

博 士 論 文

光駆動型酸化的ラジカル-極性交差機構による
 sp^3 炭素-ヘテロ原子結合形成反応の開発

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中川 雅就

目次

序論	1
第一章 有機光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒による 脂肪族アルケンのヒドロアルコキシ化反応の開発	20
第二章 光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒による 脂肪族アミンの γ -アミノ C(sp ³)-H 官能基化反応の開発	74
第三章 有機光酸化還元触媒によるスルホンアミドの 脱炭酸型アルキル化反応の開発	161
総括	188
論文目録	189
謝辞	190

略語表

Ac	Acetyl
Ar	Aryl
BDE	Bond Dissociation Energy
Bn	Benzyl
Boc	<i>tert</i> -Butoxycarbonyl
BOM	Benzyloxymethyl
bpy	2,2'-Bipyridyl
Bu	Butyl
Bz	Benzoyl
CAN	Ceric Ammonium Nitrate
Cbz	Carbobenzoxy
Cy	Cyclohexyl
DCM	Dichloromethane
DG	Directing Group
DIPEA	<i>N,N</i> -Diisopropylethylamine
DMF	<i>N,N</i> -Dimethylformamide
DMSO	Dimethyl Sulfoxide
dtbbpy	4,4'-Di- <i>tert</i> -butyl-2,2'-bipyridine
e	Electron
EDA	Electron-Donor-Acceptor
EDG	Electron Donating Group
Et	Ethyl
EWG	Electron Withdrawing Group
HAT	Hydrogen Atom Transfer
HFIP	1,1,1,3,3,3-Hexafluoro-2-propanol
HOMO	Highest Occupied Molecular Orbital
iPr	Isopropyl
LED	Light Emitting Diode
LG	Leaving Group
Me	Methyl
Mes	Mesityl
MHAT	Metal-hydride Hydrogen Atom Transfer
MOM	Methoxymethyl
NMR	Nuclear Magnetic Resonance
Nu	Nucleophile
ORPC	Oxidative Radical–Polar Crossover

PC	Photocatalyst
PFBI	Perfluorobenziodoxole
Ph	Phenyl
Phth	Phthaloyl
POX	Phenoxazine
ppy	2-Phenylpyridinato
Pr	Propyl
PTH	Phenothiazine
RPC	Radical Polar Crossover
SCE	Saturated Calomel Electrode
SET	Single Electron Transfer
TBS	<i>tert</i> -Butyldimethylsilyl
TEMPO	2,2,6,6-Tetramethylpiperidine 1-Oxyl
Tf	Trifluoromethanesulfonyl
THF	Tetrahydrofuran
THP	2-Tetrahydropyranyl
TMS	Trimethylsilyl
Ts	Toluenesulfonyl
TTF	Tetrathiafulvalene

序論

第一節 カルボカチオン種を用いた炭素-ヘテロ原子結合形成反応

カルボカチオン種は、 S_N1 反応に代表されるように、ヘテロ原子求核剤と反応することで炭素-ヘテロ原子結合形成反応を可能にする重要な反応中間体である。

1920 から 30 年代にかけて、Meerwein、Ingold、Whitmore らによる一連の先駆的な研究を通じて、カルボカチオンが有機反応における反応中間体として関与することが明らかにされた。¹ とりわけ Ingold らは、カルボカチオンの生成とそれに続く求核剤の攻撃から成る S_N1 機構を提唱し、カルボカチオンを基盤とする炭素-ヘテロ原子結合形成反応の初期的研究を行った。^{1a} さらに 1958 年に Doering らが初めてカルボカチオン種を NMR で観測し、² 1960 年代には Olah らが超酸を用いることで様々なカルボカチオン種を安定に生成・観測することに成功し、カルボカチオンの存在が実験的に示された結果、有機化学における反応中間体として広く受け入れられるようになった。³ これらの研究を契機として、現在に至るまで、カルボカチオンを活用した炭素-ヘテロ原子結合形成反応が数多く開発されてきた。一方で、カルボカチオンの生成手法は反応開発における重要な課題であり続けている。一般に、カルボカチオンの発生方法は、1) 基質から直接カルボカチオンを発生させる手法と 2) 基質から炭素ラジカルを経由してカルボカチオンを発生させる手法に大別され、これまでに多くの反応例が報告されている。

1) 基質から直接カルボカチオンを発生させる手法

基質から直接カルボカチオンが生成する手法は、(i)炭素-ヘテロ原子結合のヘテロリシス⁴ と (ii) π 結合の求電子的活性化⁵ の二つに大別される (Figure P1)。(i)炭素-ヘテロ原子結合のヘテロリシスでは、ハロゲン化アルキルやアルコールなどの基質が、強力なブレンステッド酸またはルイス酸により活性化され、結合のヘテロリシスが起こり、カルボカチオン種が生成する。(ii) π 結合の求電子的な活性化を経る経路は、アルケンなどの π 結合を有する基質にプロトンが付加することで、対応するカルボカチオン種が生成する。

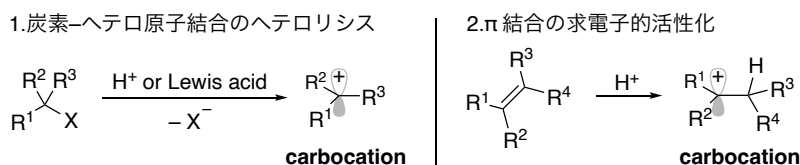


Figure P1. 基質から直接カルボカチオンが生成する手法

本カルボカチオン発生法は、1900 年代前半より利用されてきた古典的手法である。近年では、研究の進展に伴い、不安定なカルボカチオン種を精密に制御し、求核剤との反応による触媒的なエナンチオ選択的な炭素-ヘテロ原子結合形成も達成されている。⁶ しかしながら、基質の活性化に必要な酸はその強力さ故に、官能基許容性の低下を招き、多様な官能基

が共存する医薬品・天然物合成への応用を阻んでいる。近年、超臨界状態の二酸化炭素中において、強酸条件を用いることなくハロゲン化アルキルからカルボカチオン種を生成し、アルコールなどの求核剤と反応させる手法が報告されている。⁷さらに、レーザーフラッシュフォトリシスを用いた炭素-ヘテロ原子結合のヘテロリシスを介するカルボカチオン生成も知られている。⁸

2) 基質から炭素ラジカルを経由してカルボカチオンを発生させる手法

基質から直接カルボカチオン種を生成するためには過酷な反応条件が必要とされることから、基質から炭素ラジカルを経由し、カルボカチオンを生成する手法が注目を集めている。具体的には、1)ラジカルカチオン種のメソリティック開裂反応と 2)酸化的ラジカル-極性交差 (Oxidative Radical-Polar Crossover, ORPC) 反応の二つが挙げられる (Figure P2)。メソリティック開裂は基質を一電子酸化することで生じたラジカルカチオン種が結合開裂を起こすことで、ラジカル種とカルボカチオン種が生成する。ORPC 反応は基質から発生させた、アルキルラジカルの一電子酸化によってカルボカチオン種が生成する。これらの過程では、強酸の代わりに一電子移動で基質を活性化することで、古典的な手法と比較して、温和な反応条件と高い官能基許容性を実現している。

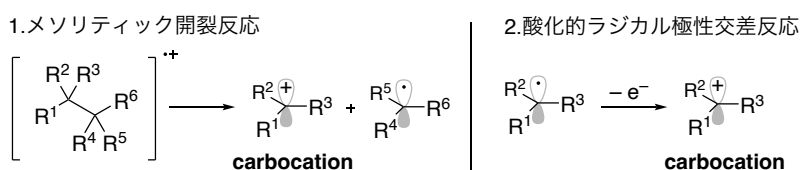


Figure P2. 基質から炭素ラジカルを経由してカルボカチオンが発生する手法

第二節では、具体的なラジカル反応を介するカルボカチオン発生と求核剤との反応への適用を示す。

第二節 ラジカル反応を介するカルボカチオン発生と反応への適用

1)メソリティック開裂によるカルボカチオン種の発生

1973 年、Trahanovsky らは、1,2-ジフェニルエタンと酸化剤の硝酸アンモニウムセリウム (IV) (CAN) と反応させることで、ベンズアルデヒド、ベンジルアルコールと硝酸ベンジルが得られることを見出している (Figure P3)。^{9a} この結果は、基質が一電子酸化を受けてラジカルカチオン種となった後、メソリティック開裂を経て、ベンジルカチオンおよびベンジルラジカルが生成することを示している。

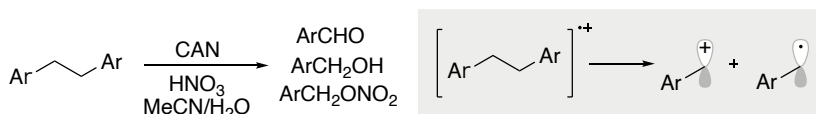


Figure P3. メソリティック開裂によるカルボカチオンの生成を活用した反応

この報告を起点として、メソリティック開裂によるカルボカチオンの発生とアルコールを中心とした求核剤との反応が数多く報告された。⁹Knowles らは近年、光酸化還元触媒存在下でアルコキシアミン (1) を一電子酸化し、安定な TEMPO の生成を駆動力とするメソリティック開裂により、従来困難であった安定化されていないカルボカチオン種を触媒的に発生させる手法を報告している (Figure P4)。^{10a}発生したカルボカチオン種はアルコール、アミンなどの求核剤との結合形成に活用された。¹⁰

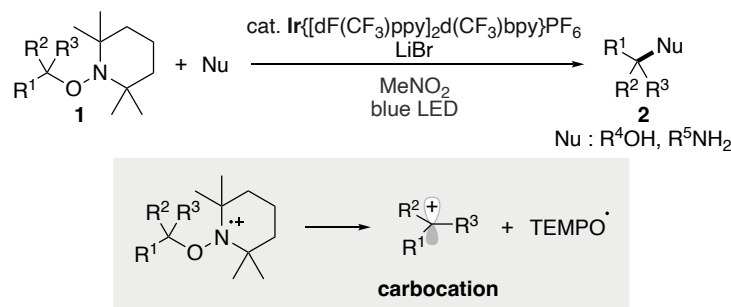


Figure P4. TEMPO の生成を駆動力とするカルボカチオン種の生成

2) 酸化ラジカル-極性交差 (Oxidative Radical-Polar Crossover, ORPC) によるカルボカチオン種の発生

酸化ラジカル-極性交差 (Oxidative Radical-Polar Crossover, ORPC) 反応の起源は 1902 年に Hofer および Moest によって報告された電解酸化反応に遡る (Figure P5)。^{11a}この電解反応では、カルボン酸が陽極にて一電子酸化されて生じたアシロキシラジカルが脱炭酸を起こし、アルキルラジカルが生成する。このアルキルラジカルは、一電子酸化されることでカルボカチオン種に変換される。生じたカルボカチオン種はその後、様々な求核剤と反応することが報告されている。¹¹

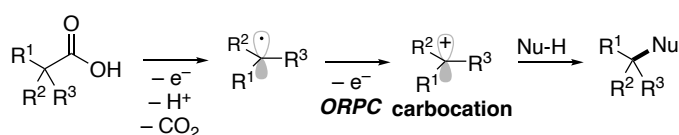


Figure P5. カルボン酸の電解酸化反応によるカルボカチオン種の生成と求核剤との反応

上記の電解反応では、反応過程で高反応性のカルボカチオン種を経由するため、求核剤による捕捉が速やかに進行する条件設定が重要であった。そのため、求核剤を過剰量共存させる手法が一般的に採用されており、また、酸化されやすい求核剤の適用には一定の工夫が求められていた。庄野、吉田らは、カルボカチオンを配位子で安定化して一旦蓄える「カチオンプール法」を開発し、求核剤を後入れできるように改良した。これにより、カルボカチオン源よりも酸化されやすい求核剤も利用できるようになった。¹²さらに近年、Baran らは Hofer-Moest 反応の反応条件を精査・改良することで、求核剤の当量を大幅に低減しつつ、副反応を抑制することに成功した。これにより、脂肪族カルボン酸と第一級から第三級アル

コールとの脱炭酸型クロスカップリングが可能となり、嵩高いジアルキルエーテルの合成を達成している。^{11b}

一方で、電気化学的な手法とは独立して、金属酸化剤による一電子酸化を活用したカルボカチオン種生成の手法も報告されてきた。1960 年から 70 年代にかけて、Kochi らは、Cu(II)、Co(III)、Pb(IV)などの金属塩を酸化剤として用いて、カルボン酸から脱炭酸反応を経てカルボカチオン種を発生できることを報告している。¹³ この反応でも同様に、カルボン酸由来のアルキルラジカルが生じ、続く一電子酸化によりカルボカチオン種へと変換され、水などの求核剤との反応が進行することが示された。

1993 年に Lee-Ruf らは、ハロゲン化アルキルの光開裂によってカルボカチオン種が発生することを報告している。¹⁴ 紫外線照射によって、炭素-ハロゲン結合のホモリシスが行われ、アルキルラジカルとハロゲン原子が生じる。続いて、アルキルラジカルからハロゲン原子に一電子移動が起こり、カルボカチオン種が生じる。生じたカルボカチオン種は水やアルコールによって捕捉され、炭素-ヘテロ原子結合が形成される。

なお、1993 年の Murphy らの報告にて、Radical-Polar Crossover (RPC) は明確に定義づけられた。^{15a} Murphy らは、分子内にアルケンを有するジアゾニウム塩 (**3**) と過剰量のメタノールを触媒量のテトラチアフルバレン (TTF) 存在下反応させると、アルケンのアリールアルコキシ化が進行し、ベンゾフラン環を含むジアルキルエーテル (**4**) を与えることを見出した (Figure P6)。本反応では、TTF が電子移動触媒として機能している。TTF から基質への一電子移動によりアルキルラジカルが生成し、生成したアルキルラジカルが TTF ラジカルカチオンと再結合することでアルキルスルホニウム種を与える。このスルホニウム種はカルボカチオン等価体としてアルコールによる加溶媒分解を受け、**5** を与える。

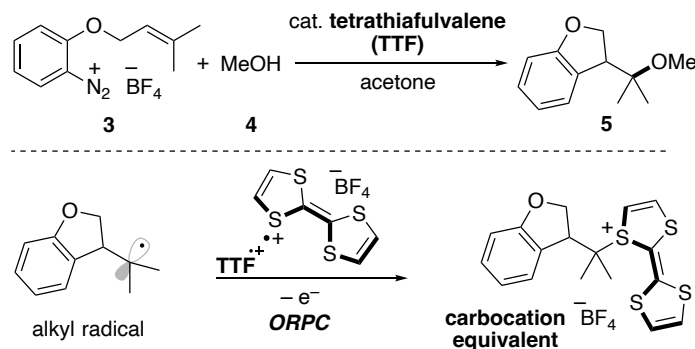


Figure P6. TTF 触媒を用いた RPC 反応によるエーテル合成

Murphy らは、アルキルラジカルがカルボカチオン種へと変換される過程を RPC として提唱した。その後も、Murphy らによって TTF を用いた一電子移動を基盤とする RPC 型の変換反応が精力的に開発され、様々なカルボカチオン等価体の生成とアルコール、アミンなど

を求核剤として用いた結合形成反応が報告されてきた。¹⁵ しかしながら、TTF の還元力が低く、利用できるラジカル源はジアゾニウム塩のような還元されやすい分子に限られていた。

第三節では近年見出されている、光酸化還元触媒による ORPC 反応を活用した反応について示す。

第三節 光酸化還元触媒を活用した ORPC 反応によるカルボカチオン発生と反応への応用

光酸化還元触媒は、光エネルギーを一電子移動またはエネルギー移動を介して化学エネルギーへと変換することができ、熱エネルギーでは困難であった反応を可能にする。¹⁶ 光励起された光酸化還元触媒は基底状態と比較して強力な一電子還元剤および酸化剤として働くことが知られている。近年、光酸化還元触媒を ORPC に活用することで、利用できるラジカル源とラジカル種は大幅に拡張された。¹⁷ さらに、アルケンへのラジカル付加、水素原子移動や開裂反応のような様々なラジカル反応と ORPC 反応を組み合わせることで、多岐にわたる分子変換反応が開発された。代表的な反応形式ごとに後述する。(Figure P7)。

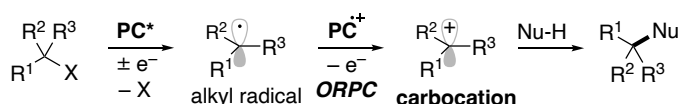


Figure P7. 光酸化還元触媒の一電子移動を活用した ORPC 反応による炭素-ヘテロ原子結合の形成

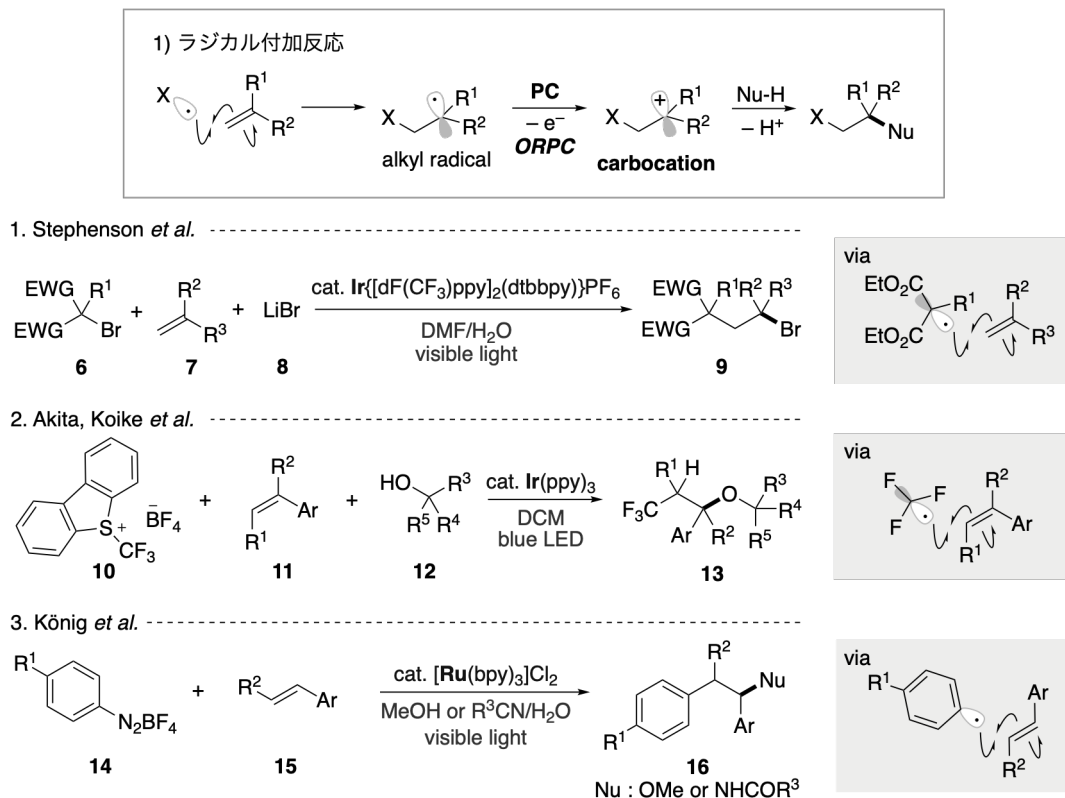


Figure P8. ラジカル付加によるアルキルラジカルの生成とカルボカチオン種の発生

光酸化還元触媒を用いた ORPC の反応形式で最も多いのが、アルケンへのラジカル付加と ORPC 反応を組み合わせたアルケンの二官能基化である。光酸化還元触媒からラジカル前駆体への一電子移動により生成したラジカル種をアルケンへと付加させた後、生成したアルキルラジカルがカルボカチオン種へと一電子酸化され、様々な求核剤と反応する (Figure P8)。付加するラジカル種およびカルボカチオン種と反応する求核剤には違いが見られる。

Stephenson らは、臭化アルキル (6) をラジカル源、臭化物イオン (8) を求核剤とするアルケンのアルキル臭素化反応を報告している (Figure P8.1)。¹⁸ 穂田、小池らは、梅本試薬 (10) を一電子還元することで生じるトリフルオロメチルラジカルをビニルアレーン (11) へ付加させて、生成したカルボカチオンをアルコール (12) で捕捉することで官能基化されたジアルキルエーテル (13) の合成に成功している (Figure P8.2)。^{19a} 続けて、穂田、小池らは、生じたカルボカチオン種に対して、アセトニトリル/水^{19b}やカルボン酸^{19c}を求核剤として反応させ、アミドやエステルの合成に応用している。さらに König らは、アリールジアゾニウム塩 (14) をアリールラジカル源として本反応形式に利用できることを見出した。生じたカルボカチオン種は Ritter 反応やアルコキシ化反応へと応用可能であることを示している (Figure P8.3)。²⁰

これらの先駆的な報告をもとに、様々なラジカル源と求核剤を組み合わせたアルケンの二官能基化反応が報告され、ORPC 反応のコンセプトは大幅に拡張された²¹。最近では、アレニルラジカル^{22a}やジアゾメチルラジカル^{22b}などの官能基を有する複雑なラジカル種の導入例や、ヘテロ環を含む複雑な環形成^{23,24}も報告されている。

光酸化還元触媒による一電子移動により生じたラジカル種を水素原子移動に利用し、生成したアルキルラジカルをカルボカチオンへと変換して求核剤と反応させることで、位置選択的な sp^3 炭素—水素結合の官能基化にも応用されている (Figure P9)。

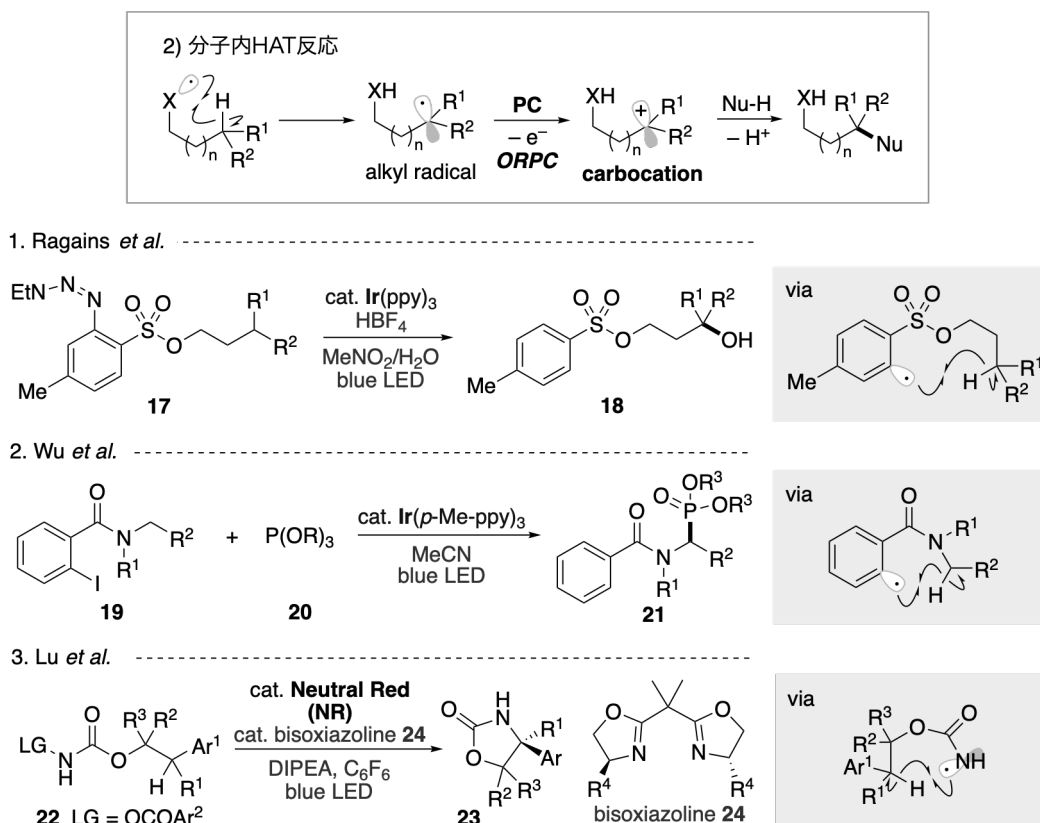


Figure P9. 分子内水素原子移動によるアルキルラジカルの生成とカルボカチオン種の発生

Ragains らは、Tz^o (アリールトリアゼン) スルホン酸エステル (**17**) を配向基として用いて、遠隔位の炭素(sp³)-水素結合ヒドロキシ化を達成している (Figure P9.1)。本反応では **17** から生じるアリールラジカルによる HAT 反応を活用することで、遠隔位の第三級炭素-水素結合または第二級、第三級ベンジル炭素-水素結合を位置選択的に切断し、酸化することに成功した。²⁵

Wu らは 2-ヨードベンゾイル保護されたアルキルアミン (**19**) と垂リン酸エステル (**20**) を基質とした α-アミノホスホン酸エステル (**21**) の合成反応を報告している (Figure P9.2)。²⁶ 本反応ではアミンに導入された 2-ヨードベンゾイル部位から生じるアリールラジカルが窒素 α 位の水素原子を引き抜き、α-アミノアルキルラジカルが生成し、イミニウム中間体へ導かれる。本反応では効率的な分子内 HAT 反応を利用することで、通常はラジカルとの反応性が高く、達成が困難な炭素-リン結合形成を可能にした。

Lu らは、N-ベンゾイロキシカルバミン酸エステル (**22**) からオキサゾリジノン (**23**) が高い光学収率で得る反応を報告している (Figure P9.3)。²⁷ 生成したアミジルラジカルは分子内 HAT 反応を起点にして、生じたカルボカチオン種は分子内環化反応を経て、**23** を与える。キラル添加剤として用いるキラルビスオキサゾリン触媒 (**24**) は反応中間体であるカルボカチオン種との水素結合や π-π 相互作用を介して不斉環境を形成し、エナンチオ選択性を制

御していることが提唱されている。

さらに、ラジカルの開裂反応と組み合わせた手法も報告されている。2018年に Shi らは、シクロケトキシムエステル (**25**) の開環を伴った転位反応を報告した (Figure P10)。^{28a} 本反応では、**25** の一電子還元により、イミニルラジカルと芳香族カルボン酸アニオンを与える。続いて、イミニルラジカルは β -開裂を起こし、シアノアルキルラジカルを与える。生成したシアノアルキルラジカルはカルボカチオン種へと変換され、芳香族カルボン酸アニオンの求核攻撃を受けることで目的物 **26** が得られる。さらに、生成したカルボカチオン種に DMSO を反応させることでケトン合成、フェノールおよびアルコールなどの求核剤を反応させることでエーテル合成へと応用されている。^{28b-d}

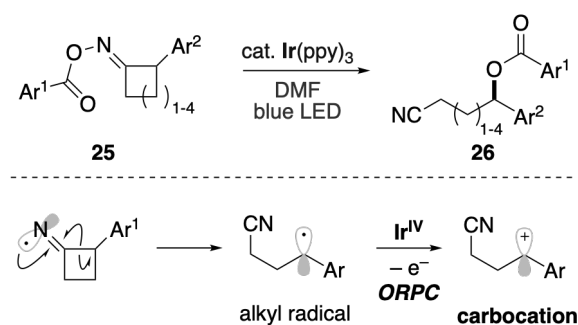


Figure P10. シクロケトキシムエステルのラジカル開環反応を介した転位反応

上述の報告では、一電子移動によって生じたラジカルがアルケンへの付加や開環を起こすため、最初に生じたラジカルとカルボカチオンの生成位置は異なる。一方で、アルキルラジカルの生成位置を保持したまま、ORPCを起こす反応形式も報告されている。

初期の報告では、炭素(sp^3)-水素結合から生成したアルキルラジカルを ORPC 過程に組み込んだ反応が報告されている。2013年に Pandey らは、酸素雰囲気下、ベンジル位炭素-水素結合のアルコキシ化反応を報告した (Figure P11)。^{29a} 本反応では、基質 **27** 中の電子豊富な芳香環が一電子酸化を受け、対応するラジカルカチオン種が生成し、続いて脱プロトン化が進行することでベンジルラジカルが発生する。生成したベンジルラジカルは、カルボカチオン種へと導かれ、基質 **27** のアルコール部位の分子内求核置換反応が進行することで、目的物 **28** が得られる。本手法の続報により、求核剤や基質の芳香環の基質適用範囲が拡張され、医薬品部位を持つ基質の官能基化に適用可能であることが示されている。²⁹

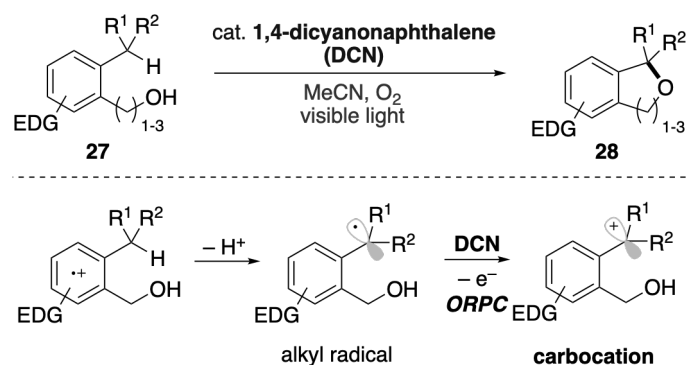


Figure P11. 有機光酸化還元触媒によるベンジル位 C-H アルコキシ化反応

系中で生じるラジカル種による分子間の水素原子移動 (HAT) 反応を経て、基質の炭素 (sp^3)-水素結合から生じるアルキルラジカルを ORPC 反応に利用した例も報告されている。

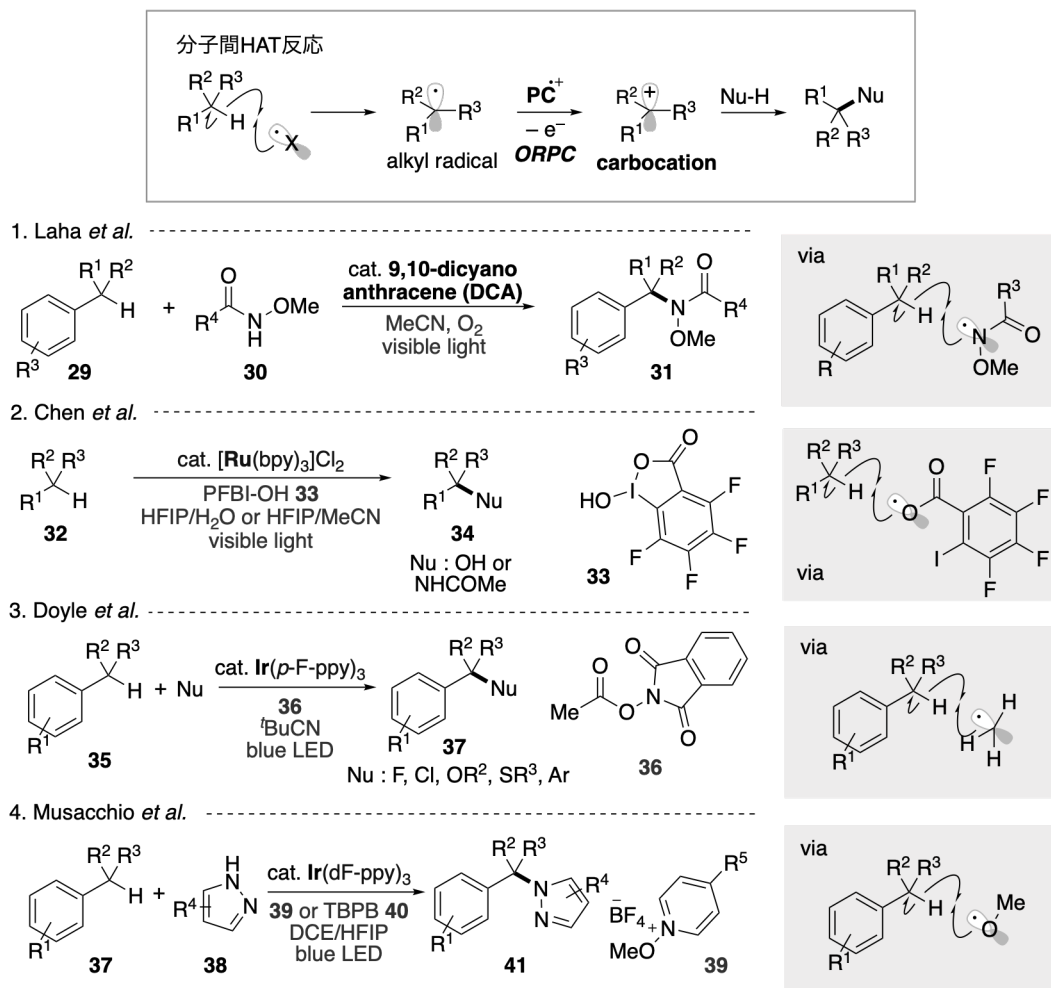


Figure P12. HAT 反応と ORPC 反応を組み合わせたカルボカチオン種の発生

2015 年に Laha らは、酸素存在下でトルエンをはじめとするアルキル置換芳香族化合物 **29** のベンジル位炭素-水素結合のアミノ化を報告している (Figure P12-1)。³⁰ 基質のアミン (**30**) から生じるアミニルラジカルが基質 **31** のベンジル位水素原子を引き抜き、アルキルラジカルを与える。続いて、ベンジルカチオンに導かれたのち、**30** による求核攻撃を受け、目的物 **31** が生成する。

2017 年に Chen らは、HAT 剤として超原子価ヨウ素試薬 (PFBI-OH) (**33**) を用いた、ベンジル位炭素-水素結合の水酸化およびアミド化反応を報告している (Figure P12-2)。³¹ **33** からアシロキシラジカルが生じ、基質 **32** の第三級またはベンジル位の炭素-水素結合から水素原子を引き抜くことで、対応するアルキルラジカルを与える。このアルキルラジカルはカルボカチオン種へと導かれ、最終的に、このカルボカチオン種に対して水による求核攻撃、またはリッター反応が進行することで、目的物 **34** が得られる。

先に示した HAT 反応と ORPC 反応を組み合わせた炭素(sp³)-水素官能基化手法では、化学量論量以上の酸化剤や、反応性の高い酸化剤を必要とする場合が多い。一方、2021 年に Doyle らは、酢酸由来のレドックス活性エステル (**36**) から生成するメチルラジカルを HAT 剤として利用することで、強力な酸化剤を必要としない手法を報告している (Figure P12-3)。^{32a} この温和な条件では、第二級および第三級ベンジル位またはアリル位の炭素-水素結合に対して、フッ素化、塩素化、水酸化、エーテル化、チオエーテル化、アジド化、アリアル化が達成された。

2023 年、Musacchio らは^{33a}、*N*-アルコキシピリジニウム (**39**) または *tert*-ブチルベンゾイルペルオキシド (TBPB) (**40**) から生じるアルコキシラジカルを HAT 剤として利用し、アルキル化されたアゾール (**41**) を得る反応を開発している (Figure P12-4)。本反応は、入手容易で、HAT 剤の置換基導入により還元電位を容易に調節できる **39** を用いることで、アゾール (**38**) をカルボカチオン種と反応させることができる。同時期に、Doyle らは同様の HAT と ORPC 反応の組み合わせにおいて、適用範囲をアミド、カルバメート、スルホンアミド、アゾールなどの多様な窒素求核剤に拡大している。^{33b}

2020 年に著者が所属する研究室では、フェノチアジン型有機光酸化還元触媒による、レドックス活性エステル (**42**) とアルコール (**43**) を基質とした炭素-酸素結合形成反応を報告している (Figure P13)。^{34a} 本反応では、**42** を一電子還元することで、アルキルラジカルが生じる。アルキルラジカルはカルボカチオン等価体である、アルキルスルホニウム種へと導かれ、アルコール求核剤と反応し、対応するジアルキルエーテル (**44**) を与える。本手法は求核剤にアルキルラジカルとカルボカチオン種を安定化するヘテロ原子や芳香環を含むアルキル鎖だけでなく、様々な脂肪族第三級アルキル鎖の導入が可能であった。また、チオール、アミド、水が求核剤として適用可能であることが示され、多種多様な炭素-ヘテロ原子結合形成に応用できる。³⁴ また、同時期に Doyle らは、同様の ORPC 過程を介したレドックス活性エステルを用いたフッ素化反応を報告している。^{34b}

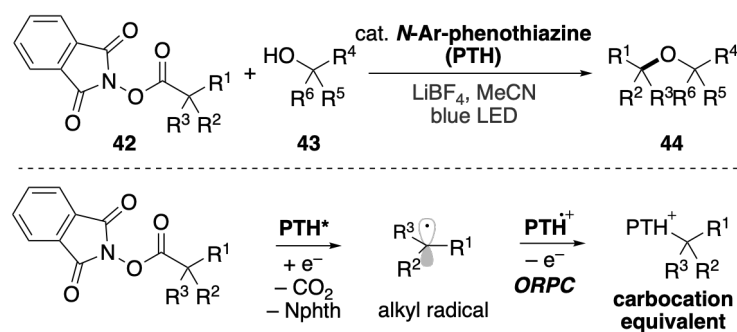


Figure P13. 有機光酸化還元触媒によるレドックス活性エステルとアルコールのジアルキルエーテル合成

上記の報告では、カルボン酸を活性エステルへ誘導して用いる必要があった。伊丹・村上らは、カルボン酸 (45) と超原子価ヨウ素試薬 (46) からヨードカルボキシレート種を系中で形成させることで、カルボン酸を直接アルキル源として用いることができる手法を見出した (Figure P14) ^{35a}。本反応では、ヨードカルボキシレート種から生じたアルキルラジカルが光酸化還元触媒による一電子酸化を受け、カルボカチオン種へと導かれる。生じたカルボカチオン種に対して超原子価ヨウ素試薬由来のカルボン酸が反応することで、目的のエステル (47) が生成する。その後、Terret らや伊丹らによって、生成したカルボカチオン種がアルコール、ジスルホンイミド、アゾール、スルホンアミドなど、多様な求核剤と反応できることが示された。 ³⁵

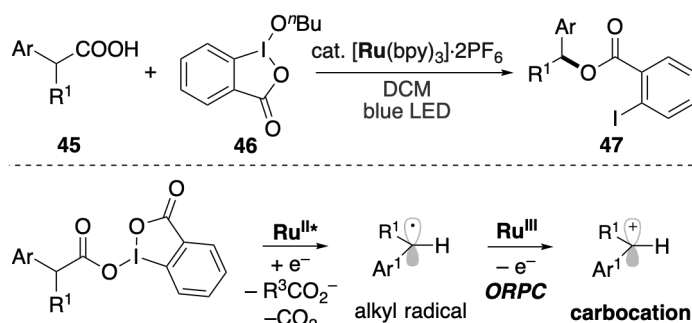


Figure P14. 光酸化還元触媒および超原子価ヨウ素試薬を用いた、カルボン酸の脱炭酸型炭素-酸素結合形成反応

2020 年に Hu らは、可視光照射下、イリジウム光酸化還元触媒を用いて電子求引性置換基を含む臭化アルキル (48) をアルキル化剤とした芳香族化合物のフリーデル・クラフツ反応を報告している (Figure P15)。 ^{36a} 本反応では、ORPC 戦略を用いることで、ルイス酸を用いた古典的な手法では困難なカルボカチオンの発生に成功している。一電子還元により基質 48 の一電子還元によりアルキルラジカルが生じ、続いて、一電子酸化を受け、カルボカチオン種に導かれる。続いて、カルボカチオン種と芳香族化合物 (49) の求電子的芳香族置換反応が進行し、目的物 50 が生成する。生じたカルボカチオン種は芳香族化合物の他、アル

コールや、フッ素アニオンが反応することが示されている。³⁶

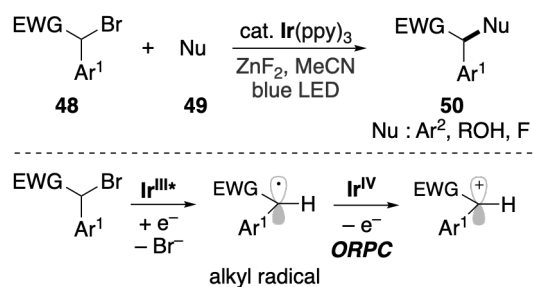


Figure P15. 光酸化還元触媒によるベンジル位 C-Br 結合の官能基化反応

Kang らは 2020 年に、カルバゾール型の有機光酸化還元触媒を用いた α,β -不飽和アミド (51) の α 位選択的求核付加反応を報告している (Figure P16)。³⁷ 本反応では、基質 51 のアルケン部位が、一電子還元、続くプロトン化を経てカルボニル α 位にアルキルラジカルが生成する。アルキルラジカルから生じるカルボカチオン種がアルコールあるいはフッ化物イオンによる求核攻撃を受けることで、目的物 53 を与える。本反応は ORPC 経路を介してカルボニル α 位にカルボカチオン種を発生でき、 α,β -不飽和アミドの極性転換を可能にし、本来の求核付加反応の位置選択性とは異なる生成物を与える。

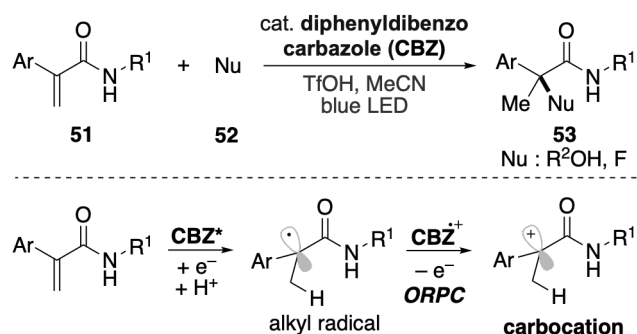


Figure P16. 有機光酸化還元触媒による電子不足アルケンのヒドロ官能基化反応

本論文概要

上述のように、光酸化還元触媒による一電子酸化を介してアルキルラジカルをカルボカチオン種へと変換する ORPC 反応を活用することで、求核剤を用いた炭素-ヘテロ原子結合形成が可能となった。一方で、これまでに報告されている例の多くは、ベンジル位やヘテロ原子 α 位など、アルキルラジカルおよび対応するカルボカチオン種が比較的安定化される基質に限定されている。さらに、アルキルラジカルを発生させるために、複雑な官能基を事前に基質へ導入する必要がある場合が多い。従って、合成可能な化合物の骨格はいまだ限定的であり、入手容易な基質から多様かつ複雑な骨格を直接構築可能な ORPC 反応の開発が求められている。

このような背景を踏まえ、本論文では、光酸化還元触媒を用いた ORPC 反応を基盤とし、触媒的なカルボカチオン等価体生成を活用した炭素-ヘテロ原子結合形成反応を開発した。これらの反応により、アルキルラジカルおよび対応するカルボカチオン種の安定化に依存しない炭素-ヘテロ原子結合形成が可能となった（第一章、第三章）。また、複雑な官能基を事前に導入することなく、入手容易な基質から直接的に多様な骨格構築を行うことが可能となった（第一章、第二章）。

第一章 有機光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒による脂肪族アルケンのヒドロアルコキシ化反応の開発

第一章では、可視光照射下、フェノチアジン有機光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒の協働触媒によるアルコールを用いた脂肪族アルケンのヒドロアルコキシ化反応を示す (Figure P17)。³⁸ 本反応は、1)系中で生成するコバルトヒドリド種による金属ヒドリド水素原子移動 (MHAT) 反応が進行し、アルケン (54) からアルキルラジカルが生成する 2)アルキルラジカル等価体であるアルキルコバルト(III)種が光酸化還元触媒により一電子酸化され、カルボカチオン等価体のアルキルコバルト(IV)種に変換される 3)カルボカチオン等価体とアルコール (55) が反応して目的物 56 を与える。本手法では用いるブレンステッド酸触媒は弱酸であり、従来法と比較して脂肪族アルケンのヒドロアルコキシ化を温和な条件で実現できた。結果、酸による分解が引き起こされるアセタール、Boc 保護されたアミンや医薬品骨格を含む基質を適用することができた。

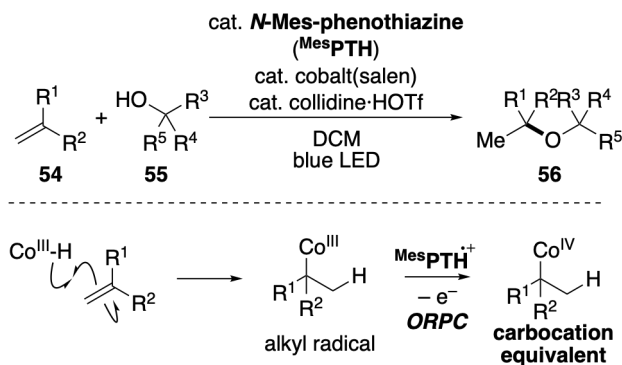


Figure P17. 有機光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒による脂肪族アルケンのヒドロアルコキシ化反応

第二章 光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒による脂肪族アミンの γ -アミノ C(sp³)-H 官能基化反応の開発

第二章では、第一章で見出した光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒からなる協働触媒系とビニルスルホニル基を活用することで、アルキルアミンからアゼチジンおよび γ 位官能基化されたアミンを合成する手法を示す (Figure P18)。³⁹ 本反応では、1)基質57におけるビニルスルホニル基由来の電子不足ラジカルを利用した1,6-HATにより窒素 γ 位にアルキルラジカル種が生じる 2)光酸化還元触媒により、アルキルコバルト(III)種は一電子酸化され、アルキルコバルト(IV)種に導かれる 3)分子内求核置換または外部求核剤による求核置換反応により目的物が生成する。本手法は、入手容易なアルキルアミンを基質として、アゼチジンの合成に加え、アミン γ 位C(sp³)-H結合のアルコキシ化、アミノ化、ならびにアリール化が可能になった。

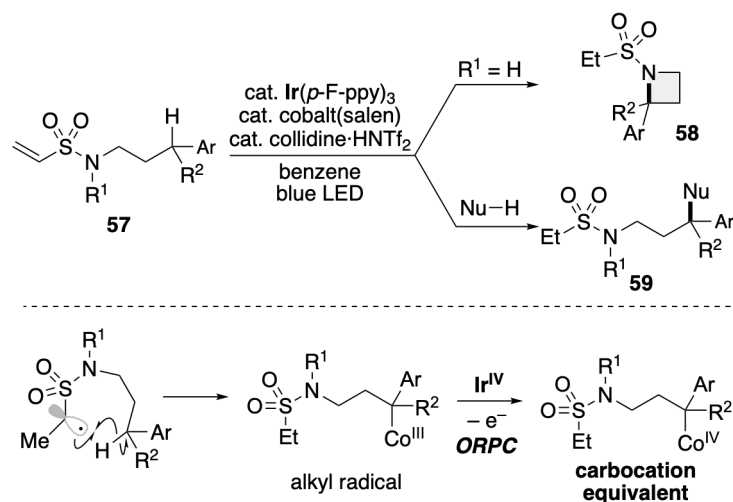


Figure P18. 光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒による脂肪族アミンの γ -アミノ $C(sp^3)$ -H 官能基化反応

第三章 有機光酸化還元触媒によるスルホンアミドの脱炭酸型アルキル化反応の開発

第三章では、可視光照射下、フェノチアジン有機光酸化還元触媒を用い、レドックス活性エステル (60) とスルホンアミド (61) との脱炭酸型クロスカップリングが進行することを示す (Figure P19)。⁴⁰本反応では、1)光励起されたフェノチアジン触媒による一電子移動により60からアルキルラジカルが生成する 2)アルキルラジカルがフェノチアジン触媒のラジカルカチオンにより、カルボカチオン等価体へ導かれる 3)61とカルボカチオン等価体が反応し、*N*-アルキル化が進行する。本手法により、強酸を用いない温和な条件で嵩高いアルキル鎖が導入されたスルホンアミド (62) の合成が達成できた。

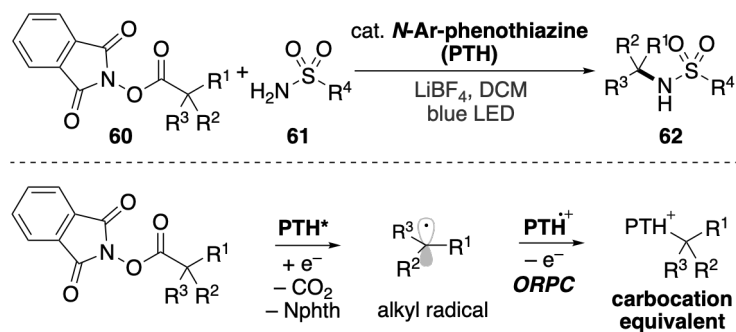


Figure P19. 有機光酸化還元触媒によるスルホンアミドの *N*-アルキル化反応

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第一章 有機光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒による脂肪族アルケンのヒドロアルコキシ化反応の開発

第一節 研究の背景

ジアルキルエーテルは医薬品・天然物に見られる重要な構造の一つである。ジアルキルエーテル構造の最も単純な構築法の一つとして、アルケンのマルコフニコフ型ヒドロアルコキシ化が挙げられる。しかし、脂肪族アルケンのように HOMO 準位が低い基質では、炭素-炭素二重結合を二電子的に活性化するために、硫酸 ($\text{pK}_a = -2.5$ in DCE) に代表される強力なブレンステッド酸を必要とする場合が多い。¹ また、 π 酸性を有する遷移金属触媒を用い、金属中心がアルケンの π 結合へ配位することで二重結合を活性化し、続くアルコールの付加を促進する手法も開発されてきた (Figure 1-1)。² しかしながら、これらの手法はいずれも強酸条件や高いルイス酸性を有する金属種に依存するため、分子内に多様な官能基を有する医薬品や天然物合成への応用には制約が残されていた。

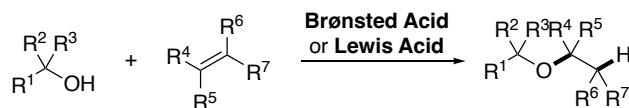


Figure 1-1. アルケンのヒドロアルコキシ化

第二節 着想の経緯

コバルトは多様な原子価状態を取り得る遷移金属であり、それぞれの原子価状態が特有の化学的性質を示すことが知られている。本研究では、以下の三点に着目した (Figure 1-2)。

まず、低原子価の Co(I) 種はプロトンと反応して Co(III)-H 種を形成する。³ この過程は電気化学的な水分解反応における重要な素反応として知られており、形式的にはプロトンがヒドリドへと極性転換される反応として捉えることができる。

次に、Co(III)-H 種は、脂肪族アルケンを含む種々のアルケンに対して金属ヒドリド水素原子移動 (Metal-hydride Hydrogen Atom Transfer, MHAT) 反応を起こし、アルキルラジカル種と Co(II) 種、あるいはアルキルコバルト(III) 種を生成する。⁴ この MHAT 反応は発熱的に進行し、アルケンからアルキルラジカルを生成することができ、向山水和反応に代表されるラジカル反応を介する分子変換に展開されてきた。

加えて、アルキルコバルト(IV) 種はカルボカチオン等価体として振る舞い、求核剤との置換反応を起こすことが知られている。⁵ アルキルコバルト(III) 種を化学的または電気化学的に一電子酸化することで対応するアルキルコバルト(IV) 種へと変換でき、その化学的性質および反応性について多くの研究がなされてきた。

これら三つの特性は、これまでそれぞれが独立した触媒反応として報告されているものの、単一の触媒サイクル内で連続的に進行する例は報告されていない。この点に着目し、本研究では可視光駆動型の光酸化還元触媒を用いることで、プロトンおよび電子移動を精密に制御し、Co(I) から Co(IV) に至る原子価の変換を伴う反応を単一の触媒サイクル内で連結する反応設計を着想した。これにより、強酸を用いることなく、原子効率に優れたマルコフニコ

フ型ヒドロアルコキシ化反応が実現可能になると考えた。

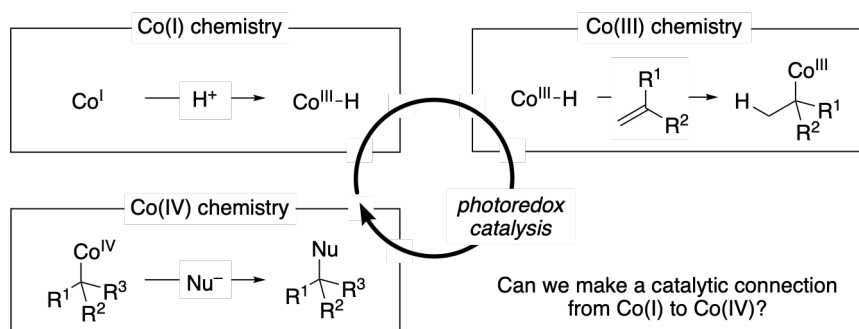


Figure 1-2. コバルトの各原子価特性とそれらの触媒的な連結

第三節 作業仮説

著者はコバルト触媒の知見をもとに、光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒の協働触媒システムの作業仮説を確立した (Figure 1-3)。可視光励起された光酸化還元触媒 (A) は高い還元力を持ち (B)、Co(II) (C) に一電子移動を引き起こす。この一電子移動により、Co(I)、光酸化還元触媒のラジカルカチオンを含むラジカルイオン対 (D) が形成する。次に、ブレンステッド酸が Co(I) と反応し、Co(III)-H (E) と光酸化還元触媒のラジカルカチオン (F) を与える。E とアルケン (2) による MHAT 反応により、Co(II) (G) とアルキルラジカル (H) が得られる。その後、F による I の一電子酸化により、カルボカチオン等価体であるアルキルコバルト(IV)種 (J) が生成する。最後に J とアルコール求核剤 (1) の求核置換反応が起こり、目的のジアルキルエーテル (3) と Co(II) (C) が得られる。本反応系では、光酸化還元触媒を介した一電子移動によってコバルト触媒の原子価の変換が効率的に制御され、各段階で必要な活性種が触媒的に供給される点が特徴である。したがって、本協働触媒系の反応効率は光酸化還元触媒の選択に大きく依存すると考えられた。本触媒サイクルには、Co(II) 種の一電子還元 ($E_{\text{red}} = -1.31 \text{ V vs SCE}$) ^{3a} およびアルキルコバルト(III) 種の一電子酸化 ($E_{\text{ox}} = 0.39 \text{ V vs SCE}$) ⁶ が含まれるため、励起状態で高い還元力を有し、かつラジカルカチオン状態で適度な酸化力を示す光酸化還元触媒が必要であると判断した。

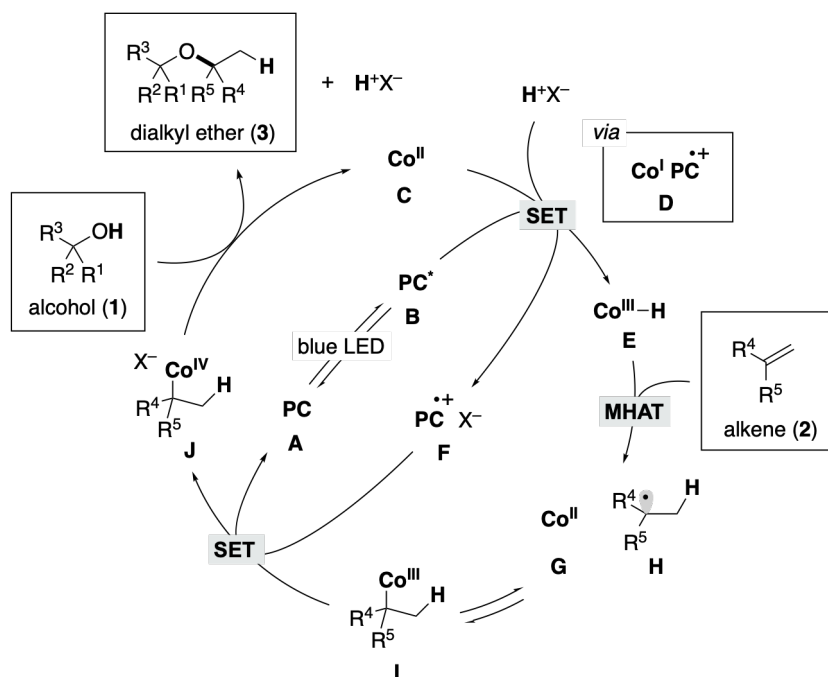


Figure 1-3. 作業仮説

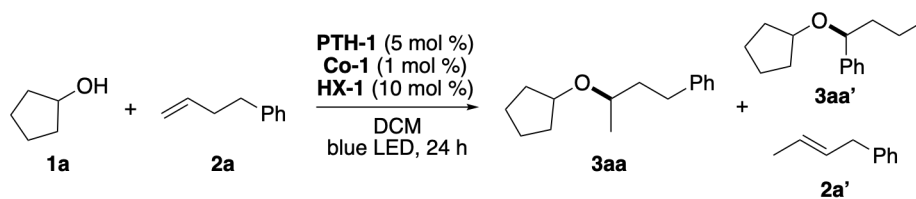
第四節 反応条件の最適化および基質適用範囲の検討

上述した作業仮説をもとに、*N*-メシチルベンゾ[*b*]フェノチアジン (PTH-1)、コバルトサロフェン錯体 (Co-1)、コリジニウムトリフラート (HX-1) を触媒量用いて駆動するハイブリッド触媒システムを構築した。シクロペンタノール (1a) と 4-フェニル-1-ブテン (2a) が可視光照射下で効率的に反応し、目的のジアルキルエーテル (3aa) を得た。同時に、ベンジルエーテル (3aa') と異性化アルケン (2a') が生成したことを確認している (Table 1-1)。

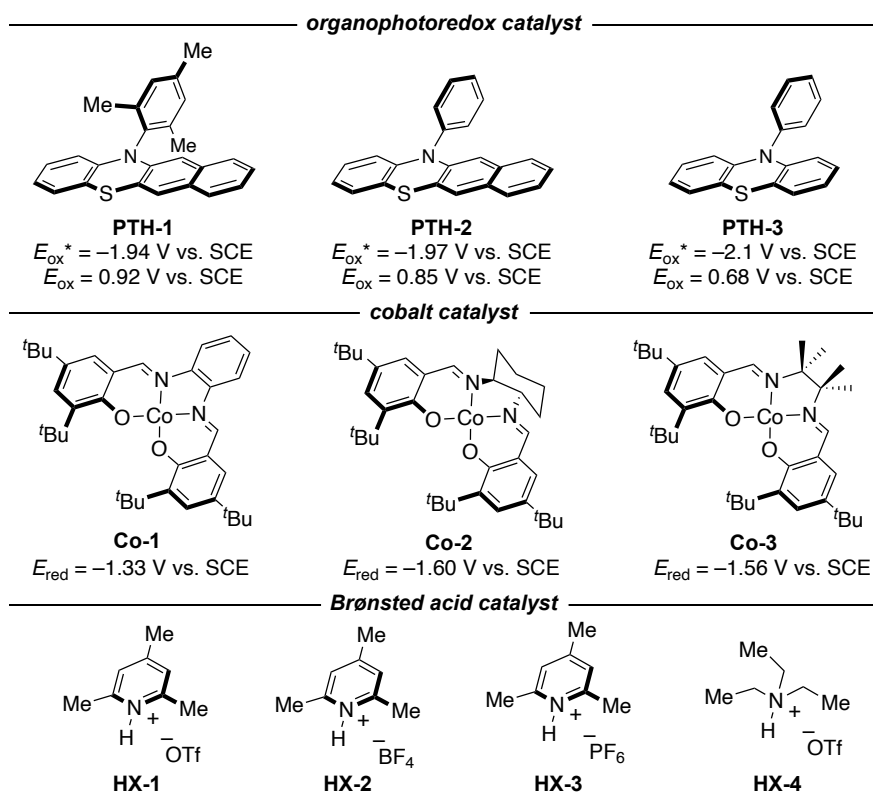
PTH-1 の酸化還元特性 ($E_{ox}^* = -1.94$ V vs SCE, $E_{ox} = 0.92$ V vs SCE) は、光酸化還元触媒として用いた場合に最も優れた反応性を示した。PTH-1 の酸化電位はサイクリックボルタメトリーと吸収波長、蛍光波長を計測することにより求めた (Figure 1-4-7)。PTH-2 では同程度の収率で目的物を与えたが (entry 2)、PTH-3 を用いた場合は収率が低下した (entry 3)。この結果は、酸化電位 ($E_{ox} = 0.85$ V vs SCE : PTH-2, $E_{ox} = 0.68$ V vs SCE : PTH-3) ^{7,8} と可視光領域の吸収波長 ($\lambda_{max} = 362$ nm : PTH-1, $\lambda_{max} = 365$ nm : PTH-2, $\lambda_{max} = 320$ nm : PTH-3)

(Figure 1-5) ^{7,8} の違いによるものと推測している。また、Ir(ppy)₃ を用いた場合も同様に高収率で目的物を得た (entry 4)。コバルト触媒に関しては Co-1 の代わりに錯体構造の異なる Co-2 および Co-3 を使用すると、2a の変換率が低くなった (entries 5,6)。ブレンステッド酸触媒では対イオンの影響が見られた。トリフラートをテトラフルオロボラートまたはヘキサフルオロホスフェートにした場合、生成物の収率が大幅に低下した (entries 7,8)。また、トリエチルアンモニウムトリフラート (HX-4) は効果がなかった (entry 9)。コントロール実験より、三種類の触媒と光照射が反応の進行に必須であった (entries 10,11)。

Table 1-1. 反応条件の最適化



Entry	Change from standard conditions	Yield of 3aa (%) ^b	Yield of 3aa' (%) ^b	Yield of 2a' (%) ^b
1	none	75 (74)	6	8
2	PTH-2 instead of PTH-1	71	14	14
3	PTH-3 instead of PTH-1	0	0	0
4	Ir(ppy) ₃ (1 mol%) instead of PTH-1	71	10	9
5	Co-2 instead of Co-1	29	0	9
6	Co-3 instead of Co-1	6	0	2
7	HX-2 instead of HX-1	17	0	5
8	HX-3 instead of HX-1	5	0	2
9	HX-4 instead of HX-1	5	0	8
10	w/o PTH-1 or Co-1 or HX-1	0	0	0
11	under dark	0	0	0



^aReaction was carried out with **1a** (0.6 mmol), **2a** (0.2 mmol), photoredox catalyst (0.01 mmol), Co catalyst (0.002 mmol), and Brønsted acid catalyst (0.02 mmol) in DCM (0.5 mL) under blue LED (450 nm) irradiation for 24 h. ^{b1}H NMR yield based on **2a**.

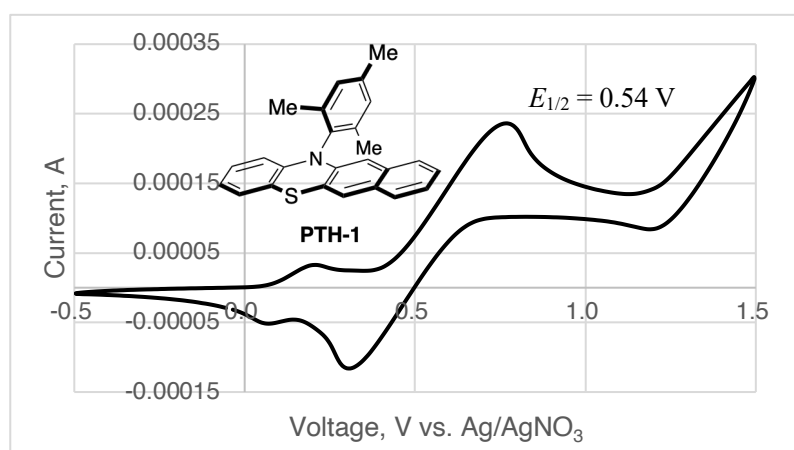


Figure 1-4. PTH-1 のサイクリックボルタンメトリー

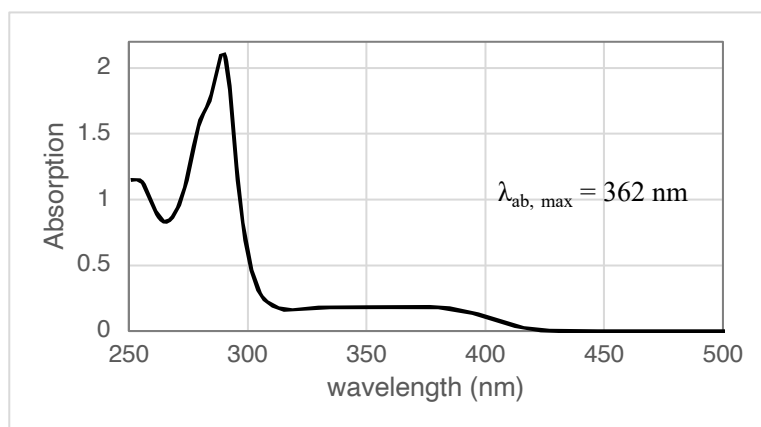


Figure 1-5. PTH-1 の UV-Vis スペクトル ^a

^a UV-Vis adsorption spectrum of organophotocatalyst **PTH-1** was measured with 40 μ M acetonitrile solution.

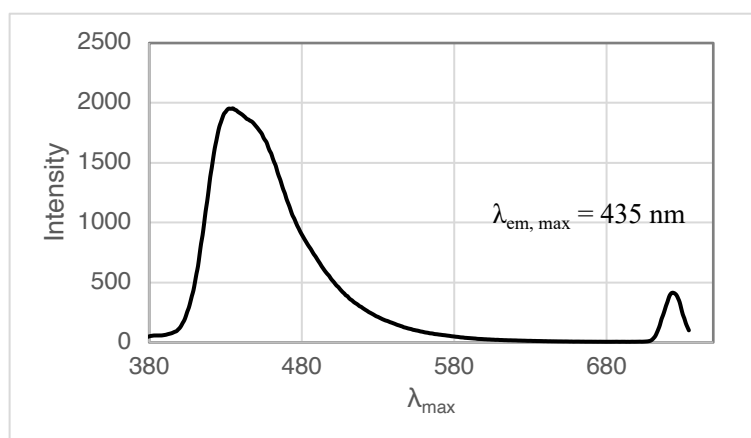


Figure 1-6. PTH-1 の 蛍光スペクトル ^a

^a Fluorescence spectrum of **PTH-1** was scanned from 372 to 734 nm after excitation at 362 nm.

	PTH-1
$E_{1/2} (^2PC^{*+}/^1PC)$ (V vs $Ag/AgNO_3$) ^a	0.54
$E_{1/2} (^2PC^{*+}/^1PC)$ (V vs SCE) ^b	0.92
$\lambda_{max,em}$ (nm)	435
$E_{S1, exp}$ (eV) ^c	2.85
$E^{0*}_{S1, exp} (^2PC^{*+}/^1PC^*)$ (V vs SCE) ^d	-1.94

Figure 1-7. PTH-1 の各パラメーター

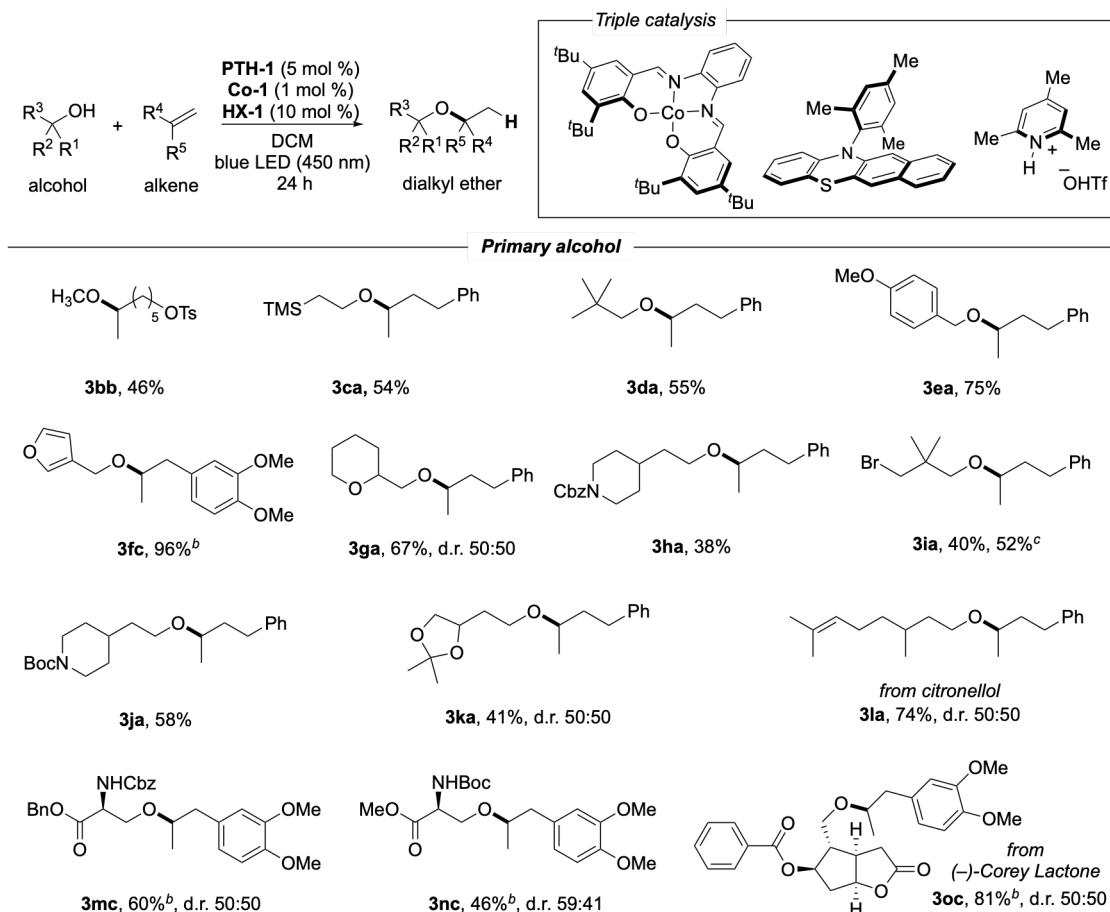
^a Determined by CV experiments. ^b $E_{1/2}$ ($Ag/AgNO_3$) (V vs SCE) = 0.38 V. ^c Singlet energies were calculated using the maximum wavelength of emission. ^d Singlet excited state reduction potentials were calculated using the singlet energies and the $E_{1/2}$.

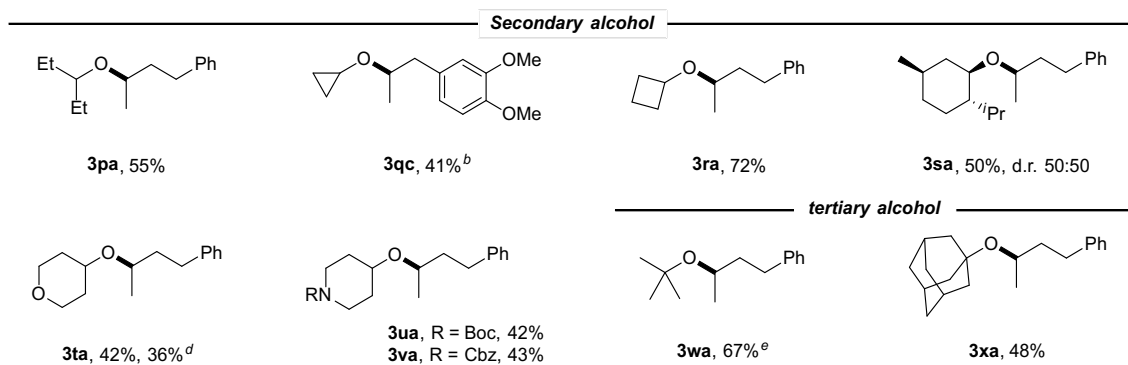
前述の検討で得られた最適条件に基づき、本反応におけるアルコール及びアルケンの適用範囲の検討を行った。

本反応条件では、様々な第一級アルコールが適用可能であった (Figure 1-8)。メタノール (3bb)、嵩高い置換基 (3ca, 3da)、電子豊富な芳香族 (3ea, 3fc)、テトラヒドロピラン (3ga)、カルバミン酸ベンジル (3ha) ハロゲン化アルキル (3ia) を構造中に有するアルコールを用いて目的のジアルキルエーテル得られた。酸に弱いカルバーメートやアセタールなどの置換基を持つ基質に関しても、分解は見られず反応が進行した (3ja, 3ka)。シトロネロールをアルコール求核剤として用いた場合、シトロネロールの三置換アルケンにヒドロアルコキシル化を受けなかった (3la)。天然物や医薬品化合物の *O*-アルキル化が可能であり、複雑な骨格を有するジアルキルエーテル (3la–3oc) を合成することができた。

鎖状、環状第二級 (3pa–3va)、嵩の高い第三級 (3wa–3xa) アルコールを用いた場合でも、同様の条件、またはわずかな条件変更を行うことで目的のジアルキルエーテルが得られた。

Figure 1-8. アルコールの基質適用範囲 ^a

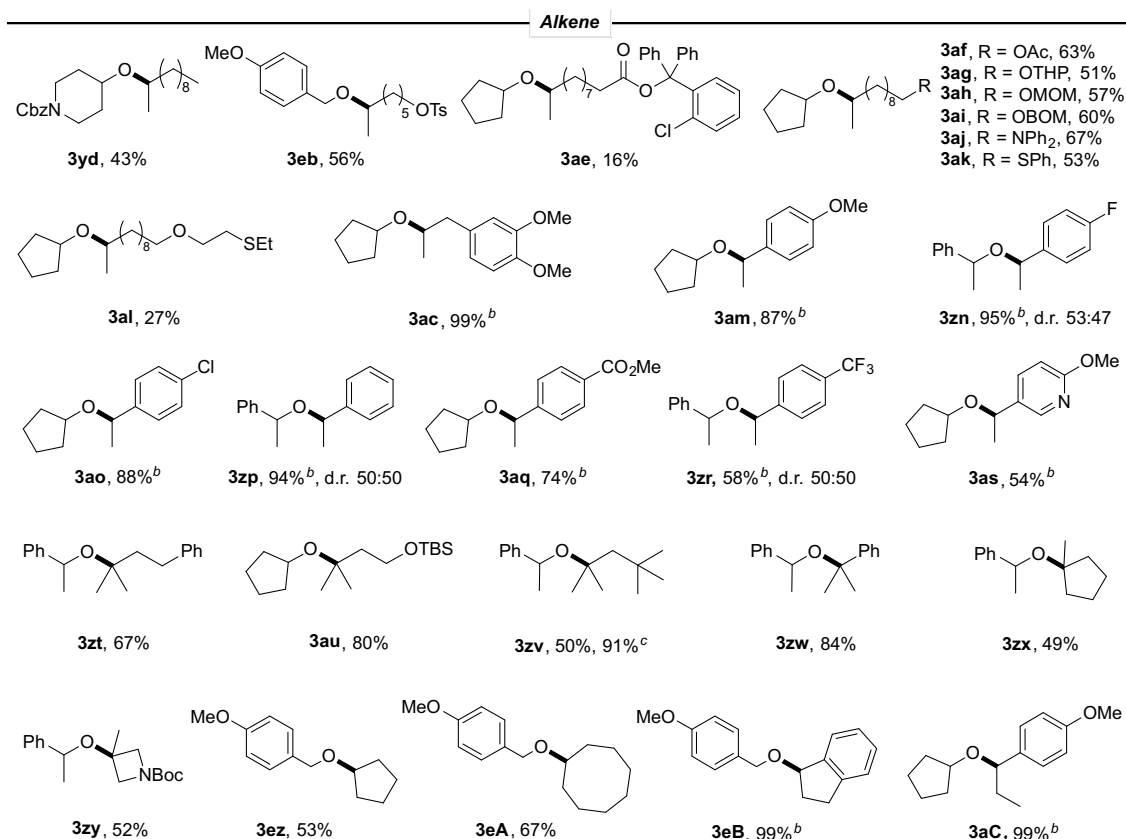




^aReaction was carried out with **1** (0.6 mmol), **2** (0.2 mmol), **PTH-1** (0.01 mmol), **Co-1** (0.002 mmol), and **HX-1** (0.02 mmol) in DCM (0.5 mL) under blue LED (450 nm) irradiation for 24 h. ^b**1** (0.2 mmol) was used. ^cIr(ppy)₃ (0.002 mmol) was used instead of **PTH-1**. ^d**1** (0.2 mmol) and **2** (0.4 mmol) were used. ^e**1** (2.0 mmol) was used.

続いて、アルケンの基質適用範囲を示す (Figure 1-9)。酸または酸化によって容易に分解する官能基をもつ基質に対しても、官能基が損なわれることなく本反応は適用可能であった (**3ae–3al**)。反応基質の中でも、3,4-ジメトキシアリルベンゼンは特に高い反応性を示した (**3ac**)。また、ビニルアレーンを基質として用いることで、ベンジルエーテルが効率よく合成できた (**3am–3as**)。本反応系に適用することで、1,1-二置換脂肪族アルケンに第三級アルキル化試薬として扱うことができ、嵩高い鎖状脂肪族鎖を持つジアルキルエーテルを合成することができた (**3zt–3zw**)。シクロペンタン (**3zx**) とアゼチジン (**3zy**) などの環状アルカンも効率よくエーテル骨格に導入することができた。加えて、内部アルケンも本反応系に適用でき、目的のジアルキルエーテルを得た (**3ez–3aC**)。

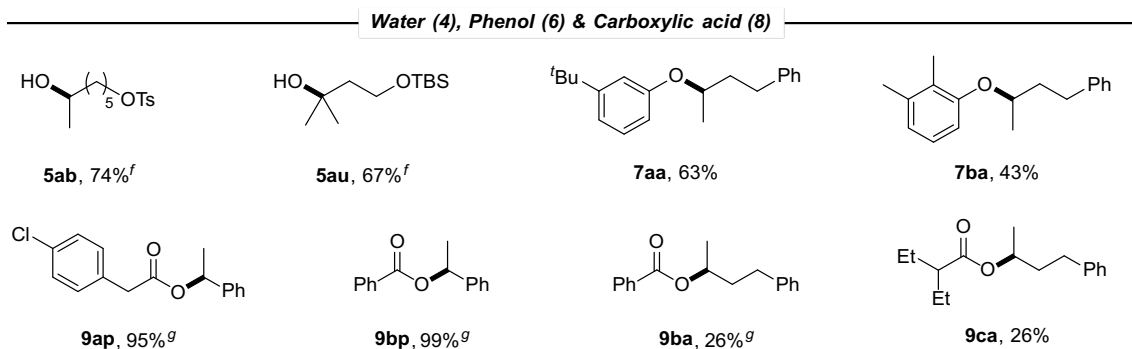
Figure 1-9. アルケンの基質適用範囲 ^a



^aReaction was carried out with **1** (0.6 mmol), **2** (0.2 mmol), **PTH-1** (0.01 mmol), **Co-1** (0.002 mmol), and **HX-1** (0.02 mmol) in DCM (0.5 mL) under blue LED (450 nm) irradiation for 24 h. ^b**1** (0.2 mmol) was used. ^cIr(ppy)₃ (0.002 mmol) was used instead of **PTH-1**.

また、本反応系では、アルコール以外の酸素求核剤に対しても適用可能であった (Figure 1-10)。末端一置換及び二置換アルケンの両方が、水の存在下で対応する第二級または第三級脂肪族アルコールに変換が可能であった (**5ab**, **5au**)。フェノール誘導体 (**7aa**, **7ba**) および脂肪族および芳香族カルボン酸 (**9ap**–**9ca**) も同様に本反応系で求核剤として用いることができた。

Figure1-10. その他求核剤の基質適用範囲.



^aReaction was carried out with **4**, **6**, or **8** (0.6 mmol), **2** (0.2 mmol), **PTH-1** (0.01 mmol), **Co-1** (0.002 mmol), and **HX-1** (0.02 mmol) in DCM (0.5 mL) under blue LED (450 nm) irradiation for 24 h. ^cIr(ppy)₃ (0.002 mmol) was used instead of **PTH-1**. ^d**1** (0.2 mmol) and **2** (0.4 mmol) were used. ^fAcetone was used instead of DCM. ^g α,α,α -Trifluorotoluene was used instead of DCM.

本反応の反応機構を明らかにすべく、機構実験を行った (Figure 1-11)。まず、重水素化実験を行った (Figure 1-11A)。求核剤としてメタノール- d_1 (**1b-D**) を用いた場合、重水素原子がアルケンの末端位置に付加した生成物 (**3bb-D**) が得られた。また、重水素化された目的物が 86 %収率で得られ、完全な重水素化は進行しなかった。これらの結果から、Co(III)-H 形成時のプロトン源は **HX-1** 由来であることがわかった。また、メタノール- d_4 (**1b-D'**) を用いた場合、 CD_3 が含まれたジアルキルエーテル (**3bb-D'**) が得られた。

さらに、アルコール求核剤による置換段階における Co-1 の役割についても検討した (Figure 1-11B)。著者らの研究室では以前、フェノチアジン触媒を用い、レドックス活性エステルから生成するアルキルラジカルを経由したアルコールの脱炭酸アルキル化反応を報告している。⁷ 当該反応では、さまざまな第三級アルキルレドックス活性エステルが適用可能であったが、第二級アルキルレドックス活性エステル **10a** を用いた場合には、目的のエーテル **11Aa** は得られなかった。これは、第二級アルキルラジカルの ORPC 反応が進行しないことが原因である。一方、**Co-1** を添加すると、目的の反応が進行し、**11Aa** を得ることができた。**Co-1** 錯体はアルキルラジカルを捕捉し、その後の ORPC 過程を促進していることが示唆された。

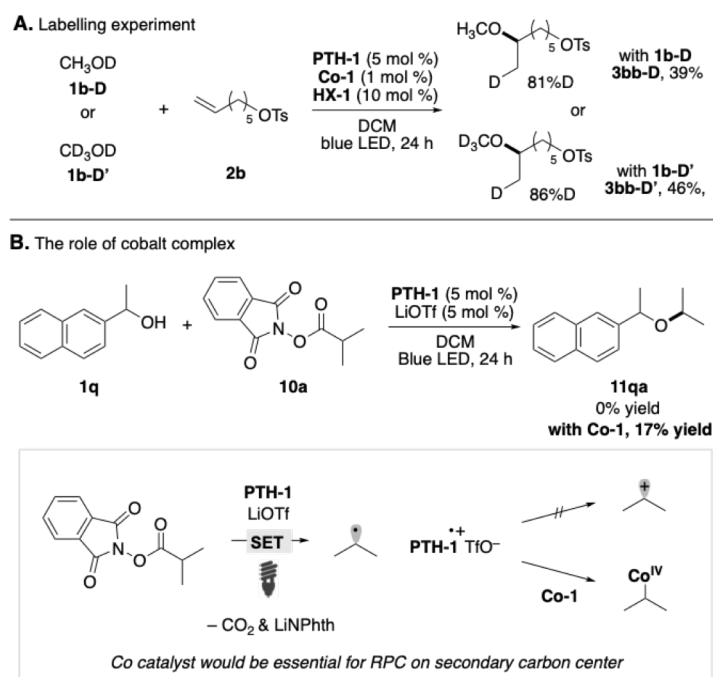


Figure 1-11. 機構研究

フェノチアジン光酸化還元触媒による一電子還元過程の詳細を検討するため、消光実験を行った (Figure 1-12)。その結果、コバルト触媒の添加により励起状態のフェノチアジン触媒が効率的に消光されることが確認された。一方、コバルト触媒に加えてブレンステッド酸触媒を添加した場合でも、消光の効率に顕著な変化は認められなかった。

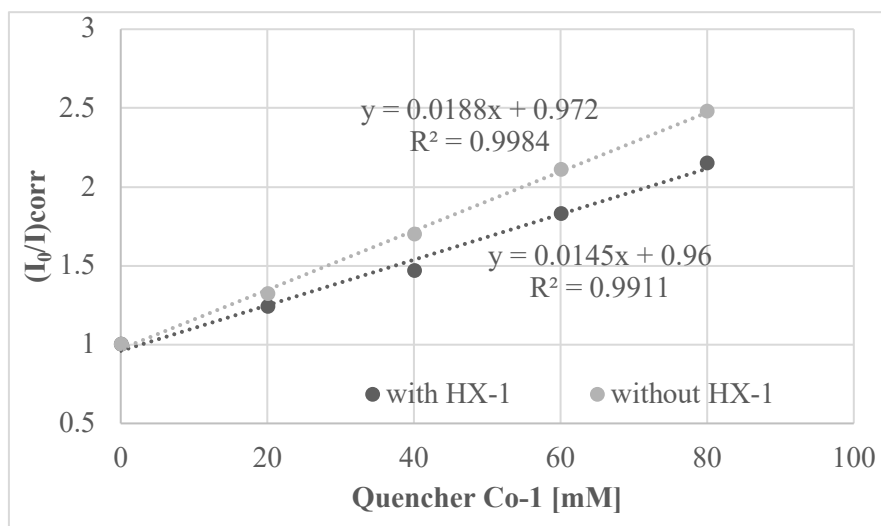


Figure 1-12. 光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒を用いた消光実験

加えて、ブレンステッド酸のみを消光剤として用いて消光実験を行った場合、イリジウム光酸化還元触媒の消光は確認されなかった (Figure 1-13)。

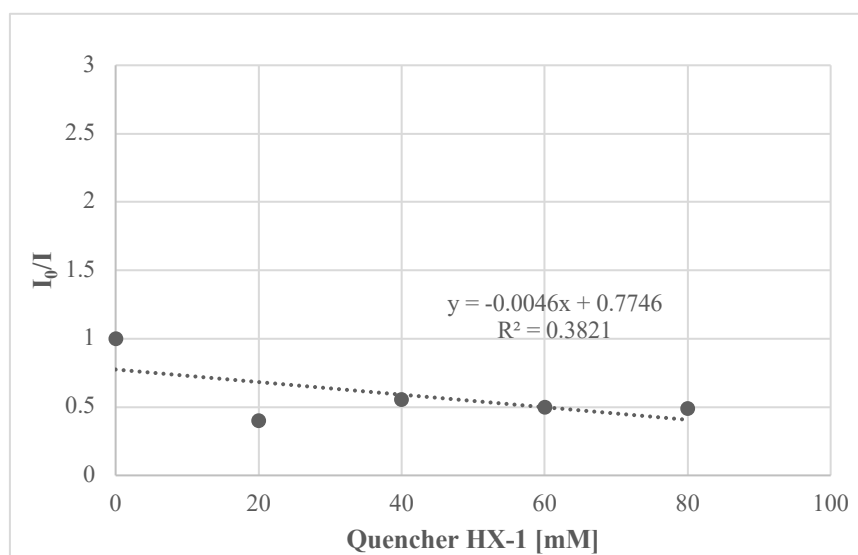


Figure 1-13. 光酸化還元触媒、ブレンステッド酸触媒を用いた消光実験

これらの結果から、励起されたフェノチアジン光酸化還元触媒は、ブレンステッド酸の関与なしにコバルト触媒を一電子還元していることが明らかとなった。

結論

著者はアルケンのマルコフニコフヒドロアルコキシ化反応を可視光駆動の光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒の協働触媒反応を開発した。三つの触媒によるプロトンと電子の精密な制御は、強酸や外部の還元剤/酸化剤を用いずに、容易に入手できるアルコールとアルケンから価値あるジアルキルエーテルを得る新しいアプローチとなる。

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実験項

Instrumentation and Chemicals

NMR spectra were recorded on a Bruker AVANCE NEO 400N spectrometer, operating at 400 MHz for ^1H NMR, 100.6 MHz for ^{13}C NMR. Chemical shift values for ^1H and ^{13}C are referenced to Me_4Si and the residual solvent resonances, respectively. Chemical shifts were reported in δ ppm. Mass spectra were obtained with JMS-T100TD (DART). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Wakosil[®] 60, 64~210 μm) was used for column chromatography. Biotage Selekt was used for purification. IR spectra were measured with a Thermo Scientific iD7 ATR Accessory for the Thermo Scientific Nicolet iS5 FT-IR Spectrometer. Melting points were measured on a Stanford Research Systems MPA100. CV measurements were recorded with a Hokuto Denko HZ-7000 potentiostat. UV-Vis absorption spectra were recorded on a Shimadzu UV-1900. Fluorescence spectra were recorded on a Shimadzu RF-6000. Kessil A160W Tuna Blue (highest blue and intensity setting) was used as a light source. TEKNOS MG9 was used as a fan.

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. Dichloromethane and acetonitrile were purchased from FUJIFILM Wako Pure Chemical Co., stored under nitrogen, and used as received. $\text{Ir}(\text{ppy})_3$ was purchased from Aldrich Chemical Co., stored under nitrogen, and used as received. LiOTf was purchased from Tokyo Chemical Industry Co., stored under nitrogen, and used as received. Cobalt catalysts **Co-1–3** were prepared by the reported procedure.¹ **PTH-2** and **PTH-3** were prepared by the reported procedure.^{2,3} **HX-2** was prepared by the reported procedure.⁴ The redox active ester **10a** was prepared by the reported procedure.⁵

Synthesis and Characterization of Organophotoredox Catalyst PTH-1

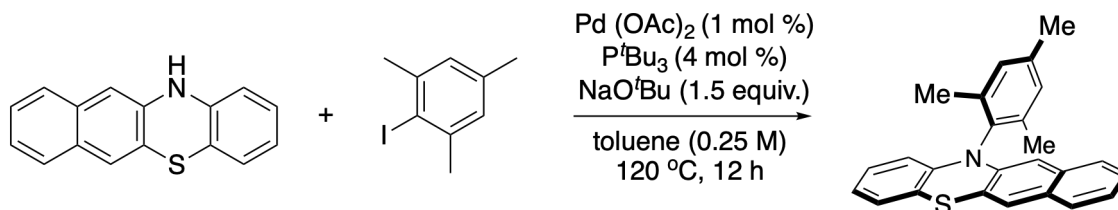
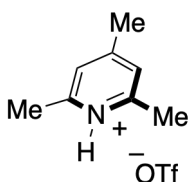


Figure S1-1. Synthesis of PTH-1.

In a glovebox, to an oven-dried vial with a stirring bar was added palladium acetate (4.5 mg, 0.02 mmol), tri-*tert*-butyl phosphine (16.2 mg, 0.08 mmol) and toluene (8 mL). After stirring at room temperature for 10 min, benzo[*b*]phenoxazine (498.7 mg, 2.0 mmol), mesityl iodide (639.8 mg, 2.6 mmol) and sodium *tert*-butoxide (288.3 mg, 3.0 mmol) were sequentially added to the reaction solution. After sealing the vial with a cap and removed from the glove box, the reaction was stirred at 120 °C overnight and quenched with NH₄Cl aq. The resultant reaction solution was extracted with ethyl acetate three times, and the combined organic layer was dried over Na₂SO₄ and filtered. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 0:100–4:96, dichloromethane/hexane) gave the coupling product **PTH-1** (173.0 mg, 0.47 mmol, 23% isolated yield). White solid. **M.p.** 240–242 °C. **IR** (neat) 743, 907, 1247, 1314, 1336, 1448, 1478, 1572, 2917, 3052 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.48 (m, 1H), 7.35 (s, 1H), 7.27 (m, 1H), 7.19–7.12 (m, 2H), 7.11 (s, 2H), 6.96 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.79 (dd, *J* = 7.2, 1.6 Hz, 1H), 6.73 (td, *J* = 7.6, 1.6 Hz, 1H), 6.11 (s, 1H), 5.93 (dd, *J* = 7.2, 1.6 Hz, 1H), 2.41 (s, 3H), 2.15 (s, 6H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 140.1, 138.6, 138.3, 137.8 (×2C), 134.9, 133.7, 130.4, 130.1, 127.1, 126.6, 126.1, 126.1, 125.8, 123.9, 121.5, 121.2, 117.9, 114.4, 108.7, 21.1, 17.8. **HRMS–DART** (*m/z*): [M+H]⁺ calcd for C₂₅H₂₂NS, 368.1467; found, 368.1469.

Synthesis and Characterization of Brønsted Acid Catalysts HX-1 and 3

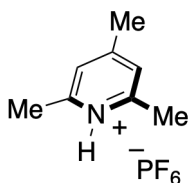
Synthesis of HX-1. To a 30 ml round bottom flask with a stirring bar was added collidine (1.05 mL, 8.0 mmol) and TfOH (1.20 g, 8.0 mmol) at 0 °C. After stirring at 0 °C for 10 min, the obtained white solid was washed with ether and dried under reduced pressure to afford collidine·HOTf (**HX-1**, 1.37 g, 5.1 mmol, 63% isolated yield).



White solid. **M.p.** 79–81 °C. **IR** (neat) 515, 638, 1029, 1155, 1224, 1242, 1286, 1639, 2974, 3080 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 14.53 (brs, 1H), 7.30 (s, 2H), 2.80 (s, 6H), 2.57 (s, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 159.3, 153.0, 125.3, 120.3 (q, *J*_{C-F} = 318.6 Hz), 22.1, 19.4. **¹⁹F NMR**

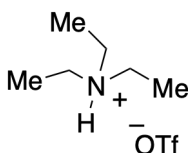
(376.5 MHz, CDCl₃) δ -78.4. **HRMS-DART** (m/z): [M-OTf]⁺ calcd for C₈H₁₂N; 122.0964, found 122.0959.

Synthesis of HX-3. To a 30 ml round bottom flask with a stirring bar was added collidine (0.66 mL, 5.0 mmol) and HPF₆ solution (20 wt%, 3.65 g) at 0 °C. After stirring at 0 °C for 10 min, the obtained white solid was washed with ether and dried under reduced pressure to afford collidine·HPF₆ (**HX-3**, 0.53 g, 2.0 mmol, 40% isolated yield).



White solid. **M.p.** 230–233 °C. **IR** (neat) 516, 712, 765, 990, 1011, 1039, 1073, 1637, 2996, 3191 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 13.35 (brs, 1H), 7.32 (s, 2H), 2.80 (s, 6H), 2.58 (s, 3H). **¹³C NMR** (100.6 MHz, D₂O) δ 160.1, 151.6, 125.1, 21.1, 18.3. **¹⁹F NMR** (376.5 MHz, CDCl₃) δ -149.7, -149.8. **HRMS-DART** (m/z): [M-PF₆]⁺ calcd for C₈H₁₂N; 122.0964, found 122.0966.

Synthesis of HX-4. To a 30 ml round bottom flask with a stirring bar was added Et₃N (1.25 mL, 9.0 mmol) in DCM (0.5 M, 6.0 mL) and TfOH (0.45 g, 3.0 mmol) at 0 °C. After stirring at 0 °C for 30 min, the organic layer was dried over Na₂SO₄ and filtered. the obtained colorless oil was washed with ether and dried under reduced pressure to afford and dried under reduced pressure to afford Et₃N·HOTf (**HX-3**, 0.46 g, 1.8 mmol, 62% isolated yield).



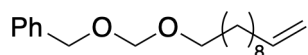
A colorless gel. **IR** (neat) 518, 638, 1028, 1158, 1224, 1239, 1279, 1477, 2821, 3059 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 8.87 (brs, 1H), 3.18 (q, J = 7.2 Hz, 6H), 1.38 (t, J = 7.2 Hz, 9H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 120.2 (q, J_{C-F} = 319.1 Hz), 46.9, 8.6. **¹⁹F NMR** (376.5 MHz, CDCl₃) δ -78.4. **HRMS-DART** (m/z): [M-OTf]⁺ calcd for C₆H₆N; 102.1277, found 102.1279.

Synthesis and Characterization of Alkenes

{[(Undec-10-en-1-yloxy)methoxy]methyl}benzene (**2i**)

Alkene **2i** was synthesized according to the modified procedure.⁶ A flask was placed under N₂ atmosphere by three cycles of evacuating and N₂ backfilling and charged with undec-10-en-1-ol (801 μ L, 4.0 mmol, 1.0 equiv.). Dry CH₂Cl₂ (10 mL) and DIPEA (1.40 mL, 8.0 mmol, 2.0 equiv.) were added and the solution was cooled to 0 °C. BOMCl (1.04 mL, 1.90 mmol, 1.9 equiv.) was added

dropwise. After stirring for 15 min, the ice bath was removed and the reaction mixture was stirred for 16 h at room temperature. The solution was diluted with CH₂Cl₂, washed with sat. aq. NaHCO₃, dried over Na₂SO₄ and the solvent was removed under reduced pressure. The oily residue was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–93:7, hexane/EtOAc) to afford the desired product **2i** (577 mg, 2.0 mmol, 50%) as a colorless oil.

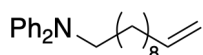


IR (neat) 697, 734, 908, 994, 1028, 1046, 1113, 1455, 2854, 2925 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.36–7.26 (m, 5H), 5.81 (m, 1H), 5.01–4.92 (m, 2H), 4.76 (s, 2H), 4.60 (s, 2H), 3.58 (t, *J* = 6.8 Hz, 2H), 2.04 (dt, *J* = 7.2, 6.8 Hz, 2H), 1.63–1.56 (m, 2H), 1.37–1.29 (m, 12H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 139.2, 138.0, 128.4, 127.9, 127.6, 114.1, 94.6, 69.2, 68.1, 33.8, 29.7, 29.5, 29.4 ($\times 2$ C), 29.1, 28.9, 26.2. **HRMS–DART** (*m/z*): [M+NH₄]⁺ calcd for C₁₉H₃₄NO₂, 308.2584; found, 308.2584.

***N*-Phenyl-*N*-(undec-10-en-1-yl)aniline (**2j**)**

Alkene **2j** was synthesized according to the modified procedure.⁷ The undec-10-en-1-ol (3.41 g, 20 mmol, 1.0 equiv.) and trimethylamine (4.16 ml, 30 mmol, 1.5 equiv.) were added to a round-bottom flask containing dry DCM (6.7 mL). The flask was sealed with a rubber septum and purged with nitrogen. The mixture was cooled to 0 °C, and methanesulfonylchloride (2.63 g, 34 mmol, 1.48 equiv.) was added to the mixture while being stirred vigorously. After 1h, the mixture was washed with HCl 2mol/L, saturated NaHCO₃ and brine, dried over Na₂SO₄ and concentrated under reduced pressure, afforded brown liquid. The mesylated product (5.68 g, >20 mmol, >99% yield) was used in the next step without further purification.

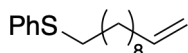
Diphenylamine (1.33 g, 7.8 mmol, 1.12 equiv.) was dissolved in anhydrous THF (42 mL) and the solution was cooled to –78 °C. A 13.6 mL portion of *n*-butyllithium (7.91 mmol, 1.13 equiv.) was added dropwise. The mixture was stirred at –78 °C for 30 min then kept at room temperature for 2 h. The suspension was cooled to –20 °C and transferred into a second flask containing a cold (–78 °C) solution of the mesylated product (7.0 mmol, 1.0 equiv.) in anhydrous THF (12 mL). The reaction mixture was stirred at –78 °C for 30 min and then at room temperature overnight. The precipitate was filtered off and the solvents were removed in vacuo. The resulting oil was hydrolyzed with deionized water. The aqueous layer was washed dichloromethane. The organic fractions were combined, dried over magnesium sulfate, and the solvent was evaporated off. The oily residue was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–95:5, hexane/EtOAc) to afford the desired **2j** (960 mg, 3.0 mmol, 43 %) as a colorless oil.



IR (neat) 692, 745, 908, 1244, 1363, 1494, 1574, 1588, 2852, 2923 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃)

δ 7.27–7.23 (m, 4H), 6.99–6.97 (m, 4H), 6.93 (t, $J = 7.2$ Hz, 2H), 5.81 (m, 1H), 5.01–4.91 (m, 2H), 3.67 (t, $J = 7.6$ Hz, 2H), 2.03 (dt, $J = 7.2, 6.8$ Hz, 2H), 1.69–1.61 (m, 2H), 1.38–1.26 (m, 12H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 148.1, 139.2, 129.2, 121.0, 120.9, 114.1, 52.3, 33.8, 29.5, 29.4, 29.4, 29.1, 28.9, 27.4, 27.1. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{32}\text{N}$, 322.2529; found, 322.2529.

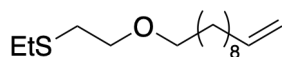
Alkene **2k** was synthesized according to the modified procedure.⁸ To a solution of thiophenol (0.31 ml, 330 mg, 3.0 mmol) in DMF (6.5 ml) was added K_2CO_3 (539 mg, 3.9 mmol), followed by the 11-Bromo-1-undecene (0.65 ml, 700 mg, 3 mmol). The reaction was stirred at room temperature overnight and then diluted with water. The combined hexane extracts were dried with Na_2SO_4 and the solvent was removed under reduced pressure. The oily residue was purified by flash chromatography on silica gel (Biotage Selekt, 100:0, hexane/EtOAc). The oily precipitate was dried in vacuo to afford the desired **2k** (780 mg, 3.0 mmol, 99 %) as a colorless oil.



IR (neat) 690, 736, 909, 1025, 1438, 1465, 1480, 2852, 2924, 3074 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.33–7.25 (m, 4H), 7.16 (t, $J = 7.2$ Hz, 1H), 5.81 (m, 1H), 5.01–4.92 (m, 2H), 2.91 (t, $J = 7.2$ Hz, 2H), 2.04 (q, $J = 7.2$ Hz, 2H), 1.64 (quintet, $J = 7.2$ Hz, 2H), 1.43–1.27 (m, 12H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 139.2, 137.0, 128.8, 128.8, 125.6, 114.1, 33.8, 33.6, 29.4, 29.4, 29.1 ($\times 2\text{C}$), 29.1, 28.9, 28.8. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{27}\text{S}$, 263.1828; found, 263.1825.

Ethyl[2-(undec-10-en-1-yloxy)ethyl]sulfane (**2l**)

A flask was placed under N_2 atmosphere by three cycles of evacuating and N_2 backfilling and charged with NaH (0.48 g, 60 wt.% dispersion in oil, 12.0 mmol, 1.5 equiv.) in dry DMF (40 mL). 2-(Ethylthio)ethan-1-ol (0.83 mL, 8.0 mmol, 1.0 equiv.) was added and stirred for 1 h. 11-Bromoundec-1-ene (1.73 mL, 8.0 mmol, 1.0 equiv.) was added dropwise at 0 $^\circ\text{C}$. The reaction was stirred at room temperature overnight and then diluted with water. The water layer was extracted with Et_2O three times. The combined Et_2O layer was dried with Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–96:4, hexane/EtOAc) to afford the desired product **2l** (1.00 g, 3.9 mmol, 48 %) as a colorless oil.



IR (neat) 637, 909, 993, 1107, 1265, 1358, 1456, 1640, 2853, 2924 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 5.81 (m, 1H), 5.02–4.91 (m, 2H), 3.58 (t, $J = 7.2$ Hz, 2H), 3.44 (t, $J = 6.8$ Hz, 2H), 2.71 (t, $J = 7.2$ Hz, 2H), 2.59 (q, $J = 7.2$ Hz, 2H), 2.04 (dt, $J = 7.6, 6.8$ Hz, 2H), 1.60–1.53 (m, 2H), 1.42–1.25 (m, 15H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 139.2, 114.1, 71.2, 70.5, 33.8, 31.1, 29.7, 29.5, 29.4, 29.4, 29.1, 28.9, 26.4, 26.1, 14.9. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{15}\text{H}_{34}\text{NOS}$, 276.2356; found,

276.2364.

Procedures for Hydroalkoxylation of Alkenes by A Triple Catalysis

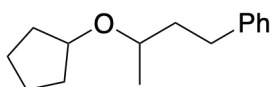
The reaction in Table 1-1, entry 1 is representative (limiting reagent: alkene). In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst **PTH-1** (3.7 mg, 0.01 mmol), **Co-1** (1.2 mg, 0.002 mmol), **HX-1** (5.4 mg, 0.02 mmol) and DCM (500 μ L). Then, cyclopentanol **1a** (54.4 μ L, 0.6 mmol) and 4-phenyl-1-butene **2a** (30.0 μ L, 0.2 mmol) were added to the reaction mixture. After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 $^{\circ}$ C (Figure S1-2). After 24 h, the reaction was quenched with a short plug of silica gel using diethyl ether. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (100:0–98:2, hexane/Et₂O) gave the **3aa** (32.3 mg, 0.15 mmol, 74% isolated yield) as a pale yellow oil.



Figure S1-2. Light set up

Characterization Data for Coupling Products

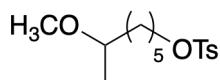
[3-(Cyclopentyloxy)butyl]benzene (**3aa**)



The product **3aa** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et₂O) (Table 1-1, entry 1; 32.3 mg, 0.15 mmol, 74% isolated yield. Table 1-1, entry 13; 37.6 mg, 0.17 mmol, 86% isolated yield.). Pale yellow oil. **IR** (neat) 698, 745, 1091, 1132, 1337, 1371, 1453, 1495, 2869, 2961 cm^{-1} . **¹H NMR** (400 MHz, CDCl₃) δ 7.27 (t, J = 8.0 Hz, 2H), 7.20–7.15 (m, 3H), 3.98 (quintet, J = 5.2 Hz, 1H), 3.38 (m, 1H), 2.75 (m, 1H), 2.61 (m, 1H), 1.86–1.49 (m, 10H), 1.16 (d, J = 6.4 Hz,

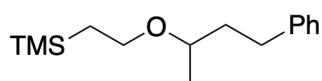
3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.6, 128.4, 128.3, 125.6, 78.8, 72.6, 38.8, 33.2, 32.5, 32.1, 23.4, 23.3, 20.4. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{23}\text{O}$; 219.1743, found 219.1746.

2-Methoxypropyl-4-methylbenzenesulfonate (**3bb**)



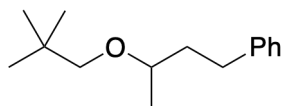
The product **3bb** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–88:12, hexane/EtOAc) (Figure 1-4; 27.6 mg, 0.09 mmol, 46% isolated yield). Pale yellow oil. **IR** (neat) 555, 664, 815, 940, 1096, 1176, 1188, 1359, 2861, 2932 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.02 (t, J = 6.4 Hz, 2H), 3.29 (s, 3H), 3.24 (m, 1H), 2.45 (s, 3H), 1.68–1.61 (m, 2H), 1.46 (m, 1H), 1.37–1.21 (m, 5H), 1.09 (d, J = 6.0 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 144.6, 133.2, 129.8, 127.8, 76.5, 70.6, 55.9, 36.1, 28.8, 25.4, 24.7, 21.6, 18.9. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{25}\text{O}_4\text{S}$; 301.1468, found 301.1461.

Trimethyl{2-[(4-phenylbutan-2-yl)oxy]ethyl}silane (**3ca**)



The product **3ca** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–97:3, hexane/EtOAc) (Figure 1-4; 27.0 mg, 0.11 mmol, 54% isolated yield). Pale yellow oil. **IR** (neat) 835, 858, 1091, 1134, 1247, 1454, 1496, 2860, 2925, 2952 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.30–7.26 (m, 2H), 7.20–7.16 (m, 3H), 3.58 (m, 1H), 3.43–3.36 (m, 2H), 2.76–2.61 (m, 2H), 1.84 (m, 1H), 1.70 (m, 1H), 1.16 (d, J = 6.0 Hz, 3H), 0.96–0.91 (m, 2H), 0.02 (s, 9H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.5, 128.4, 128.3, 125.6, 74.0, 65.3, 38.5, 31.9, 19.7, 18.6, –1.3. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{15}\text{H}_{30}\text{NOSi}$; 268.2091, found 268.2096.

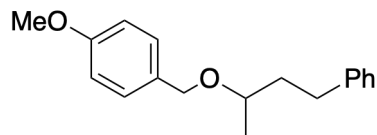
[3-(Neopentyloxy)butyl]benzene (**3da**)



The product **3da** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-4; 24.2 mg, 0.11 mmol, 55% isolated yield). Colorless oil. **IR** (neat) 698, 744, 1092, 1137, 1362, 1455, 1479, 1604, 2865, 2952 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.28 (t, J = 7.2 Hz, 2H), 7.20–7.15 (m, 3H), 3.35 (sextet, J = 6.4 Hz, 1H), 3.16 (d, J = 8.8 Hz, 1H), 2.96 (d, J = 8.8 Hz, 1H), 2.76 (ddd, J = 13.6, 9.2, 6.4 Hz, 1H), 2.65 (ddd, J = 13.6, 9.6, 6.4 Hz, 1H), 1.84 (m, 1H), 1.69 (m, 1H), 1.13 (d, J = 6.4 Hz, 3H), 0.92 (s, 9H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.7, 128.4, 128.3, 125.6, 78.9, 74.8, 38.7, 32.1, 31.9, 26.8, 19.6. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{25}\text{O}$; 221.1900,

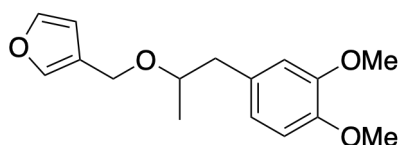
found 221.1903.

1-Methoxy-4-[[4-(4-phenylbutan-2-yl)oxy]methyl]benzene (3ea)



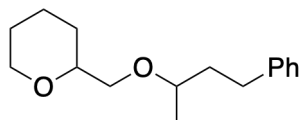
The product **3ea** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-4; 40.6 mg, 0.15 mmol, 75% isolated yield). Colorless oil. The spectrum data of product **3ea** was consistent with the literature.⁹

3-([1-(3,4-Dimethoxyphenyl)propan-2-yl]oxy)methylfuran (3fc)



The reaction conditions were modified. The reaction was carried out with **1f** (17.2 μ L, 0.2 mmol), **2c** (34.3 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μ L) under blue LED irradiation for 24 h. The product **3fc** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-4; 53.1 mg, 0.19 mmol, 96% isolated yield). Colorless oil. **IR** (neat) 874, 1029, 1090, 1141, 1157, 1237, 1262, 1515, 2835, 2933 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.36 (s, 1H), 7.33 (s, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.74–6.73 (m, 2H), 6.30 (s, 1H), 4.42 (d, J = 12.0 Hz, 1H), 4.29 (d, J = 12.0 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.68 (m, 1H), 2.84 (dd, J = 13.6, 6.0 Hz, 1H), 2.62 (dd, J = 13.6, 6.0 Hz, 1H), 1.18 (d, J = 6.0 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 148.6, 147.4, 143.2, 140.2, 131.7, 122.8, 121.3, 112.7, 112.0, 110.3, 76.0, 62.1, 55.9, 55.8, 42.8, 19.6. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{16}\text{H}_{24}\text{NO}_4$; 294.1699, found 294.1696.

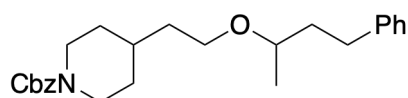
2-([4-(4-Phenylbutan-2-yl)oxy]methyl)tetrahydro-2H-pyran (3ga)



The product **3ga** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–95:5, hexane/EtOAc) (Figure 1-4; 33.3 mg, 0.13 mmol, 67% isolated yield). Colorless oil. **IR** (neat) 699, 746, 1047, 1094, 1136, 1205, 1374, 1496, 2847, 2931 cm^{-1} . The ratio (50:50) of the diastereomers was determined by ¹H NMR analysis. **¹H NMR** (400 MHz, CDCl_3) δ 7.29–7.25 (m, 2H), 7.20–7.15 (m, 3H), 4.01 (m, 1H), 3.55–3.36 (m, 4H + 0.5 $\times$ 1H), 3.24 (m, 0.5 $\times$ 1H), 2.78–2.61 (m, 2H), 1.95–

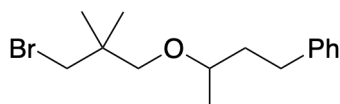
1.84 (m, 2H), 1.74–1.26 (m, 6H), 1.18–1.17 (m, 3H). Signals for two diastereomers were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.5 ($\times 2\text{C}$), 128.4 ($\times 2\text{C}$), 128.3 ($\times 2\text{C}$), 125.6, 125.6, 77.2 ($\times 2\text{C}$), 75.3 ($\times 2\text{C}$), 72.4, 72.1, 68.5, 68.5, 38.2, 38.2, 31.9 ($\times 2\text{C}$), 28.7, 28.6, 26.1, 26.0, 23.2, 23.1, 19.6 ($\times 2\text{C}$). HRMS–DART (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{25}\text{O}_2$; 249.1849, found 249.1849.

Benzyl 4-{2-[(4-Phenylbutan-2-yl)oxy]ethyl}piperidine-1-carboxylate (**3ha**)



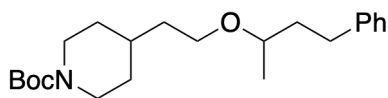
The product **3ha** was purified by flash chromatography on silica gel (99:1–85:15, hexane/EtOAc) (Figure 1-4; 30.1 mg, 0.08 mmol, 38% isolated yield). Colorless oil. IR (neat) 1087, 1135, 1208, 1238, 1276, 1364, 1429, 1696, 2856, 2924 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.36–7.25 (m, 7H), 7.19–7.17 (m, 3H), 5.12 (s, 2H), 4.16 (brs, 2H), 3.53 (m, 1H), 3.39–3.33 (m, 2H), 2.78–2.59 (m, 4H), 1.84 (m, 1H), 1.74–1.57 (m, 4H), 1.51 (quintet, $J = 6.0$ Hz, 2H), 1.16–1.13 (m, 5H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 155.2, 142.3, 136.9, 128.4, 128.3, 128.3, 127.9, 127.8, 125.7, 74.6, 66.9, 65.5, 44.2, 38.3, 36.6, 32.8, 32.0, 31.8, 19.6. HRMS–DART (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{34}\text{NO}_3$; 396.2533, found 396.2540.

[3-(3-Bromo-2,2-dimethylpropoxy)butyl]benzene (**3ia**)



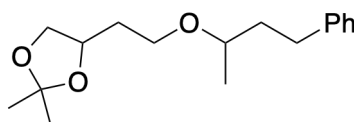
The reaction conditions were modified. The reaction was carried out with **1i** (73.7 μL , 0.6 mmol), **2a** (30.0 μL , 0.2 mmol), **Ir(ppy)₃** (1.3 mg, 0.002 mmol, 1 mol %) or **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3ia** was purified by flash chromatography on silica gel (100:0–98:2, hexane/ Et_2O) (Figure 1-4; **Ir(ppy)₃**: 31.0 mg, 0.10 mmol, 52% isolated yield, **PTH-1**: 23.9 mg, 0.08 mmol, 40 % isolated yield). Pale yellow oil. IR (neat) 698, 744, 1089, 1135, 1377, 1454, 1474, 2863, 2928, 2964. ^1H NMR (400 MHz, CDCl_3) δ 7.28 (t, $J = 7.6$ Hz, 2H), 7.21–7.16 (m, 3H), 3.45–3.35 (m, 3H), 3.29 (d, $J = 8.8$ Hz, 1H), 3.14 (d, $J = 8.8$ Hz, 1H), 2.75 (m, 1H), 2.64 (m, 1H), 1.83 (m, 1H), 1.70 (m, 1H), 1.14 (d, $J = 6.0$ Hz, 3H), 1.03 (s, 6H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.6, 128.4, 128.3, 125.6, 74.8, 74.3, 43.9, 38.6, 36.2, 31.8, 23.5, 19.5. HRMS–DART (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{24}\text{BrO}$; 299.1005, found 299.1003.

tert-Butyl 4-{2-[(4-Phenylbutan-2-yl)oxy]ethyl}piperidine-1-carboxylate (**3ja**)



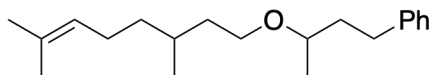
The product **3ja** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–85:15, hexane/EtOAc) (Figure 1-4; 41.9 mg, 0.12 mmol, 58% isolated yield). Colorless oil. **IR** (neat) 1138, 1171, 1245, 1277, 1365, 1421, 1693, 2856, 2926, 2970 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.29–7.26 (m, 2H), 7.19–7.16 (m, 3H), 4.06 (brs, 2H), 3.54 (dt, $J = 9.2, 6.4$ Hz, 1H), 3.41–3.34 (m, 2H), 2.76–2.60 (m, 4H), 1.85 (m, 1H), 1.75–1.65 (m, 3H), 1.61–1.49 (m, 3H), 1.45(s, 9H), 1.18–1.10 (m, 5H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 154.9, 142.3, 128.3, 128.3, 125.7, 79.1, 74.6, 65.6, 44.0 ($\times 2\text{C}$), 38.3, 36.7, 32.9, 32.2, 32.0, 31.8, 28.4, 19.6. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{36}\text{NO}_3$; 362.2690, found 362.2695.

2,2-Dimethyl-4-{2-[(4-phenylbutan-2-yl)oxy]ethyl}-1,3-dioxolane (3ka)



The product **3ka** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–90:10, hexane/EtOAc) (Figure 1-4; 22.8 mg, 0.08 mmol, 41% isolated yield). Pale yellow oil. **IR** (neat) 859, 1055, 1088, 1214, 1369, 1454, 1496, 2853, 2930, 2983 cm^{-1} . The ratio (50:50) of the diastereomers was determined by ^1H NMR analysis. **^1H NMR** (400 MHz, CDCl_3) δ 7.27 (t, $J = 7.6$ Hz, 2H), 7.20–7.16 (m, 3H), 4.25 (m, $0.5 \times 1\text{H}$), 4.20 (m, $0.5 \times 1\text{H}$), 4.08 (m, 1H), 3.66–3.54 (m, 2H), 3.48–3.35 (m, 2H), 2.76–2.59 (m, 2H), 1.94–1.77 (m, 3H), 1.68 (m, 1H), 1.41 (s, 3H), 1.36 (s, 3H), 1.16 (d, $J = 6.0$ Hz, 3H). Signals for two diastereomers were given: **^{13}C NMR** (100.6 MHz, CDCl_3) δ 142.3, 142.3, 128.4, 128.4, 128.3 ($\times 2\text{C}$), 125.7 ($\times 2\text{C}$), 108.5, 108.4, 74.7, 74.7, 74.1, 73.8, 69.7, 69.7, 64.9, 64.9, 38.4, 38.3, 34.2, 34.2, 31.8, 31.7, 26.9, 25.8, 19.5, 19.5. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{27}\text{O}_3$; 279.1955, found 279.1954.

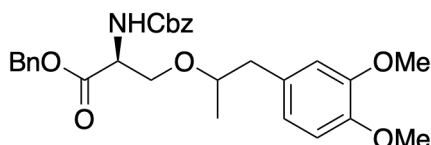
{3-[(3,7-Dimethyloct-6-en-1-yl)oxy]butyl}benzene (3la)



The product **3la** was purified by flash chromatography on silica gel (100:0–95:5, hexane/ Et_2O) (Figure 1-4; 42.7mg, 0.15 mmol, 74% isolated yield). Colorless oil. **IR** (neat) 698, 1094, 1136, 1339, 1375, 1454, 1496, 2859, 2924, 2964 cm^{-1} . The ratio (50:50) of the diastereomers was determined by ^1H -NMR analysis. **^1H NMR** (400 MHz, CDCl_3) δ 7.29–7.25 (m, 2H), 7.20–7.15 (m, 3H), 5.11 (m, 1H), 3.52 (m, 1H), 3.41–3.31 (m, 2H), 2.73 (m, 1H), 2.34 (m, 1H), 2.07–1.90 (m, 2H), 1.84 (m, 1H), 1.75–1.56 (m, 9H), 1.45–1.31 (m, 2H), 1.18–1.15 (m, 4H), 0.90 (d, $J = 6.0$ Hz, 3H). Signals for two

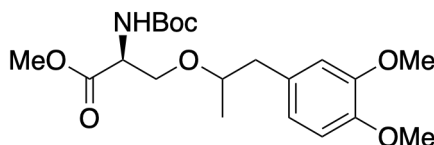
diastereomers were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.5 ($\times 2\text{C}$), 131.1 ($\times 2\text{C}$), 128.4 ($\times 4\text{C}$), 128.3 ($\times 4\text{C}$), 125.6 ($\times 2\text{C}$), 124.9 ($\times 2\text{C}$), 74.5, 74.5, 66.6 ($\times 2\text{C}$), 38.5 ($\times 2\text{C}$), 37.3, 37.2, 37.2, 37.2, 31.9, 31.9, 29.6, 29.6, 25.7 ($\times 2\text{C}$), 25.5 ($\times 2\text{C}$), 19.7, 19.7 ($\times 2\text{C}$), 19.5, 17.6 ($\times 2\text{C}$). **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{33}\text{O}$; 289.2526, found 289.2524.

Benzyl *N*-[(Benzyloxy)carbonyl]-*O*-[1-(3,4-dimethoxyphenyl)propan-2-yl]-L-serinate (3mc)



The reaction conditions were modified. The reaction was carried out with **1m** (65.9 mg, 0.2 mmol), **2c** (34.3 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3mc** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/AcOEt) (Figure 1-4; 61.2mg, 0.12 mmol, 60% isolated yield). Pale yellow oil. **IR** (neat) 1029, 1158, 1237, 1262, 1338, 1455, 1516, 1725, 2933, 3345 cm^{-1} . The ratio (50:50) of the diastereomers was determined by ^1H NMR analysis. ^1H NMR (400 MHz, CDCl_3) δ 7.37–7.25 (m, 10H), 6.73–6.63 (m, 3H), 5.59 (d, $J = 8.8$ Hz, $0.5 \times 1\text{H}$), 5.39 (d, $J = 8.8$ Hz, $0.5 \times 1\text{H}$), 5.26–4.99 (m, 4H), 4.47 (m, 1H), 4.00 (dd, $J = 8.8$, 2.4 Hz, $0.5 \times 1\text{H}$), 3.84–3.73 (m, 7H), 3.55–3.44 (m, $1\text{H} + 0.5 \times 1\text{H}$), 2.67 (m, 1H), 2.52 (m, 1H), 1.08 (d, $J = 6.0$ Hz, $0.5 \times 3\text{H}$), 1.03 (d, $J = 6.0$ Hz, $0.5 \times 3\text{H}$). Signals for two diastereomers were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 170.1, 170.1, 155.9, 155.9, 148.5, 148.4, 147.3, 147.2, 136.2, 136.0, 135.3, 135.2, 131.1, 131.0, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 121.1, 121.0, 112.6, 112.3, 110.8, 110.8, 77.6, 77.3, 68.6, 68.1, 66.9, 66.9, 66.9, 66.7, 55.6, 55.6, 55.5, 54.5, 54.4, 42.5, 42.4, 19.0, 18.9 (Only observed peaks). **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{29}\text{H}_{34}\text{NO}_7$; 508.2330, found 508.2340.

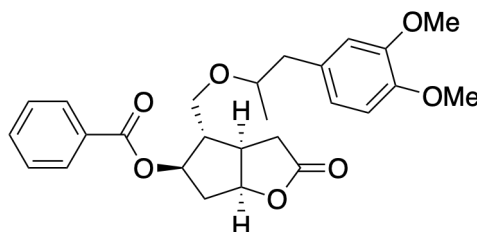
Methyl *N*-(*tert*-Butoxycarbonyl)-*O*-[1-(3,4-dimethoxyphenyl)propan-2-yl]-L-serinate (3nc)



The reaction conditions were modified. The reaction was carried out with **1n** (43.8 mg, 0.2 mmol), **2c** (34.3 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3nc** was purified by flash chromatography on silica gel (Biotage Selekt, 97:3–75:25, hexane/AcOEt) (Figure 1-4; 36.5mg, 0.09 mmol, 46% isolated yield). Pale yellow oil. **IR** (neat) 1030, 1160, 1238, 1262, 1516, 1716, 1752, 2934,

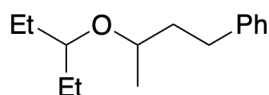
2973, 3407 cm^{-1} . The ratio (59:41) of the diastereomers was determined by ^1H NMR analysis. ^1H NMR (400 MHz, CDCl_3) δ 6.79 (m, 1H), 6.71–6.67 (m, 2H), 5.30 (d, $J = 8.4$ Hz, $0.41 \times 1\text{H}$), 5.17 (d, $J = 8.4$ Hz, $0.59 \times 1\text{H}$), 4.35 (m, 1H), 3.95–3.85 (m, $6\text{H} + 0.59 \times 1\text{H}$), 3.74–3.70 (m, $0.59 \times 3\text{H} + 0.41 \times 2\text{H}$), 3.63 (s, $0.41 \times 3\text{H}$), 3.55 (m, 1H), 3.49 (dd, $J = 9.2, 3.2$ Hz, $0.59 \times 1\text{H}$), 2.73 (m, 1H), 2.57 (m, 1H), 1.45 (s, $0.41 \times 9\text{H}$), 1.44 (s, $0.59 \times 9\text{H}$), 1.12 (d, $J = 6.0$ Hz, $0.41 \times 3\text{H}$), 1.10 (d, $J = 6.0$ Hz, $0.59 \times 3\text{H}$). Signals for two diastereomers were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 171.2, 171.2, 155.5, 148.7, 148.6, 147.5, 147.4, 131.4, 131.3, 121.3, 121.2, 112.8, 112.7, 111.0, 79.9, 79.8, 77.7, 77.4, 68.7, 68.5, 55.9, 55.8, 55.8, 54.2, 54.1, 52.3, 52.2, 42.6, 42.5, 28.3, 28.3, 19.2, 19.1 (Only observed peaks). HRMS–DART (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{32}\text{NO}_7$; 398.2173, found 398.2168.

(3aR,4S,5R,6aS)-4-([1-(3,4-Dimethoxyphenyl)propan-2-yl]oxy)methyl-2-oxohexahydro-2H-cyclopenta[b]furan-5-yl Benzoate (3oc)



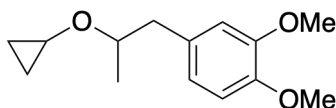
The reaction conditions were modified. The reaction was carried out with **1o** (27.6 mg, 0.1 mmol), **2c** (17.1 μL , 0.1 mmol), **PTH-1** (1.8 mg, 0.005 mmol, 5 mol %), and **HX-1** (2.7 mg, 0.01 mmol, 10 mol %) in DCM (250 μL) under blue LED irradiation for 24 h. The product **3oc** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–50:50, hexane/AcOEt) (Figure 1-4; 36.6 mg, 0.08 mmol, 81% isolated yield). Pale yellow oil. IR (neat) 714, 1027, 1108, 1263, 1273, 1451, 1516, 1714, 1771, 2965 cm^{-1} . The ratio (50:50) of the diastereomers was determined by ^1H NMR analysis. ^1H NMR (400 MHz, CDCl_3) δ 7.98 (d, $J = 7.2$ Hz, 2H), 7.55 (d, $J = 7.2$ Hz, 1H), 7.44 (t, $J = 7.2$ Hz, 2H), 6.78 (m, 1H), 6.72–6.70 (m, 2H), 5.33 (dt, $J = 6.0, 2.8$ Hz, $0.5 \times 1\text{H}$), 5.25 (dt, $J = 6.0, 2.8$ Hz, $0.5 \times 1\text{H}$), 5.01 (t, $J = 5.6$ Hz, $0.5 \times 1\text{H}$), 4.95 (t, $J = 6.0$ Hz, $0.5 \times 1\text{H}$), 3.89–3.83 (m, 6H), 3.63–3.56 (m, 2H), 3.33 (m, 1H), 2.88–2.24 (m, 8H), 1.16 (d, $J = 6.4$ Hz, $0.5 \times 3\text{H}$), 1.14 (d, $J = 6.4$ Hz, $0.5 \times 3\text{H}$). Signals for two diastereomers were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 176.8, 176.8, 166.0, 166.0, 148.7, 147.5, 133.2, 131.5, 131.4, 129.7, 129.6, 128.4, 121.3, 121.3, 112.6, 112.6, 111.1, 85.3, 85.2, 78.9, 78.7, 77.5, 77.4, 69.0, 55.9, 55.9, 53.5, 53.4, 42.9, 42.8, 40.9, 40.8, 38.8, 38.7, 36.2, 36.2, 19.4, 19.3 (Only observed peaks). HRMS–DART (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{31}\text{O}_7$; 455.2064, found 455.2060.

[3-(Pentan-3-yloxy)butyl]benzene (3pa)



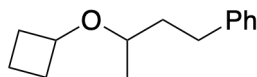
The product **3pa** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et₂O) (Figure 1-4; 24.2 mg, 0.11 mmol, 55% isolated yield). Colorless oil. The spectrum data of product **3pa** was consistent with the literature.¹⁰

4-(2-Cyclopropoxypropyl)-1,2-dimethoxybenzene (**3qc**)



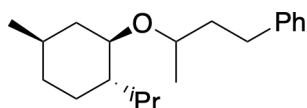
The reaction conditions were modified. The reaction was carried out with **1q** (11.7 μ L, 0.2 mmol), **2c** (34.3 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μ L) under blue LED irradiation for 24 h. The product **3qc** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-4; 19.2 mg, 0.08 mmol, 41% isolated yield). Colorless oil. **IR** (neat) 1030, 1141, 1157, 1210, 1238, 1262, 1516, 2833, 2932, 2968 cm^{-1} . **¹H NMR** (400 MHz, CDCl₃) δ 6.79 (m, 1H), 6.73–6.72 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.72 (sextet, J = 6.4 Hz, 1H), 3.30 (m, 1H), 2.83 (dd, J = 14.4, 6.4 Hz, 1H), 2.55 (dd, J = 14.4, 6.4 Hz, 1H), 1.18 (d, J = 6.4 Hz, 3H), 0.54 (m, 1H), 0.47 (m, 1H), 0.43–0.32 (m, 2H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 148.5, 147.3, 131.8, 121.3, 112.7, 110.9, 77.2, 55.8, 55.8, 51.2, 42.8, 19.8, 6.0, 5.5. **HRMS–DART** (m/z): [M+NH₄]⁺ calcd for C₁₄H₂₄NO₃; 254.1751, found 254.1755.

(3-Cyclobutoxybutyl)benzene (**3ra**)



The product **3ra** was purified by flash chromatography on silica gel (100:0–97.5:2.5, hexane/Et₂O) (Figure 1-4; 29.4 mg, 0.14 mmol, 72% isolated yield). Pale yellow oil. **IR** (neat) 698, 747, 1113, 1145, 1238, 1333, 1372, 1496, 2871, 2969 cm^{-1} . **¹H NMR** (400 MHz, CDCl₃) 7.29 (t, J = 12.0 Hz, 2H), 7.20–7.15 (m, 3H), 3.97 (quintet, J = 7.6 Hz, 1H), 3.40 (sextet, J = 6.4 Hz, 1H), 2.74 (ddd, J = 14.0, 9.2, 5.6 Hz, 1H), 2.63 (ddd, J = 14.0, 9.2, 4.8 Hz, 1H), 2.23–2.16 (m, 2H), 2.01–1.87 (m, 2H), 1.80 (m, 1H), 1.72–1.63 (m, 2H), 1.46 (m, 1H), 1.14 (d, J = 6.4 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 142.4, 128.4, 128.3, 125.6, 72.7, 71.4, 38.6, 31.9, 31.8, 31.3, 20.4, 12.7. **HRMS–DART** (m/z): [M+H]⁺ calcd for C₁₄H₂₁O; 205.1587, found 205.1586.

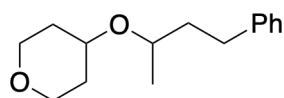
(3-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}butyl)benzene (**3sa**)



The product **3sa** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et₂O)

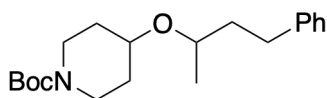
(Figure 1-4; 28.8 mg, 0.10 mmol, 50% isolated yield). Pale yellow oil. **IR** (neat) 698, 745, 1050, 1085, 1131, 1371, 1454, 2868, 2921, 2953 cm^{-1} . The ratio (50:50) of the diastereomers was determined by ^1H NMR analysis. ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.25 (m, 2H), 7.21–7.15 (m, 3H), 3.53 (m, 1H), 3.09 (dd, J = 10.8, 4.0 Hz, $0.5 \times 1\text{H}$), 3.04 (dd, J = 10.8, 4.0 Hz, $0.5 \times 1\text{H}$), 2.77–2.58 (m, 2H), 2.28 (m, 1H), 2.01 (m, 1H), 1.81 (m, 1H), 1.72 (m, 1H), 1.67–1.60 (m, 2H), 1.39–1.12 (m, 5H), 1.01–0.82 (m, 9H), 0.80–0.74 (m, 3H). Signals for two diastereomers were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.6, 142.5, 128.4, 128.3, 128.3, 128.2, 125.6, 125.6, 77.8, 76.2, 73.3, 71.9, 48.8, 48.5, 42.5, 41.7, 39.2, 38.6, 34.5, 34.5, 32.1, 31.7, 31.6, 31.6, 24.9, 23.1, 23.0, 22.4, 21.6, 21.3, 21.3, 20.1, 16.0, 16.0. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{33}\text{O}$; 289.2526, found 289.2528.

4-[(4-Phenylbutan-2-yl)oxy]tetrahydro-2H-pyran (**3ta**)



The reaction was also carried out with **1t** (19.1 μL , 0.2 mmol), **2a** (60.1 μL , 0.4 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3ta** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (Figure 1-4; 16.9 mg, 0.07 mmol, 36% isolated yield). Yellow oil. **IR** (neat) 699, 746, 871, 1002, 1088, 1130, 1372, 1454, 2853, 2925 cm^{-1} . ^1H NMR δ 7.28 (t, J = 8.0 Hz, 2H), 7.20–7.16 (m, 3H), 3.95 (dt, J = 12.0, 4.4 Hz, 2H), 3.58–3.50 (m, 2H), 3.47–3.40 (m, 2H), 2.76 (ddd, J = 12.0, 10.0, 6.4 Hz, 1H), 2.74 (ddd, J = 12.0, 10.0, 5.6 Hz, 1H), 1.88–1.79 (m, 3H), 1.72 (m, 1H), 1.65–1.52 (m, 2H), 1.17 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 142.3, 128.3, 128.3, 125.7, 71.8, 71.6, 65.9, 65.9, 38.8, 33.8, 32.8, 32.0, 20.7. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{15}\text{H}_{26}\text{NO}_2$; 252.1958, found 252.1958.

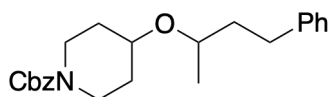
tert-Butyl 4-[(4-Phenylbutan-2-yl)oxy]piperidine-1-carboxylate (**3ua**)



The product **3ua** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (Figure 1-4; 28.0 mg, 0.08 mmol, 42% isolated yield). Colorless oil. **IR** (neat) 1037, 1089, 1132, 1172, 1236, 1365, 1422, 1693, 2861, 2928 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.29–7.26 (m, 2H), 7.19–7.16 (m, 3H), 3.80–3.77 (m, 2H), 3.56–3.46 (m, 2H), 3.10–3.03 (m, 2H), 2.75 (m, 1H), 2.61 (m, 1H), 1.87–1.68 (m, 4H), 1.55–1.44 (m, 11H), 1.16 (d, J = 6.0 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 154.9, 142.3, 128.3 ($\times 2\text{C}$), 125.7, 79.4, 72.2, 72.0, 41.5 ($\times 2\text{C}$), 38.9, 32.4, 32.0, 31.4, 28.4, 20.7.

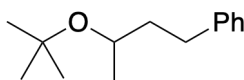
HRMS–DART (m/z): $[M+H]^+$ calcd for $C_{20}H_{32}NO_3$; 334.2377, found 334.2381.

Benzyl 4-[(4-Phenylbutan-2-yl)oxy]piperidine-1-carboxylate (3va)



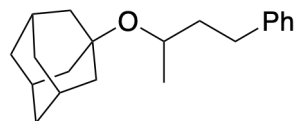
The product **3va** was purified by flash chromatography on silica gel (100:0–83:17, hexane/EtOAc) (Figure 1-4; 31.6 mg, 0.09 mmol, 43% isolated yield). Colorless oil. **IR** (neat) 698, 748, 1036, 1084, 1130, 1226, 1429, 1696, 2861, 2927 cm^{-1} . **1H NMR** (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 7H), 7.19–7.16 (m, 3H), 5.13 (s, 2H), 3.82 (brs, 2H), 3.57–3.49 (m, 2H), 3.23–3.16 (m, 2H), 2.74 (m, 1H), 2.65 (m, 1H), 1.87–1.69 (m, 4H), 1.53 (brs, 2H), 1.16 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 155.3, 142.2, 136.9, 128.5, 128.3, 128.3, 127.9, 127.8, 125.7, 72.0, 71.8, 67.0, 41.5, 41.5, 38.8, 32.3, 32.0, 31.2, 20.6. **HRMS–DART** (m/z): $[M+H]^+$ calcd for $C_{23}H_{30}NO_3$; 368.2220, found 368.2221.

[3-(*tert*-Butoxy)butyl]benzene (3wa)



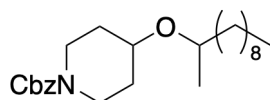
The reaction conditions were modified. The reaction was carried out with **1w** (191.3 μ L, 2.0 mmol), **2a** (30.0 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μ L) under blue LED irradiation for 24 h. The product **3ya** was purified by flash chromatography on silica gel (100:0–97:3, hexane/Et₂O) (Figure 1-4; 27.6 mg, 0.13 mmol, 67% isolated yield). Pale yellow oil. The spectrum data of product **3wa** was consistent with the literature.¹¹

1-[(4-Phenylbutan-2-yl)oxy]adamantane (3xa)



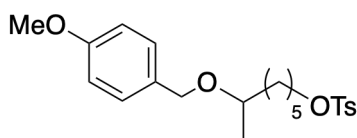
The product **3xa** was purified by flash chromatography on silica gel (100:0–98:2, hexane/EtOAc) (Figure 1-4; 27.3 mg, 0.10 mmol, 48% isolated yield). Pale yellow oil. **IR** (neat) 698, 746, 984, 1084, 1115, 1354, 1371, 1453, 2850, 2904 cm^{-1} . **1H NMR** δ 7.27 (t, $J = 7.2$ Hz, 2H), 7.20–7.15 (m, 3H), 3.80 (s, 1H), 2.72 (ddd, $J = 13.6, 10.0, 5.2$ Hz, 1H), 2.58 (ddd, $J = 13.6, 10.0, 5.2$ Hz, 1H), 2.13 (s, 3H), 1.82–1.57 (m, 14H), 1.16 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 142.7, 128.3, 128.2, 125.6, 72.5, 65.0, 42.8, 40.6, 36.4, 32.6, 30.6, 23.5. **HRMS–DART** (m/z): $[M+H]^+$ calcd for $C_{20}H_{29}O$; 285.2213, found 285.2210.

Benzyl 4-(Undecan-2-yloxy)piperidine-1-carboxylate (**3yd**)



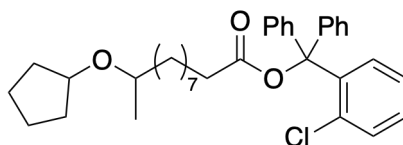
The product **3yd** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–84:16, hexane/EtOAc) (Figure 1-5; 33.5 mg, 0.09 mmol, 43% isolated yield). Pale yellow oil. **IR** (neat) 1039, 1088, 1126, 1225, 1273, 1363, 1429, 1701, 2854, 2924 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.36–7.27 (m, 5H), 5.12 (s, 2H), 3.82 (brs, 2H), 3.54–3.45 (m, 2H), 3.24–3.16 (m, 2H), 1.78 (brs, 2H), 1.49–1.44 (m, 2H), 1.37–1.18 (m, 16H), 1.11 (d, J = 6.0 Hz, 3H), 0.88 (t, J = 6.4 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 155.3, 136.9, 128.4, 127.9, 127.8, 72.7, 71.6, 67.0, 41.5, 41.5, 37.3, 31.9, 29.7, 29.6, 29.3, 25.8, 22.7, 20.6, 14.1. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{40}\text{NO}_3$; 390.3006, found 390.3003.

6-[(4-Methoxybenzyl)oxy]heptyl 4-Methylbenzenesulfonate (**3eb**)



The product **3eb** was purified by flash chromatography on silica gel (99:1–90:10, hexane/EtOAc) (Figure 1-5; 45.5 mg, 0.11 mmol, 56% isolated yield). Colorless oil. **IR** (neat) 576, 814, 937, 1173, 1245, 1356, 1512, 1612, 2860, 2933 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.78 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 4.48 (d, J = 11.2 Hz, 1H), 4.34 (d, J = 11.2 Hz, 1H), 4.01 (t, J = 6.8 Hz, 2H), 3.80 (s, 3H), 3.44 (sextet, J = 6.0 Hz, 1H), 2.44 (s, 3H), 1.66–1.59 (m, 2H), 1.50 (m, 1H), 1.43–1.21 (m, 5H), 1.14 (d, J = 6.0 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 159.0, 144.6, 133.2, 131.0, 129.8, 129.2, 127.9, 113.7, 74.2, 70.6, 69.9, 55.3, 36.4, 28.8, 25.4, 24.9, 21.6, 19.6. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{22}\text{H}_{34}\text{NO}_5\text{S}$; 424.2152, found 424.2146.

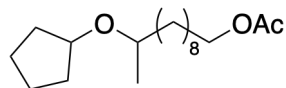
(2-Chlorophenyl)diphenylmethyl 9-(Cyclopentyloxy)decanoate (**3ae**)



The product **3ae** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–96:4, hexane/EtOAc) (Figure 1-5; 17.1 mg, 0.03 mmol, 16% isolated yield). Pale yellow oil. **IR** (neat) 700, 755, 1044, 1149, 1337, 1370, 1447, 1742, 2855, 2928 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.35–7.16 (m, 14H), 3.96 (m, 1H), 3.38 (m, 1H), 2.54 (t, J = 7.6 Hz, 2H), 1.77–1.62 (m, 6H), 1.60–1.41 (m, 4H), 1.39–1.26 (m, 12H), 1.10 (d, J = 6.0 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 172.0, 142.8,

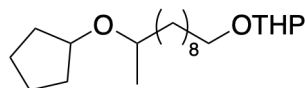
139.9, 133.7, 131.7, 131.5, 129.1, 128.0, 127.8, 127.3, 125.8, 89.5, 78.6, 73.1, 37.2, 35.0, 33.1, 32.5, 29.7, 29.5, 29.3, 29.2, 25.8, 24.8, 23.4, 23.3, 20.4. **HRMS–DART** (m/z): $[M+NH_4]^+$ calcd for $C_{35}H_{47}ClNO_3$; 564.3239, found 564.3236.

10-(Cyclopentyloxy)undecyl acetate (**3af**)



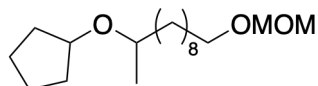
The product **3af** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–98:2, hexane/EtOAc) (Figure 1-5; 37.6 mg, 0.13 mmol, 63% isolated yield). Pale yellow oil. **IR** (neat) 1042, 1117, 1132, 1236, 1366, 1437, 1458, 1741, 1458, 1741, 2855, 2927 cm^{-1} . **1H NMR** (400 MHz, $CDCl_3$) δ 4.05 (d, $J = 6.4$ Hz, 2H), 3.97 (quintet, $J = 4.4$ Hz, 1H), 3.38 (sextet, $J = 5.2$ Hz, 1H), 2.05 (s, 3H), 1.76–1.42 (m, 11H), 1.35–1.28 (m, 13H), 1.10 (d, $J = 5.2$ Hz, 3H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 171.3, 78.6, 73.2, 64.7, 37.2, 33.1, 32.5, 29.7, 29.5, 29.5, 29.2, 28.6, 25.9, 25.8, 23.4, 23.3, 21.0, 20.4. **HRMS–DART** (m/z): $[M+NH_4]^+$ calcd for $C_{18}H_{38}NO_3$; 316.2846, found 316.2846.

2-{{10-(Cyclopentyloxy)undecyl}oxy}tetrahydro-2H-pyran (**3ag**)



The product **3ag** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-5; 34.6 mg, 0.10 mmol, 51% isolated yield). Pale yellow oil. **IR** (neat) 869, 1034, 1079, 1121, 1201, 1340, 1370, 1454, 2855, 2928 cm^{-1} . **1H NMR** (400 MHz, $CDCl_3$) δ 4.58 (m, 1H), 3.96 (m, 1H), 3.87 (m, 1H), 3.73 (m, 1H), 3.50 (m, 1H), 3.41–3.35 (m, 2H), 1.84 (m, 1H), 1.75–1.64 (m, 5H), 1.61–1.50 (m, 11H), 1.35–1.28 (13H), 1.10 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 98.8, 78.6, 73.2, 67.7, 62.3, 37.2, 33.1, 32.5, 30.8, 29.7, 29.7, 29.6, 29.6, 29.5, 26.2, 25.8, 25.5, 23.4, 23.3, 20.4, 19.7. **HRMS–DART** (m/z): $[M+NH_4]^+$ calcd for $C_{21}H_{44}NO_3$; 358.3316, found 358.3312.

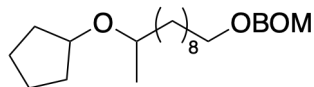
{{11-(Methoxymethoxy)undecan-2-yl}oxy}cyclopentane (**3ah**)



The product **3ah** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–95:5, hexane/EtOAc) (Figure 1-5; 34.2 mg, 0.11 mmol, 57% isolated yield). Pale yellow oil. **IR** (neat) 920, 1045, 1087, 1111, 1149, 1337, 1371, 1465, 2854, 2926 cm^{-1} . **1H NMR** (400 MHz, $CDCl_3$) δ 4.62 (s, 2H), 4.00 (quintet, $J = 4.4$ Hz, 1H), 3.52 (t, $J = 6.8$ Hz, 2H), 3.40–3.36 (m, 4H), 1.78–1.66 (m, 4H), 1.62–1.54 (m, 4H), 1.54–1.43 (m, 2H), 1.40–1.28 (m, 14H), 1.10 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 96.4, 78.6, 73.2, 67.9, 55.1, 37.2, 33.1, 32.5, 29.7, 29.7, 29.6, 29.6, 29.4, 26.2, 25.8, 23.4, 23.3, 20.4. **HRMS–DART** (m/z): $[M+NH_4]^+$ calcd for $C_{18}H_{40}NO_3$; 318.3003, found

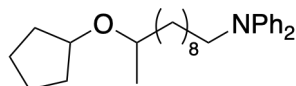
318.2990.

[[[10-(Cyclopentyloxy)undecyl]oxy}methoxy)methyl]benzene (3ai)



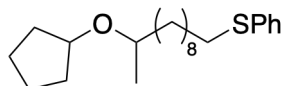
The product **3ai** was purified by flash chromatography on silica gel (100:0–90:10, hexane/EtOAc) (Figure 1-5; 45.5 mg, 0.12 mmol, 60% isolated yield). Paleyellow oil. **IR** (neat) 697, 734, 1028, 1046, 1114, 1165, 1372, 1454, 2855, 2927 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.36–7.27 (m, 5H), 4.76 (s, 2H), 4.60 (s, 2H), 3.96 (m, 1H), 3.59 (t, $J = 6.8$ Hz, 2H), 3.38 (m, 1H), 1.78–1.65 (m, 4H), 1.64–1.42 (m, 6H), 1.40–1.28 (m, 14H) 1.10 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 137.9, 128.3, 127.8, 127.6, 94.5, 78.6, 73.1, 69.2, 68.1, 37.2, 33.1, 32.4, 29.7 ($\times 2\text{C}$), 29.6, 29.5, 29.4, 26.2, 25.8, 23.3, 23.3, 20.4. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{41}\text{O}_3$; 377.3050, found 377.3051.

***N*-[10-(Cyclopentyloxy)undecyl]-*N*-phenylaniline (3aj)**



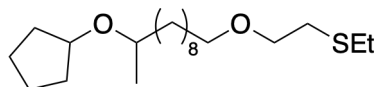
The product **3aj** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–97:3, hexane/EtOAc) (Figure 1-5; 55.0 mg, 0.13 mmol, 67% isolated yield). Paleyellow oil. **IR** (neat) 695, 748, 1046, 1240, 1371, 1496, 1589, 1741, 2854, 2928 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.28–7.23 (m, 4H), 6.99–6.97 (m, 4H), 6.93 (t, $J = 7.2$ Hz, 2H), 3.96 (quintet, $J = 4.4$ Hz, 1H), 3.68 (d, $J = 7.6$ Hz, 1H), 3.66 (d, $J = 7.6$ Hz, 1H), 3.38 (m, 1H), 1.78–1.63 (m, 6H), 1.61–1.54 (m, 2H), 1.52–1.43 (m, 3H), 1.34–1.25 (m, 13H), 1.10 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 148.1, 129.2, 121.0, 120.9, 78.6, 73.2, 52.3, 37.2, 33.1, 32.5, 29.7, 29.6, 29.6, 29.4, 27.4, 27.1, 25.8, 23.4, 23.3, 20.4. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{42}\text{NO}$; 408.3266, found 408.3268.

[10-(Cyclopentyloxy)undecyl](phenyl)sulfane (3ak)



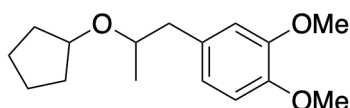
The product **3ak** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-5; 36.7 mg, 0.11 mmol, 53% isolated yield). Pale yellow oil. **IR** (neat) 690, 736, 1025, 1044, 1092, 1130, 1438, 1480, 2853, 2925 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.33–7.25 (m, 4H), 7.16 (t, $J = 7.2$ Hz, 1H), 3.96 (m, 1H), 3.38 (m, 1H), 2.91 (t, $J = 7.2$ Hz, 2H), 1.78–1.54 (m, 7H), 1.52–1.49 (m, 6H), 1.46–1.27 (m, 11H), 1.10 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 137.0, 128.8 ($\times 2\text{C}$), 125.6, 78.6, 73.2, 37.2, 33.5, 33.1, 32.5, 29.7, 29.5, 29.4, 29.1 ($\times 2\text{C}$), 28.8, 25.8, 23.4, 23.3, 20.4. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{37}\text{OS}$; 349.2560, found 349.2559.

(2-([10-(Cyclopentyloxy)undecyl]oxy)ethyl)(ethyl)sulfane (**3al**)



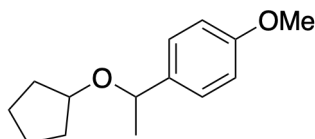
The product **3al** was purified by flash chromatography on silica gel (100:0–95:5, hexane/AcOEt) (Figure 1-5; 18.8 mg, 0.05 mmol, 27 % isolated yield). Colorless oil. **IR** (neat) 909, 993, 1110, 1265, 1358, 1456, 1641, 2854, 2925, 3075 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 3.96 (m, 1H), 3.58 (t, J = 6.8 Hz, 2H), 3.44 (t, J = 6.8 Hz, 2H), 3.38 (m, 1H), 2.71 (t, J = 6.8 Hz, 2H), 2.59 (q, J = 7.2 Hz, 2H), 1.78–1.64 (m, 4H), 1.63–1.42 (m, 7H), 1.34–1.25 (m, 16H), 1.10 (d, J = 6.0 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 78.6, 73.2, 71.2, 70.5, 37.2, 33.1, 32.5, 31.1, 29.7, 29.7, 29.6, 29.5, 29.4, 26.4, 26.1, 25.8, 23.4, 23.3, 20.4, 14.9. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{41}\text{O}_2\text{S}$; 345.2822, found 345.2829.

4-[2-(Cyclopentyloxy)propyl]-1,2-dimethoxybenzene (**3ac**)



The reaction conditions were modified. The reaction was carried out with **1a** (18.1 μL , 0.2 mmol), **2c** (34.3 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3ac** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–90:10, hexane/EtOAc) (Figure 1-5; 52.9 mg, 0.20 mmol, 99% isolated yield). Pale yellow oil. **IR** (neat) 1030, 1157, 1237, 1261, 1333, 1464, 1515, 2833, 2869, 2957 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 6.80–6.72 (m, 3H), 3.91 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.58 (sextet, J = 6.4 Hz, 1H), 2.75 (dd, J = 13.6, 6.4 Hz, 1H), 2.56 (dd, J = 13.6, 6.4 Hz, 1H), 1.73–1.41 (m, 8H), 1.13 (d, J = 6.4 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 148.4, 147.2, 132.2, 121.3, 112.9, 110.9, 79.1, 74.7, 55.9, 55.8, 43.2, 33.1, 32.4, 23.4, 23.2, 20.4. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{25}\text{O}_3$; 265.1798, found 265.1804.

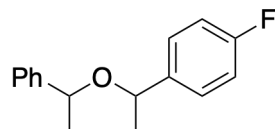
1-[1-(Cyclopentyloxy)ethyl]-4-methoxybenzene (**3am**)



The reaction conditions were modified. The reaction was carried out with **1a** (18.1 μL , 0.2 mmol), **2m** (26.8 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3am** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–95:5, hexane/EtOAc) (Figure 1-5; 38.3 mg, 0.17

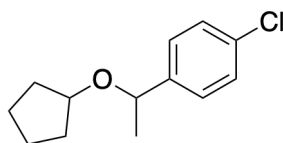
mmol, 87% isolated yield). Pale yellow oil. **IR** (neat) 831, 1038, 1091, 1171, 1243, 1441, 1511, 1611, 2869, 2955 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.24 (d, $J = 8.8$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 2H), 4.41 (q, $J = 6.4$ Hz, 1H), 3.82–3.76 (m, 4H), 1.76–1.40 (m, 8H), 1.38 (d, $J = 6.4$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 158.7, 136.7, 127.3, 113.6, 78.3, 74.9, 55.2, 33.0, 31.8, 24.6, 23.5, 23.4. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{O}_2$; 221.1536, found 221.1542.

1-Fluoro-4-[1-(1-phenylethoxy)ethyl]benzene (**3zn**)



The reaction conditions were modified. The reaction was carried out with **1z** (24.2 μL , 0.2 mmol), **2n** (23.9 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3zn** was purified by flash chromatography on silica gel (100:0–97.5:2.5, hexane/ Et_2O) (Figure 1-5; 46.4 mg, 0.19 mmol, 95% isolated yield). Pale yellow oil. **IR** (neat) 701, 761, 835, 1029, 1089, 1222, 1509, 1604, 2928, 2975 cm^{-1} . The ratio (53:47) of the diastereomers was determined by ^1H NMR analysis. **^1H NMR** (400 MHz, CDCl_3) δ 7.36 (m, 1H), 7.31–7.20 (m, 6H), 7.03 (m, 1H), 6.95 (m, 1H), 4.51 (m, 1H), 4.21 (m, 1H), 1.45 (m, 3H), 1.36 (m, 3H). Signals for two diastereomers were given: **^{13}C NMR** (100.6 MHz, CDCl_3) δ 162.1 (d, $J_{\text{C-F}} = 244.8$ Hz), 161.9 (d, $J_{\text{C-F}} = 244.8$ Hz), 144.0, 143.9, 140.0 (d, $J_{\text{C-F}} = 2.9$ Hz), 139.8 (d, $J_{\text{C-F}} = 3.3$ Hz), 128.5, 128.3, 127.8 (d, $J_{\text{C-F}} = 7.7$ Hz), 127.8 (d, $J_{\text{C-F}} = 7.5$ Hz), 127.4, 127.2, 126.3, 126.2, 115.3 (d, $J_{\text{C-F}} = 21.2$ Hz), 115.0 (d, $J_{\text{C-F}} = 21.3$ Hz), 74.7, 74.6, 73.9, 73.8, 24.7, 24.6, 23.1, 22.9. Signals for two diastereomers (53:47) were given: **^{19}F NMR** (376.5 MHz, CDCl_3) δ –115.4, –115.9. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{16}\text{H}_{21}\text{FNO}$; 262.1602, found 262.1606.

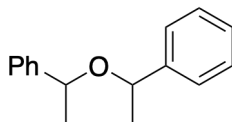
1-Chloro-4-[1-(cyclopentyloxy)ethyl]benzene (**3ao**)



The reaction conditions were modified. The reaction was carried out with **1a** (18.1 μL , 0.2 mmol), **2o** (25.4 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3ao** was purified by flash chromatography on silica gel (100:0–98:2, hexane/ Et_2O) (Figure 1-5; 39.6 mg, 0.18 mmol, 88% isolated yield, 12 h : 90% NMR yield). Pale yellow oil. **IR** (neat) 546, 781, 826, 1014, 1088, 1336, 1367, 1488, 2869, 2958 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.30 (d, $J = 8.4$ Hz, 2H), 7.25 (d, $J = 8.4$ Hz, 2H), 4.43 (q, $J = 6.4$ Hz, 1H), 3.78 (quintet, $J = 4.8$ Hz, 1H), 1.78–1.40 (m, 8H), 1.37 (d, $J =$

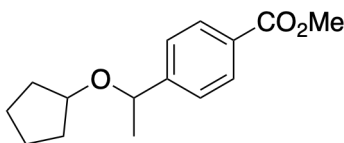
6.4 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 143.3, 132.7, 128.4, 127.6, 78.8, 74.8, 33.0, 31.9, 24.6, 23.5, 23.4. HRMS–DART (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{18}\text{ClO}$; 225.1041, found 225.1040.

[Oxybis(ethane-1,1-diyl)]dibenzene (**3zp**)



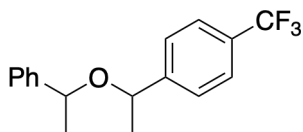
The reaction conditions were modified. The reaction was carried out with **1z** (24.2 μL , 0.2 mmol), **2p** (20.8 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3zp** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-5; 42.4 mg, 0.19 mmol, 94% isolated yield). Colorless oil. The ratio (51:49) of the diastereomers was determined by ^1H NMR analysis. The spectrum data of product **3zp** was consistent with the literature.¹²

Methyl 4-[1-(Cyclopentyloxy)ethyl]benzoate (**3aq**)



The reaction conditions were modified. The reaction was carried out with **1a** (18.1 μL , 0.2 mmol), **2q** (32.4 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3aq** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–95:5, hexane/EtOAc) (Figure 1-5; 36.8 mg, 0.15 mmol, 74% isolated yield). Pale yellow oil. IR (neat) 773, 857, 1092, 1110, 1275, 1435, 1611, 1721, 2870, 2952 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 8.01 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 4.51 (q, J = 6.4 Hz, 1H), 3.91 (s, 3H), 3.79 (quintet, J = 4.4 Hz, 1H), 1.76–1.42 (m, 8H), 1.40 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 167.0, 150.3, 129.7, 129.0, 126.1, 79.1, 75.2, 52.0, 33.0, 31.9, 24.5, 23.5, 23.4. HRMS–DART (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{15}\text{H}_{24}\text{NO}_3$; 266.1751, found 266.1752.

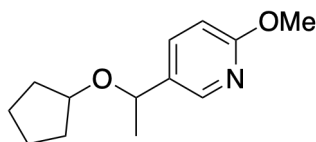
1-[1-(1-Phenylethoxy)ethyl]-4-(trifluoromethyl)benzene (**3zr**)



The reaction conditions were modified. The reaction was carried out with **1z** (24.2 μL , 0.2 mmol), **2r** (34.2 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10

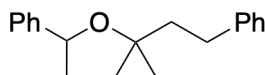
mol %) in DCM (500 μ L) under blue LED irradiation for 24 h. The product **3zr** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–95:5, hexane/EtOAc) (Figure 1-5; 34.1 mg, 0.12 mmol, 58% isolated yield). Colorless oil. **IR** (neat) 700, 761, 841, 1018, 1066, 1088, 1122, 1163, 1323, 2976 cm^{-1} . The ratio (50:50) of the diastereomers was determined by ^1H NMR analysis. ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, J = 8.0 Hz, $0.5 \times 2\text{H}$), 7.52 (d, J = 8.0 Hz, $0.5 \times 2\text{H}$), 7.41–7.33 (m, 3H), 7.32–7.20 (m, 4H), 4.54 (m, 1H), 4.31 (q, J = 6.4 Hz, $0.5 \times 1\text{H}$), 4.20 (q, J = 6.4 Hz, $0.5 \times 1\text{H}$), 1.47 (m, 3H), 1.39 (m, 3H). Signals for two diastereomers were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 148.4, 148.4, 143.7, 143.6, 129.6 (q, $J_{\text{C-F}}$ = 32.5 Hz), 129.6 (q, $J_{\text{C-F}}$ = 33.0 Hz), 128.5, 128.3, 127.6, 127.3, 126.5 ($\times 2\text{C}$), 126.4 ($\times 2\text{C}$), 126.2, 126.2, 125.5 (q, $J_{\text{C-F}}$ = 3.7 Hz), 125.2 (q, $J_{\text{C-F}}$ = 3.9 Hz), 75.1 ($\times 2\text{C}$), 74.1, 74.0, 24.6, 24.6, 23.3, 22.9. Signals for two diastereomers were given: ^{19}F NMR (376.5 MHz, CDCl_3) δ –62.4, –62.4. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{17}\text{H}_{21}\text{F}_3\text{NO}$; 312.1570, found 312.1568.

5-[1-(Cyclopentyloxy)ethyl]-2-methoxypyridine (**3as**)



The reaction conditions were modified. The reaction was carried out with **1a** (18.1 μ L, 0.2 mmol), **2s** (27.0 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol % or 10.8 mg, 0.04 mmol, 20 mol %) in DCM (500 μ L) under blue LED irradiation for 24 h. The product **3as** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–97:3, hexane/EtOAc) (Figure 1-5; 21.6 mg, 0.10 mmol, 49% isolated yield, 20 mol % Collidine HOTf: 54% isolated yield). Pale yellow oil. **IR** (neat) 1028, 1093, 1252, 1282, 1323, 1397, 1492, 1608, 2871, 2955 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 8.06 (d, J = 2.4 Hz, 1H), 7.58 (dd, J = 8.4, 2.4 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H), 4.43 (q, J = 6.4 Hz, 1H), 3.93 (s, 3H), 3.78 (m, 1H), 1.74–1.42 (m, 8H), 1.40 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 163.7, 144.8, 136.9, 132.5, 110.9, 78.5, 72.7, 53.4, 33.0, 31.9, 24.2, 23.4, 23.4. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{20}\text{NO}_2$; 222.1489, found 222.1482.

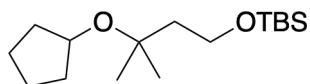
[3-Methyl-3-(1-phenylethoxy)butyl]benzene (**3zt**)



The reaction conditions were modified. The reaction was carried out with **1z** (72.6 μ L, 0.6 mmol), **2t** (29.2 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μ L) under blue LED irradiation for 48 h. The product **3zt** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-5; 36.1 mg, 0.13 mmol, 67%

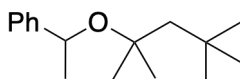
isolated yield). Colorless oil. The spectrum data of product **3zt** was consistent with the literature.¹³

***tert*-Butyl[3-(cyclopentyloxy)-3-methylbutoxy]dimethylsilane (**3au**)**



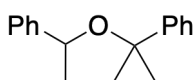
The product **3au** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-5; 45.6 mg, 0.16 mmol, 80% isolated yield). Red oil. **IR** (neat) 774, 836, 1045, 1091, 1152, 1255, 1362, 1472, 2857, 2956 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 3.99 (m, 1H), 3.71 (t, $J = 7.2$ Hz, 2H), 1.81–1.64 (m, 6H), 1.49–1.42 (m, 4H), 1.15 (s, 6H), 0.89 (s, 9H), 0.05 (s, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 73.9, 73.1, 59.7, 43.8, 34.9, 27.1, 26.0, 23.6, 18.3, -5.3 . **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{35}\text{O}_2\text{Si}$; 287.2401, found 287.2403.

{1-[(2,4,4-Trimethylpentan-2-yl)oxy]ethyl}benzene (3zv**)**



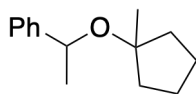
The reaction conditions were modified. The reaction was carried out with **1z** (72.6 μL , 0.6 mmol), **2v** (31.2 μL , 0.2 mmol), **Ir(ppy)₃** (1.3 mg, 0.002 mmol, 1 mol %) or **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3zv** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-5; **Ir(ppy)₃**: 42.5 mg, 0.18 mmol, 91% isolated yield, **PTH-1**: 23.4 mg, 0.10 mmol, 50% isolated yield). Colorless oil. **IR** (neat) 700, 759, 1020, 1028, 1081, 1125, 1213, 1365, 1383, 2952 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.35–7.26 (m, 4H), 7.19 (t, $J = 7.2$ Hz, 1H), 4.65 (q, $J = 6.4$ Hz, 1H), 1.52 (s, 2H), 1.34 (d, $J = 6.4$ Hz, 3H), 1.22 (s, 3H), 1.05 (s, 3H), 1.02 (s, 9H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 147.9, 128.0, 126.4, 125.7, 69.6, 54.9, 31.8, 31.3, 28.7, 27.2, 26.8. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{16}\text{H}_{30}\text{NO}$; 252.2322, found 252.2324.

[2-(1-Phenylethoxy)propan-2-yl]benzene (3zw**)**



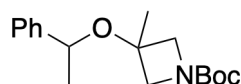
The reaction conditions were modified. The reaction was carried out with **1z** (24.2 μL , 0.2 mmol), **2w** (26.0 μL , 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μL) under blue LED irradiation for 24 h. The product **3zw** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-5; 40.6 mg, 0.17 mmol, 84% isolated yield). Colorless oil. The spectrum data of product **3zw** was consistent with the literature.¹⁴

{1-[(1-Methylcyclopentyl)oxy]ethyl}benzene (3zx**)**



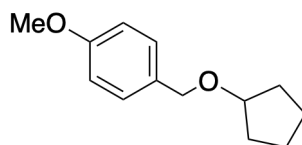
The reaction conditions were modified. The reaction was carried out with **1z** (72.6 μ L, 0.6 mmol), **2x** (21.1 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μ L) under blue LED irradiation for 48 h. The product **3zx** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-5; 20.0 mg, 0.10 mmol, 49% isolated yield). Pale yellow oil. **IR** (neat) 700, 759, 954, 1028, 1082, 1203, 1374, 1448, 2870, 2966 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.36–7.28 (m, 4H), 7.20 (tt, J = 7.2, 1.6 Hz, 1H), 4.58 (q, J = 6.8 Hz, 1H), 1.89 (m, 1H), 1.82–1.70 (m, 2H), 1.62–1.41 (m, 4H), 1.37–1.36 (m, 4H), 1.20 (s, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 147.4, 128.1, 126.4, 125.5, 85.6, 70.9, 39.0, 38.4, 26.7, 24.9, 23.9, 23.7. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{14}\text{H}_{24}\text{NO}$; 222.1852, found 222.1850.

***tert*-Butyl 3-Methyl-3-(1-phenylethoxy)azetidine-1-carboxylate (**3zy**)**



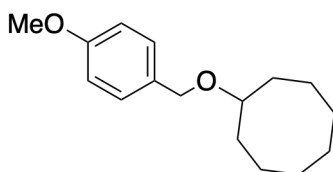
The product **3zy** was purified by flash chromatography on silica gel (100:0–70:30, hexane/EtOAc) (Figure 1-5; 30.4 mg, 0.10 mmol, 52% isolated yield). Yellow oil. **IR** (neat) 701, 1081, 1106, 1149, 1366, 1399, 1702, 2882, 2929, 2974 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.33–7.32 (m, 4H), 7.25 (m, 1H), 4.56 (q, J = 6.4 Hz, 1H), 3.93 (d, J = 8.8 Hz, 1H), 3.81 (d, J = 8.8 Hz, 1H), 3.66 (d, J = 8.8 Hz, 1H), 3.54 (d, J = 8.8 Hz, 1H), 1.43–1.42 (m, 15H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 156.5, 145.1, 128.4, 127.3, 125.7, 79.5, 72.6, 72.5, 60.8, 28.4, 25.6, 24.2. **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{26}\text{NO}_3$; 292.1907, found 292.1905.

1-[(Cyclopentyloxy)methyl]-4-methoxybenzene (3ez**)**



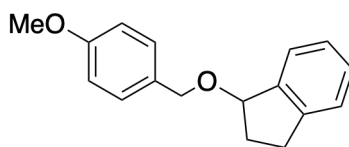
The reaction conditions were modified. The reaction was carried out with **1e** (83.0 mg, 0.6 mmol), **2z** (17.7 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol%), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol%) in DCM (500 μ L) under blue LED irradiation for 48 h. The product **3ez** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-5; 21.8 mg, 0.11 mmol, 53% isolated yield). Paleyellow oil. The spectrum data of product **3ez** was consistent with the literature.¹⁵

[(4-Methoxybenzyl)oxy]cyclooctane (3eA**)**



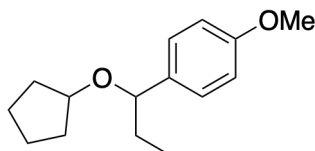
The reaction conditions were modified. The reaction was carried out with **1e** (83.0 mg, 0.6 mmol), **2A** (25.9 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol%), and **HX-1** (5.4 mg, 0.02 mmol, 10 mol%) in DCM (500 μ L) under blue LED irradiation for 48 h. The product **3eA** was purified by flash chromatography on silica gel (100:0–95:5, hexane/AcOEt) (Figure 1-5; 33.5 mg, 0.13 mmol, 67% isolated yield). Pale yellow oil. **IR** (neat) 820, 1037, 1071, 1171, 1246, 1465, 1512, 1613, 2852, 2921. **¹H NMR** (400 MHz, CDCl₃) δ 7.26 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.50 (m, 1H), 1.89–1.82 (m, 2H), 1.77–1.67 (m, 4H), 1.62–1.49 (m, 5H), 1.46–1.39 (m, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 158.9, 131.4, 129.0, 113.7, 78.4, 69.6, 55.2, 31.4, 27.3, 25.4, 23.1. **HRMS–DART** (m/z): [M+NH₄]⁺ calcd for C₁₆H₂₈NO; 266.2115, found 266.2111.

1-[(4-Methoxybenzyl)oxy]-2,3-dihydro-1H-indene (**3eB**)



The product **3eB** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–93:7, hexane/EtOAc) (Figure 1-5; 50.9 mg, 0.2 mmol, 99% isolated yield). Colorless oil. **IR** (neat) 756, 1034, 1074, 1246, 1301, 1460, 1512, 1611, 2850, 2934 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.40 (d, J = 6.8 Hz, 1H), 7.31 (dt, J = 8.4, 2.0 Hz, 2H), 7.25–7.19 (m, 3H), 6.88 (d, J = 6.8 Hz, 2H), 5.00 (dd, J = 6.4, 4.4 Hz, 1H), 4.59 (d, J = 11.6 Hz, 1H), 4.55 (d, J = 11.6 Hz, 1H), 3.80 (s, 3H), 3.09 (m, 1H), 2.81 (m, 1H), 2.34 (m, 1H), 2.13 (m, 1H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 159.1, 144.0, 142.9, 130.9, 129.3, 128.3, 126.3, 125.1, 124.8, 113.8, 82.3, 70.2, 55.3, 32.4, 30.2. **HRMS–DART** (m/z): [M+NH₄]⁺ calcd for C₁₇H₂₂NO₂; 272.1645, found 272.1648.

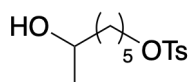
1-[1-(Cyclopentyloxy)propyl]-4-methoxybenzene (**3aC**)



The reaction conditions were modified. The reaction was carried out with **1a** (18.1 μ L, 0.2 mmol), **2C** (29.9 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μ L) under blue LED irradiation for 24 h. The product **3aC** was purified by flash

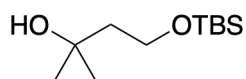
chromatography on silica gel (Biotage Selekt, 100:0–90:10, hexane/EtOAc) (Figure 1-5; 46.9 mg, 0.2 mmol, 99% isolated yield). Pale yellow oil. **IR** (neat) 1039, 1055, 1100, 1171, 1247, 1302, 1511, 1611, 2871, 2958 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.21 (d, $J = 8.4$ Hz, 2H), 6.87 (d, $J = 8.4$ Hz, 2H), 4.10 (dd, $J = 7.2, 6.0$ Hz, 1H), 3.80 (s, 3H), 3.76 (m, 1H), 1.78–1.39 (m, 10H), 0.88 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 158.7, 135.7, 127.8, 113.5, 80.8, 78.4, 55.2, 33.1, 31.6, 23.4, 10.6. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{15}\text{H}_{26}\text{NO}_2$; 252.1958, found 255.1961.

6-Hydroxyheptyl 4-Methylbenzenesulfonate (**5ab**)



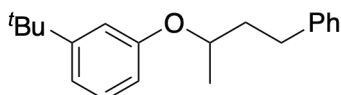
The reaction conditions were modified. The reaction was carried out with **4a** (10.8 μL , 0.2 mmol), **2b** (40.1 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in acetone (500 μL) under blue LED irradiation for 24 h. The product **5ab** was purified by flash chromatography on silica gel (100:0–65:35, hexane/EtOAc) (Figure 1-6; 42.2 mg, 0.15 mmol, 74% isolated yield). Pale yellow oil. **IR** (neat) 555, 664, 815, 938, 1175, 1189, 1356, 2862, 2933, 3400 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.79 (d, $J = 8.0$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 4.03 (t, $J = 6.4$ Hz, 2H), 3.74 (m, 1H), 2.45 (s, 3H), 1.69–1.62 (m, 2H), 1.43–1.26 (m, 6H), 1.17 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 144.7, 133.2, 129.8, 127.9, 70.5, 67.9, 39.0, 28.8, 25.3, 25.1, 23.6, 21.6. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{14}\text{H}_{26}\text{NO}_4\text{S}$; 304.1577, found 304.1578.

4-[(*tert*-Butyldimethylsilyl)oxy]-2-methylbutan-2-ol (**5au**)



The reaction conditions were modified. The reaction was carried out with **4a** (10.8 μL , 0.2 mmol), **2u** (48.1 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in acetone (500 μL) under blue LED irradiation for 24 h. The product **5au** was purified by flash chromatography on silica gel (100:0–90:10, hexane/EtOAc) (Figure 1-6; 29.2 mg, 0.13 mmol, 67% isolated yield). Pale yellow oil. The spectrum data of product **5au** was consistent with the literature.¹⁶

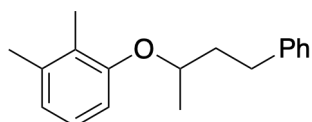
1-(*tert*-Butyl)-3-[(4-phenylbutan-2-yl)oxy]benzene (**7aa**)



The product **7aa** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-6; 35.5 mg, 0.13 mmol, 63% isolated yield). Pale yellow oil. **IR** (neat) 698, 1222, 1273,

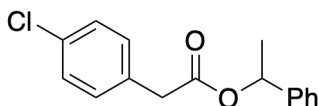
1289, 1486, 1579, 1604, 2866, 2963, 3026 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.29–7.25 (m, 2H), 7.21–7.17 (m, 4H), 6.97 (m, 1H), 6.91 (t, $J = 2.4$ Hz, 1H), 6.67 (dd, $J = 8.0, 2.4$ Hz, 1H), 4.37 (m, 1H), 2.85–2.70 (m, 2H), 2.08 (m, 1H), 1.88 (m, 1H), 1.33 (d, $J = 6.0$ Hz, 3H), 1.30 (s, 9H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 157.9, 153.0, 141.9, 128.9, 128.5, 128.4, 125.8, 117.7, 113.9, 112.0, 72.6, 38.3, 34.7, 31.9, 31.3, 19.8. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{20}\text{H}_{30}\text{NO}$; 300.2322, found 300.2322.

1,2-Dimethyl-3-[(4-phenylbutan-2-yl)oxy]benzene (7ba)



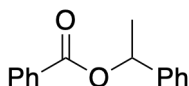
The product **7ba** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-6; 22.0 mg, 0.09 mmol, 43% isolated yield). Colorless oil. **IR** (neat) 699, 768, 1100, 1256, 1454, 1470, 1584, 2928, 2971, 3026 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.29–7.25 (m, 2H), 7.20–7.17 (m, 3H), 7.01 (m, 1H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.65 (d, $J = 8.0$ Hz, 1H), 4.34 (m, 1H), 2.84–2.71 (m, 2H), 2.27 (s, 3H), 2.22 (s, 3H), 2.08 (m, 1H), 1.91 (m, 1H), 1.31 (d, $J = 6.0$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 155.9, 142.0, 138.0, 128.5, 128.3, 126.2, 125.8, 125.6, 122.0, 110.7, 73.1, 38.5, 31.9, 20.2, 19.9, 11.9. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{18}\text{H}_{26}\text{NO}$; 272.2009, found 272.2006.

1-Phenylethyl 2-(4-Chlorophenyl)acetate (9ap)



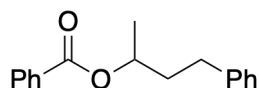
The reaction conditions were modified. The reaction was carried out with **8a** (102.4 mg, 0.6 mmol), **2p** (20.8 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in PhCF_3 (500 μL) under blue LED irradiation for 24 h. The product **9ap** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-6; 52.4 mg, 0.19 mmol, 95% isolated yield). Yellow oil. **IR** (neat) 699, 1063, 1092, 1159, 1251, 1492, 1732, 2359, 2980, 3032 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.35–7.27 (m, 7H), 7.19 (d, $J = 8.4$ Hz, 2H), 5.88 (q, $J = 6.8$ Hz, 1H), 3.60 (s, 2H), 1.52 (d, $J = 6.8$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 170.3, 141.3, 133.0, 132.4, 130.6, 128.6, 128.5, 127.9, 126.0, 73.0, 40.9, 22.1. **HRMS–DART** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{16}\text{H}_{19}\text{ClINO}_2$; 292.1099, found 292.1091.

1-Phenylethyl Benzoate (9bp)



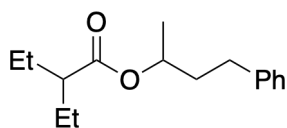
The reaction conditions were modified. The reaction was carried out with **8b** (73.3 mg, 0.6 mmol), **2p** (20.8 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in PhCF₃ (500 μ L) under blue LED irradiation for 24 h. The product **9bp** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-6; 45.0 mg, 0.20 mmol, 99% isolated yield). Colorless oil. The spectrum data of product **9bp** was consistent with the literature.¹⁷

4-Phenylbutan-2-yl Benzoate (**9ba**)



The reaction conditions were modified. The reaction was carried out with **8b** (73.3 mg, 0.6 mmol), **2a** (30.0 μ L, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in PhCF₃ (500 μ L) under blue LED irradiation for 24 h. The product **9ba** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (Figure 1-6; 13.2 mg, 0.05 mmol, 26% isolated yield). Yellow oil. The spectrum data of product **9ba** was consistent with the literature.¹⁸

4-Phenylbutan-2-yl 2-Ethylbutanoate (**9ca**)



The product **9ca** was purified by flash chromatography on silica gel (100:0–97:3, hexane/EtOAc) (Figure 1-6; 12.9 mg, 0.05 mmol, 26% isolated yield). Pale yellow oil. **IR** (neat) 699, 1130, 1150, 1181, 1728, 2360, 2876, 2934, 2964, 3027 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.30–7.26 (m, 2H), 7.20–7.17 (m, 3H), 4.99 (m, 1H), 2.69 (ddd, J = 14.0, 10.4, 5.2 Hz, 1H), 2.60 (ddd, J = 14.0, 10.4, 5.2 Hz, 1H), 2.19 (m, 1H), 1.93 (m, 1H), 1.81 (m, 1H), 1.68–1.49 (m, 4H), 1.25 (d, J = 5.2 Hz, 3H), 0.94–0.90 (m, 6H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 175.9, 141.6, 128.4, 128.3, 125.9, 70.0, 49.3, 37.8, 31.8, 25.2, 25.1, 20.1, 11.9, 11.9. **HRMS–DART** (m/z): [M+NH₄]⁺ calcd for C₁₆H₂₈NO₂; 266.2115, found 266.2113.

Labelling Experiments

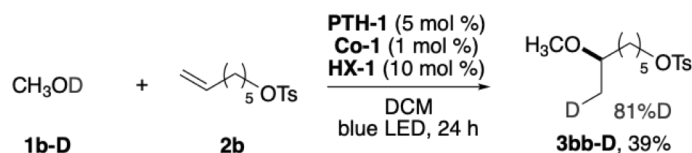


Figure S1-3.

The reaction with 1b-D (Figure 1-11A, top). In a glovebox, to an oven-dried vial equipped with a stirring bar was added **1b-D** (24.2 μ L, 0.6 mmol), **2b** (53.7 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol,

5 mol %), **Co-1** (1.2 mg, 0.002mmol, 1 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in DCM (500 μ L). After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away), with a cooling fan to keep the temperature at around 40 $^{\circ}$ C (Figure S1-2). After 24 h, the reaction was quenched with a short plug of silica gel using AcOEt. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 92:8–82:18, hexane/EtOAc) gave the coupling product **3bb-D** (Figure 1-11A; 23.5 mg, 0.08 mmol, 39% isolated yield: mixture of deuterated and nondeuterated compounds, 81:19) as a pale yellow oil. The ratio (81%D) of deuterium incorporation was determined by ^1H NMR analysis: ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 4.02 (t, J = 6.4 Hz, 2H), 3.29 (s, 3H), 3.23 (m, 1H), 2.45 (s, 3H), 1.68–1.61 (m, 2H), 1.45 (m, 1H), 1.38–1.22 (m, 5H), 1.10–1.06 (m, 2H + 0.19 $\times$ 1H). Signals for deuterated and nondeuterated compounds were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 144.6, 133.3, 129.8, 127.9, 76.5, 76.5, 70.6, 55.9, 36.1, 36.1, 28.8, 25.5, 24.7, 21.6, 18.9, 18.7 (t, $J_{\text{C-D}}$ = 19.1 Hz). **HRMS–DART** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{24}\text{DO}_4\text{S}$; 302.1531, found 302.1524.

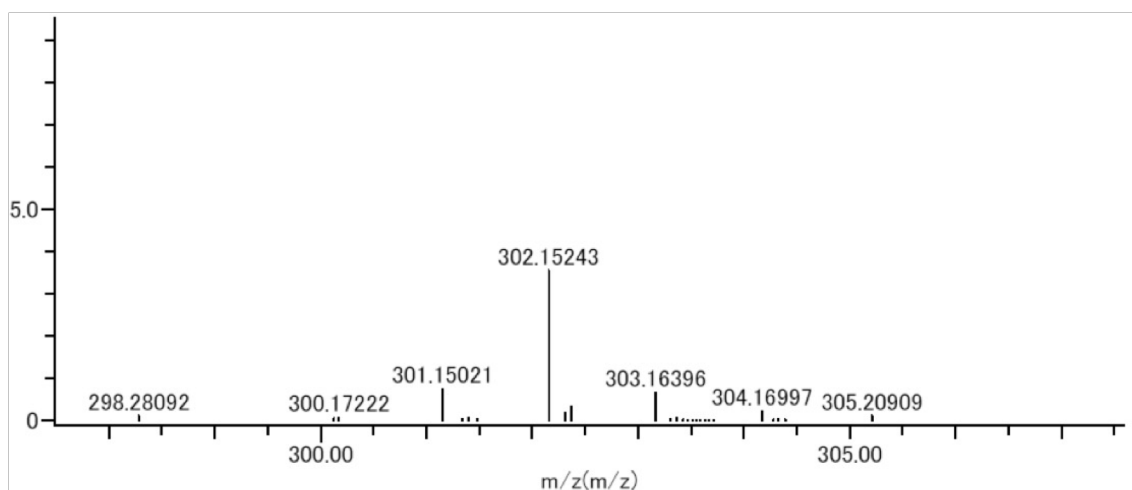


Figure S1-4. HRMS spectrum of **3bb-D**

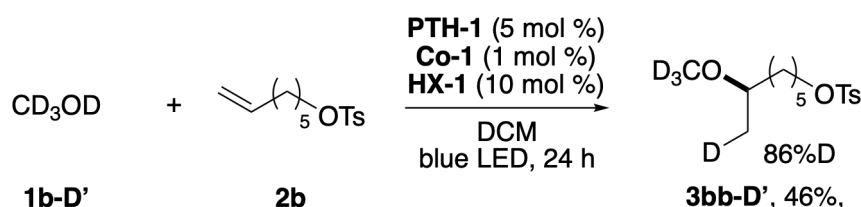


Figure S1-5.

The reaction with 1b-D' (Figure 1-11A, top). In a glovebox, to an oven-dried vial equipped with a stirring bar was added **1b-D'** (24.3 μ L, 0.6 mmol), **2b** (53.7 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), **Co-1** (1.2 mg, 0.002mmol, 1 mol %) and **HX-1** (5.4 mg, 0.02 mmol, 10 mol %) in

DCM (500 μ L). After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away), with a cooling fan to keep the temperature at around 40 $^{\circ}$ C. After 24 h, the reaction was quenched with a short plug of silica gel using AcOEt. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 98:2–88:12, hexane/EtOAc) gave the coupling product **3bb-D'** (Figure 1-11A; 28.0 mg, 0.09 mmol, 46% isolated yield: mixture of deuterated and nondeuterated compounds, 86:14) as a pale yellow oil. The ratio (86%D) of deuterium incorporation was determined by ^1H NMR analysis: ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 4.02 (t, J = 6.4 Hz, 2H), 3.23 (m, 1H), 2.45 (s, 3H), 1.68–1.61 (m, 2H), 1.45 (m, 1H), 1.38–1.22 (m, 5H), 1.10–1.06 (m, $0.86 \times 2\text{H} + 0.14 \times 3\text{H}$). Signals for deuterated and nondeuterated compounds were given: ^{13}C NMR (100.6 MHz, CDCl_3) δ 144.6, 133.1, 129.8, 127.8, 76.4, 76.3, 70.5, 55.0 (quintet, $J_{\text{C-D}}$ = 21.7 Hz), 36.0, 36.0, 28.7, 25.4, 24.7, 21.6, 18.9, 18.6 (t, $J_{\text{C-D}}$ = 19.2 Hz). HRMS–DART (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{21}\text{D}_4\text{O}_4\text{S}$; 305.1719, found 305.1718.

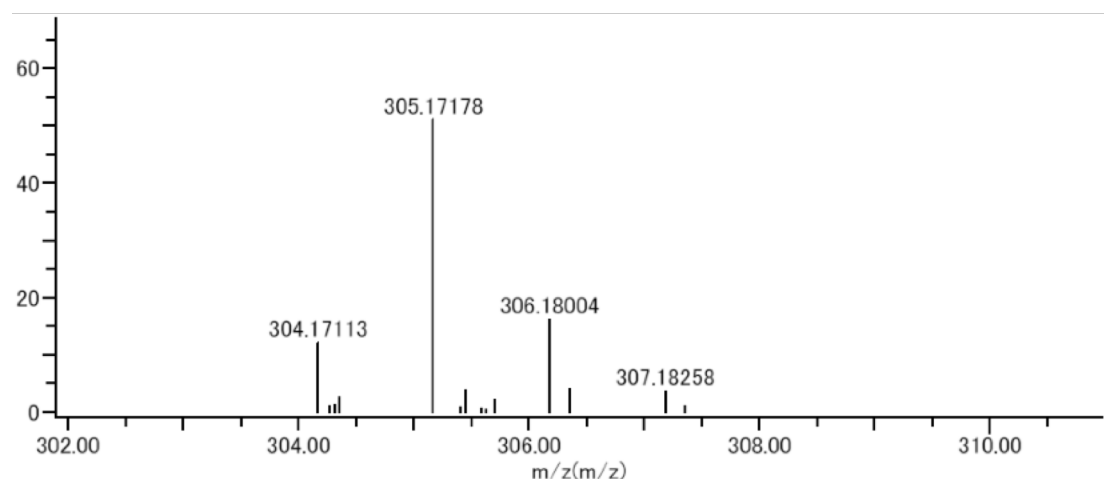


Figure S1-6. HRMS spectrum of **3bb-D'**

Decarboxylative Cross-Coupling of Secondary Aliphatic Redox Active Ester

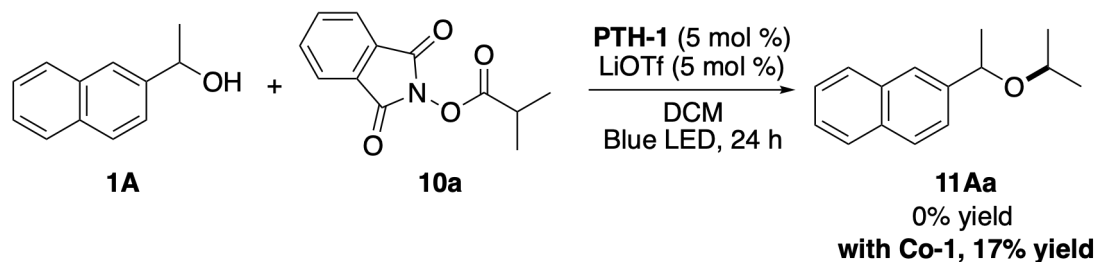


Figure S1-7.

Figure 1-11B. In a glovebox, to an oven-dried vial equipped with a stirring bar was added **1A** (103.3 mg, 0.6 mmol), **10a** (46.6 mg, 0.2 mmol), **PTH-1** (3.7 mg, 0.01 mmol, 5 mol %), lithium triflate (1.6 mg, 0.01 mmol), **Co-1** (1.2 mg, 0.01 mmol, 1 mol %) in DCM (500 μ L). After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away), with a cooling fan to keep the temperature at around 40 $^{\circ}$ C. After 24 h, the reaction was quenched with a short plug of silica gel using AcOEt. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (100:0–95:5, hexane/EtOAc) gave the coupling product **11Aa** (Figure 1-7B; 10.5 mg, 0.05 mmol, 24% isolated yield) as a pale yellow oil. The spectrum data of product **11Aa** was consistent with the literature.¹⁹

Cyclic Voltammetry Experiments

CV measurements were carried out under nitrogen atmosphere in organic solutions with 0.1 M of tetrabutylammonium perchlorate (Bu_4NClO_4) as a supporting electrolyte. Measurements were made with a glassy carbon electrode (area = 0.07 cm^2), an Ag/AgNO₃ reference electrode, and a Pt wire counter electrode. The sample solution prepared with appropriate concentration and the sweep rates were set to 100 mV/s. Ferrocene was used as an internal standard.

While the $E_{1/2}$ of **Co-1** did not change with or without **HX-1** (Figure S1-11 vs. Figure S1-8), the cathodic current corresponding to Co(I) to Co(II) with **HX-1** (Figure S1-11) became weaker than one in Figure S1-8. This result implied that Co(III)–H species was generated through single electron reduction of Co(II) to Co(I) by excited state of **PTH-1** followed by fast protonation of Co(I) by **HX-1**. The concerted mechanism involving Brønsted acidic activation of Co(II) by **HX-1** under the single electron transfer would not be feasible.

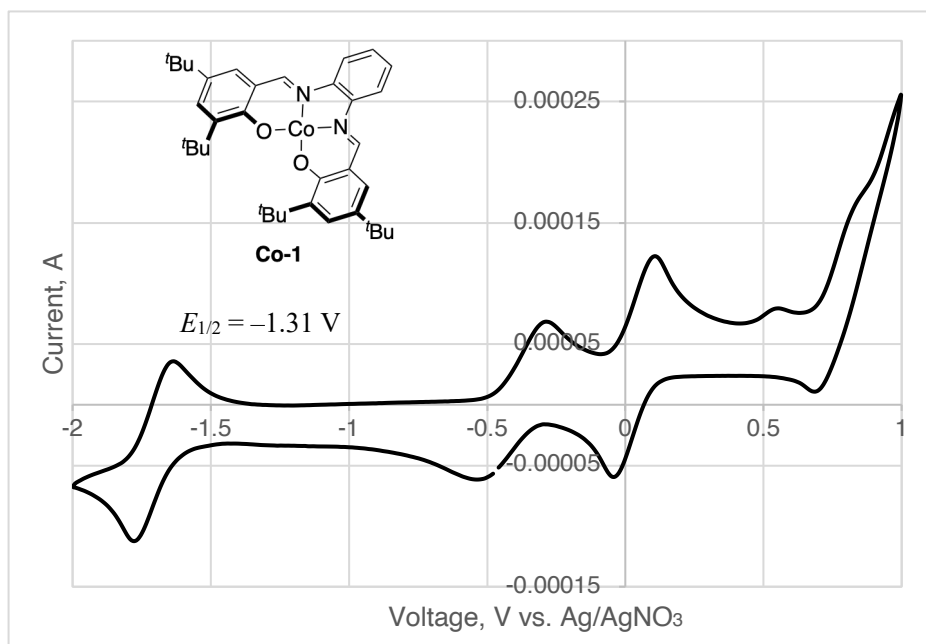


Figure S1-8. Cyclic voltammogram of **Co-1** in DMF (10 mM).

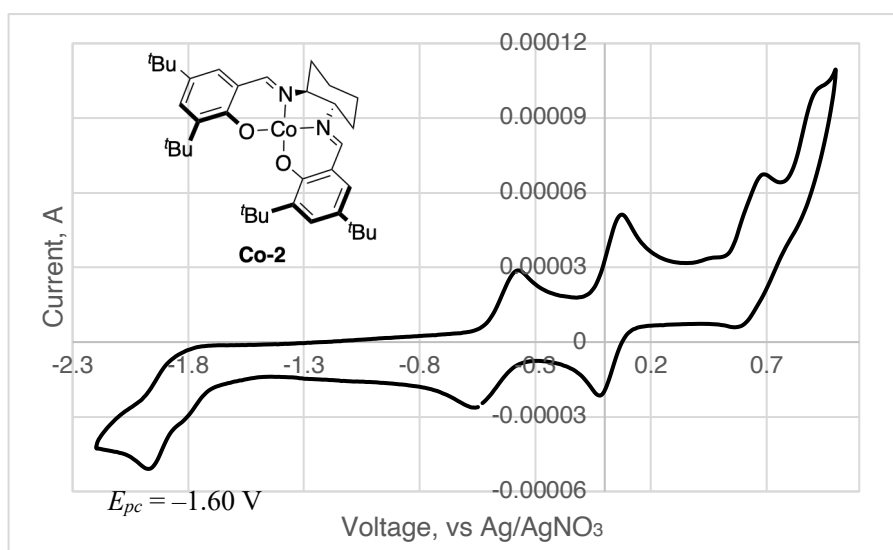


Figure S1-9. Cyclic voltammogram of **Co-2** in DMF (3 mM).

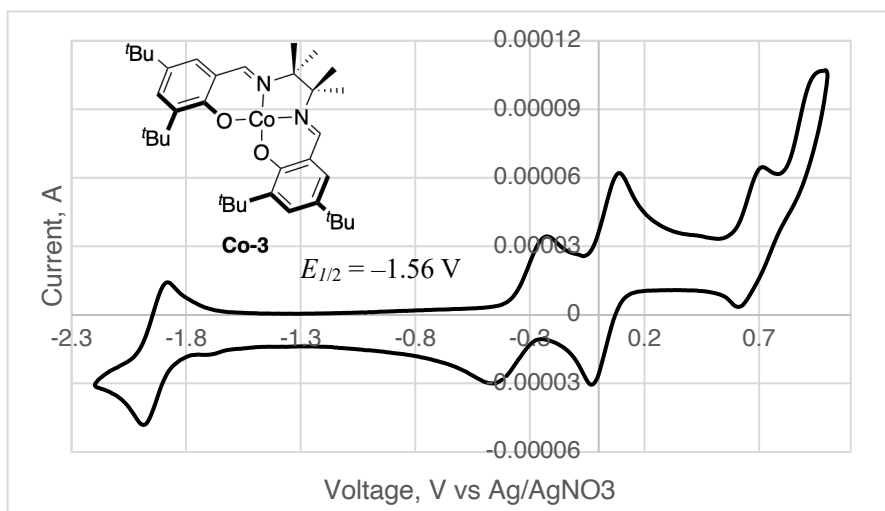


Figure S1-10. Cyclic voltammogram of **Co-3** in DMF (3 mM).

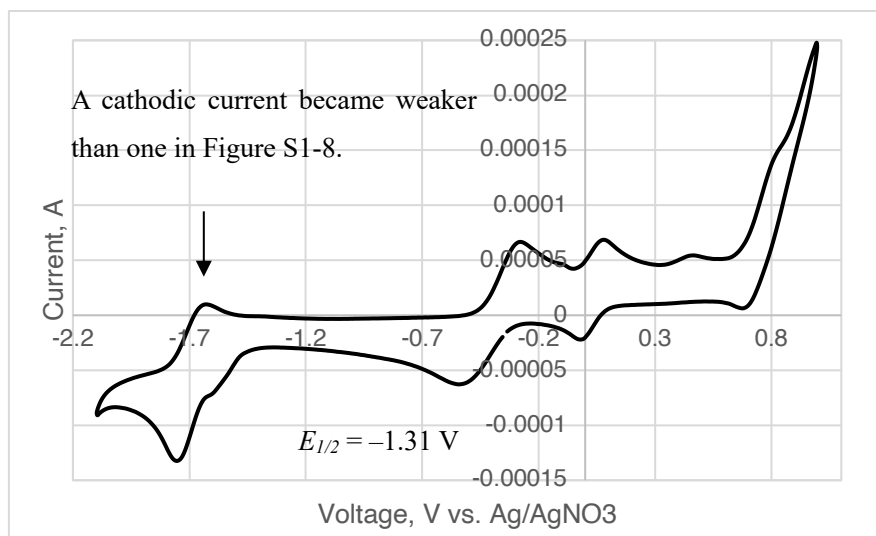


Figure S1-11. Cyclic voltammogram of **Co-1** (0.1 M) and **HX-1** (0.1 M) in DMF (10 mM).

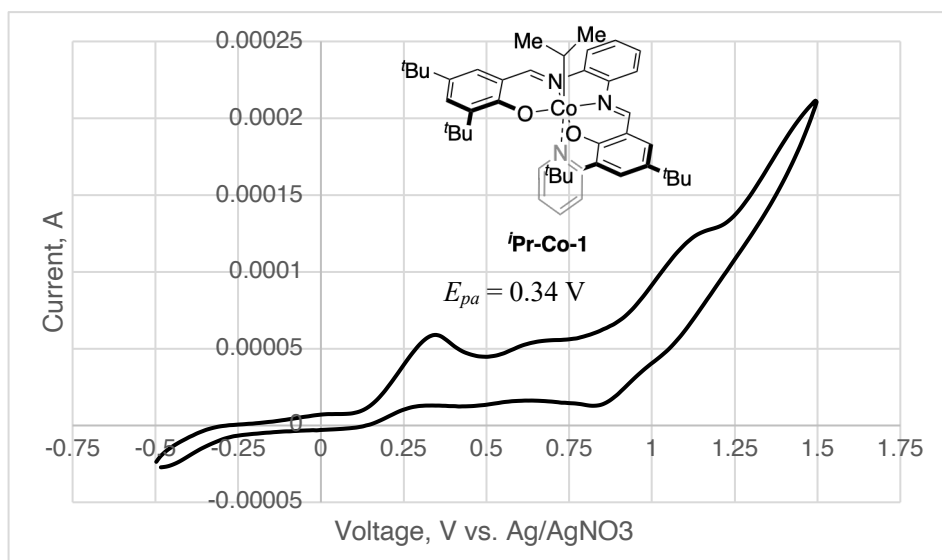


Figure S1-12. Cyclic voltammogram of **1Pr-Co-1** in DCM (3 mM).

UV-Vis Adsorption Spectra Experiments

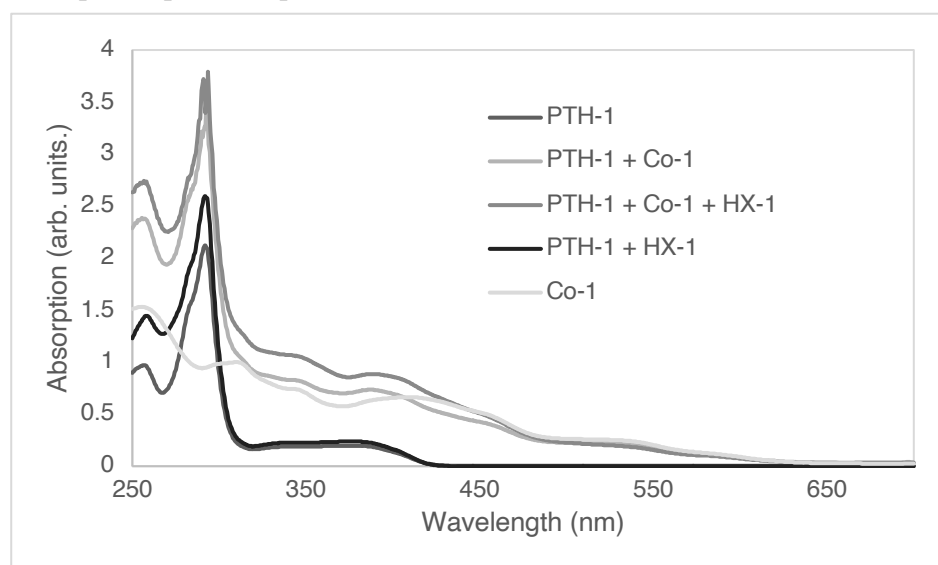


Figure S1-13. UV-Vis spectra of **PTH-1**, **Co-1** and **HX-1** (40 μ M)

Summary of Redox Properties of Organophotocatalysts

	PTH-1	PTH-2 ^a	PTH-3 ^b
$E_{1/2} (^2\text{PC}^{*+}/^1\text{PC})$ (V vs Ag/AgNO ₃) ^c	0.54	—	—
$E_{1/2} (^2\text{PC}^{*+}/^1\text{PC})$ (V vs SCE) ^d	0.92	(0.85)	0.68
$\lambda_{\text{max,em}}$ (nm)	435	439	—
$E_{\text{S1, exp}}$ (eV) ^e	2.85	2.82	2.80
$E_{\text{S1, exp}}^0 (^2\text{PC}^{*+}/^1\text{PC}^*)$ (V vs SCE) ^f	−1.94	(−1.97)	−2.1

^a ref 2. ^b ref 20. ^c Determined by CV experiments. ^d $E_{1/2} (\text{Ag}/\text{AgNO}_3)$ (V vs SCE) = 0.38 V. ^e Singlet energies were calculated using the maximum wavelength of emission. ^f Singlet excited state reduction potentials were calculated using the singlet energies and the $E_{1/2}$.

Stern-Volmer Luminescence Quenching Analysis

Several Stern-Volmer luminescence quenching experiments were carried out.

1. Quencher **Co-1** with or without collidinium salt **HX-1** (Figure S1-14)

The cobalt complex **Co-1** has a broad absorption in visible light region (Figure S1-13). To consider the inner filter effect of **Co-1**, the quenching ratio I_0/I , based on the measured steady-state emission intensity (I at 432 nm) of the excited state of **PTH-1** has been corrected followingly.¹⁹

$$(I_0/I)_{\text{corr}} = (I_0/I) \frac{\text{Abs (PTH-1)}}{\text{Abs (PTH-1)} + \text{Abs (Co-1)}} \frac{1-10^{-[\text{Abs(PTH-1)}+\text{Abs(Co-1)}]}}{1-10^{-\text{Abs(PTH-1)}}}$$

Procedure without HX-1: In a glovebox, to a screw-top 1.0 cm quartz cuvette was added 40 μM solution of **PTH-1** in degassed DCE and cobalt-salen complex **Co-1** (quencher) of appropriate concentration in degassed DCE (quencher concentration = 20 μM , 40 μM , 60 μM , 80 μM). The fluorescence intensity was measured at $\lambda = 430$ nm after excitation at $\lambda = 362$ nm in the quartz cuvette.

Procedure with HX-1: In a glovebox, to a screw-top 1.0 cm quartz cuvette was added 40 μM solution of PTH in degassed DCE, collidinium salt **HX-1** of appropriate concentration in degassed DCE (concentration = 40 μM), and cobalt-salen complex (quencher) of appropriate concentration in degassed DCE (quencher concentration = 20 μM , 40 μM , 60 μM , 80 μM). The fluorescence intensity was measured at $\lambda = 430$ nm after excitation at $\lambda = 362$ nm in the quartz cuvette.

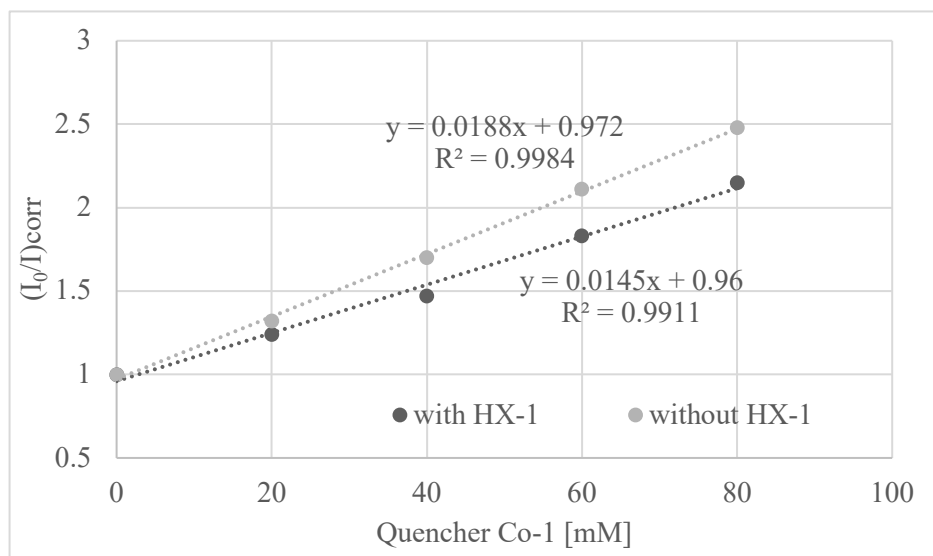


Figure S1-14.

2. Quencher: collidinium salt **HX-1** (Figure S1-15)

Procedure: In a glovebox, to a screw-top 1.0 cm quartz cuvette was added 40 μM solution of PTH in degassed DCE and collidinium salt (quencher) of appropriate concentration in degassed DCE (quencher concentration = 20 μM , 40 μM , 60 μM , 80 μM). The fluorescence intensity was measured at $\lambda = 430$ nm after excitation at $\lambda = 362$ nm in the quartz cuvette.

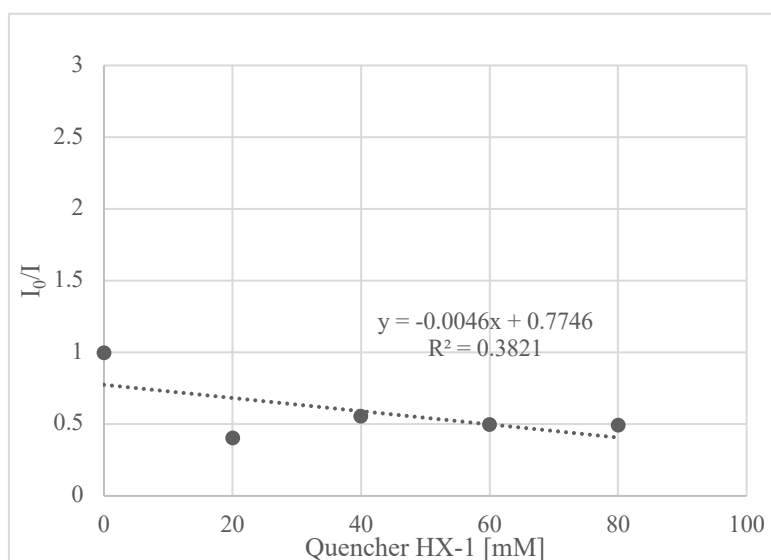


Figure S1-15.

The Stern-Volmer experiments revealed that the fluorescence of **PTH-1** is quenched by **Co-1**, but not by **HX-1** (Figure S1-14 and S1-15) .

Isolation of *N*-Phenyl Benzo[*b*]phenothiazine Radical Cation

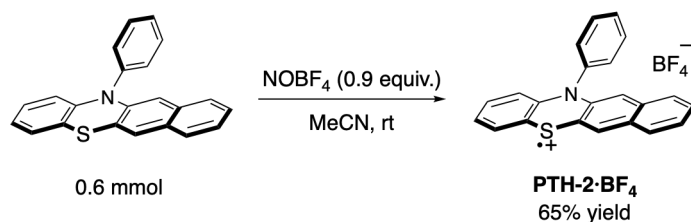


Figure S1-16. Preparation of **PTH-2·BF₄**

Figure S1-16. **PTH-2·BF₄** was prepared according to the reported procedure.²¹ In a Schlenk tube, **PTH-2** (195.3 mg, 0.6 mmol, 1.0 equiv.) was dissolved in 2 mL anhydrous MeCN. Then the mixture was cooled to 0 °C and nitrosonium tetrafluoroborate (63.1 mg, 0.54 mmol, 0.90 equiv.) was slowly added to the mixture. The mixture turned deep purple immediately and was stirred for a further 20 min. The mixture was freeze-pump-thawed for three cycles to remove the generated NO. Then the mixture was warmed to room temperature and the solvent removed. The solid was then dissolved in DCM (1.5 mL). A purple solid precipitated upon addition of hexanes. The purple solid was washed with hexanes three times to remove excess **PTH-2** then dried under reduced pressure. The obtained **PTH-2·BF₄** (150 mg, 0.39 mmol, 65%) was characterized by its absorption spectrum.

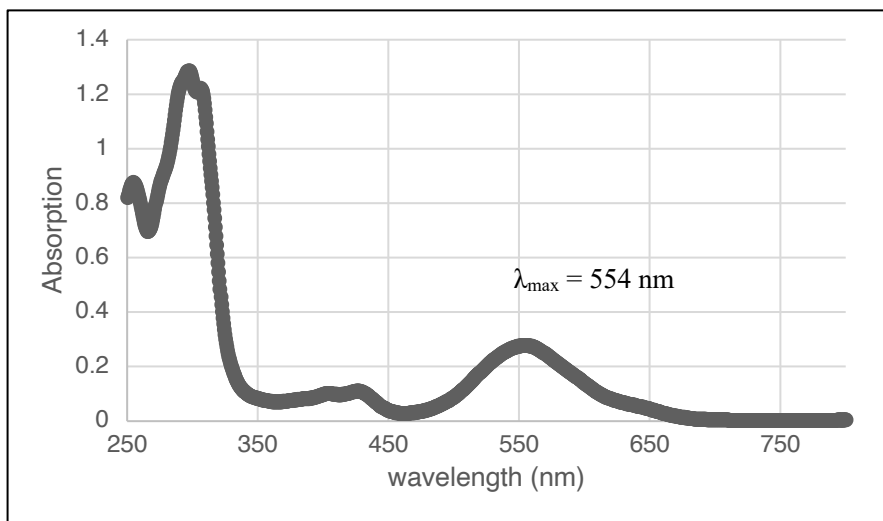


Figure S1-17. UV-Vis absorption spectrum of **PTH-2·BF₄**

Stoichiometric Reaction

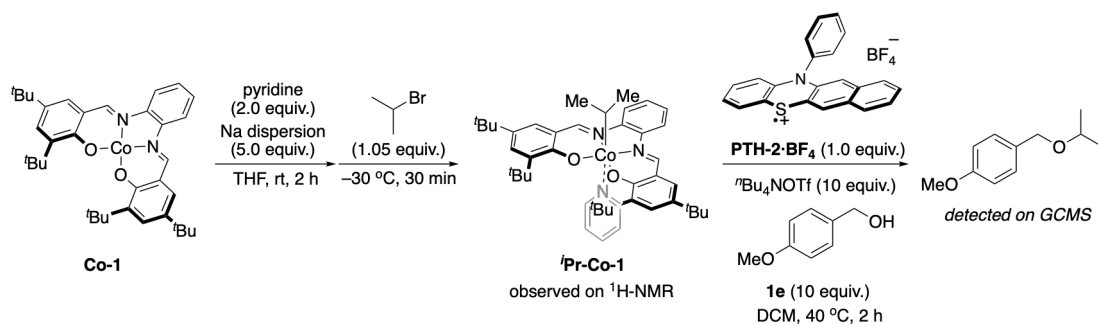


Figure S1-18. Stoichiometric Reaction

***i*Pr-Co-1** was prepared according to the literature procedure.²² In a glove box, an oven-dried 4 mL vial equipped with a Teflon-coated magnetic stir bar was charged with **Co-1** (59.8 mg, 0.10 mmol) and anhydrous THF (1.0 mL). Pyridine (16.1 μ L, 0.20 mmol) and Na dispersion (27.6 mg, 0.3 mmol, 25%wt) were sequentially added via syringe. The resulting red suspension was stirred at ambient temperature for 2 hours until a dark green solution was formed. After the vial was wrapped aluminum foil to avoid light and cooled at $-30\text{ }^{\circ}\text{C}$, 2-bromopropane (9.9 μ L, 0.11 mmol, 1.05 equiv.) was added. After stirring for 30 min at $-30\text{ }^{\circ}\text{C}$, the solution was passed through a short pad of silica gel (3 mm high) with small amount of DCM (50 μ L) to remove unreacted Na. Then, methyl benzoate (7.0 mg, 0.051 mmol) was added to the reaction mixture and the aliquot (10 μ L) was used to determine the yield of ***i*Pr-Co-1** (0.031 mmol, 31% yield, Figure S26) on $^1\text{H-NMR}$ (benzene- d_6) analysis (we have already confirmed that ***i*Pr-Co-1** was not decomposed by silica gel). The resulting mixture was kept in the refrigerator in the glovebox and used as a stock solution ($[\textbf{iPr-Co-1}] = 0.031\text{ mol/L}$). Although we could not fully characterize the ***i*Pr-Co-1** on $^1\text{H-NMR}$, the signals $\delta -0.41$ and 4.35 were consistent with ones of reported *i*Pr-Co(III) complex.²³

In a glovebox, an aliquot of ***i*Pr-Co-1** solution (160 μ L, 5 μ mol), tetrabutylammonium triflate (19.6 mg, 50 μ mol) and **PTH-2 $\cdot$ BF₄** (2.1 mg, 50 μ mol) were added to an oven-dried 4 mL vial equipped with a Teflon-coated magnetic stir bar. To the reaction mixture, DCM solution (130 μ L) of *p*-methoxy benzylalcohol **1e** (6.9 mg, 50 μ mol) was added. After sealing the vial with a cap, the reaction mixture was stirred at $40\text{ }^{\circ}\text{C}$ for 2 h. Then, the solution was passed through a short pad of silica gel and evacuated. The residue was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) and a trace amount of desired product was detected on GCMS.

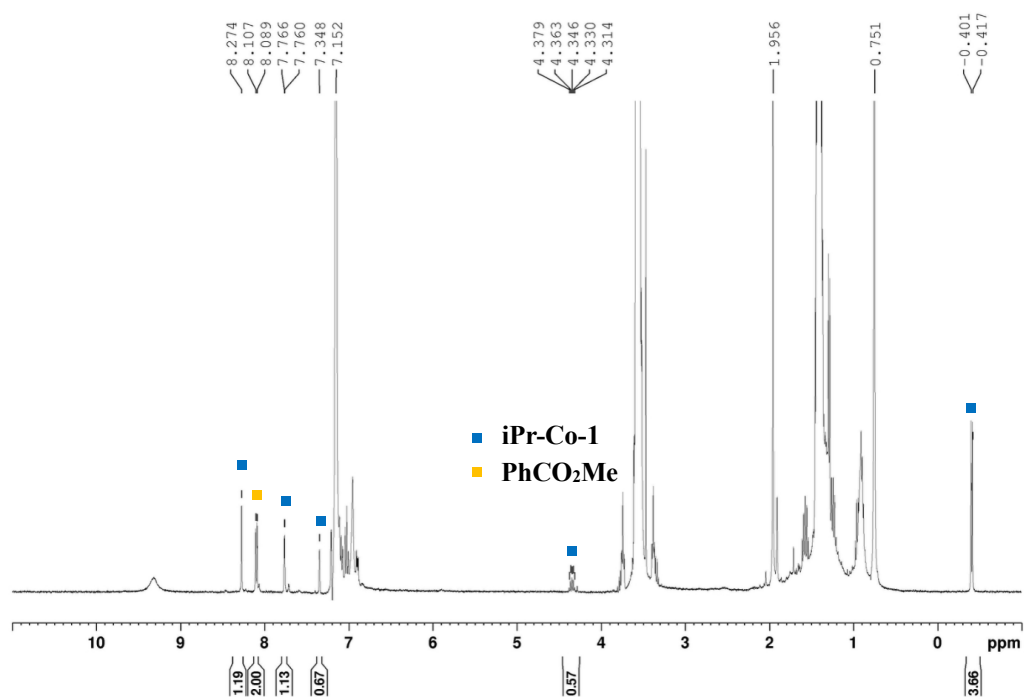


Figure S1-19. ^1H -NMR of $i\text{Pr-Co-1}$

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第二章 光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒による脂肪族アミンの γ -アミノ $C(sp^3)$ -H 官能基化反応の開発

第一節 着想背景および作業仮説

脂肪族アミンの位置選択的 $C(sp^3)$ -H 官能基化は、医薬品、農薬、天然物に見られる複雑な含窒素三次元骨格を迅速かつ直接的に構築できる有力な手法として注目されている。中でも、脂肪族アミンの γ 位 $C(sp^3)$ -H 結合を活性化し、求核剤を分子内または分子間反応により導入できれば、医薬品化学で重要なアゼチジン、1,3-ジアミン、1,3-アミノアルコール骨格を直接合成する手法となる。^{1,2} しかしながら、 γ 位 $C(sp^3)$ -H 結合の切断と、それに続く γ 位での官能基導入を両立させることは依然として困難であり、現時点で利用できる手法は限定的である。報告例の多くは配向基を活用した遷移金属触媒反応に依存しているが、求核剤に応じた反応条件の最適化が必要であるため、分子内反応および分子間反応の両方に適用可能な一般的な手法はいまだ確立されていない (Figure 2-1)。³

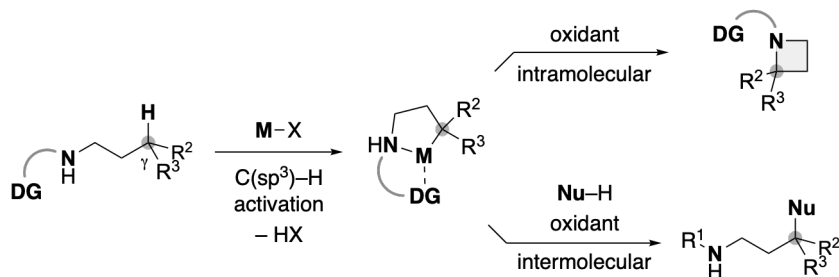


Figure 2-1. 遷移金属触媒による脂肪族アミンの γ 位 $C(sp^3)$ -H 官能基化

ラジカルを介した水素原子移動 (Hydrogen Atom Transfer, HAT) は、脂肪族アミンの位置選択的 $C(sp^3)$ -H 官能基化に対する有力な代替戦略として注目されている。しかし、これまで α 位または δ 位選択的な HAT 反応および続く官能基化^{4,5} は広く検討されてきた一方で、 γ 位選択的 HAT は報告例が少ない。⁶ ラジカル配向基を用いた脂肪族アミンの γ 位選択的 HAT 反応は報告されているものの、生成する炭素中心ラジカルとイオン性求核剤との反応性の不一致により、求核剤を官能基として導入できる例は限りがある。

この課題を克服するため、著者は光酸化還元触媒が駆動する、HAT 反応と酸化的ラジカル-極性交差 (Oxidative Radical-Polar Crossover, ORPC) 反応に着目した (Figure 2-2)。^{7,8} 具体的には、光酸化還元触媒の一電子還元により生成したラジカル中間体による脂肪族アミンの γ 位選択的 HAT により、 γ -アミノアルキルラジカルが生成する。続いて、生じたアルキルラジカルが光酸化還元触媒由来のラジカルカチオンによる一電子酸化を受けて、対応するカルボカチオン種へと変換される。最終的に、このカルボカチオン種が分子内または分子間の求核剤と反応し、 γ 位が官能基化されたアミンが得られる。

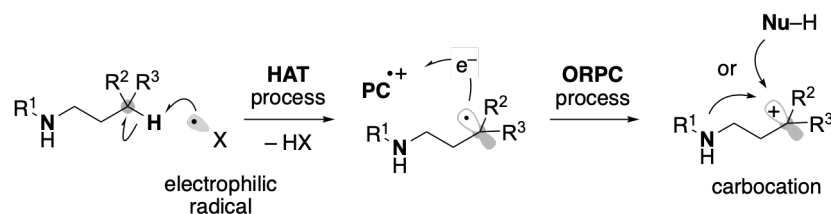


Figure 2-2. 光酸化還元触媒を用いた HAT-ORPC 戦略による γ -アミノ $C(sp^3)$ -H 官能基化

HAT-ORPC戦略を実現するため、脂肪族アミンに対する γ 位選択的HATを引き起こすラジカル配向基としてビニルスルホニル基に着目した (Figure 2-3)。⁶ビニルスルホニル基は、Co(III)-Hによるアルケンへの金属ヒドリド水素原子移動 (Metal-hydride Hydrogen Atom Transfer, MHAT) ⁹を経て α -スルホニルラジカルを生成する。生成した α -スルホニルラジカルは電子不足なアルキルラジカルであり、分子内HAT反応により γ -アミノ $C(sp^3)$ -H結合から水素原子を引き抜くことが知られている。また、著者は第一章において、光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒を用いたアルケンのマルコフニコフ選択的ヒドロ官能基化反応を見出したことを示した。¹⁰本反応では、Co(II)錯体が光酸化還元触媒およびブレンステッド酸触媒からそれぞれ一電子還元とプロトン化を受け、Co(III)-H種を生成する。続いて、Co(III)-H種がアルケンに対してMHAT反応を起こし、アルキルラジカルが生じる。これらの知見に基づき、ビニルスルホニル基からMHAT反応で生じるアルキルラジカルによる位置選択的な分子内HAT反応と、光酸化還元/コバルト/ブレンステッド酸触媒系を組み合わせることで、脂肪族アミンの γ 位 $C(sp^3)$ -H結合の官能基化が達成できると着想した。

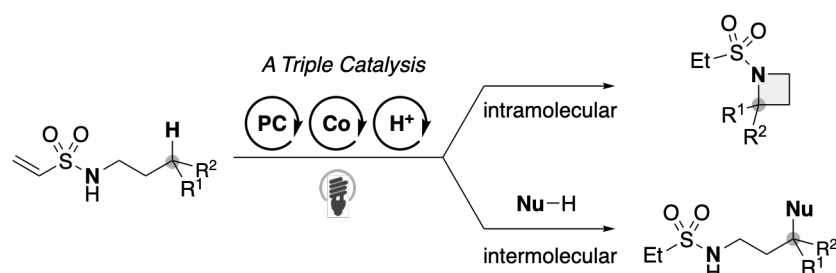


Figure 2-3. 光酸化還元触媒/コバルト触媒/ブレンステッド酸触媒による脂肪族アミンの γ -アミノ $C(sp^3)$ -H官能基化反応

第二節 作業仮説

分子内 γ -アミノ $C(sp^3)$ -H結合の官能基化反応についての作業仮説を示す (Scheme 2-4)。励起状態の光酸化還元触媒 (B) からCo(II) (C) への一電子移動により、Co(I)、光酸化還元触媒のラジカルカチオンを含むラジカルイオン対 (E) が形成する。続いて、コリジニウム塩 (D) がブレンステッド酸としてEと反応し、Co(III)-H種 (F) および光酸化還元触媒のラジカルカチオン (G) を与える。その後、Fはビニルスルホンアミド (1) に対してMHAT反応を起こし、アルキルコバルト(III)種 (I) を形成する。このアルキルコバルト(III)種は、Co(II)

種 (**J**) および電子不足なアルキルラジカル (**K**) と平衡状態となる。生成した電子不足なアルキルラジカルは、1,6-HAT反応を経て γ -アミノC-H結合から水素原子を引き抜く。^{6a}生じたアルキルラジカルはCo(II)種と結合を形成し、アルキルコバルト(III)種 (**L**) を与える。続いて、**G**が**L**を一電子酸化することで、光酸化還元触媒 (**A**) および対応するアルキルコバルト(IV)種 (**M**) が生成する。生成したアルキルコバルト(IV)種はカルボカチオン等価体として振る舞い、¹¹コリジン (**H**) の存在下で分子内求核置換反応が進行することで、アゼチジン (**2**) を与え、同時に**C**および**D**が再生される。¹²

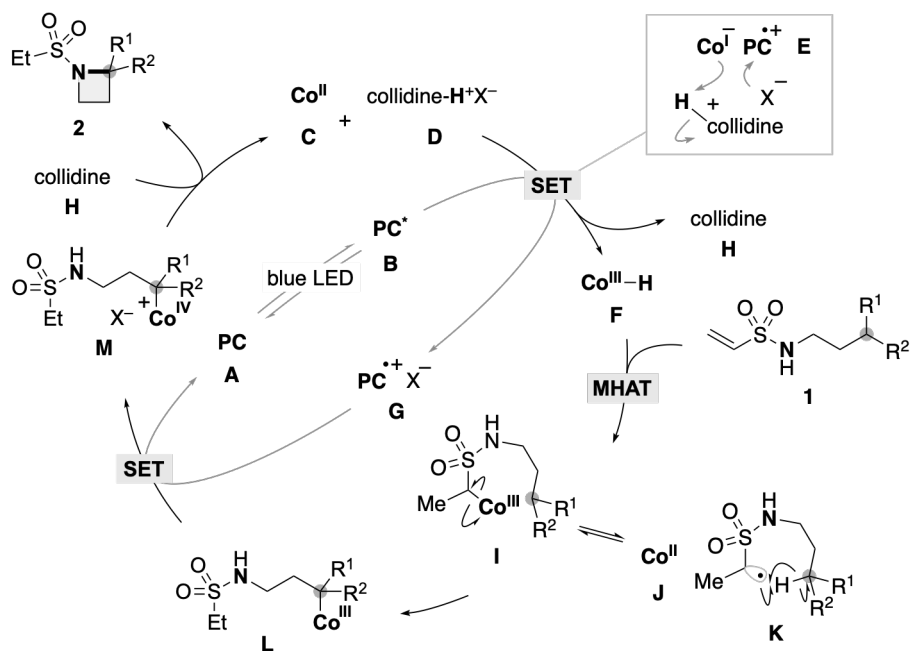
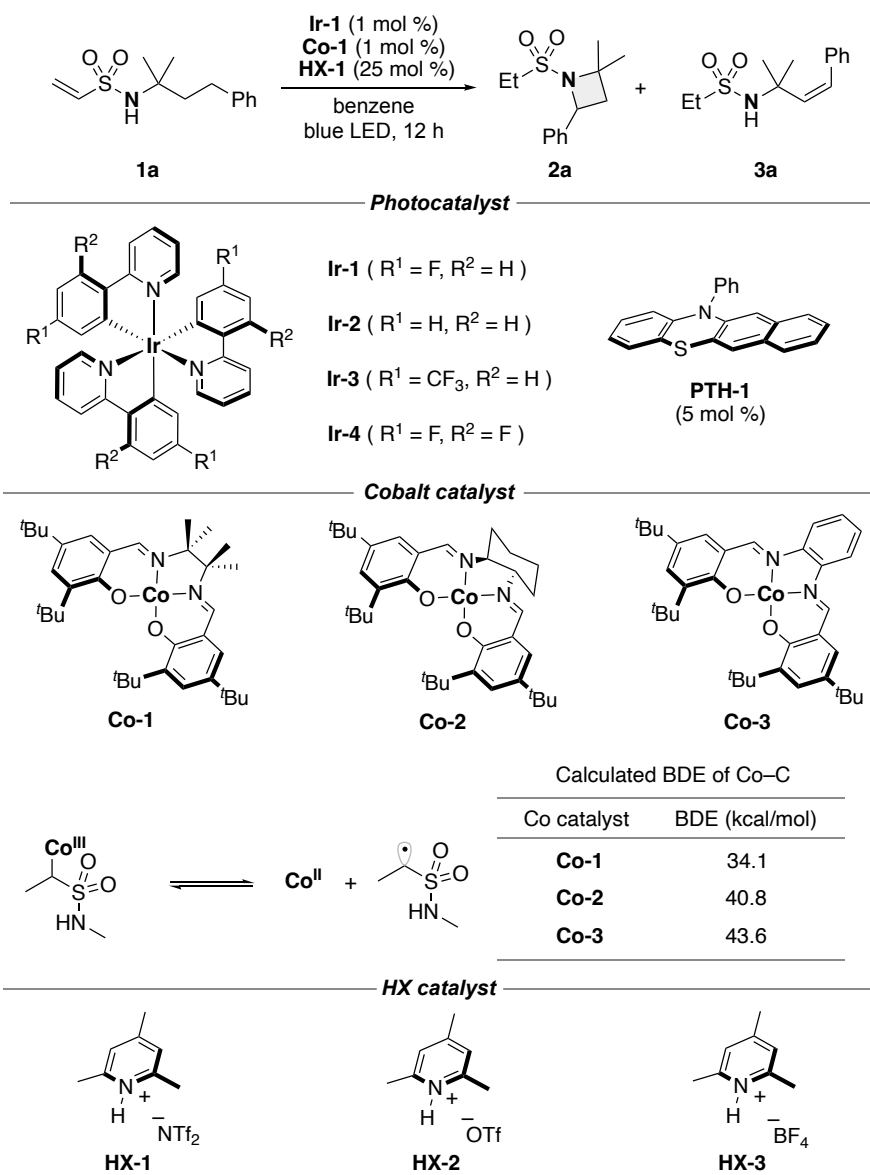


Figure 2-4. 作業仮説

第三節 反応条件の最適化および基質適用範囲の検討

N-ビニルスルホニル基を導入した脂肪族アミンを基質とした、アゼチジン合成における条件検討を示す (Table 2-1)。青色 LED 照射下、Ir(*p*-F-ppy)₃ (**PC-1**)、サレン型コバルト錯体 (**Co-1**)、およびコリジニウムビストリフルイミド (**HX-1**) を用いることで、2-メチル-4-フェニルブタン-2-アミン由来のビニルスルホンアミド (**1a**) が効率的に反応し、目的とするアゼチジン (**2a**) が高収率で得られた (Table 2-1, entry 1)。本手法は、先行研究の遷移金属触媒反応で必要とされていた高温条件や化学量論量の酸化剤を必要としない温和な条件でのアゼチジン合成を可能にした。

Table 2-1. 反応条件の最適化 ^a



Entry	Change from standard conditions	Yield of 2a (%) ^a	Yield of 3a (%) ^a	Yield of 1a (%) ^a
1	none	81 (76)	0	0
2	Ir-2 instead of Ir-1	76	0	0
3	Ir-3 instead of Ir-1	76	0	0
4	Ir-4 instead of Ir-1	81	0	0
5	PTH-1 (5 mol%) instead of Ir-1	71	0	5
6	4CzIPN instead of Ir-1	0	0	<99

7	Ir[dF(CF ₃)ppy] ₂ (dtbbpy)PF ₆ instead of Ir-1	0	0	98
8	Co-2 instead of Co-1	28	0	47
9	Co-3 instead of Co-1	30	0	53
10	HX-2 instead of HX-1	70	11	0
11	HX-3 instead of HX-1	71	0	0
12	toluene instead of benzene	74	0	0
13	trifluorotoluene instead of benzene	73	0	0
14	benzene (0.4 M)	62	0	0
15	w/o Ir-1 or Co-1 or HX-1	0	0	<88
16	under dark	0	0	97

^a Reaction was carried out with **1a** (0.1 mmol), photoredox catalyst (0.001 mmol), Co catalyst (0.001 mmol) and Brønsted acid catalyst (0.025 mmol) in benzene (1.0 mL, 0.1 M) under blue LED irradiation for 12 h. ^b ¹H NMR yield based on **1a**.

本反応においては、Ir(*p*-F-ppy)₃ (**Ir-1**) が最適な光酸化還元触媒であった。その他のイリジウム光酸化還元触媒 **Ir-2-4** および *N*-フェニルベンゾ[*b*]フェノチアジン触媒 **PTH-1** も、同程度の反応性を示した (entries 2-5)。一方、4CzIPN および Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ を用いた際には目的物が得られなかった (entries 6,7)。これは、触媒の還元力が十分でないこと (4CzIPN : $E_{\text{red}} = -1.24$ V vs SCE, Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ : $E_{\text{red}} = -1.37$ V vs SCE) ^{12,13} に起因し、Co(II)種 (**Co-1**, $E_{1/2 \text{ red}} = -1.56$ V vs SCE) の還元が非効率であったためと考えられる。さらに、*trans*-1,2-シクロヘキサンジアミンおよび *o*-フェニレンジアミン由来のコバルト触媒 **Co-2** および **Co-3** を用いた場合、生成物の収率は低下した (entries 8,9)。DFT 計算の結果、中間体 **I** における C-Co(III)結合の結合解離エネルギー (BDE) に差が生じることが明らかとなった。中でも、最適触媒の **Co-1** 由来のアルキルコバルト種における炭素-コバルト結合が最も弱いことが示され、この弱い結合が電子不足なアルキルラジカルの生成を促進し、後続する 1,6-HAT 段階を有利にすると考えられる。トリフルオロメタンスルホナートおよびテトラフルオロボラートなどの弱配位性アニオンについても検討を行ったところ、ビス(トリフルオロメチルスルホニル)イミデートと同程度の反応性を示すことが明らかとなった (entries 10,11)。溶媒としてはベンゼンが最適であったが、トルエンまたはトリフルオロトルエンを用いた際にも反応は進行した (entries 12,13)。一方で、反応濃度を高めた場合には、収率の低下が認められた (entry 14)。さらに、コントロール実験の結果、本反応の進行には三つの触媒と光照射が不可欠であることが示された (entries 15, 16)。

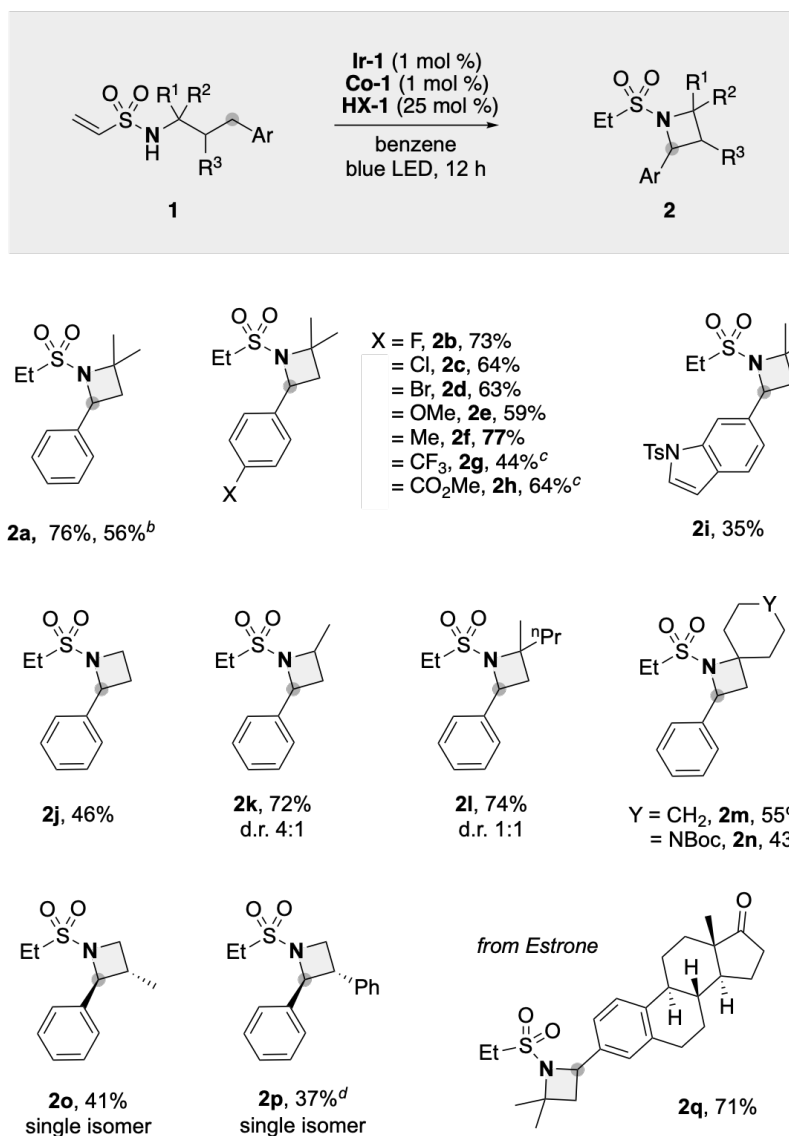


Figure 2-3. Substrate scope of azetidine synthesis. ^aReaction was carried out with **1** (0.1 mmol), **Ir-1** (0.001 mmol), **Co-1** (0.001 mmol) and **HX-1** (0.025 mmol) in benzene (1.0 mL) under blue LED irradiation for 12 h. ^b1.0 mmol scale. ^c**Ir-3** (0.001 mmol) was used instead of **Ir-1**. ^d**Ir-4** (0.001 mmol) was used instead of **Ir-1**.

本手法により、従来のベンジル位 C-H 官能基化の手法では合成が困難であった、様々な置換パターンを有する 2 位にアリール置換基が導入されたアゼチジンが合成可能であった (Figure 2-3)。本反応は、ハロゲン原子 (**2b–2d**)、電子供与性基 (**2e–2f** および **2i**)、ならびに電子求引性基 (**2g, 2h**) を有する基質に対して、中程度から高収率で反応が進行した。電子不足な芳香環を有する基質においては、**Ir-3** 触媒を用いることで、より効率的にアゼチジンが得られた (**2g, 2h**)。これは、比較的高い酸化力を有する **Ir-3** が、電子求引性基をもつ基質から生じるベンジルコバルト(III)種の酸化に適していることを示唆している。単純な 3-フェニルプロピルアミン誘導体も、本反応系に適用可能な基質であった (**2j**)。しかしなが

ら、**2a** と比較すると **2j** の収率は低く、これは α -アミノ置換基による Thorpe–Ingold 効果が **2a** における 1,6-HAT 段階を促進しているためと考えられる。実際に、 α 位に置換基を有する脂肪族アミンでは、目的とするアゼチジンが高収率で得られた (**2k**, **2l**)。さらに、本手法はシクロヘキサン骨格やピペリジン骨格を有するスピロアゼチジンの合成にも適用可能であった (**2m**, **2n**)。 β,γ -二置換脂肪族アミンを基質とした場合にも反応は良好に進行し、単一のジアステレオマーが得られた (**2o**, **2p**)。また、エストロン由来の基質を用いた場合にもアゼチジンが得られ、本手法の官能基許容性の高さが示された (**2q**)。

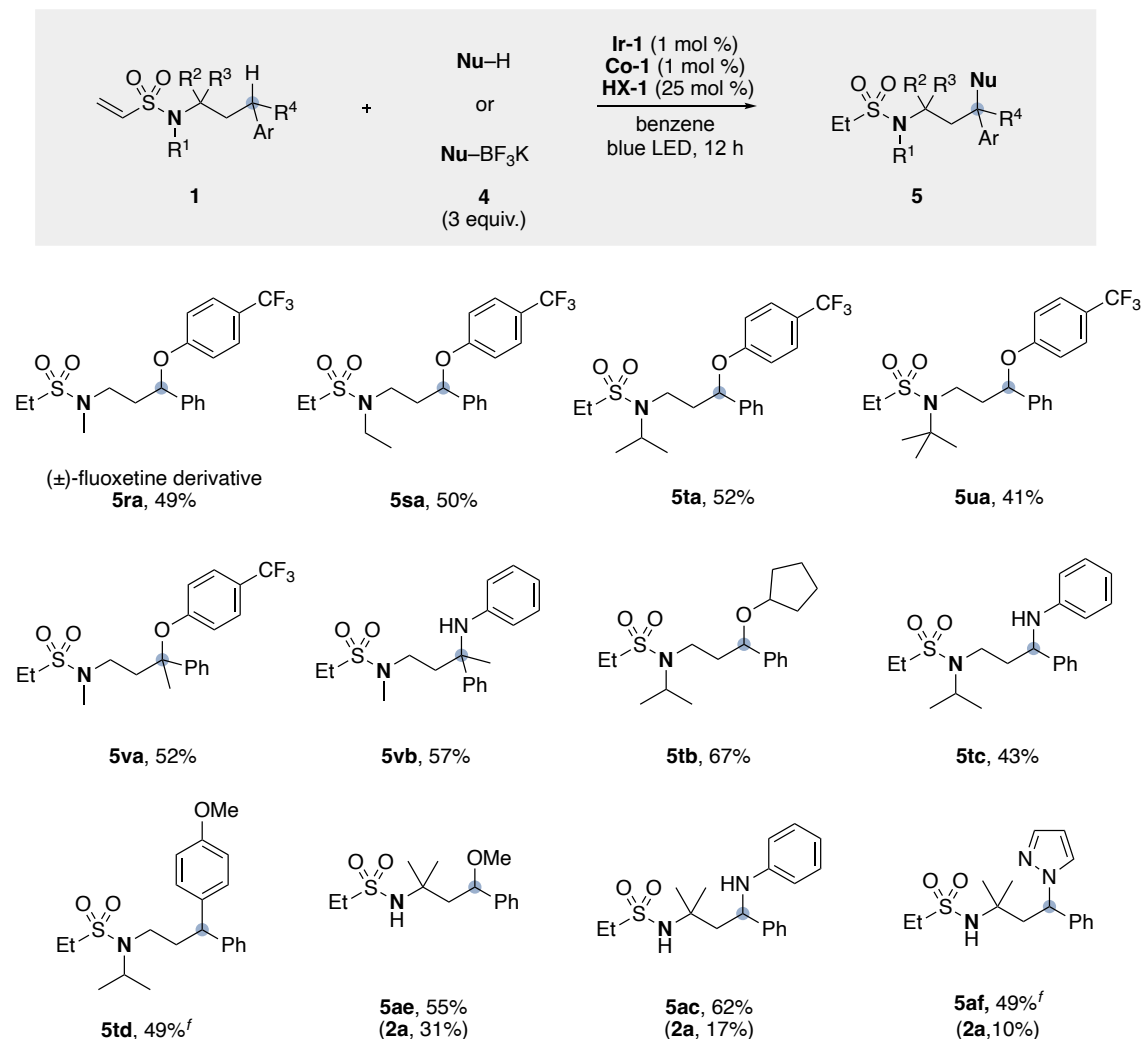


Figure 2-4. Substrate scope of intermolecular γ -amino $C(sp^3)$ -H functionalization. ^eReaction was carried out with **1** (0.1 mmol), **Ir-1** (0.001 mmol), **Co-1** (0.001 mmol) and **HX-1** (0.025 mmol) in benzene (1.0 mL) under blue LED irradiation for 12 h. ^f**HX-1** (0.1 mmol) was used.

次に、求核剤を用いた分子間反応の検討を行った (Figure 2-4)。その結果、*N*-メチル-3-フェニルプロパン-1-アミン誘導体 (**1r**) と 4-トリフルオロメチルフェノール (**4a**) との反応は、反応条件を大きく変更することなく効率的に進行し、目的の γ 位アルコキシ化生成物 (**5ra**) を与えた。本生成物はフルオキセチン骨格を有しており、本手法が医薬品合成へ応

用可能であることが示された。窒素原子上の置換基としては、第一級、二級、三級アルキル鎖のいずれも許容され、高い基質一般性が確認された (**5sa–5ua**)。さらに、本反応系は第三級ベンジル位 C(sp³)-H 結合の活性化にも適用可能であり、求核剤と反応し炭素-酸素結合形成が達成された (**5va, 5vb**)。また、シクロペンタノールおよびアニリンを求核剤として用いた場合にも、それぞれ対応するベンジルエーテル (**5tb**) およびベンジルアミン (**5tc**) が得られた。これにより、本手法が医薬品や天然物によく見られる 1,3-ジアミンおよび 1,3-アミノアルコール骨格の構築に有効であることが示された。第一級アミン誘導体を基質として用いた場合には、アゼチジン形成よりも分子間反応が優先的に進行した (**5ac, 5ac, 5af**)。加えて、テトラブチルアンモニウム (4-メトキシフェニル) トリフルオロボラートを求核剤として用いた場合には、フリーデル-クラフツ反応が進行し、 γ 位へのアリール基の導入が可能であった (**5td, 5rd**)。

第四節 反応機構解析

反応機構に関する知見を得るために、機構実験を行った。Table 2-1 の entry 10 において、主生成物 **2a** とともに副生成物 **3a** が得られていたことから、**3a** が反応中間体として関与している可能性があった。(Figure 2-5)。**3a** は光増感剤存在下で **3b** から容易に異性化することが知られているため、¹³ 最適反応条件下で **3b** を用いて反応を行った。しかしながら、反応はほとんど進行しなかった。この結果から、**3a** および **3b** の生成はいずれも本反応においての主経路ではないことが示唆された。

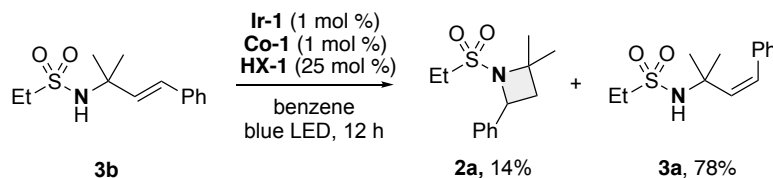


Figure 2-5. **3b** を用いた反応

次に、反応系に TEMPO を添加したところ、主生成物 **2a** とともに α -スルホニルアルコキシルアミン **5j** が得られた (Figure 2-6)。この結果は、反応途中に α -スルホニルラジカルが生成していることを示唆している。

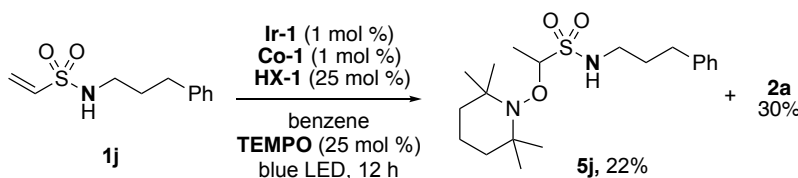


Figure 2-6. ラジカルトラップ実験

続いて、 γ -アミノ位に第二級ベンジル位 C-H 結合および第三級脂肪族 C-H 結合の両方を有する基質と **4a** との反応を検討した (Figure 2-7)。その結果、第三級脂肪族アルキル鎖の反応した生成物 **6w'** に対して、ベンジル位のアルコキシ化体 **6w** が相対的に多く生成する傾

向が見られた。この位置選択性は、C(sp³)-H 結合の結合解離エネルギーの差（第三級脂肪族 C-H : 96.5 kcal/mol、第二級ベンジル位 C-H : 85.4 kcal/mol）に起因すると考えられる。¹⁴

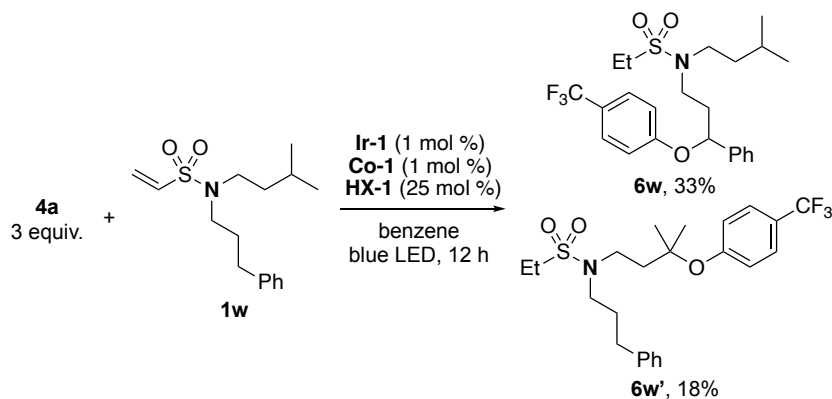


Figure 2-7. 競合実験

次に、RPC 段階の反応機構の詳細を計算によって明らかにした。ベンジルラジカルがベンジルコバルト(III)種へと直接酸化される経路と、ベンジルコバルト(III)種が酸化されてベンジルコバルト(IV)種を与える経路の2つが考えられる。先行研究に基づき、DFT 計算を用いてベンジルコバルト(III)種とベンジルラジカルとの安定性を比較した (Figure 2-8)。その結果、ベンジルラジカルの方がベンジルコバルト(III)種よりも安定であることが示され、ベンジルラジカルがベンジルコバルト(III)種へと直接酸化される経路が優先的に進行し得ることが示された。

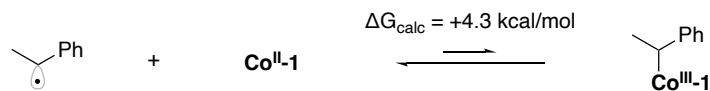


Figure 2-8. 計算による RPC 機構における反応機構の調査

さらに、分子間 HAT 試薬を用いた検討を行った (Figure 2-9)。まず、単純なビニルスルホンアミド **1x** または **1y** を分子間の HAT 試薬として用い、基質 **1z** との反応を行ったが、いずれの場合も目的生成物は得られなかった。

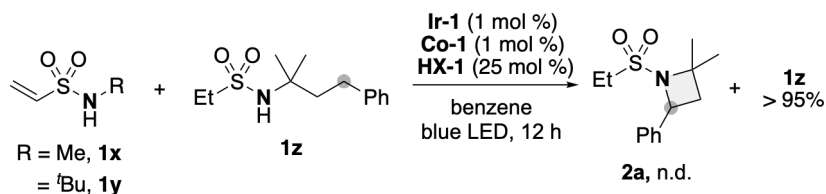


Figure 2-9. 分子間 HAT 試薬の検討

加えて、Musacchio^{7b} らおよび Doyle^{7c} らによって報告されている他の光酸化還元触媒を用いた分子間 HAT-ORPC 反応条件を **1z** に適用したが、いずれの反応も効率的に進行しなかった (Figure 2-10)。これらの結果は、本反応系における分子内の HAT 反応が高い選択性を有することを示している。

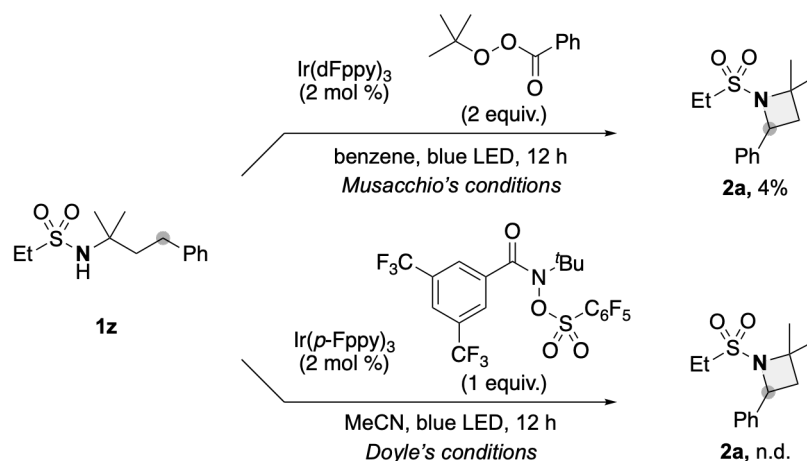


Figure 2-10. その他分子間 HAT 試薬による検討

イリジウム光酸化還元触媒による一電子還元過程の詳細を検討するため、消光実験を行った (Figure 2-11)。その結果、コバルト触媒の添加により励起状態のイリジウム触媒が効率的に消光されることが確認された。一方、コバルト触媒に加えてブレンステッド酸触媒を添加した場合は、消光の効率は下がった。

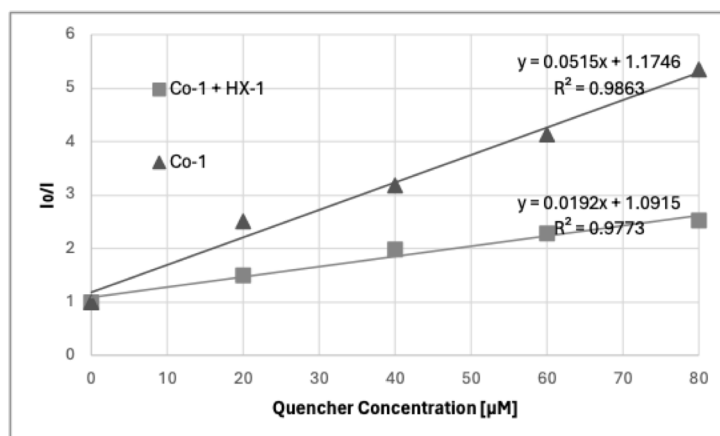


Figure 2-11. イリジウム光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒を用いた消光実験

加えて、ブレンステッド酸のみを消光剤として用いて消光実験を行った場合、イリジウム光酸化還元触媒の消光は確認されなかった (Figure 2-12)。

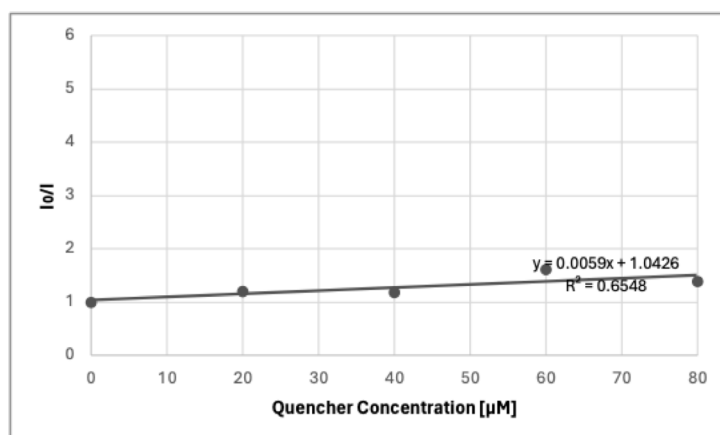


Figure 2-12. イリジウム光酸化還元触媒、ブレンステッド酸触媒を用いた消光実験

以上の結果から、励起されたイリジウム光酸化還元触媒は、ブレンステッド酸の関与なしにコバルト触媒を一電子還元していることが明らかとなった。

アゼチジン **2a** に導入したスルホンアミド型の配向基は、 LiAlH_4 により除去可能であり、85%収率で遊離アゼチジン **2a'**を得た (Figure 2-13)。したがって、本手法により脂肪族アミンからアゼチジンへの合成が可能であることが示された。

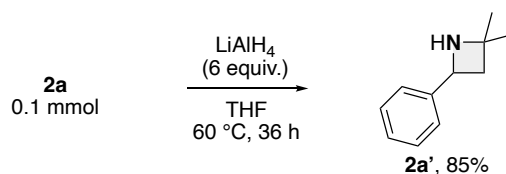


Figure 2-13. 配向基の除去

第五節 結論

本研究では、*N*-ビニルスルホニル基を導入した脂肪族アミンを基質とし、光酸化還元触媒/コバルト触媒/ブレinsted酸触媒を用いることで、分子内および分子間 γ -アミノ C(sp³)-H 官能基化反応を開発した。本反応で達成された γ -アミノ C(sp³)-H 官能基化により、アゼチジンならびに 1,3-ジアミン、1,3-アミノアルコール誘導体といった γ -アミノ官能化生成物を得ることができた。

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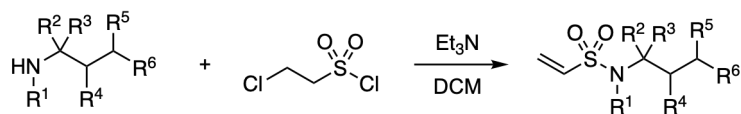
第二章 実験項

Instrumentation and Chemicals

NMR spectra were recorded on a Bruker AVANCE NEO 400N spectrometer, operating at 400 MHz for ^1H NMR, 100.6 MHz for ^{13}C NMR, 376.5 MHz for ^{19}F NMR. Chemical shift values for ^1H and ^{13}C are referenced to Me $_4\text{Si}$ and the residual solvent resonances, respectively. Chemical shifts were reported in δ ppm. Mass spectra were obtained with Bruker timsTOF mass spectrometer (ESI). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F $_{254}$. Silica gel (Wakosil $^{\text{®}}$ 60, 64–210 μm) was used for column chromatography. Biotage Selekt was used for purification. IR spectra were measured with a ATR Accessory (QATR-S) for the Shimadzu IRSpirit FT-IR Spectrometer. Melting points were measured on a Stanford Research Systems MPA100. CV measurements were recorded with a Hokuto Denko HZ-7000 potentiostat. UV-Vis absorption spectra were recorded on a Shimadzu UV-1900. Fluorescence spectra were recorded on a Shimadzu RF-6000. Kessil A160W Tuna Blue (highest blue and intensity setting) was used as a light source. TEKNOS MG9 was used as a fan.

All reactions were carried out under nitrogen atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. Benzene and toluene were purchased from FUJIFILM Wako Pure Chemical Co., stored under nitrogen, and used as received. Trifluorotoluene, **Ir-2** and $\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$ were purchased from Aldrich Chemical Co., stored under nitrogen, and used as received. Cobalt catalysts **Co-1–3** were prepared by the reported procedures.¹ **Ir-1**, **3**, **4**, and **4CzIPN** were prepared by the reported procedures.² **PTH-1** was prepared by the reported procedure.³ **HX-1–3** were prepared by the reported procedures.⁴ **4d** was prepared by the reported procedure.⁵

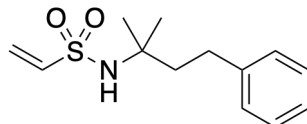
Synthesis and Characterization of Vinyl Sulfonamide



Aliphatic amines were prepared according to the conditions of the literatures.⁶ Vinyl sulfonamides were prepared according to the modified conditions of the literatures.⁷ The aliphatic amine (1.0 equiv.) was added to a round bottom flask and put under nitrogen. The flask was then charged with dichloromethane (0.2 M with respect to amine) and triethylamine (3.5 equiv.) and stirred at 0 $^{\circ}\text{C}$. Then, 2-chloroethanesulfonyl chloride (1.1 equiv.) was added dropwise via syringe. After the addition, the reaction was allowed to slowly warm to room temperature at 2 h. The reaction was diluted with additional dichloromethane and quenched with 1M HCl. The organic phase was separated, washed with a saturated brine solution, dried over Na_2SO_4 , filtered and concentrated to provide the crude vinyl

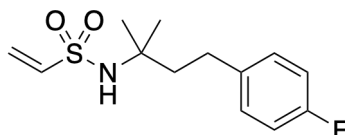
sulfonamide which was purified via column chromatography.

***N*-(2-Methyl-4-phenylbutan-2-yl)ethenesulfonamide (1a)**



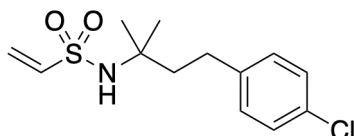
The product **1a** was purified by flash chromatography on silica gel (4.1 mmol scale, 769 mg, 75% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 699, 701, 733, 975, 1001, 1143, 1321, 1387, 1419, 3282 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.31–7.26 (m, 2H), 7.21–7.17 (m, 3H), 6.61 (dd, J = 16.4, 9.6 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 5.85 (d, J = 9.6 Hz, 1H), 4.17 (s, 1H), 2.71–2.67 (m, 2H), 1.92–1.88 (m, 2H), 1.39 (s, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 141.6, 139.5, 128.5, 128.3, 126.0, 124.7, 57.2, 44.8, 30.4, 28.0. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_2\text{SNa}$; 276.1029, found 276.1029.

***N*-[4-(4-Fluorophenyl)-2-methylbutan-2-yl]ethenesulfonamide (1b)**



The product **1b** was purified by flash chromatography on silica gel (0.7 mmol scale, 122 mg, 64% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Yellow solid. **M.p.** 61–63 °C. **IR** (neat) 668, 827, 1001, 1143, 1219, 1324, 1510, 1602, 2978, 3283 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.16–7.12 (m, 2H), 6.99–6.94 (m, 2H), 6.62 (dd, J = 16.4, 9.6 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 5.85 (d, J = 9.6 Hz, 1H), 4.20 (s, 1H), 2.69–2.64 (m, 2H), 1.90–1.86 (m, 2H), 1.37 (s, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 161.3 (d, $J_{\text{C-F}}$ = 243.7 Hz), 139.5, 137.2 (d, $J_{\text{C-F}}$ = 3.1 Hz), 129.7 (d, $J_{\text{C-F}}$ = 7.9 Hz), 124.8, 115.2 (d, $J_{\text{C-F}}$ = 21.1 Hz), 57.1, 44.8, 29.6, 28.0. **^{19}F NMR** (376.5 MHz, CDCl_3) δ –117.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{18}\text{NO}_2\text{SFNa}$; 294.0934, found 294.0931.

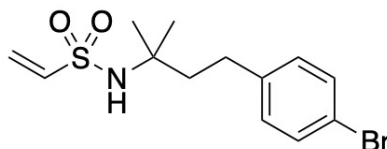
***N*-[4-(4-Chlorophenyl)-2-methylbutan-2-yl]ethenesulfonamide (1c)**



The product **1c** was purified by flash chromatography on silica gel (1.1 mmol scale, 109 mg, 34% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). Grey solid. **M.p.** 77–79 °C. **IR** (neat) 661, 733, 807, 1015, 1094, 1145, 1324, 1387, 1492, 3282 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.26–7.23 (m, 2H), 7.14–7.11 (m, 2H), 6.62 (dd, J = 16.4, 10.0 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 5.85 (d, J = 10.0 Hz, 1H), 4.20 (s, 1H), 2.68–2.64 (m, 2H), 1.90–1.85 (m, 2H), 1.37 (s, 6H). **^{13}C NMR** (100.6 MHz,

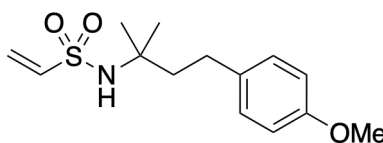
CDCl_3) δ 140.1, 139.4, 131.7, 129.7, 128.6, 124.9, 57.1, 44.6, 29.8, 28.0. **HRMS-ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{18}\text{ClNO}_2\text{SNa}$; 310.0639, found 310.0630.

***N*-[4-(4-Bromophenyl)-2-methylbutan-2-yl]ethenesulfonamide (1d)**



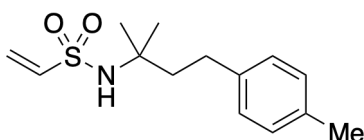
The product **1d** was purified by flash chromatography on silica gel (0.83 mmol scale, 209 mg, 76% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). Yellow solid. **M.p.** 71–74 °C. **IR** (neat) 483, 543, 678, 730, 801, 958, 975, 1013, 1145, 1321 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.41–7.38 (m, 2H), 7.09–7.06 (m, 2H), 6.61 (dd, J = 16.4, 9.6 Hz, 1H), 6.25 (dd, J = 16.4 Hz, 1H), 5.85 (d, J = 9.6 Hz, 1H), 4.20 (s, 1H), 2.67–2.63 (m, 2H), 1.90–1.85 (m, 2H), 1.37 (s, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 140.6, 139.4, 131.5, 130.1, 124.9, 119.7, 57.1, 44.5, 29.9, 28.0. **HRMS-ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{18}\text{NO}_2\text{SBrNa}$; 354.0134, found 354.0128.

***N*-[4-(4-Methoxyphenyl)-2-methylbutan-2-yl]ethenesulfonamide (1e)**



The product **1e** was purified by flash chromatography on silica gel (0.74 mmol scale, 126 mg, 60% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). Yellow solid. **M.p.** 47–49 °C. **IR** (neat) 668, 741, 822, 1001, 1145, 1245, 1320, 1512, 2975, 3282 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.12–7.09 (m, 2H), 6.85–6.81 (m, 2H), 6.61 (dd, J = 16.4, 10.0 Hz, 1H), 6.24 (d, J = 16.4 Hz, 1H), 5.84 (d, J = 10.0 Hz, 1H), 4.18 (s, 1H), 3.79 (s, 3H), 2.65–2.61 (m, 2H), 1.88–1.84 (m, 2H), 1.38 (s, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 157.8, 139.5, 133.6, 129.2, 124.7, 113.9, 57.1, 55.3, 45.0, 29.5, 28.0. **HRMS-ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{22}\text{NO}_3\text{S}$; 284.1315, found 284.1310.

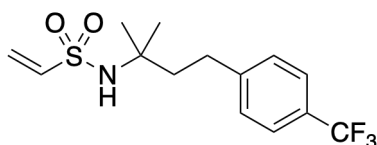
***N*-[2-Methyl-4-(p-tolyl)butan-2-yl]ethenesulfonamide (1f)**



The product **1f** was purified by flash chromatography on silica gel (0.98 mmol scale, 99 mg, 38% yield; Biotage Selekt, 98:2–84:16, hexane/AcOEt). Brown oil. **IR** (neat) 669, 731, 810, 971, 1003, 1145, 1321, 1387, 1515, 3281 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.11–7.06 (m, 4H), 6.61 (dd, J = 16.4, 9.6 Hz, 1H), 6.24 (d, J = 16.4 Hz, 1H), 5.85 (d, J = 9.6 Hz, 1H), 4.17 (s, 1H), 2.66–2.62 (m, 2H),

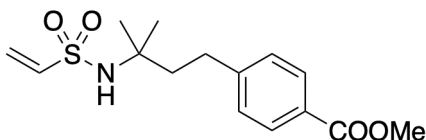
2.32 (s, 3H), 1.89–1.85 (m, 2H), 1.38 (s, 6H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 139.5, 138.4, 135.5, 129.2, 128.2, 124.7, 57.2, 45.0, 30.0, 28.0, 21.0. HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{NO}_2\text{SNa}$; 290.1185, found 290.1178.

***N*-{2-Methyl-4-[4-(trifluoromethyl)phenyl]butan-2-yl}ethenesulfonamide (1g)**



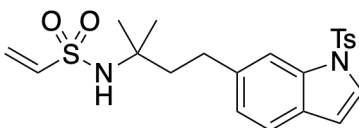
The product **1g** was purified by flash chromatography on silica gel (0.59 mmol scale, 129 mg, 68% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). Colorless oil. IR (neat) 669, 734, 824, 968, 1018, 1067, 1102, 1119, 1321, 1419 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.53 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 6.63 (dd, J = 16.4, 9.6 Hz, 1H), 6.26 (d, J = 16.4 Hz, 1H), 5.86 (d, J = 9.6 Hz, 1H), 4.27 (s, 1H), 2.78–2.74 (m, 2H), 1.93–1.89 (m, 2H), 1.38 (s, 6H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 145.8, 139.4, 128.7, 128.3 (q, $J_{\text{C-F}}$ = 32.2 Hz), 125.4 (q, $J_{\text{C-F}}$ = 3.7 Hz), 124.9, 124.3 (q, $J_{\text{C-F}}$ = 272.6 Hz), 57.0, 44.3, 30.4, 28.1. ^{19}F NMR (376.5 MHz, CDCl_3) δ –62.3. HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_2\text{SF}_3\text{Na}$; 344.0903, found 344.0910.

Methyl 4-[3-Methyl-3-(vinylsulfonamido)butyl]benzoate (1h)



The product **1h** was purified by flash chromatography on silica gel (0.69 mmol scale, 191 mg, 89% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). Pale yellow oil. IR (neat) 669, 968, 1020, 1145, 1281, 1317, 1436, 1718, 2978, 3283 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.97–7.94 (m, 2H), 7.28–7.26 (m, 2H), 6.62 (dd, J = 16.4, 9.6 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 5.86 (d, J = 9.6 Hz, 1H), 4.23 (s, 1H), 3.91 (s, 3H), 2.77–2.73 (m, 2H), 1.94–1.90 (m, 2H), 1.38 (s, 6H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 167.1, 147.2, 139.4, 129.8, 128.4, 128.0, 124.9, 57.1, 52.0, 44.2, 30.6, 28.0. HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_4\text{SNa}$; 334.1083, found 334.1080.

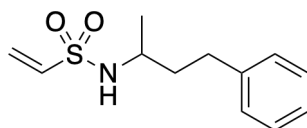
***N*-[2-Methyl-4-(1-tosyl-1*H*-indol-6-yl)butan-2-yl]ethenesulfonamide (1i)**



The product **1i** was purified by flash chromatography on silica gel (0.27 mmol scale, 80 mg, 67%

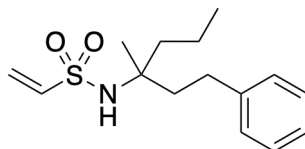
yield; Biotage Selekt, 97:3–65:35, hexane/AcOEt). Pale yellow oil. **IR** (neat) 504, 582, 677, 814, 1000, 1125, 1173, 1268, 1323, 1370 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.81 (s, 1H), 7.77–7.75 (m, 2H), 7.50 (d, J = 3.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.07 (dd, J = 8.0, 1.6 Hz, 1H), 6.67–6.60 (m, 2H), 6.26 (d, J = 16.4 Hz, 1H), 5.87 (d, J = 10.0 Hz, 1H), 4.18 (s, 1H), 2.82–2.78 (m, 2H), 2.35 (s, 3H), 1.95–1.91 (m, 2H), 1.40 (s, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 144.9, 139.5, 138.5, 135.2, 135.2, 129.9, 128.9, 126.8, 125.9, 124.8, 124.1, 121.2, 113.0, 108.9, 57.2, 45.1, 30.9, 28.0, 21.5. **HRMS–ESI** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{22}\text{H}_{30}\text{N}_3\text{O}_4\text{S}_2$; 464.1672, found 464.1682.

***N*-(4-Phenylbutan-2-yl)ethenesulfonamide (1k)**



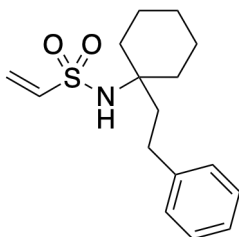
The product **1k** was purified by flash chromatography on silica gel (5 mmol scale, 1.1 g, 96% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). White solid. **M.p.** 30–32 °C. **IR** (neat) 552, 662, 699, 734, 968, 1132, 1319, 1151, 1456, 3275 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.31–7.27 (m, 2H), 7.21–7.17 (m, 3H), 6.52 (dd, J = 16.4, 9.6 Hz, 1H), 6.23 (d, J = 16.4 Hz, 1H), 5.89 (d, J = 9.6 Hz, 1H), 4.11 (s, 1H), 3.41 (m, 1H), 2.76–2.62 (m, 2H), 1.84–1.75 (m, 2H), 1.26 (d, J = 6.4 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 141.1, 137.0, 128.5, 128.3, 126.1, 126.0, 49.8, 39.3, 32.1, 22.3. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_2\text{SNa}$; 262.0872, found 262.0872.

***N*-(3-Methyl-1-phenylhexan-3-yl)ethenesulfonamide (1l)**



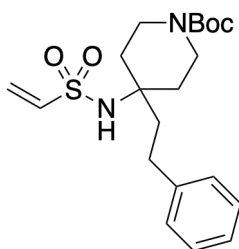
The product **1l** was purified by flash chromatography on silica gel (0.75 mmol scale, 146 mg, 69% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 547, 669, 699, 740, 968, 995, 1143, 1324, 2959, 3279 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.31–7.26 (m, 2H), 7.21–7.17 (m, 3H), 6.61 (dd, J = 16.4, 9.6 Hz, 1H), 6.24 (d, J = 16.4 Hz, 1H), 5.83 (d, J = 9.6 Hz, 1H), 4.10 (s, 1H), 2.68–2.63 (m, 2H), 1.91–1.86 (m, 2H), 1.62–1.58 (m, 2H), 1.42–1.33 (m, 5H), 0.94 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 141.7, 139.5, 128.5, 128.3, 125.9, 124.6, 59.9, 42.8, 42.4, 30.1, 24.6, 16.8, 14.2. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{23}\text{NO}_2\text{SNa}$; 304.1342, found 304.1341.

***N*-(1-Phenethylcyclohexyl)ethenesulfonamide (1m)**



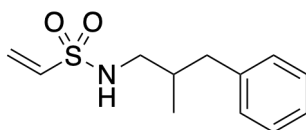
The product **1m** was purified by flash chromatography on silica gel (0.4 mmol scale, 80 mg, 68% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). White solid. **M.p.** 71–73 °C. **IR** (neat) 668, 699, 734, 965, 990, 1145, 1329, 1456, 2934, 3282 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.30–7.26 (m, 2H), 7.23–7.16 (m, 3H), 6.64 (dd, J = 16.4, 9.6 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 5.83 (d, J = 9.6 Hz, 1H), 4.08 (brs, 1H), 2.72–2.68 (m, 2H), 2.02–1.98 (m, 2H), 1.90–1.81 (m, 2H), 1.55–1.49 (m, 7H), 1.38 (m, 1H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 142.0, 139.4, 128.4 ($\times$ 4C), 125.8, 124.6, 59.8, 41.0, 36.1, 29.4, 25.4, 21.8. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{23}\text{NO}_2\text{SNa}$; 316.1342, found 316.1342.

***tert*-Butyl-4-phenethyl-4-(vinylsulfonamido)piperidine-1-carboxylate (1n)**



The product **1n** was purified by flash chromatography on silica gel (1.7 mmol scale, 292 mg, 43% yield; Biotage Selekt, 97:3–70:30, hexane/AcOEt). White solid. **M.p.** 138–140 °C. **IR** (neat) 666, 735, 982, 1145, 1248, 1366, 1423, 1668, 1689, 3273 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.31–7.26 (m, 2H), 7.21–7.18 (m, 3H), 6.64 (dd, J = 16.4, 9.6 Hz, 1H), 6.27 (d, J = 16.4 Hz, 1H), 5.89 (d, J = 9.6 Hz, 1H), 4.14 (brs, 1H), 3.67 (brs, 2H), 3.28–3.23 (m, 2H), 2.73–2.69 (m, 2H), 2.06–2.01 (m, 2H), 1.94–1.90 (m, 2H), 1.65–1.56 (m, 2H), 1.46 (s, 9H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 154.6, 141.3, 139.0, 128.5, 128.3, 126.1, 125.4, 79.8, 58.2, 41.3, 35.2, 35.1, 29.2, 28.4. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_4\text{SNa}$; 417.1818, found 417.1818.

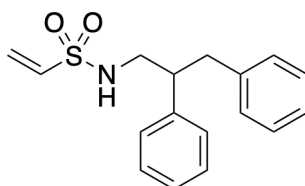
***N*-(2-Methyl-3-phenylpropyl)ethenesulfonamide (1o)**



The product **1o** was purified by flash chromatography on silica gel (3 mmol scale, 328 mg, 46% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 701, 740, 970, 1064,

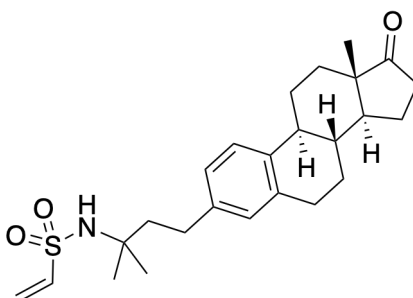
1148, 1323, 1425, 1454, 2929, 3289 cm^{-1} . $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.31–7.25 (m, 2H), 7.21 (m, 1H), 7.15–7.13 (m, 2H), 6.47 (dd, $J=16.4, 9.6$ Hz, 1H), 6.21 (d, $J=16.4$ Hz, 1H), 5.92 (d, $J=9.6$ Hz, 1H), 4.20 (s, 1H), 2.98 (m, 1H), 2.87 (m, 1H), 2.69 (dd, $J=13.6, 6.4$ Hz, 1H), 2.69 (dd, $J=13.6, 8.0$ Hz, 1H), 1.98 (m, 1H), 0.94 (d, $J=6.4$ Hz, 3H). $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 139.7, 135.7, 129.0, 128.4, 126.7, 126.2, 48.5, 40.6, 35.5, 17.4. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_2\text{SNa}$; 262.0872, found 262.0871.

***N*-(2,3-Diphenylpropyl)ethenesulfonamide (1p)**



The product **1p** was purified by flash chromatography on silica gel (3.3 mmol scale, 934 mg, 94% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). White solid. **M.p.** 77–79 °C. **IR** (neat) 574, 699, 968, 1073, 1149, 1327, 1454, 1495, 3028, 3292 cm^{-1} . $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33–7.29 (m, 2H), 7.27–7.20 (m, 3H), 7.19–7.12 (m, 3H), 7.06–7.03 (m, 2H), 6.30 (dd, $J=16.4, 9.6$ Hz, 1H), 6.13 (d, $J=16.4$ Hz, 1H), 5.86 (d, $J=9.6$ Hz, 1H), 3.96 (m, 1H), 3.33 (m, 1H), 3.20 (m, 1H), 3.10 (m, 1H), 2.98–2.89 (m, 2H). $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 140.8, 138.9, 135.5, 129.0, 128.9, 128.3, 127.8, 127.3, 126.7, 126.3, 47.7, 47.3, 40.2. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_2\text{SNa}$; 324.1029, found 324.1031.

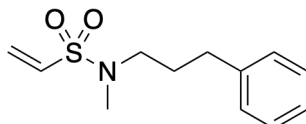
***N*-(2-Methyl-4-[(8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl]butan-2-yl)ethenesulfonamide (1q)**



The product **1q** was purified by flash chromatography on silica gel (1.5 mmol scale, 350 mg, 56% yield; Biotage Selekt, 98:2–70:30, hexane/AcOEt). Brown oil. **IR** (neat) 669, 734, 976, 1005, 1145, 1324, 1735, 2860, 2932, 3278 cm^{-1} . $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.22 (d, $J=8.0$ Hz, 1H), 6.98 (m, 1H), 6.94 (s, 1H), 6.62 (dd, $J=16.4, 10.0$ Hz, 1H), 6.25 (d, $J=16.4$ Hz, 1H), 5.85 (d, $J=10.0$ Hz, 1H), 4.24 (brs, 1H), 2.91–2.88 (m, 2H), 2.64–2.60 (m, 2H), 2.50 (m, 1H), 2.42 (m, 1H), 2.28 (m, 1H), 2.19–1.94 (m, 4H), 1.90–1.86 (m, 2H), 1.68–1.41 (m, 6H), 1.38 (s, 6H), 0.91 (s, 3H). $^{13}\text{C NMR}$ (100.6

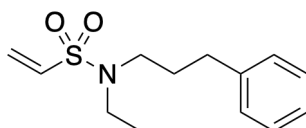
MHz, CDCl₃) δ 220.8, 139.5, 139.0, 137.1, 136.3, 128.8, 125.6, 125.2, 124.3, 56.8, 50.2, 47.8, 44.7, 44.0, 38.0, 35.7, 31.4, 29.7, 29.2, 27.7, 26.3, 25.5, 21.4, 13.6. **HRMS–ESI** (m/z): [M+H]⁺ calcd for C₂₅H₃₆NO₃S; 430.2410, found 430.2420.

***N*-Methyl-*N*-(3-phenylpropyl)ethenesulfonamide (1r)**



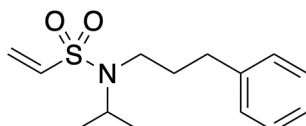
The product **1r** was purified by flash chromatography on silica gel (5.7 mmol scale, 380 mg, 28% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 485, 553, 699, 744, 768, 964, 1146, 1336, 1383, 1455 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.31–7.25 (m, 2H), 7.21–7.18 (m, 3H), 6.41 (dd, J = 16.4, 10.0 Hz, 1H), 6.20 (d, J = 16.4 Hz, 1H), 5.96 (d, J = 10.0 Hz, 1H), 3.13 (t, J = 7.2 Hz, 2H), 2.78 (s, 3H), 2.66 (t, J = 7.2 Hz, 2H), 1.95–1.87 (m, 2H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 141.1, 132.9, 128.4, 128.3, 127.5, 126.0, 49.5, 34.4, 32.7, 29.5. **HRMS–ESI** (m/z): [M+H]⁺ calcd for C₁₂H₁₈NO₂S; 240.1053, found 240.1049.

***N*-Ethyl-*N*-(3-phenylpropyl)ethenesulfonamide (1s)**



The product **1s** was purified by flash chromatography on silica gel (5 mmol scale, 411 mg, 32% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 488, 553, 699, 934, 967, 1143, 1333, 1383, 1454, 1497 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.31–7.25 (m, 2H), 7.22–7.18 (m, 3H), 6.41 (dd, J = 16.4, 10.0 Hz, 1H), 6.18 (d, J = 16.4 Hz, 1H), 5.88 (d, J = 10.0 Hz, 1H), 3.22 (q, J = 7.2 Hz, 2H), 3.15 (t, J = 7.6 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H), 1.96–1.89 (m, 2H), 1.17 (t, J = 7.2 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 141.1, 135.2, 128.4, 128.3, 126.1, 126.0, 46.8, 42.4, 32.9, 30.5, 14.3. **HRMS–ESI** (m/z): [M+Na]⁺ calcd for C₁₃H₁₉NO₂SN_a; 276.1029, found 276.1031.

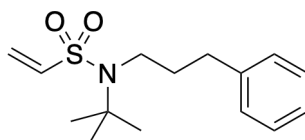
***N*-Isopropyl-*N*-(3-phenylpropyl)ethenesulfonamide (1t)**



The product **1t** was purified by flash chromatography on silica gel (4 mmol scale, 481 mg, 45% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Colorless oil. **IR** (neat) 560, 701, 748, 965, 1049, 1139, 1189, 1334, 1385, 1454 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.31–7.25 (m, 2H), 7.21–7.18 (m,

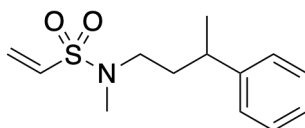
3H), 6.40 (dd, $J = 16.4, 10.0$ Hz, 1H), 6.16 (d, $J = 16.4$ Hz, 1H), 5.84 (d, $J = 10.0$ Hz, 1H), 3.98 (sep, $J = 6.8$ Hz, 1H), 3.07–3.03 (m, 2H), 2.63 (t, $J = 7.6$ Hz, 2H), 2.05–1.95 (m, 2H), 1.15 (d, $J = 6.8$ Hz, 6H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 141.2, 136.0, 128.4, 128.3, 126.0, 125.4, 49.6, 42.5, 33.2, 33.1, 21.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{NO}_2\text{SNa}$; 290.1185, found 290.1189.

***N*-(*tert*-Butyl)-*N*-(3-phenylpropyl)ethenesulfonamide (1u)**



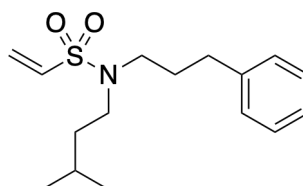
The product **1u** was purified by flash chromatography on silica gel (5 mmol scale, 924 mg, 66% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 500, 682, 737, 947, 1094, 1138, 1255, 1329, 1454, 2979 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.30–7.26 (m, 2H), 7.20–7.17 (m, 3H), 6.48 (dd, $J = 16.4, 10.0$ Hz, 1H), 6.12 (d, $J = 16.4$ Hz, 1H), 5.77 (d, $J = 10.0$ Hz, 1H), 3.21–3.17 (m, 2H), 2.59 (t, $J = 7.6$ Hz, 2H), 2.05–1.97 (m, 2H), 1.38 (s, 9H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 141.1, 138.6, 128.3, 128.2, 125.9, 123.9, 59.0, 45.8, 33.8, 33.1, 30.2. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{23}\text{NO}_2\text{SNa}$; 304.1342, found 304.1343.

***N*-Methyl-*N*-(3-phenylbutyl)ethenesulfonamide (1v)**



The product **1v** was purified by flash chromatography on silica gel (3.7 mmol scale, 332 mg, 36% yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 554, 646, 702, 763, 882, 938, 971, 1151, 1339, 1456 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.33–7.28 (m, 2H), 7.22–7.18 (m, 3H), 6.36 (dd, $J = 16.4, 10.0$ Hz, 1H), 6.16 (d, $J = 16.4$ Hz, 1H), 5.93 (d, $J = 10.0$ Hz, 1H), 3.06 (m, 1H), 2.93 (m, 1H), 2.82–2.73 (m, 4H), 1.92–1.84 (m, 2H), 1.28 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 146.3, 132.9, 128.5, 127.4, 126.8, 126.2, 48.5, 37.2, 36.1, 34.4, 22.3. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_2\text{SNa}$; 276.1029, found 276.1031.

***N*-Isopentyl-*N*-(3-phenylpropyl)ethenesulfonamide (1w)**



The product **1w** was purified by flash chromatography on silica gel (3.7 mmol scale, 827 mg, 76%

yield; Biotage Selekt, 98:2–80:20, hexane/AcOEt). Pale yellow oil. **IR** (neat) 649, 699, 748, 776, 964, 1145, 1336, 1455, 1497, 2950 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.31–7.26 (m, 2H), 7.22–7.18 (m, 3H), 6.40 (dd, $J=16.4, 10.0$ Hz, 1H), 6.18 (d, $J=16.4$ Hz, 1H), 5.88 (d, $J=10.0$ Hz, 1H), 3.16–3.11 (m, 4H), 2.64 (t, $J=7.6$ Hz, 2H), 1.96–1.88 (m, 2H), 1.59–1.51 (m, 1H), 1.46–1.40 (m, 2H), 0.89 (d, $J=6.4$ Hz, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 141.1, 135.0, 128.4, 128.3, 126.1, 126.0, 47.2, 46.3, 37.5, 32.9, 30.4, 25.8, 22.4. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{25}\text{NO}_2\text{SNa}$; 318.1498, found 318.1501.

Procedures for Construction of Azetidine by A Triple Catalysis

The reaction in Table 2-1, entry 1 is representative. In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst **Ir-1** (0.7 mg, 0.001 mmol), **Co-1** (0.6 mg, 0.001 mmol), **HX-1** (10.1 mg, 0.025 mmol) and benzene (1.0 mL). Then, *N*-(2-Methyl-4-phenylbutan-2-yl)ethenesulfonamide **1a** (25.3 mg, 0.1 mmol) was added to the reaction mixture. After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-1). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) gave the **2a** (19.3 mg, 0.08 mmol, 76% isolated yield) as white solid.

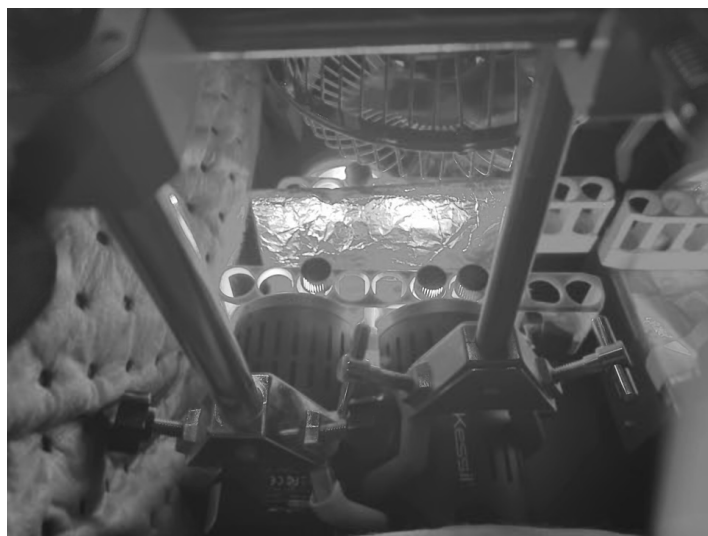


Figure S2-1. Light set up

The reaction without glovebox. To an oven-dried vial with a stirring bar was added photoredox catalyst **Ir-1** (0.7 mg, 0.001 mmol), **Co-1** (0.6 mg, 0.001 mmol), **HX-1** (10.1 mg, 0.025 mmol) and benzene (1.0 mL). Then, *N*-(2-Methyl-4-phenylbutan-2-yl)ethenesulfonamide **1a** (25.3 mg, 0.1 mmol) was added to the reaction mixture. After sealing the vial with a septum rubber cap, the resulting

mixture was degassed by N₂ bubbling for 5 min. The reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-1). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate and analyzed by ¹H NMR relative to 1,1,2,2-tetrachloroethane as an internal standard to afford the desired **2a** (0.08 mmol, 79% isolated yield).

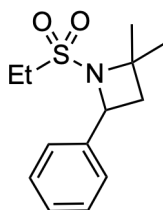
1 mmol scale reaction of 2a. In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst **Ir-1** (7.1 mg, 0.01 mmol), **Co-1** (6.1 mg, 0.01 mmol), **HX-1** (100.6 mg, 0.25 mmol) and benzene (5 mL). Then, *N*-(2-Methyl-4-phenylbutan-2-yl)ethanesulfonamide **1a** (253.4 mg, 1.0 mmol) was added to the reaction mixture. After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with two 34W blue LEDs (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-2). After 16 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) gave the **2a** (141.9 mg, 0.56 mmol, 56% isolated yield) as white solid.



Figure S2-2. Light set up for scale-up reaction

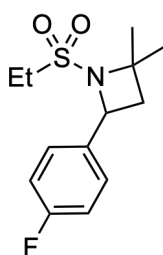
Characterization Data for Azetidienes

1-(Ethylsulfonyl)-2,2-dimethyl-4-phenylazetidine (**2a**)



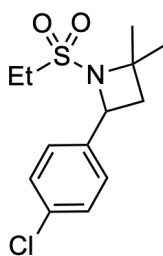
The product **2a** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) (Figure 2-3; 19.3 mg, 0.08 mmol, 76% isolated yield). White solid. **M.p.** 72–75 °C. **IR** (neat) 626, 733, 764, 783, 1001, 1047, 1133, 1319, 1458, 2969 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.48–7.46 (m, 2H), 7.40–7.31 (m, 3H), 5.15 (t, $J = 8.4$ Hz, 1H), 2.48 (dq, $J = 14.4, 7.2$ Hz, 1H), 2.38–2.25 (m, 2H), 2.16 (dd, $J = 10.4, 8.4$ Hz, 1H), 1.79 (s, 3H), 1.60 (s, 3H), 1.13 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 139.8, 128.7, 128.6, 127.3, 67.5, 60.7, 48.4, 41.4, 29.8, 25.9, 7.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_2\text{SNa}$; 276.1029, found 276.1034.

1-(Ethylsulfonyl)-4-(4-fluorophenyl)-2,2-dimethylazetidine (**2b**)



The product **2b** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–88:12, hexane/EtOAc) (Figure 2-3; 19.8 mg, 0.07 mmol, 73% isolated yield). White solid. **M.p.** 85–87 °C. **IR** (neat) 398, 744, 838, 1047, 1133, 1225, 1320, 1511, 2364, 2972 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.47–7.43 (m, 2H), 7.09–7.05 (m, 2H), 5.14 (t, $J = 8.4$ Hz, 1H), 2.50 (m, 1H), 2.38–2.25 (m, 2H), 2.12 (dd, $J = 10.4, 8.4$ Hz, 1H), 1.78 (s, 3H), 1.59 (s, 3H), 1.14 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 162.7 (d, $J_{\text{C-F}} = 247.3$ Hz), 135.7 (d, $J_{\text{C-F}} = 3.0$ Hz), 129.0 (d, $J_{\text{C-F}} = 8.2$ Hz), 115.7 (d, $J_{\text{C-F}} = 21.5$ Hz), 67.5, 60.0, 48.5, 41.5, 29.9, 25.9, 7.5. **^{19}F NMR** (376.5 MHz, CDCl_3) δ –113.2. **HRMS–ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{18}\text{NO}_2\text{SFNa}$; 294.0934, found 294.0938.

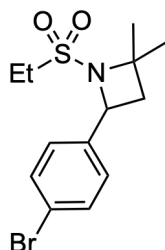
4-(4-Chlorophenyl)-1-(ethylsulfonyl)-2,2-dimethylazetidine (**2c**)



The product **2c** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–85:15, hexane/EtOAc) (Figure 2-3; 18.4 mg, 0.06 mmol, 64% isolated yield). White solid. **M.p.** 77–79 °C. **IR** (neat) 619, 737, 781, 827, 1013, 1090, 1133, 1320, 1491, 2970 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.43–7.39 (m, 2H), 7.37–7.34 (m, 2H), 5.13 (t, $J = 8.4$ Hz, 1H), 2.51 (m, 1H), 2.38–2.28 (m, 2H), 2.10 (dd, $J = 10.4, 8.4$ Hz, 1H), 1.78 (s, 3H), 1.59 (s, 3H), 1.15 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (100.6

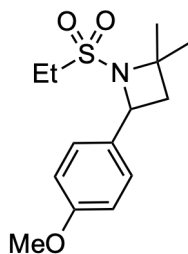
MHz, CDCl₃) δ 138.4, 134.3, 129.0, 128.6, 67.6, 60.0, 48.5, 41.4, 29.9, 25.9, 7.5. **HRMS–ESI** (m/z): [M+Na]⁺ calcd for C₁₃H₁₈NO₂SClNa ; 310.0639, found 310.0649.

4-(4-Bromophenyl)-1-(ethylsulfonyl)-2,2-dimethylazetidine (2d)



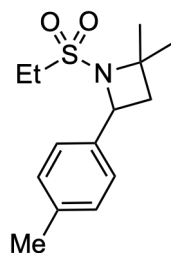
The product **2d** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–88:12, hexane/EtOAc) (Figure 2-3; 20.9 mg, 0.06 mmol, 63% isolated yield). White solid. **M.p.** 95–96 °C. **IR** (neat) 737, 823, 1010, 1046, 1072, 1133, 1320, 1370, 1487, 2970 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.52–7.49 (m, 2H), 7.36–7.33 (m, 2H), 5.12 (t, J = 8.4 Hz, 1H), 2.51 (m, 1H), 2.38–2.29 (m, 2H), 2.09 (dd, J = 10.4, 8.4 Hz, 1H), 1.78 (s, 3H), 1.59 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 139.0, 131.9, 128.9, 122.5, 67.7, 60.1, 48.5, 41.4, 29.9, 25.9, 7.5. **HRMS–ESI** (m/z): [M+Na]⁺ calcd for C₁₃H₁₈NO₂SBrNa ; 354.0134, found 354.0144.

1-(Ethylsulfonyl)-4-(4-methoxyphenyl)-2,2-dimethylazetidine (2e)



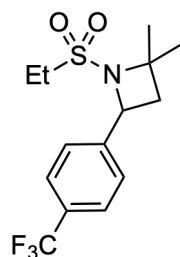
The product **2e** was purified by flash chromatography on silica gel (Biotage Selekt, 97:3–85:15, hexane/EtOAc) (Figure 2-3; 16.8 mg, 0.06 mmol, 59% isolated yield). Yellow solid. **M.p.** 57–60 °C. **IR** (neat) 743, 832, 1034, 1132, 1247, 1317, 1456, 1515, 1612, 2966 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.41–7.38 (m, 2H), 6.92–6.88 (m, 2H), 5.10 (t, J = 8.4 Hz, 1H), 3.82 (s, 3H), 2.47 (m, 1H), 2.35–2.23 (m, 2H), 2.14 (dd, J = 10.4, 8.4 Hz, 1H), 1.78 (s, 3H), 1.59 (s, 3H), 1.12 (t, J = 7.2 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 159.7, 131.8, 128.6, 114.0, 67.1, 60.3, 55.3, 48.4, 41.5, 29.8, 25.8, 7.6. **HRMS–ESI** (m/z): [M+Na]⁺ calcd for C₁₄H₂₁NO₃SNa ; 306.1134, found 306.1135.

1-(Ethylsulfonyl)-2,2-dimethyl-4-(*p*-tolyl)azetidine (2f)



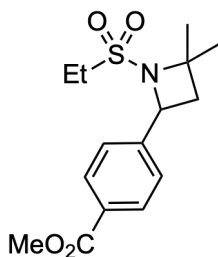
The product **2f** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–90:10, hexane/EtOAc) (Figure 2-3; 20.6 mg, 0.08 mmol, 77% isolated yield). Yellow oil. **IR** (neat) 743, 817, 971, 1046, 1133, 1247, 1320, 1370, 1456, 2970 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.35 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.11 (t, J = 8.4 Hz, 1H), 2.47 (m, 1H), 2.35 (s, 3H), 2.34–2.25 (m, 2H), 2.13 (dd, J = 10.4, 8.4 Hz, 1H), 1.78 (s, 3H), 1.59 (s, 3H), 1.13 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 138.4, 136.8, 129.4, 127.2, 67.3, 60.5, 48.4, 41.5, 29.8, 25.9, 21.2, 7.6. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{NO}_2\text{SNa}$; 290.1185, found 290.1184.

1-(Ethylsulfonyl)-2,2-dimethyl-4-[4-(trifluoromethyl)phenyl]azetidine (**2g**)



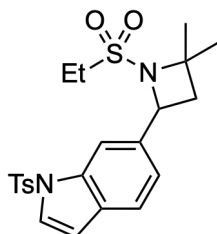
The reaction conditions were modified. The reaction was carried out with **1g** (32.1 mg, 0.1 mmol), **Ir-3** (0.9 mg, 0.001 mmol, 1 mol %), **Co-1** (0.6 mg, 0.001 mmol, 1 mol %) and **HX-1** (10.1 mg, 0.025 mmol, 25 mol %) in benzene (1 mL) under blue LED irradiation for 12 h. The product **2g** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–85:15, hexane/EtOAc) (Figure 2-3; 14.2 mg, 0.04 mmol, 44% isolated yield). Yellow oil. **IR** (neat) 734, 840, 1017, 1067, 1096, 1132, 1323, 1375, 1541, 2972 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.65 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 5.23 (t, J = 8.4 Hz, 1H), 2.53 (m, 1H), 2.43–2.33 (m, 2H), 2.11 (dd, J = 10.6, 8.4 Hz, 1H), 1.80 (s, 3H), 1.62 (s, 3H), 1.19 (t, J = 8.4 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 144.0, 130.7 (q, $J_{\text{C-F}}$ = 32.6 Hz), 127.4, 125.8 (q, $J_{\text{C-F}}$ = 3.6 Hz), 123.9 (q, $J_{\text{C-F}}$ = 272.1 Hz), 68.0, 60.1, 48.6, 41.5, 29.9, 26.0, 7.5. **^{19}F NMR** (376.5 MHz, CDCl_3) δ –62.6. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_2\text{SF}_3\text{Na}$; 344.0903, found 344.0913.

Methyl 4-[1-(Ethylsulfonyl)-4,4-dimethylazetidin-2-yl]benzoate (**2h**)



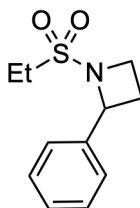
The reaction conditions were modified. The reaction was carried out with **1h** (31.1 mg, 0.1 mmol), **Ir-3** (0.9 mg, 0.001 mmol, 1 mol %), **Co-1** (0.6 mg, 0.001 mmol, 1 mol %) and **HX-1** (10.1 mg, 0.025 mmol, 25 mol %) in benzene (1 mL) under blue LED irradiation for 12 h. The product **2h** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–88:12, hexane/EtOAc) (Figure 2-3; 19.9 mg, 0.06 mmol, 64% isolated yield). Yellow solid. **M.p.** 80–83 °C. **IR** (neat) 774, 1001, 1094, 1112, 1135, 1280, 1321, 1370, 1724, 2362 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 8.07–8.04 (m, 2H), 7.56–7.54 (m, 2H), 5.21 (t, J = 8.4 Hz, 1H), 3.93 (s, 3H), 2.50 (m, 1H), 2.42–2.28 (m, 2H), 2.13 (dd, J = 10.4, 8.4 Hz, 1H), 1.80 (s, 3H), 1.62 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 166.6, 144.9, 130.4, 130.1, 127.2, 67.9, 60.2, 52.2, 48.5, 41.3, 29.9, 26.0, 7.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_4\text{Na}$; 334.1083, found 334.1084.

6-[1-(Ethylsulfonyl)-4,4-dimethylazetidin-2-yl]-1-tosyl-1H-indole (**2i**)



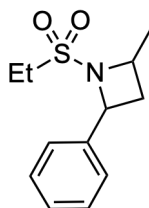
The reaction was carried out with **1i** (22.3 mg, 0.05 mmol), **Ir-1** (0.4 mg, 0.0005 mmol, 1 mol %), **Co-1** (0.3 mg, 0.0005 mmol, 1 mol %) and **HX-1** (5.1 mg, 0.0125 mmol, 25 mol %) in benzene (500 μL) under blue LED irradiation for 12 h. The product **2i** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–78:22, hexane/EtOAc) (Figure 2-3; 7.9 mg, 0.02 mmol, 35% isolated yield). Yellow oil. **IR** (neat) 580, 675, 734, 817, 1132, 1172, 1319, 1370, 1432, 2967 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 8.08 (s, 1H), 7.78 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 3.6 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.4 Hz, 2H), 6.65 (d, J = 3.6 Hz, 1H), 5.27 (t, J = 8.0 Hz, 1H), 2.43–2.32 (m, 5H), 2.23–2.12 (m, 2H), 1.82 (s, 3H), 1.65 (s, 3H), 1.05 (t, J = 7.2 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 145.1, 136.7, 135.2, 134.8, 130.9, 129.9, 127.2, 126.9, 122.4, 121.6, 112.4, 108.6, 67.4, 61.0, 48.5, 42.0, 30.0, 26.0, 21.6, 7.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}_4\text{S}_2\text{Na}$; 469.1226, found 469.1234.

1-(Ethylsulfonyl)-2-phenylazetidine (**2j**)



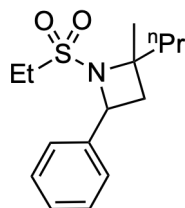
The reaction was carried out with **1j** (45.1 mg, 0.2 mmol), **Ir-1** (1.4 mg, 0.002 mmol, 1 mol %), **Co-1** (1.2 mg, 0.002 mmol, 1 mol %) and **HX-1** (20.1 mg, 0.05 mmol, 25 mol %) in benzene (2 mL) under blue LED irradiation for 12 h. The product **2j** was purified by flash chromatography on silica gel (Biotage Selekt, 96:4–78:22, hexane/EtOAc) (Figure 2-3; 20.8 mg, 0.09 mmol, 46% isolated yield). Pale yellow oil. **IR** (neat) 544, 629, 698, 745, 761, 955, 1043, 1135, 1317, 2917 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.48–7.45 (m, 2H), 7.40–7.36 (m, 2H), 7.32 (m, 1H), 5.30 (t, J = 8.4 Hz, 1H), 4.21 (dt, J = 10.0, 7.6 Hz, 1H), 3.69 (ddd, J = 8.8, 7.6, 3.6 Hz, 1H), 2.79–2.62 (m, 2H), 2.53 (m, 1H), 2.33 (dq, J = 10.0, 8.8 Hz, 1H), 1.20 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 140.5, 128.7, 128.4, 126.7, 64.8, 46.7, 45.7, 25.2, 7.4. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{NO}_2\text{Na}$; 248.0716, found 248.0708.

1-(Ethylsulfonyl)-2-methyl-4-phenylazetidine (**2k**)



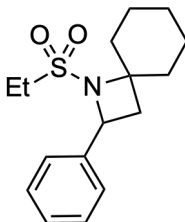
The reaction was carried out with **1k** (47.9 mg, 0.2 mmol), **Ir-1** (1.4 mg, 0.002 mmol, 1 mol %), **Co-1** (1.2 mg, 0.002 mmol, 1 mol %) and **HX-1** (20.1 mg, 0.05 mmol, 25 mol %) in benzene (2 mL) under blue LED irradiation for 12 h. The product **2k** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–84:16, hexane/EtOAc) (Figure 2-3; 34.4 mg, 0.14 mmol, 72% isolated yield). White solid. **M.p.** 36–38 °C. **IR** (neat) 530, 609, 763, 1017, 1080, 1139, 1286, 1320, 1456, 2970 cm^{-1} . The ratio (4:1) of the diastereomers was determined by ^1H NMR analysis. **^1H NMR** (400 MHz, CDCl_3) δ 7.52–7.44 (m, 2H), 7.41–7.29 (m, 3H), 5.33 (t, J = 8.0 Hz, $0.2 \times 1\text{H}$), 5.10 (t, J = 8.4 Hz, $0.8 \times 1\text{H}$), 4.50 (m, 1H), 2.75–2.40 (m, 3H), 2.20 (m, $0.2 \times 1\text{H}$), 1.88 (dt, J = 10.8, 8.0 Hz, $0.8 \times 1\text{H}$), 1.74 (d, J = 6.4 Hz, $0.2 \times 3\text{H}$), 1.47 (d, J = 6.4 Hz, $0.8 \times 3\text{H}$), 1.20–1.13 (m, 3H). Peaks for the minor rotamer were enclosed in parenthesis. **^{13}C NMR** (100.6 MHz, CDCl_3) δ 140.6, (139.9), (128.7), 128.7, (128.6), 128.3, (127.2), 126.9, (63.8), 61.4, (59.6), 54.2, (48.1), 47.5, (33.8), 33.6, 22.5, (20.9), (7.6), 7.4. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_2\text{SNa}$; 262.0872, found 262.0874.

1-(Ethylsulfonyl)-2-methyl-4-phenyl-2-propylazetidine (2l)



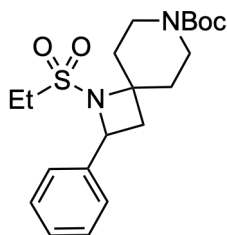
The product **2l** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–88:12, hexane/EtOAc) (Figure 2-3; 20.8 mg, 0.07 mmol, 74% isolated yield). Yellow solid. **M.p.** 35–37 °C. **IR** (neat) 702, 735, 783, 1027, 1066, 1139, 1324, 1458, 2364, 2966 cm^{-1} . The ratio (1:1) of the diastereomers was determined by ^1H NMR analysis. **^1H NMR** (400 MHz, CDCl_3) δ 7.49–7.46 (m, 2H), 7.40–7.31 (m, 3H), 5.14 (m, 1H), 2.54–2.43 (m, $0.5 \times 1\text{H} + 1\text{H}$), 2.37–2.17 (m, 3H), 2.05 (dd, $J = 10.8, 8.0$ Hz, $0.5 \times 1\text{H}$), 1.89 (m, 1H), 1.77 (s, $0.5 \times 3\text{H}$), 1.60 (s, $0.5 \times 3\text{H}$), 1.51–1.39 (m, 2H), 1.13 (t, $J = 7.2$ Hz, 3H), 1.04–0.98 (m, 3H). Peaks for two diastereomers were given. **^{13}C NMR** (100.6 MHz, CDCl_3) δ 139.9 ($\times 2\text{C}$), 128.7 ($\times 2\text{C}$), 128.6, 128.5, 127.4 ($\times 2\text{C}$), 71.3, 70.4, 61.1, 60.9, 48.7, 48.5, 44.7, 40.5, 39.1, 38.3, 27.6, 23.8, 18.0, 17.4, 14.5, 14.4, 7.6, 7.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{23}\text{NO}_2\text{SNa}$; 304.1342, found 304.1335.

1-(Ethylsulfonyl)-2-phenyl-1-azaspiro[3.5]nonane (2m)



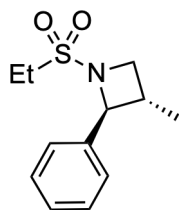
The product **2m** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–90:10, hexane/EtOAc) (Figure 2-3; 16.3 mg, 0.06 mmol, 55% isolated yield). Yellow solid. **M.p.** 63–66 °C. **IR** (neat) 519, 701, 733, 766, 783, 1066, 1138, 1320, 1456, 2932 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.49–7.46 (m, 2H), 7.40–7.30 (m, 3H), 5.15 (t, $J = 8.4$ Hz, 1H), 2.52–2.25 (m, 5H), 2.10–1.97 (m, 3H), 1.82–1.72 (m, 2H), 1.60 (m, 1H), 1.32–1.18 (m, 3H), 1.13 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 140.1, 128.7, 128.5, 127.3, 71.5, 60.9, 48.3, 39.1, 38.4, 34.3, 24.9, 23.3, 23.0, 7.6. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{23}\text{NO}_2\text{SNa}$; 316.1342, found 316.13424.

tert-Butyl 1-(Ethylsulfonyl)-2-phenyl-1,7-diazaspiro[3.5]nonane-7-carboxylate (2n)



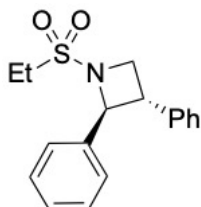
The product **2n** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) (Figure 2-3; 16.9 mg, 0.04 mmol, 43% isolated yield). White solid. **M.p.** 114–116 °C. **IR** (neat) 701, 767, 1066, 1139, 1241, 1323, 1419, 1458, 1685, 2361 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.48–7.46 (m, 2H), 7.41–7.32 (m, 3H), 5.20 (t, $J = 8.4$ Hz, 1H), 4.17 (brs, 2H), 2.74–2.45 (m, 5H), 2.36–2.18 (m, 3H), 2.12 (m, 1H), 1.99 (m, 1H), 1.46 (s, 9H), 1.23 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 154.5, 139.5, 128.8, 128.8, 127.2, 79.8, 68.9, 60.9, 48.4, 38.3, 37.4, 33.7, 28.4, 7.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_4\text{SNa}$; 417.1818, found 417.1810.

1-(Ethylsulfonyl)-3-methyl-2-phenylazetidine (**2o**)



The product **2o** was purified by flash chromatography on silica gel (Biotage Selekt, 99:1–85:15, hexane/EtOAc) (Figure 2-3; 9.8 mg, 0.04 mmol, 41% isolated yield). Yellow oil. **IR** (neat) 610, 698, 730, 914, 1015, 1139, 1287, 1317, 1456, 2965 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.45–7.42 (m, 2H), 7.40–7.36 (m, 2H), 7.32 (m, 1H), 4.76 (d, $J = 7.8$ Hz, 1H), 3.79 (d, $J = 7.8$ Hz, 2H), 2.80–2.54 (m, 3H), 1.24–1.20 (m, 6H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 139.9, 128.7, 128.4, 126.7, 72.2, 52.9, 46.7, 34.5, 17.4, 7.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_2\text{SNa}$; 262.0872, found 262.0864.

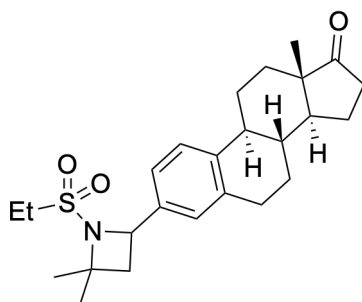
1-(Ethylsulfonyl)-2,3-diphenylazetidine (**2p**)



The reaction conditions were modified. The reaction was carried out with **1p** (30.1 mg, 0.1 mmol), **Ir-4** (0.8 mg, 0.001 mmol, 1 mol %), **Co-1** (0.6 mg, 0.001 mmol, 1 mol %) and **HX-1** (10.1 mg, 0.025 mmol, 25 mol %) in benzene (1 mL) under blue LED irradiation for 12 h. The product **2p** was purified

by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) (Figure 2-3; 11.2 mg, 0.04 mmol, 37% isolated yield). The relative configuration was determined by NOESY experiment. White solid. **M.p.** 61–62 °C. **IR** (neat) 698, 724, 754, 790, 1066, 1139, 1321, 1456, 2363, 3031 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.47–7.45 (m, 2H), 7.41–7.31 (m, 5H), 7.29–7.26 (m, 3H), 5.27 (d, J = 8.0 Hz, 1H), 4.36 (dd, J = 8.4, 7.6 Hz, 1H), 4.05 (t, J = 7.6 Hz, 1H), 3.71 (q, J = 8.4 Hz, 1H), 2.87–2.71 (m, 2H), 1.26 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 139.5, 138.9, 128.8, 128.8, 128.6, 127.5, 127.2, 126.8, 72.3, 52.1, 47.0, 43.6, 7.5. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_2\text{SNa}$; 324.1029, found 324.1022.

(8*R*,9*S*,13*S*,14*S*)-3-[1-(Ethylsulfonyl)-4,4-dimethylazetidin-2-yl]-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (2q)



The product **2q** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) (Figure 2-3; 30.5 mg, 0.07 mmol, 71% isolated yield). Colorless oil. **IR** (neat) 570, 738, 823, 886, 1007, 1047, 1132, 1317, 1735, 2930 cm^{-1} . The ratio (1:1) of the diastereomers was determined by ^1H NMR analysis. **^1H NMR** (400 MHz, CDCl_3) δ 7.33–7.23 (m, 2H), 7.17 (s, 0.5 $\times$ 1H), 7.13 (s, 0.5 $\times$ 1H), 5.09 (t, J = 8.4 Hz, 1H), 2.98–2.84 (m, 2H), 2.57–2.48 (m, 2H), 2.44–2.27 (m, 4H), 2.20–1.96 (m, 5H), 1.78 (s, 3H), 1.69–1.40 (m, 9H), 1.20–1.15 (m, 3H), 0.92 (s, 3H). Only observed peaks were shown. **^{13}C NMR** (100.6 MHz, CDCl_3) δ 220.7, 140.1, 140.1, 137.3, 136.8, 136.7, 128.0, 127.7, 125.8, 125.7, 124.4, 124.2, 67.3, 60.5, 60.5, 50.5, 48.4, 47.9, 44.3, 41.7, 41.6, 38.0, 38.0, 35.8, 31.5, 29.8, 29.4, 29.3, 26.4, 25.9, 25.7, 25.6, 21.5, 13.8. **HRMS–ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{36}\text{NO}_3\text{S}$; 430.2410, found 430.2402.

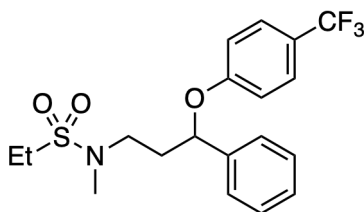
1. Procedure for Intermolecular γ -Amino C–H Functionalization

The reaction in Figure 1 (5ra) is representative. In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst **Ir-1** (0.7 mg, 0.001 mmol), **Co-1** (0.6 mg, 0.001 mmol), **HX-1** (10.1 mg, 0.025 mmol) and benzene (1.0 mL). Then, *N*-Methyl-*N*-(3-phenylpropyl)ethanesulfonamide **1r** (23.9 mg, 0.1 mmol) and 4-trifluoromethylphenol **4a** (48.6 mg, 0.3 mmol) were added to the reaction mixture. After sealing the vial with a cap and removal from the

glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-2). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 97:3–68:32, hexane/EtOAc) gave the **5ra** (19.5 mg, 0.05 mmol, 49% isolated yield) as colorless oil.

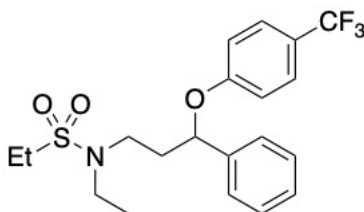
Characterization of γ -Functionalized Sulfonamides

N-Methyl-*N*-{3-phenyl-3-[4-(trifluoromethyl)phenoxy]propyl}ethanesulfonamide (**5ra**)



The product **5ra** was purified by flash chromatography on silica gel (Biotage Selekt, 97:3–68:32, hexane/EtOAc) (Figure 2-4; 19.5 mg, 0.05 mmol, 49% isolated yield). Colorless oil. **IR** (neat) 702, 757, 838, 1067, 1110, 1152, 1251, 1324, 1517, 1614 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.43 (d, J = 8.4 Hz, 2H), 7.37–7.32 (m, 4H), 7.27 (m, 1H), 6.90 (d, J = 8.4 Hz, 2H), 5.28 (dd, J = 8.8, 4.0 Hz, 1H), 3.48 (m, 1H), 3.34 (m, 1H), 2.96 (q, J = 7.6 Hz, 2H), 2.90 (s, 3H), 2.27 (m, 1H), 2.12 (m, 1H), 1.34 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 160.2, 140.4, 128.9, 128.1, 126.8 (q, $J_{\text{C-F}}$ = 3.6 Hz), 125.7, 124.3 (q, $J_{\text{C-F}}$ = 271.3 Hz), 123.0 (q, $J_{\text{C-F}}$ = 32.5 Hz), 115.8, 77.3, 47.0, 44.1, 37.6, 35.1, 7.9. **^{19}F NMR** (376.5 MHz, CDCl_3) δ -62.6. **HRMS–ESI** (m/z): $[\text{M}+\text{K}]^+$ calcd for $\text{C}_{19}\text{H}_{22}\text{F}_3\text{NO}_3\text{SK}$; 440.0904, found 440.0900.

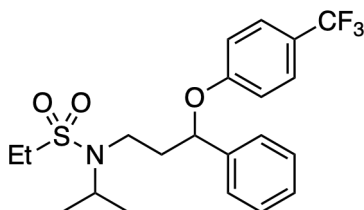
N-Ethyl-*N*-{3-phenyl-3-[4-(trifluoromethyl)phenoxy]propyl}ethanesulfonamide (**5sa**)



The product **5sa** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) (Figure 2-4; 20.6 mg, 0.05 mmol, 50% isolated yield). Pale yellow oil. **IR** (neat) 702, 836, 1067, 1110, 1136, 1248, 1323, 1517, 1614, 2980 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.43 (d, J = 8.4 Hz, 2H), 7.37–7.25 (m, 5H), 6.89 (d, J = 8.4 Hz, 2H), 5.26 (dd, J = 8.8, 4.0 Hz, 1H), 3.51–3.36 (m, 2H), 3.34–3.28 (m, 2H), 2.95 (q, J = 7.6 Hz, 2H), 2.31–2.13 (m, 2H), 1.33 (t, J = 7.6 Hz, 3H), 1.12 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 160.2, 140.3, 128.9, 128.3, 126.8 (q, $J_{\text{C-F}}$ = 3.8 Hz), 125.7, 124.3 (q, $J_{\text{C-F}}$ = 271.0 Hz), 123.0 (q, $J_{\text{C-F}}$ = 32.7 Hz), 115.7, 77.6, 46.2, 43.9, 42.7, 38.4,

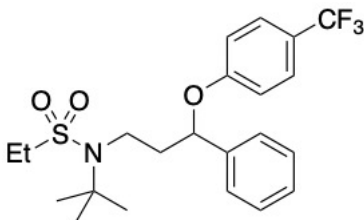
14.3, 8.1. ^{19}F NMR (376.5 MHz, CDCl_3) δ -61.6. HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{24}\text{F}_3\text{NO}_3\text{SNa}$; 438.1321, found 438.1314.

***N*-Isopropyl-*N*-{3-phenyl-3-[4-(trifluoromethyl)phenoxy]propyl}ethanesulfonamide (5ta)**



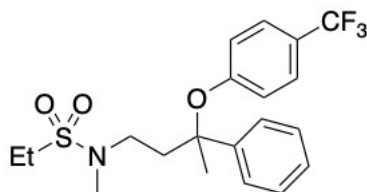
The product **5ta** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–88:12, hexane/EtOAc) (Figure 2-4; 22.4 mg, 0.05 mmol, 52% isolated yield). Colorless oil. IR (neat) 702, 837, 1067, 1112, 1139, 1251, 1326, 1518, 1614, 2979 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.43 (d, J = 8.4 Hz, 2H), 7.36–7.25 (m, 5H), 6.89 (d, J = 8.4 Hz, 2H), 5.23 (dd, J = 8.2, 4.6 Hz, 1H), 4.00 (sep, J = 6.8 Hz, 1H), 3.42–3.28 (m, 2H), 2.94 (q, J = 7.2 Hz, 2H), 2.34–2.21 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H), 1.23 (d, J = 6.8 Hz, 3H), 1.18 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 160.3, 140.3, 128.9, 128.0, 126.8 (q, $J_{\text{C-F}}$ = 3.7 Hz), 125.6, 123.8 (q, $J_{\text{C-F}}$ = 269.7 Hz), 122.9 (q, $J_{\text{C-F}}$ = 32.8 Hz), 115.7, 78.2, 49.7, 46.9, 40.9, 39.6, 22.0, 21.4, 8.3. ^{19}F NMR (376.5 MHz, CDCl_3) δ -61.6. HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{F}_3\text{NO}_3\text{SNa}$; 452.1478, found 452.1482.

***N*-(*tert*-Butyl)-*N*-{3-phenyl-3-[4-(trifluoromethyl)phenoxy]propyl}ethanesulfonamide (5ua)**



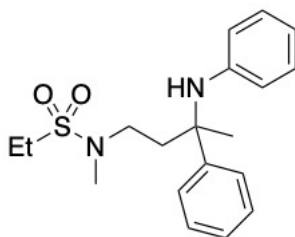
The product **5ua** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) (Figure 2-4; 18.2 mg, 0.04 mmol, 41% isolated yield). Pale yellow oil. IR (neat) 701, 836, 912, 1067, 1109, 1247, 1321, 1517, 1614, 2980 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.43 (d, J = 8.4 Hz, 2H), 7.36–7.25 (m, 5H), 6.88 (d, J = 8.4 Hz, 2H), 5.18 (dd, J = 8.8, 4.0 Hz, 1H), 3.53 (m, 1H), 3.43 (m, 1H), 3.06–3.01 (m, 2H), 2.37–2.19 (m, 2H), 1.44 (s, 9H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 160.3, 140.3, 128.8, 128.0, 126.8 (q, $J_{\text{C-F}}$ = 3.7 Hz), 125.6, 124.3 (q, $J_{\text{C-F}}$ = 268.4 Hz), 122.9 (q, $J_{\text{C-F}}$ = 32.7 Hz), 115.7, 78.6, 58.8, 50.4, 43.4, 41.4, 30.2, 8.6. ^{19}F NMR (376.5 MHz, CDCl_3) δ -61.6. HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{28}\text{F}_3\text{NO}_3\text{SNa}$; 466.1628, found 466.1634.

***N*-Methyl-*N*-{3-phenyl-3-[4-(trifluoromethyl)phenoxy]butyl}ethanesulfonamide (5va)**



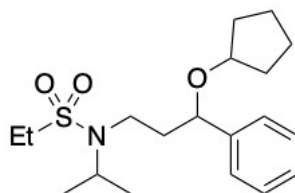
The product **5va** was purified by flash chromatography on silica gel (Biotage Selekt, 97:3–74:26, hexane/EtOAc) (Figure 2-4; 21.8 mg, 0.05 mmol, 52% isolated yield). Colorless oil. **IR** (neat) 702, 761, 842, 955, 1066, 1110, 1158, 1245, 1324, 1514 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.39–7.29 (m, 7H), 6.72 (d, $J = 8.4$ Hz, 2H), 3.39 (m, 1H), 3.21 (m, 1H), 2.92 (q, $J = 7.6$ Hz, 2H), 2.79 (s, 3H), 2.35–2.21 (m, 2H), 1.78 (s, 3H), 1.32 (t, $J = 7.6$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 158.2, 143.9, 128.8, 127.7, 126.3 (q, $J_{\text{C-F}} = 3.6$ Hz), 125.2, 124.3 (q, $J_{\text{C-F}} = 271.2$ Hz), 123.2 (q, $J_{\text{C-F}} = 32.6$ Hz), 119.1, 81.7, 45.7, 44.6, 43.0, 34.6, 23.8, 8.0. **^{19}F NMR** (376.5 MHz, CDCl_3) δ –61.7. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{24}\text{F}_3\text{NO}_3\text{SNa}$; 438.1321, found 438.1319.

***N*-Methyl-*N*-[3-phenyl-3-(phenylamino)butyl]ethanesulfonamide (5vb)**



The product **5vb** was purified by flash chromatography on silica gel (Biotage Selekt, 97:3–70:30, hexane/EtOAc) (Figure 2-4; 95.6 mg, 0.06 mmol, 57% isolated yield). Pale yellow oil. **IR** (neat) 699, 751, 947, 1138, 1324, 1446, 1498, 1600, 2978, 3394 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.49–7.46 (m, 2H), 7.36–7.32 (m, 2H), 7.27–7.23 (m, 1H), 7.03–6.98 (m, 2H), 6.63 (m, 1H), 6.37–6.34 (m, 2H), 4.19 (s, 1H), 3.33 (s, 1H), 3.00 (s, 1H), 2.86 (q, $J = 7.2$ Hz, 2H), 2.69 (s, 3H), 2.36 (m, 1H), 2.22 (m, 1H), 1.65 (s, 3H), 1.29 (t, $J = 7.2$ Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 145.9, 145.5, 128.7, 128.6, 126.7, 125.8, 117.4, 115.4, 57.6, 46.0, 44.5, 39.9, 34.6, 27.7, 7.9. **HRMS–ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$; 347.1788, found 347.1784.

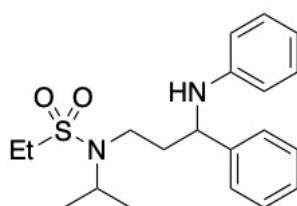
***N*-[3-(Cyclopentyloxy)-3-phenylpropyl]-*N*-isopropylethanesulfonamide (5tb)**



The product **5tb** was purified by flash chromatography on silica gel (Biotage Selekt, 97:3–74:26,

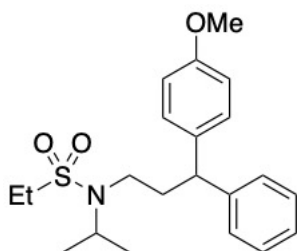
hexane/EtOAc) (Figure 2-4; 24.0 mg, 0.07 mmol, 67% isolated yield). Colorless oil. **IR** (neat) 702, 761, 842, 955, 1066, 1110, 1158, 1245, 1324, 1514 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.36–7.24 (m, 5H), 4.28 (t, J = 6.4 Hz, 1H), 3.96 (sep, J = 6.8 Hz, 1H), 3.78 (m, 1H), 3.97 (sep, J = 6.8 Hz, 1H), 3.32 (m, 1H), 3.17 (m, 1H), 2.92 (q, J = 7.6 Hz, 2H), 2.00–1.94 (m, 2H), 1.74–1.41 (m, 6H), 1.32 (t, J = 7.6 Hz, 3H), 1.19 (d, J = 6.8 Hz, 3H), 1.17 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 142.7, 128.3, 127.4, 126.5, 78.7, 49.6, 47.3, 40.7, 39.9, 33.1, 31.5, 23.3, 21.9, 21.4, 8.3. **HRMS–ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{31}\text{NO}_3\text{S}$; 354.2097, found 354.2096.

***N*-Isopropyl-*N*-[3-phenyl-3-(phenylamino)propyl]ethanesulfonamide (5tc)**



The product **5tc** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–77:23, hexane/EtOAc) (Figure 2-4; 15.5 mg, 0.04 mmol, 43% isolated yield). Pale yellow oil. **IR** (neat) 749, 873, 1028, 1139, 1283, 1320, 1454, 1502, 1602, 2978 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.36–7.30 (m, 4H), 7.23 (m, 1H), 7.11–7.06 (m, 2H), 6.64 (t, J = 7.6 Hz, 1H), 6.52 (d, J = 7.6 Hz, 2H), 4.34–4.31 (m, 2H), 3.97 (sep, J = 6.8 Hz, 1H), 3.37 (m, 1H), 3.14 (m, 1H), 2.95 (q, J = 7.6 Hz, 2H), 2.21–2.08 (m, 2H), 1.34 (t, J = 7.6 Hz, 3H), 1.15 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 147.2, 143.2, 129.1, 128.7, 127.2, 126.1, 117.3, 113.3, 56.5, 49.4, 47.0, 41.3, 40.2, 22.1, 21.4, 8.3. **HRMS–ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{29}\text{N}_2\text{O}_2\text{S}$; 361.1944, found 361.1944.

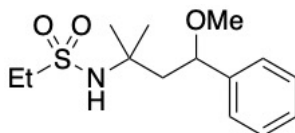
***N*-Isopropyl-*N*-[3-(4-methoxyphenyl)-3-phenylpropyl]ethanesulfonamide (5td)**



The reaction conditions were modified. The reaction was carried out with **1t** (26.7 mg, 0.1 mmol), tetrabutylammonium(4-methoxyphenyl)trifluoroborate **4d** (125.2 mg, 0.3 mmol), **Ir-1** (0.7 mg, 0.001 mmol, 1 mol %), **Co-1** (0.6 mg, 0.001 mmol, 1 mol %) and **HX-1** (40.4 mg, 0.1 mmol, 100 mol %) in benzene (1 mL) under blue LED irradiation for 12 h. The product **5td** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/EtOAc) (Figure 2-4; 18.2 mg, 0.05 mmol, 49% isolated yield). Brown oil. **IR** (neat) 701, 965, 1031, 1136, 1250, 1324, 1454, 1511, 1610,

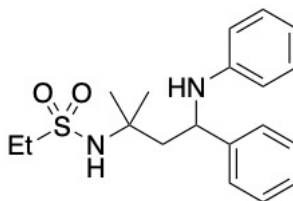
2976 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.30–7.15 (m, 7H), 6.85–6.81 (m, 2H), 3.95 (sep, *J* = 6.8 Hz, 1H), 3.84 (t, *J* = 8.0 Hz, 1H), 3.77 (s, 3H), 3.07–3.02 (m, 2H), 2.91 (q, *J* = 7.2 Hz, 2H), 2.41–2.35 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 6H). ¹³C NMR (100.6 MHz, CDCl₃) δ 158.0, 144.4, 136.0, 128.6, 128.5, 127.5, 126.3, 113.9, 55.2, 49.5, 48.5, 47.0, 41.8, 37.7, 21.8, 21.7, 8.3. HRMS–ESI (*m/z*): [M+H]⁺ calcd for C₂₁H₃₀NO₃S; 376.1941, found 376.1934.

***N*-(4-Methoxy-2-methyl-4-phenylbutan-2-yl)ethanesulfonamide (5ae)**



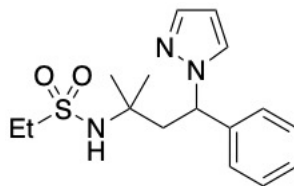
The product **5ae** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–84:16, hexane/EtOAc) (Figure 2-4; 15.7 mg, 0.06 mmol, 55% isolated yield). Pale yellow oil. IR (neat) 539, 703, 753, 1007, 1050, 1100, 1133, 1320, 2363, 2978 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.39–7.35 (m, 2H), 7.32–7.26 (m, 3H), 6.05 (s, 1H), 4.49 (dd, *J* = 12.0, 2.0 Hz, 1H), 3.22 (s, 3H), 3.07 (q, *J* = 7.2 Hz, 2H), 2.07 (dd, *J* = 15.0, 10.0 Hz, 1H), 1.57–1.54 (m, 4H), 1.42–1.38 (m, 6H). ¹³C NMR (100.6 MHz, CDCl₃) δ 141.3, 128.7, 128.0, 126.3, 81.6, 56.4, 56.1, 51.6, 50.4, 28.7, 27.2, 8.7. HRMS–ESI (*m/z*): [M+Na]⁺ calcd for C₁₄H₂₃NO₃SSNa; 308.1291, found 308.1283.

***N*-[2-Methyl-4-phenyl-4-(phenylamino)butan-2-yl]ethanesulfonamide (5ac)**



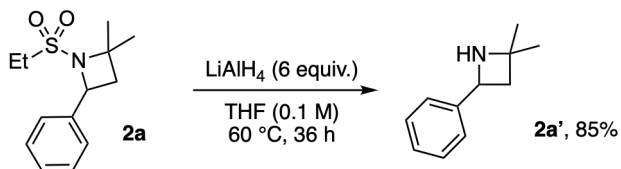
The product **5ac** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–70:30, hexane/EtOAc) (Figure 2-4; 15.7 mg, 0.06 mmol, 62% isolated yield). Pale yellow oil. IR (neat) 701, 750, 994, 1133, 1311, 1425, 1508, 1602, 2363, 2976 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.32–7.27 (m, 4H), 7.19 (m, 1H), 7.11–7.06 (m, 4H), 6.67 (m, 1H), 6.63–6.60 (m, 2H), 5.15 (s, 1H), 4.66 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.11–2.98 (m, 2H), 2.29 (dd, *J* = 15.2, 10.4 Hz, 1H), 1.88 (dd, *J* = 15.2, 2.8 Hz, 1H), 1.48 (s, 3H), 1.46 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100.6 MHz, CDCl₃) δ 146.2, 143.8, 129.2, 128.8, 127.1, 126.0, 118.3, 114.3, 56.5, 55.1, 50.8, 50.5, 29.0, 28.1, 8.5. HRMS–ESI (*m/z*): [M+H]⁺ calcd for C₁₉H₂₇NO₃S; 347.1788, found 347.1778.

N-[2-Methyl-4-phenyl-4-(1*H*-pyrazol-1-yl)butan-2-yl]ethanesulfonamide (**5af**)



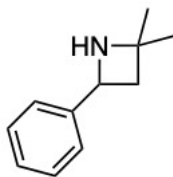
The reaction conditions were modified. The reaction was carried out with **1a** (25.4 mg, 0.1 mmol), 1*H*-pyrazole **4f** (20.4 mg, 0.3 mmol), **Ir-1** (0.7 mg, 0.001 mmol, 1 mol %), **Co-1** (0.6 mg, 0.001 mmol, 1 mol %) and **HX-1** (40.4 mg, 0.1 mmol, 100 mol %) in benzene (1 mL) under blue LED irradiation for 12 h. The product **5ac** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–70:30, hexane/EtOAc) (Figure 2-4; 15.6 mg, 0.05 mmol, 49% isolated yield). Colorless oil. **IR** (neat) 701, 753, 1000, 1129, 1221, 1308, 1398, 1455, 2978, 3238 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.58 (d, *J* = 1.6 Hz, 1H), 7.42 (d, *J* = 2.4 Hz, 1H), 7.35–7.24 (m, 5H), 6.28 (dd, *J* = 2.4, 1.6 Hz, 1H), 5.66 (dd, *J* = 10.4, 2.8 Hz, 1H), 4.97 (s, 1H), 3.02–2.94 (m, 3H), 2.34 (dd, *J* = 15.2, 2.8 Hz, 1H), 1.42 (s, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.18 (s, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 141.5, 139.3, 129.5, 128.8, 127.9, 126.5, 106.4, 62.4, 56.1, 50.4, 47.8, 28.6, 27.6, 8.5. **HRMS–ESI** (*m/z*): [M+H]⁺ calcd for C₁₆H₂₃N₃O₂S; 322.1584, found 322.1574.

Deprotection Method



Deprotection was carried out according to the modified conditions in the literature.⁸ To a suspension of lithium aluminium hydride (22.8 mg, 0.6 mmol) in tetrahydrofuran (1.0 mL) was added **2a** (25.3 mg, 0.10 mmol) at room temperature. After being stirred for 36 hours at 60 °C, water (22 μ L), 4M NaOH aq. (22 μ L), and water (68 μ L) were added at 0°C. The mixture was filtered with Celite pad. The mother liquid was concentrated. The residue was purified by flash column chromatography (2:98, Et₃N/EtOAc) to obtain **2a'** (13.7 mg, 85%).

2,2-Dimethyl-4-phenylazetidine (**2a'**)



IR (neat) 699, 753, 1069, 1132, 1263, 1321, 1367, 1456, 2863, 2956 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.31–7.32 (m, 2H), 7.28–7.24 (m, 2H), 7.15 (m, 1H), 4.73 (t, *J* = 8.0 Hz, 1H), 2.36 (dd, *J* =

10.8, 8.0 Hz, 1H), 2.04 (dd, $J = 10.8, 8.0$ Hz, 1H), 1.93 (m, 1H), 1.43 (s, 3H), 1.24 (s, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 145.5, 128.3, 126.7, 126.0, 55.5, 53.7, 42.3, 31.8, 29.1. HRMS–ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{16}\text{N}$; 162.1277, found 162.1270.

Stern-Volmer Luminescence Quenching Analysis

Several Stern-Volmer luminescence quenching experiments were carried out.

1. Quencher Co-1 with or without collidinium salt HX-1 (Figure S2-3)

Procedure without HX-1: In a glovebox, to a screw-top 1.0 cm quartz cuvette was added 5 μM solution of **Ir-1** in degassed benzene and cobalt-salen complex **Co-1** (quencher) of appropriate concentration in degassed benzene (quencher concentration = 20 μM , 40 μM , 60 μM , 80 μM). The fluorescence intensity was measured at $\lambda = 483$ nm after excitation at $\lambda = 380$ nm in the quartz cuvette.

Procedure with HX-1: In a glovebox, to a screw-top 1.0 cm quartz cuvette was added 5 μM solution of **Ir-1** in degassed benzene, collidinium salt **HX-1** of appropriate concentration in degassed benzene (concentration = 40 μM), and cobalt-salen complex (quencher) of appropriate concentration in degassed benzene (quencher concentration = 20 μM , 40 μM , 60 μM , 80 μM). The fluorescence intensity was measured at $\lambda = 483$ nm after excitation at $\lambda = 380$ nm in the quartz cuvette.

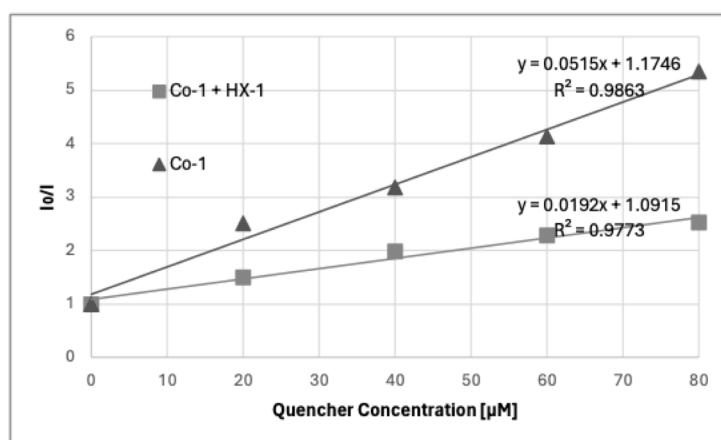


Figure S2-3.

2. Quencher: collidinium salt HX-1 (Figure S2-4)

Procedure: In a glovebox, to a screw-top 1.0 cm quartz cuvette was added 5 μM solution of **Ir-1** in degassed benzene and collidinium salt (quencher) of appropriate concentration in degassed benzene (quencher concentration = 20 μM , 40 μM , 60 μM , 80 μM). The fluorescence intensity was measured at $\lambda = 483$ nm after excitation at $\lambda = 380$ nm in the quartz cuvette.

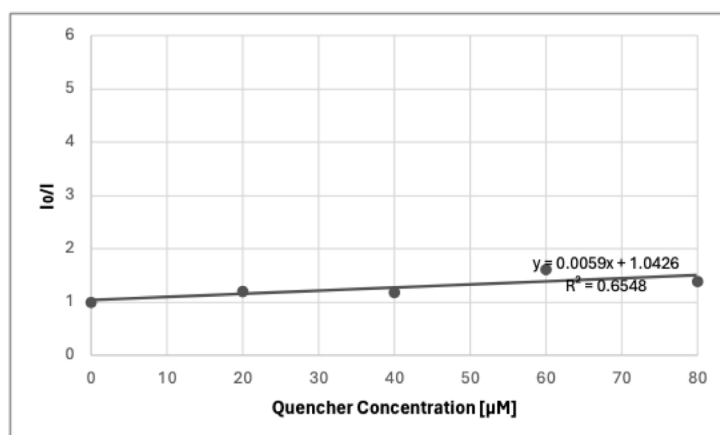


Figure S2-4.

The results of Stern-Volmer experiments revealed that the fluorescence of **Ir-1** is quenched by **Co-1**, but not by **HX-1** (Figure S2-3 and S2-4).

Radical Trapping Experiment.

Radical Trapping with TEMPO. In a glovebox, an oven-dried vial with a stirring bar was added **Ir-1** (0.7 mg, 0.001 mmol, 1.0 mol %), **Co-1** (0.6 mg, 0.001 mmol), **HX-1** (10.1 mg, 0.025 mmol), *N*-(3-Phenylpropyl)ethanesulfonamide **1j** (22.5 mg, 0.1 mmol, 1.0 equiv.), (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO, 3.9 mg, 0.025 mmol, 25 mol %) and benzene (1.0 mL). After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-1). After 16 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 99:1–90:10, hexane/EtOAc) gave the **5j** (8.4 mg, 0.02 mmol, 22% isolated yield) as colorless oil.

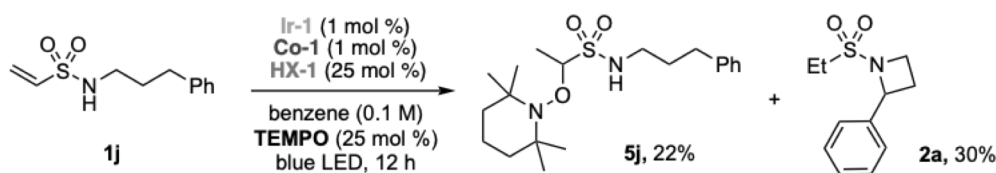
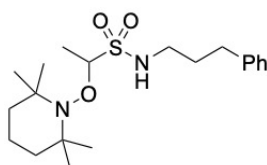


Figure S2-5.

N-(3-Phenylpropyl)-1-[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]ethane-1-sulfonamide (**5j**)



IR (neat) 699, 747, 1107, 1142, 1153, 1326, 1363, 1453, 2871, 2929 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.31–7.26 (m, 2H), 7.21–7.17 (m, 3H), 4.96 (q, $J = 6.4$ Hz, 1H), 4.21 (t, $J = 6.4$ Hz, 1H), 3.31–3.21 (m, 2H), 2.71 (t, $J = 7.6$ Hz, 2H), 1.97–1.89 (m, 2H), 1.65 (d, $J = 6.4$ Hz, 3H), 1.63–1.43 (m, 6H), 1.38–1.08 (m, 12H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 140.9, 128.5, 128.4, 126.1, 92.1, 61.6, 59.9, 43.2, 40.3, 33.9, 33.5, 32.9, 32.3, 29.7, 20.6, 20.6, 17.0, 14.8. **HRMS–ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{34}\text{N}_2\text{O}_3\text{S}$; 383.2363, found 383.2371.

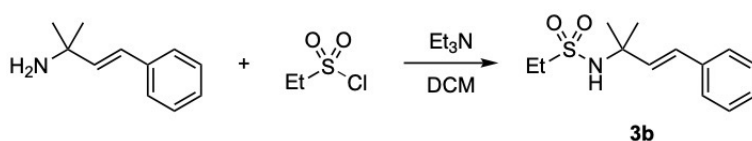
Photoisomerization by Photoredox Catalysts



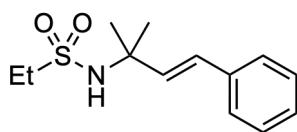
Figure S2-6.

In a glovebox, to a n oven-dried vial with a stirring bar was added **Ir-1** (0.4 mg, 0.0005 mmol, 1.0 mol %), (*E*)-*N*-(2-methyl-4-phenylbut-3-en-2-yl)ethanesulfonamide **3b** (12.7 mg, 0.05 mmol, 1.0 equiv.) and benzene (0.5 mL). After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-1). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate and analyzed by ^1H NMR relative to 1,1,2,2-tetrachloroethane (19.4 mg, 0.12 mmol, 2.31 equiv.) as an internal standard. The mixture of **3b** and **3a** was obtained.

Synthesis and Characterization of (*E*)-*N*-(2-methyl-4-phenylbut-3-en-2-yl)ethanesulfonamide (**3b**)



(*E*)-2-Methyl-4-phenyl-3-buten-2-amine was prepared according to the conditions of the literature.⁹ The amine (102.8 mg, 0.64 mmol, 1.0 equiv.) was added to a round bottom flask and put under nitrogen. The flask was then charged with dichloromethane (0.2 M with respect to amine) and triethylamine (106.5 μL , 0.77 mmol, 1.2 equiv.) and stirred at 0 °C. Then, ethanesulfonyl chloride (66.2 μL , 0.70 mmol, 1.1 equiv.) was added dropwise via syringe. After the addition, the reaction was allowed to slowly warm to room temperature at 2 h. The reaction was diluted with additional dichloromethane and quenched with 1M HCl. The organic phase was separated, washed with a saturated brine solution, dried over Na_2SO_4 , and concentrated in vacuo. The residue was purified by flash column chromatography (Biotage Selekt, 98:2–80:20, hexane/EtOAc) to afford **3b** (70 mg, 0.27 mmol, 43%).



White solid. **M.p.** 68–69 °C. **IR** (neat) 695, 750, 970, 995, 1132, 1319, 1383, 1449, 2979, 3273 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.40–7.37 (m, 2H), 7.35–7.31 (m, 2H), 7.26 (m, 1H), 6.57 (d, J = 16.4 Hz, 1H), 6.34 (d, J = 16.4 Hz, 1H), 4.23 (s, 1H), 3.05 (q, J = 7.6 Hz, 2H), 1.57 (s, 6H), 1.36 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 136.3, 134.4, 128.7, 128.7, 127.9, 126.5, 56.7, 49.9, 28.6, 8.6. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_2\text{SNa}$; 276.1029, found 276.1031.

Reaction with **3b**

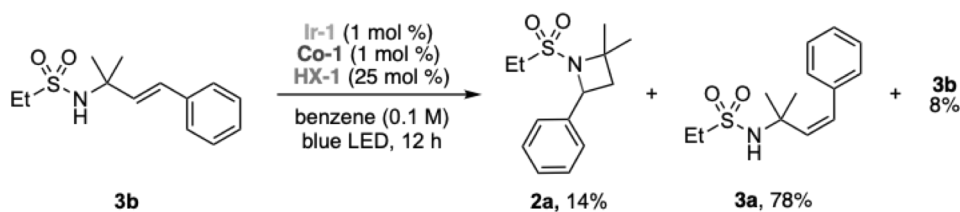
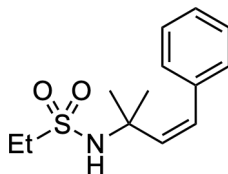


Figure S2-7

In a glovebox, to an oven-dried vial with a stirring bar was added **Ir-1** (0.7 mg, 0.001 mmol, 1.0 mol %), **Co-1** (0.6 mg, 0.001 mmol), **HX-1** (10.1 mg, 0.025 mmol), (*E*)-*N*-(2-methyl-4-phenylbut-3-en-2-yl)ethanesulfonamide **3b** (25.4 mg, 0.1 mmol, 1.0 equiv.) and benzene (1.0 mL). After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-1). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, and analyzed by ^1H NMR relative to 1,1,2,2-tetrachloroethane (20.0 mg, 0.12 mmol, 1.2 equiv.) as an internal standard. The residue was purified by flash column chromatography on silica gel (Biotage Selekt, 97:3–70:30, hexane/EtOAc) gave the mixture **3a** and **3b** (13.3 mg, **3a** : **3b** = 0.89 : 0.11).

(*Z*)-*N*-(2-Methyl-4-phenylbut-3-en-2-yl)ethanesulfonamide



IR (neat) 702, 757, 994, 1130, 1283, 1314, 1380, 1456, 2979, 3273 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.38–7.25 (m, 5H), 6.59 (d, J = 12.8 Hz, 1H), 5.78 (d, J = 12.8 Hz, 1H), 4.16 (s, 1H), 2.96 (q, J = 7.2 Hz, 2H), 1.44 (s, 6H), 1.27 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 137.7, 137.4, 129.5, 128.6, 128.1, 127.1, 57.5, 50.2, 30.0, 8.4. **HRMS–ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for

C₁₃H₁₉NO₂SNa ; 276.1029, found 276.1037.

Competition Experiment

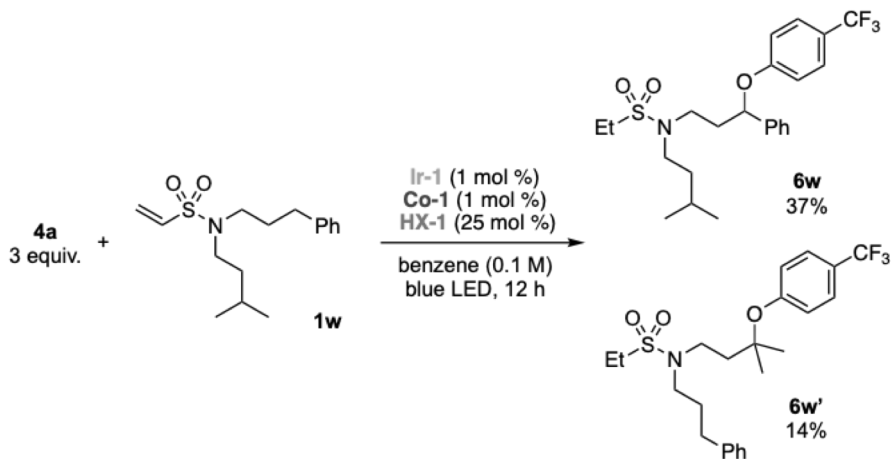
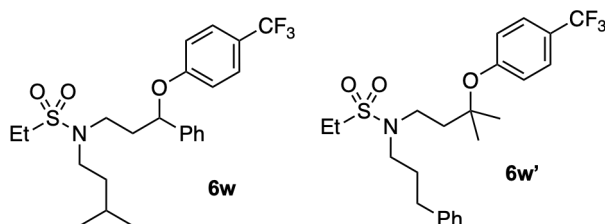


Figure S2-8

In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst **Ir-1** (0.7 mg, 0.001 mmol), **Co-1** (0.6 mg, 0.001 mmol), **HX-1** (10.1 mg, 0.025 mmol) and benzene (1.0 mL). Then, *N*-isopentyl-*N*-(3-phenylpropyl)ethanesulfonamide **1w** (29.5 mg, 0.1 mmol) and 4-trifluoromethylphenol **4a** (48.6 mg, 0.3 mmol) were added to the reaction mixture. After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-8). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 97:3–74:26, hexane/EtOAc) gave the mixture **6w** and **6w'** (23.2 mg, 51%, **6w** : **6w'** = 0.73 : 0.27) as colorless oil.



IR (neat) 701, 753, 1067, 1112, 1161, 1251, 1326, 1517, 1614, 2873 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.52 (d, *J* = 8.4 Hz, 0.27 $\times$ 2H), 7.43 (d, *J* = 8.4 Hz, 0.73 $\times$ 2H), 7.37–7.17 (m, 0.27 $\times$ 5H + 0.73 $\times$ 5H), 7.03 (d, *J* = 8.4 Hz, 0.27 $\times$ 2H), 6.89 (d, *J* = 8.4 Hz, 0.73 $\times$ 2H), 5.26 (dd, *J* = 8.4, 4.0 Hz, 1H), 3.48–3.34 (m, 0.27 $\times$ 2H + 0.73 $\times$ 2H), 3.27–3.19 (m, 0.27 $\times$ 2H + 0.73 $\times$ 2H), 2.99–2.92 (m, 0.27 $\times$ 2H + 0.73 $\times$ 2H), 2.64 (t, *J* = 7.8 Hz, 0.27 $\times$ 2H), 2.30–2.15 (m, 0.73 $\times$ 2H), 2.00 (m, 0.27 $\times$ 1H), 1.92 (m, 0.27 $\times$ 1H), 1.58–1.38 (m, 0.27 $\times$ 2H + 0.73 $\times$ 3H), 1.37–1.28 (m, 0.27 $\times$ 9H + 0.73 $\times$ 3H), 0.87 (dd, *J* = 6.4, 3.6 Hz, 0.73 $\times$ 6H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 160.1, (158.1), (141.0),

140.3, 128.9, (128.5), (128.3), 128.0, 126.8 (q, J_{C-F} = 3.7 Hz), (126.5 (q, J_{C-F} = 3.6 Hz)), (126.1), (125.1 (q, J_{C-F} = 32.9 Hz)), 123.0 (q, J_{C-F} = 34.0 Hz), (122.8), 115.7, (79.9), 77.5, (47.6), 46.7, (46.1), 45.9, 44.4, (43.5), (41.5), 38.4, 37.7, (32.9), (30.5), 26.6, 25.8, 22.4, (22.3), 8.2, (8.1). ^{19}F NMR (376.5 MHz, CDCl_3) δ -61.8, (-61.6). **HRMS-ESI** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{23}\text{H}_{34}\text{F}_3\text{N}_2\text{O}_3\text{S}$; 475.2237, found 475.2257.

2. Reactions with Intermolecular HAT Reagents

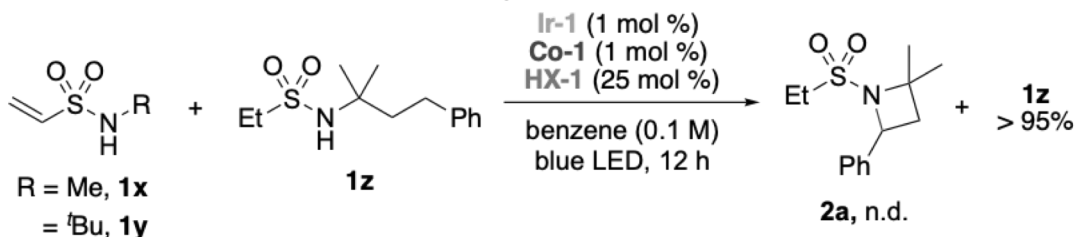
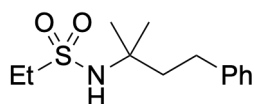


Figure S2-9

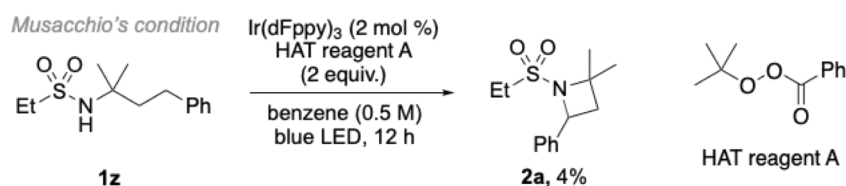
In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst **Ir-1** (0.7 mg, 0.001 mmol), **Co-1** (0.6 mg, 0.001 mmol), **HX-1** (10.1 mg, 0.025 mmol) and benzene (1.0 mL). Then, HAT reagent **1x** or **1y** (0.1 mmol) and ethylsulfonamide **1z** (25.5 mg, 0.1 mmol) were added to the reaction mixture. After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-1). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate and analyzed by ^1H NMR relative to 1,1,2,2-tetrachloroethane as an internal standard.

N-(2-Methyl-4-phenylbutan-2-yl)ethanesulfonamide (**1z**)

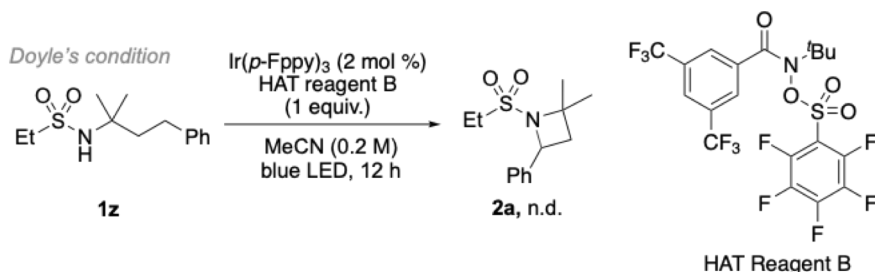


Ethyl sulfonamide **1z** was prepared according to the conditions of the synthesis **3b**. The product **1z** was purified by flash chromatography on silica gel (Biotage Selekt, 98:2–80:20, hexane/AcOEt) (1.3 mmol scale, 227 mg, 72% yield). Pale yellow oil. **IR** (neat) 540, 701, 744, 1001, 1129, 1317, 1387, 1455, 2978, 3282 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.26 (m, 2H), 7.21–7.17 (m, 3H), 4.02 (s, 1H), 3.08 (q, J = 7.2 Hz, 1H), 2.72–2.67 (m, 2H), 1.94–1.90 (m, 2H), 1.42 (s, 6H), 1.39 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100.6 MHz, CDCl_3) δ 141.6, 128.5, 128.3, 126.0, 57.0, 50.5, 45.0, 30.6, 27.9, 8.7. **HRMS-ESI** (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{21}\text{NO}_2\text{SNa}$; 278.1185, found 278.1188.

Other HAT reagents



Musacchio's condition. The reaction was carried out according to the conditions of the literature.¹⁰ In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst Ir(dFppy)₃ (1.5 mg, 0.002 mmol), HAT reagent A (38.0 μ L, 0.2 mmol) and benzene (0.2 mL). Then, ethanesulfonamide **1z** (25.5 mg, 0.1 mmol) was added to the reaction mixture. After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C (Figure S2-1). After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate and analyzed by ¹H NMR relative to 1,1,2,2-tetrachloroethane as an internal standard.



Doyle's condition. The reaction was carried out according to the conditions of the literature.¹¹ In a glovebox, to an oven-dried vial with a stirring bar was added photoredox catalyst Ir(p-Fppy)₃ (1.4 mg, 0.002 mmol), HAT reagent B (55.9 mg, 0.1 mmol) and MeCN (0.5 mL). Then, ethanesulfonamide **1z** (25.5 mg, 0.1 mmol) was added to the reaction mixture. After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 °C. After 12 h, the reaction was quenched with a short plug of silica gel using ethyl acetate and analyzed by ¹H NMR relative to 1,1,2,2-tetrachloroethane as an internal standard.

X-ray Structure of 2a

Details of the crystal data and a summary of the intensity data collection parameters for **2a** are listed in Table S1. A suitable crystal obtained by recrystallization from dichloromethane and hexane was mounted with mineral oil on a Cargille Immersion Oil Type B and transferred to Bruker Single Crystal CCD X-ray Diffractometer (SMART APEX II) (Graphite-monochromated Mo K α radiation ($\lambda = 0.71073$ Å)). Cell parameters were determined and refined, and raw frame data were integrated using APEX 3 (Bruker) and a multi-scan absorption correction using an empirical method was applied. The structures were solved by direct methods with SHELXT and refined by full-matrix least-squares techniques against F^2 (SHELXL-2018/3) by using Yadokari-XG software package. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were refined isotropically on calculated positions using a riding model with their U_{iso} values constrained to 1.5 times the U_{eq} of their pivot atoms for terminal sp³ carbon atoms and 1.2 times for all other carbon atoms. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. CCDC 2328158 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

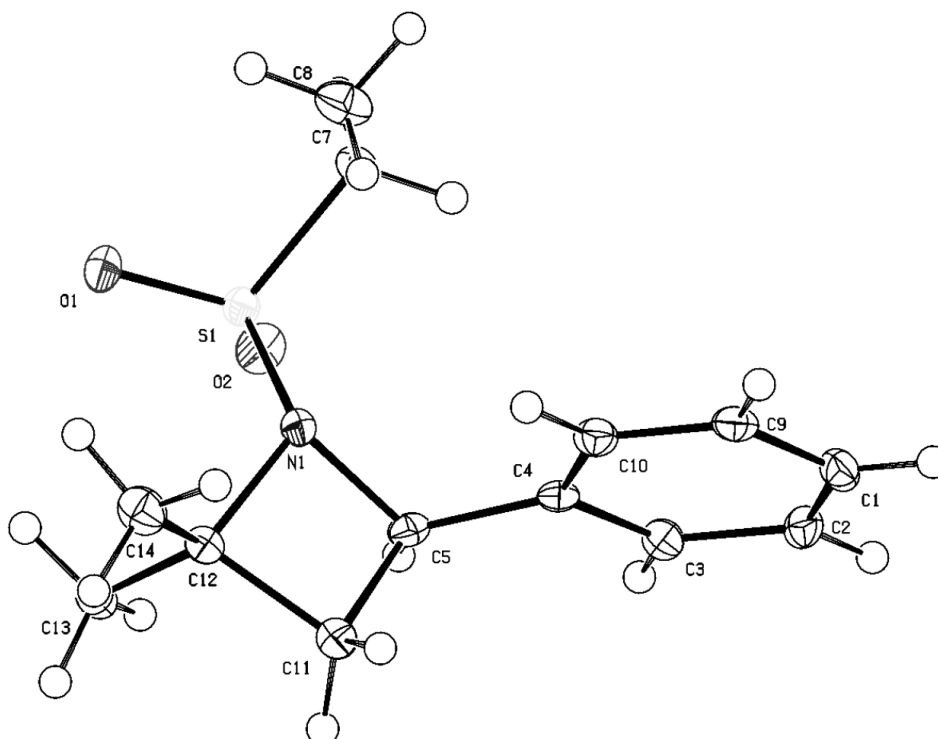


Table S2-1. Crystallographic data and structure refinement details of **2a**

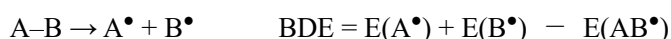
	2a
CCDC No.	2328158
formula	C ₁₃ H ₁₉ NO ₂ S
fw	253.36
<i>T</i> (K)	86(2)
λ (Å)	0.71073
cryst syst	orthorhombic
space group	Pna2 ₁
<i>a</i> (Å)	11.909 (4)
<i>b</i> (Å)	11.677 (4)
<i>c</i> (Å)	9.648 (3)
α (deg)	90
β (deg)	90
γ (deg)	90
<i>V</i> (Å ³)	1341.6(2)
<i>Z</i>	4
<i>D</i> _{calc} (g·cm ⁻³)	1.254
μ (mm ⁻¹)	0.232
F(000)	480
cryst size (mm ³)	0.16 × 0.20 × 0.22
2 θ range (deg)	2.45 to 25.09
reflns collected	12383
params	157
GOF on <i>F</i> ²	1.149
<i>R</i> ₁ , <i>wR</i> ₂ (all data)	0.0255, 0.0720
Flack parameter	0.02 (2)

Computational Studies

Calculation of Bond Dissociation Energies of Cobalt–Carbon Bonds

To gain the mechanistic insight into the effects of the ligand (Table 1 entries 1, 8 and 9), the computational studies were carried out based on the Zhu's report.¹² All the restricted and unrestricted density functional theory (DFT) calculations were performed with the Gaussian 16 package¹³. The method (U)B3LYP-D3(BJ) functional with the 6-31G(d,p) basis set was used for the geometry optimization and normal vibrational mode analysis with SMD¹⁴ model (PhCF₃). The dispersion-corrected method (U)BP86¹⁵-D3(BJ)¹⁶ functional with the 6-311+G(d,p) basis set was used to calculate single-point energies with SMD model (PhCF₃). SMD solvation model was implied in all geometry pre-optimizations and optimizations, where the solvent was replaced with toluene in the pre-optimizations, and data for PhCF₃ ($\epsilon = 9.22^{17}$, $n_{20}^2 = 1.9923^{18}$, $\alpha = 0.00^{19}$, $\beta = 0.109^{19}$, $\gamma = 34.4^{20}$, $\varphi = 0.600$, $\psi = 0.300$) were used.

Bond dissociation energies (BDE) were calculated according to²¹



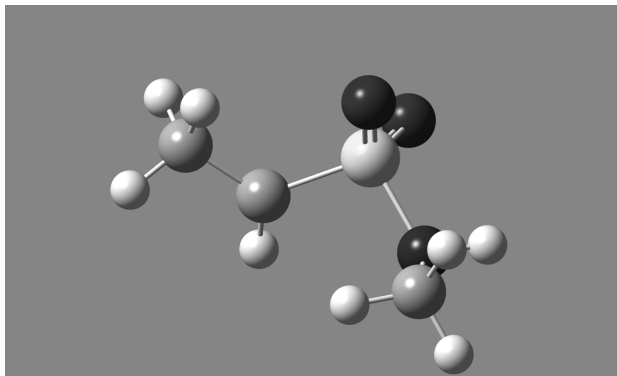
where E is the sum of electronic energy and zero point vibration energy.

Table S2-2. DFT calculation results of Cobalt, alkyl radical(A) and cobalt complex.^a

	ZPE / a.u.	E(BP-86) / a.u.	BDE / kcal mol ⁻¹
Alkyl radical (A)	0.126036	-722.4714661	
Co-1	0.879233	-3047.183723	
Co-2	0.859071	-3045.994201	
Co-3	0.787199	-3042.442921	
Co-C (Co-1)	1.011128	-3769.709511	34.1
Co-C (Co-2)	0.990681	-3768.530738	40.8
Co-C (Co-3)	0.918988	-3764.983842	43.6

^a Calculated at (U)BP86-D3(BJ)/6-311+G(d,p)/SMD(PhCF₃)/(U)B3LYP-D3(BJ)/6-31G(d,p)/SMD(PhCF₃) level theory. Abbreviations: ZPE—zero-point energy.

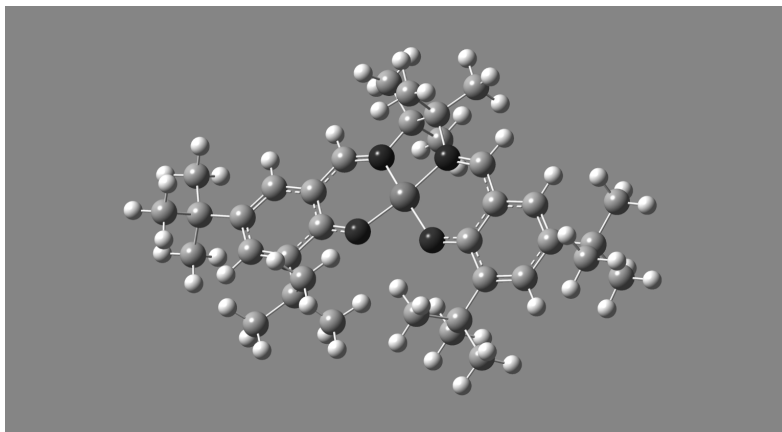
Alkyl radical (A)



Charge = 0 Multiplicity = 2

C	2.38123	-0.95474	0.02636
H	2.21805	-1.04857	-1.04993
H	2.7231	-1.91396	0.4293
H	3.19933	-0.23289	0.1803
C	1.15021	-0.51959	0.7233
H	1.01656	-0.60516	1.79701
S	-0.0299	0.50111	-0.06996
N	-1.4601	-0.08479	0.58441
H	-2.12239	0.68846	0.63723
C	-2.01974	-1.29748	-0.02805
H	-1.29281	-2.10942	0.05359
H	-2.90725	-1.57617	0.54364
H	-2.29078	-1.16455	-1.08062
O	0.07502	1.88909	0.41995
O	0.0606	0.25701	-1.52141

Co-1



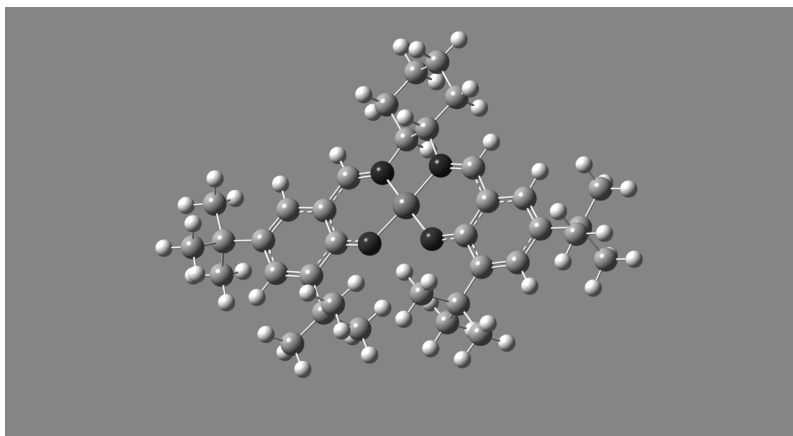
Charge = 0 Multiplicity = 2

C	4.74061	-1.49194	-0.1621
C	3.36241	-1.6113	-0.23597
C	2.57017	-0.42226	-0.06497
C	3.2517	0.81327	0.14629
C	4.66764	0.86053	0.20936
C	5.43449	-0.27508	0.06343
H	5.3367	-2.38703	-0.28398
C	2.54329	2.04584	0.28713
H	5.1284	1.82854	0.37514
H	3.16297	2.92425	0.45413
C	0.63579	3.53643	0.45759
C	1.58189	4.69536	0.12444
C	-0.63579	3.53643	-0.4576
H	2.36511	4.79174	0.88062
C	-1.58188	4.69536	-0.12444
H	-2.05736	4.57119	0.85101
C	-2.54329	2.04584	-0.28713
H	-3.16297	2.92425	-0.45414
C	-3.2517	0.81327	-0.14628
C	-4.66764	0.86053	-0.20936
C	-2.57017	-0.42226	0.06497
C	-5.43449	-0.27508	-0.06342
H	-5.1284	1.82854	-0.37514
C	-3.36241	-1.6113	0.23597
C	-4.74061	-1.49194	0.1621
H	-5.3367	-2.38703	0.28399
O	1.26571	-0.49488	-0.10609
O	-1.26571	-0.49488	0.10609
N	-1.25064	2.19596	-0.22931
N	1.25064	2.19596	0.2293
C	2.68616	-2.96684	-0.49755
C	1.75208	-3.32097	0.68028
C	1.87666	-2.89244	-1.81154
C	3.70668	-4.10837	-0.64395
H	2.32257	-3.39408	1.61346

H	0.97862	-2.56495	0.8026
H	1.27306	-4.29051	0.50309
H	1.37136	-3.84651	-2.00017
H	1.12503	-2.10459	-1.76429
H	2.54117	-2.69044	-2.65946
H	3.17195	-5.04511	-0.83177
H	4.39125	-3.94529	-1.48314
H	4.30406	-4.24543	0.26375
C	-2.68616	-2.96684	0.49755
C	-1.75208	-3.32097	-0.68029
C	-1.87667	-2.89245	1.81154
C	-3.70668	-4.10837	0.64393
H	-2.32256	-3.39407	-1.61346
H	-0.97861	-2.56495	-0.80259
H	-1.27306	-4.29051	-0.5031
H	-2.54117	-2.69045	2.65946
H	-1.37136	-3.84651	2.00017
H	-1.12503	-2.1046	1.76429
H	-3.17195	-5.04512	0.83176
H	-4.39125	-3.9453	1.48313
H	-4.30405	-4.24543	-0.26377
C	-6.96715	-0.28115	-0.12639
C	-7.5384	1.12225	-0.38124
C	-7.43194	-1.20865	-1.26955
C	-7.53617	-0.80057	1.21143
H	-7.2652	1.82184	0.4156
H	-7.18892	1.53513	-1.3333
H	-8.63144	1.07468	-0.42087
H	-7.08566	-2.23635	-1.12404
H	-8.52635	-1.23001	-1.32372
H	-7.04983	-0.85913	-2.23463
H	-8.63159	-0.81656	1.18073
H	-7.19446	-1.81671	1.4302
H	-7.22811	-0.1566	2.04209
C	6.96715	-0.28115	0.1264
C	7.43194	-1.20865	1.26956

C	7.53617	-0.80057	-1.21142
C	7.5384	1.12225	0.38125
H	7.04983	-0.85913	2.23464
H	7.08566	-2.23635	1.12405
H	8.52635	-1.23001	1.32373
H	7.22811	-0.1566	-2.04208
H	8.63159	-0.81656	-1.18071
H	7.19446	-1.81671	-1.43019
H	8.63144	1.07468	0.42088
H	7.2652	1.82184	-0.41559
H	7.18891	1.53513	1.33331
Co	0.	0.84427	0.
H	2.05736	4.57118	-0.85102
H	-2.36511	4.79173	-0.88063
H	1.03118	5.63803	0.11957
H	-1.03117	5.63803	-0.11958
C	0.25216	3.60281	1.94634
H	1.14537	3.44197	2.5565
H	-0.16357	4.58028	2.20262
H	-0.4778	2.82974	2.19887
C	-0.25216	3.60281	-1.94635
H	-1.14537	3.44196	-2.55651
H	0.16358	4.58027	-2.20263
H	0.4778	2.82973	-2.19887

Co-2



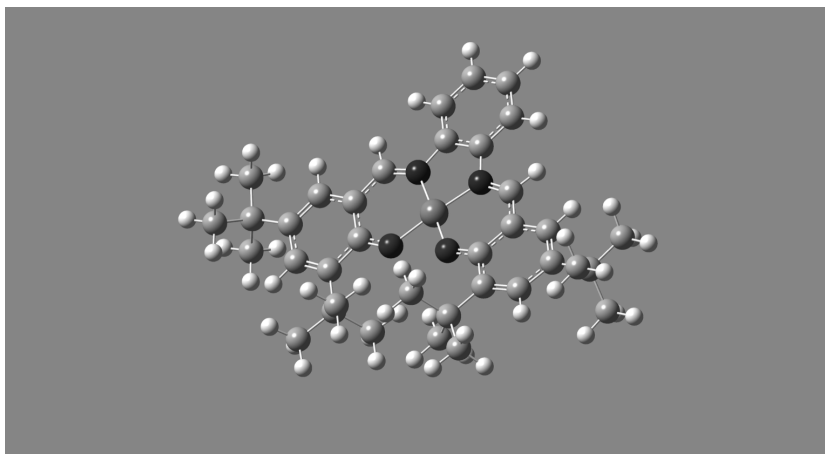
Charge = 0 Multiplicity = 2

C	0.38	-0.60132	0.
C	1.75758	-0.73507	-0.05958
C	2.55546	0.46381	-0.08304
C	1.87095	1.71709	-0.10039
C	0.45509	1.77782	-0.0491
C	-0.31327	0.63637	0.01507
H	-0.21753	-1.50317	0.02951
C	2.57914	2.95106	-0.21129
H	-0.00308	2.76101	-0.06319
H	1.96486	3.84523	-0.30101
C	4.50514	4.39365	-0.45669
C	3.65298	5.63651	-0.20814
C	5.76059	4.39366	0.4182
C	4.49495	6.89928	-0.44335
H	2.7847	5.64922	-0.87378
C	6.61274	5.63651	0.16965
C	5.77078	6.89928	0.40486
H	4.76601	6.95534	-1.5059
H	6.98875	5.62	-0.86151
H	6.37266	7.78736	0.18492
C	7.68659	2.95106	0.1728
H	8.30087	3.84523	0.2625
C	8.39477	1.71709	0.06189
C	9.81063	1.77782	0.01059
C	7.71027	0.46381	0.04455

C	10.57899	0.63637	-0.05358
H	10.2688	2.76101	0.02466
C	8.50814	-0.73507	0.02109
C	9.88572	-0.60132	-0.03851
H	10.48326	-1.50317	-0.06802
O	3.86112	0.38308	-0.09958
O	6.40461	0.38308	0.06111
N	6.39074	3.07801	0.19329
N	3.87498	3.07801	-0.23177
C	2.42181	-2.11878	-0.1398
C	3.41229	-2.30923	1.02833
C	1.39789	-3.2649	-0.07348
C	3.16509	-2.23326	-1.4893
H	4.19077	-1.54975	1.00276
H	2.88979	-2.24546	1.99
H	3.88032	-3.2981	0.96581
H	0.68354	-3.23146	-0.90284
H	1.92768	-4.22111	-0.13474
H	0.83395	-3.25893	0.86552
H	2.45679	-2.16224	-2.32257
H	3.90604	-1.44114	-1.59579
H	3.67608	-3.19986	-1.56242
C	7.84392	-2.11878	0.10131
C	8.86784	-3.2649	0.03499
C	7.10065	-2.23326	1.45082
C	6.85344	-2.30923	-1.06681
H	9.5822	-3.23145	0.86435
H	8.33805	-4.22111	0.09626
H	9.43177	-3.25894	-0.90401
H	7.80895	-2.16224	2.28409
H	6.35969	-1.44115	1.55731
H	6.58966	-3.19987	1.52394
H	7.37593	-2.24547	-2.02848
H	6.38541	-3.2981	-1.00429
H	6.07495	-1.54975	-1.04123
C	12.11124	0.6435	-0.12303

C	12.68744	-0.10378	1.09883
C	12.5705	-0.06641	-1.41455
C	12.68014	2.07077	-0.12791
H	13.7827	-0.11103	1.06101
H	12.38197	0.38163	2.0319
H	12.34894	-1.14363	1.1352
H	12.18462	0.44871	-2.30073
H	13.66466	-0.0779	-1.4763
H	12.22371	-1.10348	-1.4519
H	12.41215	2.61709	0.78245
H	13.7729	2.03279	-0.18254
H	12.32379	2.64579	-0.98894
C	-1.84552	0.6435	0.0845
C	-2.41442	2.07077	0.08933
C	-2.4217	-0.10382	-1.13735
C	-2.3048	-0.06637	1.37603
H	-2.14642	2.61706	-0.82105
H	-3.50718	2.03279	0.14396
H	-2.05807	2.64582	0.95034
H	-2.08319	-1.14367	-1.17369
H	-3.51696	-0.11107	-1.09954
H	-2.11622	0.38157	-2.07043
H	-3.39895	-0.07786	1.43776
H	-1.95801	-1.10344	1.41342
H	-1.91892	0.44878	2.2622
Co	5.13286	1.72162	-0.01924
H	4.84017	4.40228	-1.50386
H	5.42556	4.40228	1.46537
H	3.27698	5.62	0.82302
H	3.89306	7.78736	-0.22341
H	5.49971	6.95534	1.46741
H	7.48103	5.64922	0.83529

Co-3



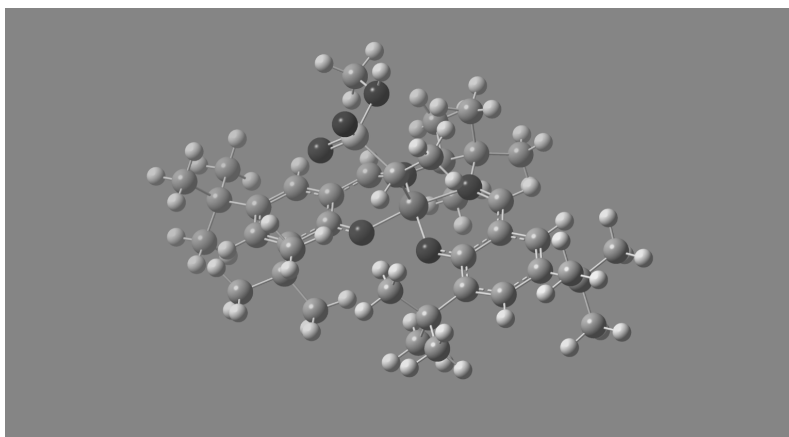
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C	4.72151	-1.5031	0.11602
C	3.34512	-1.6127	0.20348
C	2.56184	-0.4103	0.08183
C	3.25779	0.83081	-0.07883
C	4.67821	0.86357	-0.15547
C	5.42926	-0.28437	-0.06981
H	5.30943	-2.40787	0.19723
C	2.57623	2.07194	-0.11803
H	5.14862	1.83264	-0.28097
H	3.20768	2.95523	-0.18473
C	0.7031	3.53491	-0.03221
C	1.40011	4.74814	-0.05998
C	-0.7031	3.53491	0.03221
C	0.6983	5.95024	-0.03007
H	2.48199	4.76858	-0.10519
C	-1.40011	4.74814	0.05998
C	-0.6983	5.95025	0.03007
H	-1.24363	6.88811	0.05323
C	-2.57623	2.07194	0.11803
H	-3.20768	2.95523	0.18473
C	-3.25779	0.83081	0.07883
C	-4.67821	0.86357	0.15547
C	-2.56184	-0.4103	-0.08183
C	-5.42926	-0.28437	0.0698
H	-5.14862	1.83264	0.28097

C	-3.34512	-1.6127	-0.20348
C	-4.72151	-1.5031	-0.11602
H	-5.30943	-2.40787	-0.19724
O	1.25996	-0.47302	0.12808
O	-1.25996	-0.47302	-0.12808
N	-1.27259	2.23606	0.0594
N	1.27259	2.23606	-0.0594
C	2.66206	-2.96979	0.43484
C	1.70587	-3.28223	-0.73634
C	3.67565	-4.12299	0.52951
C	1.87983	-2.92587	1.76663
H	0.93574	-2.51872	-0.82514
H	2.26052	-3.3327	-1.68044
H	1.22297	-4.25293	-0.57868
H	4.37555	-3.99119	1.36147
H	3.13564	-5.06019	0.69837
H	4.25592	-4.23786	-0.39224
H	2.56406	-2.7563	2.60577
H	1.13546	-2.1298	1.76061
H	1.3682	-3.87972	1.93706
C	-2.66206	-2.96979	-0.43484
C	-3.67565	-4.12299	-0.52951
C	-1.87982	-2.92587	-1.76663
C	-1.70587	-3.28223	0.73634
H	-4.37555	-3.99119	-1.36147
H	-3.13564	-5.06019	-0.69837
H	-4.25593	-4.23786	0.39224
H	-2.56405	-2.7563	-2.60577
H	-1.13546	-2.1298	-1.76061
H	-1.3682	-3.87972	-1.93705
H	-2.26052	-3.3327	1.68044
H	-1.22297	-4.25293	0.57868
H	-0.93574	-2.51872	0.82515
C	-6.96039	-0.3087	0.1493
C	-7.53386	-0.89089	-1.16062
C	-7.39921	-1.19482	1.33474

C	-7.54797	1.09629	0.35187
H	-8.62846	-0.92015	-1.1178
H	-7.24279	-0.27747	-2.01995
H	-7.18056	-1.91066	-1.34101
H	-7.01367	-0.79945	2.28051
H	-8.4925	-1.23004	1.40019
H	-7.03872	-2.22246	1.22863
H	-7.29404	1.76516	-0.47705
H	-8.63959	1.03525	0.40661
H	-7.19327	1.55349	1.28145
C	6.96039	-0.3087	-0.1493
C	7.54797	1.09629	-0.35187
C	7.53387	-0.89089	1.16062
C	7.39921	-1.19483	-1.33475
H	7.29404	1.76516	0.47704
H	8.63959	1.03525	-0.40662
H	7.19327	1.55349	-1.28146
H	7.18056	-1.91066	1.341
H	8.62847	-0.92015	1.11779
H	7.2428	-0.27746	2.01994
H	8.49249	-1.23004	-1.40019
H	7.03872	-2.22246	-1.22863
H	7.01367	-0.79945	-2.28051
Co	0.	0.86816	0.
H	1.24363	6.88811	-0.05323
H	-2.48199	4.76858	0.10519

Co-C(**Co-1**)



Charge = 0 Multiplicity = 1

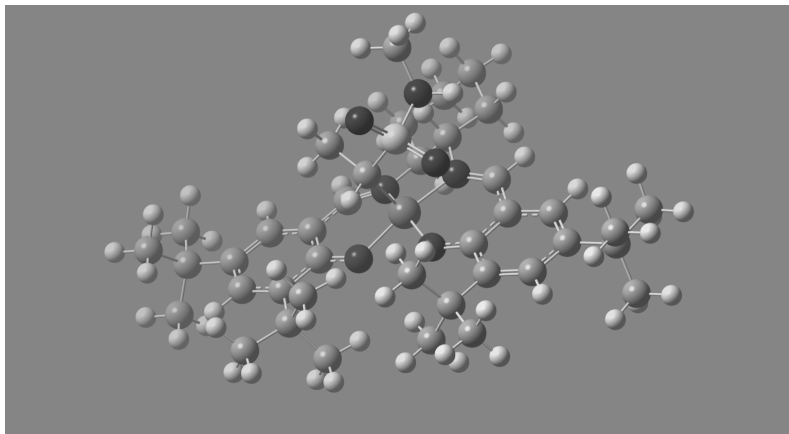
C	4.51241	1.86467	-0.42743
C	3.13832	1.94164	-0.27602
C	2.37096	0.73631	-0.45191
C	3.07939	-0.46285	-0.7618
C	4.48838	-0.4661	-0.91197
C	5.22991	0.68218	-0.74666
H	5.08986	2.76951	-0.28926
C	2.39548	-1.68842	-0.98524
H	4.96372	-1.40983	-1.1576
H	3.00742	-2.48629	-1.40317
C	0.55829	-3.16388	-1.42468
C	1.47279	-4.3851	-1.25547
C	-0.83765	-3.40078	-0.76447
H	2.34363	-4.32519	-1.91188
C	-1.71924	-4.29819	-1.6483
H	-2.05987	-3.78934	-2.55226
C	-2.70083	-1.88091	-0.63071
H	-3.31763	-2.76026	-0.80227
C	-3.42807	-0.65934	-0.47363
C	-4.84121	-0.74636	-0.43363
C	-2.76436	0.59997	-0.38388
C	-5.62762	0.37813	-0.29912
H	-5.28399	-1.73379	-0.50695
C	-3.57703	1.78199	-0.27679
C	-4.95337	1.62305	-0.22997
H	-5.56436	2.51128	-0.13601
O	1.07011	0.76737	-0.37353
O	-1.46269	0.69717	-0.43085
N	-1.41247	-2.03144	-0.58197
N	1.12801	-1.92878	-0.78887
C	2.4527	3.26045	0.11254
C	1.41479	3.65413	-0.9596
C	1.75957	3.08644	1.48122
C	3.45195	4.42277	0.24173
H	1.9015	3.80197	-1.93088

H	0.65577	2.88194	-1.06486
H	0.926	4.59512	-0.68291
H	1.24416	4.0109	1.76559
H	1.03259	2.27769	1.44794
H	2.49486	2.85243	2.25771
H	2.90812	5.3327	0.51579
H	4.20044	4.23981	1.01977
H	3.97639	4.62191	-0.6991
C	-2.93108	3.17574	-0.24604
C	-1.92916	3.27866	0.92422
C	-2.20634	3.41543	-1.58899
C	-3.96955	4.29654	-0.06802
H	-2.43254	3.09361	1.88022
H	-1.12234	2.55874	0.81029
H	-1.49902	4.2856	0.96131
H	-2.92398	3.40437	-2.4172
H	-1.7099	4.39218	-1.58587
H	-1.4555	2.64617	-1.77053
H	-3.45336	5.26176	-0.04939
H	-4.69251	4.32672	-0.88985
H	-4.52241	4.19853	0.87251
C	-7.15926	0.34302	-0.22857
C	-7.70602	-1.09007	-0.31765
C	-7.62539	0.95874	1.10816
C	-7.74924	1.16102	-1.3974
H	-7.43059	-1.57116	-1.26198
H	-7.34044	-1.71491	0.5039
H	-8.79911	-1.0723	-0.26069
H	-7.295	1.99655	1.21323
H	-8.71933	0.94859	1.17257
H	-7.22863	0.39237	1.95746
H	-8.84433	1.14815	-1.35789
H	-7.42757	2.20629	-1.36417
H	-7.43812	0.7441	-2.3612
C	6.75622	0.73805	-0.88111
C	7.1428	1.74829	-1.98242

C	7.37284	1.18895	0.46046
C	7.35079	-0.62972	-1.25051
H	6.72184	1.45158	-2.94909
H	6.78149	2.75545	-1.75391
H	8.23244	1.80134	-2.08724
H	7.12147	0.48438	1.26031
H	8.4648	1.24144	0.38186
H	7.01197	2.17752	0.7599
H	8.43891	-0.54808	-1.33956
H	7.13598	-1.38432	-0.48674
H	6.96511	-0.99357	-2.20868
Co	-0.1559	-0.64571	-0.29101
H	1.82123	-4.48818	-0.22624
H	-2.59571	-4.64948	-1.09844
H	0.93527	-5.29506	-1.53106
H	-1.15804	-5.18698	-1.94527
C	0.40731	-2.83724	-2.92396
H	1.37529	-2.52962	-3.32796
H	0.0668	-3.70767	-3.48875
H	-0.30121	-2.01772	-3.0785
C	-0.71898	-4.05512	0.6185
H	-1.70606	-4.07606	1.0895
H	-0.37623	-5.08831	0.52216
H	-0.0328	-3.51126	1.26758
C	-0.26386	-0.48142	1.65705
S	1.17937	-0.84554	2.69316
O	2.42425	-0.34222	2.09632
O	0.82952	-0.39937	4.06138
N	1.2889	-2.53748	2.74994
H	0.95227	-2.83517	3.66267
C	2.58391	-3.13625	2.40825
H	3.38486	-2.88062	3.11108
H	2.4496	-4.22093	2.40265
H	2.88005	-2.81552	1.41099
C	-1.49612	-1.06501	2.33672
H	-2.39492	-0.75576	1.80437

H	-1.47718	-2.15459	2.37006
H	-1.57727	-0.68977	3.36159
H	-0.29201	0.6079	1.74329

Co-C(**Co-2**)



Charge = 0 Multiplicity = 1

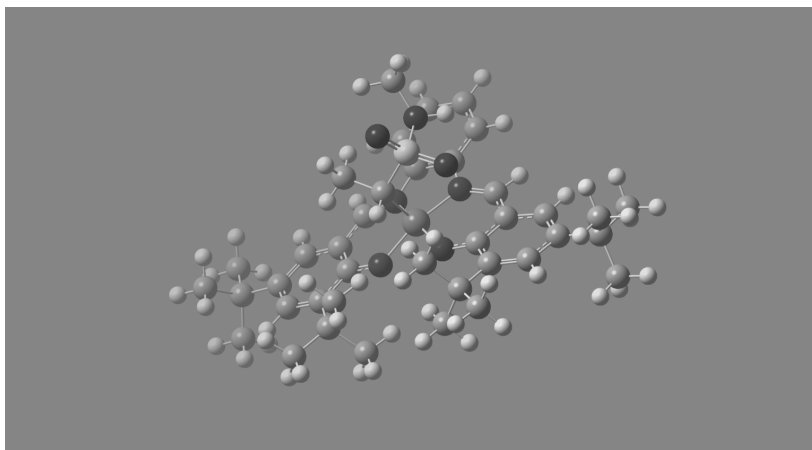
C	-4.8882	-1.75891	-0.23695
C	-3.5108	-1.91836	-0.23285
C	-2.69612	-0.76228	-0.49232
C	-3.36036	0.47064	-0.77361
C	-4.77349	0.55534	-0.78679
C	-5.56149	-0.54135	-0.50679
H	-5.50062	-2.62558	-0.0251
C	-2.62318	1.65687	-1.08527
H	-5.21592	1.51901	-1.01514
H	-3.20729	2.48895	-1.47568
C	-0.68304	3.05548	-1.38648
C	-1.51054	4.33945	-1.3129
C	0.58353	3.17332	-0.53992
C	-0.65144	5.54176	-1.73247
H	-2.38702	4.27826	-1.96411
C	1.45563	4.34344	-0.98211
C	0.63755	5.64105	-0.91013
H	-0.39494	5.44331	-2.79557
H	1.81314	4.18127	-2.0073
H	1.24629	6.48166	-1.25946
C	2.45406	1.64429	-0.74599

H	3.07692	2.51194	-0.95714
C	3.12924	0.38699	-0.70662
C	4.52756	0.39596	-0.92928
C	2.44116	-0.82474	-0.39559
C	5.28009	-0.75571	-0.84043
H	4.98966	1.34848	-1.16659
C	3.22523	-2.02197	-0.25197
C	4.58833	-1.94211	-0.48743
H	5.17518	-2.84611	-0.3872
O	-1.3928	-0.86663	-0.51299
O	1.14338	-0.88274	-0.26416
N	1.18601	1.8311	-0.53752
N	-1.34479	1.81099	-0.93156
C	-2.8659	-3.29363	0.00093
C	-1.84938	-3.23216	1.16206
C	-3.9057	-4.37187	0.35172
C	-2.15638	-3.72882	-1.30045
H	-1.03439	-2.54957	0.93254
H	-2.33776	-2.89944	2.0854
H	-1.43229	-4.22868	1.34502
H	-4.63326	-4.52443	-0.45219
H	-3.39192	-5.32485	0.5138
H	-4.4535	-4.12996	1.26897
H	-2.88335	-3.84148	-2.1127
H	-1.41029	-2.99353	-1.60268
H	-1.65589	-4.69325	-1.15891
C	2.56264	-3.33943	0.18071
C	3.57505	-4.49182	0.29482
C	1.91239	-3.14835	1.56937
C	1.49256	-3.7579	-0.84995
H	4.35539	-4.28427	1.03461
H	3.05072	-5.39843	0.6143
H	4.05977	-4.71152	-0.66267
H	2.67501	-2.91939	2.32113
H	1.19543	-2.3295	1.55632
H	1.39851	-4.06728	1.87438

H	1.94737	-3.91673	-1.83494
H	1.02147	-4.69855	-0.54276
H	0.72412	-2.99306	-0.94034
C	6.79338	-0.8052	-1.08423
C	7.50706	-1.31176	0.18731
C	7.09415	-1.76882	-2.25232
C	7.36422	0.57646	-1.43932
H	8.59035	-1.35485	0.02655
H	7.31397	-0.64468	1.03418
H	7.17218	-2.31483	0.46791
H	6.60876	-1.42821	-3.17322
H	8.17332	-1.82342	-2.43596
H	6.74002	-2.78256	-2.04203
H	7.20711	1.29939	-0.63197
H	8.44286	0.49811	-1.6096
H	6.91219	0.97951	-2.35164
C	-7.09432	-0.50382	-0.47926
C	-7.6411	0.89405	-0.80746
C	-7.65468	-1.50007	-1.51696
C	-7.59125	-0.90194	0.92697
H	-7.3416	1.22184	-1.80844
H	-8.73528	0.87918	-0.77658
H	-7.29845	1.6428	-0.08568
H	-7.3323	-2.52519	-1.31113
H	-8.75041	-1.48694	-1.50548
H	-7.32149	-1.23934	-2.52718
H	-8.68643	-0.88693	0.96362
H	-7.26245	-1.90829	1.2031
H	-7.21532	-0.20606	1.68456
Co	-0.11123	0.49389	-0.33983
H	-0.37458	2.89091	-2.4292
H	0.27728	3.35008	0.49723
H	-1.87281	4.47129	-0.28523
H	-1.23733	6.46162	-1.63297
H	0.38465	5.84582	0.13861
H	2.33625	4.42474	-0.3362

C	-0.4079	0.55924	1.57972
C	-1.59674	1.38876	2.0471
H	-0.57281	-0.49629	1.81581
H	-1.76263	1.25703	3.12117
H	-2.50073	1.05994	1.53441
H	-1.45573	2.45322	1.84519
S	0.9977	0.93527	2.66221
N	1.25637	2.60508	2.48529
H	2.21601	2.71805	2.16715
C	0.93063	3.46883	3.62581
H	1.49479	3.23163	4.53408
H	1.15208	4.49635	3.32602
H	-0.1347	3.39905	3.84829
O	0.53968	0.68865	4.04679
O	2.23531	0.27883	2.21175

Co-C(**Co-3**)



Charge = 0 Multiplicity = 1

C	-4.88253	-1.77208	-0.26155
C	-3.50878	-1.90519	-0.1549
C	-2.69656	-0.74627	-0.4142
C	-3.35994	0.47514	-0.76264
C	-4.77549	0.52801	-0.87499

C	-5.55735	-0.57539	-0.62293
H	-5.49451	-2.64119	-0.05893
C	-2.64695	1.68043	-0.99188
H	-5.21866	1.47863	-1.15043
H	-3.23781	2.52458	-1.34309
C	-0.76918	3.13093	-0.97995
C	-1.43992	4.35612	-1.06155
C	0.63628	3.09272	-1.02673
C	-0.70843	5.53054	-1.21969
H	-2.5195	4.40418	-0.98002
C	1.36475	4.2778	-1.17539
C	0.68894	5.49086	-1.28119
H	1.25463	6.41079	-1.38761
C	2.42738	1.53998	-1.14633
H	3.01524	2.33389	-1.60457
C	3.09831	0.3171	-0.92395
C	4.48724	0.27284	-1.22375
C	2.42986	-0.82254	-0.36852
C	5.24386	-0.84237	-0.95419
H	4.93262	1.1605	-1.65946
C	3.22807	-1.97416	-0.03494
C	4.57547	-1.93947	-0.34432
H	5.17469	-2.8079	-0.10385
O	-1.39746	-0.83905	-0.36406
O	1.14095	-0.8586	-0.20464
N	1.17705	1.80244	-0.83574
N	-1.36429	1.8617	-0.7954
C	-2.85715	-3.25284	0.19301
C	-1.92393	-3.10694	1.41598
C	-3.90124	-4.3296	0.53542
C	-2.05786	-3.74509	-1.03378
H	-1.1078	-2.41756	1.21061
H	-2.48249	-2.73893	2.28437
H	-1.50098	-4.08264	1.67937
H	-4.5691	-4.54303	-0.30551
H	-3.38433	-5.261	0.78736

H	-4.51417	-4.04627	1.39792
H	-2.72954	-3.91552	-1.88263
H	-1.30472	-3.01475	-1.33003
H	-1.55417	-4.6911	-0.80648
C	2.59477	-3.19215	0.65614
C	3.63001	-4.28565	0.9698
C	1.96077	-2.75277	1.99437
C	1.51543	-3.81179	-0.25606
H	4.42163	-3.92508	1.63517
H	3.12845	-5.11814	1.4737
H	4.09795	-4.68362	0.06307
H	2.72165	-2.34287	2.66678
H	1.20044	-1.99043	1.835
H	1.49565	-3.61232	2.49024
H	1.95535	-4.14871	-1.20186
H	1.06342	-4.68201	0.23327
H	0.73373	-3.08748	-0.47436
C	6.74372	-0.94849	-1.25314
C	7.51596	-1.18059	0.06323
C	6.9944	-2.13723	-2.20577
C	7.28865	0.32573	-1.91618
H	8.59058	-1.26463	-0.13446
H	7.36053	-0.34827	0.75778
H	7.19673	-2.09935	0.56436
H	6.46321	-1.99669	-3.15319
H	8.06398	-2.23086	-2.42518
H	6.66017	-3.08386	-1.77056
H	7.16823	1.20168	-1.27033
H	8.35782	0.20775	-2.1195
H	6.78949	0.53152	-2.86884
C	-7.08843	-0.57082	-0.70361
C	-7.63787	0.79969	-1.12771
C	-7.55323	-1.62117	-1.73505
C	-7.67399	-0.92349	0.68058
H	-7.27017	1.09535	-2.11586
H	-8.73058	0.75909	-1.17796

H	-7.36764	1.58394	-0.41297
H	-7.2274	-2.62964	-1.46315
H	-8.64693	-1.63121	-1.80078
H	-7.15401	-1.39493	-2.72944
H	-8.769	-0.93186	0.64046
H	-7.34546	-1.91042	1.02018
H	-7.36594	-0.1893	1.43257
Co	-0.11267	0.51909	-0.33564
H	-1.22876	6.481	-1.27648
H	2.44866	4.26405	-1.17706
C	-0.2706	0.68163	1.59524
C	-1.57309	1.27601	2.11262
H	-0.17957	-0.35782	1.92216
H	-1.63469	1.17377	3.20067
H	-2.42263	0.74352	1.68414
H	-1.66865	2.33397	1.85832
S	1.10516	1.47361	2.45592
N	0.99793	3.09455	1.99344
H	1.85052	3.33544	1.49657
C	0.61395	4.08716	3.00049
H	1.32466	4.17367	3.82992
H	0.54168	5.04992	2.48825
H	-0.36781	3.84029	3.40588
O	0.82615	1.38766	3.90519
O	2.39762	0.96849	1.96174

Relative Stability of Benzyl Cobalt(III) and Benzyl Radical

To compare the stability of a benzyl cobalt(III) and a benzyl radical (**Figure 2-8**), the computational studies were carried out based on Lin's report.²² Geometry optimizations were also carried out in benzene solution using the SMD solvation model, M06-L functional,²³ def2-SVP basis set,²⁴ and W06 auxiliary basis set as a benchmark.²⁵ On the basis of the optimized structures, single-point energy refinements were performed at the SMD(benzene)/M06-L/def2-TZVPP/W06 level. As a benchmark, the method (U)B3LYP-D3(BJ) functional with the 6-31G(d,p) basis set was used for the geometry optimization and normal vibrational mode analysis with SMD¹⁴ model (benzene). The method (U)B3LYP-D3(BJ)¹⁶ functional with the 6-311+G(d,p) basis set was used to calculate single-point energies with SMD model (benzene).

Table S2-3. Results of M06-L.

	M06-L				
	SPE ^a / a.u.	TCG ^a / a.u. (a)	SPE ^b / a.u. (b)	Sum of E (a+b)	ΔG / kcal mol ⁻¹
Alkylradical (B)	-309.9768208	0.109358	-310.3081849	-310.1988269	+4.3
Co-1	-3045.660362	0.757739	-3047.63302	-3046.875281	
Alkylcobalt	-3355.672617	0.900751	-3357.967963	-3357.067212	

^a Calculated at SMD(benzene)/M06-L/def2-SVP/W06 level theory. ^b Calculated at SMD(benzene)/M06-L/def2-TZVPP/W06 level theory. Abbreviations: SPE—single-point energy, TCG—thermal correction to Gibbs energy.

Table S2-4. Results of B3LYP

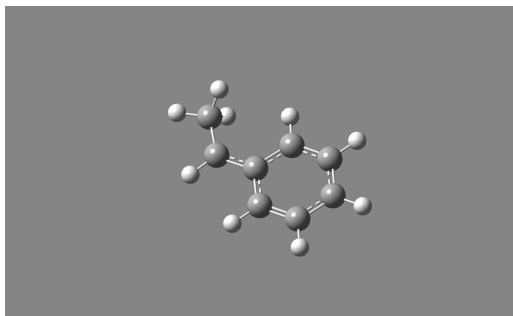
	B3LYP				
	SPE ^a / a.u.	TCG ^a / a.u. (a)	SPE ^b / a.u. (b)	Sum of E (a+b)	ΔG / kcal mol ⁻¹
Alkylradical (B)	-310.2849335	0.110507	-310.353664	-310.24316	+4.4
Co-1	-3047.432197	0.763242	-3047.904224	-3047.141	
Alkylcobalt	-3357.752936	0.906938	-3358.284012	-3357.3771	

^a Calculated at (U)B3LYP-D3(BJ)/6-31G(d,p)/SMD(Benzene) level theory. ^b Calculated at (U)B3LYP-D3(BJ)/6-311+G(d,p)/SMD(Benzene) level theory. Abbreviations: SPE—single-point energy, TCG—thermal correction to Gibbs

energy.

M06L

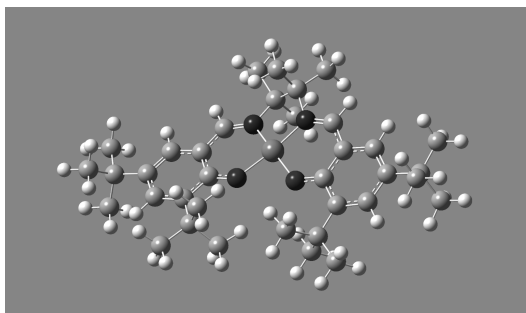
Benzyl radical(B)



Charge = 0 Multiplicity = 2

C	2.38006	-0.95673	0.02553
H	2.21558	-1.05182	-1.05044
H	2.72154	-1.91572	0.42934
H	3.19897	-0.2354	0.17761
C	1.15021	-0.51959	0.7233
H	1.0177	-0.60364	1.79727
C	0.11193	0.37845	0.02537
C	-0.96203	-0.19597	-0.65516
C	0.2451	1.76606	0.07366
C	-1.90218	0.6171	-1.28781
H	-1.06631	-1.28999	-0.6937
C	-0.69579	2.57955	-0.55829
H	1.09139	2.21896	0.61014
C	-1.76926	2.00533	-1.23908
H	-2.74837	0.1644	-1.82477
H	-0.59076	3.6736	-0.5197
H	-2.51069	2.64621	-1.73793

Co-1



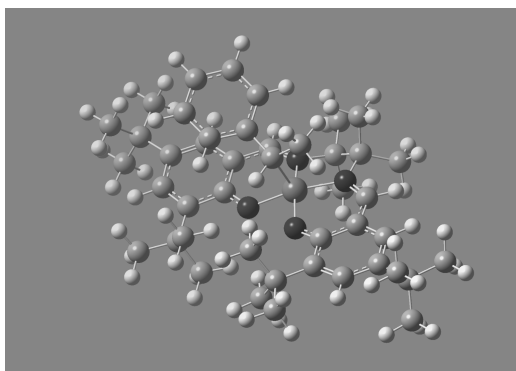
Charge = 0 Multiplicity = 2

C	4.73246	-1.49217	-0.16617
C	3.35578	-1.60967	-0.24242
C	2.56646	-0.41914	-0.06892
C	3.25045	0.81466	0.147
C	4.66678	0.8583	0.21216
C	5.42976	-0.2775	0.06391
H	5.32645	-2.38833	-0.28973
C	2.54325	2.04365	0.28912
H	5.13082	1.82422	0.38177
H	3.16317	2.92192	0.45847
C	0.63601	3.53621	0.45794
C	1.58185	4.69607	0.12443
C	-0.63601	3.53621	-0.45794
H	2.36415	4.79724	0.88121
C	-1.58185	4.69607	-0.12443
H	-2.06007	4.57199	0.84969
C	-2.54325	2.04365	-0.28912
H	-3.16317	2.92192	-0.45847
C	-3.25045	0.81466	-0.147
C	-4.66678	0.8583	-0.21216
C	-2.56646	-0.41914	0.06892
C	-5.42976	-0.2775	-0.06391
H	-5.13082	1.82422	-0.38177
C	-3.35578	-1.60967	0.24242
C	-4.73246	-1.49217	0.16617
H	-5.32645	-2.38833	0.28973
O	1.26365	-0.48831	-0.11221
O	-1.26365	-0.48831	0.11221

N	-1.24936	2.19721	-0.22868
N	1.24936	2.19721	0.22868
C	2.67563	-2.96186	-0.50762
C	1.74171	-3.31641	0.67004
C	1.86682	-2.88154	-1.82153
C	3.69362	-4.10509	-0.65716
H	2.31133	-3.38805	1.60363
H	0.96605	-2.56339	0.79309
H	1.26386	-4.28644	0.49328
H	1.3578	-3.83293	-2.01277
H	1.11724	-2.09216	-1.77452
H	2.5318	-2.67959	-2.66897
H	3.15791	-5.04034	-0.84882
H	4.37892	-3.94233	-1.49594
H	4.28935	-4.24867	0.25072
C	-2.67563	-2.96186	0.50762
C	-1.74171	-3.31641	-0.67004
C	-1.86682	-2.88154	1.82153
C	-3.69362	-4.10509	0.65716
H	-2.31133	-3.38805	-1.60363
H	-0.96605	-2.56339	-0.79309
H	-1.26386	-4.28644	-0.49328
H	-2.5318	-2.67959	2.66897
H	-1.3578	-3.83293	2.01277
H	-1.11724	-2.09216	1.77452
H	-3.15791	-5.04034	0.84882
H	-4.37892	-3.94234	1.49594
H	-4.28935	-4.24867	-0.25072
C	-6.96189	-0.28899	-0.12941
C	-7.53801	1.11175	-0.38753
C	-7.42157	-1.21887	-1.27252
C	-7.53174	-0.80713	1.20836
H	-7.26956	1.81398	0.40859
H	-7.18984	1.52427	-1.3402
H	-8.63085	1.06228	-0.42895
H	-7.07313	-2.24561	-1.12665

H	-8.51569	-1.24475	-1.33091
H	-7.03703	-0.87076	-2.23681
H	-8.62711	-0.82744	1.17776
H	-7.18773	-1.82137	1.43153
H	-7.22612	-0.16175	2.03845
C	6.96189	-0.28899	0.12941
C	7.42157	-1.21887	1.27252
C	7.53174	-0.80713	-1.20836
C	7.53801	1.11175	0.38753
H	7.03703	-0.87076	2.23681
H	7.07313	-2.24561	1.12665
H	8.51569	-1.24475	1.33091
H	7.22612	-0.16175	-2.03845
H	8.62711	-0.82744	-1.17776
H	7.18773	-1.82137	-1.43153
H	8.63085	1.06228	0.42895
H	7.26956	1.81398	-0.40859
H	7.18984	1.52427	1.3402
Co	0.	0.84633	0.
H	2.06007	4.57199	-0.84969
H	-2.36415	4.79724	-0.88121
H	1.03344	5.64027	0.11726
H	-1.03344	5.64027	-0.11726
C	0.2512	3.60483	1.94651
H	1.14107	3.43505	2.55897
H	-0.15728	4.58457	2.20707
H	-0.48323	2.83602	2.19775
C	-0.25121	3.60484	-1.94651
H	-1.14107	3.43505	-2.55897
H	0.15728	4.58457	-2.20707
H	0.48323	2.83602	-2.19775

Benzyl cobalt



Charge = 0 Multiplicity = 1

C	-4.39693	-1.72852	-0.59402
C	-3.02288	-1.82723	-0.73305
C	-2.25141	-0.61373	-0.67573
C	-2.96334	0.62384	-0.6171
C	-4.37184	0.64986	-0.50053
C	-5.11033	-0.51191	-0.44922
H	-4.9751	-2.64354	-0.59888
C	-2.28381	1.86405	-0.80375
H	-4.85109	1.62054	-0.43715
H	-2.91911	2.71347	-1.04995
C	-0.39492	3.24039	-1.41224
C	-1.30501	4.47335	-1.34448
C	0.96892	3.48102	-0.68332
H	-2.14626	4.38116	-2.03593
C	1.90341	4.36065	-1.53039
H	2.2955	3.83091	-2.4008
C	2.81618	1.96177	-0.38791
H	3.44695	2.84257	-0.49729
C	3.52798	0.74004	-0.192
C	4.93888	0.82399	-0.07959
C	2.86164	-0.52418	-0.15444
C	5.71891	-0.29888	0.08036
H	5.3864	1.81131	-0.12447
C	3.6709	-1.70429	0.01728
C	5.04115	-1.54432	0.12579
H	5.64694	-2.43125	0.25832
O	-0.94959	-0.66216	-0.71099

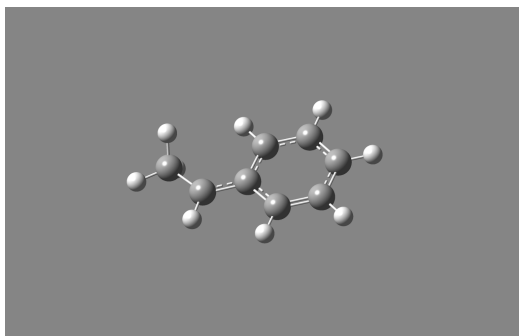
O	1.57315	-0.63044	-0.2971
N	1.5256	2.11309	-0.44864
N	-0.99497	2.0331	-0.77706
C	-2.32906	-3.18263	-0.94207
C	-1.54917	-3.15175	-2.27568
C	-1.35813	-3.47298	0.22125
C	-3.33346	-4.34481	-1.01575
H	-2.23174	-2.98262	-3.11621
H	-0.8004	-2.35991	-2.27259
H	-1.04189	-4.109	-2.44092
H	-0.84474	-4.42648	0.05478
H	-0.61043	-2.68745	0.30479
H	-1.9025	-3.55076	1.16926
H	-2.7901	-5.28005	-1.18483
H	-3.90053	-4.46013	-0.08575
H	-4.04537	-4.22423	-1.83927
C	3.01592	-3.09125	0.11556
C	2.117	-3.1311	1.3708
C	2.17841	-3.38249	-1.149
C	4.0551	-4.21738	0.25247
H	2.71421	-2.9729	2.27568
H	1.35009	-2.35944	1.32618
H	1.6224	-4.10492	1.45785
H	2.81347	-3.36303	-2.04219
H	1.72931	-4.37963	-1.08
H	1.38448	-2.64876	-1.27199
H	3.53598	-5.17936	0.31146
H	4.73124	-4.26064	-0.60822
H	4.65959	-4.11719	1.1602
C	7.24606	-0.26535	0.21368
C	7.7993	1.16583	0.13502
C	7.65722	-0.86936	1.57348
C	7.88235	-1.09282	-0.92351
H	7.56142	1.64053	-0.82266
H	7.40542	1.79772	0.93785
H	8.88949	1.14899	0.23326

H	7.32207	-1.90586	1.67509
H	8.74746	-0.86039	1.68536
H	7.225	-0.29712	2.40091
H	8.97518	-1.08354	-0.84111
H	7.55735	-2.13714	-0.89765
H	7.61103	-0.68384	-1.90232
C	-6.63099	-0.54511	-0.25913
C	-7.29441	-1.23633	-1.46914
C	-6.96607	-1.33352	1.02497
C	-7.22341	0.86587	-0.12301
H	-7.07337	-0.6964	-2.39577
H	-6.94452	-2.26565	-1.59235
H	-8.38288	-1.26902	-1.34513
H	-6.52456	-0.84966	1.90176
H	-8.05071	-1.38602	1.17388
H	-6.58643	-2.35878	0.98242
H	-8.30614	0.80229	0.02625
H	-6.80042	1.39963	0.73417
H	-7.04923	1.46777	-1.02102
Co	0.26254	0.71366	-0.32985
H	-1.70103	4.63618	-0.33969
H	2.74839	4.72282	-0.93936
H	-0.75242	5.36656	-1.6441
H	1.36868	5.2467	-1.88029
C	-0.16822	2.86215	-2.89088
H	-1.11404	2.53276	-3.32872
H	0.1972	3.71307	-3.47086
H	0.54899	2.04163	-2.98374
C	0.76203	4.16919	0.67296
H	1.691	4.14109	1.24781
H	0.48272	5.21701	0.53774
H	-0.01751	3.67639	1.24961
C	0.04215	0.4808	1.63639
C	1.12772	1.16078	2.45879
H	2.12352	0.94058	2.06992
H	1.01764	2.24439	2.51289

H	1.09068	0.78212	3.49003
H	0.23047	-0.59241	1.64613
C	-1.34178	0.69859	2.14677
C	-2.19548	-0.40627	2.3108
C	-1.84814	1.95857	2.50448
C	-3.49559	-0.26339	2.78788
H	-1.82324	-1.39155	2.05605
C	-3.15239	2.11249	2.9697
H	-1.21436	2.83341	2.42396
C	-3.98695	1.00164	3.11034
H	-4.12766	-1.13957	2.89376
H	-3.51633	3.10218	3.2322
H	-5.00288	1.12134	3.47508

(U)B3LYP

Benzyl radical (B)

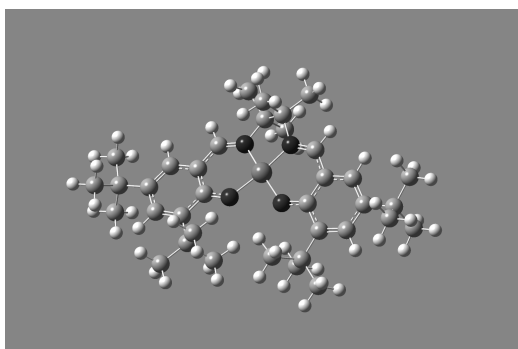


Charge = 0 Multiplicity = 2

C	2.95521000	-0.33391800	-0.00000300
H	2.92617300	-0.99296600	0.87973200
H	3.92384200	0.17191800	-0.00004900
H	2.92611900	-0.99302200	-0.87969500
C	1.83163100	0.65028800	0.00000400
H	2.07551700	1.70937400	0.00000200
C	0.46158300	0.29891800	0.00000100
C	0.02037900	-1.05564200	0.00000200
C	-0.54178500	1.31067400	0.00000000
C	-1.33158000	-1.36645700	0.00000000
H	0.75466000	-1.85445600	0.00000200
C	-1.88888300	0.98831100	-0.00000100

H	-0.23091100	2.35200100	0.00000100
C	-2.29773900	-0.35266300	-0.00000100
H	-1.64218200	-2.40749800	0.00000200
H	-2.63216000	1.78051400	-0.00000200
H	-3.35394900	-0.60292900	-0.00000200

Co-1



Charge = 0 Multiplicity = 2

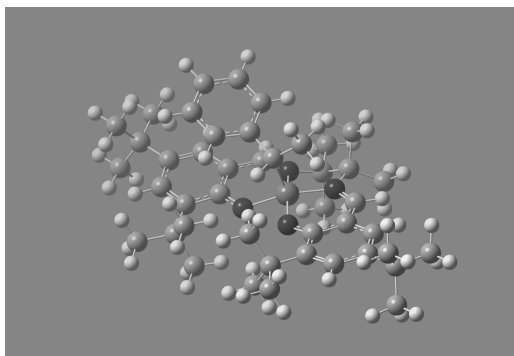
C	-4.73246	-1.49217	0.16617
C	-3.35578	-1.60967	0.24242
C	-2.56646	-0.41914	0.06892
C	-3.25045	0.81466	-0.147
C	-4.66678	0.8583	-0.21216
C	-5.42976	-0.2775	-0.06391
H	-5.32645	-2.38833	0.28973
C	-2.54325	2.04365	-0.28912
H	-5.13082	1.82422	-0.38177
H	-3.16317	2.92192	-0.45847
C	-0.63601	3.53621	-0.45794
C	-1.58185	4.69607	-0.12443
C	0.63601	3.53621	0.45794
H	-2.36415	4.79724	-0.88121
C	1.58185	4.69607	0.12443
H	2.06007	4.57199	-0.84969
C	2.54325	2.04365	0.28912
H	3.16317	2.92192	0.45847
C	3.25045	0.81466	0.147
C	4.66678	0.8583	0.21216

C	2.56646	-0.41914	-0.06892
C	5.42976	-0.2775	0.06391
H	5.13082	1.82422	0.38177
C	3.35578	-1.60967	-0.24242
C	4.73246	-1.49217	-0.16617
H	5.32645	-2.38833	-0.28973
O	-1.26365	-0.48831	0.11221
O	1.26365	-0.48831	-0.11221
N	1.24936	2.19721	0.22868
N	-1.24936	2.19721	-0.22868
C	-2.67563	-2.96186	0.50762
C	-1.74171	-3.31641	-0.67004
C	-1.86682	-2.88154	1.82153
C	-3.69362	-4.10509	0.65716
H	-2.31133	-3.38805	-1.60363
H	-0.96605	-2.56339	-0.79309
H	-1.26386	-4.28644	-0.49328
H	-1.3578	-3.83293	2.01277
H	-1.11724	-2.09216	1.77452
H	-2.5318	-2.67959	2.66897
H	-3.15791	-5.04034	0.84882
H	-4.37892	-3.94233	1.49594
H	-4.28935	-4.24867	-0.25072
C	2.67563	-2.96186	-0.50762
C	1.74171	-3.31641	0.67004
C	1.86682	-2.88154	-1.82153
C	3.69362	-4.10509	-0.65716
H	2.31133	-3.38805	1.60363
H	0.96605	-2.56339	0.79309
H	1.26386	-4.28644	0.49328
H	2.5318	-2.67959	-2.66897
H	1.3578	-3.83293	-2.01277
H	1.11724	-2.09216	-1.77452
H	3.15791	-5.04034	-0.84882
H	4.37892	-3.94234	-1.49594
H	4.28935	-4.24867	0.25072

C	6.96189	-0.28899	0.12941
C	7.53801	1.11175	0.38753
C	7.42157	-1.21887	1.27252
C	7.53174	-0.80713	-1.20836
H	7.26956	1.81398	-0.40859
H	7.18984	1.52427	1.3402
H	8.63085	1.06228	0.42895
H	7.07313	-2.24561	1.12665
H	8.51569	-1.24475	1.33091
H	7.03703	-0.87076	2.23681
H	8.62711	-0.82744	-1.17776
H	7.18773	-1.82137	-1.43153
H	7.22612	-0.16175	-2.03845
C	-6.96189	-0.28899	-0.12941
C	-7.42157	-1.21887	-1.27252
C	-7.53174	-0.80713	1.20836
C	-7.53801	1.11175	-0.38753
H	-7.03703	-0.87076	-2.23681
H	-7.07313	-2.24561	-1.12665
H	-8.51569	-1.24475	-1.33091
H	-7.22612	-0.16175	2.03845
H	-8.62711	-0.82744	1.17776
H	-7.18773	-1.82137	1.43153
H	-8.63085	1.06228	-0.42895
H	-7.26956	1.81398	0.40859
H	-7.18984	1.52427	-1.3402
Co	0.	0.84633	0.
H	-2.06007	4.57199	0.84969
H	2.36415	4.79724	0.88121
H	-1.03344	5.64027	-0.11726
H	1.03344	5.64027	0.11726
C	-0.2512	3.60483	-1.94651
H	-1.14107	3.43505	-2.55897
H	0.15728	4.58457	-2.20707
H	0.48323	2.83602	-2.19775
C	0.25121	3.60484	1.94651

H	1.14107	3.43505	2.55897
H	-0.15728	4.58457	2.20707
H	-0.48323	2.83602	2.19775

Benzyl cobalt



Charge = 0 Multiplicity = 1

C	4.51241	1.86467	-0.42743
C	3.13832	1.94164	-0.27602
C	2.37096	0.73631	-0.45191
C	3.07939	-0.46285	-0.7618
C	4.48838	-0.4661	-0.91197
C	5.22991	0.68218	-0.74666
H	5.08986	2.76951	-0.28926
C	2.39548	-1.68842	-0.98524
H	4.96372	-1.40983	-1.1576
H	3.00742	-2.48629	-1.40317
C	0.55829	-3.16388	-1.42468
C	1.47279	-4.3851	-1.25547
C	-0.83765	-3.40078	-0.76447
H	2.34363	-4.32519	-1.91188
C	-1.71924	-4.29819	-1.6483
H	-2.05987	-3.78934	-2.55226
C	-2.70083	-1.88091	-0.63071
H	-3.31763	-2.76026	-0.80227
C	-3.42807	-0.65934	-0.47363
C	-4.84121	-0.74636	-0.43363
C	-2.76436	0.59997	-0.38388
C	-5.62762	0.37813	-0.29912

H	-5.28399	-1.73379	-0.50695
C	-3.57703	1.78199	-0.27679
C	-4.95337	1.62305	-0.22997
H	-5.56436	2.51128	-0.13601
O	1.07011	0.76737	-0.37353
O	-1.46269	0.69717	-0.43085
N	-1.41247	-2.03144	-0.58197
N	1.12801	-1.92878	-0.78887
C	2.4527	3.26045	0.11254
C	1.41479	3.65413	-0.9596
C	1.75957	3.08644	1.48122
C	3.45195	4.42277	0.24173
H	1.9015	3.80197	-1.93088
H	0.65577	2.88194	-1.06486
H	0.926	4.59512	-0.68291
H	1.24416	4.0109	1.76559
H	1.03259	2.27769	1.44794
H	2.49486	2.85243	2.25771
H	2.90812	5.3327	0.51579
H	4.20044	4.23981	1.01977
H	3.97639	4.62191	-0.6991
C	-2.93108	3.17574	-0.24604
C	-1.92916	3.27866	0.92422
C	-2.20634	3.41543	-1.58899
C	-3.96955	4.29654	-0.06802
H	-2.43254	3.09361	1.88022
H	-1.12234	2.55874	0.81029
H	-1.49902	4.2856	0.96131
H	-2.92398	3.40437	-2.4172
H	-1.7099	4.39218	-1.58587
H	-1.4555	2.64617	-1.77053
H	-3.45336	5.26176	-0.04939
H	-4.69251	4.32672	-0.88985
H	-4.52241	4.19853	0.87251
C	-7.15926	0.34302	-0.22857
C	-7.70602	-1.09007	-0.31765

C	-7.62539	0.95874	1.10816
C	-7.74924	1.16102	-1.3974
H	-7.43059	-1.57116	-1.26198
H	-7.34044	-1.71491	0.5039
H	-8.79911	-1.07229	-0.26069
H	-7.295	1.99655	1.21323
H	-8.71933	0.94859	1.17257
H	-7.22863	0.39237	1.95746
H	-8.84433	1.14815	-1.35789
H	-7.42757	2.20629	-1.36417
H	-7.43812	0.7441	-2.3612
C	6.75622	0.73805	-0.88111
C	7.1428	1.74829	-1.98242
C	7.37284	1.18895	0.46046
C	7.35079	-0.62972	-1.25051
H	6.72184	1.45158	-2.94909
H	6.78149	2.75545	-1.75391
H	8.23244	1.80134	-2.08724
H	7.12147	0.48438	1.26031
H	8.4648	1.24144	0.38186
H	7.01197	2.17752	0.7599
H	8.43891	-0.54808	-1.33956
H	7.13598	-1.38432	-0.48674
H	6.96511	-0.99357	-2.20868
Co	-0.1559	-0.64571	-0.29101
H	1.82123	-4.48818	-0.22624
H	-2.59571	-4.64948	-1.09844
H	0.93527	-5.29506	-1.53106
H	-1.15804	-5.18698	-1.94527
C	0.40731	-2.83724	-2.92396
H	1.37529	-2.52962	-3.32796
H	0.0668	-3.70767	-3.48875
H	-0.30121	-2.01772	-3.0785
C	-0.71898	-4.05512	0.6185
H	-1.70606	-4.07606	1.0895
H	-0.37623	-5.08831	0.52216

H	-0.0328	-3.51126	1.26758
C	-0.26386	-0.48142	1.65705
C	-1.49612	-1.06501	2.33672
H	-2.39492	-0.75576	1.80437
H	-1.47718	-2.15459	2.37006
H	-1.57727	-0.68977	3.36159
H	-0.29201	0.6079	1.74329
C	0.96167	-0.79061	2.53687
C	1.50188	0.20257	3.35432
C	1.53154	-2.06355	2.51661
C	2.61214	-0.07703	4.15081
H	1.05285	1.20625	3.36948
C	2.64153	-2.34368	3.31402
H	1.10578	-2.8465	1.87252
C	3.18196	-1.35066	4.13095
H	3.03838	0.70593	4.79469
H	3.09039	-3.34755	3.29816
H	4.05732	-1.57089	4.75908

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第三章 有機光酸化還元触媒によるスルホンアミドの脱炭酸型アルキル化反応の開発

第一節 着想背景および作業仮説

炭素-窒素結合形成は、医薬品化学において最も広く利用されている反応の一つである。中でもスルホンアミドは、農薬および医薬品に多く含まれる官能基であり重要な基質である。¹ スルホンアミドとアリール求電子剤との遷移金属触媒による C-N クロスカップリング反応は、多様な *N*-アリール化スルホンアミドを与える手法として確立されている。² 一方、近年、天然物由来の生理活性化合物に見られる sp^3 リッチな骨格は、三次元的な化学空間を有し、創薬分子の立体構造を精密に制御可能であることから注目を集めている。³ これらの背景のもと、*N*-アリール化に加えて、スルホンアミドの *N*-アルキル化反応の重要性も高まっているが、同様に遷移金属触媒に依存してきた (Figure 3-1)。アルケンの分子内または分子間ヒドロアミノ化反応、⁴ 金属ナイトレノイドを介した $C(sp^3)$ -H アミノ化反応、⁵ ならびにアルコールを用いた脱水的アルキル化反応⁶、強酸⁷や超原子価ヨウ素試薬⁸を用いる手法などが報告されている。しかし、強酸を必要とする厳しい条件であるため、これらの条件下で適用可能なスルホンアミドおよびアルキル基に制限が生じる。

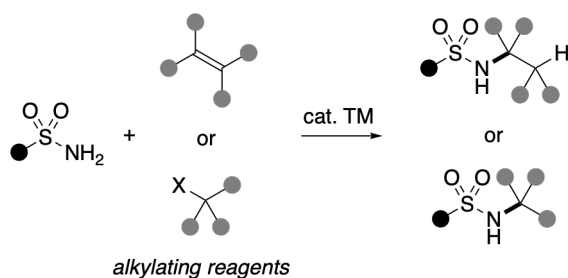


Figure 3-1. 遷移金属触媒によるスルホンアミドの *N*-アルキル化反応

著者の所属する研究室では、序章に示したように、有機光酸化還元触媒のフェノチアジン触媒を用いた脂肪族カルボン酸由来のレッドクス活性エステルとヘテロ原子求核剤との脱炭酸クロスカップリング反応を報告している (Figure P13)。^{9,10} 本反応では、光励起されたフェノチアジン触媒がレッドクス活性エステルに対して一電子移動を引き起こすことで、脱炭酸を伴いながら、対応するアルキルラジカルとフェノチアジンラジカルカチオンを生成する。生成したアルキルラジカルは、フェノチアジンラジカルカチオンによる一電子酸化を伴う RPC 機構を経て、カルボカチオン等価体へと変換される。¹¹ このカルボカチオン等価体は、脂肪族アルコール、アミド、チオールなど、様々なヘテロ原子求核剤と反応する。本手法により、遷移金属触媒を用いることなく、温和な条件下で炭素-ヘテロ原子結合の構築が可能となった。著者は、この温和な条件で、触媒的に生成したカルボカチオン種がスルホンアミド求核剤とも反応し、*N*-アルキル化スルホンアミドを与えることができると着想した。

以上の背景を踏まえ、本研究では、フェノチアジン型有機光酸化還元触媒を用いることで、可視光照射下、スルホンアミドとレッドックス活性エステルとの脱炭酸型クロスカップリング反応が進行することを示した (Figure 3-2)。本反応は遷移金属触媒や強酸を必要とせず、温和な条件下で進行し、高い官能基許容性を示すことから、多様な *N*-アルキル化スルホンアミドの合成が可能である。

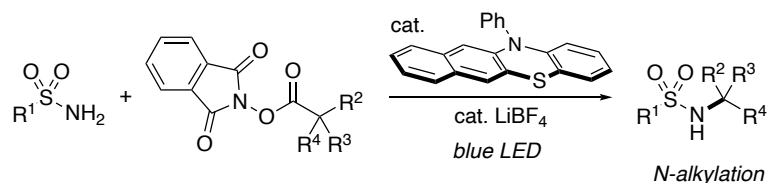


Figure 3-2. 有機光酸化還元触媒によるスルホンアミドの *N*-アルキル化反応

第二節 反応条件の最適化および基質適用範囲の検討

スルホンアミドの *N*-アルキル化反応の条件を、*p*-トルエンスルホンアミド (**1a**) とピバル酸由来のレッドックス活性エステル (**2a**) をモデル基質として用いて検討した (Table 3-1)。先行研究の知見を元に、*N*-フェニルベンゾ[*b*]フェノチアジン (**PTH-1**) を光酸化還元触媒、テトラフルオロホウ酸リチウムを添加剤として用い、溶媒にジクロロメタンを用いて、青色 LED 照射下で反応を開始した。その結果、反応は良好に進行し、*N,N*-ジアルキル化副生成物を与えることなく、目的とする *N*-アルキル化生成物 **3aa** が 83% の単離収率で得られた (Table 3-1, entry 1)。

光酸化還元触媒の構造は、本反応の進行に大きな影響を与えた。(entries 2–4)。ベンゾ[*a*]フェノチアジン骨格を有する **PTH-2** を用いた場合、基質の変換率は低かった (entry 2)。また、**PTH-1** の代わりに単純なフェノチアジン骨格を有する触媒 **PTH-3** を用いると、生成物の収率は大きく低下した (entry 3)。さらに、*N*-フェニルベンゾ[*b*]フェノキサジン (**POX-1**) を光酸化還元触媒として用いた場合にも、低収率にとどまった (entry 4)。添加剤および溶媒も、本反応において重要な役割を果たすことが分かった。テトラフルオロホウ酸リチウム塩の添加は反応促進に重要であり、十分な反応効率を確保するには 10 mol % 以上の添加が必要であった。(entries 5–7)。一方、酢酸エチル、アセトン、アセトニトリルなどの他の溶媒を用いた場合には、目的物は得られなかった (entries 8–10)。また、**2a** を制限基質として用いた場合にも、同程度の収率が得られた (entry 11)。

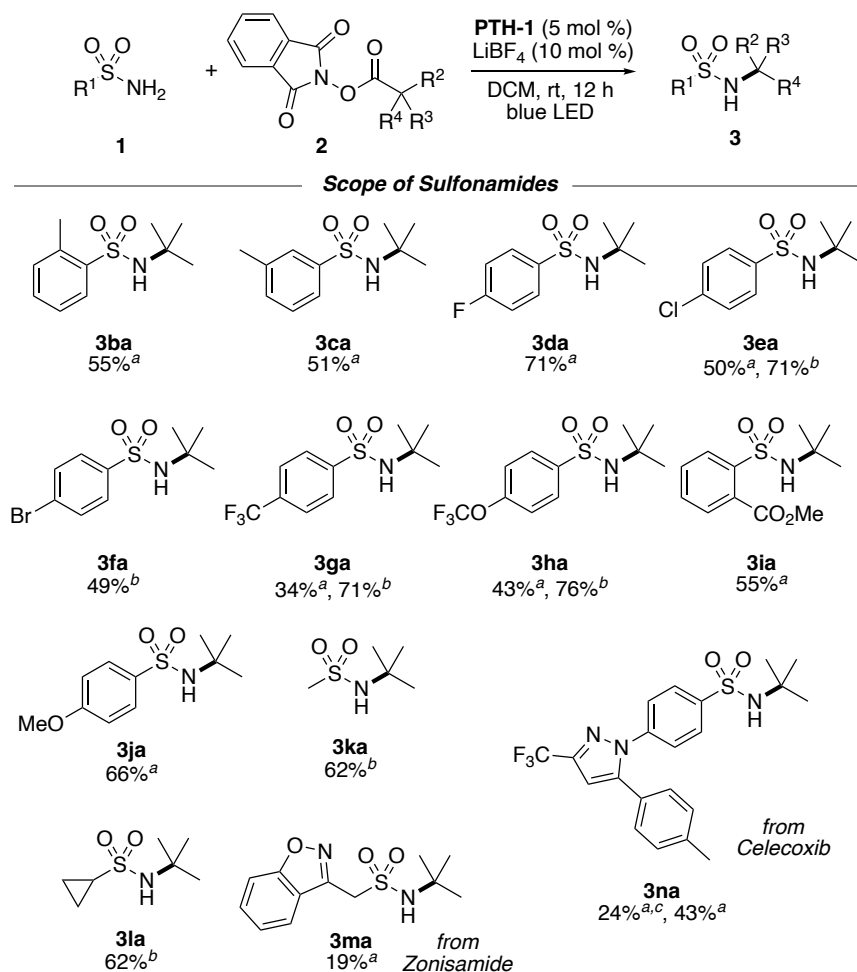
Table 3-1. 反応条件の最適化 ^a

Entry	Change from standard conditions	Yield of 3aa (%) ^b
1	none	99 (83)
2	PTH-2 instead of PTH-1	22
3	PTH-3 instead of PTH-1	3
4	POX-1 instead of PTH-1	28
5	without LiBF ₄	10
6	LiBF ₄ (5 mol %)	32
7	LiBF ₄ (20 mol %)	99
8	EtOAc instead of DCM	0
9	Acetone instead of DCM	0
10	MeCN instead of DCM	0
11	1a (0.6 mmol), 2a (0.2 mmol) and DCM (0.3 mL) for 18 h	87 (64)

^a The number in parentheses is the isolated yield. The reaction was carried out with **1a** (0.2 mmol), **2a** (0.3 mmol), **PTH-1-3** or **POX-1** (0.01 mmol, 5 mol %), and LiBF₄ (0.02 mmol, 10 mol %) in DCM (0.5 mL, 0.4 M) under blue LED irradiation for 24 h. ^b ¹H NMR yield based on **3aa**. Yield of the isolated product is in parentheses.

ピバル酸から誘導されたレドックス活性エステル (**2a**) を用いて、スルホンアミドの基質適用範囲を検討した (Scheme 3-1)。オルトおよびメタトルエンスルホンアミドとの反応では、対応する *N*-アルキル化生成物が中程度の収率で得られた (**3ba**, **3ca**)。ハロゲン原子を持つスルホンアミドに対しても本反応は適用可能であった (**3da-3fa**)。さらに、電子求引性基および電子供与性基のいずれも反応効率に大きな影響を与えなかった (**3ha-3ja**)。脂肪族スルホンアミドを用いた際は中程度の収率で反応が進行し、sp³リッチなスルホンアミド骨格を与えた (**3ka**, **3la**)。また、本手法は、ゾニサミドおよびセレコキシブといったスルホンアミド骨格を含む医薬品のアルキル化にも適用可能であった (**3ma**, **3na**)。

Scheme 3-1. スルホンアミドの基質適用範囲 ^a

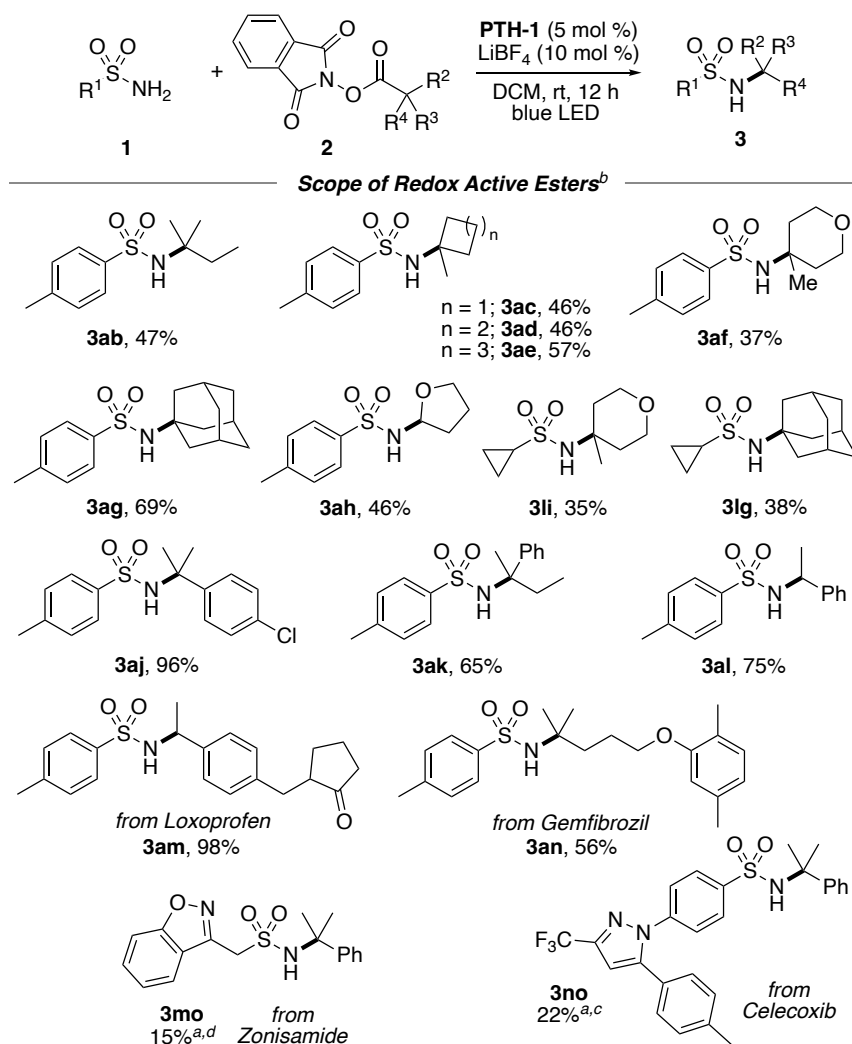


^a The reaction was carried out with **1 a** (0.6 mmol), **2 a** (0.2 mmol), **PTH-1** (0.01 mmol, 5 mol %), and LiBF₄ (0.02 mmol, 10 mol %) in DCM (0.3 mL, 0.7 M) under blue LED irradiation for 18 h. ^b The reaction was carried out with **1 a** (0.2 mmol), **2 a** (0.3 mmol), **PTH-1** (0.01 mmol, 5 mol %), and LiBF₄ (0.02 mmol, 10 mol %) in DCM (0.5 mL, 0.4 M) under blue LED irradiation for 24 h. ^c DCM (0.9 mL, 0.2 M) was used.

次に、4-メチルベンゼンスルホンアミド (**1a**) をカップリングパートナーとして用い、レドックス活性エステルの基質適用範囲を検討した (Scheme 3-2)。本手法は、イソペンチル基の導入も可能であった (**3ab**)。また、多様なサイズの環状アルキル鎖を中程度の効率で導入することができた (**3ac–3ae**)。テトラヒドロピラニル基や、アダマンチル基を有するレドックス活性エステルも、アルキル化剤として反応に適用可能であった (**3af, 3ag**)。また、 α -アルコキシ置換基を有する基質も本反応条件下で良好な収率で目的物を与えた (**3ah**)。本アルキル化反応は脂肪族スルホンアミドにも同様に環状アルキル鎖の導入が可能であった (**3li, 3lg**)。さらに、第三級および第二級ベンジル位を有するレドックス活性エステルを用いた場合にも反応は良好に進行し、対応するアルキル化生成物が中から高収率で得られた。

(**3aj–3al**)。加えて、ロキソプロフェンやゲムフィブロジルなどのカルボン酸部位を持つ医薬品を、スルホンアミドのアルキル化剤として用いることが可能であった (**3am, 3an**)。さらに、**2o** を用いた反応により、二種のスルホンアミド部位を持つ医薬品から目的とするアルキル化生成物が得られた (**3mo, 3no**)。

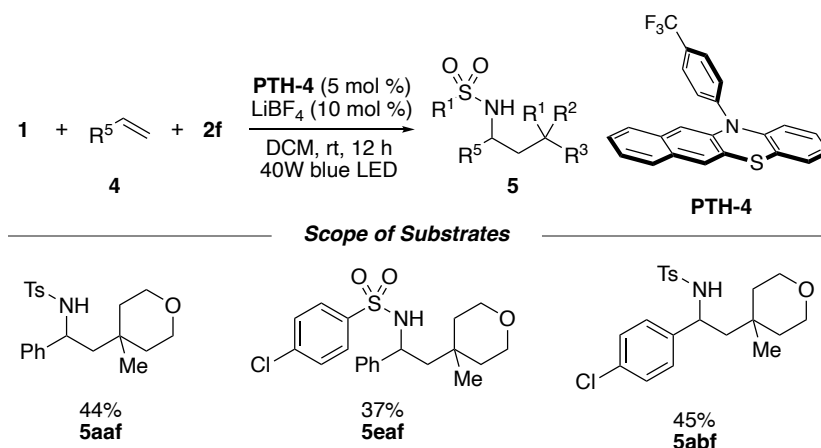
Scheme 3-2. レドックス活性エステルの基質適用範囲^a



^a The reaction was carried out with **1 a** (0.6 mmol), **2 a** (0.2 mmol), **PTH-1** (0.01 mmol, 5 mol %), and LiBF₄ (0.02 mmol, 10 mol %) in DCM (0.3 mL, 0.7 M) under blue LED irradiation for 18 h. ^b The reaction was carried out with **1 a** (0.2 mmol), **2 a** (0.3 mmol), **PTH-1** (0.01 mmol, 5 mol %), and LiBF₄ (0.02 mmol, 10 mol %) in DCM (0.5 mL, 0.4 M) under blue LED irradiation for 24 h. ^c DCM (0.9 mL, 0.2 M) was used. ^d EtOAc (0.9 mL, 0.2 M) was used.

次に、本反応の適用範囲をさらに拡張するため、多成分カップリング反応への応用を検討した (Scheme 3-3)。本反応経路におけるラジカル反応の特性を活かし、アルケンのラジカ

ルリレー型二官能化反応へと展開した。¹² 有機光酸化還元触媒を用いたアルケン二官能化に関する先行研究をもとに、触媒として **PTH-4** を用いた。^{9b} 収率は中程度にとどまったものの、本反応により、スルホンアミド、スチレン、ならびにレドックス活性エステルを一挙に組み合わせ、複雑なベンジルスルホンアミド骨格を構築することが可能であった (**5aaf**, **5eaf**, **5abf**)。



Scheme 3-3. 三成分カップリング

第三節 機構実験

反応機構に関する知見を得るため、テトラフルオロホウ酸リチウム塩の存在下、**PTH-1** と 1-アダマンタンカルボン酸由来のレドックス活性エステル (**2g**) を用いた化学量論反応を行った (Figure 3-3)。青色光照射下を 6 時間反応させた後、DART-HRMS により、アルキルスルホニウム中間体 **PTH-1-2g** に対応するピークが検出された。この結果は、アルキルスルホニウム中間体の存在を支持する結果である。一方、**2g** の代わりに **2a** を用いて同様の検討を行った場合には反応は進行せず、これは第三級ブチルカチオンまたは対応するアルキルスルホニウム種の不安定性に起因すると考えられる。



Figure 3-3. アルキルスルホニウム中間体の検出

第四節 推定反応機構

推定反応機構を Figure 3-4 に示す。**PTH-1** とレドックス活性エステル **2** は、可視光領域に吸収を有する EDA (Electron Donor–Acceptor) 錯体 **A** を形成する。^{9b} 続いて、光励起された **PTH-1** から **2** への一電子移動が起こり、**PTH-1** のラジカルカチオン種 **B** および **2** のラジカルアニオン種 **C** が生成する。**C** は二酸化炭素を放出し、対応するアルキルラジカル **D** を与える。次に、**D** と **B** がラジカル–ラジカルカップリング、あるいは一電子移動を経て再結合

することで、アルキルスルホニウム中間体 **E** が生成する。最終的に、**E** がスルホンアミド **1** と反応し、*N*-アルキル化生成物 **3** を与えるとともに、**PTH-1** が再生される。

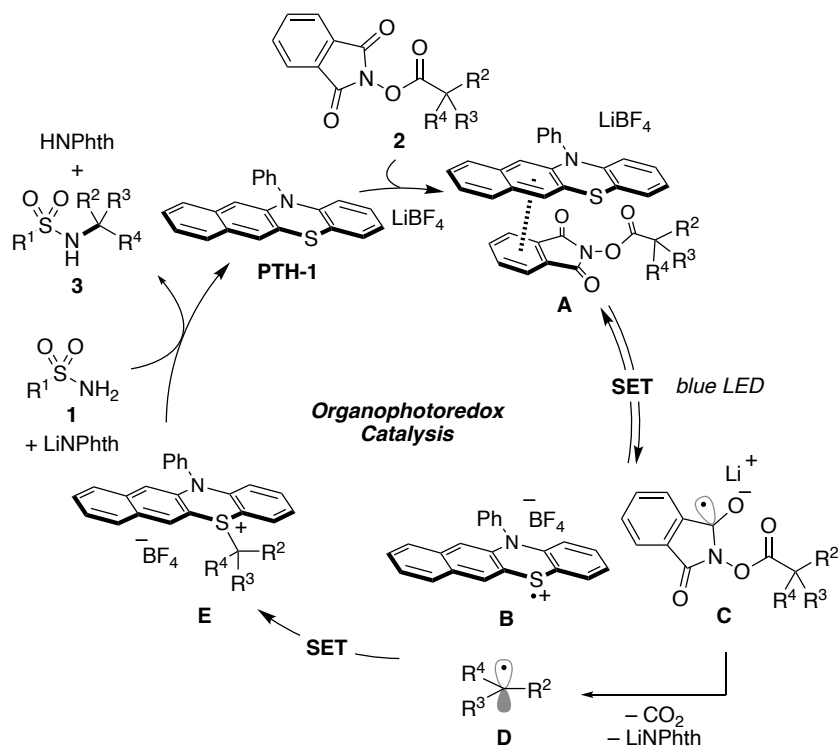


Figure 3-4. 推定反応機構

第三章 結論

本研究では、有機光酸化還元触媒を用いた嵩高いアルキル鎖導入反応をスルホンアミドの *N*-アルキル化へと展開した。温和かつ遷移金属を用いない条件下で、*N*-アルキル化スルホンアミドを合成することに成功した。本手法は、カルボン酸部位あるいはスルホンアミド部位を有する医薬品基質の官能基化にも適用可能であった。さらに、アルケンのラジカルリレー型二官能化反応に適用し、三成分を組み合わせた複雑なスルホンアミド骨格の構築も達成した。

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実験項

1. Instrumentation and Chemicals

NMR spectra were recorded on a JNM-ECS400, operating at 400 MHz for ^1H NMR and 100.5 MHz for ^{13}C NMR, JNM-ECA600, operating at 600 MHz for ^1H NMR and 150.9 MHz for ^{13}C NMR, and Bruker Avance NEO 400N, operating at 400 MHz for ^1H NMR and 100.6 MHz for ^{13}C NMR. Bruker Ultra Shield-300, operating at 300 MHz for ^1H NMR and 75.0 MHz for ^{13}C NMR. Chemical shift values for ^1H and ^{13}C are referenced to Me_4Si and the residual solvent resonances, and for ^{19}F is referenced to trifluorotoluene, respectively. Chemical shifts are reported in δ ppm. Mass spectra were obtained with JMS-T100TD (DART). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Wakosil[®] 60, 64~210 μm) and Aluminum oxide 90 standardized (Merck Millipore) were used for column chromatography. Preparative HPLC was performed with Gilson 159UV-VIS as a UV detector. The column was YMC-Actus Triant C18 (50 $\times$ 20 mm I.D., 5 μm) with a flow rate of 25 mL/min at room temperature. The eluent was concentrated down using a Biotage[®] Turbovap, and the samples dried on a Biotage[®] V-10 Touch. Gel Permeation Chromatography (GPC) was performed with LaboACE LC-5060 using UV Detector and Refractive Index Detector. IR spectra were measured with a Thermo Scientific iD7 ATR Accessory for the Thermo Scientific Nicolet iS5 FT-IR Spectrometer. Melting points were measured on a Stanford Research System MPA100 (OptiMelt) apparatus. CV measurements were recorded with a Hokuto Denko HZ-7000 potentiostat. UV-Vis absorption spectra were recorded on a Shimadzu UV-1900. Fluorescence spectra were recorded on a Shimadzu RF-6000. Kessil A160WE 40W Tuna Blue (highest blue and intensity setting) was used as a light source. TEKNOS MG9 was used as a fan.

All reactions were carried out under nitrogen atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. LiBF_4 was purchased from Aldrich Chemical Co., stored under nitrogen, and used as received. Dichloromethane, acetonitrile, ethyl acetate and acetone were purchased from FUJIFILM Wako Pure Chemical Co., stored under nitrogen, and used as received. The sulfonamides **1** were obtained from commercial suppliers. The redox active esters **2** were prepared by the reported procedure.¹ **PTH-1**², **PTH-2**³, **PTH-3**⁴ and **PTH-4**⁵ were prepared by the reported procedures.

2. Synthesis of N-Phenylbenzo[b]phenoxazine (POX-1)

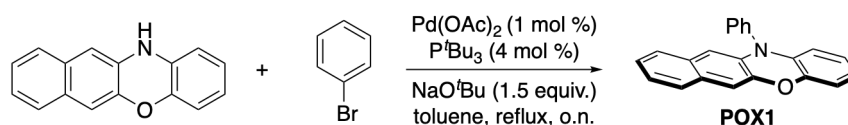


Figure S3-1. Synthesis of POX-1.

In a glovebox, to an oven-dried vial with a stirring bar was added palladium acetate (0.9 mg, 0.004 mmol), tri-*tert*-butyl phosphine (3.2 mg, 0.016 mmol) and toluene (1.6 mL). After stirring at room

temperature for 10 min, benzo[*b*]phenoxazine (93.2 mg, 0.4 mmol), bromobenzene (50.4 μ L, 0.48 mmol) and sodium *tert*-butoxide (57.7 mg, 0.6 mmol) were sequentially added to the reaction solution. After sealing the vial with a cap and removed from the glove box, the reaction was stirred at 120 °C overnight and quenched with NH₄Cl aq. The resultant reaction solution was extracted with ethyl acetate and the combined organic layer was dried over Na₂SO₄ and filtered. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 0:100–10:90, dichloromethane/hexane) gave the coupling product **POX-1** (101.5 mg, 0.33 mmol, 82% isolated yield). White solid. **M.p.** 166–169 °C. **IR** (neat) 572, 699, 742, 1276, 1297, 1326, 1472, 1493, 1591, 3059 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.66 (t, *J*=7.6 Hz, 2H), 7.55 (t, *J*=7.2 Hz, 1H), 7.49 (d, *J*=7.2 Hz, 1H), 7.40 (t, *J*=7.6 Hz, 2H), 7.25 (d, *J*=7.2 Hz, 1H), 7.17–7.11 (m, 2H), 7.06 (s, 1H), 6.81 (d, *J*=7.6 Hz, 1H), 6.69 (t, *J*=7.6 Hz, 1H), 6.64 (t, *J*=7.6 Hz, 1H), 6.12 (s, 1H), 5.98 (d, *J*=7.6 Hz, 1H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 144.3, 143.1, 138.6, 134.1, 133.0, 131.2 ($\times 2$ C), 131.2, 130.7 ($\times 2$ C), 129.9, 128.8, 126.3, 126.0, 124.9, 123.9, 123.1, 121.1, 115.5, 113.4, 110.9, 108.0. **DART–HRMS** (*m/z*): [M+H]⁺ calcd for C₂₂H₁₆NO, 310.1226; found, 310.1221.

3. Procedures for Organophotoredox-Catalyzed Decarboxylative Alkylation of Sulfonamides

Condition A (Table 3-1, entry 11 is representative; redox active ester as a limiting reagent, glovebox free). To an oven-dried vial equipped with a stirring bar was added **PTH-1** (3.3 mg, 0.01 mmol), LiBF₄ (1.9 mg, 0.02 mmol), redox active ester **2a** (49.4 mg, 0.2 mmol) and sulfonamide **1a** (103 mg, 0.6 mmol) in dichloromethane (300 μ L). After sparging with Ar for 10 seconds, the vial was sealed, and the reaction mixture was stirred and irradiated with two 34W blue LEDs (0.5 cm away from both sides) with a cooling fan to maintain the temperature at around 40 °C for 18 h. The crude material was purified by preparative HPLC (90:10–0:100, 10mM NH₄CO₃ in H₂O/MeCN) to give the coupling product **3aa** (Table 3-1, entry 11; 29.3 mg, 0.13 mmol, 64% isolated yield).

Condition B (Table 3-1, entry 1 is representative; sulfonamide as a limiting reagent). In a glovebox, to an oven-dried vial equipped with a stirring bar was added **PTH-1** (3.3 mg, 0.01 mmol), LiBF₄ (1.9 mg, 0.02 mmol), redox active ester **2a** (74.2 mg, 0.3 mmol) and sulfonamide **1a** (34.2 mg, 0.2 mmol) in dichloromethane (500 μ L). After sealing the vial with a cap and removal from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away), with a cooling fan to keep the temperature at around 40 °C (Figure S3-2). After 24 h, the reaction was quenched by 0.5 M NaOH aq. solution (1.5 ml). The aqueous layer was thrice extracted with dichloromethane (500 μ L), dried over Na₂SO₄ and then, filtered. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) gave the coupling product **3aa** (Table 3-1, entry 1; 38.6 mg, 0.17 mmol, 83% isolated yield).

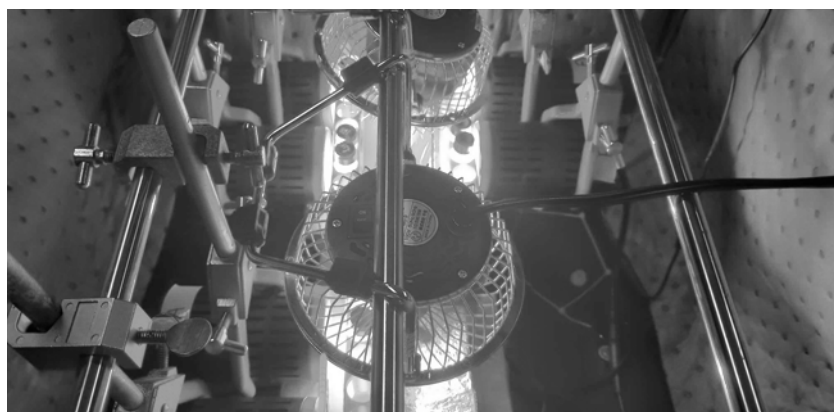
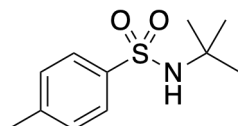


Figure S3-2. Light set up

4. Characterization Data for N-Alkylated Sulfonamides

N-(*tert*-Butyl)-4-methylbenzenesulfonamide (**3aa**)



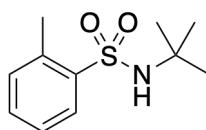
The reactions were carried out with conditions A and B.

Condition A. The product **3aa** was purified by preparative HPLC (90:10–0:100, 10mM NH₄CO₃ in H₂O/MeCN) (Scheme3-1; 29.3 mg, 0.13 mmol, 64% isolated yield).

Condition B. The product **3aa** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Table 3-1, entry 1; 38.6 mg, 0.17 mmol, 83% isolated yield).

The spectrum data of product **3aa** was consistent with the literature.⁶

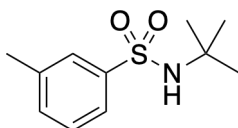
N-(*tert*-Butyl)-2-methylbenzenesulfonamide (**3ba**)



The reaction carried out with condition A. The product **3ba** was purified by preparative HPLC (90:10–0:100, 10mM NH₄CO₃ in H₂O/MeCN) (Scheme 3-1; 25.0 mg, 0.11 mmol, 55% isolated yield).

The spectrum data of product **3ba** was consistent with the literature.⁷

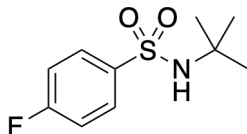
N-(*tert*-Butyl)-3-methylbenzenesulfonamide (**3ca**)



The reaction was carried out with condition A. The product **3ca** was purified by preparative HPLC (90:10–0:100, 10mM NH₄CO₃ in H₂O/MeCN) (Scheme 3-1; 23.0 mg, 0.10 mmol, 51% isolated yield).

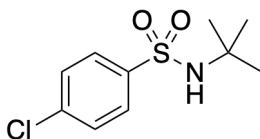
The spectrum data of product **3ca** was consistent with the literature.⁷

***N*-(*tert*-Butyl)-4-fluorobenzenesulfonamide (3da)**



The reaction was carried out with condition A. The reaction mixture was poured into water at room temperature and extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over MgSO₄ and concentrated *in vacuo*. The product **3da** was purified by flash chromatography on silica gel (75:25–75:25, hexane/EtOAc) (Scheme 3-1; 32.6 mg, 0.14 mmol, 71% isolated yield). Brown solid. **M.p.** 85–87 °C. **IR** (neat) 982, 1057, 1116, 1154, 1285, 1327, 1429, 1709, 2975, 3289 cm⁻¹. **¹H NMR** (300 MHz, DMSO-*d*₆) δ 7.93–7.83 (m, 2H), 7.56 (s, 1H), 7.47–7.34 (m, 2H), 1.09 (s, 9H). **¹³C NMR** (75 MHz, DMSO-*d*₆) δ 163.7 (d, J_{C-F} = 249.8 Hz), 140.7 (d, J_{C-F} = 3.3 Hz), 129.2 (d, J_{C-F} = 9.4 Hz), 116.1 (q, J_{C-F} = 22.6 Hz), 53.3, 29.7. **DART-HRMS** (m/z): [M+H]⁺ calcd for C₁₀H₁₅FNO₂S, 232.0820; found, 232.0799.

***N*-(*tert*-Butyl)-4-chlorobenzenesulfonamide (3ea)**



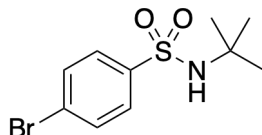
The reactions were carried out with conditions A and B.

Condition A. The product **3ea** was purified by preparative HPLC (90:10–0:100, 10mM NH₄CO₃ in H₂O/MeCN) (Scheme 3-1; 24.8 mg, 0.10 mmol, 50% isolated yield).

Condition B. The product **3ea** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Scheme 3-1; 34.6 mg, 0.14 mmol, 71% isolated yield).

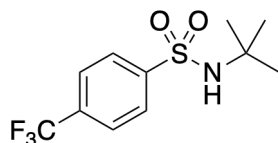
The spectrum data of product **3ea** was consistent with the literature.⁷

4-Bromo-*N*-(*tert*-butyl)benzenesulfonamide (3fa)



The reaction was carried out with condition B. The product **3fa** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–70:30, hexane/EtOAc) (Scheme 3-1; 17.4 mg, 0.06 mmol, 49% isolated yield). The spectrum data of product **3fa** was consistent with the literature.⁸

***N*-(*tert*-Butyl)-4-(trifluoromethyl)benzenesulfonamide (3ga)**



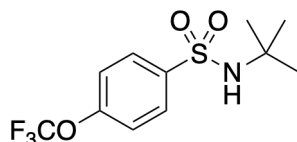
The reactions were carried out with conditions A and B.

Condition A. The mixture was poured into water and extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over MgSO_4 and concentrated *in vacuo*. The product **3ga** was purified by preparative HPLC (80:20–0:100, 10mM NH_4CO_3 in $\text{H}_2\text{O}/\text{MeCN}$) (Scheme 3-1; 19.3 mg, 0.07 mmol, 34% isolated yield).

Condition B. The product **3ga** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Scheme 3-1; 39.3 mg, 0.14 mmol, 71% isolated yield).

The spectrum data of product **3ga** was consistent with the literature.⁹

***N*-(*tert*-Butyl)-4-(trifluoromethoxy)benzenesulfonamide (3ha)**

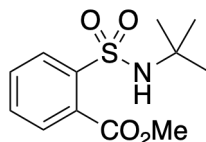


The reactions were carried out with conditions A and B.

Condition A. The product **3ha** was purified by flash chromatography on silica gel (95:5–70:30, hexane/EtOAc) (Scheme 3-1; 26.0 mg, 0.09 mmol, 43% isolated yield).

Condition B. The product **3ha** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Condition B: Scheme 3-1; 44.6 mg, 0.15 mmol, 76% isolated yield). Brown solid. **M.p.** 46–48 °C. **IR** (neat) 613, 854, 989, 1090, 1144, 1169, 1249, 1433, 2976, 3291 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.94 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 4.60 (bs, 1H), 1.25 (s, 9H). **^{13}C NMR** (150.9 MHz, CDCl_3) δ 151.7, 141.8, 129.0, 120.7, 120.2 (q, $J_{\text{C-F}}$ = 257.4 Hz), 55.0, 30.1. **DART–HRMS** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{NF}_3\text{NO}_3\text{S}$, 298.0719; found, 298.0714.

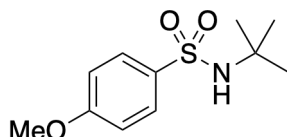
Methyl 2-[*N*-(*tert*-butyl)sulfamoyl]benzoate (3ia)



The reaction was carried out with condition A. The mixture was poured into water and extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over MgSO_4 and concentrated *in vacuo*. The product **3ia** was purified by preparative HPLC (80:20–0:100, 10mM

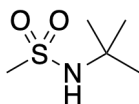
NH₄CO₃ in H₂O/MeCN) (Scheme 3-1; 29.9 mg, 0.11 mmol, 55% isolated yield). Yellow solid. **M.p.** 72–76 °C. **IR** (neat) 773, 865, 1000, 1068, 1131, 1147, 1308, 1392, 2972, 3285 cm⁻¹. **¹H NMR** (400 MHz, DMSO-*d*₆) δ 7.98 (br d, *J* = 7.2 Hz, 1H), 7.65–7.75 (m, 2H), 7.61 (m, 1H), 7.29 (s, 1H), 3.84 (s, 3H), 1.11 (s, 9H). **¹³C NMR** (75 MHz, CDCl₃) δ 168.3, 143.1, 131.73, 131.69, 130.6, 130.0, 129.0, 54.9, 53.3, 30.2. **DART–HRMS** (*m/z*): [M+H]⁺ calcd for C₁₂H₁₈NO₄S, 272.0951; found, 272.0961.

***N*-(*tert*-Butyl)-4-methoxybenzenesulfonamide (3ja)**



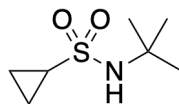
The reaction was carried out with condition A. The product **3ja** was purified by preparative HPLC (90:10–0:100, 10mM NH₄CO₃ in H₂O/MeCN) (Scheme 3-1; 32.0 mg, 0.13 mmol, 66% isolated yield). White solid. **M.p.** 102–104 °C. **IR** (neat) 561, 669, 992, 1147, 1259, 1318, 1499, 1597, 2974, 3275 cm⁻¹. **¹H NMR** (300 MHz, DMSO-*d*₆) δ 7.81–7.69 (m, 2H), 7.34 (s, 1H), 7.13–7.03 (m, 2H), 3.83 (s, 3H), 1.07 (s, 9H). **¹³C NMR** (75 MHz, DMSO-*d*₆) δ 161.6, 136.0, 128.4, 114.0, 55.5, 53.0, 29.7. **DART–HRMS** (*m/z*): [M+H]⁺ calcd for C₁₁H₁₈NO₃S, 244.1002; found, 244.1000.

***N*-(*tert*-Butyl)methanesulfonamide (3ka)**



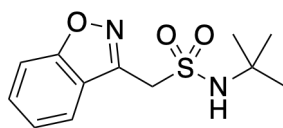
The reaction was carried out with condition B. The product **3ka** was purified by flash chromatography on silica gel (95:5–80:20, hexane/EtOAc) (Scheme 3-1; 14.0 mg, 0.09 mmol, 46% isolated yield). The spectrum data of product **3ka** was consistent with the literature.⁹

***N*-(*tert*-Butyl)cyclopropanesulfonamide (3la)**



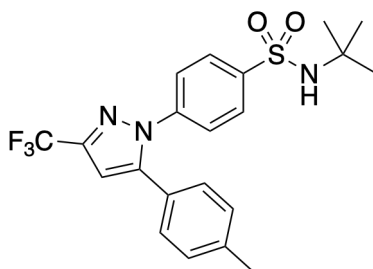
The reaction was carried out with condition B. The product **3la** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–70:30, hexane/EtOAc). (Scheme 3-1; 21.9 mg, 0.12 mmol, 62% isolated yield). The spectrum data of product **3la** was consistent with the literature.¹⁰

1-(Benzo[*d*]isoxazol-3-yl)-*N*-(*tert*-butyl)methanesulfonamide (3ma)



The reaction was carried out with condition A. The reaction mixture was poured into 1M NaOH solution (50 mL), from which the crude product was extracted thrice with EtOAc (3 x 20 mL). The combined organic extracts were washed with 1N NaOH (50 mL) and brine (50 mL), before being dried over Na₂SO₄. The drying agent was filtered off and the solvent removed *in vacuo*. The product **3ma** was purified by flash chromatography on silica gel (95:5–75:25, hexane/EtOAc) (Scheme 3-1; 10.1 mg, 0.04 mmol, 19% isolated yield). Off-white solid. **M.p.** 138–142 °C. **IR** (neat) 656, 751, 1004, 1150, 1325, 1437, 1611, 2359, 2973, 3284 cm⁻¹. **¹H NMR** (300 MHz, CDCl₃) δ 7.91 (dt, J = 8.0, 1.0 Hz, 1H), 7.60 (d, J = 1.0 Hz, 1H), 7.58 (m, 1H), 7.37 (m, 1H), 4.70 (s, 2H), 4.25 (br s, 1H), 1.40 (s, 9H). **¹³C NMR** (75 MHz, CDCl₃) δ 163.7, 150.3, 130.4, 124.1, 122.6, 120.9, 109.9, 55.4, 52.1, 30.1. **DART–HRMS** (m/z): [M+H]⁺ calcd for C₁₂H₁₇BN₂O₃S, 269.0954; found, 269.0950.

***N*-(*tert*-Butyl)-4-[5-(*p*-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (3na)**



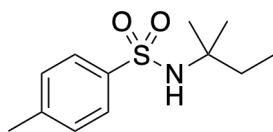
The reactions were carried out with conditions A and B.

Condition A (DCM 900 μ L was used). The product **3na** was purified by preparative HPLC (50:50–0:100, 10mM NH₄CO₃ in H₂O/MeCN) (Scheme 3-1; 20.6 mg, 0.05 mmol, 24% isolated yield).

Condition B. The product **3na** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Condition B: Scheme 3-1; 35.0 mg, 0.08 mmol, 43% isolated yield).

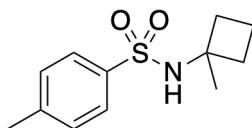
Yellow Solid. **M.p.** 163–165 °C. **IR** (neat) 845, 973, 1103, 1114, 1235, 1324, 1500, 1599, 2983, 3295 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.88 (dd, J = 6.8, 2.4 Hz, 2H), 7.44 (dd, J = 6.8, 2.4 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 6.74 (s, 1H), 4.51 (bs, 1H), 2.38 (s, 3H), 1.23 (s, 9H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 145.2, 144.0 (q, J_{C-F} = 38.4 Hz), 142.9, 142.0, 139.7, 129.7, 128.7, 128.0, 125.7, 125.4, 121.0 (q, J_{C-F} = 269.2 Hz), 106.1 (q, J_{C-F} = 2.0 Hz), 54.9, 30.1, 21.3. **DART–HRMS** (m/z): [M+H]⁺ calcd for C₂₁H₂₃F₃N₃O₂S, 438.1460; found, 438.1460.

4-Methyl-*N*-(*tert*-pentyl)benzenesulfonamide (3ab)



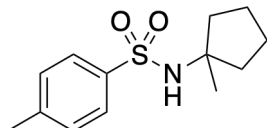
The reaction was carried out with condition B. The product **3ab** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Scheme 3-2; 21.7 mg, 0.09 mmol, 47% isolated yield). The spectrum data of product **3ab** was consistent with the literature.⁶

4-Methyl-N-(1-methylcyclobutyl)benzenesulfonamide (**3ac**)



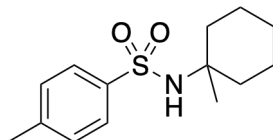
The reaction was carried out with condition B. The product **3ac** was purified by flash chromatography on silica gel (97:3–60:40, hexane/EtOAc) and GPC (Scheme 3-2; 22.0 mg, 0.09 mmol, 46% isolated yield). White solid. **M.p.** 70–72 °C. **IR** (neat) 661, 814, 883, 997, 1092, 1147, 1417, 2937, 2968, 3267 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.77 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 4.67 (bs, 1H), 2.42 (s, 3H), 2.16 (q, J = 11.2 Hz, 2H), 1.86–1.81 (m, 2H), 1.76–1.59 (m, 2H), 1.37 (s, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 143.0, 139.9, 129.5, 126.9, 56.2, 35.6, 25.8, 21.5, 14.3. **DART–HRMS** (m/z): [M+H]⁺ calcd for C₁₂H₁₈NO₂S, 240.1053; found, 240.1051.

4-Methyl-N-(1-methylcyclopentyl)benzenesulfonamide (**3ad**)



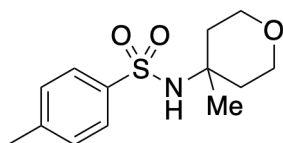
The reaction was carried out with condition B. The product **3ad** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc). (Scheme 3-2; 27.6 mg, 0.09 mmol, 46% isolated yield). The spectrum data of product **3ad** was consistent with the literature.¹¹

4-Methyl-N-(1-methylcyclohexyl)benzenesulfonamide (**3ae**)



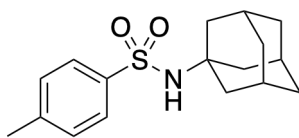
The reaction was carried out with condition B. The product **3ae** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc). (Scheme 3-2; 29.4 mg, 0.11 mmol, 57% isolated yield). The spectrum data of product **3ae** was consistent with the literature.¹¹

4-Methyl-*N*-(4-methyltetrahydro-2H-pyran-4-yl)benzenesulfonamide (**3af**)



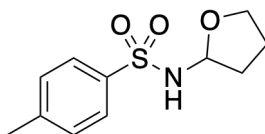
The reaction was carried out with condition B. The product **3af** was purified by flash chromatography on silica gel (Biotage Selekt, 93:7–60:40, hexane/EtOAc) (Scheme 3-2; 19.9mg, 0.07 mmol, 37% isolated yield). Yellow solid. **M.p.** 23–25 °C. **IR** (neat) 816, 1000, 1091, 1148, 1307, 1320, 1426, 2862, 2924, 3251 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.77 (d, J = 7.6 Hz, 2H), 7.29 (d, J = 7.6 Hz, 2H), 4.42 (s, 1H), 3.58 (t, J = 4.8 Hz, 4H), 2.43 (s, 3H), 1.83 (t, J = 4.0 Hz, 1H), 1.79 (t, J = 4.0 Hz, 1H), 1.63–1.58 (m, 2H), 1.27 (s, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 143.1, 140.4, 129.6, 126.9, 63.5, 54.3, 38.1, 27.3, 21.5. **DART–HRMS** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{13}\text{H}_{20}\text{NO}_3\text{S}$, 270.1158; found, 270.1152.

N-[(3*s*,5*s*,7*s*)-Adamantan-1-yl]-4-methylbenzenesulfonamide (**3ag**)



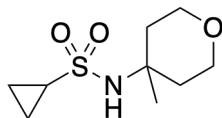
The reaction was carried out with condition B. The product **3ag** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Scheme 3-2; 42.7 mg, 0.14 mmol, 69% isolated yield). The spectrum data of product **3ag** was consistent with the literature.⁶

4-Methyl-*N*-(tetrahydrofuran-2-yl)benzenesulfonamide (**3ah**)



The reaction was carried out with condition B. The product **3ah** was purified by flash chromatography on silica gel (Biotage Selekt, 93:7–60:40, hexane/EtOAc) (Scheme 3-2; 22.2 mg, 0.09 mmol, 46% isolated yield). The spectrum data of product **3ah** was consistent with the literature.¹²

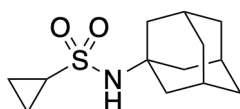
N-(4-Methyltetrahydro-2H-pyran-4-yl)cyclopropanesulfonamide (**3li**)



The reaction was carried out with condition B. The product **3li** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–69:40) (Scheme 3-2; 15.3 mg, 0.07 mmol, 35%

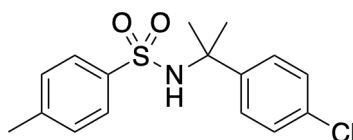
isolated yield). Yellow solid. **M.p.** 88–92 °C. **IR** (neat) 599, 703, 890, 1003, 1106, 1173, 1302, 1322, 2961, 3275 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 4.08 (s, 1H), 3.82–3.76 (m, 2H), 3.73–3.67 (m, 2H), 2.47 (m, 1H), 1.92–1.87 (m, 2H), 1.76–1.69 (m, 2H), 1.52 (s, 3H), 1.21 (dd, J = 4.8, 2.0 Hz, 2H), 1.02 (dd, J = 4.8, 2.0 Hz, 2H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 63.7, 54.0, 38.5, 33.8, 27.8, 6.61. **DART–HRMS** (m/z): [M+H]⁺ calcd for C₉H₁₈NO₃S, 220.1002; found, 200.1002.

***N*–[(3*s*,5*s*,7*s*)–Adamantan-1-yl]cyclopropanesulfonamide (3lg)**



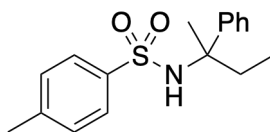
The reaction was carried out with condition B. The product **3lg** was purified by flash chromatography on silica gel (Biotage Selekt, 100:0–80:20, hexane/EtOAc) (Scheme 3-2; 19.2 mg, 0.08 mmol, 38% isolated yield). Yellow solid. **M.p.** 109–110 °C. **IR** (neat) 697, 890, 995, 1089, 1145, 1359, 1455, 2851, 2907, 3271 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 4.06 (s, 1H), 2.47 (m, 1H), 2.11 (s, 3H), 1.97 (s, 6H), 1.67 (s, 6H), 1.19 (dd, J = 10.8, 6.0 Hz, 2H), 0.99 (dd, J = 10.8, 6.0 Hz, 2H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 54.6, 43.6, 35.9, 34.1, 29.6, 6.6. **DART–HRMS** (m/z): [M+H]⁺ calcd for C₁₃H₂₂NO₂S, 256.1366; found, 256.1370.

***N*–[2-(4-Chlorophenyl)propan-2-yl]–4-methylbenzenesulfonamide (3aj)**



The reaction was carried out with condition B. The product **3aj** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc). (Scheme 3-2; 62.1 mg, 0.19 mmol, 96% isolated yield). Yellow solid. **M.p.** 122–124 °C. **IR** (neat) 563, 666, 808, 913, 984, 1087, 1144, 1323, 1490, 3233 cm⁻¹. **¹H NMR** (400 MHz, CDCl₃) δ 7.49 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.8 Hz, 2H), 4.88 (bs, 1H), 2.41 (s, 3H), 1.62 (s, 6H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 143.1, 142.8, 139.3, 132.7, 129.2, 127.9, 127.2, 126.8, 57.8, 29.8, 21.4. **DART–HRMS** (m/z): [M+H]⁺ calcd for C₁₆H₁₉ClNO₂S, 324.0820; found, 324.0814.

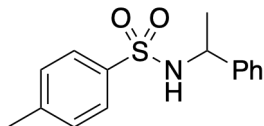
4-Methyl-*N*–(2-phenylbutan-2-yl)benzenesulfonamide (3ak)



The reaction was carried out with condition B. The product **3ak** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc). (Scheme 3-2; 39.4 mg,

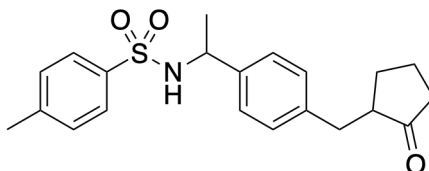
0.13 mmol, 65% isolated yield). The spectrum data of product **3ak** was consistent with the literature.⁶

4-Methyl-*N*-(1-phenylethyl)benzenesulfonamide (**3al**)



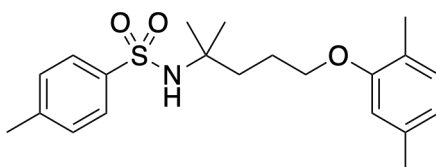
The reaction was carried out with condition B. The product **3al** was purified by flash chromatography on silica gel (Biotage Selekt, 93:7–70:30, hexane/EtOAc). (Scheme 3-2; 41.1 mg, 0.15 mmol, 75% isolated yield). The spectrum data of product **3al** was consistent with the literature.¹³

4-Methyl-*N*-(1-{4-[(2-oxocyclopentyl)methyl]phenyl}ethyl)benzenesulfonamide (**3am**)



The reaction was carried out with condition B. The product **3am** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc). (Scheme 3-2; 71.9 mg, 0.19 mmol, 97% isolated yield). The ratio of diastereomers is 1:1. Yellow solid. **M.p.** 102–105 °C. **IR** (neat) 552, 666, 962, 1090, 1158, 1325, 1432, 1734, 2970, 3274 cm⁻¹. The diastereo ratio has not been determined. **¹H NMR** (400 MHz, CDCl₃) δ 7.63 (d, J = 7.6 Hz, 2H), 7.19 (d, J = 7.6 Hz, 2H), 7.01 (dd, J = 8.8, 8.8 Hz, 4H), 4.81 (m, 1H), 4.43 (quin, J = 7.6 Hz, 1H), 3.07 (dd, J = 14.0, 9.6 Hz, 1H), 2.46 (dd, J = 14.0, 9.6 Hz, 1H), 2.39 (s, 3H), 2.39–2.23 (m, 2H), 2.15–1.93 (m, 3H), 1.74 (m, 1H), 1.50 (m, 1H), 1.40 (d, J = 6.8 Hz, 3H). **¹³C NMR** (100.6 MHz, CDCl₃) δ 220.2, 143.0, 140.0, 139.2, 137.7, 129.4 ($\times 2$ C), 128.9, 128.9, 127.1 ($\times 2$ C), 126.2 ($\times 2$ C), 53.2, 50.9, 38.1, 35.1, 29.1, 23.4, 21.5, 20.5. **DART–HRMS** (m/z): [M+H]⁺ calcd for C₂₁H₂₆NO₃S, 372.1628; found, 372.1634.

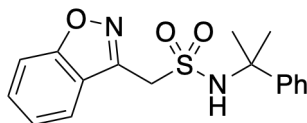
N-[5-(2,5-Dimethylphenoxy)-2-methylpentan-2-yl]-4-methylbenzenesulfonamide (**3an**)



The reaction was carried out with condition B. The product **3an** was purified by flash chromatography on silica gel (Biotage Selekt, 90:10–60:40, hexane/EtOAc) (Scheme 3-2; 41.3 mg, 0.11 mmol, 56% isolated yield). Brown solid. **M.p.** 84–88 °C. **IR** (neat) 597, 660, 732, 806, 1020,

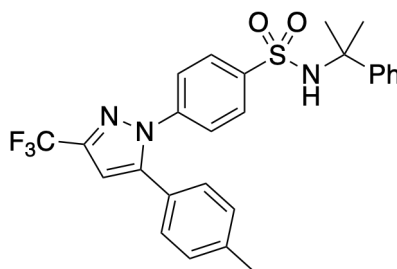
1145, 1319, 1509, 2919, 3255 cm^{-1} . $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.77 (d, $J = 8.4$ Hz, 2H), 7.27 (d, $J = 8.4$ Hz, 2H), 7.00 (d, $J = 7.6$ Hz, 1H), 6.77 (d, $J = 7.6$ Hz, 1H), 6.58 (s, 1H), 4.51 (s, 1H), 3.84 (t, $J = 5.6$ Hz, 2H), 2.39 (s, 1H), 2.31 (s, 1H), 2.15 (s, 1H), 1.83–1.74 (m, 2H), 1.71–1.67 (m, 2H), 1.57 (s, 2H), 1.22 (s, 6H). $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 156.8, 142.9, 140.4, 136.5, 130.3, 129.5, 127.0, 123.5, 120.8, 111.9, 67.6, 56.9, 39.3, 27.7, 24.1, 21.4, 15.8. **DART-HRMS** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{30}\text{NO}_3\text{S}$, 376.1941; found, 376.1938.

1-(Benzo[d]isoxazol-3-yl)-*N*-(2-phenylpropan-2-yl)methanesulfonamide (**3mo**)



The reaction was carried out with condition A. (EtOAc 900 μL was used). The reaction mixture was poured into 1M NaOH solution (50 mL), from which the crude product was extracted thrice with EtOAc (3 x 20 mL). The combined organic extracts were washed with 1N NaOH (50 mL) and brine (50 mL), before being dried over Na_2SO_4 . The drying agent was filtered off and the solvent removed *in vacuo*. The product **3mo** was purified by preparative HPLC (80:20–0:100, 10mM NH_4CO_3 in $\text{H}_2\text{O}/\text{MeCN}$) (Scheme 3-2; 10.2 mg, 0.03 mmol, 15% isolated yield). White solid. **M.p.** 112–114 $^\circ\text{C}$. **IR** (neat) 562, 701, 754, 997, 1146, 1328, 1381, 1610, 2938, 3278 cm^{-1} . $^1\text{H NMR}$ (300 MHz, $\text{DMSO}-d_6$) δ 7.88 (m, 1H), 7.86 (s, 1H), 7.78 (m, 1H), 7.67 (m, 1H), 7.54–7.49 (m, 2H), 7.42 (ddd, $J = 8.1, 7.2, 0.9$ Hz, 1H), 7.37–7.29 (m, 2H), 7.24 (m, 1H), 4.63 (s, 2H), 1.63 (s, 6H). $^{13}\text{C NMR}$ (75 MHz, $\text{DMSO}-d_6$) δ 162.7, 150.6, 147.0, 130.5, 128.0, 126.6, 125.5, 123.9, 123.3, 121.0, 109.6, 58.1, 51.3, 29.7. **DART-HRMS** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_3\text{S}$, 331.1111; found, 331.1110.

N-(2-Phenylpropan-2-yl)-4-[5-(*p*-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (**3no**)



The reaction was carried out with condition A. (DCM 900 μL was used). The mixture was poured into water at room temperature and extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over MgSO_4 and concentrated *in vacuo*. The product **3no** was purified by flash chromatography on NH silica gel (80:20–0:100, hexane/EtOAc) (Scheme 3-2; 22.0 mg, 0.04 mmol, 22% isolated yield) White solid. **M.p.** 187–189 $^\circ\text{C}$. **IR** (neat) 765, 976, 1149, 1237, 1328, 1472,

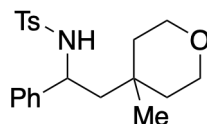
1498, 1597, 2983, 3278 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.63 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.29–7.20 (m, 5H), 7.16 (d, J = 7.6 Hz, 2H), 7.08 (d, J = 7.6 Hz, 2H), 6.73 (s, 1H), 4.84 (s, 1H), 2.38 (s, 3H), 1.55 (s, 9H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 145.1, 144.5, 143.8 (q, $J_{\text{C-F}}$ = 38.4 Hz), 142.1, 141.9, 139.7, 129.7, 128.7, 128.3, 127.9, 127.4, 125.7, 125.5, 125.2, 121.1 (q, $J_{\text{C-F}}$ = 269.2 Hz), 106.2, 59.0, 29.8, 21.3. **DART-HRMS** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{25}\text{F}_3\text{N}_3\text{O}_2\text{S}$, 500.1614; found, 500.1621.

5. Procedure for Three Component Coupling

In a glovebox, to an oven-dried vial equipped with a stirring bar was added **PTH-4** (3.9 mg, 0.01 mmol), LiBF_4 (1.9 mg, 0.02 mmol), redox active ester **2** (0.2 mmol), sulfonamide **1** (0.2 mmol) and styrene **4** (0.4 mmol) in dichloromethane (600 μl). After sealing the vial with a cap and removing it from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature at around 40 $^\circ\text{C}$. (Figure S3-3) After 12 h, the reaction was quenched by filtration through a short plug of SiO_2 with ethyl acetate. After volatiles were removed under reduced pressure, purification by flash column chromatography on silica gel gave the coupling product **5**.

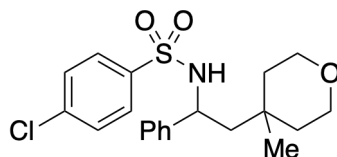
6. Characterization of Three Component Coupling Products

4-Methyl-*N*-[2-(4-methyltetrahydro-2H-pyran-4-yl)-1-phenylethyl]benzenesulfonamide (**5aaf**)



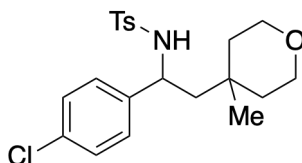
The product **5aaf** was purified by flash chromatography on silica gel (100:0–80:20, hexane/EtOAc and 50:50–80:20, hexane/diethyl ether), GPC and recrystallization (DCM/hexane) (Scheme 3-3; 32.9 mg, 0.09 mmol, 44% isolated yield). White solid. **M.p.** 127–129 $^\circ\text{C}$. **IR** (neat) 701, 813, 945, 1094, 1156, 1323, 1456, 1599, 2921, 3273 cm^{-1} . **¹H NMR** (400 MHz, CDCl_3) δ 7.44 (d, J = 7.6 Hz, 2H), 7.11 (m, 3H), 7.05 (d, J = 7.6 Hz, 2H), 6.94 (m, 2H), 4.72 (m, 1H), 4.49 (dd, J = 14.0, 6.8 Hz, 1H), 3.67 (dt, J = 12.0, 4.4 Hz, 1H), 3.61–3.47 (m, 3H), 2.33 (s, 3H), 1.82 (dd, J = 14.4, 7.2 Hz, 1H), 1.75 (dd, J = 14.4, 7.2 Hz, 1H), 1.53 (m, 1H), 1.42 (d, J = 13.6 Hz, 1H), 1.30 (m, 1H), 1.11 (d, J = 13.6 Hz, 1H), 1.03 (s, 3H). **¹³C NMR** (100.6 MHz, CDCl_3) δ 142.9, 142.0, 137.5, 129.1, 128.5, 127.3, 127.0, 126.3, 63.6, 63.6, 55.1, 50.7, 38.3, 38.0, 31.0, 23.4, 21.4. **DART-HRMS** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{21}\text{H}_{31}\text{N}_2\text{O}_3\text{S}$, 391.2050; found, 391.2046.

4-Chloro-*N*-[2-(4-methyltetrahydro-2H-pyran-4-yl)-1-phenylethyl]benzenesulfonamide (**5eaf**)



The product **5eaf** was purified by flash chromatography on silica gel (7:3–5:5, hexane/diethyl ether) and GPC (Scheme 3-3; 28.8 mg, 0.07 mmol, 37% isolated yield). Yellow solid. **M.p.** 138–140 °C. **IR** (neat) 666, 813, 1014, 1092, 1157, 1324, 1598, 1700, 2922, 3274 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.43 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.11–7.08 (m, 3H), 6.92 (d, J = 6.8 Hz, 2H), 4.97 (bs, 1H), 4.54 (dd, J = 14.0, 6.8 Hz, 1H), 3.69 (m, 1H), 3.62–3.50 (m, 3H), 1.81 (dd, J = 14.0, 6.8 Hz, 1H), 1.74 (dd, J = 14.0, 6.8 Hz, 1H), 1.56 (m, 1H), 1.45 (d, J = 13.6 Hz, 1H), 1.33 (m, 1H), 1.14 (d, J = 13.6 Hz, 1H), 1.07 (s, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 141.5, 139.1, 138.5, 128.7, 128.6, 128.4, 127.5, 126.3, 63.6 ($\times 2\text{C}$), 55.3, 50.9, 38.4, 37.9, 31.1, 23.3. **DART–HRMS** (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{25}\text{ClNO}_3\text{S}$, 394.1238; found, 394.1238.

***N*-[1-(4-Chlorophenyl)-2-(4-methyltetrahydro-2H-pyran-4-yl)ethyl]-4-methylbenzenesulfonamide (5abf)**



The product **5abf** was purified by flash chromatography on silica gel (7:3–5:5, hexane/diethyl ether) and recrystallization (Scheme 3-3; 36.6 mg, 0.09 mmol, 45% isolated yield). Yellow solid. **M.p.** 144–146 °C. **IR** (neat) 700, 752, 825, 1093, 1158, 1325, 1476, 1586, 2922, 3274 cm^{-1} . **^1H NMR** (400 MHz, CDCl_3) δ 7.42 (d, J = 7.6 Hz, 2H), 7.05 (t, J = 8.0 Hz, 4H), 6.88 (d, J = 8.0 Hz, 2H), 4.96 (bs, 1H), 4.48 (dd, J = 14.0, 6.8 Hz, 1H), 3.66 (m, 1H), 3.59–3.48 (m, 3H), 2.36 (s, 3H), 1.77 (dd, J = 14.4, 7.2 Hz, 1H), 1.67 (dd, J = 14.4, 7.2 Hz, 1H), 1.52 (m, 1H), 1.40 (d, J = 13.6 Hz, 1H), 1.31 (m, 1H), 1.12 (d, J = 13.6 Hz, 1H), 1.03 (s, 3H). **^{13}C NMR** (100.6 MHz, CDCl_3) δ 143.3, 140.5, 137.4, 133.1, 129.2, 128.6, 127.8, 127.0, 63.6, 63.6, 54.4, 50.8, 38.3, 38.0, 31.1, 23.3, 21.4. **DART–HRMS** (m/z): $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{21}\text{H}_{30}\text{ClN}_2\text{O}_3\text{S}$, 425.1660; found, 425.1655.

7. Stoichiometric Reaction

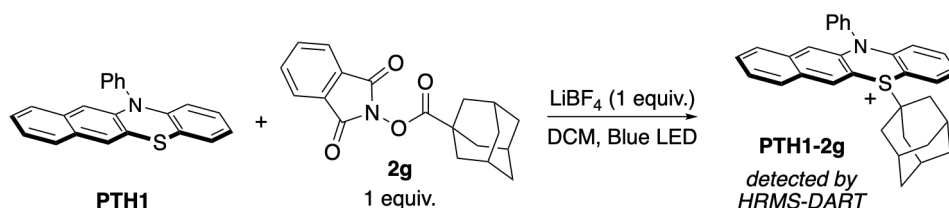


Figure S3-3. Stoichiometric Reaction

Figure S3-3 (Figure 3-3). In a glovebox, to an oven-dried vial equipped with a stirring bar was added redox active ester **2g** (16.3 mg, 0.05 mmol), **PTH-1** (16.3 mg, 0.05 mmol), LiBF_4 (4.7 mg, 0.05 mmol) and dichloromethane (375 μl). After sealing the vial with a cap and removed from the glove box, the reaction was stirred and irradiated with a 34W blue LED (0.5 cm away) with a cooling fan to keep the temperature around 40 $^{\circ}\text{C}$ (Figure S3-3). After 6 h, the reaction solution was directly used for MS analysis (**DART-HRMS**). **PTH-1-2g**: **DART-HRMS** (m/z): $[\text{M-BF}_4]^+$ calcd for $\text{C}_{32}\text{H}_{30}\text{NS}$, 460.2094; found, 460.2087.

8. Cyclic Voltammetry of POX-1

CV measurements were carried out under nitrogen atmosphere in acetonitrile solutions with 0.1 M of tetrabutylammonium tetrafluoroborate (Bu_4NBF_4) as a supporting electrolyte. Measurements were made with a glassy carbon electrode (area = 0.07 cm^2), an Ag/AgCl reference electrode, and a Pt wire counter electrode. The concentration of the sample solution was fixed at 10 mM and the sweep rates were set to 100 mV/s.

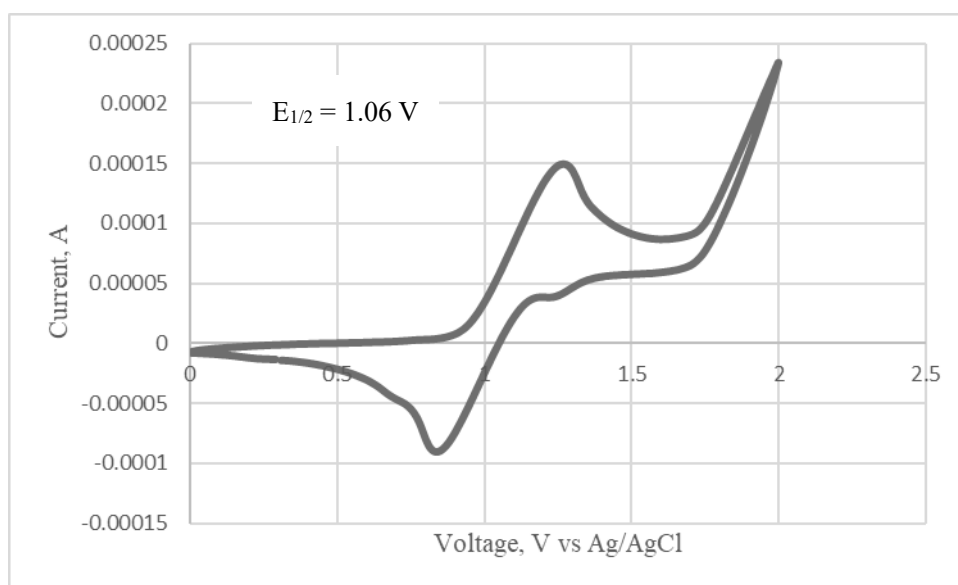


Figure S3-4. Cyclic voltammogram of **POX-1**.

9. UV-Vis Spectra of POX1

UV-Vis adsorption spectra of organophotocatalysts were measured with 40 μM acetonitrile solution.

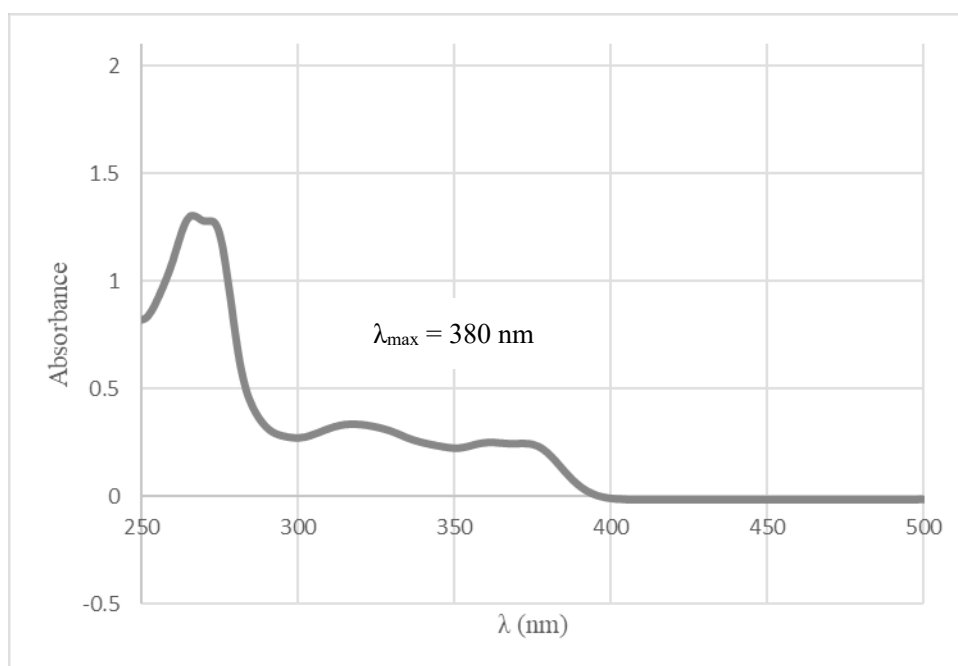


Figure S3-5. UV-vis spectrum of **POX1**.

10. Fluorescence spectra of POX1

Fluorescence spectra of organophotocatalysts were measured with 40 μM acetonitrile solution.

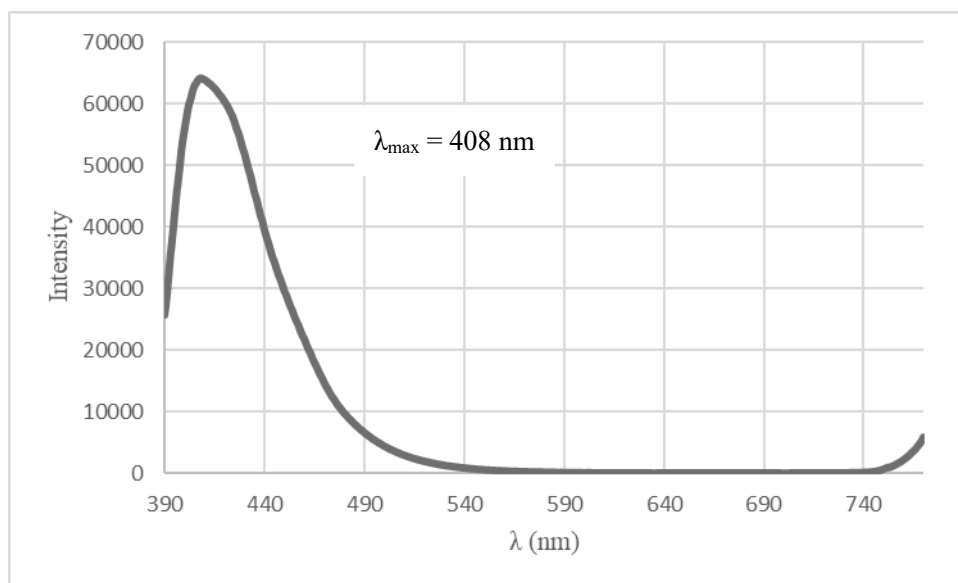


Figure S3-6. Fluorescence spectrum of **POX1** was scanned from 390 to 770 nm after excitation at 380 nm.

第三章 実験項 参考文献

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総括

第一章 可視光照射下、フェノチアジン有機光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒の協働触媒によるアルコールを用いた脂肪族アルケンのヒドロアルコキシ化反応の開発に成功した。本反応は、光酸化還元触媒によるコバルト触媒の一電子還元を起点として、アルケンからMHAT反応によってアルキルコバルト(III)種が生成する。続いて、アルキルコバルト(III)種が光酸化還元触媒により一電子酸化され、カルボカチオン等価体のアルキルコバルト(IV)種に変換されるORPC反応が進行する。カルボカチオン等価体とアルコールが反応して目的物を与える。本手法では、強酸を用いない温和な条件かつ還元剤と酸化剤を用いないアトムエコノミーに優れた条件でアルケンのヒドロアルコキシ化が可能である。

第二章 可視光照射下、イリジウム光酸化還元触媒、コバルト触媒、ブレンステッド酸触媒からなる協働触媒系とビニルスルホニル基を活用することで、アルキルアミンの γ 位選択的な官能基化に成功した。本反応では、ビニルスルホニル基由来の電子不足ラジカルによる分子内HAT反応が進行し、窒素 γ 位にアルキルコバルト(III)種が生じる。光酸化還元触媒により、アルキルコバルト(III)種は一電子酸化され、カルボカチオン等価体のアルキルコバルト(IV)種に変換されるORPC反応が進行する。カルボカチオン等価体は分子内求核置換反応または外部求核剤による求核置換反応により目的物が生成する。本手法により、入手容易なアルキルアミンから、アゼチジン、1,3-ジアミン、1,3-アミノアルコール誘導体などの γ -アミノ官能基化生成物が得られた。

第三章 可視光照射下、フェノチアジン有機光酸化還元触媒を用い、スルホンアミドとレッドックス活性エステルとの脱炭酸型クロスカップリング反応の開発に成功した。本反応では、光励起されたフェノチアジン触媒による一電子移動によりレッドックス活性エステルからアルキルラジカルが生成する。アルキルラジカルがフェノチアジン触媒のラジカルカチオンにより、カルボカチオン等価体に変換されるORPC反応が進行する。スルホンアミドとカルボカチオン等価体が反応し、*N*-アルキル化が進行する。本手法は、強酸を用いない温和な条件で進行することから、医薬品構造を含むカルボン酸やスルホンアミドを適用することが可能であった。

以上、著者は光酸化還元触媒の一電子酸化による ORPC 反応を活用した、三つの新規分子変換反応の開発に成功した。これらの手法により、温和な条件で、入手容易な原料から、複雑な骨格を持ち合成手法が限られている化合物の合成を可能にした。本論文によって得られた成果は、本論文によって得られた成果は、従来の ORPC 反応の適用範囲を拡張するものとして、今後、創薬研究における探索合成や合成研究の現場において、有用な分子変換手法として活用されることが期待される。

論文目録

第一章

“A Triple Photoredox/Cobalt/Brønsted Acid Catalysis Enabling Markovnikov Hydroalkoxylation of Unactivated Alkenes”

Masanari Nakagawa, Yuki Matsuki, Kazunori Nagao, Hirohisa Ohmiya

J. Am. Chem. Soc. **2022**, *144*, 7953–7959.

第二章

“ γ -Amino C(sp³)-H Functionalization of Aliphatic Amines through a Light-Driven Triple Catalysis”

Masanari Nakagawa, Kazunori Nagao, Hirohisa Ohmiya

ACS Catal. **2024**, *14*, 8005–8012.

第三章

“Organophotoredox-Catalyzed Decarboxylative N-Alkylation of Sulfonamides”

Masanari Nakagawa, Kazunori Nagao, Zenichi Ikeda, Matthew Reynolds, Ignacio Ibáñez, Junsu Wang,

Norihito Tokunaga, Yusuke Sasaki, Hirohisa Ohmiya

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