129.1, 123.4, 82.1, 67.2, 32.0, 23.5.

IR (film): ν (cm⁻¹) 2951, 2868, 1788, 1726, 1611, 1464, 1373, 1329, 1283, 1230, 1184, 1127, 1091, 979, 876, 786, 700, 518.

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2-(2-((2,3-Dihydro-1H-inden-2-yl)oxy)ethoxy)isoindoline-1,3-dione (25d)

Following the general procedure, 2-((1-tosylazetidin-3-yl)oxy)ethanol (0.660 g, 3.7 mmol) was converted to N-alkoxyphthalimide 25d (1.135 g, 3.5 mmol, yield: 95%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.90–7.62 (m, 4H), 7.19–7.05 (d, $J = 1.5$ Hz, 4H), 4.49–4.29 (m, 3H), 3.96–3.77 (m, 2H), 3.09 (dd, $J = 16.2, 6.6$ Hz, 2H), 2.87 (dd, $J = 16.2, 4.6$ Hz, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 163.4, 140.7, 134.3, 128.9, 126.4, 124.6, 123.4, 81.0, 67.5, 39.0.

All spectroscopic data were in agreement with the literature.$^{24}$

2-(2-(Cyclohexyloxy)ethoxy)isoindoline-1,3-dione (25e)

Following the general procedure, 2-(cyclohexyloxy)ethanol (0.596 g, 4.1 mmol) was converted to N-alkoxyphthalimide 25e (0.664 g, 2.3 mmol, yield: 56%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.82 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.73 (dd, $J = 5.5, 3.1$ Hz, 2H), 4.42–4.28 (m, 2H), 3.88–3.65 (m, 2H), 3.35–3.15 (m, 1H), 1.77 (dq, $J = 13.1, 8.4, 6.3$ Hz, 2H), 1.68–1.57 (m, 2H), 1.52–1.36 (m, 1H), 1.30–1.01 (m, 5H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 163.4, 134.3, 129.1, 123.4, 77.9, 66.1, 31.8, 25.7, 23.9.

IR (film): $\nu$ (cm$^{-1}$) 2928, 2853, 1784, 1720, 1609, 1453, 1369, 1241, 1181, 1119, 1027, 983, 951, 851, 790, 698, 693, 609, 513.

HRMS (ESI, $m/z$) calcd for C$_{16}$H$_{19}$NO$_4$Na [M+Na]$^+$: 312.1206, found: 312.1206.

2-(2-(Cycloheptyloxy)ethoxy)isoindoline-1,3-dione (25f)
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Following the general procedure, 2-(cycloheptyloxy)ethanol (0.316 g, 2.0 mmol) was converted to N-alkoxyphthalimide 25f (0.371 g, 1.2 mmol, yield: 61%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.86–7.78 (m, 2H), 7.75–7.68 (m, 2H), 4.40–4.29 (m, 2H), 3.79–3.70 (m, 2H), 3.50–3.35 (m, 1H), 1.88–1.71 (m, 2H), 1.60–1.38 (m, 8H), 1.34–1.18 (m, 2H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 163.4, 134.3, 129.1, 123.3, 80.6, 77.3, 66.6, 33.5, 28.3, 22.8.

IR (film): \(\nu\) (cm\(^{-1}\)) 2920, 2876, 1723, 1609, 1441, 1360, 1228, 1177, 1110, 1025, 1000, 987, 851, 789, 690, 610, 513.

HRMS (ESI, \(m/z\)) calcd for C\(_{17}\)H\(_{21}\)NO\(_4\)Na [M+Na\(^+\)]: 326.1363, found: 326.1363.

2-(2-((1-Tosylpiperidin-4-yl)oxy)ethoxy)isoindoline-1,3-dione (25g)

Following the general procedure, 2-((1-tosylpiperidin-4-yl)oxy)ethanol (0.596 g, 4.0 mmol) was converted to N-alkoxyphthalimide 25g (1.422 g, 3.2 mmol, yield: 80%) as a white solid.

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.83–7.71 (m, 4H), 7.61 (d, \(J = 8.2\) Hz, 2H), 7.30 (d, \(J = 8.0\) Hz, 2H), 4.31–4.26 (m, 2H), 3.79–3.67 (m, 2H), 3.46–3.34 (m, 1H), 3.26–3.10 (m, 2H), 2.90–2.74 (m, 2H), 2.42 (s, 3H), 1.92–1.74 (m, 2H), 1.68–1.54 (m, 2H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 163.3, 143.4, 134.4, 133.5, 129.6, 128.9, 127.6, 123.4, 77.2, 73.5, 66.4, 43.1, 30.1, 21.5.

IR (film): \(\nu\) (cm\(^{-1}\)) 2953, 2860, 1833, 1786, 1726, 1599, 1460, 1374, 1332, 1249, 1149, 1112, 1031, 938, 878, 800, 698, 647, 543.

HRMS (ESI, \(m/z\)) calcd for C\(_{22}\)H\(_{24}\)N\(_2\)O\(_6\)SNa [M+Na\(^+\)]: 467.1247, found: 467.1244.

2-(2-((1-Tosylazetidin-3-yl)oxy)ethoxy)isoindoline-1,3-dione (25h)

Following the general procedure, 2-((1-tosylazetidin-3-yl)oxy)ethanol (0.600 g, 2.2 mmol) was converted to N-alkoxyphthalimide 25h (0.559 g, 1.3 mmol, yield: 61%) as a white solid.
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$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.89–7.77 (m, 4H), 7.74 (d, $J$ = 8.3 Hz, 2H), 7.38 (d, $J$ = 8.0 Hz, 2H), 4.32–4.19 (m, 3H), 4.03–3.92 (m, 2H), 3.72–3.67 (m, 2H), 3.66–3.58 (m, 2H), 2.48 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 163.3, 144.0, 134.6, 131.7, 129.7, 128.8, 128.4, 123.6, 67.4, 67.3, 57.9, 21.6.

IR (film): $\nu$ (cm$^{-1}$) 3046, 2998, 2951, 2873, 1791, 1721, 1600, 1463, 1367, 1336, 1296, 1155, 1125, 1090, 1004, 956, 923, 809, 748, 700, 665, 601, 745, 513.

HRMS (ESI, $m/z$) calcd for C$_{20}$H$_{20}$N$_2$O$_6$SNa [M+Na]$^+$: 439.0931, found: 439.0934.

2-(2-(Methylthio)ethoxy)isoindoline-1,3-dione (25k)

Following the general procedure, 2-(methylthio)ethanol (0.461 g, 5.0 mmol) was converted to $N$-alkoxyphthalimide 25k (1.103 g, 4.65 mmol, yield: 93%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.85–7.60 (m, 4H), 4.27 (t, $J$ = 7.2 Hz, 2H), 2.80 (t, $J$ = 7.2 Hz, 2H), 2.10 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 163.2, 134.3, 128.6, 123.3, 76.9, 31.3, 15.7.

IR (film): $\nu$ (cm$^{-1}$) 2922, 1780, 1721, 1611, 1458, 1362, 1293, 1181, 1118, 1075, 1021, 980, 872, 793, 759, 699, 597, 553, 515.

HRMS (ESI, $m/z$) calcd for C$_{11}$H$_{11}$NO$_3$SNa [M+Na]$^+$: 260.0352, found: 260.0352.

2-(2-(Isopropylthio)ethoxy)isoindoline-1,3-dione (25l)

Following the general procedure, 2-(isopropylthio)ethanol (0.601 g, 5.0 mmol) was converted to $N$-alkoxyphthalimide 25l (1.035 g, 3.9 mmol, yield: 78%) as a white solid.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.92–7.80 (m, 2H), 7.78–7.70 (m, 2H), 4.32 (t, $J$ = 7.5 Hz, 2H), 3.10–2.85 (m, 3H), 1.28 (d, $J$ = 6.7 Hz, 6H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 163.5, 134.5, 128.9, 123.6, 77.6, 35.4, 28.1, 23.5.
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IR (film): $\nu$ (cm$^{-1}$) 2960, 2920, 2864, 1781, 1717, 1610, 1459, 1366, 1288, 1231, 1181, 1124, 1077, 1014, 976, 872, 784, 696, 606, 550, 515.

HRMS (ESI, m/z) calcd for C$_{13}$H$_{15}$NO$_3$SNa [M+Na]$^+$: 288.0665, found: 288.0665.

5.5.2 Rhodium-Catalyzed Photoredox Reactions

**General catalysis procedure.** A dried 10 mL Schlenk tube was charged with the catalyst fac-[Ir(ppy)$_3$] (1 mol%), $\Delta$-RhS (8 mol%), Hantzsch ester (0.30 mmol, 1.5 eq.), 2-acyl pyrazoles 24a-j (0.40 mmol, 2.0 eq.), and the corresponding N-alkoxyphthalimides 25a-l (0.20 mmol, 1.0 eq.). The tube was purged with nitrogen and THF (1.0 mL) was added via syringe. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the tube was sealed and positioned approximately 5 cm from a 23 W compact fluorescent lamp (CFL). The reaction was stirred at room temperature for the indicated time (monitored by TLC) under nitrogen atmosphere. Afterwards, the mixture was diluted with DCM (2 mL). The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:10 to 1:5) to afford the products 26a-j, 26m-y. Racemic samples were obtained by carrying out the reactions with rac-RhS. The enantiomeric excess was determined by chiral HPLC analysis.

**Exemplary reaction setup:**
(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-(2-hydroxyethoxy)-3-methylbutan-1-one (26a)

\[
\begin{align*}
\text{Starting from 2-acyl pyrazole } & \text{24a (65.7 mg, 0.40 mmol) and } N\text{-alkoxyphthalimide } \text{25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26a as a pale yellow oil (33.6 mg, 0.140 mmol, yield: 70%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, } ee = 92\% \text{(HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t_r (major) = 8.1 min, t_r (minor) = 8.7 min). } \alpha_l^{25} = +14.5^\circ (c 0.4, \text{CH}_2\text{Cl}_2). \\
\text{^1H NMR (300 MHz, CDCl}_3\text{)} & \delta 5.94 (s, 1H), 3.68–3.60 (m, 2H), 3.56–3.46 (m, 2H), 3.44–3.32 (m, 2H), 3.24 (dd, J = 15.9, 6.8 Hz, 1H), 2.90 (dd, J = 15.9, 6.8 Hz, 1H), 2.56–2.46 (m, 4H), 2.44–2.37 (m, 1H), 2.22 (s, 3H), 1.02 (d, J = 6.8 Hz, 3H). \\
\text{^13C NMR (75 MHz, CDCl}_3\text{)} & \delta 173.5, 151.8, 144.0, 111.0, 75.8, 72.1, 61.7, 39.5, 30.6, 17.2, 14.6, 13.7. \\
\text{IR (film): } & \nu (\text{cm}^{-1}) 3477, 2993, 2923, 2861, 1724, 1582, 1479, 1445, 1384, 1345, 1251, 1212, 1117, 1064, 1028, 995, 968, 893, 845, 738, 695, 614, 589, 554, 507. \\
\text{HRMS (ESI, } m/z & \text{) calcd for C}_{12}\text{H}_{20}\text{N}_2\text{O}_3\text{Na [M+Na]^+: 263.1366, found: 263.1367.}
\end{align*}
\]

(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-((2-hydroxyethoxy)methyl)pentan-1-one (26b)

\[
\begin{align*}
\text{Starting from 2-acyl pyrazole } & \text{24b (71.3 mg, 0.40 mmol) and } N\text{-alkoxyphthalimide } \text{25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26b as a pale yellow oil (34.1 mg, 0.134 mmol, yield: 67%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, } ee = 93\% \text{(HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t_r (major) = 7.1 min, t_r (minor) = 7.7 min). } \alpha_l^{25} = +14.0^\circ (c 0.3, \text{CH}_2\text{Cl}_2). \\
\text{^1H NMR (300 MHz, CDCl}_3\text{)} & \delta 5.95 (s, 1H), 3.65–3.56 (m, 2H), 3.54–3.35 (m, 4H), 3.22 (dd, J = 15.9, 8.0 Hz, 1H), 2.99 (dd, J = 15.9, 5.4 Hz, 1H), 2.53 (s, 3H), 2.41–2.26 (m, 2H), 2.22 (s, 3H), 1.55–1.35 (m, 2H), 0.95 (t, J = 7.5 Hz, 3H). \\
\text{^13C NMR (75 MHz, CDCl}_3\text{)} & \delta 173.9, 151.8, 144.0, 111.1, 73.7, 72.1, 61.7, 37.5, 37.3, 24.5, 14.6, 13.7, 11.4.
\end{align*}
\]
IR (film): $\nu$ (cm$^{-1}$) 3404, 2925, 2867, 1721, 1581, 1457, 1378, 1337, 1257, 1119, 1063, 999, 964, 890, 804, 744, 652, 588.

HRMS (ESI, $m/z$) calcd for C$_{13}$H$_{22}$N$_2$O$_3$Na [M+Na]$^+$: 277.1523, found: 277.1523.

(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-((2-hydroxyethoxy)methyl)hexan-1-one (26c)

Starting from 2-acyl pyrazole 24c (76.9 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26c as a pale yellow oil (35.0 mg, 0.130 mmol, yield: 65%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, $ee = 92\%$ (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, $t_r$ (major) = 6.5 min, $t_r$ (minor) = 6.8 min). [$\alpha$]$D_{25} = +27.5^\circ$ (c 0.2, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.95 (s, 1H), 3.64–3.51 (m, 2H), 3.53–3.44 (m, 3H), 3.43–3.35 (m, 4H), 3.21 (dd, $J$ = 15.8, 8.1 Hz, 1H), 2.99 (dd, $J$ = 15.8, 5.2 Hz, 1H), 2.53 (s, 3H), 2.48–2.28 (m, 2H), 2.22 (s, 3H), 1.43–1.32 (m, 4H), 0.96–0.87 (m, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) 174.0, 151.8, 144.0, 111.1, 74.2, 72.1, 61.7, 37.9, 35.5, 34.0, 20.1, 14.6, 14.2, 13.7.

IR (film): $\nu$ (cm$^{-1}$) 3433, 2955, 2926, 2866, 1721, 1581, 1458, 1409, 1378, 1333, 1257, 1174, 1119, 1061, 992, 963, 890, 802, 742, 649, 589, 530.

HRMS (ESI, $m/z$) calcd for C$_{14}$H$_{24}$N$_2$O$_3$Na [M+Na]$^+$: 291.1679, found: 291.1680.

(S)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-((2-hydroxyethoxy)methyl)-4-methylpentan-1-one (26d)

Starting from 2-acyl pyrazole 24d (78.9 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26d as a pale yellow oil (33.3 mg, 0.124 mmol, yield: 62%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, $ee = 94\%$ (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, $t_r$ (major) = 6.8 min, $t_r$ (minor) = 7.5 min). [$\alpha$]$D_{25} = -8.4^\circ$ (c 0.3, CH$_2$Cl$_2$).
1H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 5.94 (s, 1H), 3.61–3.38 (m, 6H), 3.20 (dd, \(J = 15.7, 8.8\) Hz, 1H), 2.98 (dd, \(J = 15.7, 4.4\) Hz, 1H), 2.52 (s, 3H), 2.45–2.26 (m, 2H), 2.22 (s, 3H), 1.91–1.73 (m, 1H), 0.95 (d, \(J = 6.9\) Hz, 6H).

13C NMR (75 MHz, CDCl\textsubscript{3}) \(\delta\) 174.4, 151.8, 144.0, 111.1, 72.6, 72.1, 61.6, 41.5, 35.2, 29.1, 19.8, 19.6, 14.6, 13.7.

IR (film): \(\nu\) (cm\textsuperscript{-1}) 3435, 2950, 2923, 2876, 1725, 1578, 1467, 1411, 1389, 1333, 1257, 1170, 1119, 1065, 998, 956, 891, 743, 649, 530.

HRMS (ESI, \(m/z\)) calcd for C\textsubscript{14}H\textsubscript{24}N\textsubscript{2}O\textsubscript{3}Na: \([\text{M+Na}]^+\): 291.1679, found: 291.1680.

\((R)-1-(3,5-\text{Dimethyl-1H-pyrazol-1-yl})-3-((2-\text{hydroxyethoxy})\text{methyl})-5-\text{methylhexan-1-one (26e)}\)

\[
\begin{align*}
\text{N} & \text{N} \\
\text{O} & \text{O} \\
im\text{Bu} & \text{OH}
\end{align*}
\]

Starting from 2-acyl pyrazole 24e (82.5 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26e as a pale yellow solid (35.0 mg, 0.124 mmol, yield: 62\%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, \(ee = 91\%\) (HPLC: OD-H, 254 nm, hexane/isopropanol = 98:2, flow rate 0.5 mL/min, 25 °C, \(t_r\) (major) = 18.9 min, \(t_r\) (minor) = 19.6 min). \([\alpha]_D^{25} = +8.0^\circ\) (c 0.4, CH\textsubscript{2}Cl\textsubscript{2}).

1H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 5.95 (s, 1H), 3.66–3.55 (m, 2H), 3.53–3.41 (m, 3H), 3.40–3.31 (m, 1H), 3.17 (dd, \(J = 15.5, 8.5\) Hz, 1H), 2.99 (dd, \(J = 15.5, 4.7\) Hz, 1H), 2.58–2.32 (m, 5H), 2.22 (s, 3H), 1.77–1.58 (m, \(J = 6.7\) Hz, 1H), 1.24 (t, \(J = 7.1\) Hz, 2H), 0.92 (d, \(J = 6.6\) Hz, 6H).

13C NMR (75 MHz, CDCl\textsubscript{3}) \(\delta\) 174.1, 151.8, 144.0, 111.1, 74.5, 72.2, 61.7, 41.2, 38.4, 33.8, 25.4, 22.8, 22.6, 14.6, 13.7.

IR (film): \(\nu\) (cm\textsuperscript{-1}) 3435, 2953, 2927, 2868, 1722, 1622, 1580, 1464, 1410, 1377, 1333, 1258, 1170, 1119, 1058, 1000, 962, 888, 803, 746, 648, 588, 550.

HRMS (ESI, \(m/z\)) calcd for C\textsubscript{15}H\textsubscript{26}N\textsubscript{2}O\textsubscript{3}Na [M+Na]^+: 305.1836, found: 305.1837.
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(S)-3-Cyclohexyl-1-(3,5-dimethyl-1H-pyrazol-1-yl)-4-(2-hydroxyethoxy)butan-1-one (26f)

Starting from 2-acyl pyrazole 24f (92.9 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26f as a white solid (45.6 mg, 0.148 mmol, yield: 74%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, \( ee = 91\% \) (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, \( t_r \) (major) = 6.1 min, \( t_r \) (minor) = 6.8 min). \([\alpha]_D^{25} = -4.3^\circ \) (c 0.5, CH₂Cl₂).

\(^1\)H NMR (300 MHz, CDCl₃) \( \delta \) 5.94 (s, 1H), 3.62–3.49 (m, 3H), 3.48–3.42 (m, 2H), 3.22 (dd, \( J = 15.8, 8.7 \) Hz, 1H), 3.00 (dd, \( J = 15.8, 4.5 \) Hz, 1H), 2.52 (s, 3H), 2.46–2.27 (m, 2H), 2.22 (s, 3H), 1.81–1.59 (m, 5H), 1.54–1.38 (m, 1H), 1.34–0.98 (m, 6H).

\(^13\)C NMR (75 MHz, CDCl₃) \( \delta \) 174.5, 151.8, 144.0, 111.0, 72.5, 72.1, 61.6, 40.9, 39.5, 35.6, 30.3, 30.2, 26.63, 26.61, 26.5, 14.6, 13.7.

IR (film): \( \nu \) (cm\(^{-1}\)) 3424, 2922, 2853, 1723, 1581, 1446, 1410, 1378, 1333, 1237, 1172, 1118, 1057, 963, 889, 801, 748, 649, 588.

HRMS (ESI, \( m/z \)) calcd for C₁₇H₂₈N₂O₃Na \([\text{M+Na}]^+\): 331.1992, found: 331.1994.

(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-ethoxy-4-(2-hydroxyethoxy)butan-1-one (26g)

Starting from 2-acyl pyrazole 24g (77.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26g as a pale yellow oil (43.2 mg, 0.160 mmol, yield: 80%). Enantiomeric excess established by HPLC analysis using a Chiralpak IC column, \( ee = 97\% \) (HPLC: IC, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, \( t_r \) (major) = 30.0 min, \( t_r \) (minor) = 32.3 min). \([\alpha]_D^{25} = -11.0^\circ \) (c 0.5, CH₂Cl₂).
1H NMR (300 MHz, CDCl$_3$) δ 5.94 (s, 1H), 4.21–4.05 (m, 1H), 3.72–3.66 (m, 2H), 3.64–3.55 (m, 5H), 3.41 (dd, $J$ = 16.0, 6.5 Hz, 1H), 3.29 (dd, $J$ = 16.1, 6.1 Hz, 1H), 3.15 (q, $J$ = 7.3, 6.3 Hz, 1H), 2.52 (s, 3H), 2.31–2.11 (m, 4H), 1.16 (t, $J$ = 7.0 Hz, 3H).

13C NMR (75 MHz, CDCl$_3$) δ 171.8, 152.0, 144.0, 111.2, 74.9, 72.8, 72.7, 65.5, 61.7, 38.2, 15.4, 14.4, 13.7.

IR (film): $\nu$ (cm$^{-1}$) 3414, 2971, 2925, 2873, 1721, 1582, 1440, 1380, 1335, 1249, 1121, 1063, 995, 963, 846, 747, 662, 592, 588.

HRMS (ESI, $m/z$) calcd for C$_{13}$H$_{22}$N$_2$O$_4$Na [M+Na]$^+$: 293.1472, found: 293.1473.

(R)-3-(Benzyloxy)-1-(3,5-dimethyl-1H-pyrazol-1-yl)-4-(2-hydroxyethoxy)butan-1-one (26h)

Starting from 2-acyl pyrazole 24h (102.5 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26h as a white solid (52.0 mg, 0.156 mmol, yield: 78%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, $ee = 97\%$ (HPLC: AD-H, 254 nm, hexane/isopropanol = 94:6, flow rate 1.0 mL/min, 25 °C, $t_r$ (minor) = 20.0 min, $t_r$ (major) = 22.0 min). [$\alpha$]$_D^{25} = -6.1^\circ$ (c 0.5, CH$_2$Cl$_2$).

1H NMR (300 MHz, CDCl$_3$) δ 7.41–7.20 (m, 5H), 5.99 (s, 1H), 4.78–4.64 (m, 2H), 4.36–4.25 (m, 1H), 3.75–3.65 (m, 4H), 3.64–3.58 (m, 2H), 3.53 (dd, $J$ = 15.9, 6.7 Hz, 1H), 3.39 (dd, $J$ = 15.9, 6.0 Hz, 1H), 2.74–2.62 (m, 1H), 2.56 (s, 3H), 2.25 (s, 3H).

13C NMR (75 MHz, CDCl$_3$) δ 171.6, 152.1, 144.0, 138.3, 128.3, 127.8, 127.6, 111.2, 74.8, 72.8, 72.6, 72.2, 61.7, 38.3, 14.5, 13.7.

IR (film): $\nu$ (cm$^{-1}$) 3477, 2993, 2923, 2861, 1724, 1582, 1479, 1445, 1384, 1345, 1251, 1212, 1117, 1064, 1028, 995, 968, 893, 845, 738, 695, 614, 589, 554, 507.

HRMS (ESI, $m/z$) calcd for C$_{18}$H$_{24}$N$_2$O$_4$Na [M+Na]$^+$: 355.1628, found: 355.1625.
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(S)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(2,4-dimethylphenyl)-4-(2-hydroxyethoxy)butan-1-one (26i)

Starting from 2-acyl pyrazole 24i (101.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26i as a white solid (33.7 mg, 0.102 mmol, yield: 51%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, ee = 91% (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t<sub>r</sub> (minor) = 8.9 min, t<sub>r</sub> (major) = 12.1 min). [α]<sub>D</sub> = –24.6° (c 0.3, CH<sub>2</sub>Cl<sub>2</sub>).

1H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.14 (d, J = 7.7 Hz, 1H), 7.05–6.91 (m, 2H), 5.95 (s, 1H), 4.05–3.87 (m, 1H), 3.69–3.42 (m, 7H), 3.37 (dd, J = 15.9, 6.3 Hz, 1H), 2.50 (s, 3H), 2.42 (s, 3H), 2.33–2.21 (d, J = 10.3 Hz, 7H).

13C NMR (75 MHz, CDCl<sub>3</sub>) δ 173.1, 151.9, 144.0, 136.7, 136.1, 136.0, 131.3, 126.8, 126.1, 111.0, 75.0, 72.2, 61.6, 39.1, 37.0, 20.9, 19.6, 14.5, 13.7.

IR (film): ν (cm<sup>−1</sup>) 3429, 2923, 2863, 1722, 1616, 1580, 1501, 1445, 1409, 1377, 1339, 1256, 1169, 1118, 1056, 1000, 961, 884, 813, 739, 702, 654, 579.

HRMS (ESI, m/z) calcd for C<sub>19</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>Na [M+Na]<sup>+</sup>: 353.1836, found: 353.1832.

(S)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-(2-hydroxyethoxy)-3-(4-methoxyphenyl)butan-1-one (26j)

Starting from 2-acyl pyrazole 2j (102.5 mg, 0.40 mmol) and N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol) according to the general procedure to give 26j as a white solid (37.9 mg, 0.114 mmol, yield: 57%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, ee = 82%
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(HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t_r (major) = 17.3 min, t_r (minor) = 20.2 min). [α]_D\textsuperscript{25} = –8.0° (c 0.4, CH₂Cl₂).

\( ^1 \text{H} \text{NMR} \) (300 MHz, CDCl\(_3\)) \( δ \) 7.22 (d, \( J = 8.7 \) Hz, 2H), 6.84 (d, \( J = 8.7 \) Hz, 2H), 5.93 (s, 1H), 3.77 (s, 3H), 3.69–3.58 (m, 6H), 3.54–3.47 (m, 2H), 3.44–3.30 (m, 1H), 2.48 (s, 3H), 2.38–2.28 (m, 1H), 2.24 (s, 3H).

\( ^{13} \text{C} \text{NMR} \) (75 MHz, CDCl\(_3\)) \( δ \) 172.8, 158.4, 151.9, 144.1, 133.7, 128.7, 113.9, 111.1, 75.3, 72.1, 61.6, 55.2, 41.1, 38.8, 14.5, 13.8.

IR (film): \( ν \) (cm\(^{-1}\)) 3450, 2924, 2880, 1726, 1610, 1582, 1501, 1453, 1375, 1324, 1242, 1175, 1112, 1032, 960, 891, 823, 745, 634, 561, 527.

HRMS (ESI, \( m/z \)) calcd for C\(_{18}\)H\(_{24}\)N\(_2\)O\(_4\)Na [M+Na]\(^+\): 355.1625, found: 355.1624.

(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-(2-hydroxyethoxy)-3,4-dimethylpentan-1-one (26m)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and \( N \)-alkoxyphthalimide 25b (49.9 mg, 0.20 mmol) according to the general procedure to give 26m as a white solid (45.1 mg, 0.168 mmol, yield: 84%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, \( ee = 91\% \) (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t_r (major) = 6.3 min, t_r (minor) = 6.7 min). [α]_D\textsuperscript{25} = +25.2° (c 0.5, CH₂Cl₂).

\( ^1 \text{H} \text{NMR} \) (300 MHz, CDCl\(_3\)) \( δ \) 5.93 (s, 1H), 3.63–3.53 (m, 2H), 3.50–3.36 (m, 3H), 2.70 (dd, \( J = 15.5, 8.4 \) Hz, 1H), 2.52 (s, 3H), 2.49–2.35 (m, 2H), 2.22 (s, 3H), 1.16 (d, \( J = 14.2 \) Hz, 6H), 0.98 (d, \( J = 6.9 \) Hz, 3H).

\( ^{13} \text{C} \text{NMR} \) (75 MHz, CDCl\(_3\)) \( δ \) 174.4, 151.7, 144.0, 111.0, 77.2, 62.2, 62.1, 38.7, 37.6, 23.7, 20.6, 15.9, 14.6, 13.7.

IR (film): \( ν \) (cm\(^{-1}\)) 3425, 2974, 2873, 1721, 1581, 1514, 1461, 1376, 1326, 1246, 1153, 1049, 992, 960, 927, 888, 801, 757, 707, 657, 561, 524.

HRMS (ESI, \( m/z \)) calcd for C\(_{14}\)H\(_{24}\)N\(_2\)O\(_3\)Na [M+Na]\(^+\): 291.1679, found: 291.1680.
(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(1-(2-hydroxyethoxy)cyclopentyl)butan-1-one (26n)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25c (55.1 mg, 0.20 mmol) according to the general procedure to give 26n as a pale yellow oil (43.0 mg, 0.146 mmol, yield: 73%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, ee = 93% (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t_r (major) = 6.7 min, t_r (minor) = 7.7 min), [α]_D^{25} = +24.5° (c 0.2, CH₂Cl₂).

^1H NMR (300 MHz, CDCl₃) δ 5.94 (s, 1H), 3.71–3.63 (m, 2H), 3.55–3.47 (m, 1H), 3.46–3.35 (m, 2H), 2.81 (dd, J = 15.6, 9.7 Hz, 1H), 2.68–2.57 (m, 1H), 2.53 (s, 3H), 2.45–2.28 (m, 1H), 2.22 (s, 3H), 1.83–1.52 (m, 8H), 0.99 (d, J = 6.8 Hz, 3H).

^13C NMR (75 MHz, CDCl₃) δ 174.2, 151.8, 144.0, 111.0, 89.6, 62.43, 62.36, 38.3, 34.6, 32.8, 32.5, 24.7, 24.6, 15.7, 14.6, 13.7.

IR (film): ν (cm⁻¹) 3422, 2957, 2870, 1721, 1581, 1456, 1409, 1377, 1326, 1243, 1180, 1139, 1055, 965, 893, 803, 755, 658, 613, 553.


(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(2-(2-hydroxyethoxy)-2,3-dihydro-1H-inden-2-yl)butan-1-one (26o)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25d (64.7 mg, 0.20 mmol) according to the general procedure to give 26o as a pale yellow oil (52.0 mg, 0.152 mmol, yield: 76%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, ee = 94% (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t_r (major) = 13.7 min, t_r (minor) = 15.8 min), [α]_D^{25} = +4.8° (c 0.6, CH₂Cl₂).
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.24–7.09 (m, 4H), 5.96 (s, 1H), 3.56–3.41 (m, 3H), 3.36–3.20 (m, 2H), 3.19–3.04 (m, 4H), 2.96 (dd, $J = 15.7, 8.6$ Hz, 1H), 2.75–2.60 (m, 1H), 2.55 (s, 3H), 2.42–2.30 (m, 1H), 2.24 (s, 3H), 1.06 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 174.0, 151.8, 144.0, 141.5, 141.3, 126.59, 126.55, 124.04, 124.01, 111.1, 88.7, 63.9, 62.2, 41.3, 40.4, 38.3, 38.2, 16.0, 14.6, 13.8.

IR (film): $\nu$ (cm$^{-1}$) 3426, 2928, 2871, 1721, 1581, 1514, 1460, 1410, 1377, 1326, 1289, 1217, 1092, 1044, 964, 888, 802, 740, 655, 582, 551.

HRMS (ESI, $m/z$) calcd for C$_{20}$H$_{26}$N$_2$O$_3$Na $[\text{M+Na}]^+$: 365.1836, found: 365.1835.

(S)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(2-(2-hydroxyethoxy)-2,3-dihydro-1H-inden-2-yl)-4-methylpentan-1-one (26p)

Starting from 2-acyl pyrazole 24d (78.9 mg, 0.40 mmol) and $N$-alkoxyphthalimide 25d (64.7 mg, 0.20 mmol) according to the general procedure to give 26p as a pale yellow oil (58.1 mg, 0.170 mmol, yield: 85%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, $ee = 97\%$ (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, $t_r$ (major) = 9.3 min, $t_r$ (minor) = 10.8 min). $[\alpha]_{D}^{25} = -9.1\degree$ ($c$ 0.6, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.21–7.09 (m, 4H), 5.98 (s, 1H), 3.60–3.39 (m, 3H), 3.22–3.09 (m, 5H), 3.05–2.93 (m, 2H), 2.65–2.58 (m, 1H), 2.56 (s, 3H), 2.48–2.39 (m, 1H), 2.26 (s, 3H), 2.20–2.09 (m, 1H), 1.00 (d, $J = 6.9$ Hz, 6H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 175.3, 152.0, 144.1, 141.6, 141.4, 126.6, 126.5, 123.83, 123.79, 111.2, 89.5, 64.0, 62.2, 49.0, 42.6, 41.5, 31.5, 28.4, 23.6, 18.7, 14.7, 13.8.

IR (film): $\nu$ (cm$^{-1}$) 3445, 2929, 2871, 1722, 1581, 1461, 1411, 1379, 1314, 1279, 1234, 1173, 1094, 1053, 989, 961, 803, 737, 674, 583, 540.

HRMS (ESI, $m/z$) calcd for C$_{22}$H$_{30}$N$_2$O$_3$Na $[\text{M+Na}]^+$: 393.2149, found: 393.2149.
(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(1-(2-hydroxyethoxy)cyclohexyl)butan-1-one (26q)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25e (57.9 mg, 0.20 mmol) according to the general procedure to give 26q as a pale yellow oil (50.0 mg, 0.162 mmol, yield: 81%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, ee = 94% (HPLC: OD-H, 254 nm, hexane/isopropanol = 99:1, flow rate 1.0 mL/min, 25 °C, t<sub>r</sub> (major) = 14.2 min, t<sub>r</sub> (minor) = 15.5 min). [α]<sub>D</sub><sup>25</sup> = +8.5° (c 0.6, CH₂Cl₂).

¹H NMR (300 MHz, CDCl₃) δ 5.93 (s, 1H), 3.80–3.68 (m, 2H), 3.56–3.46 (m, 1H), 3.44–3.30 (m, 2H), 2.80 (dd, J = 15.8, 10.7 Hz, 1H), 2.58–2.36 (m, 5H), 2.21 (s, 3H), 2.20–1.33 (m, 9H), 1.22–1.07 (m, 1H), 0.94 (d, J = 6.9 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 174.4, 151.7, 144.0, 111.0, 77.1, 62.6, 60.3, 37.0, 34.6, 30.1, 29.9, 25.8, 21.6, 21.4, 15.0, 14.6, 13.7.

IR (film): ν (cm⁻¹) 3424, 2930, 2860, 1722, 1581, 1449, 1410, 1377, 1327, 1218, 1146, 1055, 965, 899, 804, 755, 705, 659, 600, 548.


(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(1-(2-hydroxyethoxy)cycloheptyl)butan-1-one (26r)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25f (60.7 mg, 0.20 mmol) according to the general procedure to give 26r as a pale yellow oil (40.0 mg, 0.124 mmol, yield: 62%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, ee = 95% (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, t<sub>r</sub> (major) = 5.7 min, t<sub>r</sub> (minor) = 6.3 min). [α]<sub>D</sub><sup>25</sup> = +21.1° (c 0.4, CH₂Cl₂).

¹H NMR (300 MHz, CDCl₃) δ 5.93 (s, 1H), 3.71 (t, J = 4.7 Hz, 2H), 3.57–3.46 (m, 1H), 3.44–3.37 (m, 1H), 3.32 (dd, J = 15.8, 2.6 Hz, 1H), 2.85 (dd, J = 15.8, 10.7 Hz, 1H), 2.57–2.39 (m, 5H), 2.21 (s, 3H), 1.82–1.40 (m, 12H), 0.95 (d, J = 6.8 Hz, 3H).
\( ^{13} \text{C NMR (75 MHz, CDCl}_3 \) \( \delta \) 174.3, 151.7, 144.0, 111.0, 80.7, 62.5, 61.0, 37.2, 36.7, 34.8, 34.5, 29.4, 29.3, 22.6, 22.5, 15.1, 14.6, 13.7. \\
IR (film): \( \nu \) (cm\(^{-1}\)) 3430, 2925, 2860, 1723, 1581, 1460, 1410, 1379, 1331, 1218, 1171, 1048, 963, 892, 805, 751, 664, 593, 555. \\
HRMS (ESI, \( m/z \)) calcd for C\(_{18}\)H\(_{30}\)N\(_2\)O\(_3\)Na [M+Na]\(^+\): 345.2149, found: 345.2149.

(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(4-(2-hydroxyethoxy)-1-tosylpiperidin-4-yl)butan-1-one (26s)

Starting from 2-acyl 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25g (88.9 mg, 0.20 mmol) according to the general procedure to give 26s as a white solid (67.0 mg, 0.144 mmol, yield: 72%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, \( ee = 93\% \) (HPLC: OD-H, 254 nm, hexane/isopropanol = 80:20, flow rate 1.0 mL/min, 25 \( ^\circ \)C, t, (major) = 10.6 min, t, (minor) = 13.1 min). \( [\alpha]_D^{25} = +25.6^\circ \) (c 0.8, CH\(_2\)Cl\(_2\)).

\( ^1\text{H NMR (300 MHz, CDCl}_3 \) \( \delta \) 7.63 (d, \( J = 8.0 \) Hz, 2H), 7.30 (d, \( J = 7.9 \) Hz, 2H), 5.93 (s, 1H), 3.70–3.49 (m, 4H), 3.47–3.38 (m, 1H), 3.35–3.17 (m, 2H), 2.74 (dd, \( J = 15.7, 10.6 \) Hz, 1H), 2.62 (td, \( J = 11.9, 3.0 \) Hz, 1H), 2.56–2.36 (d, \( J = 25.5 \) Hz, 8H), 2.18 (s, 3H), 2.12–1.98 (m, 1H), 1.90–1.61 (m, 4H), 0.90 (d, \( J = 6.8 \) Hz, 3H).

\( ^{13} \text{C NMR (75 MHz, CDCl}_3 \) \( \delta \) 173.5, 151.9, 144.0, 143.4, 133.4, 129.5, 127.6, 111.1, 74.8, 62.1, 60.7, 41.8, 41.7, 36.6, 33.7, 29.2, 28.8, 21.4, 14.8, 14.5, 13.6. \\
IR (film): \( \nu \) (cm\(^{-1}\)) 3411, 2930, 2866, 1720, 1586, 1459, 1408, 1378, 1327, 1248, 1216, 1159, 1088, 1050, 968, 893, 846, 815, 762, 651, 545. \\
HRMS (ESI, \( m/z \)) calcd for C\(_{23}\)H\(_{38}\)N\(_4\)O\(_5\)Na [M+Na]\(^+\): 486.2033, found: 486.2034.
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(5)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(2,4-dimethylphenyl)-3-(4-(2-hydroxyethoxy)-1-tosylpiperidin-4-yl)propan-1-one (26t)

Starting from 2-acyl pyrazole 24i (101.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25g (88.9 mg, 0.20 mmol) according to the general procedure to give 26t as a white solid (60.0 mg, 0.108 mmol, yield: 54%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, ee = 92% (HPLC: OD-H, 254 nm, hexane/isopropanol = 85:15, flow rate 1.0 mL/min, 25 °C, t_r (major) = 12.6 min, t_r (minor) = 18.9 min). [α]_D^25 = −19.7° (c 0.4, CH₂Cl₂).

1H NMR (300 MHz, CDCl₃) δ 7.59 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 7.9 Hz, 1H), 7.00–6.89 (m, 2H), 5.87 (s, 1H), 4.11 (dd, J = 9.2, 5.2 Hz, 1H), 3.78–3.51 (m, 5H), 3.50–3.41 (m, 1H), 3.40–3.31 (m, 1H), 2.65 (td, J = 12.1, 3.1 Hz, 1H), 2.50–2.36 (m, 4H), 2.35–2.24 (m, 9H), 2.23–2.10 (m, 4H), 2.02 (td, J = 12.7, 4.7 Hz, 1H), 1.95–1.81 (m, 2H), 1.44–1.22 (m, 2H).

13C NMR (75 MHz, CDCl₃) δ 172.7, 151.8, 144.0, 143.9, 137.1, 136.3, 134.2, 133.3, 131.5, 129.5, 128.0, 127.6, 126.8, 110.9, 76.4, 62.2, 61.2, 41.9, 41.7, 39.7, 35.8, 30.7, 28.2, 21.5, 20.9, 20.4, 14.3, 13.7.

IR (film): v (cm⁻¹) 3560, 2928, 2865, 1721, 1585, 1548, 1410, 1378, 1321, 1248, 1161, 1087, 1049, 992, 959, 811, 768, 726, 653, 585, 545.


(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-3-(3-(2-hydroxyethoxy)-1-tosylazetidin-3-yl)butan-1-one (26u)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25h (83.2 mg, 0.20 mmol) according to the general procedure to give 26u as a white solid (50.0 mg, 0.114 mmol, yield:
57%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, $ee = 86\%$ (HPLC: AD-H, 254 nm, hexane/isopropanol = 90:10, flow rate 1.0 mL/min, 25 °C, $t_t$ (major) = 27.8 min, $t_t$ (minor) = 30.8 min). [$\alpha$]$_D^{25} = +15.8^\circ$ (c 0.4, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 7.8$ Hz, 2H), 5.94 (s, 1H), 3.86–3.68 (m, 4H), 3.52 (t, $J = 4.7$ Hz, 2H), 3.39 (ddd, $J = 9.0$, 5.1, 3.7 Hz, 1H), 3.34–3.25 (m, 1H), 3.11 (dd, $J = 15.6$, 4.8 Hz, 1H), 2.80 (dd, $J = 15.5$, 8.3 Hz, 1H), 2.49 (s, 3H), 2.46–2.34 (m, 4H), 2.25–2.08 (m, 4H), 0.95 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 172.9, 152.1, 144.3, 144.0, 131.6, 129.7, 128.3, 111.3, 64.4, 61.6, 57.8, 57.1, 56.7, 36.6, 35.3, 21.5, 14.5, 14.1, 13.7.

IR (film): $\nu$ (cm$^{-1}$) 3533, 2930, 2877, 1722, 1634, 1590, 1451, 1381, 1336, 1157, 1089, 966, 842, 756, 705, 667, 607, 548.

HRMS (ESI, $m/z$) calcd for C$_{21}$H$_{29}$N$_3$O$_5$SNa [M+Na]$^+$: 458.1720, found: 458.1719.

(3R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-(2-hydroxyethoxy)-3-methyl-4-(naphthalen-2-yl)butan-1-one (26v)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxypthalimide 25i (69.3 mg, 0.20 mmol) according to the general procedure to give 26v as a pale yellow oil (52.0 mg, 0.142 mmol, yield: 71%, $dr = 3:1$). Enantiomeric excess established by HPLC analysis using a Chiralpak OJ-H column, $ee = 97\%$ (major product) (HPLC: OJ-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, $t_t$ (minor) = 16.7 min, $t_t$ (major) = 27.3 min). The $dr$ value was determined by $^1$H NMR of 26v (after purification by flash chromatography).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.84–7.78 (m, 3H), 7.74 (s, 1H), 7.48–7.42 (m, 3H), 5.90 (s, 1H), 4.48 (d, $J = 5.6$ Hz, 1H), 3.74–3.66 (m, 2H), 3.61–3.51 (m, 1H), 3.45–3.33 (m, 2H), 2.91 (dd, $J = 16.2$, 6.8 Hz, 1H), 2.78–2.66 (m, 1H), 2.64–2.58 (m, 1H), 2.47 (s, 3H), 2.23 (s, 3H), 1.07 (d, $J = 6.8$ Hz, 3H) (major product).
\begin{align*}
^{13}\text{C NMR (75 MHz, CDCl}_3\text{) } & \delta 173.3, 151.8, 143.9, 137.7, 133.04, 133.02, 128.0, 127.8, 127.6, 126.4, \\
& 126.0, 125.8, 125.0, 111.1, 85.2, 70.6, 62.0, 38.7, 36.7, 15.5, 14.5, 13.7 \text{ (major product).} \\
\text{IR (film): } & \nu (\text{cm}^{-1}) 3431, 2963, 2927, 2868, 1720, 1582, 1460, 1410, 1377, 1328, 1270, 1168, 1105, \\
& 1058, 963, 818, 740, 658, 588, 554. \\
\text{HRMS (ESI, } & m/z \text{) calcd for C}_{22}\text{H}_{26}\text{N}_2\text{O}_3\text{Na [M+Na]}^+: 389.1836, \text{ found: 389.1841.} \\
\end{align*}

\((3R)-1-(3,5-\text{Dimethyl-1H-pyrazol-1-yl})-4-(2-\text{hydroxyethoxy})-4\text{-mesityl}-3\text{-methylbutan-1-one} \) 

\((26w)\)

Starting from 2-acyl pyrazole \textit{24a} (65.7 mg, 0.40 mmol) and \textit{N}-alkoxyphthalimide \textit{25j} (68.1 mg, 0.20 mmol) according to the general procedure to give \textit{26w} as a pale yellow oil (45.1 mg, 0.126 mmol, yield: 63\%, \textit{dr} = 3:1). Enantiomeric excess established by HPLC analysis using a Chiralpak IC column, \textit{ee} = 97\% (major product) (HPLC: IC, 254 nm, hexane/isopropanol = 94:6, flow rate 0.7 mL/min, 25 °C, \textit{t}_r (major) = 12.2 min, \textit{t}_r (minor) = 16.0 min). The \textit{dr} value was determined by \textit{¹H NMR} of \textit{26w} (after purified by flash chromatography).

\textit{¹H NMR (300 MHz, CDCl}_3\text{) } \delta 6.78 (s, 1H), 6.66 (s, 1H), 5.86 (s, 1H), 4.54 (d, \textit{J} = 8.6 Hz, 1H), 3.67 (t, \textit{J} = 4.6 Hz, 2H), 3.41–3.25 (m, 2H), 3.02–2.86 (m, 2H), 2.81–2.70 (m, 1H), 2.51–2.37 (m, 7H), 2.27–2.14 (m, 9H), 1.21 (d, \textit{J} = 6.3 Hz, 3H) (major product). \\
\textit{¹C NMR (75 MHz, CDCl}_3\text{) } \delta 172.8, 151.4, 143.8, 136.7, 132.3, 131.4, 131.2, 128.9, 128.8, 110.8, 83.1, \\
\text{IR (film): } & \nu (\text{cm}^{-1}) 3433, 2923, 1723, 1610, 1581, 1455, 1411, 1376, 1324, 1210, 1104, 1055, 964, 894, \\
& 854, 802, 746, 655, 586, 536. \\
\text{HRMS (ESI, } & m/z \text{) calcd for C}_{22}\text{H}_{26}\text{N}_2\text{O}_3\text{Na [M+Na]}^+: 381.2149, \text{ found: 381.2145.} \\
\end{align*}
(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-((2-hydroxyethyl)thio)-3-methylbutan-1-one (26x)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25k (47.5 mg, 0.20 mmol) according to the general procedure to give 26x as a pale yellow oil (25.1 mg, 0.098 mmol, yield: 49%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, $ee = 86\%$ (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, $t_r$ (major) = 11.2 min, $t_r$ (minor) = 12.5 min). $[\alpha]_D^{25} = +54.6^\circ$ (c 0.2, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.94 (s, 1H), 3.72 (t, $J = 5.9$ Hz, 2H), 3.32 (dd, $J = 16.6$, 6.2 Hz, 1H), 2.97 (dd, $J = 16.6$, 7.2 Hz, 1H), 2.73 (t, $J = 5.9$ Hz, 2H), 2.66–2.45 (m, 6H), 2.38 (dt, $J = 13.4$, 6.7 Hz, 1H), 2.22 (s, 3H), 1.10 (d, $J = 6.7$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 173.0, 151.9, 144.0, 111.1, 60.4, 41.1, 38.7, 35.7, 30.1, 19.7, 14.5, 13.7.

IR (film): $\nu$ (cm$^{-1}$) 3421, 2960, 2925, 2874, 1721, 1582, 1463, 1410, 1377, 1328, 1247, 1165, 1048, 998, 963, 904, 747, 639, 586, 557.

HRMS (ESI, $m/z$) calcd for C$_{12}$H$_{20}$N$_2$O$_2$SNa $[M+Na]^+$: 279.1138, found: 279.1139.

(R)-1-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-((2-hydroxyethyl)thio)-3,4-dimethylpentan-1-one (26y)

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25l (53.1 mg, 0.20 mmol) according to the general procedure to give 26y as a pale yellow oil (41.0 mg, 0.144 mmol, yield: 72%). Enantiomeric excess established by HPLC analysis using a Chiralpak OD-H column, $ee = 93\%$ (HPLC: OD-H, 254 nm, hexane/isopropanol = 95:5, flow rate 1.0 mL/min, 25 °C, $t_r$ (major) = 9.3 min, $t_r$ (minor) = 14.3 min). $[\alpha]_D^{25} = +55.6^\circ$ (c 0.4, CH$_2$Cl$_2$).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.94 (s, 1H), 3.73 (t, $J = 6.1$ Hz, 2H), 3.32 (dd, $J = 16.4$, 3.1 Hz, 1H), 2.98 (dd, $J = 16.4$, 10.1 Hz, 1H), 2.79 (td, $J = 6.0$, 2.2 Hz, 2H), 2.53 (s, 3H), 2.49–2.33 (m, 1H), 2.31–2.15 (s, 4H), 1.38 (s, 3H), 1.28 (s, 3H), 1.04 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 173.9, 151.8, 144.0, 111.1, 61.4, 49.1, 38.7, 38.2, 31.4, 27.5, 24.9, 15.4, 14.6, 13.8.
IR (film): $\nu$ (cm$^{-1}$) 3403, 2928, 2876, 1721, 1582, 1458, 1377, 1324, 1289, 1240, 1170, 1136, 1107, 1042, 994, 963, 935, 805, 769, 736, 661, 627, 587.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{24}$N$_2$O$_2$SNa [M+Na]$^+$: 307.1451, found: 307.1452.

5.5.3 Synthetic Transformations

To a solution of 26s (46.4 mg, 0.10 mmol) in THF (0.5 mL) was added $p$-toluidine (107.2 mg, 1.0 mmol). The reaction mixture was heated to 80 °C for 65 h. After cooled to room temperature, the reaction residue was purified by flash silica gel column chromatography to afford 27 as a colorless oil (43.0 mg, 91%). Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 93% (HPLC: AD-H, 254 nm, hexane/isopropanol = 80:20, flow rate 1.0 mL/min, 25 °C, $t_r$ (minor) = 25.4 min, $t_r$ (major) = 28.0 min). $[\alpha]_D^{25} = +8.7^\circ$ (c 0.4, CH$_2$Cl$_2$).

(R)-3-(4-(2-Hydroxyethoxy)-1-tosylpiperidin-4-yl)-N-(p-tolyl)butanamide (27)

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.04 (s, 1H), 7.63 (d, $J = 8.3$ Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.07 (d, $J = 8.1$ Hz, 2H), 3.67–3.50 (m, 4H), 3.46–3.33 (m, 1H), 3.26–3.15 (m, 1H), 2.63 (ddd, $J = 24.5$, 12.9, 2.6 Hz, 2H), 2.52–2.40 (m, 4H), 2.39–2.20 (m, 5H), 1.90–1.77 (m, 1H), 1.76–1.56 (m, 3H), 1.44 (dd, $J = 13.8$, 2.7 Hz, 1H), 0.93 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 171.3, 143.6, 135.7, 133.7, 133.5, 129.6, 129.3, 127.6, 119.7, 74.8, 62.2, 60.8, 41.9, 41.7, 38.8, 35.0, 29.1, 28.9, 21.5, 20.8, 15.0.

IR (film): $\nu$ (cm$^{-1}$) 3502, 2928, 2870, 1664, 1601, 1526, 1457, 1405, 1325, 1246, 1160, 1086, 977, 930, 816, 725, 651, 551.

HRMS (ESI, m/z) calcd for C$_{25}$H$_{34}$N$_2$O$_5$SNa [M+Na]$^+$: 497.2080, found: 497.2083.
Chapter 5: Experimental Part

To a solution of 26s (46.4 mg, 0.10 mmol) in THF/H$_2$O (v/v = 4:1, 1.0 mL) at 0 ºC was added NaBH$_4$ (37.3 mg, 1.0 mmol). The reaction mixture was stirred at room temperature overnight. The reaction was quenched with aqueous 2 N HCl and extracted with DCM. The combined organic layers were dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (100% EtOAc) to afford 28 (35.3 mg, yield: 95%) as a colorless oil. Enantiomeric excess established by HPLC analysis using a Chiralpak AD-H column, ee = 93% (HPLC: AD-H, 254 nm, hexane/isopropanol = 60:40, flow rate 1.0 mL/min, 25 ºC, t$_r$ (minor) = 5.4 min, t$_r$ (major) = 6.0 min). [$\alpha$]$^D_{25}$ = +25.5° (c 0.4, CH$_2$Cl$_2$).

\((R)-3-(4-(2-Hydroxyethoxy)-1-tosylpiperidin-4-yl)butan-1-ol\) (28)

\[
\text{HO} \hspace{1cm} \text{Me} \hspace{1cm} \text{O} \hspace{1cm} \text{OH} \hspace{1cm} \text{Ts}
\]

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.58 (d, $J = 8.3$ Hz, 2H), 7.25 (d, $J = 8.0$ Hz, 2H), 3.67 (td, $J = 6.2$, 3.1 Hz, 1H), 3.59–3.42 (m, 5H), 3.29 (dt, $J = 9.9$, 5.0 Hz, 1H), 3.11 (dt, $J = 9.5$, 4.0 Hz, 1H), 2.68–2.27 (m, 5H), 1.98–1.82 (m, 3H), 1.80–1.41 (m, 5H), 1.15–0.91 (m, 1H), 0.78 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 143.4, 133.5, 129.6, 127.6, 75.0, 62.2, 60.9, 60.4, 41.9, 41.8, 33.3, 33.1, 29.1, 29.0, 21.5, 14.1.

IR (film): $\nu$ (cm$^{-1}$) 3382, 2936, 2873, 1461, 1330, 1244, 1160, 1086, 1054, 977, 929, 894, 815, 725, 651, 573, 550.

HRMS (ESI, $m/z$) calcd for C$_{18}$H$_{29}$NO$_5$SNa [M+Na]$^+$: 394.1659, found: 394.1659.
5.5.4 Mechanistic Investigations

1) Substrate-Coordinated Rhodium Complex RhS-I

The racemic substrate-coordinated rhodium complex RhS-I was obtained by reacting substrate 24a (11.5 mg, 0.070 mmol) with racemic Δ/Λ Rhs (50.0 mg, 0.058 mmol) overnight in DCM (1.5 mL) at room temperature. After the slow addition of hexane (5.0 mL), crystals were collected after several days (39.4 mg, yield: 72%).

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) δ 7.95 (d, $J = 8.8$ Hz, 2H), 7.84–7.69 (m, 3H), 7.64–7.55 (m, 3H), 7.12 (tdd, $J = 7.5$, 2.4, 1.0 Hz, 2H), 6.98–6.86 (m, 3H), 6.73 (dq, $J = 14.9$, 1.6 Hz, 1H), 6.44–6.37 (m, 2H), 6.26 (d, $J = 7.8$ Hz, 1H), 2.66 (s, 3H), 2.10 (dd, $J = 7.1$, 1.6 Hz, 3H), 1.76 (s, 3H), 1.27 (s, 9H), 1.16 (s, 9H).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) δ 168.5, 161.3, 160.6, 160.2, 159.9, 159.6, 152.5, 152.4, 149.6, 149.4, 145.7, 140.4, 139.8, 133.89, 133.80, 131.24, 131.22, 131.10, 131.08, 128.94, 128.93, 128.86, 128.84, 126.6, 126.2, 124.9, 124.5, 124.2, 122.81, 122.78, 118.5, 117.3, 115.1, 114.5, 35.0, 34.8, 31.2, 31.1, 19.5, 15.6, 13.1.

2) Isolation of byproducts

Performed the reaction under the conditions of entry 5 in Table 8 (chapter 3.4), the expected byproducts isoindoline-1,3-dione 29 and diethyl 2,6-dimethylpyridine-3,5-dicarboxylate 30 were isolated.

Diethyl 2,6-dimethylpyridine-3,5-dicarboxylate (29)
Chapter 5: Experimental Part

1H NMR (300 MHz, CDCl$_3$) $\delta$ 8.66 (s, 1H), 4.39 (q, $J = 7.1$ Hz, 4H), 2.84 (s, 6H), 1.41 (t, $J = 7.1$ Hz, 6H).

All spectroscopic data were in agreement with the literature.$^{25}$

Isoindoline-1,3-dione (30)

\[
\text{\includegraphics[width=0.5\textwidth]{isoindoline.png}}
\]

1H NMR (300 MHz, DMSO-d$_6$) $\delta$ 11.31 (br s, 1H), 7.81 (s, 4H).

All spectroscopic data were in agreement with the literature.$^{26}$

3) Isolation of a side product

Starting from 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol) and N-alkoxyphthalimide 25h (83.2 mg, 0.20 mmol) according to the general procedure by using rac-RhS to give 26t as a white solid (51.0 mg, 0.117 mmol, yield: 59%) and a side product 2-((1-tosylazetidin-3-yl)oxy)ethanol 31 (8.3 mg, 0.030 mmol, yield: 15%).

2-((1-Tosylazetidin-3-yl)oxy)ethanol (31)

\[
\text{\includegraphics[width=0.5\textwidth]{2-tosylazetidin-3-yl-ethanol.png}}
\]

1H NMR (300 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J = 8.2$ Hz, 2H), 7.37 (d, $J = 8.0$ Hz, 2H), 4.23–4.05 (m, 1H), 4.03–3.89 (m, 2H), 3.67–3.56 (m, 4H), 3.38 (dd, $J = 5.2$, 3.9 Hz, 2H), 2.45 (s, 3H), 1.75 (s, 1H).

13C NMR (75 MHz, CDCl$_3$) $\delta$ 144.2, 131.7, 129.7, 128.4, 70.0, 67.0, 61.5, 57.9, 21.6.

4) Trapping Experiments

a) Trapping experiment with ((2-phenylallyl)sulfonyl)benzene

Using $\Delta$-RhS (8 mol%) and fac-[Ir(ppy)$_3$] (1 mol%) as dual catalysts, 2-acyl pyrazole 24a (65.7 mg, 0.40 mmol), N-alkoxyphthalimide 25a (44.2 mg, 0.20 mmol), Hantzsh ester (76.0 mg, 0.30 mmol) and ((2-phenylallyl)sulfonyl)benzene 32 (103.4 mg, 0.40 mmol)$^{27}$ according to the general procedure of synthesizing 26a-y to give 26a in 64% yield and 92% ee and 33 in 18% yield.
2-((3-Phenylbut-3-en-1-yl)oxy)ethanol (33)

\[
\begin{align*}
\text{Ph} & \quad \text{O} & \quad \text{OH}
\end{align*}
\]

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.46–7.39 (m, 2H), 7.38–7.24 (m, 3H), 5.36 (d, $J = 1.4$ Hz, 1H), 5.14 (d, $J = 1.3$ Hz, 1H), 3.68 (q, $J = 4.5$ Hz, 2H), 3.61 (t, $J = 7.0$ Hz, 2H), 3.52 (dd, $J = 5.3$, 3.8 Hz, 2H), 2.83 (td, $J = 6.9$, 1.2 Hz, 2H), 2.06–1.95 (m, 1H).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 145.4, 140.9, 128.3, 127.5, 126.0, 113.9, 71.8, 70.0, 61.8, 35.6.

IR (film): $\nu$ (cm$^{-1}$) 3434, 2927, 2872, 1720, 1682, 1597, 1488, 1447, 1364, 1282, 1218, 1114, 1054, 892, 756, 698, 658, 576, 542.

b) Trapping experiment with $N$-methyl-$N$-phenylmethacrylamide

A dried 10 mL Schlenk tube was charged with the catalyst $fac$-[Ir(ppy)$_3$] (1 mol%), $\Delta/\Lambda$-RhS (8 mol%), Hantzsch ester (0.30 mmol, 1.5 eq.), 2-acyl pyrazole 24a (0.40 mmol, 2.0 eq.), $N$-alkoxyphthalimide 25a (0.20 mmol, 1.0 eq.) and $N$-methyl-$N$-phenylmethacrylamide 34 (140.2 mg, 2.0 eq.)$^{18}$. The tube was purged with nitrogen and THF (1.0 mL) was added via syringe. The reaction mixture was degassed via freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the vial was sealed and positioned approximately 8 cm from 24 W blue LEDs. Afterwards, the mixture was diluted with DCM (2 mL). The combined organic layers were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1:10) to afford the $rac$-26a in 85% yield and 35 in 18% yield.

3-(2-(2-Hydroxyethoxy)ethyl)-1,3-dimethylindolin-2-one (35)

\[
\begin{align*}
\text{Me} & \quad \text{N} & \quad \text{O} & \quad \text{Me} & \quad \text{O} & \quad \text{OH}
\end{align*}
\]

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.32–7.24 (m, 1H), 7.20–7.15 (m, 1H), 7.07 (td, $J = 7.5$, 1.0 Hz, 1H), 6.87–6.84 (m, 1H), 3.51 (t, $J = 4.4$ Hz, 2H), 3.36–3.27 (m, 1H), 3.26–3.10 (m, 6H), 2.50–2.34 (m, 1H), 2.26–2.10 (m, 1H), 1.96 (dt, $J = 14.1$, 4.8 Hz, 1H), 1.38 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 181.0, 143.4, 133.5, 127.9, 122.6, 122.4, 108.0, 72.0, 67.5, 61.8, 46.8, 37.7, 26.2, 24.7.
IR (film): $\nu$ (cm$^{-1}$) 3434, 2926, 2870, 1692, 1610, 1466, 1425, 1377, 1349, 1308, 1247, 1163, 1121, 1064, 889, 753, 697, 640, 544.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{19}$NO$_3$Na [M+Na]$^+$: 272.1257, found: 272.1258.

5) The cross-over experiment

The reaction designed below is to explore the C(sp$^3$)-H activation occurs through intramolecular or intermolecular 1,5-HAT. When the N-alkoxyphthalimide 25l and alcohol were both subjected to the reaction conditions, the adduct 26y was isolated with no loss any of yield or enantioselectivity, whereas the product 26m was not formed in the reaction (Figure 91). It provides a good evidence that the C(sp$^3$)-H activation occurs through intramolecular 1,5-HAT.

![Chemical structure and NMR spectra](image)

**Figure 91** $^1$H NMR spectra of 26m, 26y and crude mixture.
6) Luminescence quenching experiments

The luminescence quenching experiments with the photoredox catalyst were investigated both in the absence and presence of intermediate RhS-I. Emission intensities were recorded on a Spectra Max M5 microplate reader in a 10.0 mm quartz cuvette. All fac-[Ir(ppy)_3] solutions were excited at 370 nm and the emission was measured at 515 nm. The concentration of the photoredox catalyst solution (fac-[Ir(ppy)_3] and intermediate RhS-I) was 0.2 mM in THF. The concentration of the quencher (N-alkoxyphthalimide 25a and Michael acceptor 24a) stock solution was 10 mM in THF. For each quenching experiment, 5 µL of this stock solution were titrated to a solution (1 mL) of iridium complex in a screw-top 10.0 mm quartz cuvette. The addition of 5 µL stock solution refers to an increase of the quencher concentration of 0.05 mM. After degassing with an argon stream for 5 minutes, the emission intensity was collected.

7) Light source screening

Different light sources contain CFL and blue LEDs were tested in the following reaction. It is not obvious that light intensity or wavelength effect the enantioselectivity of the product 26a. For example, the enantioselectivities obtained were almost the same when using 12 W or 2 × 20 W CFL as light source compared to 23 W CFL. However, it dropped to 86% and 76% ee when using 6 W and 24 W blue LEDs, respectively. The output wavelength of the used 6 W blue LEDs is shown in Figure 92.

<table>
<thead>
<tr>
<th>light source</th>
<th>yield</th>
<th>ee</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 12 W CFL (40 h)</td>
<td>42%</td>
<td>92%</td>
</tr>
<tr>
<td>2 23 W CFL (40 h)</td>
<td>70%</td>
<td>92%</td>
</tr>
<tr>
<td>3 2×20 W CFL (40 h)</td>
<td>68%</td>
<td>91%</td>
</tr>
<tr>
<td>4 24 W blue LEDs (20 h)</td>
<td>54%</td>
<td>76%</td>
</tr>
<tr>
<td>5 6 W blue LEDs (40 h)</td>
<td>69%</td>
<td>86%</td>
</tr>
</tbody>
</table>
Figure 92 The output wavelength of the used 6 W blue LEDs (420 nm ± 10 nm).

8) Quantum yield measurement

The quantum yield was measured by standard ferrioxalate actinometry.\textsuperscript{20} A 150 W xenon lamp (50\% of light intensity, 420 ± 5 nm bandpass filter) was used as the light source. The measured method was designed according to a published procedure with slight modifications.\textsuperscript{21,22} All the light sensitive operations were processed in the darkroom under red light.

The solutions were prepared and stored in the dark:

Potassium ferrioxalate solution (0.15 M): 736.9 mg of potassium ferrioxalate hydrate was dissolved in 10 mL of 0.05 M H₂SO₄.

Buffered solution of phenanthroline: 50 mg of 1,10-phenanthroline and 11.25 g of sodium acetate were dissolved in 50 mL of 0.5 M H₂SO₄.

\textit{a) Measurement of light intensity at 420 nm}

1000 μL of the ferrioxalate solution was added to a quartz cuvette (l = 10 mm). The actinometry solution was irradiated with 150 W Xennon Lamp (50\% of light intensity, 420 nm ± 5 nm) for specified time intervals (30, 60, 90, 120 seconds). After irradiation, 175 μL of the phenanthroline solution was added to the cuvette. The solution was kept in dark for 30 min to make sure the complete coordination. The absorbance of the actinometry solution was monitored at 510 nm. The absorbance of a non-irradiated (in dark) sample was also measured at 510 nm.

The moles of Fe²⁺ formed was determined using Beer’s Law:
Where \( V_1 (1 \text{ mL}) \) is the irradiated volume, \( V_2 (1 \text{ mL}) \) is the aliquot of the irradiated solution taken for the determination of the ferrous ions. \( V_3 (1.175 \text{ mL}) \) is the final volume after complexation with phenanthroline (all in mL), \( l \) is the path length (1 cm), and \( \Delta A(510 \text{ nm}) \) is the optical difference in absorbance between the irradiated and non-irradiated solutions, \( \epsilon(510 \text{ nm}) \) is the molar absorptivity of Fe(phen)_3^{2+} (11100 L mol^{-1} cm^{-1}).

The moles of Fe^{2+} formed for each sample (30, 60, 90, 120 seconds) are shown below:

<table>
<thead>
<tr>
<th>Irradiation time</th>
<th>30 s</th>
<th>60 s</th>
<th>90 s</th>
<th>120 s</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta A )</td>
<td>0.252</td>
<td>0.457</td>
<td>0.658</td>
<td>0.834</td>
</tr>
<tr>
<td>( \text{Fe}^{2+} (10^{-8} \text{ mol}) )</td>
<td>2.668</td>
<td>4.838</td>
<td>6.965</td>
<td>8.828</td>
</tr>
</tbody>
</table>

The moles of Fe^{2+} formed are plotted as a function of time (t). The slope is shown as:

\[
\frac{d(\text{moles Fe}^{2+})}{dt} = 7.619 \times 10^{-10}
\]

The photon flux can be calculated as:

\[
\text{photo flux (Einstein s}^{-1}) = \frac{\text{moles Fe}^{2+}}{\Phi \cdot t \cdot f} = \frac{d(\text{moles Fe}^{2+})/dt}{\Phi \cdot f} = \frac{7.619 \times 10^{-10}}{1.04 \times 1.0} = 7.32 \times 10^{-10}
\]

Where \( \Phi \) is the quantum yield for the ferrioxalate actinometer (1.05 for a 0.15 solution at 412 nm; 1.04 for a 0.15 solution at 422 nm; 1.03 for a 0.15 solution at 433 nm)\(^2\), \( t \) is the irradiated time, and \( f \) is the fraction of light absorbed at \( \lambda = 420 \text{ nm} \) (\( f = 1 - 10^{-8} \)). The measurement of the fraction of the light at 420 nm for the ferrioxalate solution was shown in Figure 93. The absorbance of the ferrioxalate solution at 420 nm is >3 indicating \( f (f = 1 - 10^{-8}) \) is >0.999.
Figure 93 Absorbance of the ferrioxalate actinometer solution (0.15 M).

b) Measurement of quantum yield:

Model reaction:

A screw-top cuvette (10.0 mm) was charged with the catalyst rac-RhS (8 mol%), photosensitizer fac-[Ir(ppy)_3] (1 mol%), 24a (0.4 mmol, 2.0 eq.), 25a (0.2 mmol, 1 eq.), Hantzsch ester (0.3 mmol, 1.5 eq.), 1.0 mL THF and a small magnetic stir bar. The cuvette was degassed with an argon stream for 10 min. After the mixture was thoroughly degassed, the vial was sealed and fixed at the same position as the measurement of photon flux. The reaction mixture was stirred and irradiated with 150 W Xenon lamp (50% of light intensity, 420 nm ± 5 nm bandpass filter high transmittance) for 10800 s (3 h). After irradiation, the reaction mixture was passed through a short silica gel column. The moles of product formed was measured by GC analysis (FID detector, column: HP-5) using dodecane as internal standard. The quantum yield calculation is then as following:

\[
\Phi = \frac{\text{moles of product}}{\text{moles of absorbed photons}} = \frac{\text{moles of product}}{\text{moles of incident photons} \times (1 - 10^{-A(420 \text{ nm})})}
\]

\[
= \frac{0.2 \times 10^{-3} \times 0.2\%}{7.32 \times 10^{-16} \times 3 \times 3600} = 0.05
\]
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5.5.5 Single-Crystal X-Ray Diffraction Studies

Single crystals of the rhodium intermediate complex \( \text{RhS-I} \) suitable for X-ray diffraction were obtained after one night from a solution of the compound in \( \text{CH}_2\text{Cl}_2 \) layered with n-hexane. Crystals of the \( (R)\)-26t were obtained by slow diffusion from a solution in \( \text{CH}_2\text{Cl}_2 \) layered with n-hexane. X-ray data of \( \text{RhS-I} \) and \( (R)\)-26t were collected with a Bruker 3 circuit D8 Quest diffractometer with MoKα radiation (microfocus tube with multilayer optics) and Photon 100 CMOS detector at 100 K. Crystal data and details of the structure determination of \( \text{RhS-I} \) and \( (R)\)-26t are presented in Appendices 6.7 The absolute configuration has been determined.
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<table>
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<th>Description</th>
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<tbody>
<tr>
<td>$^1$H NMR</td>
<td>proton nuclear magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>$^{13}$C NMR</td>
<td>carbon nuclear magnetic resonance spectroscopy</td>
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<tr>
<td>$^9$F NMR</td>
<td>fluorine nuclear magnetic resonance spectroscopy</td>
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<tr>
<td>$\delta$</td>
<td>chemical shift</td>
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<td>$J$</td>
<td>coupling constant</td>
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<tr>
<td>br</td>
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<td>triplet</td>
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<tr>
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<td>quartet</td>
</tr>
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</tr>
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<tr>
<td>AcOH</td>
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</tr>
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<td>argon</td>
</tr>
<tr>
<td>bpy</td>
<td>2,2'-bipyridine</td>
</tr>
<tr>
<td>CD</td>
<td>circular dichroism</td>
</tr>
<tr>
<td>CH$_2$Cl$_2$/DCM</td>
<td>dichloromethane</td>
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<tr>
<td>CD$_2$Cl$_2$</td>
<td>dideuteromethylenechloride</td>
</tr>
<tr>
<td>CHCl$_3$</td>
<td>chloroform</td>
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<tr>
<td>CDC$_3$</td>
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<tr>
<td>CH$_3$CN/MeCN</td>
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<tr>
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<tr>
<td>DMAP</td>
<td>4-dimethylaminopyridine</td>
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<tr>
<td>DMF</td>
<td>dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethyl sulfoxide</td>
</tr>
<tr>
<td>dr</td>
<td>diastereomeric ratio</td>
</tr>
<tr>
<td>EDA</td>
<td>electron donor-acceptor</td>
</tr>
<tr>
<td>EDC</td>
<td>1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride</td>
</tr>
<tr>
<td>ee</td>
<td>enantiomeric excesses</td>
</tr>
<tr>
<td>e.g.</td>
<td>exempli gratia (lat.: for example)</td>
</tr>
<tr>
<td>et al.</td>
<td>et alii (lat.: and others)</td>
</tr>
<tr>
<td>ESI</td>
<td>electrospray ionization</td>
</tr>
<tr>
<td>EtOH</td>
<td>ethanol</td>
</tr>
<tr>
<td>Et$_2$O</td>
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<tr>
<td>Et$_3$N</td>
<td>triethyl amine</td>
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<td>EtOAc</td>
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<tr>
<td>EWG</td>
<td>electron withdrawing group</td>
</tr>
<tr>
<td>HAT</td>
<td>hydrogen atom transfer</td>
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h  hour(s)
HPLC  high performance liquid chromatography
HRMS  high resolution mass spectrometry
Hz  Hertz
IR spectra  infrared spectra
Ir  iridium
L  liter(s)
M  mol/liter
m  meta-
min  minute(s)
mL  milliliter(s)
mmol  millimole
MS  mass spectroscopy
N₂  nitrogen
Nu  nucleophile
PCET  proton-coupled electron transfer
Ph  phenyl
PPh₃  triphenylphosphine
ppm  parts per million
ppy  2-phenylpyridine
PC  photoredox catalyst
rac  racemate
Rh  rhodium
rt  room temperature
SET  single-electron transfer
TEMPO  2,2,6,6-tetramethyl-1-piperidinyloxy
4-MeO-TEMPO  4-methoxy-2,2,6,6-tetramethyl-1-piperidinyloxy
TFA  trifluoroacetic acid
THF  tetrahydrofuran
TLC  thin layer chromatography
UV  ultraviolet
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6.5 List of Synthesized Compounds

6.5.1 List of Iridium/Rhodium Complexes

dimer-RhO

$\Lambda$-RhO

$\Lambda$-RhO

intermediate RhO-I

intermediate A

enolate complex B

intermediate IrS-I

intermediate RhS-I
6.5.2 List of Organic Compounds
6.6 List of Spectra of Compounds

6.6.1 NMR spectra of Iridium/Rhodium Complexes

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6.6.2 CD Spectra of Enantiopure Rhodium Complexes

Figure 102 CD spectrum of complex Λ-(S)-3 recorded in CH$_3$OH (0.2 mM).

Figure 103 CD spectrum of complex Δ-(R)-3 recorded in CH$_3$OH (0.2 mM).
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Figure 108 HPLC traces (Daicel Chiralpak AD-H column) of rac-5c (reference) and (R)-5c.
Figure 109 HPLC traces (Daicel Chiralpak AD-H column) of rac-5d (reference) and (R)-5d.
Figure 110 HPLC traces (Daicel Chiralpak AD-H column) of rac-5e (reference) and (R,R)-5e.
Figure 111 HPLC traces (Daicel Chiralpak AD-H column) of rac-5f (reference) and (R,R)-5f.
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Figure 114 HPLC traces (Daicel Chiralpak AD-H column) of rac-10a' (reference) and (S)-10a'.

**Table 1**: Peak RetTime Type Width Area Height Area

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<th>Height mAU</th>
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Figure 115 HPLC traces (Daicel Chiralpak AD-H column) of rac-10a (reference) and (R)-10a.
Figure 116 HPLC traces (Daicel Chiralpak OD-H column) of rac-10b (reference) and (R)-10b.
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Figure 118 HPLC traces (Daicel Chiralpak AD-H column) of rac-10d (reference) and (R)-10d.
Figure 119 HPLC traces (Daicel Chiralpak AD-H column) of rac-10e (reference) and (R)-10e.
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Figure 128 HPLC traces (Daicel Chiralpak AD-H column) of rac-16b' (reference) and (S)-16b'.
Figure 129 HPLC traces (Daicel Chiralpak AD-H column) of rac-16c' (reference) and (S)-16c'.
Figure 130 HPLC traces (Daicel Chiralpak AD-H column) of rac-16d' (reference) and (S)-16d'.

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<td>3468.69238</td>
<td>95.8713</td>
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Figure 133 HPLC traces (Daicel Chiralpak AD-H column) of rac-16d (reference) and (S)-16d.
Figure 134 HPLC traces (Daicel Chiralpak AD-H column) of rac-16e (reference) and (S)-16e.
Figure 135 HPLC traces (Daicel Chiralpak IC column) of rac-16f (reference) and (S)-16f.
Figure 136 HPLC traces (Daicel Chiralpak AD-H column) of rac-16g (reference) and (S)-16g.
Figure 137 HPLC traces (Daicel Chiralpak AD-H column) of rac-16h (reference) and (S)-16h.
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Figure 139 HPLC traces (Daicel Chiralpak AD-H column) of rac-18b (reference) and (S,R)-18b.
Figure 140 HPLC traces (Daicel Chiralpak AD-H column) of rac-18c (reference) and (S,R)-18c.
Figure 141 HPLC traces (Daicel Chiralpak AD-H column) of rac-18d (reference) and (S,R)-18d.
Figure 142 HPLC traces (Daicel Chiralpak AD-H column) of rac-18e (reference) and (S,R)-18e.
Figure 143 HPLC traces (Daicel Chiralpak AD-H column) of rac-20a (reference) and (S)-20a.
Figure 144 HPLC traces (Daicel Chiralpak OD-H column) of rac-26a (reference) and (R)-26a.
Figure 145 HPLC traces (Daicel Chiralpak OD-H column) of *rac*-26b (reference) and *(R)*-26b.
Figure 146 HPLC traces (Daicel Chiralpak OD-H column) of rac-26c (reference) and (R)-26c.
Figure 147 HPLC traces (Daicel Chiralpak OD-H column) of rac-26d (reference) and (S)-26d.
Figure 148 HPLC traces (Daicel Chiralpak OD-H column) of rac-26e (reference) and (R)-26e.
Figure 149 HPLC traces (Daicel Chiralpak OD-H column) of rac-26f (reference) and (S)-26f.
Figure 150 HPLC traces (Daicel Chiralpak IC column) of rac-26g (reference) and (R)-26g.
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Figure 152 HPLC traces (Daicel Chiralpak OD-H column) of rac-26i (reference) and (S)-26i.
Figure 153 HPLC traces (Daicel Chiralpak OD-H column) of \textit{rac-26j} (reference) and (S)-26j.
Figure 154 HPLC traces (Daicel Chiralpak OD-H column) of rac-26m (reference) and (R)-26m.
Figure 155 HPLC traces (Daicel Chiralpak OD-H column) of rac-26n (reference) and (R)-26n.
Figure 156 HPLC traces (Daicel Chiralpak OD-H column) of \textit{rac-26o} (reference) and (\textit{R})-26o.
Figure 157 HPLC traces (Daicel Chiralpak OD-H column) of \textit{rac-26p} (reference) and (S)-26p.
Figure 158 HPLC traces (Daicel Chiralpak OD-H column) of rac-26q (reference) and (R)-26q.
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Figure 160 HPLC traces (Daicel Chiralpak OD-H column) of rac-26s (reference) and (R)-26s.
Figure 161 HPLC traces (Daicel Chiralpak OD-H column) of rac-26t (reference) and (S)-26t.
Figure 162 HPLC traces (Daicel Chiralpak AD-H column) of rac-26u (reference) and (R)-26u.
Figure 163 HPLC traces (Daicel Chiralpak OJ-H column) of rac-26v (reference) and (R)-26v.
Figure 164 HPLC traces (Daicel Chiralpak IC column) of rac-26w (reference) and (R)-26w.
Figure 165 HPLC traces (Daicel Chiralpak OD-H column) of rac-26x (reference) and (R)-26x.
Figure 166 HPLC traces (Daicel Chiralpak OD-H column) of rac-26y (reference) and (R)-26y.
Figure 167 HPLC traces (Daicel Chiralpak AD-H column) of *rac*-27 (reference) and *(R)*-27.
Figure 168 HPLC traces (Daicel Chiralpak AD-H column) of rac-28 (reference) and (R)-28.
6.7 List of Crystal Structure Data

![Crystal structure of Δ-(R)-3. ORTEP drawing with 50% probability thermal ellipsoids.](image)

**Figure 169** Crystal structure of Δ-(R)-3. ORTEP drawing with 50% probability thermal ellipsoids.

**Table 9** Crystal data and structure refinement for Δ-(R)-3.

**Crystal data:**

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<tr>
<th>Identification code</th>
<th>w166_0m</th>
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<tr>
<td>Habitus, colour</td>
<td>needle, yellow</td>
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<tr>
<td>Crystal size</td>
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<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
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<tr>
<td>Space group</td>
<td>P 2₁ 2₁ 2₁</td>
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<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 13.919(6) Å, α = 90°. b = 19.144(9) Å, β = 90°. c = 28.616(11) Å, γ = 90°.</td>
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<td>Volume</td>
<td>7625(6) Å³</td>
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<td>Cell determination</td>
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<td>Empirical formula</td>
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### Data collection:

- **Diffractometer type**: Bruker D8 QUEST area detector
- **Wavelength**: 0.71073 Å
- **Temperature**: 100(2) K
- **Theta range for data collection**: 2.302 to 25.497°
- **Index ranges**: 
  - $-16 \leq h \leq 16$
  - $-23 \leq k \leq 23$
  - $-33 \leq l \leq 34$
- **Data collection software**: BRUKER APEX2
- **Cell refinement software**: SAINT V8.34A (Bruker AXS Inc., 2013)
- **Data reduction software**: SAINT V8.34A (Bruker AXS Inc., 2013)

### Solution and refinement:

- **Reflections collected**: 64188
- **Independent reflections**: 14187 [R(int) = 0.0642]
- **Completeness to theta = 25.242°**: 99.9%
- **Observed reflections**: 12148 [II > 2(I)]
- **Reflections used for refinement**: 14187
- **Absorption correction**: Numerical
- **Max. and min. transmission**: 0.96 and 0.76
- **Flack parameter (absolute struct.)**: -0.020(10)
- **Largest diff. peak and hole**: 0.569 and -0.435 e.Å$^{-3}$
- **Solution**: direct/ difmap
- **Refinement**: Full-matrix least-squares on F$^2$
- **Treatment of hydrogen atoms**: geom, constr
- **Programs used**: 
  - SHELXS-97 (Sheldrick, 2008)
  - SHELXL-2013 (Sheldrick, 2013)
  - DIAMOND (Crystal Impact)
- **Data / restraints / parameters**: 14187 / 114 / 996
- **Goodness-of-fit on F$^2$**: 1.024
- **R index (all data)**: wR2 = 0.0682
- **R index conventional [II>2sigma(I)]**: R1 = 0.0358
Figure 170 Crystal structure of Δ-RhO. ORTEP drawing with 50% probability thermal ellipsoids. The hexafluorophosphate counteranion is omitted for clarity.

Table 10 Crystal data and structure refinement for Δ-RhO.

Crystal data:

Identification code  
Habitus, colour  
Crystal size  
Crystal system  
Space group  
Unit cell dimensions  
Volume  
Cell determination  
Empirical formula  
Formula weight  
Density (calculated)  
Absorption coefficient  
F(000)
### Data collection:

- **Diffractometer type**: Bruker D8 QUEST area detector  
- **Wavelength**: 0.71073 Å  
- **Temperature**: 100(2) K  
- **Theta range for data collection**: 2.345 to 27.520°  
- **Index ranges**: -17<=h<=17, -15<=k<=17, -29<=l<=29  
- **Data collection software**: BRUKER APEX2  
- **Cell refinement software**: SAINT V8.34A (Bruker AXS Inc., 2013)  
- **Data reduction software**: SAINT V8.34A (Bruker AXS Inc., 2013)

### Solution and refinement:

- **Reflections collected**: 39009  
- **Independent reflections**: 9272 [R(int) = 0.0416]  
- **Completeness to theta = 25.242°**: 99.8 %  
- **Observed reflections**: 8540[II > 2(I)]  
- **Reflections used for refinement**: 9272  
- **Absorption correction**: Numerical  
- **Max. and min. transmission**: 0.90 and 0.75  
- **Flack parameter (absolute struct.)**: -0.033(8)  
- **Largest diff. peak and hole**: 0.511 and -0.396 e.Å⁻³  
- **Solution**: Direct methods  
- **Refinement**: Full-matrix least-squares on F²  
- **Treatment of hydrogen atoms**: Calculated positions, constr. ref.  
- **Programs used**:  
  - SHELXS-97 (Sheldrick, 2008)  
  - SHELXL-2013 (Sheldrick, 2013)  
  - DIAMOND (Crystal Impact)

- **Data / restraints / parameters**: 9272 / 168 / 590  
- **Goodness-of-fit on F²**: 1.033  
- **R index (all data)**: wR2 = 0.0579  
- **R index conventional [I>2sigma(I)]**: R1 = 0.0287
Figure 171 Crystal structure of 5d. ORTEP drawing with 50% probability thermal ellipsoids.

Table 11 Crystal data and structure refinement for 5d.

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<td>Crystal system</td>
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<td>Space group</td>
<td>P 2₁ ₂₁ ₂₁</td>
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<td>Z</td>
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<td>b = 15.3289(6) Å, β = 90°.</td>
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<td></td>
<td>c = 17.4084(9) Å, γ = 90°.</td>
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**Data collection:**

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<tr>
<td>Data collection software</td>
<td>BRUKER APEX2</td>
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<td>Cell refinement software</td>
<td>SAINT V8.34A (Bruker AXS Inc., 2013)</td>
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Data reduction software | SAINT V8.34A (Bruker AXS Inc., 2013)
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**Solution and refinement:**

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<td>Observed reflections</td>
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<td>Reflections used for refinement</td>
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<td>Numerical</td>
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<tr>
<td>Max. and min. transmission</td>
<td>0.99 and 0.95</td>
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<td>0.3(4)</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.146 and -0.203 e.Å(^3)</td>
</tr>
<tr>
<td>Solution</td>
<td>Direct methods</td>
</tr>
<tr>
<td>Refinement</td>
<td>Full-matrix least-squares on (F^2)</td>
</tr>
<tr>
<td>Treatment of hydrogen atoms</td>
<td>geom, constr</td>
</tr>
<tr>
<td>Programs used</td>
<td>SHELXS-97 (Sheldrick, 2008)</td>
</tr>
<tr>
<td></td>
<td>SHELXL-2013 (Sheldrick, 2013)</td>
</tr>
<tr>
<td></td>
<td>DIAMOND (Crystal Impact)</td>
</tr>
</tbody>
</table>

| Data / restraints / parameters | 2707 / 0 / 194 |
| Goodness-of-fit on \(F^2\) | 1.051 |
| R index (all data) | wR² = 0.0666 |
| R index conventional \([I > 2\sigma(I)]\) | R1 = 0.0291 |
Figure 172 Crystal structure of racemic 5f to verify the relative configuration. ORTEP drawing with 50% probability thermal ellipsoids.

Table 12 Crystal data and structure refinement for 5f.

Crystal data:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>w234b_0m</td>
</tr>
<tr>
<td>Habitus, colour</td>
<td>prism, colourless</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.40 x 0.30 x 0.08 mm³</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P 2₁/c</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 10.1905(5) Å</td>
</tr>
<tr>
<td></td>
<td>b = 11.5731(6) Å</td>
</tr>
<tr>
<td></td>
<td>c = 17.4203(8) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>2036.88(17) Å³</td>
</tr>
<tr>
<td>Cell determination</td>
<td>9754 peaks with Theta 2.4 to 27.5°.</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C₂₂H₂₆N₂O₄</td>
</tr>
<tr>
<td>Formula weight</td>
<td>382.45</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.247 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.086 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>816</td>
</tr>
</tbody>
</table>
### Data collection:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffractometer type</td>
<td>Bruker D8 QUEST area detector</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Temperature</td>
<td>100(2) K</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>2.118 to 27.536°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-13≤h≤13, -15≤k≤15, -22≤l≤22</td>
</tr>
<tr>
<td>Data collection software</td>
<td>BRUKER APEX2</td>
</tr>
<tr>
<td>Cell refinement software</td>
<td>SAINT V8.34A (Bruker AXS Inc., 2013)</td>
</tr>
<tr>
<td>Data reduction software</td>
<td>SAINT V8.34A (Bruker AXS Inc., 2013)</td>
</tr>
</tbody>
</table>

### Solution and refinement:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflections collected</td>
<td>47435</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>4679 [R(int) = 0.0370]</td>
</tr>
<tr>
<td>Completeness to theta = 25.242°</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Observed reflections</td>
<td>3939 [I &gt; 2σ(I)]</td>
</tr>
<tr>
<td>Reflections used for refinement</td>
<td>4679</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.99 and 0.93</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.353 and -0.349 e.Å⁻³</td>
</tr>
<tr>
<td>Solution</td>
<td>Direct methods</td>
</tr>
<tr>
<td>Refinement</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Treatment of hydrogen atoms</td>
<td>Calculated positions, constr. ref.</td>
</tr>
<tr>
<td>Programs used</td>
<td>SHELXS-97 (Sheldrick, 2008)</td>
</tr>
<tr>
<td></td>
<td>SHELXL-2013 (Sheldrick, 2013)</td>
</tr>
<tr>
<td></td>
<td>DIAMOND (Crystal Impact)</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>4679 / 0 / 258</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.122</td>
</tr>
<tr>
<td>R index (all data)</td>
<td>wR² = 0.1143</td>
</tr>
<tr>
<td>R index conventional [I&gt;2σ(I)]</td>
<td>R1 = 0.0381</td>
</tr>
</tbody>
</table>
Figure 173 Crystal structure of racemic 6 to verify the relative configuration. ORTEP drawing with 50% probability thermal ellipsoids.

Table 13 Crystal data and structure refinement for racemic 6.

Crystal data:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>w283_0m_sq</td>
</tr>
<tr>
<td>Habitus, colour</td>
<td>colourless, block</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.47 x 0.11 x 0.08 mm³</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P - 1</td>
</tr>
<tr>
<td>Z</td>
<td>2</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 9.3288(4) Å, b = 12.2132(5) Å, c = 14.0156(5) Å</td>
</tr>
<tr>
<td></td>
<td>α = 70.7804(13)°, β = 76.9655(13)°, γ = 72.0469(13)°</td>
</tr>
<tr>
<td>Volume</td>
<td>1420.69(10) Å³</td>
</tr>
<tr>
<td>Cell determination</td>
<td>9973 peaks with Theta 2.5 to 25.3°.</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C_{27}H_{26}N_{6}O_{5}</td>
</tr>
<tr>
<td>Moiety formula</td>
<td>C_{27}H_{26}N_{6}O_{5}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>514.54</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.203 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.085 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>540</td>
</tr>
</tbody>
</table>

Data collection:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffractometer type</td>
<td>Bruker D8 QUEST area detector</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Temperature</td>
<td>115(2) K</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>2.317 to 25.314°.</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-11&lt;=h&lt;=9, -14&lt;=k&lt;=14, -16&lt;=l&lt;=16</td>
</tr>
<tr>
<td>Data collection software</td>
<td>BRUKER APEX2 2014.1-1</td>
</tr>
<tr>
<td>Cell refinement software</td>
<td>SAINT V8.34A (Bruker AXS Inc., 2013)</td>
</tr>
<tr>
<td>Data reduction software</td>
<td>SAINT V8.34A (Bruker AXS Inc., 2013)</td>
</tr>
</tbody>
</table>

**Solution and refinement:**

| Reflections collected       | 31742                                           |
| Independent reflections    | 5175 [R(int) = 0.0337]                           |
| Completeness to theta = 25.242° | 99.9 %                                         |
| Observed reflections       | 4346[II > 2(I)]                                 |
| Reflections used for refinement | 5175                                    |
| Absorption correction      | Numerical                                      |
| Max. and min. transmission | 0.99 and 0.96                                  |
| Largest diff. peak and hole | 0.411 and -0.205 e.Å^{-3}                      |
| Solution                   | Direct methods                                 |
| Refinement                 | Full-matrix least-squares on F^2               |
| Treatment of hydrogen atoms | CH riding model, NH located, isotropic ref.   |
| Programs used              | SHELXS-97 (Sheldrick, 2008)                    |
|                           | SHELXL-2014 (Sheldrick, 2014)                  |
|                           | DIAMOND (Crystal Impact)                      |
| Data / restraints / parameters | 5175 / 0 / 349                      |
| Goodness-of-fit on F^2     | 1.037                                          |
| R index (all data)         | wR2 = 0.1163                                   |
| R index conventional       | R1 = 0.0426                                    |
Figure 174 Crystal structure of RhO-I. ORTEP drawing with 50% probability thermal ellipsoids. The hexafluorophosphate counteranion is omitted for clarity.

Table 14 Crystal data and structure refinement for RhO-I.

Crystal data:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>w261_0m_sq</td>
</tr>
<tr>
<td>Habitus, colour</td>
<td>needle, yellow</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.26 x 0.06 x 0.03 mm³</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>P n a 2₁</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 17.776(6) Å, b = 22.9437(8) Å, c = 13.1111(4) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>5347.4(3) Å³</td>
</tr>
<tr>
<td>Cell determination</td>
<td>9841 peaks with Theta 2.5 to 25.3°</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C₅₁ H₅₂ Cl₄ O₆ N₄ O₃ P Rh</td>
</tr>
<tr>
<td>Moiety formula</td>
<td>C₄₉ H₄₈ N₄ O₃ Rh, F₆ P, 2(C H₂ Cl₂)</td>
</tr>
<tr>
<td>Formula weight</td>
<td>1158.64</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.439 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.615 mm</td>
</tr>
<tr>
<td>F(000)</td>
<td>2368</td>
</tr>
</tbody>
</table>
Chapter 6: Appendices

Data collection:

- **Diffractometer type**: Bruker D8 QUEST area detector
- **Wavelength**: 0.71073 Å
- **Temperature**: 100(2) K
- **Theta range for data collection**: 2.113 to 25.329°
- **Index ranges**: 
  - $-21 \leqslant h \leqslant 21$
  - $-27 \leqslant k \leqslant 27$
  - $-15 \leqslant l \leqslant 15$
- **Data collection software**: BRUKER APEX2 2014.1-1
- **Cell refinement software**: SAINT V8.34A (Bruker AXS Inc., 2013)
- **Data reduction software**: SAINT V8.34A (Bruker AXS Inc., 2013)

Solution and refinement:

- **Reflections collected**: 56957
- **Independent reflections**: 9643 [R(int) = 0.0497]
- **Completeness to theta = 25.242°**: 99.9 %
- **Observed reflections**: 8691[I > 2(I)]
- **Reflections used for refinement**: 9643
- **Absorption correction**: Numerical
- **Max. and min. transmission**: 0.98 and 0.88
- **Flack parameter (absolute struct.)**: -0.015(8)
- **Largest diff. peak and hole**: 1.123 and -0.508 e.Å$^{-3}$
- **Solution**: Direct methods
- **Refinement**: Full-matrix least-squares on F$^2$
- **Treatment of hydrogen atoms**: Calculated positions, constr. ref.
- **Programs used**:
  - SHELXS-97 (Sheldrick, 2008)
  - SHELXL-2014 (Sheldrick, 2014)
  - DIAMOND (Crystal Impact)

Data / restraints / parameters: 9643 / 106 / 705

- **Goodness of-fit on F$^2$**: 1.034
- **R index (all data)**: wR2 = 0.0889
- **R index conventional [I>2sigma(I)]**: R1 = 0.0348
Figure 175 Crystal structure of an iridium enolate complex B. ORTEP drawing with 50% probability thermal ellipsoids.

Table 15 Crystal data and structure refinement for an iridium enolate complex B.

Crystal data:

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>w452_2_0m</td>
</tr>
<tr>
<td>Habitus, colour</td>
<td>prism, red</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.180 x 0.040 x 0.020 mm³</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P2₁/n</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>a = 14.5673(8) Å</td>
<td>α = 90°.</td>
</tr>
<tr>
<td>b = 13.2686(7) Å</td>
<td>β = 91.578(3)°</td>
</tr>
<tr>
<td>c = 21.6394(13) Å</td>
<td>γ = 90°.</td>
</tr>
<tr>
<td>Volume</td>
<td>4181.0(4) Å³</td>
</tr>
<tr>
<td>Cell determination</td>
<td>9213 peaks with Theta 2.3 to 25.3°.</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C₅₁H₄₅ Ir N₄ O₃</td>
</tr>
<tr>
<td>Moiety formula</td>
<td>C₅₁H₄₅ Ir N₄ O₃</td>
</tr>
<tr>
<td>Formula weight</td>
<td>954.11</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.516 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>3.242 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>1920</td>
</tr>
</tbody>
</table>
Chapter 6: Appendices

Data collection:

- Diffractometer type: Bruker D8 QUEST area detector
- Wavelength: 0.71073 Å
- Temperature: 100(2) K
- Theta range for data collection: 2.264 to 25.306°.
- Index ranges: -15<=%h%<=%17, -15<=%k%<=%15, -25<=%l%<=%26
- Data collection software: BRUKER APEX2 2014.9-0
- Cell refinement software: BRUKER SAINT
- Data reduction software: SAINT V8.34A (Bruker AXS Inc., 2013)

Solution and refinement:

- Reflections collected: 50910
- Independent reflections: 7598 [R(int) = 0.0654]
- Completeness to theta = 25.242°: 99.9 %
- Observed reflections: 6059[I>2sigma(I)]
- Reflections used for refinement: 7598
- Absorption correction: Numerical
- Max. and min. transmission: 0.94 and 0.67
- Largest diff. peak and hole: 1.311 and -0.851 e.Å⁻³
- Solution: Direct methods
- Refinement: Full-matrix least-squares on F²
- Treatment of hydrogen atoms: Calculated positions, constr. ref.
- Programs used:
  - SHELXS-97 (Sheldrick, 2008)
  - SHELXL-2014/7 (Sheldrick, 2014)
  - DIAMOND (Crystal Impact)
- Data / restraints / parameters: 7598 / 0 / 569
- Goodness-of-fit on F²: 1.039
- R index (all data): wR² = 0.0578
- R index conventional [I>2sigma(I)]: R1 = 0.0309
Figure 176 Crystal structure of (R)-10e. ORTEP drawing with 50% probability thermal ellipsoids.

Table 16 Crystal data and structure refinement for 10e.

Crystal data:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>w445c_0m</td>
</tr>
<tr>
<td>Habitus, colour</td>
<td>needle, colourless</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.51 x 0.09 x 0.04 mm^3</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>P2_12_12_1</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 9.2411(4) Å, α = 90°.</td>
</tr>
<tr>
<td></td>
<td>b = 11.5916(6) Å, β = 90°.</td>
</tr>
<tr>
<td></td>
<td>c = 23.1471(12) Å, γ = 90°.</td>
</tr>
<tr>
<td>Volume</td>
<td>2479.5(2) Å^3</td>
</tr>
<tr>
<td>Cell determination</td>
<td>3967 peaks with Theta 2.5 to 25.2°.</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C_{30}H_{24}ClN_{3}O</td>
</tr>
<tr>
<td>Moiety formula</td>
<td>C_{30}H_{24}ClN_{3}O</td>
</tr>
<tr>
<td>Formula weight</td>
<td>477.97</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.280 Mg/m^3</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.182 mm^-1</td>
</tr>
<tr>
<td>F(000)</td>
<td>1000</td>
</tr>
</tbody>
</table>
Chapter 6: Appendices

Data collection:

Diffractometer type: Bruker D8 QUEST area detector
Wavelength: 0.71073 Å
Temperature: 100(2) K
Theta range for data collection: 2.373 to 25.299°.
Index ranges: -10=<h<=11, -13=<k<=13, -27=<l<=27
Data collection software: BRUKER APEX2 2014.9-0 (APEX2 2014)
Cell refinement software: BRUKER SAINT (SAINT 2013)
Data reduction software: SAINT V8.34A (SAINT 2013)

Solution and refinement:

Reflections collected: 13057
Independent reflections: 4492 [R(int) = 0.0501]
Completeness to theta = 25.242°: 99.9 %
Observed reflections: 3776[I>2sigma(I) ]
Reflections used for refinement: 4492
Absorption correction: Semi-empirical from equivalents (SADABS 2014)
Max. and min. transmission: 0.99 and 0.91
Flack parameter (absolute struct.): 0.00(4)
Largest diff. peak and hole: 0.191 and -0.221 e.Å⁻³
Solution: Direct methods
Refinement: Full-matrix least-squares on F²
Treatment of hydrogen atoms: Calculated positions, riding model
Programs used: XT V2014/1 (Bruker AXS Inc., 2014, Sheldrick 2008))
SHELXL-2014/7 (Sheldrick 2008)
DIAMOND (Brandenburg 2014)

Data / restraints / parameters: 4492 / 0 / 316
Goodness-of-fit on F²: 1.047
R index (all data): wR2 = 0.0728
R index conventional [I>2sigma(I)]: R1 = 0.0358
Figure 177 Crystal structure of (S)-16g. ORTEP drawing with 50% probability thermal ellipsoids.

Table 17 Crystal data and structure refinement for 16g.

Crystal data:

<table>
<thead>
<tr>
<th>Identification code</th>
<th>w875chiral_0m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habitus, colour</td>
<td>block, colourless</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.45 x 0.36 x 0.22 mm³</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P2₁</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 10.4418(6) Å</td>
</tr>
<tr>
<td></td>
<td>b = 18.1671(9) Å</td>
</tr>
<tr>
<td></td>
<td>c = 12.1722(7) Å</td>
</tr>
<tr>
<td></td>
<td>α = 90°.</td>
</tr>
<tr>
<td></td>
<td>β = 106.238(2)°.</td>
</tr>
<tr>
<td></td>
<td>γ = 90°.</td>
</tr>
<tr>
<td>Volume</td>
<td>2216.9(2) Å³</td>
</tr>
<tr>
<td>Cell determination</td>
<td>9854 peaks with Theta 2.3 to 27.5°.</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C₂₄H₁₈Cl₂F₃N₃O</td>
</tr>
<tr>
<td>Moiety formula</td>
<td>C₂₄H₁₈Cl₂F₃N₃O</td>
</tr>
<tr>
<td>Formula weight</td>
<td>492.31</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.475 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.341 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>1008</td>
</tr>
</tbody>
</table>
Data collection:

Diffractometer type: Bruker D8 QUEST area detector
Wavelength: 0.71073 Å
Temperature: 100(2) K
Theta range for data collection: 2.242 to 27.544°
Index ranges: -13<=h<=13, -23<=k<=23, -15<=l<=15
Data collection software: BRUKER APEX2 2014.9-0
Cell refinement software: BRUKER SAINT [2]
Data reduction software: SAINT V8.34A (Bruker AXS Inc., 2013)

Solution and refinement:

Reflections collected: 71801
Independent reflections: 10210 [R(int) = 0.0299]
Completeness to theta = 25.242°: 99.9 %
Observed reflections: 9680 [I>2sigma(I)]
Reflections used for refinement: 10210
Absorption correction: Semi-empirical from equivalents
Max. and min. transmission: 0.93 and 0.87
Flack parameter (absolute struct.): 0.017(7)
Largest diff. peak and hole: 0.293 and -0.372 e.Å⁻³
Solution: Direct methods
Refinement: Full matrix least-squares on F²
Treatment of hydrogen atoms: CH cal. positions, constr. ref., OH located, isotr. ref.
Programs used: XT V2014/1 (Bruker AXS Inc., 2014)
                  SHELXL-2014/7 (Sheldrick, 2014)
                  DIAMOND (Crystal Impact)

Data / restraints / parameters: 10210 / 1 / 603
Goodness-of-fit on F²: 1.044
R index (all data): wR² = 0.0671
R index conventional [I>2sigma(I)]: R1 = 0.0281
Figure 178 Crystal structure of 18a. ORTEP drawing with 50% probability thermal ellipsoids.

Table 18 Crystal data and structure refinement for 18a.

Crystal data:

Identification code  w812_0m
Habitus, colour  block, colourless
Crystal size  0.26 x 0.20 x 0.19 mm³
Crystal system  Orthorhombic
Space group  \( P2_12_12_1 \)
Unit cell dimensions  
\[ \begin{align*}
    a &= 9.4488(4) \text{ Å} & \alpha &= 90^\circ \\
    b &= 15.6639(6) \text{ Å} & \beta &= 90^\circ \\
    c &= 31.2528(12) \text{ Å} & \gamma &= 90^\circ \\
\end{align*} \]
Volume  4625.6(3) Å³
Cell determination  9976 peaks with Theta 2.3 to 27.5°.
Empirical formula  \( C_{53} H_{46} Cl_2 F_6 N_6 O_2 \)
Moiety formula  \( 2(C_{26} H_{32} F_3 N_3 O), C H_2 Cl_2 \)
Formula weight  983.86
Density (calculated)  1.413 Mg/m³
Absorption coefficient  0.215 mm⁻³
F(000)  2040
Data collection:

Diffractometer type: Bruker D8 QUEST area detector
Wavelength: 0.71073 Å
Temperature: 100(2) K
Theta range for data collection: 2.252 to 27.504°.
Index ranges: 
-9<=h<=12, -20<=k<=20, -40<=l<=31
Data collection software: BRUKER APEX2 2014.9-0
Cell refinement software: BRUKER SAINT
Data reduction software: SAINT V8.34A (Bruker AXS Inc., 2013)

Solution and refinement:

Reflections collected: 23538
Independent reflections: 10598 [R(int) = 0.0221]
Completeness to theta = 25.242°: 99.9 %
Observed reflections: 9498[I>2sigma(I)]
Reflections used for refinement: 10598
Absorption correction: Semi-empirical from equivalents
Max. and min. transmission: 0.96 and 0.91
Flack parameter (absolute struct.): 0.018(17)
Largest diff. peak and hole: 0.275 and -0.374 e.Å⁻³
Solution: Direct methods
Refinement: Full-matrix least-squares on F²
Treatment of hydrogen atoms: CH cal. positions, constr. ref., OH located, isotr. ref.
Programs used:
XT V2014/1 (Bruker AXS Inc., 2014)
SHELXL-2014/7 (Sheldrick, 2014)
DIAMOND (Crystal Impact)

Data / restraints / parameters: 10598 / 0 / 640
Goodness-of-fit on F²: 1.054
R index (all data): wR² = 0.0807
R index conventional [I>2sigma(I)]: R1 = 0.0374
Figure 179 Crystal structure of rhodium intermediate RhS-I. ORTEP drawing with 50% probability thermal ellipsoids. Hexafluorophosphate counterion, hydrogen atoms and one CH$_2$Cl$_2$ molecular are omitted for clarity.

Table 19 Crystal data and structure refinement for RhS-I.

Crystal data:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>w1280_0m</td>
</tr>
<tr>
<td>Habitus, colour</td>
<td>cubic prism, yellow</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.37 x 0.28 x 0.23 mm$^3$</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P$-I$</td>
</tr>
<tr>
<td>Z</td>
<td>2</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 12.0250(5) Å</td>
</tr>
<tr>
<td></td>
<td>α = 90.447(2)$^\circ$.</td>
</tr>
<tr>
<td></td>
<td>b = 13.9944(6) Å</td>
</tr>
<tr>
<td></td>
<td>β = 111.549(2)$^\circ$.</td>
</tr>
<tr>
<td></td>
<td>c = 14.7168(7) Å</td>
</tr>
<tr>
<td></td>
<td>γ = 101.223(2)$^\circ$.</td>
</tr>
<tr>
<td>Volume</td>
<td>2250.88(17) Å$^3$</td>
</tr>
<tr>
<td>Cell determination</td>
<td>9730 peaks with Theta 2.6 to 27.5$^\circ$.</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C$<em>{44}$H$</em>{46}$Cl$_2$F$_6$N$_4$O P Rh S$_2$</td>
</tr>
<tr>
<td>Moiety formula</td>
<td>C$<em>{43}$H$</em>{44}$N$_4$O Rh S$_2$, F$_6$ P, C H Cl$_2$</td>
</tr>
<tr>
<td>Formula weight</td>
<td>1029.75</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.519 Mg/m$^3$</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.691 mm$^{-1}$</td>
</tr>
<tr>
<td>F(000)</td>
<td>1052</td>
</tr>
</tbody>
</table>
Data collection:

- **Diffactometer type**: Bruker D8 QUEST area detector
- **Wavelength**: 0.71073 Å
- **Temperature**: 100(2) K
- **Theta range for data collection**: 2.244 to 27.557°
- **Index ranges**: 
  - 15 ≤ h ≤ 15
  - 17 ≤ k ≤ 18
  - 19 ≤ l ≤ 19
- **Data collection software**: APEX3 (Bruker AXS Inc., 2015)
- **Cell refinement software**: SAINT V8.35A (Bruker AXS Inc., 2015)
- **Data reduction software**: SAINT V8.35A (Bruker AXS Inc., 2015)

Solution and refinement:

- **Reflections collected**: 56167
- **Independent reflections**: 10388 [R(int) = 0.0229]
- **Completeness to theta = 25.242°**: 99.9 %
- **Observed reflections**: 9652 [I > 2(I)]
- **Reflections used for refinement**: 10388
- **Extinction coefficient**: X = 0.0030(2)
- **Absorption correction**: Semi-empirical from equivalents
- **Max. and min. transmission**: 0.86 and 0.80
- **Largest diff. peak and hole**: 1.024 and -0.604 e.Å⁻³
- **Solution**: Direct methods
- **Refinement**: Full-matrix least-squares on F²
- **Treatment of hydrogen atoms**: Calculated positions, constr. ref.
- **Programs used**: 
  - XT V2014/1 (Bruker AXS Inc., 2014)
  - SHELXL-2014/7 (Sheldrick, 2014)
  - DIAMOND (Crystal Impact)
  - ShelXle (Hübschle, Sheldrick, Dittrich, 2011)

- **Data / restraints / parameters**: 10388 / 0 / 560
- **Goodness-of-fit on F²**: 1.054
- **R index (all data)**: wR2 = 0.0550
- **R index conventional [I>2sigma(I)]**: R1 = 0.0226
Figure 180 Crystal structure of (R)-26t. ORTEP drawing with 50% probability thermal ellipsoids.

Table 20 Crystal data and structure refinement for 26t.

Crystal data:

Identification code w1272_0m
Habitus, colour needle, colourless
Crystal size 0.44 x 0.08 x 0.08 mm³
Crystal system Monoclinic
Space group C2
Unit cell dimensions a = 19.0297(14) Å  α = 90°.
b = 8.3596(6) Å  β = 104.557(2)°.
c = 18.4008(14) Å  λ = 90°.
Volume 2833.2(4) Å³
Cell determination 9951 peaks with Theta 2.3 to 25.3°.
Empirical formula C₃₀H₃₉N₃O₅S
Moiety formula C₃₀H₃₉N₃O₅S
Formula weight 553.70
Density (calculated) 1.298 Mg/m³
Absorption coefficient 0.158 mm-1
F(000) 1184
Data collection:

Diffractometer type: Bruker D8 QUEST area detector
Wavelength: 0.71073 Å
Temperature: 100(2) K
Theta range for data collection: 2.220 to 25.328°
Index ranges: -22<=h<=20, -10<=k<=10, -22<=l<=22
Data collection software: APEX3 (Bruker AXS Inc., 2015)
Cell refinement software: SAINT V8.35A (Bruker AXS Inc., 2015)
Data reduction software: SAINT V8.35A (Bruker AXS Inc., 2015)

Solution and refinement:

Reflections collected: 33859
Independent reflections: 5163 [R(int) = 0.0549]
Completeness to theta = 25.242°: 99.9 %
Observed reflections: 4655[I > 2(I)]
Reflections used for refinement: 5163
Absorption correction: Semi-empirical from equivalents
Max. and min. transmission: 0.99 and 0.92
Flack parameter (absolute struct.): 0.00(3)
Largest diff. peak and hole: 0.177 and -0.282 e.Å⁻³
Solution: Direct Methods
Refinement: Full-matrix least-squares on F²
Treatment of hydrogen atoms: CH calculated, OH located, constr. ref.
Programs used: XT V2014/1 (Bruker AXS Inc., 2014)
               SHELXL-2014/7 (Sheldrick, 2014)
               DIAMOND (Crystal Impact)
               ShelXle (Hübschle, Sheldrick, Dittrich, 2011)
Data / restraints / parameters: 5163 / 193 / 450
Goodness-of-fit on F²: 1.093
R index (all data): wR2 = 0.0777
R index conventional [I>2sigma(I)]: R1 = 0.0348
Statement
gemäß § 10, Abs. 1 der Promotionsordnung der mathematisch-naturwissenschaftlichen Fachbereiche und des Medizinischen Fachbereichs für seine mathematisch-naturwissenschaftlichen Fächer der Philipps-Universität Marburg vom 15.07.2009

Ich erkläre, dass eine Promotion noch an keiner anderen Hochschule als der Philipps-Universität Marburg, Fachbereich Chemie, versucht wurde und versichere, dass ich meine vorgelegte Dissertation

Asymmetric Catalysis with Octahedral Chiral-at-Metal Iridium and Rhodium Complexes

selbst und ohne fremde Hilfe verfasst, nicht andere als die in ihr angegebenen Quellen oder Hilfsmittel benutzt, alle vollständig oder sinngemäß übernommenen Zitate als solche gekennzeichnet sowie die Dissertation in der vorliegenden oder ähnlichen Form noch bei keiner anderen in- oder ausländischen Hochschule anlässlich eines Promotionsgesuchs oder zu anderen Prüfungszwecken eingereicht habe.

Chuanyong Wang
Marburg, den 31.10.2016
Curriculum Vitae

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Education

08/2013–present  Ph.D. Organic Chemistry, University of Marburg, Germany
Advisor: Prof. Eric Meggers

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Ph.D. study: Directing Asymmetric Catalysis with Iridium/Rhodium Centrochirality

Publications:

M.S. study: Synthesis and Study on the Activation of Organic Molecules by Lanthanide(II) Complexes Bearing the Naphthalene-bridged Bis(guanidinate) Ligand

Publications: