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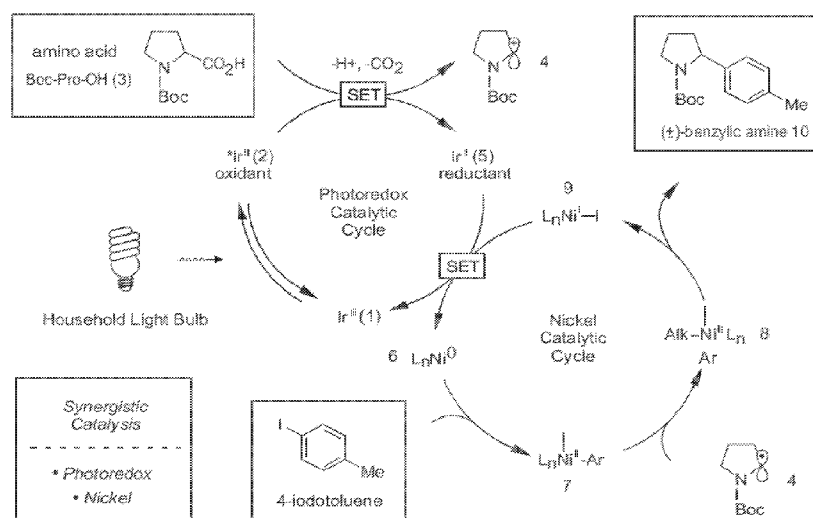
(54) **Title:** DECARBOXYLATIVE CROSS-COUPLING AND APPLICATIONS THEREOF

FIGURE 2

(57) **Abstract:** Methods described herein enable the production of numerous molecular species through decarboxylative cross-coupling via use of photoredox and transition metal catalysts. For example, methods described herein enable the production of numerous molecular species through decarboxylative cross-coupling via use of photoredox and transition metal catalysts. A method described herein, in some embodiments, comprises providing a reaction mixture including a photoredox catalyst, a transition metal catalyst, a coupling partner and a substrate having a carboxyl group. The reaction mixture is irradiated with a radiation source resulting in cross-coupling of the substrate and coupling partner via a mechanism including decarboxylation, wherein the coupling partner is selected from the group consisting of a substituted aromatic compound and a substituted aliphatic compound.

DECARBOXYLATIVE CROSS-COUPLING AND APPLICATIONS THEREOF

STATEMENT OF GOVERNMENT RIGHTS

This invention was made with government support under Grant No. GM103558 and
5 GM100985 awarded by the National Institutes of Health (NIGMS). The government has certain
rights in the invention.

RELATED APPLICATION DATA

The present application claims priority pursuant to 35 U.S.C. § 119(e) to United States
10 Provisional Patent Application Serial Number 61/975,667 filed April 4, 2014 and United States
Provisional Patent Application Serial Number 62/020,165 filed July 2, 2014, each of which is
incorporated herein by reference in its entirety.

FIELD

15 The present invention relates to decarboxylative cross-coupling and, in particular, to
decarboxylative cross-coupling via use of photoredox and transition metal catalysts.

BACKGROUND

Molecular synthesis plays a critical role in a significant number of industries including
20 the pharmaceutical, biological, biochemical and materials industries. Substantial resources and
time are invested in the construction and development of molecular libraries for the
characterization and identification of molecular species having promise for a particular
application. Such libraries, however, are often rendered incomplete by the inability to efficiently
synthesize a wide variety of chemical species. Many classes of chemical species, for example,
25 require expensive reagents, complex and time consuming synthetic pathways and/or result in the
production of hazardous by-products.

SUMMARY

In one aspect, synthetic methods are described herein operable to efficiently produce a
30 wide variety of molecular species. For example, methods described herein enable the production
of numerous molecular species through decarboxylative cross-coupling via use of photoredox
and transition metal catalysts. A method described herein, in some embodiments, comprises

providing a reaction mixture including a photoredox catalyst, a transition metal catalyst, a coupling partner and a substrate having a carboxyl group. The reaction mixture is irradiated with a radiation source resulting in cross-coupling of the substrate and coupling partner via a mechanism including decarboxylation, wherein the coupling partner is selected from the group consisting of a substituted aromatic compound and a substituted aliphatic compound. In some embodiments, the substrate of the reaction mixture is an aliphatic carboxylic acid or a keto acid. Additionally, in some embodiments, the reaction mixture further comprises a ligand component.

In another aspect, acylation methods are described herein employing decarboxylative pathways. For example, a method of acylation comprises providing a reaction mixture including an acylating agent, a photoredox catalyst, a transition metal catalyst and a substrate having a carboxyl group. The reaction mixture is irradiated with a radiation source resulting in acylation of the substrate via a mechanism including decarboxylation. In some embodiments, substrate of the reaction mixture is aliphatic carboxylic acid, and the acylating agent is acyl halide. Moreover, the reaction mixture, in some embodiments, further comprises a ligand component.

In a further aspect, methods of fluorination via decarboxylative pathways are described herein. A method of fluorination comprises providing a reaction mixture comprising a fluorination reagent, a photoredox catalyst and an aliphatic carboxylic acid. The reaction mixture is irradiated with a radiation source yielding fluoroalkane via a mechanism including decarboxylation of the aliphatic carboxylic acid and fluorination by the fluorinating reagent. In some embodiments, the reaction mixture further comprises base.

These and other embodiments are described further in the following detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates various ligand species of the ligand component of a decarboxylative cross-coupling reaction mixture according to some embodiments described herein.

Figure 2 illustrates a mechanistic pathway of decarboxylative arylation according to one example of a method described herein.

Figure 3 illustrates a mechanistic pathway of decarboxylative arylation according to one example of a method described herein.

Figure 4 illustrates a mechanistic pathway of decarboxylative fluorination according to one example of a method described herein.

Figure 5 illustrates a general reaction scheme and specific reaction product for decarboxylative arylation via sp^3 - sp^3 cross-coupling according to some embodiments described herein.

5 Figure 6 illustrates a general reaction scheme and specific reaction product for decarboxylative allylation via sp^3 - sp^3 cross-coupling according to some embodiments described herein.

Figure 7 illustrates a general reaction scheme and specific reaction product for decarboxylative alkylation via sp^3 - sp^3 cross-coupling according to some embodiments described herein.

10 Figures 8 and 9 illustrate a general reaction scheme and specific reaction product for decarboxylative acylation according to some embodiments described herein.

Figure 10 illustrates a general reaction scheme and specific reaction product for decarboxylative acylation according to some embodiments described herein.

15 Figure 11 illustrates a general reaction scheme and specific reaction product for decarboxylative acylation according to some embodiments described herein.

DETAILED DESCRIPTION

Embodiments described herein can be understood more readily by reference to the following detailed description and examples and their previous and following descriptions.

20 Elements, apparatus and methods described herein, however, are not limited to the specific embodiments presented in the detailed description and examples. It should be recognized that these embodiments are merely illustrative of the principles of the present invention. Numerous modifications and adaptations will be readily apparent to those of skill in the art without departing from the spirit and scope of the invention.

25

Definitions

The term "alkyl" as used herein, alone or in combination, refers to a straight or branched saturated hydrocarbon group. For example, an alkyl can be $C_1 - C_{30}$.

30 The term "alkenyl" as used herein, alone or in combination, refers to a straight or branched chain hydrocarbon group having at least one carbon-carbon double bond.

The term "alkynyl" as used herein, alone or in combination, refers to a straight or branched chain hydrocarbon group having at least one carbon-carbon triple bond.

The term "aryl" as used herein, alone or in combination, refers to an aromatic monocyclic or multicyclic ring system optionally substituted with one or more ring substituents

5 The term "heteroaryl" as used herein, alone or in combination, refers to an aromatic monocyclic or multicyclic ring system in which one or more of the ring atoms is an element other than carbon, such as nitrogen, oxygen and/or sulfur.

The term "cycloalkyl" as used herein, alone or in combination, refers to a non-aromatic, saturated mono- or multicyclic ring system optionally substituted with one or more ring
10 substituents.

The term "cycloalkenyl" as used herein, alone or in combination, refers to a non-aromatic, mono- or multicyclic ring system having at least one carbon-carbon double bond and is optionally substituted with one or more ring substituents.

15 The term "heterocycloalkyl" as used herein, alone or in combination, refers to a non-aromatic, saturated mono- or multicyclic ring system in which one or more of the atoms in the ring system is an element other than carbon, such as nitrogen, oxygen or sulfur, alone or in combination, and wherein the ring system is optionally substituted with one or more ring substituents.

20 The term "heterocycloalkenyl" as used herein, alone or in combination, refers to a non-aromatic, mono- or multicyclic ring system in which one or more of the atoms in the ring system is an element other than carbon, such as nitrogen, oxygen or sulfur, alone or in combination, and which contains at least one carbon-carbon double bond in the ring system and wherein the ring system is optionally substituted with one or more ring substituents.

25 The term "heteroalkyl" as used herein, alone or in combination, refers to an alkyl moiety as defined above, having one or more carbon atoms, for example one, two or three carbon atoms, replaced with one or more heteroatoms, which may be the same or different.

The term "alkoxy" as used herein, alone or in combination, refers to the moiety RO-, where R is alkyl, alkenyl or aryl defined above.

30

I. Decarboxylative Cross-Coupling

Methods described herein enable the production of numerous molecular species through decarboxylative cross-coupling via use of photoredox and transition metal catalysts. For example, a method described herein, in some embodiments, comprises providing a reaction mixture including a photoredox catalyst, a transition metal catalyst, a coupling partner and a substrate having a carboxyl group. The reaction mixture is irradiated with a radiation source resulting in cross-coupling of the substrate and coupling partner via a mechanism including decarboxylation, wherein the coupling partner is selected from the group consisting of a substituted aromatic compound and a substituted aliphatic compound. Additionally, the reaction mixture, in some embodiments, further comprises a ligand component.

A. *Carboxylic Acid Substrate*

Turning now to specific components, the reaction mixture comprises a substrate having a carboxyl group. Any substrate including a carboxyl group operable to undergo decarboxylative mechanistic pathways described herein can be employed in the reaction mixture. In some embodiments, a substrate of the reaction mixture is an aliphatic carboxylic acid. In being an aliphatic acid, the carboxyl functional group is not directly bonded to an aromatic ring, such as a phenyl ring. Aliphatic carboxylic acid, in some embodiments, is of the formula R^1-CO_2H . R^1 can be a saturated hydrocarbon or a hydrocarbon having one or more points of unsaturation. Further, saturated or unsaturated hydrocarbons can incorporate or be substituted with one or more heteroatoms including nitrogen, oxygen and/or sulfur. Therefore, R^1 can be selected from the group consisting of -alkyl, -cycloalkyl, -heteroalkyl, -heterocycloalkyl, -alkenyl, -cycloalkenyl, -heteroalkenyl, -heterocycloalkenyl, -alkynyl, -alkyl-aryl, -alkyl-heteroaryl, -alkyl-alkoxy, -alkenyl-aryl, -alkenyl-heteroaryl, -cycloalkyl-aryl, -cycloalkyl-heteroaryl, -cycloalkenyl-aryl, -heterocycloalkenyl-aryl, and -alkenyl-alkoxy.

In some embodiments, aliphatic carboxylic acid substrate of the reaction mixture is selected from the amino acids of Table I.

Table I – Amino Acids

Alanine
Arginine
Asparagine

Aspartic Acid
Cysteine
Glutamic Acid
Glutamine
Glycine
Histidine
Isoleucine
Leucine
Lysine
Methionine
Phenylalanine
Proline
Serine
Threonine
Tryptophan
Tyrosine
Valine

Further, the aliphatic carboxylic acid substrate can be one or more saturated or unsaturated fatty acids. In some embodiments, a fatty acid of the reaction mixture is selected from Table II.

5 Table II – Fatty Acids

Saturated Fatty Acids	Unsaturated Fatty Acids
Caprylic acid	Myristoleic acid
Capric acid	Palmitoleic acid
Lauric acid	Sapienic acid
Myristic acid	Oleic acid
Palmitic acid	Eladic acid
Stearic acid	Vaccenic acid
Arachidic acid	Linoleic acid
Behenic acid	α -Linoleic acid
Lignoceric acid	Arachidonic acid
Cerotic acid	Eicosapentaenoic acid
	Erucic acid
	Docosahexanoic acid

10 Keto acids, in some embodiments, can also be employed as substrate of the reaction mixture. For example, suitable keto acids include aliphatic keto acids, aryl keto acids and heteroaryl keto acids. In some embodiments, keto acids are α -keto acids. α -keto acid of the reaction mixture can be of the formula $R^2-C(O)-CO_2H$, wherein R^2 is selected from the group consisting of -alkyl, -cycloalkyl, -heteroalkyl, -heterocycloalkyl, -alkenyl, -cycloalkenyl, -heteroalkenyl, -heterocycloalkenyl, -alkynyl, -aryl, -heteroaryl, -alkyl-aryl, -alkyl-heteroaryl,

-alkyl-alkoxy, -alkenyl-aryl, -alkenyl-heteroaryl and -alkenyl-alkoxy.

The carboxyl group of the substrate can be provided to the reaction mixture in protonated form, deprotonated form, carboxylate salt, carboxylate ester or other derivative form.

5 *B. Coupling Partner*

As described herein, the reaction mixture also comprises a coupling partner selected from the group consisting of a substituted aromatic compound and a substituted aliphatic compound. Any substituted aromatic or aliphatic compound operable to undergo cross-coupling according to mechanistic pathways described herein can be employed.

10 Suitable substituted aromatic compounds can include monocyclic and multicyclic ring systems, such as fused and non-fused multicyclic ring systems. Further, substituted aryl compounds comprise heteroaryl species, including monocyclic and multicyclic heteroaryl systems. As discussed further herein, a substituted aromatic compound of the reaction mixture comprises a leaving group substituent. Chemical identity of the leaving group can be selected
15 according to several parameters including identity of the transition metal catalyst and the presence of any additional substituents appended to the aromatic compound. For example, a leaving group can be selected from the group consisting of halides (Cl, Br and I), triflates, phosphonates and tosylates. In some embodiments, the leaving group is compatible with nickel catalyst described herein.

20 Importantly, the leaving group of the substituted aromatic compound can be bonded directly to a carbon of the aromatic ring structure. In such embodiments, decarboxylative cross-coupling between the substrate and substituted aromatic compound is sp^3 - sp^2 cross-coupling. Alternatively, the leaving group of the substituted aromatic compound is not bonded directly to a carbon of the aromatic ring structure. For example, the leaving group can be coupled to the
25 aromatic ring structure by an alkyl, cycloalkyl or heteroalkyl moiety. In such embodiments, the sp^3 hybridization of the carbon bound to the leaving group is maintained resulting in sp^3 - sp^3 cross-coupling with the substrate. Further, when α -keto acids are employed as the carboxylic acid substrate, sp^2 - sp^2 and sp^2 - sp^3 cross-coupling can result, depending on the hybridization of the carbon to which the leaving group is bonded. As detailed in Figure 2 discussed below, sp^2
30 hybridization of the carbon to which the leaving group is bonded results in sp^2 - sp^2 cross-

coupling. sp^3 hybridization of the carbon to which the leaving group is bonded results in sp^2 - sp^3 cross-coupling with the α -keto acid.

Suitable substituted aliphatic compounds of the coupling partner can include saturated hydrocarbon chains or hydrocarbon chains having one or more points of unsaturation. Further, saturated or unsaturated hydrocarbon chains can incorporate or be substituted with one or more heteroatoms including nitrogen, oxygen and/or sulfur. Substituted aliphatic compounds also include a leaving group substituent. Chemical identity of the leaving group can be selected according to several parameters including identity of the transition metal catalyst and the presence of any additional substituents appended to the aliphatic compound. In some embodiments, the leaving group is selected from the group consisting of halide and carbonate. An aliphatic coupling partner, in some embodiments, is of the formula R^3 -X, wherein R^3 is selected from the group consisting of alkyl, cycloalkyl, heteroalkyl, heterocycloalkyl, alkenyl, cycloalkenyl, heteroalkenyl, heterocycloalkenyl and alkynyl, and X is a leaving group. X, in some embodiments, is selected from the group consisting of halide and carbonate.

The leaving group can be bonded directly to a sp^2 -hybridized carbon of the substituted aliphatic compound. In such embodiments, decarboxylative cross-coupling between the substrate and substituted aliphatic compound is sp^3 - sp^2 cross-coupling. Alternatively, the leaving group of the substituted aliphatic compound is bonded to a sp^3 hybridized carbon, thereby providing sp^3 - sp^3 decarboxylative cross-coupling. Additionally, when α -keto acids are employed as the carboxylic acid, sp^2 - sp^2 and sp^2 - sp^3 cross-coupling can result, depending on the hybridization of the carbon to which the leaving group is bonded as discussed above.

C. Photoredox Catalyst and Transition Metal Catalyst

The reaction mixture employs a photoredox catalyst in conjunction with a transition metal catalyst. Any photoredox catalyst operable to participate in decarboxylative mechanisms described herein can be used. Suitable photoredox catalyst can be selected from one or more iridium complexes or ruthenium complexes. In some embodiments, heteroleptic iridium complexes are selected as the photoredox catalyst. For example, iridium photoredox catalyst for use in methods described herein includes $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})^+$, $\text{Ir}(\text{ppy})_2(\text{dtbbpy})^+$ and $\text{Ir}[\text{dF}(5\text{-Me})\text{ppy}]_2(\text{tetraMePhen})^+$. Ruthenium complexes can also serve as the photoredox catalyst. Suitable ruthenium photoredox catalyst can include $\text{Ru}(\text{bpy})_3^{2+}$ and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$.

Photoredox catalyst can be present in the reaction mixture in any amount not inconsistent with the objectives of the present invention. In some embodiments, photoredox catalyst is present in the reaction mixture in an amount selected from Table III.

5 Table III – Photoredox Catalyst in Reaction Mixture

mol.%
0.1-5
0.1-1
0.5-3
0.5-2

Transition metal catalyst is present in the reaction mixture in addition to the photoredox catalyst. Any transition metal catalyst operable to participate in cross-coupling mechanisms described herein can be used. Suitable transition metal catalyst can include nickel catalyst,
 10 palladium catalyst or copper catalyst. For example, in some embodiments, transition metal catalyst can be selected from the group consisting of NiCl₂•dtbbpy, NiCl₂•bpy, NiCl₂•phen, NiCl₂•di-Ph-phen, NiBr₂•glyme, NiCl₂•glyme, Ni(OTf)₂, and Ni(COD)₂. In some
 15 embodiments, transition metal catalyst is formed in the reaction mixture by interaction of a metal catalyst precursor and the ligand component discussed in Section D below. In some
 20 embodiments, for example, NiCl₂•glyme can react with dtbbpy ligand to provide NiCl₂•dtbbpy catalyst.

Transition metal catalyst can be present in the reaction mixture in any amount not inconsistent with the objectives of the present invention. In some embodiments, transition metal catalyst is present in the reaction mixture in an amount selected from Table IV.

20

Table IV – Transition Metal Catalyst in Reaction Mixture

mol.%
1-15
4-12
5-10

D. Ligand Component

The reaction mixture, in some embodiments, also comprises a ligand component. Any
 25 ligand not inconsistent with the objectives of the present invention may be used. For example,

suitable ligand can comprise one or more pyridine moieties. In some embodiments, the ligand component comprises bipyridine or derivatives thereof. The ligand component can also be selected from the species provided in Table V.

5 Table V – Reaction Mixture Ligand

dtbbpy
bpy
diPh-bpy
diOMe-bpy
di-naphth-Py
phen
di-Ph-phen

Additional ligands of the ligand component are provided in Figure 1. The ligand component can be present in the reaction mixture in any amount not inconsistent with the objectives of the present invention. In some embodiments, the ligand component is present in the reaction mixture in an amount selected from Table VI.

Table VI – Ligand Component in Reaction Mixture

mol.%
5-50
10-40
15-30
10-20

E. Base and Solvent Components

15 In some embodiments, the reaction mixture further comprises a base. Any base not inconsistent with the objectives of the present application can be used. In some embodiments, suitable base is selected from Table VII.

Table VII – Base of the Reaction Mixture

CsHCO ₃
CsF
Cs ₂ CO ₃
CsOAc
t-BuOLi
t-BuOK
KOH

NaOH
NaOAc
CsOH·H ₂ O
Li ₂ CO ₃

Components of the reaction mixture are disposed in a solvent. Any solvent not inconsistent with the objectives of the present invention can be employed. The solvent, for example, can be an aprotic polar solvent. In some embodiments, the solvent is selected from Table VIII.

5

Table VIII – Solvent of the Reaction Mixture

DMSO
DMPU
DMF
DMA
NMP
CH ₃ CN

In one embodiment, for example, solvent of the reaction mixture is DMF at a molarity of 0.01 to 0.1M.

10 Additionally, an additive can be included in the reaction mixture. For example, pyridine can be added to the reaction mixture in various quantities. Pyridine, in some embodiments, is added to the reaction mixture in an amount of 5-50%.

As described herein, the reaction mixture is irradiated with a radiation source resulting in cross-coupling of the substrate and coupling partner via a mechanism including catalyzed
 15 decarboxylation. Advantageously, irradiation and the subsequent reaction can take place at room temperature. Radiation of any wavelength suitable for photocatalyst activation may be employed. In some embodiments, the radiation source provides radiation in the visible region of the electromagnetic spectrum, such as the blue region. In some embodiments, the radiation source comprises one or more one compact fluorescent lamps (CFL), light emitting diodes
 20 (LED) or combinations thereof. For example, blue LEDs may be used as the radiation source. While visible light is employed in the examples described herein, radiation of other region(s) of the electromagnetic spectrum are contemplated, including ultraviolet and/or infrared radiation. In some embodiments, the reaction is allowed proceed for a time period of 1 to 48 hours.

25 While not wishing to be bound by any theory, Figure 2 illustrates a mechanistic pathway of sp³ – sp² decarboxylative arylation of an α-amino acid according to one example of a method

described herein. As illustrated in Figure 2, initial irradiation of heteroleptic iridium (III) photocatalyst $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ [$\text{dF}(\text{CF}_3)\text{ppy}$ = 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine, dtbbpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine] can produce the long-lived photoexcited $^*\text{Ir}^{\text{III}}$ state **2** ($\tau = 2.3 \mu\text{s}$). Deprotonation of the α -amino acid substrate **3** with base and oxidation by the $^*\text{Ir}^{\text{III}}$ excited state via a single electron transfer event (SET) can generate a carboxyl radical which, upon rapid loss of CO_2 provides the α -amino radical **4** and the corresponding Ir^{II} species **5**. Concurrently with this photoredox cycle, addition of $\text{Ni}(0)$ species **6** into an aryl halide produces the $\text{Ni}(\text{II})$ intermediate **7**. The $\text{Ni}(\text{II})$ -aryl species **7** can intercept the α -amino radical **4**, forming the organometallic $\text{Ni}(\text{III})$ adduct **8**. Subsequent reductive elimination materializes the requisite C-C bond, while delivering the desired α -amino arylation product **10** and expelling the $\text{Ni}(\text{I})$ intermediate **9**. Finally, single-electron transfer between the Ir^{II} species **5** and the Ni complex **9** accomplishes the exergonic reduction of $\text{Ni}(\text{I})$ to $\text{Ni}(0)$, thereby completing both the photoredox and nickel catalytic cycles simultaneously.

While not wishing to be bound by any theory, Figure 3 illustrates a mechanistic pathway of sp^3 - sp^2 decarboxylative arylation of an α -keto acid according to one embodiment described herein. Irradiation of the reaction mixture generates the strongly oxidizing excited state $^*\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}](\text{dtbbpy})^+$ **2**. Base-mediated deprotonation of pyruvic acid substrate **3** and subsequent single electron oxidation of the resulting carboxylate functionality by the excited Ir^{III} photoredox catalyst **2** can generate the reduced photoredox catalyst $\text{Ir}^{\text{II}}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})$ **4** and a corresponding carboxyl radical species. The open-shell dicarbonyl intermediate rapidly extrudes CO_2 providing the acyl radical **5**. Within the same time frame, the second catalytic cycle employing Ni catalyst can initiate via oxidative addition of the Ni^0 catalyst **6** into the aryl halide partner, 4-iodotoluene **7**, to generate the Ni^{II} -aryl complex **8**. This resulting electrophilic Ni^{II} complex **8** rapidly traps the strong nucleophilic acyl radical **5** to produce Ni^{III} -acyl complex **9**. Reductive elimination from the Ni^{III} -acyl complex can forge the C-C ketone bond of compound **10**, while expelling the corresponding Ni^{I} complex. Finally, single electron transfer (SET) from the photoredox catalyst Ir^{II} species **4** to the Ni^{I} -dtbbpy complex **11** returns the Ni catalyst to the required Ni^0 oxidation state in an exergonic process. It should be noted that this second photoredox mediated SET event regenerates the ground state Ir^{III} catalyst **1** while reconstituting the requisite $\text{Ni}(0)$ complex **6**, thereby completing both photoredox and nickel cycles simultaneously.

Examples of decarboxylative cross-coupling according to this Section I are provided in the examples section below.

II. Methods of Acylation

5 In another aspect, acylation methods are described herein employing decarboxylative pathways. For example, a method of acylation comprises providing a reaction mixture including an acylating agent, a photoredox catalyst, a transition metal catalyst and a substrate having a carboxyl group. The reaction mixture is irradiated with a radiation source resulting in acylation of the substrate via a mechanism including decarboxylation. In some embodiments, substrate of
10 the reaction mixture is aliphatic carboxylic acid, and the acylating agent is acyl halide.

Moreover, the reaction mixture, in some embodiments, further comprises a ligand component.

Turning now to specific components, the reaction mixture comprises a substrate having a carboxyl group. Substrate of the reaction mixture can be aliphatic carboxylic acid, including the aliphatic carboxylic acids described in Section IA above. For example, aliphatic carboxylic acid
15 can comprise amino acids or fatty acids selected from Tables I and II of Section IA above.

Further, aliphatic carboxylic acid substrate of the reaction mixture can be of the formula R^1-CO_2H described above. In some embodiments, the carboxyl group of the substrate can be provided to the reaction mixture in protonated form, deprotonated form, carboxylate salt, carboxylate ester or other derivative form.

20 The reaction mixture also comprises an acylating agent. Any acylating agent operable to participate in catalytic mechanisms for acylation via decarboxylation can be employed. The acylating agent, for example, can be an acyl halide. In some embodiments, acyl halide is of the formula $X-C(O)R^4$, wherein X is a halide leaving group selected from the group consisting of F^- , Br^- and I^- and R^4 is selected from the group consisting of -alkyl, -cycloalkyl, -heteroalkyl,
25 -heterocycloalkyl, -alkenyl, -cycloalkenyl, -heteroalkenyl, -heterocycloalkenyl, -aryl, -heteroaryl, -alkyl-aryl, -alkyl-heteroaryl, -cycloalkyl-aryl, -cycloalkyl-heteroaryl, -aryl-alkyl, and -aryl-alkoxy.

Suitable photoredox catalyst and transition metal catalyst of the reaction mixture can comprise the catalytic species described in Section IC above. Additionally, photoredox catalyst
30 can include $Ir(4',6'-dF-5-CF_3-ppy)_2(4,4'-dtbbpy)^+$ and $Ir(4',6'-dF-5-OMe-ppy)_2(4,4'-dtbbpy)^+$. Amounts of photoredox catalyst and transition metal catalyst employed in the reaction mixture

can be selected from Tables III and IV of Section IC above. Moreover, parameters of the ligand component, reaction mixture solvent and radiation source can be selected from Sections ID and IE above.

5 Examples of acylation employing decarboxylative mechanisms described in this Section II are provided in the examples section below.

III. Methods of Fluorination

In a further aspect, methods of fluorination via decarboxylative pathways are described herein. A method of fluorination comprises providing a reaction mixture comprising a
10 fluorination reagent, a photoredox catalyst and an aliphatic carboxylic acid. The reaction mixture is irradiated with a radiation source yielding fluoroalkane via a mechanism including decarboxylation of the aliphatic carboxylic acid and fluorination by the fluorinating reagent. In some embodiments, the reaction mixture further comprises base.

Turning now to specific components, any aliphatic carboxylic acid operable to undergo
15 catalytic decarboxylation and fluorination according to pathways described herein can be employed. In some embodiments, aliphatic carboxylic acid of the reaction mixture is of the formula R^5CO_2H , wherein R^5 is selected from the group consisting of -alkyl, -heteroalkyl, -cycloalkyl, -heterocycloalkyl, -alkyl-aryl, -heteroalkyl-aryl, -alkyl-heteroaryl, -alkyl-cycloalkyl, -alkyl-heterocycloalkyl, -heteroalkyl-heteroaryl, -cycloalkyl-aryl, -cycloalkyl-
20 heteroaryl, -heterocycloalkyl-aryl, -heterocycloalkyl-heteroaryl, -cycloalkyl-alkyl, -heterocycloalkyl-alkyl, -cycloalkyl-heteroalkyl, and -heterocycloalkyl-heteroalkyl. Additionally, aliphatic carboxylic of the reaction mixture can be di-carboxylic acid. Further, carboxylic acid can be provided to the reaction mixture in protonated form, deprotonated form, carboxylate salt, carboxylate ester or other derivative form.

25 The reaction mixture can include any photoredox catalyst operable to participate in decarboxylative fluorination mechanisms described herein. Suitable photoredox catalyst can be selected from one or more iridium complexes or ruthenium complexes. In some embodiments, heteroleptic iridium or homoleptic ruthenium complexes are selected as the photoredox catalyst. Heteroleptic iridium photocatalyst can include $Ir[dF(CF_3)ppy]_2(dtbbpy)^+$ while homoleptic
30 ruthenium photocatalyst can include $Ru(bpz)_3^{2+}$ and $Ru(phen)_3^{2+}$. In some embodiments, photocatalyst is present in the reaction mixture in an amount of 0.1 to 5 mol.%.

As described herein, the reaction mixture also comprises fluorination reagent. Any fluorination reagent operable to participate in decarboxylative fluorination mechanisms described herein can be used. In some embodiments, for example, the fluorination agent is SELECTFLUOR®. The fluorination reagent can be present in the reaction mixture in any amount providing efficient fluorination following decarboxylation of the aliphatic carboxylic acid. The fluorination reagent, for example, can be present in the reaction mixture in an amount of two equivalents for every one equivalent of aliphatic carboxylic acid. The reaction mixture can also comprise base operable for deprotonation of the aliphatic carboxylic acid. In some embodiments, base of the reaction mixture comprises sodium hydrogen phosphate (Na₂HPO₄).

Solvent for the reaction mixture is selected according to the ability to sufficiently solubilize the aliphatic carboxylic acid and fluorinating reagent. Any solvent system providing such solubilization and non-interference with the catalytic decarboxylation and subsequent fluorination can be employed. In some embodiments, for example, suitable solvent is a mixture of acetonitrile and water (CH₃CN/H₂O). It is contemplated that solvent for the reaction mixture can be separate from the base component described above. However, in some embodiments, a solvent can exhibit sufficient basicity to deprotonate the aliphatic carboxylic acid and, therefore, also serve as base of the reaction mixture. Moreover, parameters of the radiation source can be selected from Section IE above.

While not wishing to be bound by any theory, Figure 4 illustrates a mechanistic pathway of decarboxylative fluorination according to one embodiment described herein. Irradiation of heteroleptic iridium (III) photoredox catalyst Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ **1** with visible light can lead to the formation of a long-lived ($\tau = 2.3 \mu\text{s}$) excited state *Ir[dF(CF₃)ppy]₂(dtbbpy)⁺ **2**, which can undergo oxidative quenching in the presence of an appropriate electron acceptor. *Ir(III) can reduce the fluorinating agent SELECTFLUOR® **3** in a single electron transfer process, resulting in the formation of radical species **4** and the strongly oxidizing Ir[dF(CF₃)ppy]₂(dtbbpy)²⁺ **5**. Base-mediated formation of an alkyl carboxylate followed by a single electron transfer oxidation using the transiently formed Ir(IV) is thermodynamically feasible to generate a carboxyl radical, which upon immediate extrusion of CO₂ can provide the SOMO species **7**. At this stage, direct F• transfer from SELECTFLUOR® to the radical species **7** is proposed to forge a new C-F bond with concomitant formation of the defluorinated analog of SELECTFLUOR®.

Examples of fluorination employing decarboxylative mechanisms described in this Section III are provided in the examples section below.

IV. EXAMPLES

5 A. Decarboxylative Arylation, sp^3 - sp^2 Cross-coupling (Examples 1-24)

Materials and Methods

The following Examples were conducted with the materials and methods described herein. Commercial reagents were purchased from Sigma Aldrich and purified prior to use following the guidelines of Perrin and Armarego, *Purification of Laboratory Chemicals*,
10 Pergamon, Oxford, ed.3 1988) (hereinafter "Perrin"). All solvents were purified by passage through columns of activated alumina. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an acetone-dry ice bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on silica gel (Fluka, 230-400 mesh). Thin layer chromatography (TLC) was performed on Analtech
15 Uniplate 250 m silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, *p*-anisaldehyde, potassium permanganate, or ceric ammonium molybdate stain. ^1H and ^{13}C NMR spectra were recorded on a Bruker 500 (500 and 125 MHz) instrument, and are internally referenced to residual protio solvent signals (note: CDCl_3 referenced at 7.26 and 77.0 ppm respectively). Data for ^1H NMR are reported as follows:
20 chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. High resolution mass spectra were obtained at Princeton University mass spectrometry facilities. All amino acids were used from commercial suppliers. All aryl and heteroaryl halides were used from
25 commercial suppliers or prepared using standard literature procedures.

General Procedure A for the Decarboxylative Arylation (Arene Scope)

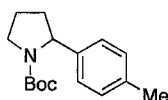
An oven-dried 40 mL vial equipped with a Teflon septum and magnetic stir bar was charged with $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (4.00 μmol , 0.01 equiv), $\text{NiCl}_2\cdot\text{glyme}$ (0.04 mmol, 0.1
30 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (0.06 mmol, 0.15 equiv), the corresponding aromatic halides (0.40 mmol, 1.0 equiv), Boc-Pro-OH (0.60 mmol, 1.5 equiv), Cs_2CO_3 (0.60 mmol, 1.5

equiv), and 20 mL of DMF. The reaction mixture was degassed by bubbling argon stream for 20 min, then irradiated with two 26 W fluorescent lamps (at approximately 2 cm away from the light source). After 72h, the reaction mixture was diluted with saturated aqueous NaHCO₃ solution, extracted with Et₂O (3 × 100 mL). The combined organic extracts were washed with water and brine, dried over MgSO₄ and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

General Procedure B for the Decarboxylative Arylation (Amino Acid Scope)

An oven-dried 40 mL vial equipped with a Teflon septum and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.00 μmol, 0.01 equiv), NiCl₂•glyme (0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (0.06 mmol, 0.15 equiv), 4-bromoacetophenone (0.40 mmol, 1.0 equiv), the corresponding amino acids (1.20 mmol, 3.0 equiv), Cs₂CO₃ (1.20 mmol, 3.0 equiv), and 20 mL of DMF. The reaction mixture was degassed by bubbling argon stream for 20 min, then irradiated with a 34 W blue LED lamp (Fan was used to keep the reaction temperature below 28 °C). After 72h, the reaction mixture was diluted with saturated aqueous NaHCO₃ solution, extracted with Et₂O (3 × 100 mL). The combined organic extracts were washed with water and brine, dried over MgSO₄ and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

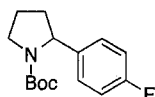
EXAMPLE 1 - *tert*-Butyl 2-(*p*-tolyl)pyrrolidine-1-carboxylate



According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-iodotoluene (89.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.60 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (15% ethyl acetate/hexane) as a pale yellow solid (81 mg, 78%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.10-7.03 (m, 4H),

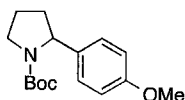
4.92 and 4.74 (2 brs, 1H, rotamer), 3.60-3.47 (m, 2H), 2.32-2.20 (m, 4H), 1.91-1.79 (m, 3H), 1.46 (s, 3H), 1.19 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 154.65 (155.41), 142.07 (141.13), 135.92, (129.04) 128.75, 125.43 (125.28), 79.10 (78.88), 61.03 (60.45), (47.31) 47.01, 36.02 (34.90), (28.54) 28.20, (23.47) 23.11, 21.05; HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_{23}\text{NNaO}_2$ [(M+Na) $^+$] 284.1626, found 284.1630.

EXAMPLE 2 - *tert*-Butyl 2-(4-fluorophenyl)pyrrolidine-1-carboxylate



10 According to the general procedure A, $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (4.5 mg, 10.0 μmol , 0.01 equiv), $\text{NiCl}_2\cdot\text{glyme}$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-fluoriodobenzene (90.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs_2CO_3 (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (15% ethyl acetate/hexane) as a
 15 pale yellow oil (69 mg, 65%). ^1H NMR (500 MHz, CDCl_3) rotameric mixture: δ 7.14-7.11 (m, 2H), 7.00-6.96 (m, 2H), 4.92 and 4.73 (2 brs, 1H, rotamer), 3.61-3.60 (m, 2H), 2.31-2.25 (m, 1H), 1.87-1.77 (m, 3H), 1.46 (s, 3H), 1.19 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 161.57 (d, $J = 242.3$ Hz), (154.71) 154.52, 140.89 (139.79), 126.96 (d, $J = 7.1$ Hz), (115.19) 114.89 (d, $J = 21.3$ Hz), 79.33
 20 (78.89), 60.72 (60.11), (47.31) 47.07, 36.10 (34.90), (28.50) 28.17, (23.46) 23.17; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{20}\text{FNNaO}_2$ [(M+Na) $^+$] 288.1376, found 288.1375.

EXAMPLE 3 - *tert*-Butyl 2-(4-methoxyphenyl)pyrrolidine-1-carboxylate

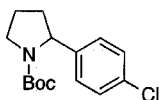


25 According to the general procedure A, $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (4.5 mg, 10.0 μmol , 0.01 equiv), $\text{NiCl}_2\cdot\text{glyme}$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-iodoanisole (96.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0

mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (15% ethyl acetate/hexane) as a yellow oil (82 mg, 74%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.08 (d, *J* = 7.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 4.90 and 4.72 (2 brs, 1H, rotamer), 3.79 (s, 3H), 3.61-3.51 (m, 2H), 2.28 (br, 1H), 1.92-1.78 (m, 3H), 1.46 (s, 3H), 1.20 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 158.22, 154.67, 137.31 (136.28), 126.60, (113.77) 113.44, 79.13, 60.74 (60.12), 55.27, (47.27) 46.99, 36.05 (34.88), (28.54) 28.21, (23.47) 23.14; HRMS (ESI) *m/z* calcd for C₁₆H₂₃NNaO₃ [(M+Na)⁺] 300.1576, found 300.1562.

10

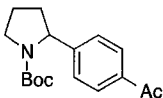
EXAMPLE 4 - *tert*-Butyl 2-(4-chlorophenyl)pyrrolidine-1-carboxylate



According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 1-chloro-4-iodobenzene (96.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (15% ethyl acetate/hexane) as a pale yellow solid (87 mg, 77%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.27 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 4.90 and 4.73 (2 brs, 1H, rotamer), 3.62-3.49 (m, 2H), 2.33-2.28 (m, 1H), 1.92-1.82 (m, 2H), 1.80-1.74 (m, 1H), 1.45 (s, 3H), 1.20 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 154.51, 143.76 (142.73), (132.19) 132.10, (128.52) 128.30, 126.91 (128.84), 79.45, 60.80 (60.25), (47.39) 47.11, 36.03 (34.87), (28.53) 28.22, (23.55) 23.19; HRMS (ESI) *m/z* calcd for C₁₅H₂₀NNaO₂Cl [(M+Na)⁺] 304.1080, found 304.1078.

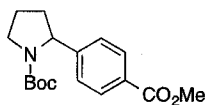
25

EXAMPLE 5 - *tert*-Butyl 2-(4-acetylphenyl)pyrrolidine-1-carboxylate

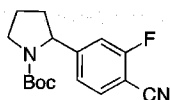


According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.80 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (81.9 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow solid (100 mg, 86%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 4.97 and 4.81 (2 brs, 1H, rotamer), 3.66-3.52 (m, 2H), 2.60-2.58 (m, 3H), 2.38-2.32 (m, 1H), 1.92-1.78 (m, 3H), 1.45 (s, 3H), 1.17 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 197.75, (154.43) 154.37, 150.79 (149.80), 135.66, (128.63) 128.41, 125.62 (125.54), (79.51) 79.45, 61.14 (60.65), (47.43) 47.11, 35.88 (34.76), (28.46) 28.12, 26.60, (23.63) 23.23; HRMS (ESI) *m/z* calcd for C₁₇H₂₃NNaO₃ [(M+Na)⁺] 312.1576, found 312.1558.

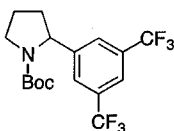
EXAMPLE 6 - *tert*-Butyl 2-(4-(methoxycarbonyl)phenyl)pyrrolidine-1-carboxylate



According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), methyl 4-bromobenzoate (88.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a yellow oil (111 mg, 90%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.97 (d, *J* = 10.0 Hz, 2H), 7.24 (d, *J* = 5.0 Hz, 2H), 4.97 and 4.80 (2 brs, 1H, rotamer), 3.91 (s, 3H), 3.65-3.52 (m, 2H), 2.37-2.31 (m, 1H), 1.92-1.77 (m, 3H), 1.45 (s, 3H), 1.16 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 166.94, 154.37, 150.58 (149.54), (129.77) 129.58, 128.47, 125.45 (125.38), 79.44, 61.19 (60.63), 51.99 (51.66), (47.37) 47.12, 35.91 (34.74), (28.44) 28.10, (23.57) 23.25; HRMS (ESI) *m/z* calcd for C₁₇H₂₃NNaO₄ [(M+Na)⁺] 328.1525, found 328.1517.

EXAMPLE 7 - *tert*-Butyl 2-(4-cyano-3-fluorophenyl)pyrrolidine-1-carboxylate

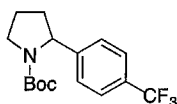
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromo-2-fluorobenzonitrile (82.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (25% ethyl acetate/hexane) as a pale yellow oil (87 mg, 75%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.56 (t, *J* = 7.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 9.5 Hz, 1H), 4.92 and 4.78 (2 brs, 1H, rotamer), 3.66-3.55 (m, 2H), 2.40-2.32 (m, 1H), 1.93-1.87 (m, 2H), 1.82-1.75 (m, 1H), 1.45 (s, 4H), 1.21 (s, 5H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (163.40) 163.27 (d, *J* = 257.3 Hz), (154.50) 154.37, 154.40 (d, *J* = 6.5 Hz) (153.45), 134.38 (d, *J* = 8.9 Hz), (133.50) 133.36, 121.97 (d, *J* = 3.1 Hz), (114.11) 114.03, 113.42 (d, *J* = 19.9 Hz), (80.04) 79.95, 60.94 (60.50), (47.46) 47.16, 35.75 (34.63), (28.40) 28.13, (23.71) 23.27; HRMS (ESI) *m/z* calcd for C₁₆H₁₉FN₂NaO₂ [(M+Na)⁺] 313.1328, found 313.1288.

EXAMPLE 8 - *tert*-Butyl 2-(3,5-bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 1,3-bis(trifluoromethyl)-5-bromobenzene (118.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (133 mg, 87%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.75-7.73 (m, 1H), 7.62-7.58 (m, 2H), 5.01 and 4.83 (2 brs, 1H, rotamer), 3.69-3.54 (m, 2H), 2.44-2.40 (m, 1H), 1.94-1.83 (m, 3H), 1.46 (s, 3H), 1.16 (s, 6H); ¹³C NMR (125 MHz,

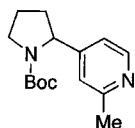
CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (154.52) 154.18, 147.92 (146.82), 131.61 (q, $J = 33.8$ Hz), 125.85 (125.59), 123.34 (q, $J = 271.3$ Hz), (120.74) 120.56, (80.08) 80.00, 60.94 (60.32), (47.46) 47.28, 36.08 (34.81), (28.32) 27.98, (23.59) 23.47; HRMS (ESI) m/z calcd for C₁₇H₁₉F₆NNaO₂ [(M+Na)⁺] 406.1218, found
5 406.1196.

EXAMPLE 9 - *tert*-Butyl 2-(4-(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate



According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μ mol,
10 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1
mg, 0.06 mmol, 0.15 equiv), 4-bromobenzotrifluoride (91.9 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-
OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of
DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane)
as a pale yellow oil (111 mg, 88%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.56 (d, J
15 = 8.0 Hz, 2H), 7.28 (d, $J = 8.0$ Hz, 2H), 4.97 and 4.81 (2 brs, 1H, rotamer), 3.66-3.55 (m, 2H),
2.38-2.32 (m, 1H), 1.91-1.86 (m, 2H), 1.82-1.77 (m, 1H), 1.46 (s, 3H), 1.18 (s, 6H); ¹³C NMR
(125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis
(): δ (154.52) 154.44, 149.29 (148.26), 128.88 (q, $J = 31.3$ Hz), 125.79 (125.72), (125.41)
125.19, 124.25 (q, $J = 270.0$ Hz), 79.60, 61.06 (60.51), 47.44 (47.14), 39.97 (34.82), (28.49)
20 28.15, (23.57) 23.23; HRMS (ESI) m/z calcd for C₁₆H₂₀F₃NNaO₂ [(M+Na)⁺] 338.1344, found
338.1324.

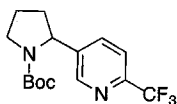
EXAMPLE 10 - *tert*-Butyl 2-(2-methylpyridin-4-yl)pyrrolidine-1-carboxylate



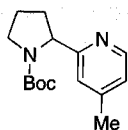
25 According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μ mol,
0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1
mg, 0.06 mmol, 0.15 equiv), 4-bromo-2-methylpyridine (71.0 mg, 0.4 mmol, 1.0 equiv), Boc-

Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (50% ethyl acetate/hexane) as a pale yellow oil (90 mg, 85%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 8.40 (d, *J* = 5.0 Hz, 1H), 6.95 (s, 1H), 6.90 (d, *J* = 5.0 Hz, 1H), 4.87-4.86 and 4.71-4.68 (2 m, 1H, rotamer), 3.63-3.49 (m, 2H), 2.53 (s, 3H), 2.36-2.29 (m, 1H), 1.90-1.85 (m, 2H), 1.81-1.76 (m, 1H), 1.46 (s, 3H), 1.20 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 158.23, 154.33 (154.21), 153.35, (149.06) 148.95, (120.15) 120.06, 117.89 (117.70), 79.58, 60.38 (59.91), (47.31) 47.02, 35.38 (34.28), (28.40) 28.07, (24.42) 24.37, (23.57) 23.16; HRMS (ESI) *m/z* calcd for C₁₅H₂₃N₂O₂ [(M+H)⁺] 263.1760, found 263.1758.

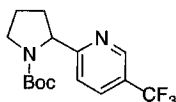
EXAMPLE 11 - *tert*-Butyl 2-(6-(trifluoromethyl)pyridin-3-yl)pyrrolidine-1-carboxylate



According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 5-bromo-2-(trifluoromethyl)pyridine (92.9 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow solid (104 mg, 82%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 8.58 (s, 1H), 7.68-7.63 (m, 2H), 5.01 and 4.86 (2 brs, 1H, rotamer), 3.67-3.57 (m, 2H), 2.43-2.40 (m, 1H), 1.96-1.91 (m, 2H), 1.84-1.82 (m, 1H), 1.45 (s, 4H), 1.17 (s, 5H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (154.47) 154.07, 148.01 (147.77), 146.61 (q, *J* = 35.0 Hz) [146.48 (q, *J* = 35.0 Hz)], 143.79 (142.80), (134.36) 134.20, 121.59 (q, *J* = 272.5 Hz), (120.16) 120.01, 79.97, 58.91 (58.58), (47.35) 47.13, 35.80 (34.55), (28.36) 28.08, (23.63) 23.28; HRMS (ESI) *m/z* calcd for C₁₅H₂₀F₃N₂O₂ [(M+H)⁺] 317.1477, found 317.1478.

EXAMPLE 12 - *tert*-Butyl 2-(4-methylpyridin-2-yl)pyrrolidine-1-carboxylate

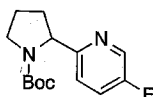
According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 2-bromo-4-methylpyridine (71.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.00 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (30% ethyl acetate/hexane) as a pale yellow oil (70 mg, 67%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 8.39-8.37 (m, 1H), 6.96-6.92 (m, 2H), 4.96-4.95 and 4.84-4.82 (2 m, 1H, rotamer), 3.67-3.50 (m, 2H), 2.38-2.26 (m, 4H), 2.01-1.96 (m, 1H), 1.91-1.84 (m, 2H), 1.46 (s, 3H), 1.20 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 163.47 (163.23), (154.63) 154.52, (149.06) 148.75, (147.32) 147.23, (122.63) 122.46, (120.88) 120.37, (79.27) 79.17, 62.72 (62.06), (47.41) 47.03, 34.17 (33.05), (28.47) 28.14, (23.75) 23.21, (21.21) 21.08; HRMS (ESI) m/z calcd for C₁₅H₂₃N₂O₂ [(M+H)⁺] 263.1760, found 263.1754.

EXAMPLE 13 - *tert*-Butyl 2-(5-(trifluoromethyl)pyridin-2-yl)pyrrolidine-1-carboxylate

According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 2-bromo-5-(trifluoromethyl)pyridine (92.9 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a yellow oil (76 mg, 60%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 8.80 (s, 1H), 7.86 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 5.04-5.02 and 4.94-4.91 (2 m, 1H, rotamer), 3.67-3.52 (m, 2H), 2.43-2.32 (m, 1H), 2.04-1.88 (m, 3H), 1.45 (s, 3H), 1.20 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in

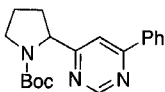
parenthesis (): δ 167.89 (166.77), (154.67) 154.28, [146.27 (q, $J = 3.8$ Hz)] 146.04 (q, $J = 3.8$ Hz), [133.62 (q, $J = 3.8$ Hz)] 133.37 (q, $J = 3.8$ Hz), 124.69 (q, $J = 32.5$ Hz), 123.61 (q, $J = 270.0$ Hz), (119.92) 119.46, (79.73) 79.67, 62.72 (62.16), (47.47) 47.12, 34.23 (32.99), (28.44) 28.15, (23.88) 23.25; HRMS (ESI) m/z calcd for $C_{15}H_{20}F_3N_2O_2$ [(M+H)⁺] 317.1477, found 5 317.1474.

EXAMPLE 14 - *tert*-Butyl 2-(5-fluoropyridin-2-yl)pyrrolidine-1-carboxylate



According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μ mol, 10 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 2-chloro-5-fluoropyridine (52.6 mg, 0.4 mmol, 1.0 equiv), Boc-Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a clear oil (68 mg, 64%). ¹H NMR (500 MHz, (CDCl₃) δ rotameric mixture: 8.38 (d, $J = 2.9$ 15 Hz, 1H), 7.39-7.29 (m, 1H), 7.22-7.14 (m, 1H), 4.97 and 4.86 (2 brs, 1H), 3.66-3.46 (m, 2H), 2.43-2.20 (m, 1H), 2.08-1.80 (m, 3H), 1.44 (s, 3H), 1.21 (s, 6H); ¹³C NMR (125 MHz, (CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 159.69 (158.52), [158.26 (d, $J = 253.9$ Hz)] 158.20 (d, $J = 253.8$ Hz), (154.67) 154.41, [137.34 (d, $J = 23.8$ Hz)] 137.03 (d, $J = 23.3$ Hz), [123.01 (d, $J = 18.1$ Hz)] 122.94 (d, $J = 18.2$ Hz), [121.22 (d, 20 $J = 4.6$ Hz)] 120.62 (d, $J = 4.1$ Hz), 79.48 (79.42), 62.20 (61.56), 47.38 (47.02), 34.28 (32.98), 28.47 (28.19), 23.82 (23.18); HRMS (ESI) m/z calcd for $C_{14}H_{19}FN_2NaO_2$ [(M+Na)⁺] 289.1328, found 289.1323.

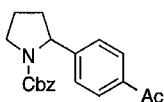
EXAMPLE 15 - *tert*-Butyl 2-(6-phenylpyrimidin-4-yl)pyrrolidine-1-carboxylate



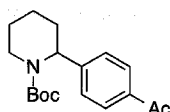
25 According to the general procedure A, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μ mol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-chloro-6-phenylpyrimidine (68.6 mg, 0.4 mmol, 1.0 equiv), Boc-

Pro-OH (129.0 mg, 0.6 mmol, 1.5 equiv), Cs₂CO₃ (195.6 mg, 0.6 mmol, 1.5 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a clear oil (85 mg, 65%). ¹H NMR (500 MHz, (CDCl₃) rotameric mixture: δ 9.17 (s, 1H), 8.09-8.02 (m, 2H), 7.57 (s, 1H), 7.52-7.47 (m, 3H), 4.97 and 4.85 (2 brs, 1H, rotamer), 3.75-3.53 (m, 2H), 2.48-2.32 (m, 1H), 2.09-1.89 (m, 3H), 1.48 (s, 3H), 1.22 (s, 6H); ¹³C NMR (125 MHz, (CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis ()): δ 172.88 (171.70), (164.30) 164.16, (158.80) 158.71, (154.69) 154.30, (137.06) 136.67, 131.04 (130.77), 129.06 (128.90), (127.23) 127.09, (113.42) 112.47, 79.86, 62.45 (61.84), (47.51) 47.20, 33.94 (32.67), (28.46) 28.21, (24.00) 23.37; HRMS (ESI) m/z calcd for C₁₉H₂₄N₃O₂ [(M+H)⁺] 326.1869, found 326.1862.

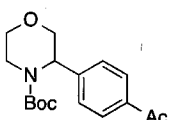
EXAMPLE 16 - Benzyl 2-(4-acetylphenyl)pyrrolidine-1-carboxylate



According to the general procedure B, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.10 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), Cbz-Pro-OH (305.0 mg, 1.2 mmol, 3.0 equiv), Cs₂CO₃ (391.2 mg, 1.2 mmol, 3.0 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane) as a pale yellow oil (120 mg, 93%). ¹H NMR (500 MHz, CDCl₃) rotameric mixture: δ 7.92-7.87 (m, 2H), 7.37-7.13 (m, 6H), 6.89 (d, *J* = 7.0 Hz, 1H), 5.17-4.92 (m, 3H), 3.71-3.62 (m, 2H), 2.60 and 2.58 (2s, 3H, rotamer), 2.40-2.33 (m, 1H), 1.93-1.89 (m, 2H), 1.87-1.82 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis ()): δ 197.64, 154.86, 149.90 (149.17), (136.85) 136.49, 135.86, (128.68) 128.62, (128.50) 128.17, (128.01) 127.93, (127.65) 127.41, 125.71, (66.87) 66.68, (61.27) 60.96, 47.73 (47.28), 35.78 (34.72), 26.65, (23.74) 23.06; HRMS (ESI) m/z calcd for C₂₀H₂₂NO₃ [(M+H)⁺] 324.1600, found 324.1586.

EXAMPLE 17 - *tert*-Butyl 2-(4-acetylphenyl)piperidine-1-carboxylate

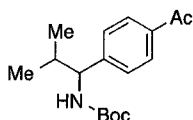
According to the general procedure B, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), Boc-Pip-OH (276 mg, 1.2 mmol, 3.0 equiv), Cs₂CO₃ (391.2 mg, 1.2 mmol, 3.0 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow oil (99 mg, 82%). ¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.43 (s, 1H), 4.07 (d, *J* = 13.0 Hz, 1H), 2.76 (td, *J* = 13.0 Hz, *J* = 3.5 Hz, 1H), 2.60 (s, 3H), 2.32-2.29 (m, 1H), 1.96-1.89 (m, 1H), 1.65-1.52 (m, 3H), 1.46 (s, 9H), 1.39-1.33 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 197.71, 155.52, 146.46, 135.44, 128.65, 126.68, 79.82, 53.42, 40.33, 28.39, 28.26, 26.60, 25.24, 19.37; HRMS (ESI) *m/z* calcd for C₁₈H₂₅NNaO₃ [(*M*+Na)⁺] 326.1732, found 326.1719.

EXAMPLE 18 - *tert*-butyl 3-(4-acetylphenyl)morpholine-4-carboxylate

According to the general procedure B, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (4.5 mg, 10.0 μmol, 0.01 equiv), NiCl₂•glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82 mg, 0.4 mmol, 1.0 equiv), Boc-Morph-OH (277.2 mg, 1.2 mmol, 3.0 equiv), Cs₂CO₃ (391.2 mg, 1.2 mmol, 3.0 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (17% ethyl acetate/hexane) as a pale yellow solid (74.0 mg, 61%). ¹H NMR (500 MHz, CDCl₃): δ 7.95 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 5.11 (br, 1H), 4.35 (d, *J* = 7.0 Hz, 1H), 3.91-3.87 (m, 2H), 3.83-3.80 (m, 1H), 3.61 (td, *J* = 11.5 Hz, *J* = 2.5 Hz, 1H), 3.11 (td, *J* = 13.0 Hz, *J* = 3.5 Hz, 1H), 2.60 (s, 3H), 1.47 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 197.70, 154.76, 144.88, 136.01, 128.52,

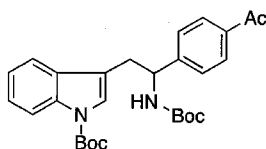
127.77, 80.56, 68.91, 66.93, 53.26, 39.97, 28.35, 26.63; HRMS (ESI) m/z calcd for $C_{17}H_{23}NNaO_4 [(M+Na)^+]$ 328.1525, found 328.1512.

EXAMPLE 19 - *tert*-Butyl (1-(4-acetylphenyl)-2-methylpropyl)carbamate



5 According to the general procedure B, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 10.0 μ mol, 0.01 equiv), $NiCl_2 \cdot glyme$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), Boc-Val-OH (260.7 mg, 1.2 mmol, 3.0 equiv), Cs_2CO_3 (391.2 mg, 1.2 mmol, 3.0 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (10% ethyl acetate/hexane) as a pale yellow solid (83 mg, 72%). 1H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, $J = 8.5$ Hz, 2H), 7.31 (d, $J = 8.0$ Hz, 2H), 5.12 (brs, 1H), 4.48 (s, 1H), 2.59 (s, 3H), 1.98 (br, 1H), 1.46 (s, 9H), 0.93 (d, $J = 7.0$ Hz, 3H), 0.85 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.83, 154.41, 147.83, 135.90, 128.46, 126.97, 79.59, 60.35, 33.58, 28.35, 26.62, 19.67; HRMS (ESI) 10 15 m/z calcd for $C_{17}H_{25}NNaO_3 [(M+Na)^+]$ 314.1732, found 314.1684.

EXAMPLE 20 - *tert*-Butyl 3-(2-(4-acetylphenyl)-2-((*tert*-butoxycarbonyl)amino)ethyl)-1*H*-indole-1-carboxylate

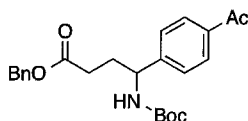


20 According to the general procedure B, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 10.0 μ mol, 0.01 equiv), $NiCl_2 \cdot glyme$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), Boc-Trp(Boc)-OH (485.0 mg, 1.2 mmol, 3.0 equiv), Cs_2CO_3 (391.2 mg, 1.2 mmol, 3.0 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (12% ethyl 25 acetate/hexane) as a yellow solid (159 mg, 83%). 1H NMR (500 MHz, $CDCl_3$) δ 8.10 (br, 1H), 7.91 (d, $J = 8.5$ Hz, 2H), 7.36 (m, 3H), 7.30 (t, $J = 7.5$ Hz, 1H), 7.26-7.22 (m, 1H), 7.19 (t, $J =$

7.5 Hz, 1H), 5.11 (br, 1H), 4.98 (br, 1H), 3.14 (s, 2H), 2.59 (s, 3H), 1.64 (s, 9H), 1.39 (br, 9H);
 ^{13}C NMR (125 MHz, CDCl_3) δ 197.76, 155.18, 149.57, 148.03, 136.16, 135.37, 130.42, 128.70,
 126.52, 124.52, 124.00, 122.57, 118.86, 115.87, 115.24, 83.65, 79.82, 54.27, 32.55, 28.32, 28.19,
 26.65; HRMS (ESI) m/z calcd for $\text{C}_{28}\text{H}_{34}\text{N}_2\text{NaO}_5$ $[(\text{M}+\text{Na})^+]$ 501.2365, found 501.2342.

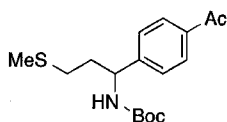
5

EXAMPLE 21 - Benzyl 4-(4-acetylphenyl)-4-((*tert*-butoxycarbonyl)amino)butanoate



According to the general procedure B, $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (4.5 mg, 10.0 μmol ,
 0.01 equiv), $\text{NiCl}_2 \cdot \text{glyme}$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1
 10 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), Boc-
 Glu(OBzl)-OH (413.0 mg, 1.2 mmol, 3.0 equiv), Cs_2CO_3 (391.2 mg, 1.2 mmol, 3.0 equiv), and
 20 mL of DMF were used. The product was isolated by flash chromatography (20% ethyl
 acetate/hexane) as a pale yellow solid (126 mg, 77%). ^1H NMR (500 MHz, CDCl_3) δ 7.92 (d, J =
 8.0 Hz, 2H), 7.39-7.33 (m, 7H), 5.11 (s, 2H), 5.01 (br, 1H), 4.72 (br, 1H), 2.59 (s, 3H), 2.45-2.37
 15 (m, 2H), 2.11-2.05 (m, 2H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 197.73, 172.88, 155.27,
 147.91, 136.20, 135.71, 128.82, 128.60, 128.35, 128.29, 126.44, 79.73, 66.53, 54.29, 31.42,
 31.09, 28.36, 26.64; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{29}\text{NNaO}_5$ $[(\text{M}+\text{Na})^+]$ 434.1943, found
 434.1924.

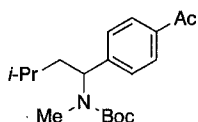
20 **EXAMPLE 22 - *tert*-Butyl (1-(4-acetylphenyl)-3-(methylthio)propyl)carbamate**



According to the general procedure B, $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (4.5 mg, 10.0 μmol ,
 0.01 equiv), $\text{NiCl}_2 \cdot \text{glyme}$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1
 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), Boc-Met-
 25 OH (300.0 mg, 1.2 mmol, 3.0 equiv), Cs_2CO_3 (391.2 mg, 1.2 mmol, 3.0 equiv), and 20 mL of
 DMF were used. The product was isolated by flash chromatography (20% ethyl acetate/hexane)

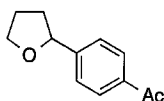
as a pale yellow solid (107 mg, 83%). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.94 (d, $J = 8.5$ Hz, 2H), 7.38 (d, $J = 8.0$ Hz, 2H), 5.00 (br, 1H), 4.82 (br, 1H), 2.59 (s, 3H), 2.49-2.43 (m, 2H), 2.10 (s, 3H), 2.06-2.01 (m, 2H), 1.41 (s, 9H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 197.74, 155.18, 147.97, 136.12, 128.78, 126.49, 79.68, 53.96, 35.94, 30.63, 28.34, 26.63, 15.51; HRMS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{25}\text{NNaO}_3\text{S}$ [(M+Na) $^+$] 346.1453, found 346.1433.

EXAMPLE 23 - *tert*-Butyl (1-(4-acetylphenyl)-3-methylbutyl)(methyl)carbamate



According to the general procedure B, $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (4.5 mg, 10.0 μmol , 0.01 equiv), $\text{NiCl}_2 \cdot \text{glyme}$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), Boc-*N*-Me-Leu-OH (296.0 mg, 1.2 mmol, 3.0 equiv), Cs_2CO_3 (391.2 mg, 1.20 mmol, 3.0 equiv), and 20 mL of DMF were used. The product was isolated by flash chromatography (9% ethyl acetate/hexane) as a pale yellow oil (117 mg, 91%). $^1\text{H NMR}$ (500 MHz, CDCl_3) rotameric mixture: δ 7.92 (d, $J = 8.0$ Hz, 2H), 7.38-7.37 (m, 2H), 5.54 and 5.33 (2 brs, 1H, rotamer), 2.60-2.57 (m, 6H), 1.86 (br, 1H), 1.68-1.64 (m, 2H), 1.49 (s, 9H), 1.00 (t, $J = 6.0$ Hz, 6H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ 197.73, 155.90 (156.17), 146.62, 136.00, 128.46, (127.56) 127.44, 80.00 (79.61), 55.54 (54.46), 39.29 (39.01), 28.47, 26.64, 24.79, 23.49, 21.80; HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{29}\text{NNaO}_3$ [(M+Na) $^+$] 342.2045, found 342.2048.

EXAMPLE 24 - 1-(4-(Tetrahydrofuran-2-yl)phenyl)ethan-1-one



According to the general procedure B, $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (4.5 mg, 10.0 μmol , 0.01 equiv), $\text{NiCl}_2 \cdot \text{glyme}$ (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (82.0 mg, 0.4 mmol, 1.0 equiv), tetrahydro-2-furoic acid (139.0 mg, 1.2 mmol, 3.0 equiv), Cs_2CO_3 (391.2 mg, 1.2 mmol, 3.0 equiv), and 20

mL of DMF were used. The product was isolated by flash chromatography (15% ethyl acetate/hexane) as a pale yellow solid (63.0 mg, 82%). ¹H NMR (500 MHz, CDCl₃): δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 4.95 (t, *J* = 7.5 Hz, 1H), 4.11 (q, *J* = 7.5 Hz, 1H), 3.97 (q, *J* = 7.0 Hz, 1H), 2.59 (s, 3H), 2.40-2.34 (m, 1H), 2.04-1.99 (m, 2H), 1.81-1.74 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 197.87, 149.21, 136.04, 128.48, 125.60, 80.14, 68.90, 34.73, 26.66, 25.98; HRMS (ESI) *m/z* calcd for C₁₂H₁₅O₂ [(M+H)⁺] 191.1072, found 191.1064.

B. Decarboxylative Arylation of Keto Acids (Examples 25-49)

Materials and Methods

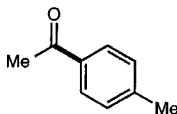
Commercial reagents were purchased from commercial suppliers and purified prior to use following the guidelines of Perrin. All solvents were purified by passage through columns of activated alumina. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an acetone-dry ice bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on silica gel (Fluka, 230-400 mesh). Thin layer chromatography (TLC) was performed on Analtech Uniplat 250 µm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, p-anisaldehyde, potassium permanganate, or ceric ammonium molybdate stain. ¹H and ¹³C NMR spectra were recorded on a Bruker 500 (500 or 501 and 125 or 126 MHz) instrument, and are internally referenced to residual protio solvent signals (note: CDCl₃ referenced at 7.26 and 77.16 ppm respectively). Data for ¹H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), integration, and coupling constant (Hz). Data for ¹³C NMR are reported in terms of chemical shift and multiplicity where appropriate, with no special nomenclature used for equivalent carbons. All known compounds are referenced herein to previous reports in the literature. High resolution mass spectra were obtained at Princeton University mass spectrometry facilities. All keto acids were used from commercial suppliers or prepared by hydrolysis of the commercially available ester. All aryl and heteroaryl halides were used from commercial suppliers.

General procedure A for the decarboxylation arylation of keto acids (acid scope): An oven-dried 40 mL vial equipped with a Teflon septum cap and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (11.2 mg, 0.01 mmol, 0.02 equiv), NiCl₂·glyme (11.2 mg, 0.05 mmol, 0.10

equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridine (20.1 mg, 0.075 mmol, 0.15 equiv), the corresponding keto acid (1.00 mmol, 2.0 equiv), 4-iodotoluene (109 mg, 0.50 mmol, 1.0 equiv), and Li₂CO₃ (73.9 mg, 1.00 mmol, 2.0 equiv) from a bottle stored in a dessicator. To this vial was added DMF (25 mL) and water (18 μL, 2.00 mmol, 2.0 equiv). The reaction mixture was degassed for 30 minutes by bubbling argon stream, then sealed with parafilm. The vial was irradiated with 34W Blue LED lamp (Kessil KSH150B LED Grow Light) for 72 hours, with cooling from a fan (vial temperature reached 37 °C). After 72 hours, the reaction was diluted with 25 mL H₂O and extracted with 3x75 mL Et₂O. The combined organic layers were washed with 3x25 mL H₂O, then dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel with a 25g column on a biotage instrument using the indicated solvent system provided the purified product.

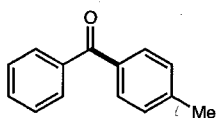
General procedure B for the decarboxylation arylation of keto acids (aryl halide scope): An oven-dried 40 mL vial equipped with a Teflon septum cap and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (11.2 mg, 0.01 mmol, 0.02 equiv), NiCl₂-glyme (11.2 mg, 0.05 mmol, 0.10 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridine (20.1 mg, 0.075 mmol, 0.15 equiv), phenylglyoxylic acid (150 mg, 1.00 mmol, 2.0 equiv), the corresponding aryl halide (0.50 mmol, 1.0 equiv), and Li₂CO₃ (73.9 mg, 1.00 mmol, 2.0 equiv) from a bottle stored in a dessicator. To this vial was added DMF (25 mL) and water (18 μL, 2.00 mmol, 2.0 equiv). The reaction mixture was degassed for 30 minutes by bubbling argon stream, then sealed with parafilm. The vial was irradiated with 34W Blue LED lamp (Kessil KSH150B LED Grow Light) for 72 hours with cooling from a fan (vial temperature reached 37 °C). After 72 hours, the reaction was diluted with 25 mL H₂O and extracted with 3x75 mL Et₂O. The combined organic layers were washed with 3x25 mL H₂O, then dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel with a 25g column on a biotage instrument using the indicated solvent system provided the purified product.

EXAMPLE 25 - 1-(*p*-Tolyl)ethan-1-one



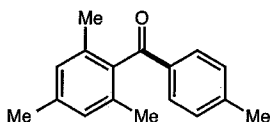
Prepared according to General Procedure A with 2-oxopropanoic acid (88.1 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a colorless viscous liquid, 38.2 mg, 57% yield. ^1H NMR (501 MHz, Chloroform-*d*) δ 7.86 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 2.58 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 198.0, 144.0, 134.83, 129.4, 128.6, 26.7, 21.8.

EXAMPLE 26 - Phenyl(*p*-tolyl)methanone



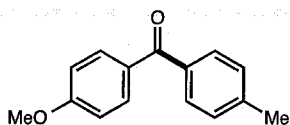
Prepared according to General Procedure A with 2-oxo-2-phenylacetic acid (150 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as an off-white solid, 86.4 mg, 88% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.82 – 7.76 (m, 2H), 7.73 (d, J = 8.1 Hz, 2H), 7.61 – 7.53 (m, 2H), 7.47 (t, J = 7.8 Hz, 1H), 7.28 (d, J = 7.8 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 196.6, 143.4, 138.1, 135.0, 132.3, 130.4, 130.1, 129.1, 128.3, 21.8.

EXAMPLE 27 - Mesityl(*p*-tolyl)methanone

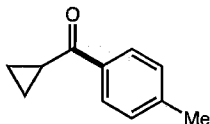


Prepared according to General Procedure A with 2-mesityl-2-oxoacetic acid (192.2 mg), purified with 2% EtOAc in hexanes as eluent, to yield the product as a pale yellow oil, 109.7 mg, 92% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.72 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 6.90 (s, 2H), 2.41 (s, 3H), 2.34 (s, 3H), 2.10 (s, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ 200.4, 144.5, 138.3, 137.1, 134.9, 134.1, 129.6, 129.5, 128.3, 21.8, 21.2, 19.4. HRMS (EI) calcd for $\text{C}_{17}\text{H}_{19}\text{O}$ [(M+H) $^+$] 238.13577, found 238.13647. IR(film) 2977, 2920, 1665, 1604, 1573, 1440, 1270, 1169 cm^{-1} .

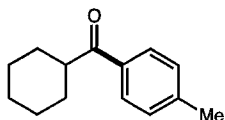
25

EXAMPLE 28 - (4-Fluorophenyl)(*p*-tolyl)methanone

Prepared according to General Procedure A with 2-(4-methoxyphenyl)-2-oxoacetic acid (180.2 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a yellow oil, 73.8 mg, 65% yield. ¹H NMR (501 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H), 2.42 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 195.4, 163.1, 142.7, 135.6, 132.5, 130.6, 130.1, 129.0, 113.6, 55.6, 21.7.

EXAMPLE 29 - Cyclopropyl(*p*-tolyl)methanone

Prepared according to General Procedure A with 2-cyclopropyl-2-oxoacetic acid (114.1 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a pale yellow solid, 70.1, mg, 88% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 2.59 (tt, *J* = 7.8, 4.5 Hz, 1H), 2.35 (s, 3H), 1.16 (dd, *J* = 4.5, 3.1 Hz, 2H), 0.95 (dd, *J* = 7.8, 3.1 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 200.3, 143.6, 135.6, 129.3, 128.2, 21.8, 17.1, 11.6.

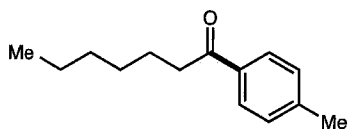
EXAMPLE 30 - Cyclohexyl(*p*-tolyl)methanone

Prepared according to General Procedure A with 2-cyclohexyl-2-oxoacetic acid (156.2 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a white solid, 80.3 mg, 80% yield. ¹H NMR (501 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz,

2H), 3.22 (m, 1H), 2.38 (s, 3H), 1.90 – 1.76 (m, 4H), 1.73 – 1.68 (m, 1H), 1.52 – 1.26 (m, 5H).

^{13}C NMR (126 MHz, CDCl_3) δ 203.6, 143.5, 133.9, 129.4, 128.5, 45.6, 29.6, 26.1, 26.0, 21.7.

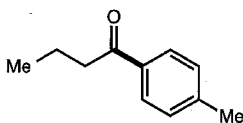
EXAMPLE 31 - 1-(*p*-Tolyl)heptan-1-one



Prepared according to General Procedure A with 2-oxooctanoic acid (158.2 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a yellow oil, 92.1 mg, 90% yield. ^1H NMR (501 MHz, Chloroform-*d*) δ 7.86 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 2.93 (t, J = 7.2 Hz, 2H), 2.41 (s, 3H), 1.72 (p, J = 7.2 Hz, 2H), 1.42 – 1.16 (m, 6H), 0.89 (t, J = 7.2 Hz, 3H).

10 ^{13}C NMR (126 MHz, CDCl_3) δ 200.5, 143.8, 134.8, 129.4, 128.4, 38.8, 31.9, 29.31, 24.7, 22.8, 21.8, 14.3.

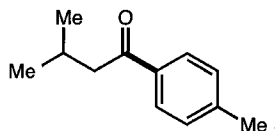
EXAMPLE 32 - 1-(*p*-Tolyl)butan-1-one



Prepared according to General Procedure A with 2-oxopentanoic acid (116.1 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a pale yellow oil, 73.4 mg, 91% yield. ^1H NMR (501 MHz, Chloroform-*d*) δ 7.86 (d, J = 8.8 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 2.92 (t, J = 7.4 Hz, 2H), 2.40 (s, 3H), 1.76 (hex, J = 7.4 Hz, 2H), 1.00 (t, J = 7.4 Hz, 3H).

20 ^{13}C NMR (126 MHz, CDCl_3) δ 200.3, 143.7, 134.8, 129.3, 128.3, 40.6, 21.8, 18.0, 14.1.

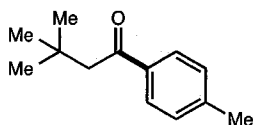
EXAMPLE 33 - 3-Methyl-1-(*p*-tolyl)butan-1-one



Prepared according to General Procedure A with 4-methyl-2-oxopentanoic acid (130.1 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a colorless oil, 73.0

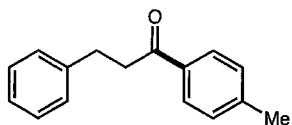
mg, 83% yield. ^1H NMR (501 MHz, Chloroform-*d*) δ 7.85 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 2.80 (d, J = 6.8 Hz, 2H), 2.40 (s, 3H), 2.29 (h, J = 6.8 Hz, 1H), 0.99 (d, J = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ 200.1, 143.7, 135.0, 129.3, 128.4, 47.5, 25.4, 22.9, 21.7.

5 **EXAMPLE 34 - 3,3-Dimethyl-1-(*p*-tolyl)butan-1-one**



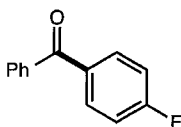
Prepared according to General Procedure A with 4,4-dimethyl-2-oxopentanoic acid (144.2 mg), purified with 3% EtOAc in hexanes as eluent, to yield the product as a colorless oil, 87.0 mg, 92% yield. ^1H NMR (501 MHz, Chloroform-*d*) δ 7.84 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 2.83 (s, 2H), 2.40 (s, 3H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 200.2, 143.5, 136.2, 129.3, 128.5, 50.1, 31.5, 30.2, 21.7.

15 **EXAMPLE 35 - 3-Phenyl-1-(*p*-tolyl)propan-1-one**



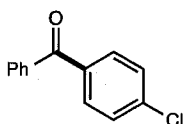
Prepared according to General Procedure A with 2-oxo-4-phenylbutanoic acid (178.2 mg), purified with 3% EtOAc in hexanes as eluent, to yield the product as a yellow oil, 103.3 mg, 92% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.85 (d, J = 8.2 Hz, 2H), 7.29 (t, J = 7.5 Hz, 2H), 7.26 – 7.21 (m, 4H), 7.21 – 7.16 (m, 1H), 3.26 (dd, J = 8.6, 6.9 Hz, 2H), 3.05 (dd, J = 8.6, 6.9 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 199.0, 144.0, 141.5, 134.5, 129.4, 128.6, 128.6, 128.3, 126.2, 40.5, 30.4, 21.8.

EXAMPLE 36 - (4-Fluorophenyl)(phenyl)methanone



Prepared according to General Procedure B with 1-fluoro-4-iodobenzene (275.0 mg, 2.5 mmol, 5.0 equiv) and Li_2CO_3 (184.8 mg, 2.5 mmol, 5.0 equiv), purified with 5% EtOAc in hexanes as eluent, to yield the product as a pale yellow solid, 70.2 mg, 70% yield. ^1H NMR (501 MHz, Chloroform-*d*) δ 7.90 – 7.81 (m, 2H), 7.79 – 7.74 (m, 2H), 7.62 – 7.56 (m, 1H), 7.49 (dd, J = 8.5, 7.1 Hz, 2H), 7.16 (t, J = 8.5 Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 195.0, 165.3 (d, J = 264.3 Hz), 137.6, 133.2 (d, J = 2.7 Hz), 133.1 (d, J = 10.1 Hz), 132.7, 129.5, 128.1, 115.6.

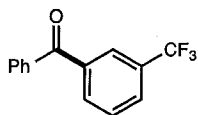
EXAMPLE 37 - (4-Chlorophenyl)(phenyl)methanone



10 Prepared according to General Procedure B with 1-chloro-4-iodobenzene (119.2 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a yellow solid, 98.9 mg, 90% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.79 – 7.74 (m, 4H), 7.63 – 7.58 (m, 1H), 7.52 – 7.44 (m, 4H). ^{13}C NMR (126 MHz, CDCl_3) δ 195.6, 139.0, 137.4, 136.0, 132.8, 131.6, 130.1, 128.8, 128.5.

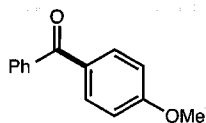
15

EXAMPLE 38 - Phenyl(3-(trifluoromethyl)phenyl)methanone

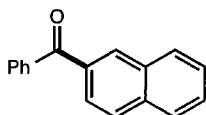


20 Prepared according to General Procedure B with 1-iodo-3-(trifluoromethyl)benzene (136.0 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a colorless solid, 110.2 mg, 88% yield. ^1H NMR (501 MHz, Chloroform-*d*) δ 8.07 (s, 1H), 7.98 (d, J = 7.8 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.80 (dd, J = 7.8, 1.4 Hz, 2H), 7.63 (t, J = 7.8 Hz, 2H), 7.52 (t, J = 7.8 Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 195.4, 138.4, 136.9, 133.3, 133.2, 131.1 (q, J = 32.9 Hz), 129.1, 129.0 (q, J = 3.6 Hz), 128.7, 126.8 (q, J = 3.8 Hz), 123.8 (d, J = 272.6 Hz).

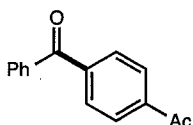
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EXAMPLE 39 - (4-Methoxyphenyl)(phenyl)methanone

- Prepared according to General Procedure B with 1-iodo-4-methoxybenzene (117.0 mg), reaction run to 84 hours, purified with 2% EtOAc in hexanes as eluent, to yield the product as a white solid, 74.4 mg, 70% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.85 – 7.79 (m, 2H), 7.78 – 7.70 (m, 2H), 7.56 (tt, *J* = 7.6, 1.3 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 6.99 – 6.94 (m, 2H), 3.88 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 195.7, 163.3, 138.4, 132.7, 132.0, 130.2, 129.8, 128.3, 113.7, 55.6.

EXAMPLE 40 - Naphthalen-2-yl(phenyl)methanone

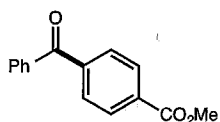
- Prepared according to General Procedure B with 2-iodonaphthalene (127.0 mg), reaction run to 90 hours, purified with 5% EtOAc in hexanes as eluent, to yield the product as a white solid, 75.8 mg, 70% yield. ¹H NMR (501 MHz, Chloroform-*d*) δ 8.27 (s, 1H), 7.95 (d, *J* = 1.0 Hz, 2H), 7.94 – 7.90 (m, 2H), 7.88 – 7.85 (m, 2H), 7.65 – 7.60 (m, 2H), 7.58 – 7.50 (m, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 196.9, 138.0, 135.4, 135.0, 132.5, 132.4, 132.0, 130.2, 129.6, 128.5, 128.5, 128.4, 128.0, 126.9, 125.9.

EXAMPLE 41 - 1-(4-Benzoylphenyl)ethan-1-one

- Prepared according to General Procedure B with 1-(4-bromophenyl)ethan-1-one (99.5 mg), purified with 16% EtOAc in hexanes as eluent, to yield the product as an off white solid, 82.3 mg, 73% yield. ¹H NMR (501 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 8.3 Hz, 2H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.79 (dd, *J* = 7.8, 1.2 Hz, 2H), 7.61 (tt, *J* = 7.8, 1.2 Hz, 1H), 7.49 (t, *J* = 7.8 Hz,

2H), 2.66 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 197.6, 196.1, 141.4, 139.7, 137.0, 133.1, 130.2, 130.2, 128.6, 128.3, 27.0.

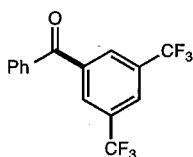
EXAMPLE 42 - Methyl 4-benzoylbenzoate



Methyl 4-benzoylbenzoate (**30**)¹: Prepared according to General Procedure B with methyl 4-bromobenzoate (107.5 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a white solid, 97.2 mg, 81% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.80 (dd, J = 7.5, 1.2 Hz, 2H), 7.61 (tt, J = 7.5 Hz, J = 1.2 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 3.96 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 196.1, 166.4, 141.4, 137.0, 133.3, 133.1, 130.2, 129.9, 129.6, 128.6, 52.6.

10

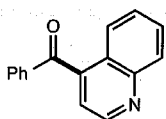
EXAMPLE 43 - (3,5-Bis(trifluoromethyl)phenyl)(phenyl)methanone



Prepared according to General Procedure B with 1-bromo-3,5-bis(trifluoromethyl)benzene (146.5 mg), purified with 5% EtOAc in hexanes as eluent, to yield the product as a colorless solid, 117.5 mg, 74% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.24 (bs, 2H), 8.10 (bs, 1H), 7.82 – 7.77 (m, 2H), 7.71 – 7.66 (m, 1H), 7.56 (t, J = 7.7 Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 193.7, 139.5, 136.0, 133.8, 132.2 (q, J = 33.9 Hz), 130.2, 130.0 (d, J = 3.8 Hz), 129.0, 125.8 (p, J = 3.7 Hz), 123.0 (q, J = 273.1 Hz).

20

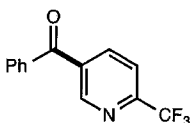
¹ Zhou, W.; Wei, S.; Han, W. *J. Org. Chem.* **2014**, *79*, 1454.

EXAMPLE 44 - Phenyl(quinolin-4-yl)methanone

Prepared according to General Procedure B with 4-bromoquinoline (104.0 mg), purified with 30% EtOAc in hexanes as eluent, to yield the product as a yellow oil, 94.1 mg, 80% yield.

- 5 $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 9.02 (d, $J = 4.3$ Hz, 1H), 8.20 (d, $J = 8.4$ Hz, 1H), 7.85 (ddd, $J = 8.4, 6.9, 1.5$ Hz, 3H), 7.75 (ddd, $J = 8.4, 6.9, 1.5$ Hz, 1H), 7.66 – 7.60 (m, 1H), 7.52 (ddd, $J = 8.4, 6.9, 1.5$ Hz, 1H), 7.47 (t, $J = 7.8$ Hz, 2H), 7.39 (d, $J = 4.3$ Hz, 1H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 196.2, 149.6, 148.7, 144.5, 136.7, 134.3, 130.4, 130.1, 128.9, 127.8, 125.5, 125.0, 119.7.

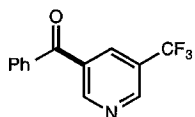
10

EXAMPLE 45 - Phenyl(6-(trifluoromethyl)pyridin-3-yl)methanone

Prepared according to General Procedure B with 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg), purified with 12% EtOAc in hexanes as eluent, to yield the product as a colorless

- 15 solid, 100.1 mg, 80% yield. $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 9.07 (bs, 1H), 8.28 (d, $J = 7.5$ Hz, 1H), 7.90 – 7.77 (m, 3H), 7.68 (t, $J = 7.5$ Hz, 1H), 7.54 (t, $J = 7.5$ Hz, 2H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 193.7, 150.9, 150.7 (q, $J = 35.2$ Hz), 138.8, 136.1, 135.7, 134.0, 130.2, 129.0, 121.3 (q, $J = 274.7$ Hz), 120.4 (q, $J = 2.7$ Hz).

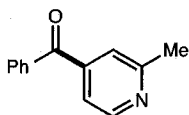
20 **EXAMPLE 46 - Phenyl(5-(trifluoromethyl)pyridin-3-yl)methanone**



Prepared according to General Procedure B with 3-bromo-5-(trifluoromethyl)pyridine (113.0 mg), purified with 12% EtOAc in hexanes as eluent, to yield the product as a yellow oil, 80.2 mg, 64% yield. $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 9.17 (d, $J = 2.2$ Hz, 1H), 9.08 (d, $J =$

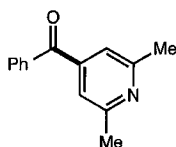
- 2.2 Hz, 1H), 8.36 (t, $J = 2.2$ Hz, 1H), 7.82 (d, $J = 7.6$ Hz, 2H), 7.69 (d, $J = 7.6$ Hz, 1H), 7.56 (t, $J = 7.6$ Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 193.4, 153.8, 149.5, 136.1, 134.4 (q, $J = 3.6$ Hz), 133.9, 133.2, 130.2, 129.1, 126.9 (q, $J = 33.6$ Hz), 123.2 (q, $J = 273.4$ Hz). HRMS (EI) calcd for $\text{C}_{13}\text{H}_9\text{F}_3\text{NO}$ [(M+H) $^+$] 251.05580, found 251.05572. IR(film) 2971, 1740, 1665, 1597, 1553, 1448, 1282 cm^{-1} .

EXAMPLE 47 - (2-Methylpyridin-4-yl)(phenyl)methanone



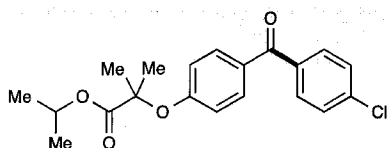
- Prepared according to General Procedure B with 4-bromo-2-methylpyridine (86.0 mg), purified with 20% EtOAc in hexanes as eluent, to yield the product as a yellow oil, 83.3 mg, 85% yield. ^1H NMR (501 MHz, Chloroform- d) δ 8.68 (d, $J = 5.0$ Hz, 1H), 7.82 (d, $J = 8.1$ Hz, 2H), 7.68 – 7.59 (m, 1H), 7.51 (t, $J = 7.8$ Hz, 2H), 7.44 (bs, 1H), 7.36 (d, $J = 5.0$ Hz, 1H), 2.65 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 195.7, 159.5, 149.8, 145.0, 136.2, 133.6, 130.3, 128.8, 122.5, 120.2, 24.7. HRMS (EI) calcd for $\text{C}_{13}\text{H}_{12}\text{NO}$ [(M+H) $^+$] 197.08406, found 197.08423. IR(film) 3035, 2971, 1739, 1666, 1598, 1579, 1446, 1338, 1265, 1134, 1084 cm^{-1} .

EXAMPLE 48 - (2,6-Dimethylpyridin-4-yl)(phenyl)methanone

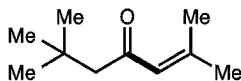


- Prepared according to General Procedure B with 4-bromo-2,6-dimethylpyridine (93.0 mg), purified with 20% EtOAc in hexanes as eluent, to yield the product as a colorless solid, 88.1 mg, 83% yield. ^1H NMR (501 MHz, Chloroform- d) δ 7.81 (d, $J = 7.0$ Hz, 2H), 7.68 – 7.58 (m, 1H), 7.51 (t, $J = 7.7$ Hz, 2H), 7.22 (s, 2H), 2.61 (s, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ 196.1, 158.7, 145.5, 136.4, 133.5, 130.3, 128.7, 119.6, 24.8.

25

EXAMPLE 49 - Fenofibrate

- An oven-dried 40 mL vial equipped with a Teflon septum cap and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (11.2 mg, 0.01 mmol, 0.02 equiv), NiCl₂·glyme (11.2 mg, 0.05 mmol, 0.10 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridine (20.1 mg, 0.075 mmol, 0.15 equiv), 2-(4-((1-isopropoxy-2-methyl-1-oxopropan-2-yl)oxy)phenyl)-2-oxoacetic acid (≥95%, 310 mg, 1.00 mmol, 2.0 equiv), 4-chloro-1-iodobenzene (120 mg, 0.50 mmol, 1.0 equiv), and Li₂CO₃ (73.9 mg, 1.00 mmol, 2.0 equiv) from a bottle stored in a desiccator. To this vial was added DMF (25 mL) and water (18 μL, 2.00 mmol, 2.0 equiv). The reaction mixture was degassed for 30 minutes by bubbling argon stream, then sealed with parafilm. The vial was irradiated with 34W Blue LED lamp (Kessil KSH150B LED Grow Light) for 72 hours with cooling from a fan (vial temperature reached 37 °C). After 96 hours, the reaction was diluted with 25 mL H₂O and extracted with 3x75 mL Et₂O. The combined organic layers were washed with 3x25 mL H₂O, then dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel with a 25g column on a biotage instrument with 5% EtOAc in hexanes as eluent, to yield **40** as an off-white solid 127.9 mg, 71% yield. ¹H NMR (501 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.08 (hept, *J* = 6.3 Hz, 1H), 1.65 (s, 6H), 1.20 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 194.4, 173.2, 159.9, 138.5, 136.5, 132.1, 131.3, 130.3, 128.7, 117.4, 79.5, 69.5, 25.5, 21.7.

C. Carbonyl *sp*²-Olefin Coupling**EXAMPLE 50 - 2,6,6-Trimethylhept-2-en-4-one**

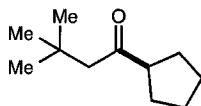
- An oven-dried 40 mL vial equipped with a Teflon septum cap and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (11.2 mg, 0.01 mmol, 0.02 equiv), NiCl₂·glyme (11.2

mg, 0.05 mmol, 0.10 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridine (20.1 mg, 0.075 mmol, 0.15 equiv), 4,4-dimethyl-2-oxopentanoic acid (144.2 mg, 1.00 mmol, 2.0 equiv), 1-bromo-2-methylprop-1-ene (68.9 mg, 0.50 mmol, 1.0 equiv), and Li₂CO₃ (73.9 mg, 1.00 mmol, 2.0 equiv) from a bottle stored in a dessicator. To this vial was added DMF (25 mL) and water (18 μL, 2.00 mmol, 2.0 equiv). The reaction mixture was degassed for 30 minutes by bubbling argon stream, then sealed with parafilm. The vial was irradiated with 34W Blue LED lamp (Kessil KSH150B LED Grow Light) for 72 hours with cooling from a fan (vial temperature reached 37 °C). After 72 hours, the reaction was diluted with 25 mL H₂O and extracted with 3x75 mL Et₂O. The combined organic layers were washed with 3x25 mL H₂O, then dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel with 2% Et₂O in pentanes as eluent, to yield **37** as a yellow oil, 56.1 mg, 73% yield. ¹H NMR (501 MHz, Chloroform-*d*) δ 6.04 (s, 1H), 2.27 (s, 2H), 2.11 (d, *J* = 1.3 Hz, 3H), 1.85 (d, *J* = 1.3 Hz, 3H), 0.99 (s, 9 H). ¹³C NMR (126 MHz, CDCl₃) δ 201.3, 154.2, 125.9, 57.0, 31.6, 30.1, 27.8, 20.7.

15

D. Carbonyl *sp*³-Alkyl Halide Coupling

EXAMPLE 51 - 1-Cyclopentyl-3,3-dimethylbutan-1-one



An oven-dried 40 mL vial equipped with a Teflon septum cap and magnetic stir bar was charged with Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (11.2 mg, 0.01 mmol, 0.02 equiv), NiCl₂·glyme (11.2 mg, 0.05 mmol, 0.10 equiv), 4,4'-di-*tert*-butyl-2,2'-bipyridine (20.1 mg, 0.075 mmol, 0.15 equiv), 4,4-dimethyl-2-oxopentanoic acid (144.2 mg, 1.00 mmol, 2.0 equiv), bromocyclopentane (76.0 mg, 0.50 mmol, 1.0 equiv), and Li₂CO₃ (73.9 mg, 1.00 mmol, 2.0 equiv) from a bottle stored in a dessicator. To this vial was added DMF (25 mL) and water (18 μL, 2.00 mmol, 2.0 equiv). The reaction mixture was degassed for 30 minutes by bubbling argon stream, then sealed with parafilm. The vial was irradiated with 34W Blue LED lamp (Kessil KSH150B LED Grow Light) for 72 hours with cooling from a fan (vial temperature reached 37 °C). After 72 hours, the reaction was diluted with 25 mL H₂O and extracted with 3x75 mL Et₂O. The combined organic

layers were washed with 3x25 mL H₂O, then dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel with 1% Et₂O in pentanes as eluent, to yield **38** as a yellow oil, 74.3 mg, 88% yield. ¹H NMR (501 MHz, Chloroform-*d*) δ 2.83 (pent, *J* = 8.0 Hz, 1H), 2.35 (s, 2H), 1.87-1.49 (m, 8H), 1.01 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 213.3, 54.3, 53.0, 31.1, 29.9, 28.9, 26.1. HRMS (EI) calcd for C₁₁H₂₁O [(M+H)⁺] 168.15142, found 168.15261. IR(film) 2954, 2869, 1705, 1465, 1364, 905, 729 cm⁻¹.

E. Decarboxylative Arylation, sp³-sp³ Cross-coupling

General Procedure - To an oven dried vial equipped with a stir bar was added Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (0.01 equiv.), the carboxylic acid (2 equiv.), the appropriate benzyl chloride (if solid, 1 equiv.) and sodium carbonate (2.0 equiv.). The vial was sealed and a stock solution of NiCl₂•glyme (0.05 equiv.) and dtbbpy (0.075 equiv.) was added in MeCN (1.68 mM). The appropriate benzyl chloride (if liquid, 1 equiv.) was added via syringe and the headspace of the vial purged with N₂ before sealing the vial with Parafilm. The reaction was stirred and irradiated with 2 x 26 W CFL lamps for 48 hours. The reaction was then diluted with sodium bicarbonate and extracted with EtOAc (× 3). The combined organic extracts were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by flash column chromatography yielded the benzylated product. Figure 5 illustrates specific examples of sp³-sp³ cross-coupled product obtain according to this general procedure.

F. Decarboxylative Allylation, sp³-sp³ Cross-coupling

General Procedure - To an oven dried vial equipped with a stir bar was added Ir[dF(5-Me)ppy]₂(tetraMePhen)PF₆ (0.01 equiv.), the carboxylic acid (2 equiv.), and cesium carbonate (1.5 equiv.). The vial was sealed and a stock solution of NiCl₂•glyme (0.03 equiv.) and dtbbpy (0.03 equiv.) was added in DME (2.91 mM). The appropriate allyl carbonate (1 equiv.) was added via syringe and the headspace of the vial purged with N₂ before sealing the vial with Parafilm. The reaction was stirred and irradiated with 2 x 34 W blue LEDs for 24 hours using a fan to keep the reaction cool. The reaction was then diluted with sodium bicarbonate and extracted with EtOAc (× 3). The combined organic extracts were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by flash column chromatography

yielded the allylated product. Figure 6 illustrates specific examples of sp^3 - sp^3 cross-coupled product obtain according to this general procedure.

G. Decarboxylative Alkylation, sp^3 - sp^3 Cross-coupling

5 General Procedure - To an oven dried vial equipped with a stir bar was added Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (0.01 equiv.), the carboxylic acid (2 equiv.), the appropriate alkyl halide (if solid, 1 equiv.) and K₃PO₄ (2.0 equiv.). The vial was sealed and a stock solution of NiCl₂·glyme (0.1 equiv.) and dtbbpy (0.15 equiv.) was added in MeCN (2.01 mM). The appropriate alkyl halide (if liquid, 1 equiv.) was added via syringe and the headspace of the vial
10 purged with N₂ before sealing the vial with Parafilm. The reaction was stirred and irradiated with 2 x 34 W blue LEDs for 48 hours using a fan to keep the reaction cool. The reaction was then diluted with sodium bicarbonate and extracted with EtOAc (× 3). The combined organic extracts were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by flash column chromatography yielded the alkylated product. Figure 7 illustrates specific examples of
15 sp^3 - sp^3 cross-coupled product obtain according to this general procedure.

H. Decarboxylative Acylation

General Procedure - Under air, an oven-dried 45 mL vial, equipped with magnetic stir bar, was charged with Ir(4',6'-dF-5-CF₃-ppy)₂(4,4'-dtbbpy)(PF₆) (0.005 mmol, 5.6 mg), NiCl₂ glyme
20 (0.025 mmol, 5.5 mg), 4,4'-dOMe-bpy (0.025 mol, 5.4 mg) and α -amino acid (0.650 mmol). MeCN (25 mL, directly from the solvent system) was added and the vial was capped. The reaction solution was stirred vigorously under nitrogen for 15 minutes. Acyl chloride (0.500 mmol) was added followed by DBU (0.650 mmol, 97 μ L). The solution was sparged with nitrogen for 30 minutes with vigorous stirring and then sealed with parafilm. The reaction
25 solution was stirred and irradiated with a 34W blue LED at a distance of 7 cm. The temperature of the reaction was maintained at room temperature by fans. After 48 hours, the reaction was quenched by exposure to air. MeCN was removed via rotovap. Crude oil was dissolved in EtOAc and the resulting organic solution was washed with NaHCO₃ (saturated aqueous solution), followed by brine. Drying with Mg₂SO₄ and removal of organic solvent yielded an
30 orange oil. Column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded

pure product. Figures 8 and 9 provide specific examples of acylated reaction product according to this general procedure.

I. Decarboxylative Acylation

5 General Procedure – Under air, an oven-dried 8 mL vial, equipped with magnetic stir bar, was charged with Ir(4',6'-dF-5-OMe-ppy)₂(4,4'-dtbbpy)(PF₆) (0.005 mmol, 5.2 mg), NiCl₂ glyme (0.025 mmol, 5.4 mg), 4,4'-dOMe-bpy (0.025 mol, 5.4 mg) and α-amino acid (0.650 mmol). Dioxane (5 mL, directly from the solvent system) was added and the vial was capped. The reaction solution was stirred vigorously under nitrogen for 15 minutes. Acyl chloride (0.500
10 mmol) was added followed by DBU (0.650 mmol 97 μL). The solution was sparged with nitrogen for 30 minutes with vigorous stirring and then sealed with parafilm. The reaction solution was stirred and irradiated with a 34W blue LED at a distance of 7 cm. The temperature of the reaction was maintained at room temperature by fans. After 48 hours, the reaction was quenched by exposure to air. Dioxane was removed via rotovap. Crude oil was dissolved in
15 EtOAc and the resulting organic solution was washed with NaHCO₃ (saturated aqueous solution), followed by brine. Drying with Mg₂SO₄ and removal of organic solvent yielded an orange oil. Column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded pure product. Figure 10 provides specific examples of acylated reaction product according to
20 this general procedure.

J. Decarboxylative Acylation

General Procedure – Under air, an oven-dried 8 mL vial, equipped with magnetic stir bar, was charged with Ir(4',6'-dF-5-OMe-ppy)₂(4,4'-dtbbpy)(PF₆) (0.005 mmol, 5.2 mg), NiCl₂ glyme (0.025 mmol, 5.4 mg), 4,4'-dOMe-bpy (0.025 mol, 5.4 mg) and α-oxy acid (0.650 mmol).
25 Dioxane (5 mL, directly from the solvent system) was added and the vial was capped. The reaction solution was stirred vigorously under nitrogen for 15 minutes. Acyl chloride (0.500 mmol) was added followed by DBU (0.650 mmol 97 μL). The solution was sparged with nitrogen for 30 minutes with vigorous stirring and then sealed with parafilm. The reaction solution was stirred and irradiated with a 34W blue LED at a distance of 7 cm. The temperature
30 of the reaction was maintained at room temperature by fans. After 48 hours, the reaction was quenched by exposure to air. Dioxane was removed via rotovap. Crude oil was dissolved in

EtOAc and the resulting organic solution was washed with NaHCO₃ (saturated aqueous solution), followed by brine. Drying with Mg₂SO₄ and removal of organic solvent yielded an orange oil. Column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded pure product. Figure 11 provides specific examples of acylated reaction product according to this general procedure.

K. Decarboxylative Fluorination (Examples 52-75)

General Information - Commercial reagents were purchased from Sigma Aldrich and purified prior to use following the guidelines of Perrin. All solvents were purified according to the method of Grubbs (Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *115*, 1518). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an acetone-dry ice bath. Chromatographic purification of products was accomplished using forced-flow chromatography according to the method of Still (Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923) on ICN 60 32-64 mesh silica gel 63. Thin-layer chromatography (TLC) was performed on Silicycle 250 mm silica gel F-254 plates. Visualization of the developed plates was performed by fluorescence quenching, potassium permanganate or ceric ammonium molybdate stain. ¹H and ¹³C NMR spectra were recorded on a Bruker 500 (500 and 125 MHz), and are internally referenced to residual protio solvent signals (for CDCl₃, δ 7.27 and 77.0 ppm, respectively). ¹⁹F NMR spectra were recorded on Bruker 300 (282 MHz) and are referenced to CFCl₃ at δ = 0 ppm. Data for ¹H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad), integration, coupling constant (Hz). ¹³C spectra were reported as chemical shifts in ppm and multiplicity where appropriate. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of wavenumber of absorption (cm⁻¹). High Resolution Mass spectra were obtained from the Princeton University Mass Spectral Facility.

Experimental Procedures and Spectral Characterization of the Starting Materials

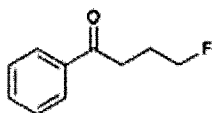
The following acids were commercially available: 4-benzoylbutanoic acid, 3,3'-(1,4-phenylene)dipropionic acid, 3-([1,1'-biphenyl]-4-yl)propanoic acid, 2-([1,1'-biphenyl]-4-yl)acetic acid, 3-phenylbutanoic acid, 3,3,3-triphenylpropanoic acid, cis-2-((*tert*-

butoxycarbonyl)amino)cyclopentane-1-carboxylic acid, trans-4-(*tert*-butyl)cyclohexane-1-carboxylic acid, 2,3-dihydro-1*H*-indene-2-carboxylic acid, 2-methyl-4-oxo-4-phenylbutanoic acid, 2-butyloctanoic acid, and (3*S*,4*S*,6*R*,6*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylic acid. The remainder of the substrates were prepared in the
5 laboratory.

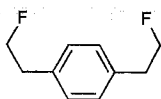
General Procedure for Photoredox-Catalyzed Decarboxylative Fluorination of Carboxylic Acid:

A solution of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), carboxylic acid (0.7 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10
10 mmol, 3 equiv.) in a mixture of acetonitrile/water (7.0 mL, 1:1 v/v) was degassed by sparging argon for 10 min, then irradiated with two 34 W blue LEDs (at approximately 4 cm from the light source). After the reaction completion, the crude reaction mixture was extracted with Et₂O (3 x 10 mL), the combined organic extracts were dried (Na₂SO₄), and concentrated *in vacuo*. Purification by flash chromatography on SiO₂ (5–10% Et₂O in pentane) afforded the desired
15 fluorinated product.

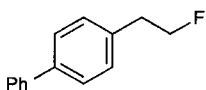
EXAMPLE 52 - 3-Fluoro-1-phenylpropan-1-one



According to the general procedure for the photoredox-catalyzed decarboxylative
20 fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 4-benzoylbutanoic acid (124.7 mg, 0.7000 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 15 h to obtain **11** as a colorless oil (82 mg, 77%). ¹H NMR (500 MHz, CDCl₃): δ 8.00–7.98 (m, 2 H), 7.80–7.57 (m, 1 H), 7.48 (t, *J* = 7.8 Hz, 2 H), 4.57 (dt, *J* = 47.3,
25 5.7 Hz, 2 H), 3.16 (t, *J* = 7.1 Hz, 2 H), 2.24–2.06 (m, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 199.1, 136.7, 133.2, 128.6, 128.0, 83.3 (d, *J* = 164.4 Hz), 34.0 (d, *J* = 4.2 Hz), 24.8 (d, *J* = 20.1 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -219.9 – -220.3 (m, 1 F); HRMS-EI (*m/z*) calcd for C₁₀H₁₁FO [*M*⁺] 166.0794, found 166.0799; IR (film): 2969, 2905, 1683, 1598, 1449, 740 cm⁻¹.

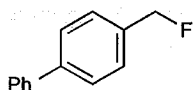
EXAMPLE 53 - 1,4-Bis(2-fluoroethyl)benzene

A mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), disodium 3,3'-(1,4-phenylene)dipropionate (186 mg, 0.700 mmol, 1 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 6 h to obtain **12** as a colorless oil (84.5 mg, 71%). ¹H NMR (500 MHz, CDCl₃): δ 7.20 (s, 4 H), 4.63 (dt, *J* = 47.1, 6.6 Hz, 4 H), 3.02 (dd, *J* = 23.2, 6.6 Hz, 4 H); ¹³C NMR (125 MHz, CDCl₃): δ 135.4 (d, *J* = 6.8 Hz, 2 C), 129.1 (4 C), 84.1 (d, *J* = 169.0 Hz, 2 C), 36.5 (d, *J* = 20.6 Hz, 2 C); ¹⁹F NMR (282 MHz, CDCl₃): δ -215.1 – -215.6 (m, 2 F); HRMS-EI (*m/z*) calcd for C₁₀H₁₂F₂ [M⁺] 170.0907, found 170.0912; IR (film): 2966, 2903, 1516, 1479, 1234, 810 cm⁻¹.

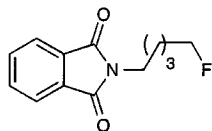
EXAMPLE 54 - 4-(2-Fluoroethyl)-1,1'-biphenyl

According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 3-([1,1'-biphenyl]-4-yl)propanoic acid (158 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 6 h to obtain **13** as a colorless oil (114 mg, 81%). ¹H NMR (500 MHz, CDCl₃): δ 7.62–7.53 (m, 4 H), 7.47–7.42 (m, 2 H), 7.37–7.30 (m, 3 H), 4.68 (dt, *J* = 47.0, 6.5 Hz, 2 H), 3.07 (dt, *J* = 23.4, 6.6 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 141.0, 139.8, 136.3 (d, *J* = 6.2 Hz), 129.5 (2 C), 128.9 (2 C), 127.5 (2 C), 127.3, 127.2 (2 C), 84.2 (d, *J* = 169.0 Hz), 36.7 (d, *J* = 20.4 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -215.1 – -215.6 (m, 1 F); HRMS-EI (*m/z*) calcd for C₁₄H₁₃F [M⁺] 200.0996, found 200.0989; IR (film): 2923, 1709, 1683, 1604, 1487, 1409, 1358, 1220, 1091, 1021, 1007, 973, 916, 886, 841, 764 cm⁻¹.

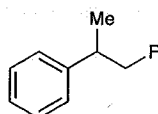
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EXAMPLE 55 - 4-(Fluoromethyl)-1,1'-biphenyl

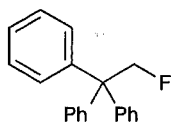
According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 2-([1,1'-biphenyl]-4-yl)acetic acid (148 mg, 0.70 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **14** as a colorless oil (113.4 mg, 87%). ¹H NMR (500 MHz, CDCl₃): δ 7.67–7.61 (m, 4 H), 7.49–7.46 (m, 4 H), 7.40–7.37 (m, 1 H), 5.45 (d, *J* = 47.9 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 141.7, 140.6, 135.1, 128.8 (2 C), 128.0 (d, *J* = 5.7 Hz, 2 C), 127.5, 127.3 (2 C), 127.1 (2 C), 84.4 (d, *J* = 165.9 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -161.4 (s, 1 F); HRMS-EI (*m/z*) calcd for C₁₃H₁₁F [(M-F)⁺] 167.0861, found 167.0855; IR (film): 3027, 1488, 1401, 1007, 909, 762, 697 cm⁻¹.

EXAMPLE 56 - 2-(3-Fluoropentyl)isoindoline-1,3-dione

According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 4-(1,3-dioxisoindolin-2-yl)butanoic acid (183 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 12 h to obtain **15** as a white solid (145 mg, 79%). ¹H NMR (500 MHz, CDCl₃): δ 7.88–7.80 (m, 2 H), 7.76–7.65 (m, 2 H), 4.44 (dt, *J* = 47.2, 6.0 Hz, 2 H), 3.70 (t, *J* = 7.2 Hz, 2 H), 1.84–1.61 (m, 4 H), 1.53–1.40 (m, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 168.6 (2 C), 134.0 (2 C), 132.2 (2 C), 123.4 (2 C), 83.9 (d, *J* = 164.6 Hz), 37.9, 30.0 (d, *J* = 19.7 Hz), 28.4, 22.7 (d, *J* = 5.32 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -218.5 (m, 1 F); HRMS-EI (*m/z*) calcd for C₁₃H₁₄FNO₂ [M⁺] 235.1003, found 235.1001; IR (film): 2942, 2866, 1772, 1704, 1614, 1466, 1437, 1394, 1364, 1337, 1187, 1171, 1153, 1053, 958, 880, 845, 793, 715 cm⁻¹.

EXAMPLE 57 - (1-Fluoropropan-2-yl)benzene

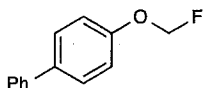
According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 3-phenylbutanoic acid (114.9 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 6 h to obtain **16** as a colorless oil (89.0 mg, 92%). ¹H NMR (500 MHz, CDCl₃): δ 7.38–7.35 (m, 2 H), 7.29–7.27 (m, 3 H), 4.49 (dddd, *J* = 47.4, 42.8, 8.8, 6.6 Hz, 2 H), 3.17 (dq, *J* = 16.5, 6.9 Hz, 1H), 1.38 (dd, *J* = 7.3, 1.3 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ 142.2 (d, *J* = 6.3 Hz), 128.6, 127.4, 126.9, 88.1 (d, *J* = 173.1 Hz), 40.4 (d, *J* = 18.9 Hz), 16.9 (d, *J* = 5.6 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -216.7 – -216.2 (m, 1 F); HRMS-EI (*m/z*) calcd for C₉H₁₁F [M⁺] 138.0845, found 138.0847; IR (film): 2967, 2896, 1479, 1233, 1000, 760, 698 cm⁻¹.

EXAMPLE 58 - (2-Fluoroethane-1,1,1-triyl)tribenzene

According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 3,3,3-triphenylpropanoic acid (212 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **17** as a white solid (159 mg, 82%). ¹H NMR (500 MHz, CDCl₃): δ 7.55–7.45 (m, 4 H), 7.44–7.37 (m, 4 H), 7.37–7.32 (m, 2 H), 7.30–7.27 (m, 2 H), 7.20–7.13 (m, 1 H), 6.80–6.74 (m, 2 H), 3.68 (d, *J* = 23.5 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 167.3, 150.56, 142.3, 142.1, 129.4 (2 C), 128.6 (2 C), 128.3 (2 C), 126.0 (2 C), 125.6 (2 C), 125.5 (2 C), 121.5 (2 C), 97.0 (d, *J* = 182.1 Hz), 45.8 (d, *J* = 24.3 Hz); ¹⁹F NMR (282

MHz, CDCl₃): t, *J* = 23.5 Hz, 1 F); HRMS-EI (*m/z*) calcd for C₂₀H₁₆ [(M-HF)⁺] 256.1247, found 256.1261; IR (film): 2921, 1852, 1592, 1492, 1449, 1360, 1227, 1192, 1161, 1134 cm⁻¹.

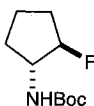
EXAMPLE 59 - 4-(Fluoromethoxy)-1,1'-biphenyl



According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 2-([1,1'-biphenyl]-4-yloxy)acetic acid (160 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **18** as a white solid (140 mg, 99%). ¹H NMR (500 MHz, CDCl₃): δ 7.58–7.53 (m, 4 H), 7.43 (t, *J* = 7.2 Hz, 2 H), 7.37–7.31 (m, 1 H), 7.21–7.13 (m, 2 H), 5.76 (d, *J* = 54.7 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 156.4, 156.4, 140.6, 136.8, 128.9 (2 C), 128.5 (2 C), 127.2, 127.0 (2 C), 117.0, 100.9 (d, *J* = 218.8 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -148.8 (t, *J* = 54.6 Hz, 1 F); HRMS-EI (*m/z*) calcd for C₁₃H₁₁FO [M⁺] 202.0788, found 202.0788;

15 IR (film): 3032, 2933, 2178, 1895, 1712, 1608, 1587, 1518, 1483, 1452, 1413, 1361, 1316, 1292, 1277, 1223, 1190, 1180, 1155, 1091, 1038, 949, 836 cm⁻¹.

EXAMPLE 60 - Trans-*tert*-butyl (2-fluorocyclopentyl)carbamate

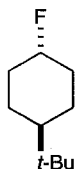


According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), cis-2-((*tert*-butoxycarbonyl)amino)cyclopentane-1-carboxylic acid (160.5 mg, 0.7000 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 15 h to obtain **19** as a white solid (116.7 mg, 82%). ¹H NMR (500 MHz, CDCl₃): δ 4.90 (dd, *J* = 52.5, 4.3 Hz, 1 H), 4.41 (br s, 1 H), 4.00 (d, *J* = 17.5 Hz, 1 H), 2.27–2.08 (m, 1 H), 1.99–1.66 (m, 3 H), 1.45 (s, 9 H); ¹³C NMR (125

25

MHz, CDCl₃): δ 155.2, 98.7 (d, *J* = 178.0 Hz), 79.7, 57.5, 30.8, 30.6, 28.3 (3 C), 21.3; ¹⁹F NMR (282 MHz, CDCl₃): δ -175.7 (s, 1 F); HRMS-EI (*m/z*) calcd for C₆H₁₁NO₂ [(M-Boc+H)⁺] 103.0797, found 103.0793; IR (film): 3342, 2973, 1681, 1524, 1366, 1251, 1167, 954 cm⁻¹.

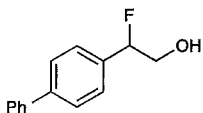
5 **EXAMPLE 61 - Trans-1-(*tert*-butyl)-4-fluorocyclohexane**



According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), trans-4-(*tert*-butyl)cyclohexane-1-carboxylic acid (129 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 15 h to obtain **20** as a colorless liquid (77.5 mg, 70%), as a mixture of *trans/cis* isomers (2.5:1 *trans:cis* ratio). ¹H NMR (500 MHz, CDCl₃): δ 4.82 (dt, *J* = 47.9, 2.3 Hz, 1 H), 4.42 (dm, *J* = 49.5 Hz, 0.4 H), 2.15–2.06 (m, 2.9 H), 1.85–1.82 (m, 0.9 H), 1.60–1.58 (m, 2.1 H), 1.52–1.33 (m, 5.1 H), 1.06–0.97 (m, 2.2 H), 0.91–0.88 (m, 0.9 H), 0.87 (s, 9 H), 0.86 (s, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 92.9 (d, *J* = 171.1 Hz), 88.8 (d, *J* = 166.2 Hz), 47.4, 46.9 (d, *J* = 1.9 Hz), 33.1, 33.0, 32.5, 31.5, 31.3, 27.6, 27.4, 25.0, 24.9, 21.2; ¹⁹F NMR (282 MHz, CDCl₃): δ -168.8 – -169.1 (m, 0.4 F), -184.8 – -185.1 (m, 1 F); HRMS-EI (*m/z*) calcd for C₁₀H₁₈ [(M-HF)⁺] 138.1409, found 138.1403; IR (film): 2942, 2869, 1479, 1441, 1367, 1179, 937, 823 cm⁻¹.

20

EXAMPLE 62 - 2-([1,1'-Biphenyl]-4-yl)-2-fluoroethan-1-ol

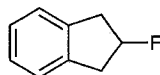


According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 2-([1,1'-biphenyl]-4-yl)-3-hydroxypropanoic acid (169.6 mg, 0.7000 mmol, 1 equiv.), Na₂HPO₄ (199 mg,

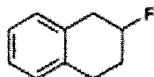
25

1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 2.10 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **21** as a white solid (121 mg, 80%). ¹H NMR (500 MHz, CDCl₃): δ 7.69–7.51 (m, 4 H), 7.48–7.41 (m, 4 H), 7.39–7.35 (m, 1 H), 5.62 (ddd, *J* = 48.6, 7.7, 3.1 Hz, 1 H), 4.18–3.58 (m, 2 H), 2.01–1.96 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 141.98, 140.6, 135.4 (d, *J* = 19.8 Hz), 129.0 (2 C), 127.7, 127.5 (2 C), 127.3 (2 C), 126.4 (d, *J* = 6.8 Hz, 2 C), 94.8 (d, *J* = 171.8 Hz), 66.7 (d, *J* = 24.8 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -186.6 – -187.1 (m, 1 F); HRMS-EI (*m/z*) calcd for C₁₄H₁₂O [(M-HF)⁺] 196.0883, found 196.0887; IR (film): 3362, 3058, 3033, 2928, 1947, 1693, 1666, 1603, 1487, 1450, 1408, 1355, 1315, 1234, 1167, 1086, 1046, 978 cm⁻¹.

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EXAMPLE 63 - 2-Fluoro-2,3-dihydro-1H-indene

According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ru(bpz)₃(PF₆)₂ (5.9 mg, 7.0 μmol, 1 mol%), 2,3-dihydro-1H-indene-2-carboxylic acid (114 mg, 0.70 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **22** as a white solid (88 mg, 92%). ¹H NMR (500 MHz, CDCl₃): δ 7.30–7.24 (m, 2 H), 7.23–7.18 (m, 2 H), 5.56–5.40 (m, 1 H), 3.31–3.23 (m, 2 H), 3.22–3.16 (m, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ = 140.1 (2 C), 127.9 (2 C), 127.0 (2 C), 94.9 (d, *J* = 176.7 Hz), 40.7 (d, *J* = 23.14 Hz, 2 C); ¹⁹F NMR (282 MHz, CDCl₃): δ -173.5 – -173.8 (m, 1 F); HRMS (*m/z*): calcd for C₉H₉F [M⁺] 136.0683, found 136.0683; IR (film): 2959, 1479, 1417, 1346, 1233, 1215, 1193, 1016, 941, 808, 739 cm⁻¹.

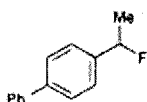
EXAMPLE 64 - 2-Fluoro-1,2,3,4-tetrahydronaphthalene

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According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ru(bpz)₃(PF₆)₂ (5.9 mg, 7.0 μmol, 1 mol%), 1,2,3,4-tetrahydronaphthalene-2-carboxylic acid (114 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg,

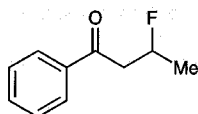
1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **23** as a colorless liquid (74 mg, 71%). ¹H NMR (500 MHz, CDCl₃): δ 7.16–7.11 (m, 4 H), 5.09 (m, 1 H), 3.19–2.99 (m, 3 H), 2.82 (dt, *J* = 16.8, 6.5 Hz, 1 H), 2.16–2.09 (m, 1 H), 2.08–2.04 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃): δ 135.4, 132.9 (d, *J* = 6.1 Hz), 129.4, 128.5, 126.1, 126.0, 88.8 (d, *J* = 169.9 Hz), 35.3 (d, *J* = 22.4 Hz), 28.5 (d, *J* = 19.9 Hz), 25.6 (d, *J* = 8.1 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -177.3 – -177.7 (m, 1 F); HRMS (*m/z*): calcd for C₁₀H₁₁F [M⁺] 150.0845, found 150.0843; IR (film): 2939, 1496, 1455, 1343, 1052, 1014, 955, 928, 835, 744 cm⁻¹.

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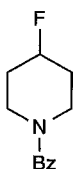
EXAMPLE 65 - 4-(1-Fluoroethyl)-1,1'-biphenyl

According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 2-([1,1'-biphenyl]-4-yl)propanoic acid (158 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **24** as a colorless oil (119.0 mg, 85%). ¹H NMR (500 MHz, CDCl₃): δ 7.67–7.56 (m, 4 H), 7.50–7.41 (m, 4 H), 7.40–7.34 (m, 1 H), 5.69 (dq, *J* = 47.7, 6.4 Hz, 1 H), 1.71 (dd, *J* = 23.9, 6.4 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ 141.4, 140.8, 140.5 (d, *J* = 19.6 Hz), 128.9 (2 C), 127.6, 127.4 (2 C), 127.3 (2 C), 125.9 (d, *J* = 6.6 Hz, 2 C), 90.9 (d, *J* = 167.4 Hz), 23.0 (d, *J* = 25.3 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -166.6 (dq, *J* = 47.7, 23.9 Hz, 1 F); HRMS-EI (*m/z*) calcd for C₁₄H₁₂ [(M–HF)⁺] 180.0934, found 180.0928; IR (film): 3027, 2971, 2926, 2871, 1600, 1485, 1449, 1404, 1367, 1300, 1182, 1089, 1076, 1007, 908 cm⁻¹.

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EXAMPLE 66 - 3-Fluoro-1-phenylbutan-1-one

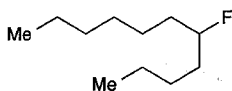
According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ru(bpz)₃(PF₆)₂ (5.9 mg, 7.0 μmol, 1 mol%), 2-methyl-4-oxo-4-phenylbutanoic acid (134.5 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **25** as a colorless oil (112 mg, 96%). ¹H NMR (500 MHz, CDCl₃): δ 8.10–7.91 (m, 2 H), 7.64–7.57 (m, 1 H), 7.49 (t, *J* = 7.8 Hz, 2 H), 5.33 (dq, *J* = 47.5, 6.2 Hz, 1 H), 3.62–3.42 (m, 1 H), 3.10 (ddd, *J* = 23.6, 16.7, 5.5 Hz, 1 H), 1.49 (dd, *J* = 24.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ 196.8 (d, *J* = 6.7 Hz), 136.8 (d, *J* = 1.5 Hz), 133.4, 128.7 (2 C), 128.1 (2 C), 87.2 (d, *J* = 165.3 Hz), 45.4 (d, *J* = 23.0 Hz), 21.2 (d, *J* = 22.2 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -172.4 – -172.9 (1 F, m); HRMS-EI (*m/z*): calcd for C₁₁H₂₂ [M⁺] 166.0794, found 166.0802; IR (film): 2984, 1684, 1598, 1385, 1214, 1134, 839, 753 cm⁻¹.

EXAMPLE 67 - (4-Fluoropiperidin-1-yl)(phenyl)methanone

According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 1-benzoylpiperidine-4-carboxylic acid (163.3 mg, 0.7000 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 6 h to obtain **26** as a colorless oil (131.0 mg, 90%). ¹H NMR (500 MHz, CDCl₃): δ 7.44–7.41 (m, 5 H), 4.98–4.86 (m, 1 H), 4.04–4.00 (m, 1 H), 3.68–3.44 (m, 3 H), 1.98–1.81 (m, 4 H); ¹³C NMR (125 MHz, CDCl₃): δ 170.5, 135.8, 129.7, 128.6, 126.8, 87.6 (d, *J* = 171.5 Hz), 43.5, 38.0; ¹⁹F NMR (282 MHz, CDCl₃): δ -183.0 – -183.4 (m, 1 F); HRMS

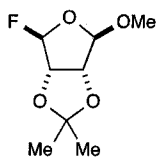
(*m/z*): calcd for C₁₂H₁₄FNO [M⁺] 207.1059, found 207.1051; IR (film): 2951, 1632, 1433, 1283, 1027, 710 cm⁻¹.

EXAMPLE 68 - 5-Fluoroundecane



5 According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 2-butyl octanoic acid (140 mg, 0.700 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 6 h to obtain **27** as a colorless oil (100 mg, 83%). ¹H NMR (500 MHz, CDCl₃): δ 4.54–4.37 (m, 1 H), 1.65–1.40 (m, 6 H), 1.37–1.26 (m, 10 H), 0.90 (t, *J* = 6.9 Hz, 6 H); ¹³C NMR (125 MHz, CDCl₃): δ 94.8 (d, *J* = 166.4 Hz), 35.3 (d, *J* = 20.9 Hz), 35.0 (d, *J* = 20.8 Hz), 31.9, 29.4, 27.5 (d, *J* = 4.5 Hz), 26.3 (d, *J* = 4.5 Hz), 22.8 (2 C), 14.2, 14.2; ¹⁹F NMR (282 MHz, CDCl₃): δ -185.1 – -185.5 (1 F, m); HRMS-EI (*m/z*): calcd for C₁₁H₂₂ [(M-HF)⁺] 154.1716, found 154.1719; IR (film): 2931, 2860, 1463, 1379, 1129, 980 cm⁻¹.

EXAMPLE 69 - (3*S*,4*R*,6*R*,6*R*)-4-Fluoro-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole

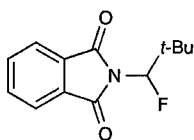


20 According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), (3*S*,4*S*,6*R*,6*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylic acid (172.7 mg, 0.7000 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **28** as a white solid (123.8 mg, 92%). ¹H NMR (500 MHz, CDCl₃): δ 5.79 (d, *J* = 60.5 Hz, 1 H), 5.17 (d, *J* = 2.9 Hz, 1 H), 4.82 (t, *J* = 6.0 Hz, 1 H), 4.67 (d, *J* = 5.7 Hz,

1 H), 3.43 (s, 3 H), 1.45 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ 115.7 (d, J = 226.5 Hz), 112.9 (d, J = 1.2 Hz), 111.4 (d, J = 1.9 Hz), 83.9 (40.0 Hz), 83.2, 55.4, 26.2, 24.8; ^{19}F NMR (282 MHz, CDCl_3): δ -119.4 (m, 1 F); HRMS (m/z): calcd for $\text{C}_8\text{H}_{12}\text{O}_4$ [(M-HF) $^{+}$] 172.0736, found 172.0746; IR (film): 2990, 1377, 1202, 1101, 1060, 995, 867, 785 cm^{-1} .

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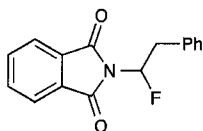
EXAMPLE 70 - 2-(1-Fluoro-2,2-dimethylpropyl)isoindoline-1,3-dione



According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (7.8 mg, 7.0 μmol , 1 mol%), 2-(1,3-dioxisoindolin-2-yl)-3,3-dimethylbutanoic acid (183 mg, 0.700 mmol, 1 equiv.), Na_2HPO_4 (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 3 h to obtain **29** as a white solid (148 mg, 90%). ^1H NMR (500 MHz, CDCl_3): δ 7.91–7.87 (m, 2 H), 7.79–7.74 (m, 2 H), 5.91 (d, J = 43.0 Hz, 1 H), 1.12 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3): δ 167.0 (2 C), 134.5 (2 C), 133.6 (2 C), 123.7 (2 C), 98.4 (d, J = 211.3 Hz), 37.2 (d, J = 23.4 Hz), 23.6 (3 C); ^{19}F NMR (282 MHz, CDCl_3): δ -173.0 (d, J = 42.8 Hz); HRMS-EI (m/z): calcd for $\text{C}_{13}\text{H}_{14}\text{FNO}_2$ [(M-HF) $^{+}$] 235.1003, found 235.0997; IR (film): 2968, 1781, 1721, 1612, 1480, 1468, 1392, 1353, 1327, 1269, 1216, 1124, 1088, 1050, 1011, 987, 898 cm^{-1} .

20

EXAMPLE 71 - 2-(1-Fluoro-2-phenylethyl)isoindoline-1,3-dione

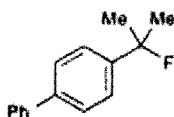


According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (7.8 mg, 7.0 μmol , 1 mol%), 2-(1,3-dioxisoindolin-2-yl)-3-phenylpropanoic acid (207 mg, 0.70 mmol, 1 equiv.), Na_2HPO_4 (199

25

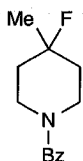
mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **30** as a white solid (170 mg, 90%). ¹H NMR (500 MHz, CDCl₃): δ 7.90–7.88 (m, 2 H), 7.78–7.76 (m, 2 H), 7.29–7.22 (m, 5 H), 6.26 (dt, *J* = 47.3, 7.4 Hz, 1 H), 3.85–3.67 (m, 2 H); ¹³C NMR (125 MHz, CDCl₃): δ 166.9 (2 C), 134.7 (2 C), 131.4, 129.2 (2 C), 128.8 (2 C), 127.2 (2 C), 124.0 (3 C), 90.3 (d, *J* = 206.0 Hz), 37.5 (d, *J* = 27.5 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -144.9 (ddd, *J* = 47.7, 19.7, 9.4 Hz, 1 F); HRMS (*m/z*): calcd for C₁₆H₁₂NO₂ [(M-HF+H)⁺] 249.07898, found 249.07895; IR (film): 1784, 1724, 1609, 1495, 1469, 1456, 1363, 1087, 998, 967, 875, 847 cm⁻¹.

10 **EXAMPLE 72 - 4-(2-fluoropropan-2-yl)-1,1'-biphenyl**



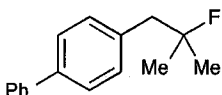
According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 2-([1,1'-biphenyl]-4-yl)-2-methylpropanoic acid (168 mg, 0.70 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **31** as a colorless oil (135.0 mg, 90%). ¹H NMR (500 MHz, CDCl₃): δ 7.64–7.55 (m, 4 H), 7.50–7.41 (m, 4 H), 7.37–7.33 (m, 1 H), 1.73 (d, *J* = 21.9 Hz, 6 H); ¹³C NMR (125 MHz, CDCl₃): δ 145.0 (d, *J* = 22.1 Hz), 140.9, 140.4, 128.9 (2 C), 127.5, 127.3 (2 C), 127.2 (2 C), 124.4 (d, *J* = 8.8 Hz, 2 C), 95.8 (d, *J* = 168.9 Hz), 29.5 (d, *J* = 25.8 Hz, 2 C); ¹⁹F NMR (282 MHz, CDCl₃): δ -137.0 (hept, *J* = 22.0 Hz, 1 F); HRMS-EI (*m/z*) calcd for C₁₅H₁₄ [(M-HF)⁺] 194.1090, found 194.1094; IR (film): 3034, 2985, 2937, 1714, 1682, 1600, 1486, 1451, 1402, 1367, 1287, 1203, 1165, 1155, 1155, 1103, 1005, 937 cm⁻¹.

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EXAMPLE 73 - (4-Fluoro-4-methylpiperidin-1-yl)(phenyl)methanone

According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 1-benzoyl-4-methylpiperidine-4-carboxylic acid (173.1 mg, 0.7000 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 15 h to obtain **32** as a white solid (111.5 mg, 72%). ¹H NMR (500 MHz, CDCl₃): δ 7.43–7.40 (m, 5 H), 4.55–4.52 (m, 1 H), 3.62–3.59 (m, 1 H), 3.40–3.34 (m, 1 H), 3.20–3.15 (m, 1 H), 1.99–1.96 (m, 1 H), 1.81–1.78 (m, 1 H), 1.69–1.54 (m, 2 H), 1.41 (d, *J* = 21.5 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ 170.4, 135.9, 129.6, 128.5 (2 C), 126.8 (2 C), 92.3 (d, *J* = 168.8 Hz), 43.7, 38.2, 36.5 (dd, *J* = 122.9, 21.1 Hz, 2 C), 27.0 (d, *J* = 24.1 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -153.55 – -153.96 (m, 1 F); HRMS (*m/z*): calcd for C₁₃H₁₇FNO [(M+H)⁺] 222.1294, found 222.1293; IR (film): 2935, 1632, 1435, 1290, 1264, 1149, 1114, 968, 709 cm⁻¹.

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EXAMPLE 74 - 4-(2-Fluoro-2-methylpropyl)-1,1'-biphenyl

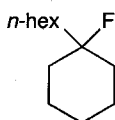
According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (7.8 mg, 7.0 μmol, 1 mol%), 3-([1,1'-biphenyl]-4-yl)-2,2-dimethylpropanoic acid (178.0 mg, 0.7000 mmol, 1 equiv.), Na₂HPO₄ (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (496 mg, 1.40 mmol, 2 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 1 h to obtain **33** as a colorless oil (140.6 mg, 88%). ¹H NMR (500 MHz, CDCl₃): δ 7.62–7.57 (m, 2 H), 7.56–7.51 (m, 2 H), 7.45–7.40 (m, 2 H), 7.36–7.31 (m, 1 H), 7.31–7.27 (m, 2 H), 2.95 (d, *J* = 20.5 Hz, 2 H), 1.38 (d, *J* = 21.3 Hz, 6 H); ¹³C NMR (125 MHz, CDCl₃): δ 140.9, 139.4, 136.1 (d, *J* = 3.9 Hz), 130.8 (2 C), 128.7

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(2 C), 127.1, 127.0 (2 C), 126.8 (2 C), 95.3 (d, $J = 168.0$ Hz), 47.2 (d, $J = 22.9$ Hz), 26.7 (d, $J = 24.4$ Hz, 2 C); ^{19}F NMR (282 MHz, CDCl_3): δ -137.0 (hept, $J = 21.2$ Hz, 1 F); HRMS (m/z): calcd for $\text{C}_{16}\text{H}_{16}$ [(M-HF) $^{+}$] 209.1332, found 209.1325; IR (film): 3032, 2980, 2918, 1487, 1408, 1372, 1225, 1185, 1130 cm^{-1} .

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EXAMPLE 75 - 1-Fluoro-1-hexylcyclohexane



According to the general procedure for the photoredox-catalyzed decarboxylative fluorination, a mixture of $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ (7.8 mg, 7.0 μmol , 1 mol%), 1-hexylcyclohexane-1-carboxylic acid (148.6 mg, 0.7000 mmol, 1 equiv.), Na_2HPO_4 (199 mg, 1.40 mmol, 2 equiv.), and SELECTFLUOR® (744 mg, 2.10 mmol, 3 equiv.) in acetonitrile/water (7.0 mL, 1:1 v/v) was irradiated for 15 h to obtain **34** as a colorless oil (103.0 mg, 79%).

^1H NMR (500 MHz, CD_2Cl_2): δ 1.80–1.76 (m, 2 H), 1.63–1.28 (m, 18 H), 0.94–0.87 (m, 3 H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ 40.4, 40.2, 35.2, 35.0, 31.9, 29.8, 25.5, 22.9 (d, $J = 4.5$ Hz), 22.7, 22.2 (d, $J = 3.6$ Hz); ^{19}F NMR (282 MHz, CD_2Cl_2): δ -155.4 (s, 1 F); HRMS (m/z): calcd for $\text{C}_{12}\text{H}_{23}$ [(M-F) $^{+}$] 167.1800, found 167.1794; IR (film): 2932, 2859, 1449, 1375, 1149, 960, 928, 829 cm^{-1} .

Various embodiments of the invention have been described in fulfillment of the various objectives of the invention. It should be recognized that these embodiments are merely illustrative of the principles of the present invention. Numerous modifications and adaptations thereof will be readily apparent to those skilled in the art without departing from the spirit and scope of the invention.

CLAIMS

1. A method of cross-coupling comprising:
providing a reaction mixture including a photoredox catalyst, a transition metal catalyst, a
coupling partner and a substrate having a carboxyl group; and
5 irradiating the reaction mixture with a radiation source resulting in cross-coupling of the
substrate and coupling partner via a mechanism including decarboxylation, wherein the coupling
partner is selected from the group consisting of a substituted aromatic compound and substituted
aliphatic compound.
- 10 2. The method of claim 1, wherein the substrate is an aliphatic carboxylic acid.
3. The method of claim 2, wherein the aliphatic carboxylic acid is an amino acid.
4. The method of claim 2, wherein the aliphatic carboxylic acid is a fatty acid.
- 15 5. The method of claim 2, wherein the aliphatic carboxylic acid is of formula R^1-CO_2H ,
wherein R^1 is selected from the group consisting of -alkyl, -cycloalkyl, -heteroalkyl,
-heterocycloalkyl, -alkenyl, -cycloalkenyl, -heteroalkenyl, -heterocycloalkenyl, -alkynyl,
-alkyl-aryl, -alkyl-heteroaryl, -alkyl-alkoxy, -alkenyl-aryl, -alkenyl-heteroaryl, -cycloalkyl-aryl,
20 -cycloalkyl-heteroaryl, -cycloalkenyl-aryl, -heterocycloalkenyl-aryl, and -alkenyl-alkoxy.
6. The method of claim 1, wherein the substrate is a keto acid.
7. The method of claim 6, wherein the keto acid is an aliphatic keto acid.
- 25 8. The method of claim 6, wherein the keto acid is an aryl keto acid or heteroaryl keto acid.
9. The method of claim 6, wherein the keto acid is of the formula $R^2-C(O)-CO_2H$, wherein
 R^2 is selected from the group consisting of -alkyl, -cycloalkyl, -heteroalkyl,
30 -heterocycloalkyl, -alkenyl, -cycloalkenyl, -heteroalkenyl, -heterocycloalkenyl, -alkynyl,

-aryl, -heteroaryl, -alkyl-aryl, -alkyl-heteroaryl, -alkyl-alkoxy, -alkenyl-aryl, -alkenyl-heteroaryl and -alkenyl-alkoxy.

10. The method of claim 1, wherein the cross-coupling is a sp^3-sp^2 cross-coupling.

5

11. The method of claim 1, wherein the cross-coupling is a sp^3-sp^3 cross-coupling.

12. The method of claim 1, wherein the substituted aromatic compound is a substituted aryl or substituted heteroaryl.

10

13. The method of claim 12, wherein the substituted aryl or substituted heteroaryl comprises a halide leaving group.

14. The method of claim 1, wherein the substituted aliphatic compound comprises one or more points of unsaturation.

15

15. The method of claim 14, wherein the substituted aliphatic compound is an allyl carbonate.

20 16. The method of claim 1, wherein the substituted aliphatic compound is saturated.

17. The method of claim 16, wherein the substituted aliphatic compound comprises a halide leaving group.

25 18. The method of claim 17, wherein the substituted aliphatic compound is of the formula R^3-X , wherein X is the halide leaving group and R^3 is selected from the group consisting of -alkyl, -cycloalkyl, -heteroalkyl, -heterocycloalkyl, -alkenyl, -cycloalkenyl, -heteroalkenyl, -heterocycloalkenyl, -alkynyl, -alkyl-aryl, -alkyl-heteroaryl, -alkyl-alkoxy, -alkenyl-aryl, -alkenyl-heteroaryl and -alkenyl-alkoxy.

30

19. The method of claim 1, wherein the photoredox catalyst is an iridium complex or ruthenium complex.
20. The method of claim 19, wherein the photoredox catalyst is a heteroleptic iridium
5 complex.
21. The method of claim 20, wherein the heteroleptic iridium complex is selected from the group consisting of $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})^+$, $\text{Ir}(\text{ppy})_2(\text{dtbbpy})^+$ and $\text{Ir}[\text{dF}(5\text{-Me})\text{ppy}]_2(\text{tetraMePhen})^+$.
10
22. The method of claim 19, wherein the photoredox catalyst is present in the reaction mixture in an amount of 0.1 to 5 mol.%.
23. The method of claim 1, wherein the transition metal catalyst is selected from the group
15 consisting of nickel catalyst, copper catalyst and palladium catalyst.
24. The method of claim 23, wherein the transition metal catalyst is present in the reaction mixture in an amount of 1 to 15 mol.%.
- 20 25. The method of claim 23, wherein the transition metal catalyst is selected from the group consisting of $\text{NiCl}_2 \cdot \text{dimethoxyethane}$ and $\text{NiCl}_2 \cdot \text{dtbbpy}$.
26. The method of claim 1, wherein the reaction mixture further comprises a ligand component.
25
27. The method of claim 26, wherein the ligand component comprises one or more pyridine moieties.
28. The method of claim 26, wherein the ligand component is present in the reaction mixture
30 in an amount of 5 to 50 mol%.

29. A method of acylation comprising:
providing a reaction mixture including an acylating agent, a photoredox catalyst, a transition metal catalyst and a substrate having a carboxyl group; and
irradiating the reaction mixture with a radiation source resulting in acylation of the substrate via a mechanism including decarboxylation.
30. The method of claim 29, wherein the substrate is an aliphatic carboxylic acid.
31. The method of claim 30, wherein the aliphatic carboxylic acid is an amino acid.
32. The method of claim 30, wherein the aliphatic carboxylic acid is an α -oxy acid.
33. The method of claim 29, wherein the acylating agent is an acyl halide.
34. The method of claim 33, wherein the acylating agent is of the formula $X-C(O)R^4$, wherein X is a halide leaving group and R^4 is selected from the group consisting of -alkyl, -cycloalkyl, -heteroalkyl, -heterocycloalkyl, -alkenyl, -cycloalkenyl, -heteroalkenyl, -heterocycloalkenyl, -aryl, -heteroaryl, -alkyl-aryl, -alkyl-heteroaryl, -cycloalkyl-aryl, -cycloalkyl-heteroaryl, -aryl-alkyl and -aryl-alkoxy.
35. The method of claim 29, wherein the photoredox catalyst is a heteroleptic iridium complex.
36. The method of claim 35, wherein the heteroleptic iridium complex is selected from the group consisting of $Ir(4',6'\text{-dF-5-CF}_3\text{-ppy})_2(4,4'\text{-dtbbpy})^+$ and $Ir(4',6'\text{-dF-5-OMe-ppy})_2(4,4'\text{-dtbbpy})^+$.
37. The method of claim 29, wherein the transition metal catalyst is selected from the group consisting of nickel catalyst, copper catalyst and palladium catalyst.

38. A method of fluorination comprising:
providing a reaction mixture comprising a fluorination reagent, a photoredox catalyst and
an aliphatic carboxylic acid; and
irradiating the reaction mixture with a radiation source yielding fluoroalkane via a
5 mechanism including decarboxylation of the aliphatic carboxylic acid and fluorination by the
fluorinating reagent.
39. The method of claim 38, wherein the aliphatic carboxylic acid is of the formula R^5CO_2H ,
wherein R^5 is selected from the group consisting of -alkyl, -heteroalkyl, -cycloalkyl,
10 -heterocycloalkyl, -alkyl-aryl, -heteroalkyl-aryl, -alkyl-heteroaryl, -alkyl-cycloalkyl, -alkyl-
heterocycloalkyl, -heteroalkyl-heteroaryl, -cycloalkyl-aryl, -cycloalkyl-heteroaryl,
-heterocycloalkyl-aryl, -heterocycloalkyl-heteroaryl, -cycloalkyl-alkyl,
-heterocycloalkyl-alkyl, -cycloalkyl-heteroalkyl, and -heterocycloalkyl-heteroalkyl.
- 15 40. The method of claim 38, wherein the photoredox catalyst is a heteroleptic iridium
complex or homoleptic ruthenium complex.
41. The method of claim 40, wherein the photoredox catalyst is selected from the group
consisting of $Ir[dF(CF_3)ppy]_2(dtbbpy)^+$, $Ru(bpz)_3^{2+}$ and $Ru(phen)_3^{2+}$.
- 20 42. The method of claim 38, wherein the fluorinating reagent comprises 1-(chloromethyl)-4-
fluoro-1,4-diazoniabicyclo[2.2.2]octane ditetrafluoroborate.
43. The method of claim 38, wherein the reaction mixture further comprises a base.
- 25 44. The method of claim 38, wherein the reaction mixture is a homogeneous solution of the
aliphatic carboxylic acid, photoredox catalyst and fluorinating reagent.
45. The method of claim 44, where solvent of the reaction mixture is CH_3CN/H_2O .

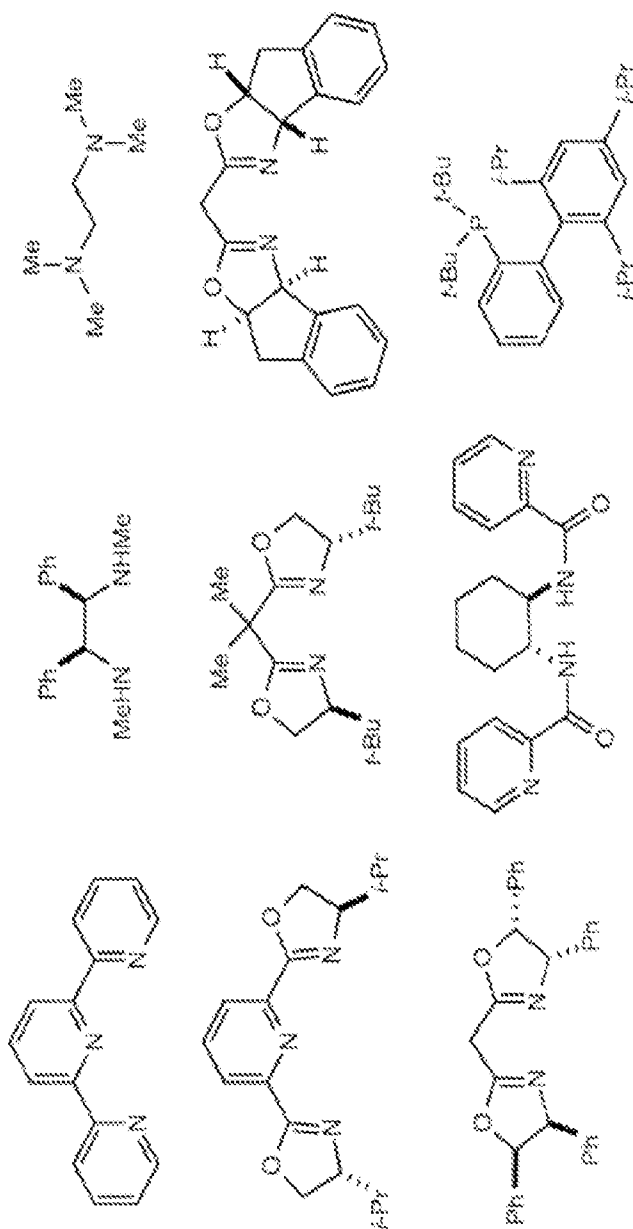


FIGURE 1

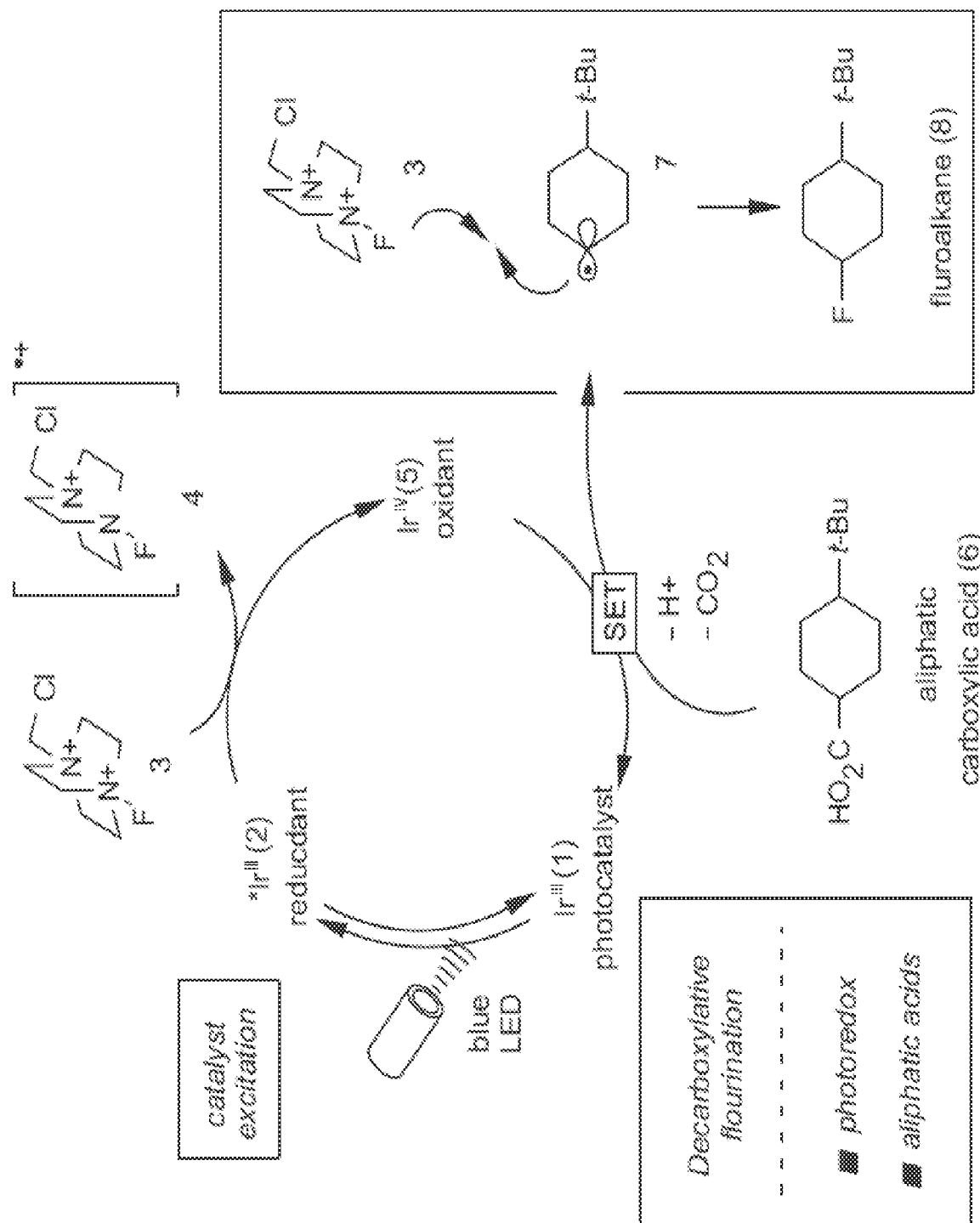
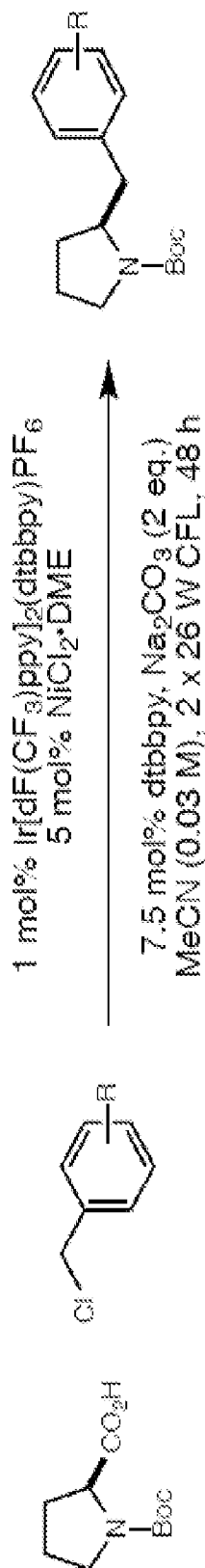


FIGURE 4

Reaction Scheme



Specific Examples

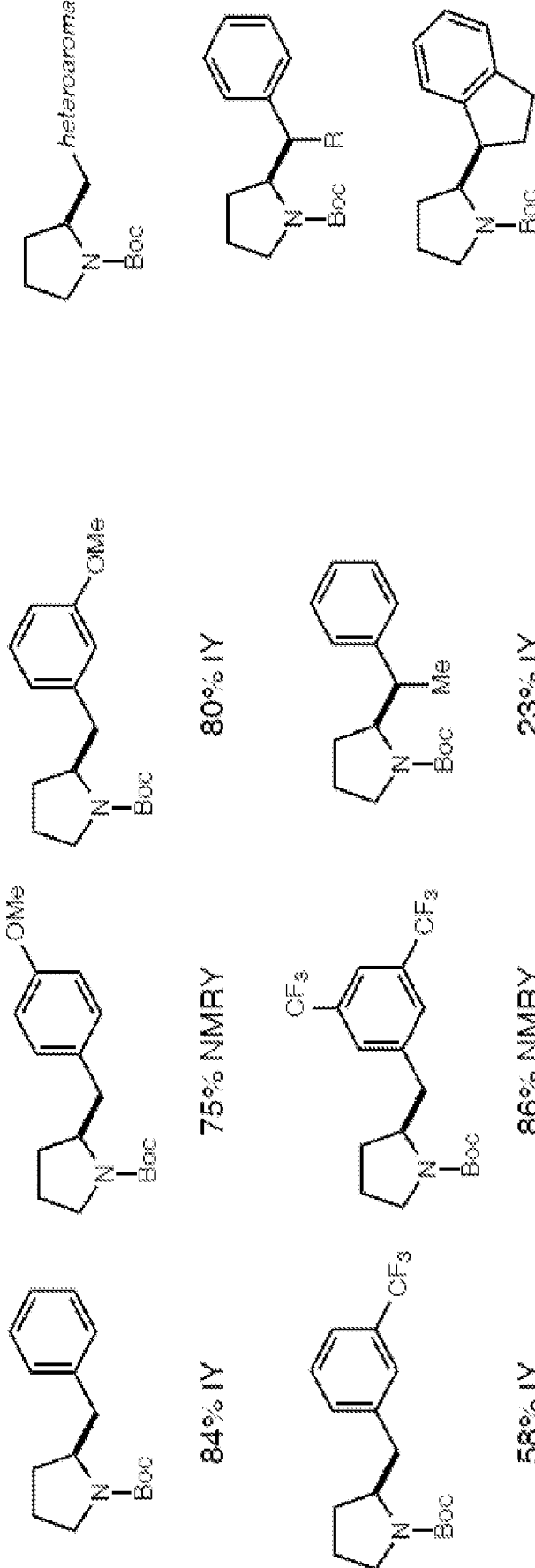
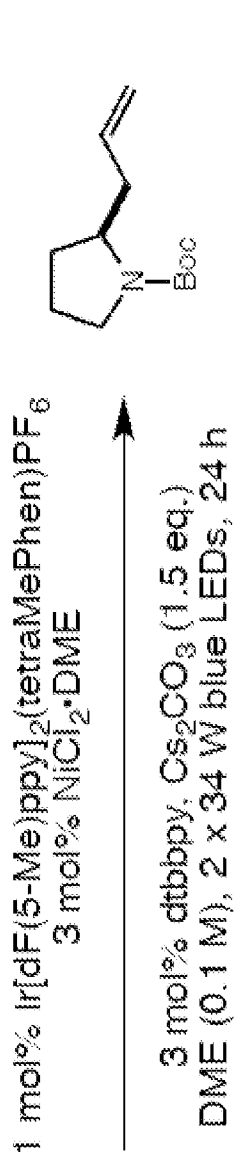
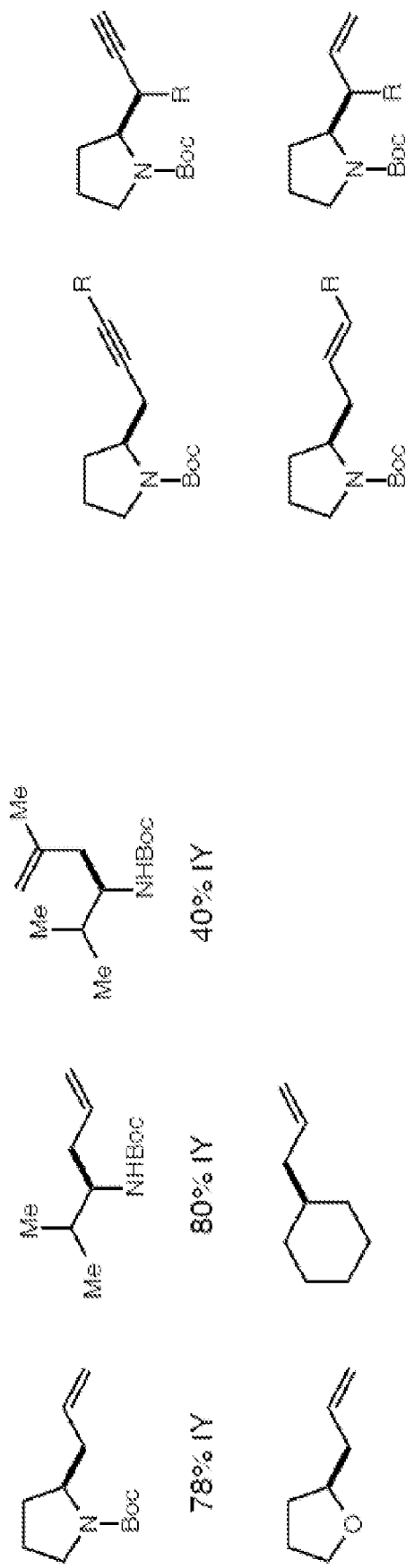


FIGURE 5

Reaction Scheme



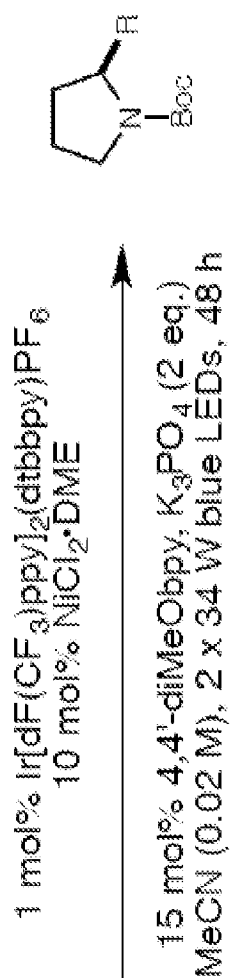
Specific Examples



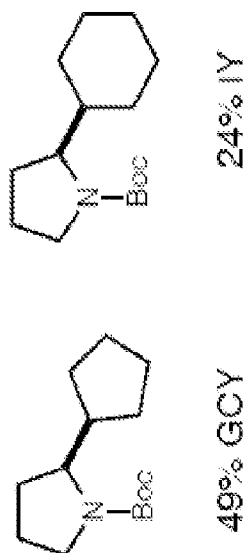
¹ performed in acetone
² performed with Ir[dF(5-OMe)ppy]₂(dtbbpy)PF₆ in DMA

FIGURE 6

Reaction Scheme



Specific Examples



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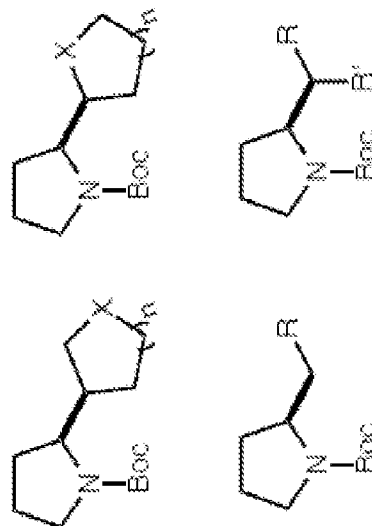
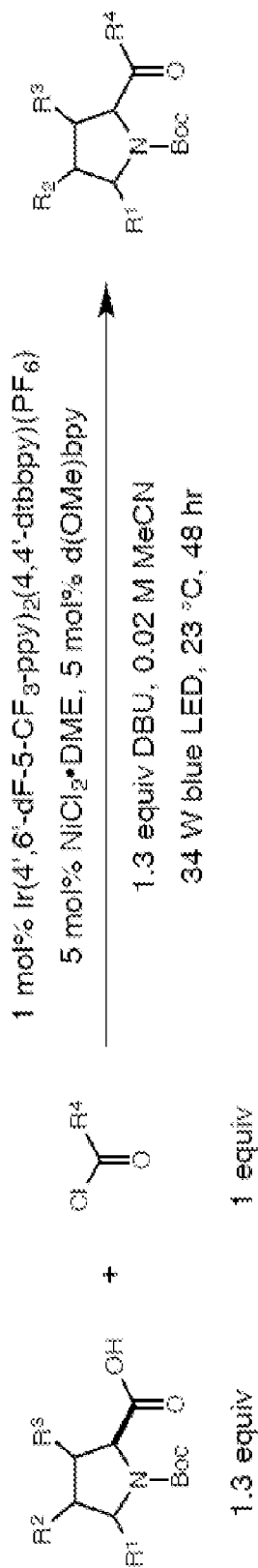


FIGURE 7

Reaction Scheme



Specific Examples

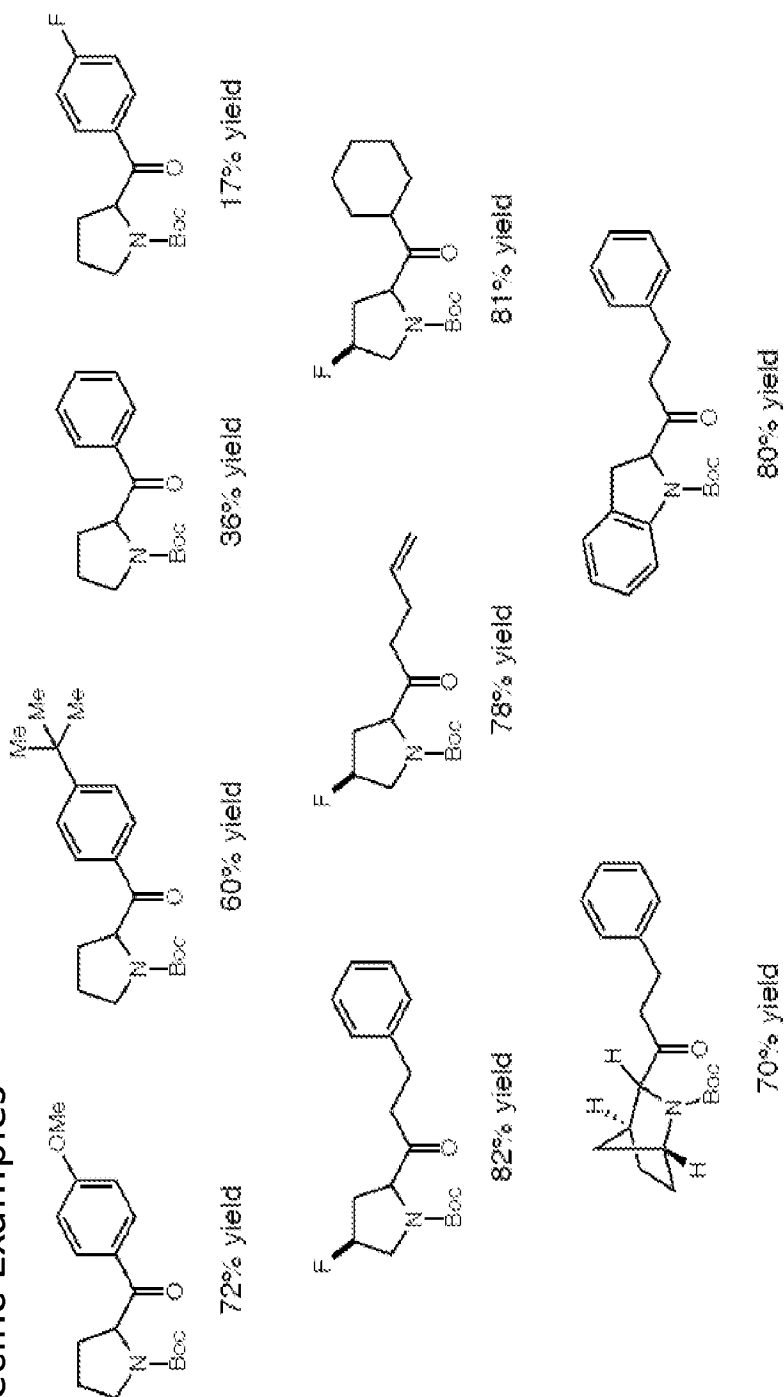
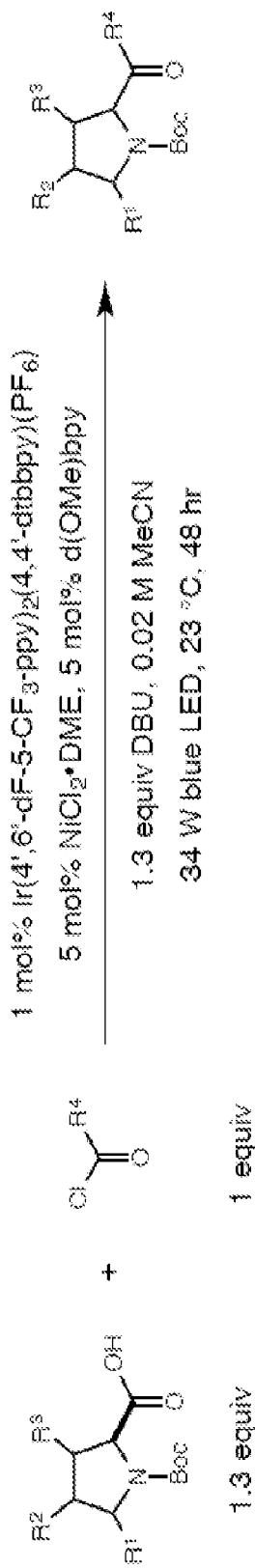


FIGURE 8

Reaction Scheme



Specific Examples

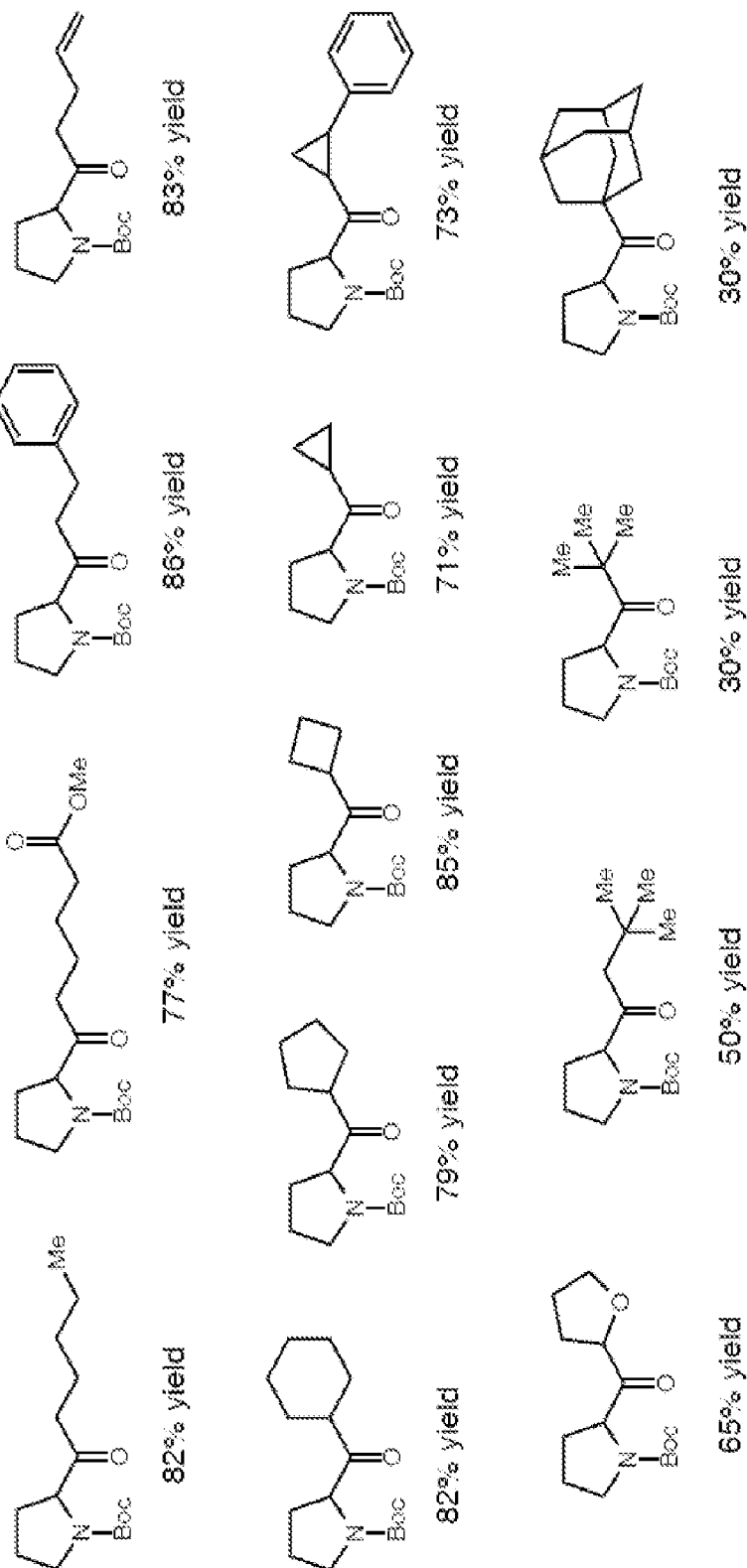


FIGURE 9

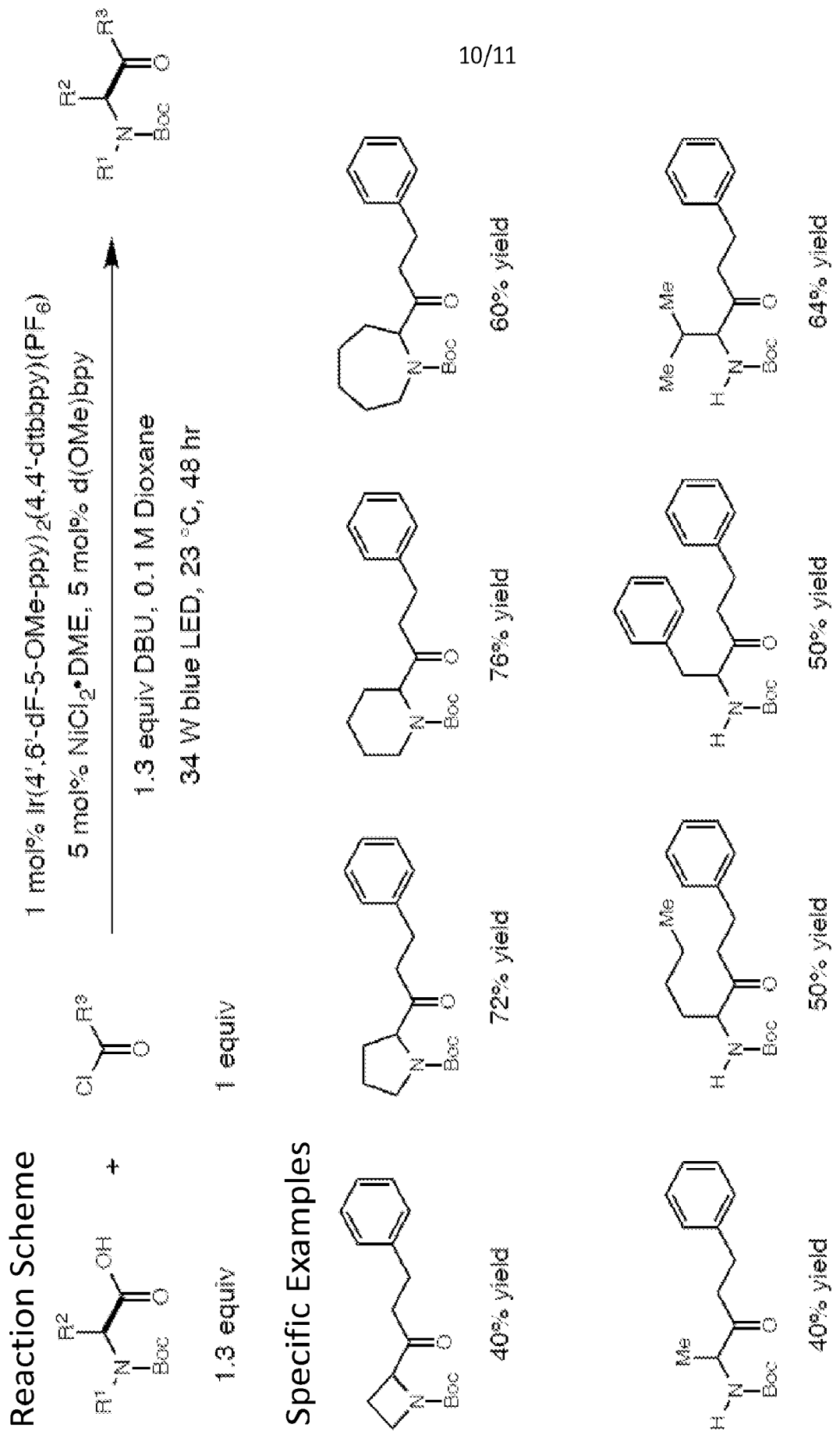
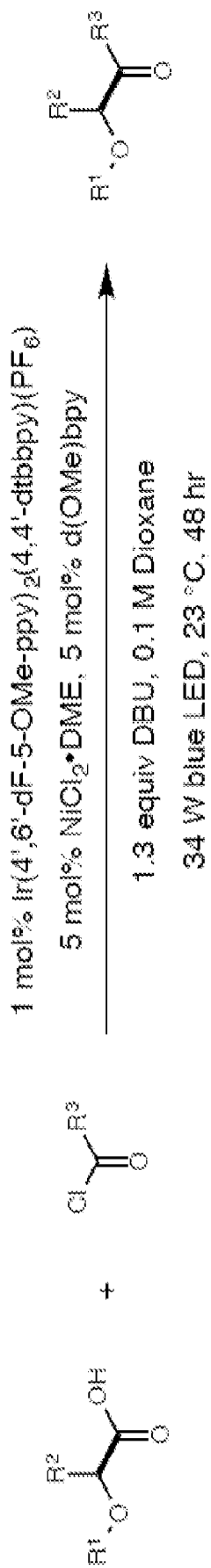


FIGURE 10

Reaction Scheme



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Specific Examples

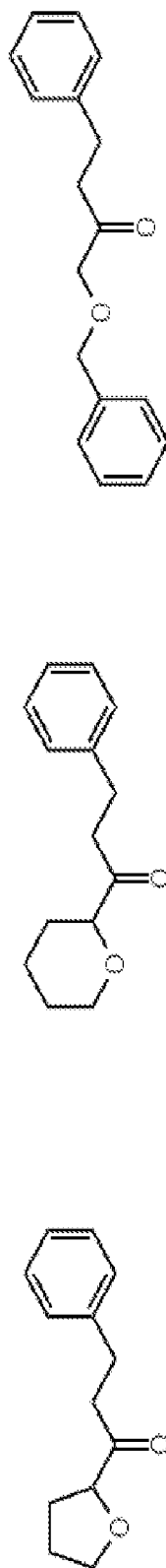


FIGURE 11