博　士　論　文

可視光励起を活用した触媒的分子変換反応の開発

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目次

序論

古典的なラジカル生成法

炭素中心ラジカルは一般に不対電子に由来する反応性の高い種であり、有機合成化学において合成上有用な中間体を提供する[1]。Ingold らにより、熱力学的あるいは速度論的に安定化した半減期が長い炭素中心ラジカルは長寿命なラジカルとして、一方で反応性の高い炭素中心ラジカルは短寿命なラジカル（半減期 $<10^{-3}$ 秒）として定義されている[2]。Kolbe 電解反応[3]、ピナコールカップリング[4]、Borodin-Hundsdiecker 反応[5]など、有機合成におけるラジカル反応は 19 世紀から存在している。対照的に、炭素中心ラジカルは、1900 年に Gomberg らが難分解性のトリチルラジカル（半減期 $=10^{-2.2}$ 秒）を発見したことによって初めて明確に確認された[6]。炭素中心ラジカルは、カルバニオン、カルボカチオン、カルベンといった従来の二電子的な極性反応とは異なり、一電子反応に基づく特異な反応性と化学選択性を与える。ラジカル反応の化学選択性は、主に反応基質の結合解離エネルギー（Bond Dissociation Energy = BDE）と電子的極性に支配される[7]。ラジカル化学は、一般に極性反応では阻害されるようなアルコール、カルボン酸、水などのプロトン性官能基存在下での反応を可能にする。その合成上の有用性にもかかわらず、炭素中心ラジカルは、Birch 還元反応[8]や Kharasch 反応[9]（原子移動ラジカル付加反応、ATRA）のようなわずかな例外を除いて、合成化学において重要な役割を担ってこなかった。この原因としては、これまで短寿命な炭素中心ラジカルの一般的な生成法が確立されていなかったためであり、炭素中心ラジカルを分子構築に適用する反応設計は困難であった。

このような背景のもと、van der Kerk らのスズヒドリドを用いた炭素中心ラジカル生成法の報告を皮切りにラジカル化学が発展してきた[10]。同時期に、Walling らがラジカル極性効果[11]を報告し、Barton 反応によりステロイド化学が大きく発展した[12]。典型的なラジカル付加反応である Giese 反応[13]や Minisci 反応[14]は、合成化学的に有用であるため、現在でも天然物、医薬品、ポリマー合成に応用されている。炭素中心ラジカルに基づく変換と並行して、その生成法が数多く開発されてきた（**Figure P1**）。スズヒドリドを用いた炭素中心ラジカル生成法は優れた手法であるが[8a,15]、残留する毒性の高いスズ化合物が医薬品合成などで問題となり、安全面での改良が求められていた。1967 年、Davies らは、酸素と有機ホウ素化合物との反応により、炭素−ホウ素結合の均等開裂により炭素中心ラジカル形成が起こることを報告し[16]、その後、ラジカル開始剤を触媒量で運用するに発展し[17]、より汎用性の高い手法に昇華した。キサンテート構造を鍵としたプロセスである Barton-McCombie 反応により、アルコールを足がかりとした炭素中心ラジカルの生成が可能になった[18]。同様に Barton らは、N-ヒドロキシチオピリドンとカルボン酸から誘導される酸化還元活性エステル、いわゆる Barton エステルを、熱的にあるいはスタナンや UV 照射によって、脱炭酸を介し炭素中心ラジカルを生成することを報告している[19]。澤本[20a]および Matyjaszewski[20b]は、Kharasch 反応に基づく原子移動

ラジカル重合（ATRP）を独自に報告し、キサンテート化学は、炭素中心ラジカルの付加/開裂に基づく可逆的付加−開裂連鎖移動（RAFT）重合[21]の開発につながった。

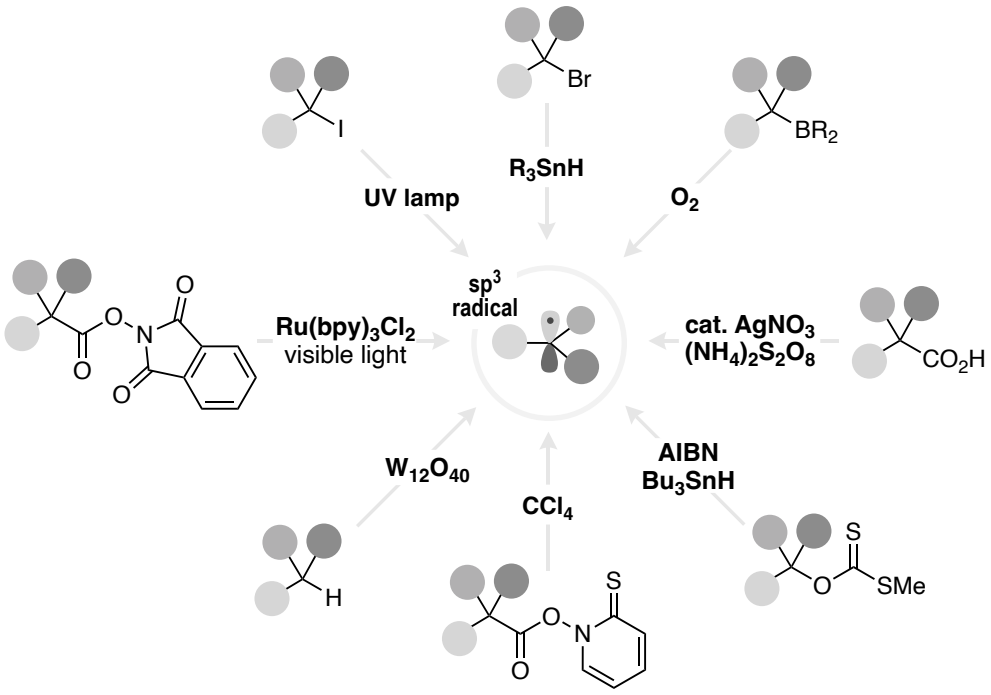
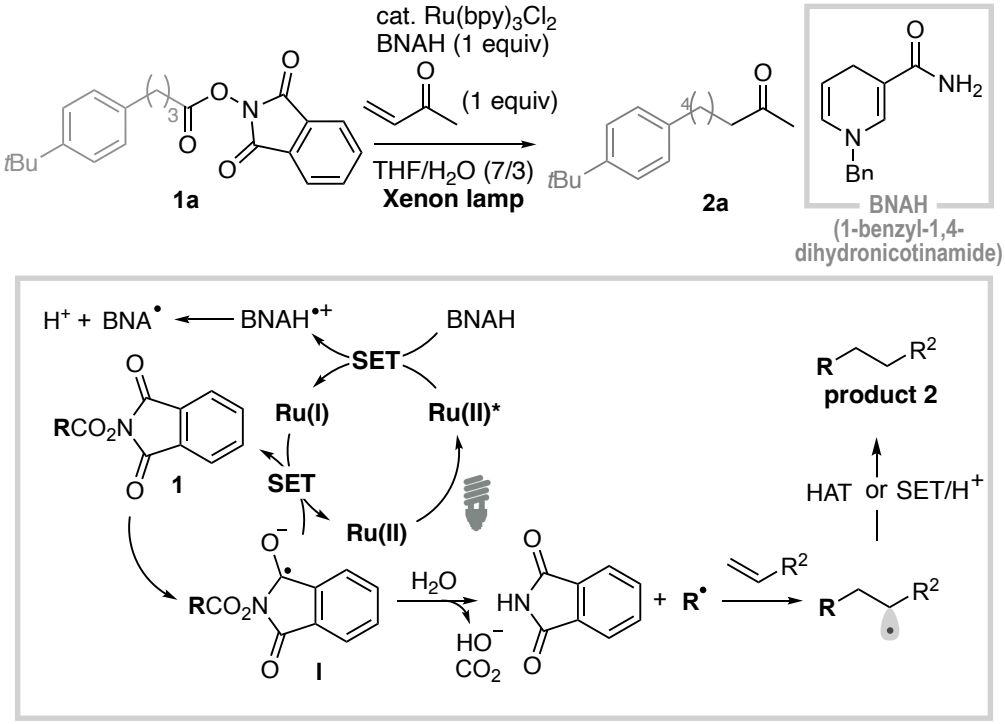


Figure P1. Selected conventional alkyl radical generation methods.

1988 年、岡田と小田は、N-(アシルオキシ)フタルイミド **1a** からの可視光を介した炭素中心ラジカル生成を報告した。その直後、彼らは $Ru(bpy)_3Cl_2$ 錯体と 1-ベンジル-1,4-ジヒドロニコチンアミド（BNAH）を一電子還元剤として用いる触媒系を開発し[22b]、Giese 付加生成物 **2a** を得た（**Scheme P1**）。



Scheme P1. Ru-Catalyzed decarboxylative alkyl radical generation.

光酸化還元触媒を用いた分子変換

過去半世紀にわたり、無数のラジカル反応や炭素中心ラジカルの生成法が開発され、ラジカル化学は知識の蓄積と汎用性の向上とともに徐々に発展してきた。しかし、ラジカル化学は、それでもなおラジカル種の制御と反応性の予測が困難であるため、有機合成において主たる方法論にはなっていなかった。1980 年代には、**Scheme P1** に示した岡田・小田らの報告に加えて、Kellogg [23a]、Pac [23b]、福住と田中 [23c] による光酸化還元化学の先駆的研究が報告された。この 20 年後、Yoon、MacMillan、Stephenson がそれぞれ独自の光酸化還元反応を発表し [24]、これが現代の光酸化還元触媒化学の原型となった。光酸化還元触媒化学の基本原理は、まず可視光照射下で励起された光酸化還元触媒が、一電子受容体または一電子供与体のいずれかに一電子移動 (SET) を引き起こす。この SET によって、触媒は電子を失うか（酸化的消光機構）、基質から電子を獲得する（還元的消光機構）。その後、光酸化還元触媒はそれぞれ全く逆のプロセスを経て、他の基質と SET を進行し、触媒サイクルを完結する（**Figure P2**）[25]。本プロセスは、可視光を化学エネルギーに変換することで機能し、強塩基も強酸も必要としない上、室温という非常に温和な条件下で炭素中心ラジカルの生成を可能とする。触媒–基質間あるいは基質–基質間の SET 過程は、励起状態あるいは基底状態の酸化還元電位から容易に予測できるため、精密な触媒反応設計が可能である。

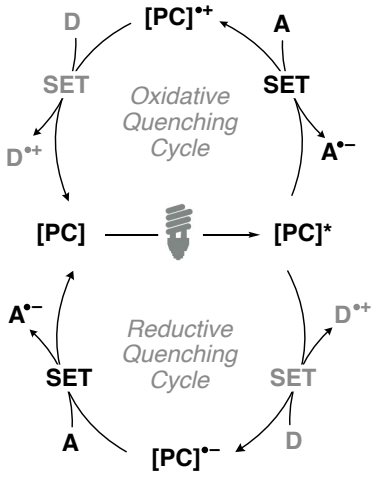
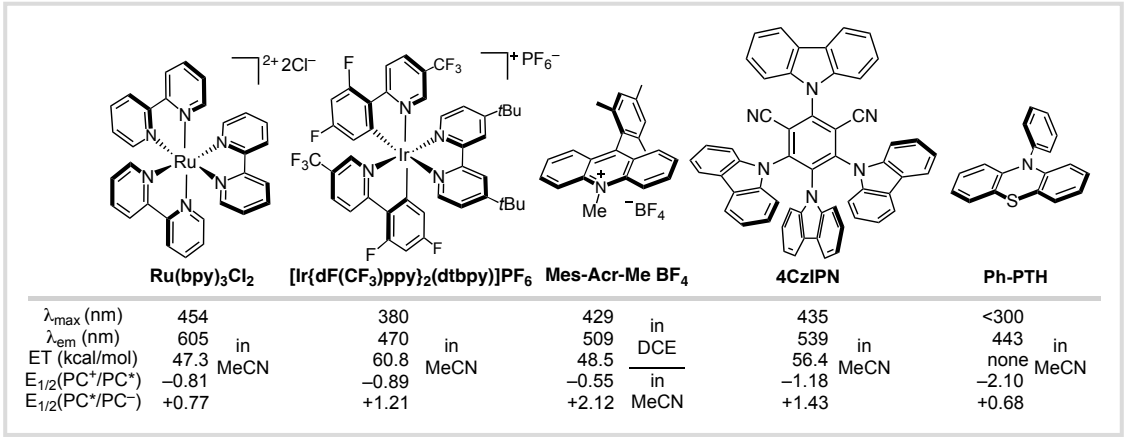


Figure P2. General catalytic mechanism of photoredox catalysis [PC].

$Ru(bpy)_3Cl_2$ 錯体に加え、多くの Ru 錯体や Ir 錯体が光酸化還元触媒として設計・合成されており、これらは現在の光酸化還元分野で最も広く用いられている[26]。これと並行して、新規有機光酸化還元触媒の設計・合成も、汎用される有機蛍光色素を光酸化還元触媒として応用することで発展してきた（**Figure P3**）[26f]。さらに、酸化的消光型[22,27]（酸化還元活性エステルや Katritzky ピリジニウム塩など）や還元的消光型[28]（ケイ酸塩、ジヒドロピリジン、ホウ酸塩など）のさまざまなラジカル前駆体が開発されてきた。各ラジカル前駆体の酸化還元電位に応じて、酸化的または還元的消光が起こり、炭素中心ラジカルが生成する。それぞれの光酸化還元触媒とラジカル前駆体の固有の酸化還元電位に基づいて、所望の触媒反応を設計できる（**Figure P4**）。

SET とは別の現象として、水素原子移動（HAT）とエネルギー移動（EnT）もまた、光駆動型合成化学における重要なプロセスとして認識されている。他のラジカルプロセスと同様に、HAT は BDE に大きく影響されるため、第三級 $C(sp^3)$–H 結合の HAT は、第二級 $C(sp^3)$–H 結合や第一級 $C(sp^3)$–H 結合の HAT よりも優先的に起こり、極性反応では困難な後期段階における C–H 官能基化を可能にする[29]。また EnT は、励起状態の光酸化還元触媒を介して、基底状態の反応基質に対して起こりうるプロセスである[24a, 30]。



	$Ru(bpy)_3Cl_2$		$[Ir\{dF(CF_3)ppy\}_2(dtbpy)]PF_6$		Mes-Acr-Me BF_4		4CzIPN		Ph-PTH	
λ_{max} (nm)	454		380		429	in DCE	435		<300	
λ_{em} (nm)	605	in	470	in	509		539	in	443	in
ET (kcal/mol)	47.3	MeCN	60.8	MeCN	48.5		56.4	MeCN	none	MeCN
$E_{1/2}(PC^+/PC^*)$	–0.81		–0.89		–0.55	in MeCN	–1.18		–2.10	
$E_{1/2}(PC^*/PC^-)$	+0.77		+1.21		+2.12		+1.43		+0.68	

λ_{max}=maximum absorption wavelength, λ_{em}= emission wavelength, ET=triplet energy, $E_{1/2}(PC^+/PC^*)$ = oxidative potential, $E_{1/2}(PC^+/PC^*)$ = reductive potential.

Figure P3. Widely used photoredox catalysts and their photophysical properties.

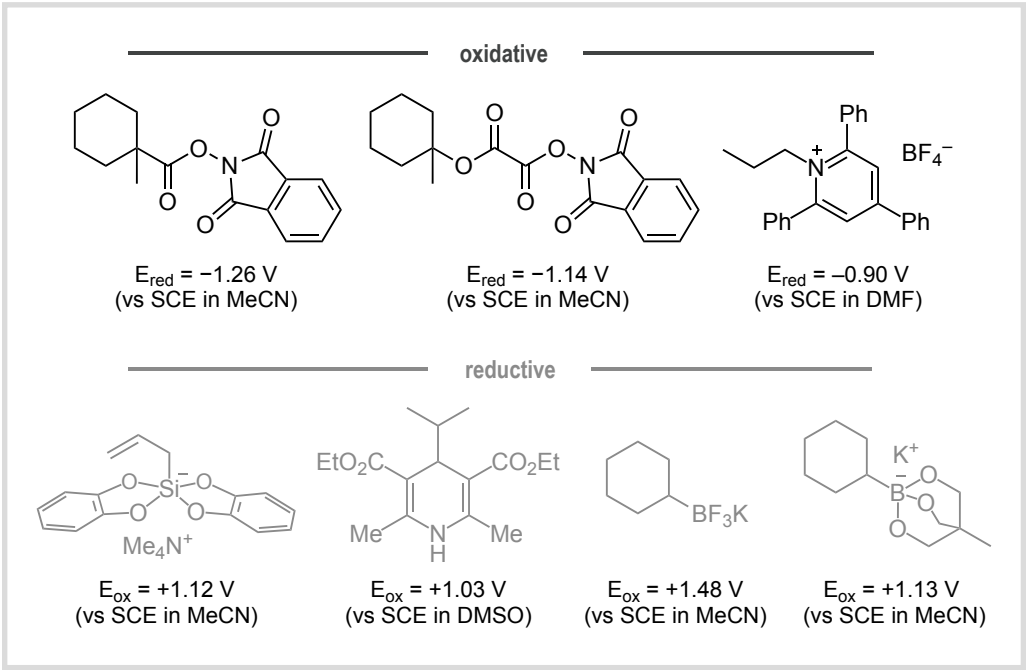
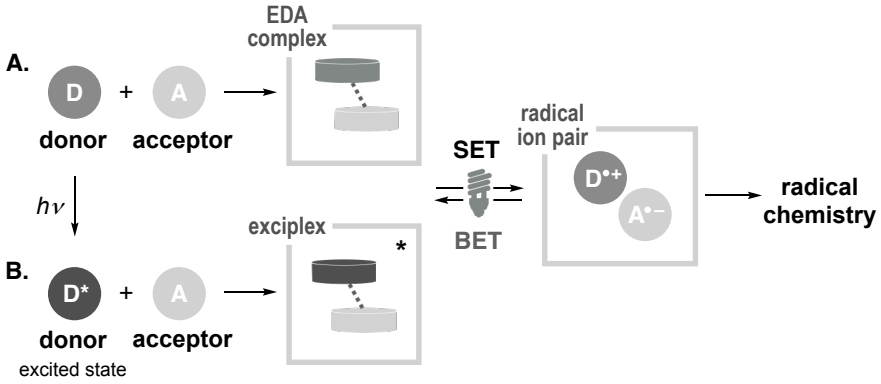


Figure P4. Widely used radical precursors in photoredox catalysis and their redox potentials.

<u>EDA 錯体に基づく合成戦略</u>

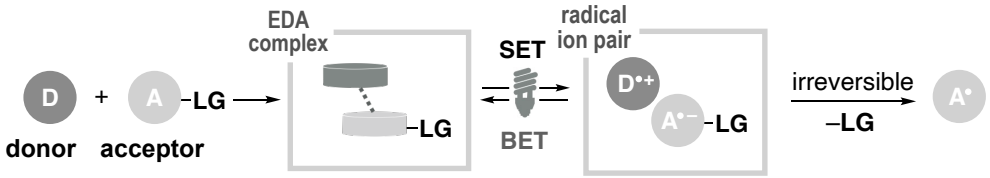
電子供与性分子と電子受容性分子は、基底状態で電荷移動（CT）錯体を形成できる。形成した複合体は電子供与–受容（EDA）錯体と呼ばれ、元の 2 分子が個々では紫外領域でしか吸収できない場合でも、しばしば可視光を吸収する。EDA 錯体に基づく合成戦略は、外因性の光酸化還元触媒を用いずに固有の光化学を可能にするため、近年、ラ

ジカル化学における魅力的なアプローチとして再注目が集まっている [31]。EDA 錯体の光物理学的な特性は 1950 年代から広く研究されてきたが、合成化学への応用は限定的であった。1949 年、Benesi と Hildebland は、ヨウ素と芳香族炭化水素との相互作用による分光学的変化を報告した [32]。その後、Mulliken らは量子力学で EDA 錯体形成の理論を提唱した [33]。基底状態で形成される安定な電荷移動錯体は一般に、非結合性構造の寄与が大きく、電荷移動錯体構造の寄与は小さい。対照的に、EDA 錯体の光励起は、熱的経路では到達できない分極した電荷移動状態をもたらし、続く SET プロセスによってラジカルイオン対が生成する（**Scheme P2A**）。また Leonhart と Weller は、基底状態では電荷移動相互作用は観測されないが、電子供与体または電子受容体の励起状態では励起錯体（エキサイプレックス）[34] と呼ばれる EDA 錯体の形成を提唱した（**Scheme P2B**）。どちらの過程でも、適切な分子設計により望みの有機ラジカル種が生成する。しかし、SET 過程が効率よく起こり、EDA 錯体からラジカルイオン対が形成されたとしても、逆電子移動（BET）がしばしば望みのラジカル種生成、ひいては EDA 錯体の有機合成への応用を妨げる。



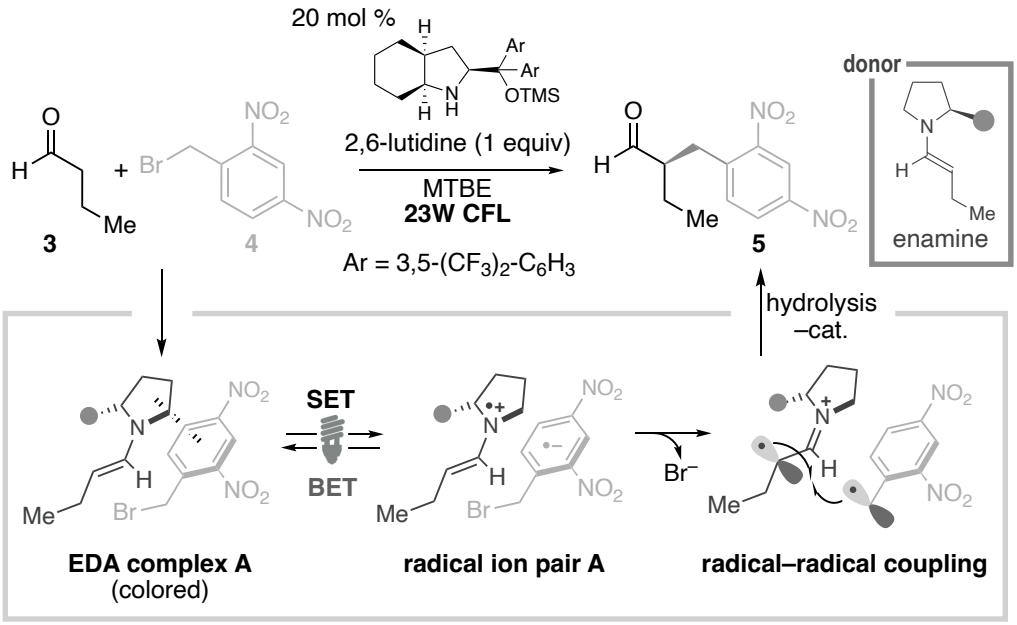
Scheme P2. Schematic pathway of EDA complex (A) and exciplex (B).

BET に由来する上記の制限は、脱離基（LG）を導入した一電子受容体を用いることで緩和された。LG の脱離は BET と競合し、基底状態の EDA 錯体への消光を妨げる。不可逆的プロセスである脱離の効率が十分に高ければ、平衡が傾きラジカル種が生成するため、化学合成への適用が可能となる（**Scheme P3**）。いくつかのグループが、電子供与体と LG を導入した電子受容体から形成される EDA 錯体を用いたアプローチに関する先駆的な研究を行ったが、EDA 錯体に関する明確な実験的証拠は得られなかった。



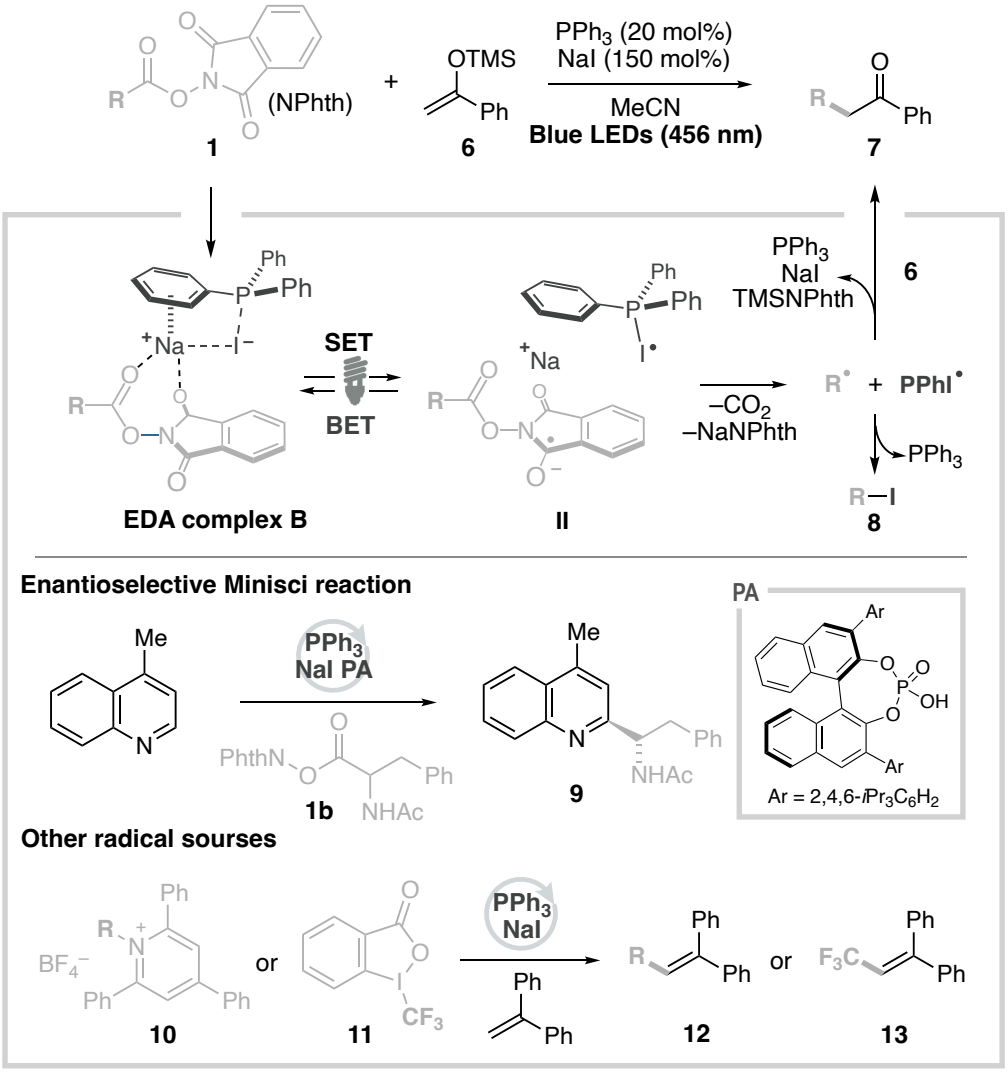
Scheme P3. A radical generation strategy based on LG-installed EDA complex.

2013 年、Melchiorre らは、アルデヒドの α-アルキル化を可能にする不斉有機触媒反応に基づく EDA 錯体戦略を報告した[35]。電子不足の臭化ベンジル **4** と、アルデヒド **3** からアミン触媒を用いて反応系中で形成したキラルエナミンから、着色した EDA 錯体を形成した。このキラル EDA 錯体 **A** は可視光照射下で励起でき、SET が起こってラジカルイオン対 **A** が形成される。電子受容体からブロモアニオンが脱離すると、炭素中心ラジカルが生成し、さらにラジカル–ラジカルカップリングが起こって生成物 **5** が得られる（**Scheme P4**）。



Scheme P4. Enantioselective catalytic α-alkylation of aldehydes.

EDA 錯体に関する研究は加速し、上述の報告をきっかけとして、現在では光酸化還元化学における戦略の一つとして認識されている。酵素を利用した形成も含め、多種多様な EDA 複合体が対応する機構論的根拠とともに報告されている。EDA 錯体に基づく様々な方法論に関する報告が増えていることから、触媒的 EDA 錯体戦略も魅力的な選択肢である。このような触媒的 EDA 錯体戦略は、Melchiorre らにより例示されているように、触媒とカルボニル基のような足場を持つ基質との反応によって、EDA 錯体形成を促進するような電子供与体が提供されるという反応形式である。

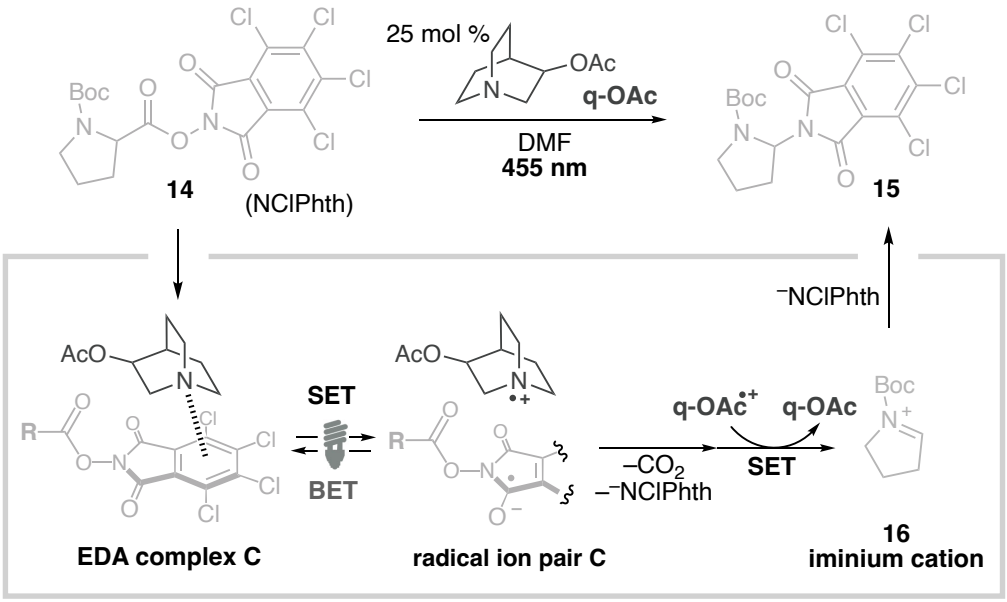


Scheme P5. PPh_3-catalysed radical generation based on catalytic formation of a three-component EDA complex.

Shang と Fu のグループは、トリフェニルホスフィン（PPh_3）とヨウ化アルカリ金属（MI）の組み合わせが触媒的電子供与体として働き、電子受容体と EDA 錯体を形成することを発見した（**Scheme P5**）[36]。PPh_3 と NaI を電子供与体として酸化還元活性エステル **1** と混合すると、三成分から可視光吸収性の EDA 錯体 **B** が生成する。この EDA 錯体 **B** は、光照射下で中間体 **II** を介して炭素中心ラジカルと長寿命ラジカル $PPh_3I^{\cdot}$を与え、生成物 **7** を得る。ラジカル捕捉基質 **6** を用いない反応では、生成した炭素中心ラジカルを単純にヨウ素化した生成物 **8** を形成した。このプロトコルでは、ラジカル捕捉基質との相互作用も、触媒活性化のために必要としない。不斉リン酸触媒（PA）を加えることで、レピジンと **1b** のエナンチオ選択的 Minisci 反応も可能であった。さらに、PPh_3 と NaI の組み合わせは、酸化還元活性エステルだけでなく、Katrizky 塩 **10** と Togni

試薬 **11** を活性化し、生成物 **12** と **13** を得た。

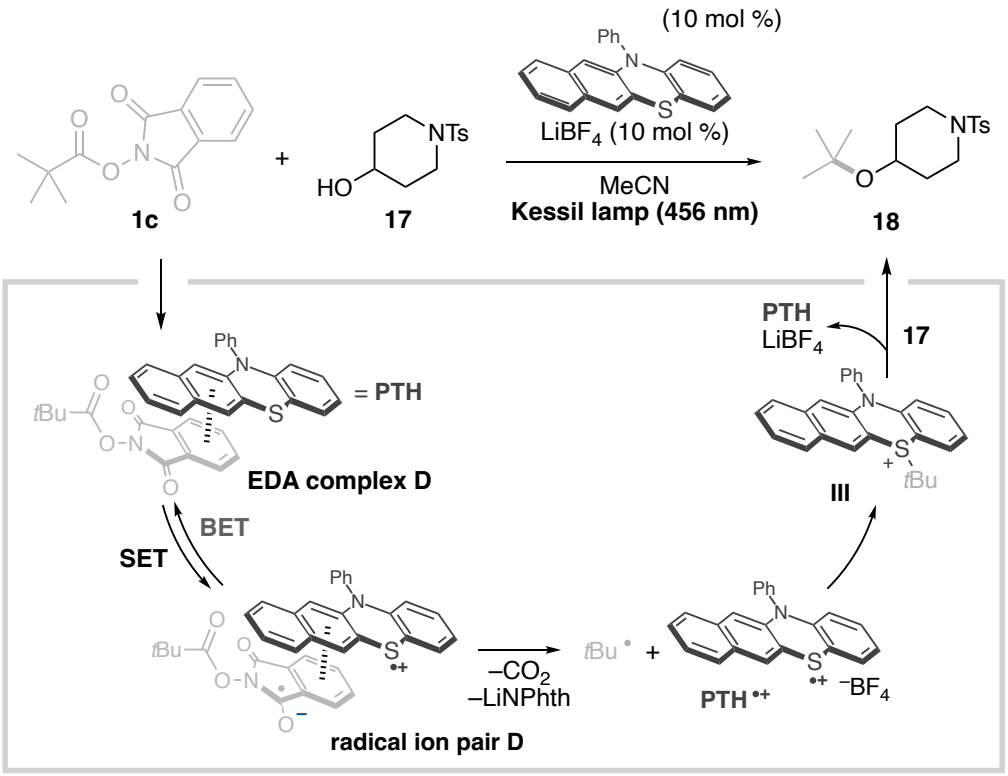
Bosque と Bach は、ラジカル捕捉基質との相互作用を伴わない別の触媒的 EDA 錯体形成を報告している（**Scheme P6**）[37]。3-アセトキシキヌクリジン（q-OAc）は、テトラクロロ-N-フタルイミド（NClPhth）酸化還元活性エステル **14** を触媒的に活性化し、EDA 錯体を形成する。興味深いことに、**14** を用いた q-OAc では、着色した EDA 錯体 **C** による明るい黄色の溶液が観察されたが、対応する N-フタルイミドのみでは無色の溶液が得られた。この違いの主な理由は、**14** の還元電位（E_{red} = −0.70〜−0.54 V vs. SCE）が、



Scheme P6. Catalytic formation of EDA complex-mediated decarboxylative α-amidation using quinuclidine as a catalyst.

N-フタルイミド酸化還元エステルの還元電位（E_{red} = −1.24〜−1.38 V vs. SCE）に比べてはるかに高いためである。光照射により、EDA 錯体 **C** からキヌクリジルラジカルカチオン（q-OAc$^{\cdot+}$）を含むラジカルイオン対 **C** の形成が促進された。α-アミノラジカルは q-OAc$^{\cdot+}$によってさらに酸化され、q-OAc 触媒の再生とともにイミニウムカチオン **16** を与え、最終的に **16** をアミド化して生成物 **15** を得た。

大宮は、π-スタッキング相互作用を利用した触媒的 EDA 錯体戦略に基づく、有機光酸化還元触媒による脱炭酸エーテル化反応を開発した（**Scheme P7**）[38]。本触媒系では、有機光酸化還元触媒であるフェノチアジン（PTH）が、酸化還元活性エステル **1c** と EDA 錯体 **D** を形成する。光照射下で EDA 錯体 **D** から誘導されたラジカルイオン対 **D** は、炭素中心ラジカルとラジカルカチオン PTH$^{\cdot+}$を生成した。炭素中心ラジカルと PTH$^{\cdot+}$の再結合によりカチオン種 **III** が得られ、続くアルコール **17** からの求核攻撃により、エーテル **18** が生成した。

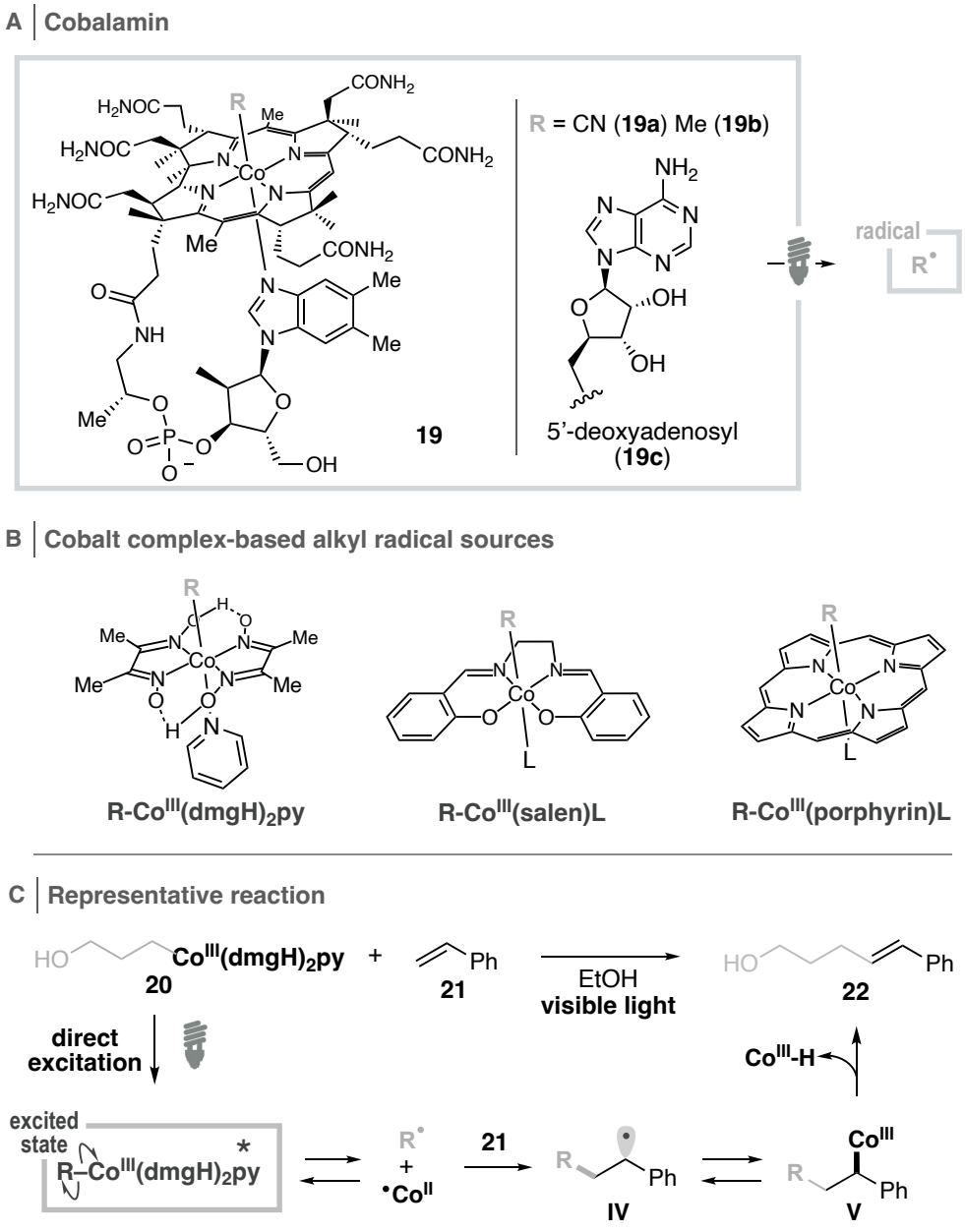


Scheme P7. Organophotoredox catalyst enabling radical polar crossover via π-stacking-driven formation of an EDA complex.

反応基質の直接光励起に基づく分子変換

EDA 錯体を介した合成戦略は優れた方法論であり、最近の光合成化学の発展に大きく貢献しているが、可視光照射下で反応基質を直接励起する手法は、EDA 錯体形成や高価な光酸化還元触媒を必要としないため、炭素中心ラジカルの発生に最も直截的であるといえる。古典的には、ビタミン B12 が可視光で直接励起され、炭素–コバルト結合の均等開裂を介して炭素中心ラジカルを生成できる最も研究されている分子である（**Scheme P8A**）[39]。Co–C 結合を含む化合物群には、シアノ、メチル、5'-デオキシアデノシルコバラミン（**19a–c**）が含まれる。その中でも、**19b** と **19c** に含まれる比較的反応性の高い Co–C 結合は、酵素反応におけるラジカル源として機能し[39b]、このラジカル生成は光照射によって促進される。光励起コバラミンについては、構造特性、反応性、有機合成、高分子合成、ケージドプローブへの応用など、幅広い分野で数多く報告されている。さらに、コバラミンを基本骨格として、可視光で直接励起される有機コバルト錯体も報告されている（**Scheme P8B**）。例えば、アルキル基を持つ(ピリジン)ビス(ジメチルグリオキシマト)コバルト(III)、Co(dmgH)$_2$py **20**[39c] とオレフィン **21** との反応は、可視光照射下で溝呂木・Heck 型生成物 **22** を与えた（**Scheme P8C**）[39d]。R-Co(dmgH)$_2$py **20** の

直接光励起により反応が開始し、C–Co 結合の均等開裂が起こり、長寿命 Co^{II} 錯体と短寿命炭素中心ラジカルが形成される。生成した炭素中心ラジカルと Co^{II} 錯体との逆反応



Scheme P8. Direct photo-excitation of bioinspired cobalt-based complexes.

も、Co^{II} 錯体に由来する長寿命ラジカル効果（PRE）により、効率的に起こり、アルキル Co^{III} 錯体を形成する。オレフィン **21** への選択的なラジカル付加は、ホモカップリングより優先して進行する。ベンジルラジカル **IV** と Co^{II} の再結合により、中間体としてベンジル Co^{III} 錯体 **V** が形成され、β-水素脱離により生成物 **22** が得られる。光化学の引

き金となる最も基本的な要因は、光化学第一法則（Grotthuss-Draper 則）に従って、光を吸収する分子、中間体、または触媒のみが可視光励起を開始できることである。直接光励起では、反応基質またはその場で形成した中間体が自ら光を吸収し、獲得したエネルギーが結合切断に関与する。こうして結合が切断されると、光誘起ラジカル種が生成する（**Figure P5**）。

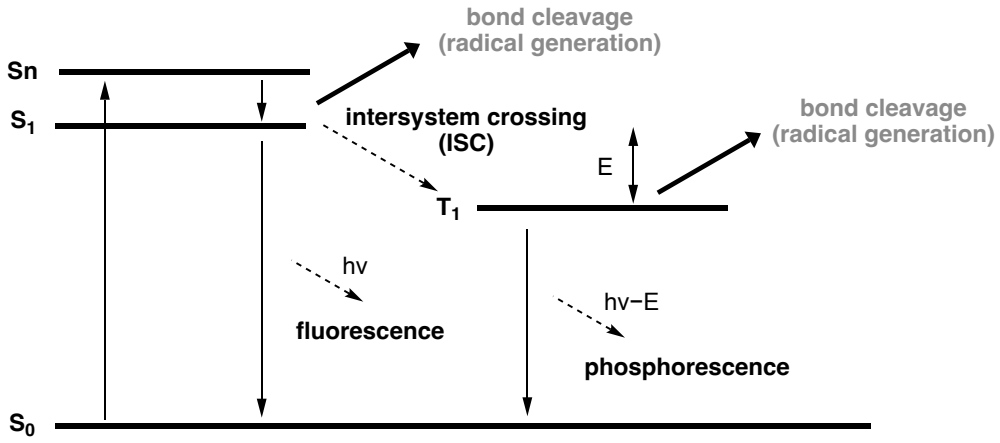
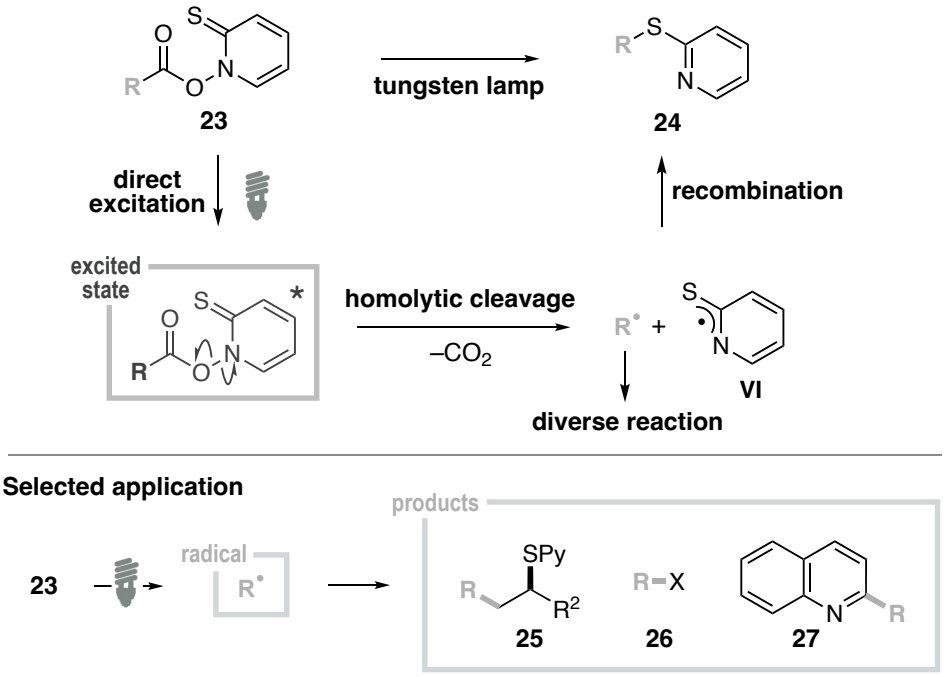


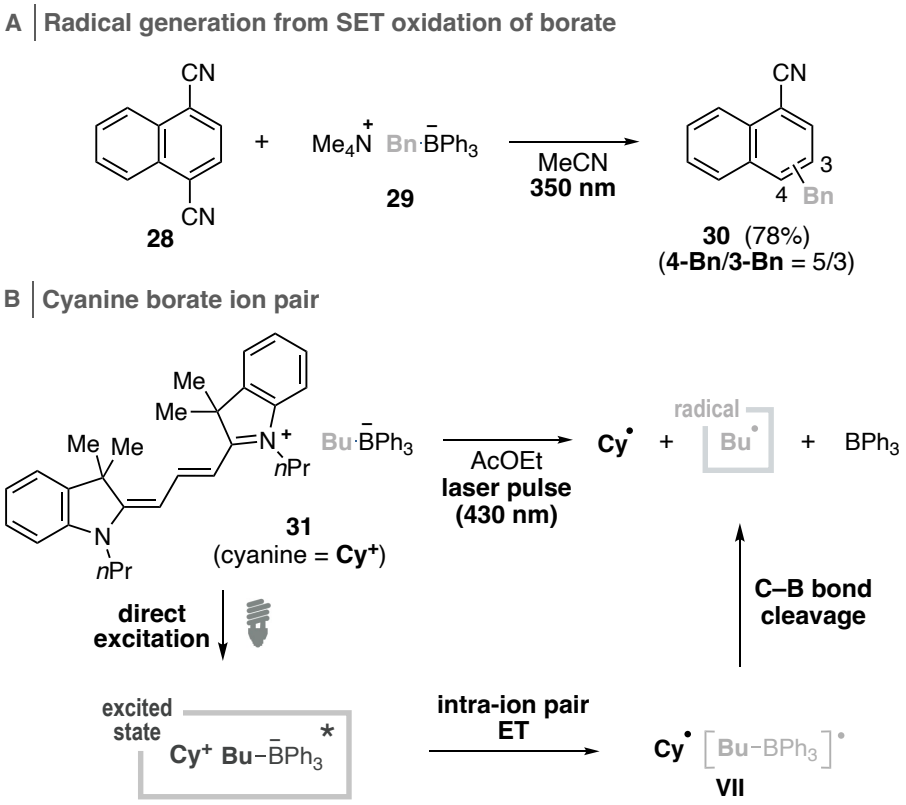
Figure P5. Jablonski diagram of bond cleavage following direct excitation.

遷移金属を用いない初期の例として、N-アシルオキシ-ピリジン-2-チオン、いわゆる Barton エステル **23** は、タングステンランプ照射下で脱炭酸を伴った転位により、2-ピリジルスルフィド **24** を生成した（**Scheme P9**）[19,40]。本反応は、スルフィド **24** の単純な合成に加えて、オレフィンのビシナルアルキルチオ化反応による **25** の生成[40a]、ハロゲン化反応による **26** の生成[40b]、Minisci 反応による **27** の生成[40c]など、さまざまなラジカル化学反応に応用されている。



Scheme P9. Alkyl radical generation from direct photo-excitation of Barton ester.

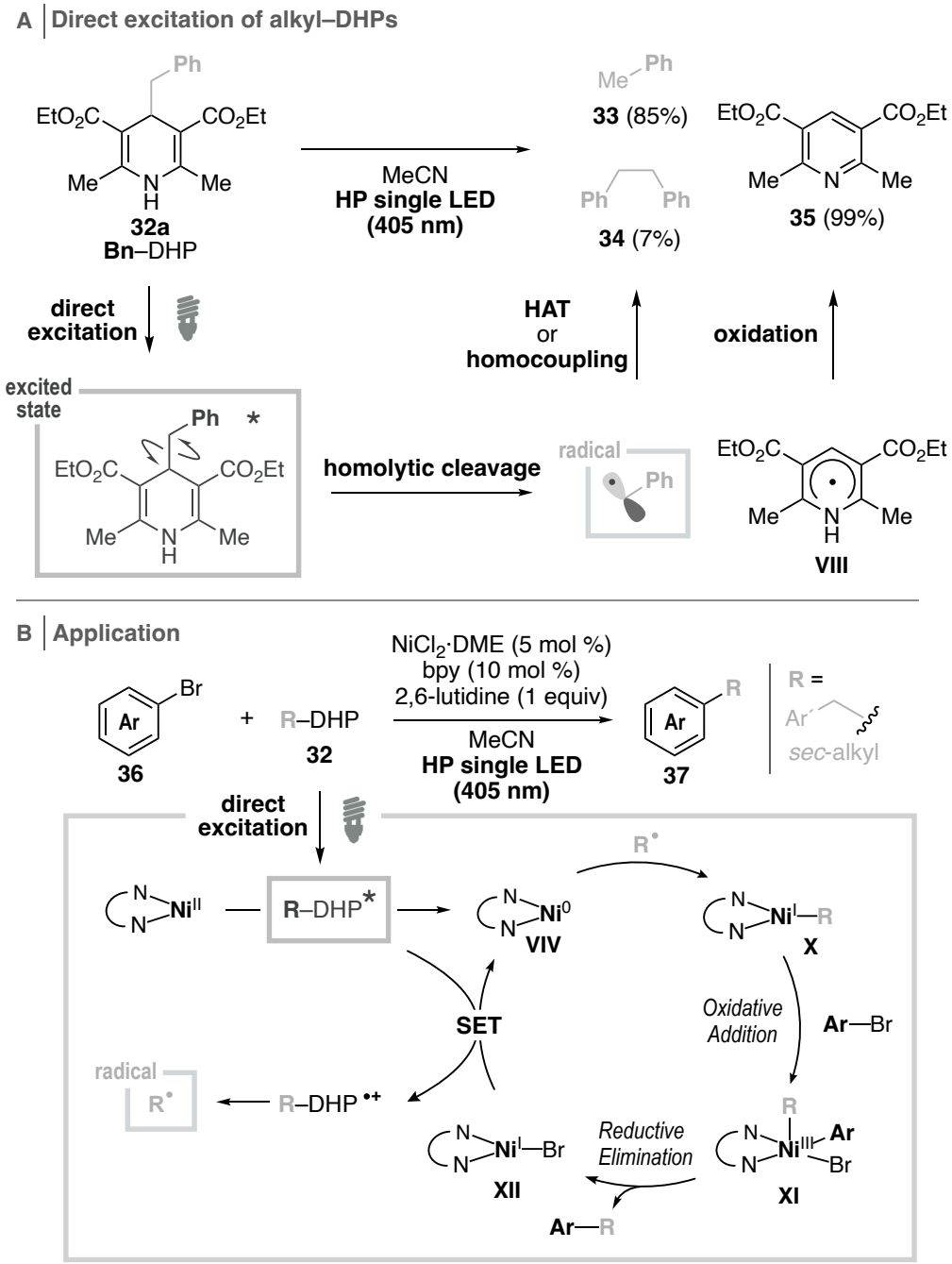
Schuster らは、一電子酸化に続くホウ酸塩の C–B 結合開裂に基づく、ホウ素アート錯体からの光駆動型炭素中心ラジカル生成について報告している [41]。彼らは、1,4-ジシアノナフタレン **28** とアルキル(トリアリール)ボレート **29** との反応により、350 nm の照射下で脱シアノアルキル化が起こり、位置異性体混合物 **30** が生成することを見出した。この生成物から、光照射によって **28** が活性化され、その励起種がホウ素アート錯体との SET によって還元され、炭素中心ラジカルが生成したことが示された（**Scheme P10A**）[41a]。この反応に付随して、Schuster らは、ホウ素アート錯体の対カチオンを可視光吸収性分子と置換することで、ホウ素アート錯体自身の直接励起に基づき、対応する炭素中心ラジカルを生成できると報告した。実際、対カチオンをインドカルボシアニン（Cy^+）と置換してブチルホウ素アート錯体 **31** を調製すると、430 nm のレーザーパルス照射下でホウ素アート錯体の直接励起が起こった。励起された $Cy^+[BuBPh_3]^-$は、イオン内対電子移動を介してシアニンラジカル $Cy^{\cdot}$とボラニルラジカル **VII** に変換された（**Scheme P10B**）[41b]。ボラニルラジカルアニオンのフラグメント化により、トリフェニルボランとブチルラジカルが得られ、適切なモノマーの存在下で重合 反応に適用できた。



Scheme P10. (A) Radical generation from single electron oxidation of alkylborate. (B) Exchanging the borate countercation enabled direct excitation under visible-light irradiation.

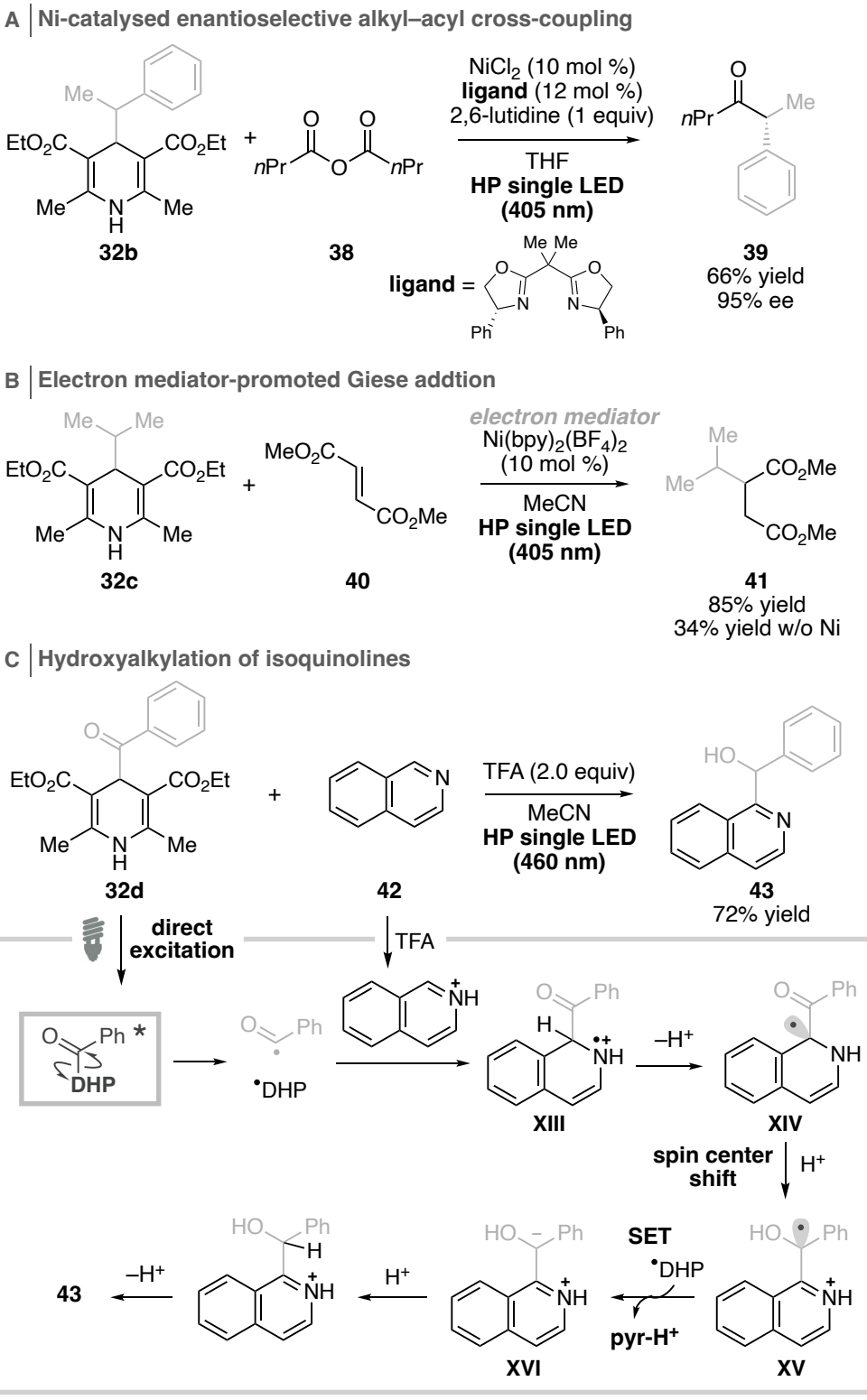
4-アルキル-1,4-ジヒドロピリジン（アルキル-DHP）は、光酸化還元触媒の還元的ラジカル前駆体であるにもかかわらず（**Figure P4**）、Melchiorre らは、アルキル-DHP が可視光照射下で直接励起され、対応する炭素中心ラジカルを生成できることを発見した[42a]。MeCN 中のベンジル-DHP **32a** を HP シングル LED（405 nm）照射下で直接励起すると、DHP ラジカル中間体 **VIII** の酸化からトルエン **33**（85%）、1,2-ジフェニルエタン **34**（7%）、定量的にピリジン誘導体 **35** が生成した（**Scheme P11A**）。収率は低いものの、1,2-ジフェニルエタン **34** が観測されたことから、ベンジルラジカルの介在が示唆された。このプロトコルには高出力の光源が必要であるが、Ni 触媒を用いた臭化アリール **36** とアルキル-DHP **32** のクロスカップリングは、外部の光酸化還元触媒を用いずに、一電子トランスメタル化[42b]に基づいて進行する（**Scheme P11B**）。光励起されたアルキル-DHP は強力な還元剤（$E(32^{\cdot+}/32^{*}) \approx -1.6$ V vs. Ag/Ag^{+} in CH_3CN）として働けるため、アルキル-DHP **32** の励起状態による一電子還元（$Ep(Ni^{II}/Ni^{0}) = -1.2$ V vs. SCE in DMF）を介して活性な Ni^0 触媒 **VIV** が生成し、炭素中心ラジカルが得られる。生成した炭素中心ラジカルと Ni^0 触媒 **VIV** との反応により、アルキル–Ni^I 錯体 **X** が形成し、続いて臭化アリール **36** が酸化的付加して **XI** を形成する。**XI** からの還元的脱離により、Ni^I-Br 錯体 **XII** とクロスカップリング生成物が得られ、一電子還元により活性な Ni^0 触媒 **VIV** と炭素中心

ラジカルが再生される。この先駆的な研究により、反応基質の直接光励起[42c]によって、光酸化還元触媒を用いない反応系を構築できることが実証された。



Scheme P11. (A) Radical generation *via* direct excitation of alkyl-DHPs. (B) Ni-Catalyzed cross-coupling based on direct excitation of alkyl-DHP.

Melchiorre らは、上記の方法論をいくつかの変換に応用した（**Scheme P12**）[43]。キラル配位子としてビス(オキサゾリン)を有する触媒量の Ni 錯体の存在下、可視光照射下で、第二級ベンジル-DHP **32b** とアルキルカルボン酸無水物 **38** を用いて、エナンチオ選択的アシル–アルキルクロスカップリングを進行させ、キラル生成物 **39** を得た（**Scheme P12A**）[43a]。その後、アルキル-DHP **32c** の直接励起に基づく Giese 付加が報告され、この系では、$Ni(bpy)_3BF_4$ が触媒的な電子メディエーターとして働くことで、効率よく進行した。この Ni 錯体は可視光（405 nm）をほとんど吸収せず、光励起されたアルキル-DHP によって還元される（$Ep(Ni^{II}/Ni^{I}) = -1.35$ V vs. SCE）（**Scheme P12B**）[43b]。また、アシル-DHP はアルキル-DHP よりも長波長の 460 nm で直接励起されることも見いだした。アシル-DHP **32d** を 460 nm の可視光照射下でイソキノリン **42** との反応に適用すると、通常とは異なる Minisci 反応が進行し、ヒドロキシアルキル化生成物 **43** が得られる（**Scheme P12C**）[43c]。プロトン化イソキノリンと、直接光励起アシル-DHP から生成したアシルラジカルとの反応により、ラジカルカチオン **XIII** が得られ、続いて脱プロトン化が起こり、比較的安定な α-アミノラジカル **XIV** に変換された。その後、スピン中心シフトが起こり、再芳香族化によって **XV** が形成された。DHP ラジカル（$DHP^{\cdot}$）による **XV** の一電子還元は、対応するピリジニウムカチオン $pyr\text{-}H^{+}$とアニオン **XVI** を与え、続くプロトン移動と脱プロトン化により最終生成物 **43** が得られた。



Scheme P12. Applications of alkyl-DHP protocol. (A) Ni-catalyzed enantioselective alkylation of carbonate ester. (B) Electron mediator-promoted Giese addition. (C) Hydroxyalkylation of isoquinoline *via* spin center shift.

本論概要

可視光励起ホウ素アート錯体の設計とクロスカップリング反応への適用（第 1 章）

分子内にホウ素を有する五環性化合物8,9-dioxa-8a-**bora**benzo[*fg*]tetra**cene**（boracene）から得られるホウ素アート錯体を設計・合成した。本ホウ素アート錯体は、boraceneに対して、有機リチウムあるいはグリニャール反応剤を作用させることで、定量的に得られ、空気や水中でも取り扱い可能である。さらに、可視光を照射することで直接光励起が起こり、励起状態において、優れた炭素中心ラジカル生成能および一電子移動能を獲得するため、脱シアノアルキル化反応、Giese反応、およびNi触媒を用いた二成分および三成分カップリング反応など種々の炭素–炭素結合形成反応へと展開できた（**Figure P6**）。

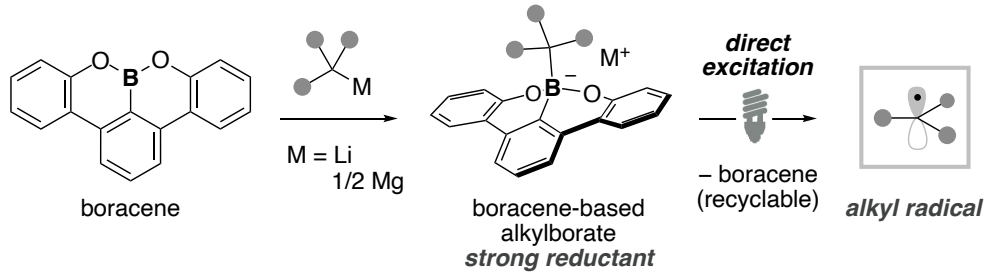


Figure P6. Generation of an alkyl radical through direct excitation of boracene-based alkylborates.

可視光励起ホウ素アート錯体を用いた N-ヘテロ環カルベン触媒反応（第 2 章）

有機ホウ素アート錯体の可視光励起を活用した、N-ヘテロ環カルベン（NHC）触媒反応を開発した。可視光照射下、NHC触媒を用いることで、ホウ素アート錯体とカルボン酸誘導体であるアシルイミダゾールのクロスカップリングが進行し、かさ高いケトンを

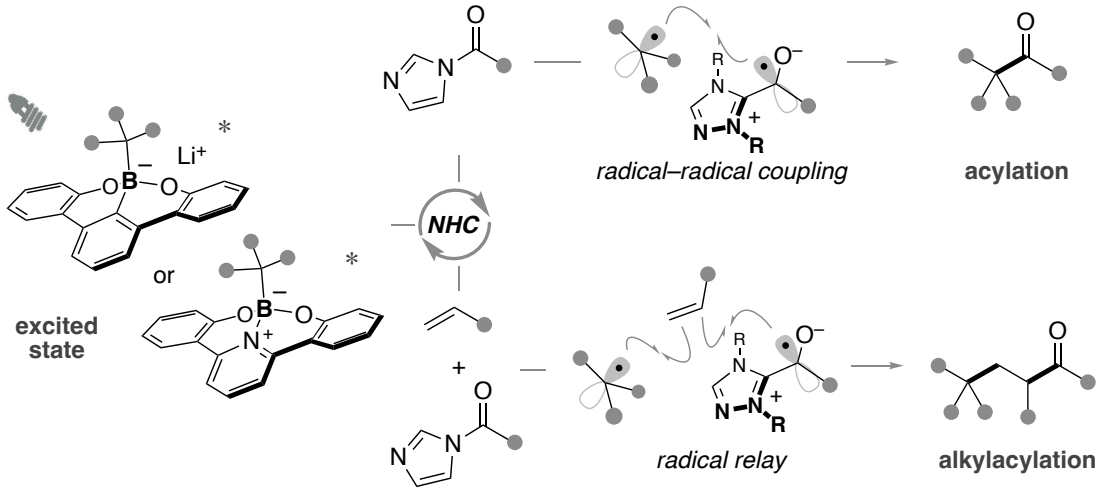


Figure P7. Light-driven *N*-Heterocyclic carbene catalysis using alkylborates.

与える。本触媒系では、NHC触媒とアシルイミダゾールが反応し、アシルアゾリウム中間体が形成する。このアシルアゾリウム中間体と可視光励起されたホウ素アート錯体の間で一電子移動が起こり、ケチルラジカルとアルキルラジカルがそれぞれ形成される。これら二種類のラジカル種のラジカル–ラジカルカップリングにより、目的生成物を与えるとともに、NHC触媒が再生する。本触媒系は、ホウ素アート錯体とアシルイミダゾールを用いたアルケンのアルキルアシル化にも適用可能であった（**Figure P7**）。

可視光駆動型 N-ヘテロ環カルベン触媒を用いたアルケンのアミドアシル化反応（第 3 章）

可視光駆動型プロトン共役電子移動（PCET）に基づく NHC 触媒系を用いた、アルケンのアミドアシル化反応を開発した。可視光照射下、光酸化還元触媒と塩基を用いることで、酸化的 PCET 機構に基づき、分子内にアルケンを有するアミド化合物の窒素中心にラジカルが発生する。生じた窒素中心ラジカルは速やかに分子内環化が進行し、アルキルラジカルを与える。一方で、アシルイミダゾールと NHC 触媒から生じるアシルアゾリウム中間体に対する還元状態の光酸化還元触媒からの一電子還元により、ケチルラジカルが生じる。これら各々の触媒サイクルから生じた２種類の異なるラジカル種同士がラジカル–ラジカルカップリングを起こすことで、かさ高い β-アミドケトン体がジアステレオ選択的に得られる（**Figure P8**）。

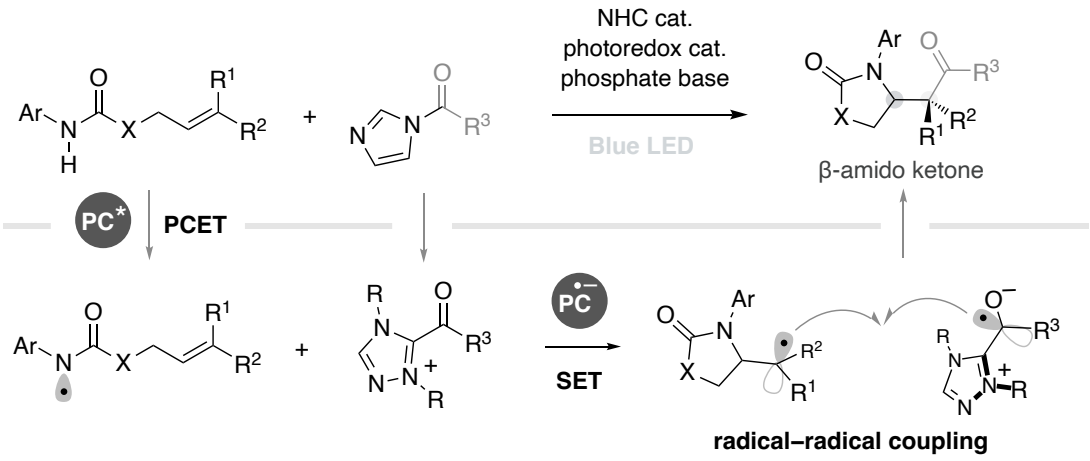


Figure P8. *N*-Heterocyclic carbene-catalyzed radical-radical coupling incorporating PCET

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第１章　可視光励起ホウ素アート錯体の設計とクロスカップリング反応への適用

第１節　着想背景および作業仮説

序論でも述べた通り、可視光を利用した化学変換は、有機ラジカル種を経由することで、かさ高い有機基の導入、高い化学選択性を実現できる。また太陽光などの光エネルギーを利用した分子変換を可能にすることから、高難度な化学変換開発と環境調和型プロセスの両面から高い注目を集めている。近年発展している光酸化還元触媒化学は、炭素中心ラジカルの極めて温和な生成と自在な制御を実現するため、世界的な潮流になっている。

一方で、光酸化還元触媒を必要としない可視光エネルギーを利用した炭素中心ラジカル生成法の開発も並行して精力的に開発されている。例えば、反応基質同士が静電的相互作用により、一電子授受が可能となるEDA錯体の形成に基づく戦略が挙げられる。このEDA錯体が可視光により励起されて炭素中心ラジカルが生成し、特有の分子変換が可能となっている。しかし、これはEDA錯体の形成が必須となるため、基質の制限が大きく、汎用性に乏しい。ごく最近、反応基質として4位にアルキル基を有するジヒドロピリジン類を用いると直接励起され、光酸化還元触媒やその他の添加物を必要とすることなく、炭素中心ラジカルを生じることが報告されている（**序論, Scheme P11, 12**）。これは直截的で魅力的な炭素中心ラジカル生成法であるものの、生成可能な炭素中心ラジカルに制限があり、また強力な光源が必要であった。

Schusterらは有機ホウ素アート錯体の光化学における先駆的な例として、ホウ素分子の対カチオンにシアニン色素化合物を有する複合体を調製し、これが可視光照射により対応する有機ラジカルが生成することを報告している（**序論, Scheme P10**）。すなわち、光励起された対カチオンからイオン内対電子移動、続く炭素–ホウ素結合の均等開裂により対応する炭素中心ラジカルが形成する。しかしながら、この反応形式ではイオン対間での電子移動を経由するため、その電子移動効率や逆電子移動を考慮する必要があった。

このような背景を踏まえ、分子内にホウ素原子を含む五環性化合物8,9-dioxa-8a-**bora**benzo[*fg*]-tetra**cene**（**1**, **ボラセン**）から誘導されるホウ素アート錯体**2**に着目した（**Figure 1-1**）。このホウ素アート錯体はボラセン**1**と有機リチウム試薬あるいはグリニャール反応剤との反応により、定量的に得られ、空気や水中で安定である上、特別な精製操作を必要とせずに、続く化学変換へと適用可能であった。本ホウ素アート錯体は母骨格の広いπ-共役構造に基づき、可視光により直接励起され、より効率的に光エネルギーを活用できるため、より網羅的な炭素中心ラジカルの生成を実現できると想定した。

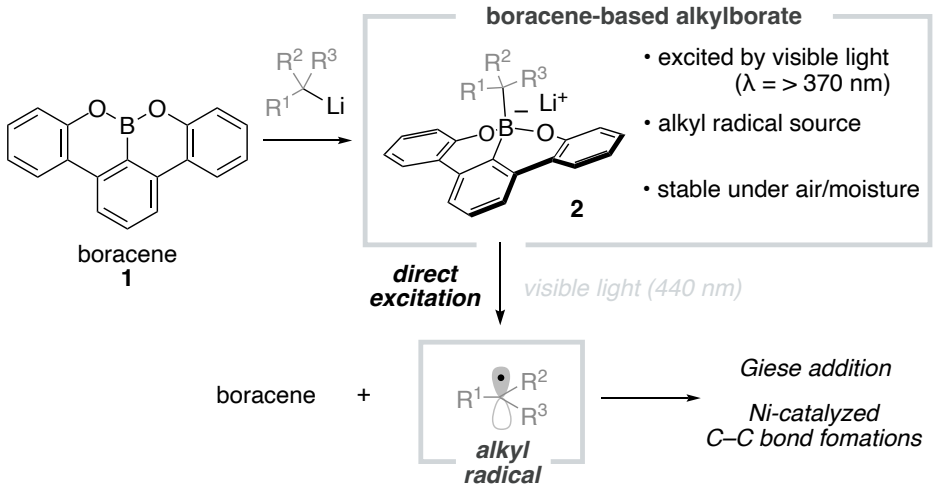


Figure 1-1. An alkyl radical from direct excitation of boron-based precursor.

第 2 節　ホウ素アート錯体の構造および光物性解析

ボラセン **1** は benzo[*fg*]tetracene 骨格が部分的に酸素–ホウ素–酸素結合に置換された構造であり、高い平面性と剛直性、化学安定性を有する。まず、ボラセン **1** と *t*-ブチルリチウムより調製した第三級アルキルホウ素アート錯体の構造および光感受性に対する解析を行った[1]。このホウ素アート錯体 **2a** は、単結晶 X 線結晶構造解析よりホウ素原子が四配位アート錯体となることで四面体構造を有していることが判明した。また、このホウ素アート錯体 **2a** の２つの酸素原子がリチウムカチオンに配位しており、そのリチウムカチオンに対して２または３分子のテトラヒドロフラン分子が配位することで、この錯体の安定性に寄与していることが示唆された（**Figure 1-2**）。

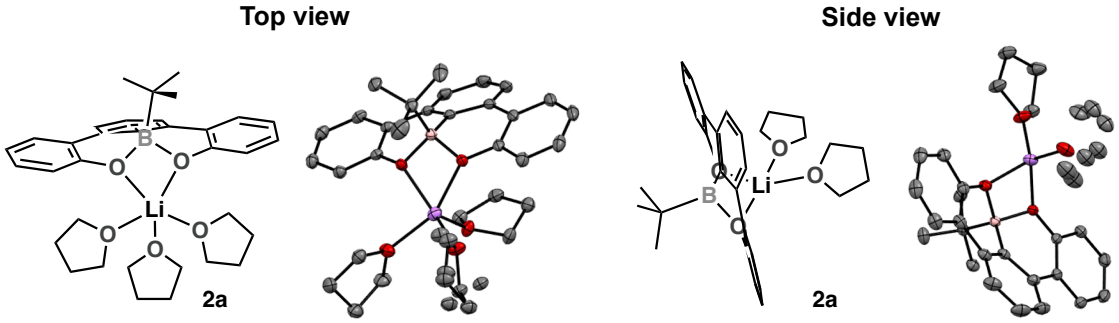


Figure 1-2. X-ray structure of boracene-based alkylborate **2a**.

このホウ素アート錯体 **2a** が光化学反応において適切な反応基質であるかを検討するべく光物性解析を行った。紫外可視吸光スペクトルにおいて、緑線で示されたボラセン **1** の吸収極大波長は 335 nm（20 mM in DMA）である一方で、黄線で示されたホウ素アート錯体 **2a** の吸収スペクトルはおよそ 370 nm に長波長シフトしており、その裾野が

400 nm に達していた。また励起波長 370 nm において対応する蛍光スペクトルが、最大発光波長（410 nm）に得られた（**Figure 1-3**）。

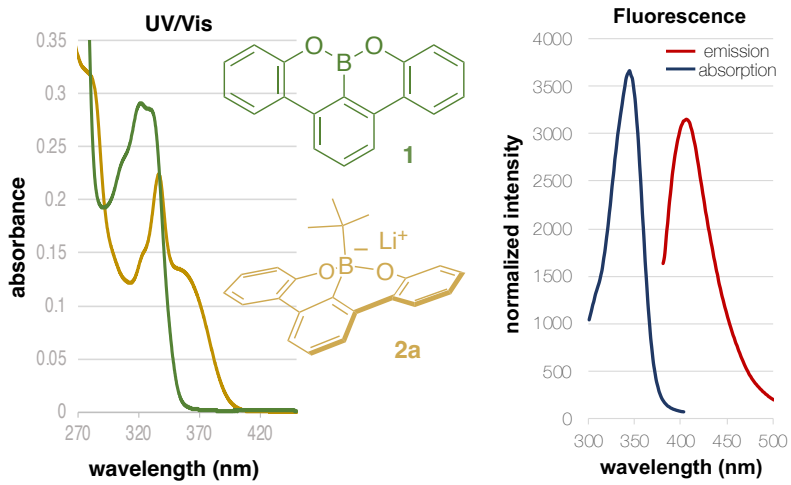


Figure 1-3. Photophysical property of **2a**.

このホウ素アート錯体 **2a** の吸収波長の長波長シフト化の要因を調査するべく、DFT 計算により HOMO および LUMO をそれぞれ算出した（**Figure 1-4**）。その結果、HOMO-LUMO のエネルギーギャップが 4.451 eV とかなり小さい値が得られた。これは上述の単結晶 X 線結晶構造解析の結果を踏まえると、本ホウ素アート錯体が平面性を崩した構造を有しているために、HOMO が炭素–ホウ素結合に、一方で LUMO が母骨格の benzo[*fg*]tetracene 部分に局在化する、すなわち分子内電荷移動錯体として機能することで、長波長での光励起が可能となると推測される [2]。

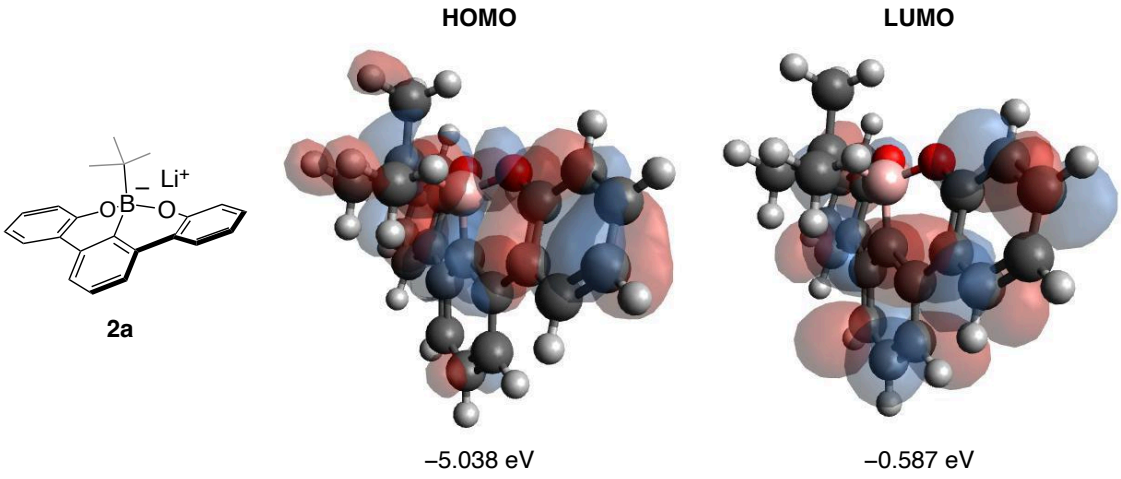


Figure 1-4. Kohn–Sham orbitals of **2a** in the S0 states, calculated at the B3LYP/6-31++G(d,p) level.

このホウ素アート錯体 **2a** の励起状態における一電子移動能に関する知見を得るために、サイクリックボルタンメトリーによる酸化還元電位の測定を行った（**Figure 1-5**）。このホウ素アート錯体 **2a** の酸化還元電位は比較的高い値（+0.78 V vs. SCE in MeCN）を与え、有機合成に広く用いられているアルキルトリフルオロボレート塩（<+1.26 V vs. SCE in MeCN）と比べて、基底状態においても高い還元能を示した。上述した蛍光スペクトルとサイクリックボルタンメトリーの結果を用いて、Rehm−Weller 式より、励起状態におけるホウ素アート錯体 **2a** の酸化還元電位[E(**2a**$^{\bullet+}$/**2a***)]は−2.2 V 程度であることが推定された[3]。

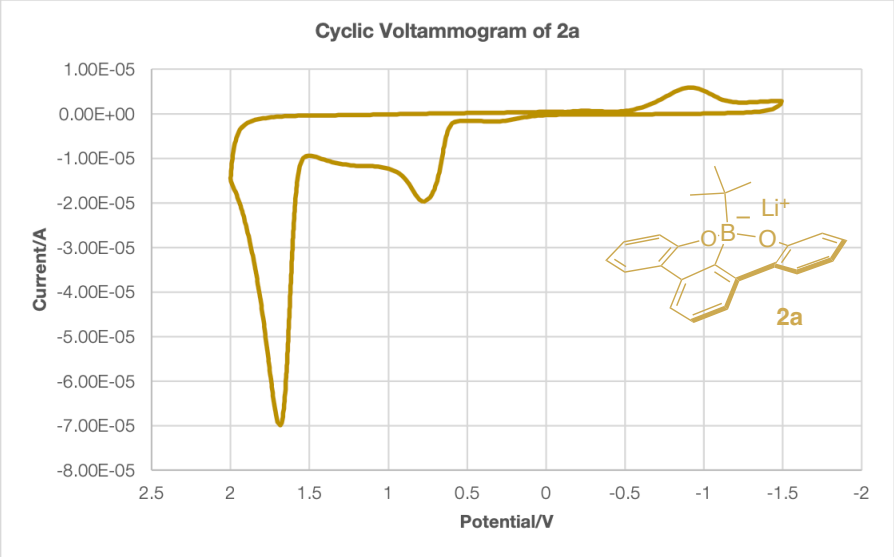
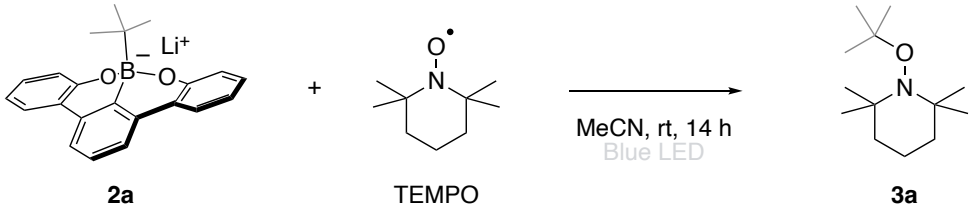


Figure 1-5. Cyclic voltammogram of **2a**.

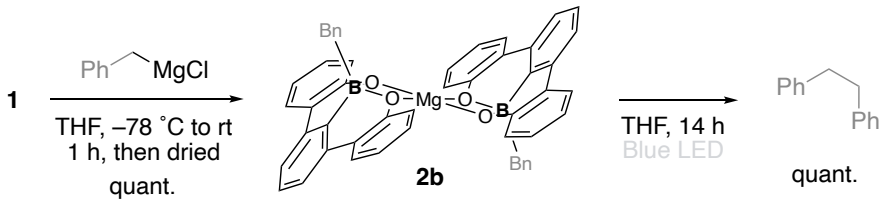
第 3 節　ホウ素アート錯体の励起状態における反応性の評価実験

ボラセン由来のアルキルホウ素アート錯体の対応するアルキルラジカルの生成能を評価するべく、いくつかの実験を行った。可視光照射下、ホウ素アート錯体 **2a** とラジカル捕捉剤である TEMPO を反応させたところ、*t*-ブチルラジカルが捕捉された付加体 **3a** が 64%収率で得られた（**Scheme 1-1**）。さらに、ボラセン **1** とベンジルマグネシウムクロリドとの反応によりホウ素アート錯体 **2b** が定量的に得られ、単結晶 X 線結晶構造



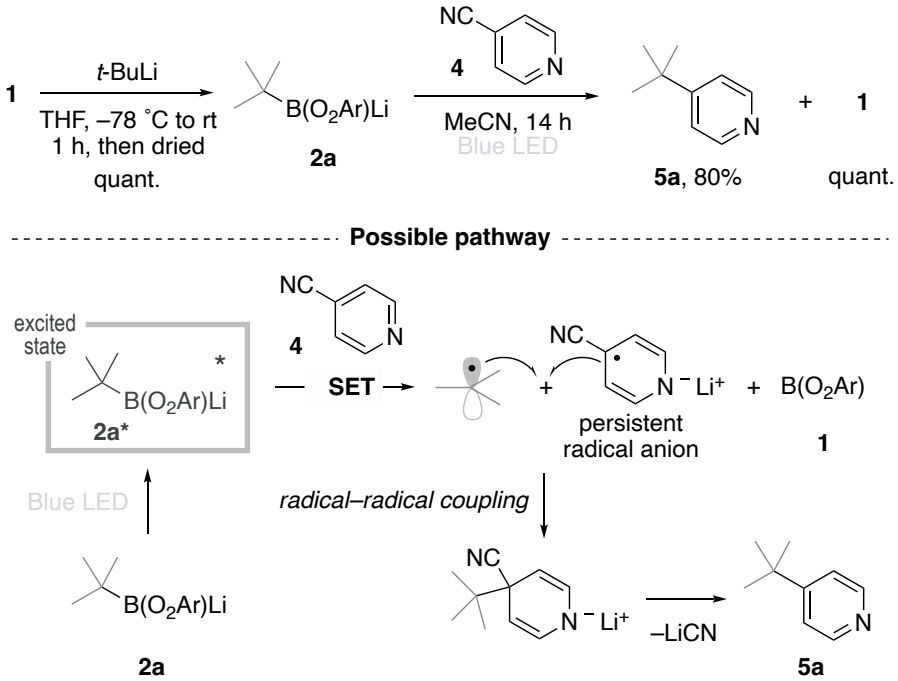
Scheme 1-1. Radical trap experiment.

解析より 1 分子の Mg に対して、2 分子のボラセンが配位した構造を有することが確認された。このベンジルホウ素アート作体に対して、添加物を加えずに光照射を行ったところ、二量化体であるビベンジルが定量的に得られた（**Scheme 1-2**）。これらの結果より、このホウ素アート錯体は可視光照射のみで、対応する炭素中心ラジカルを生成することが示唆された。



Scheme 1-2. Dimerization via direct excitation.

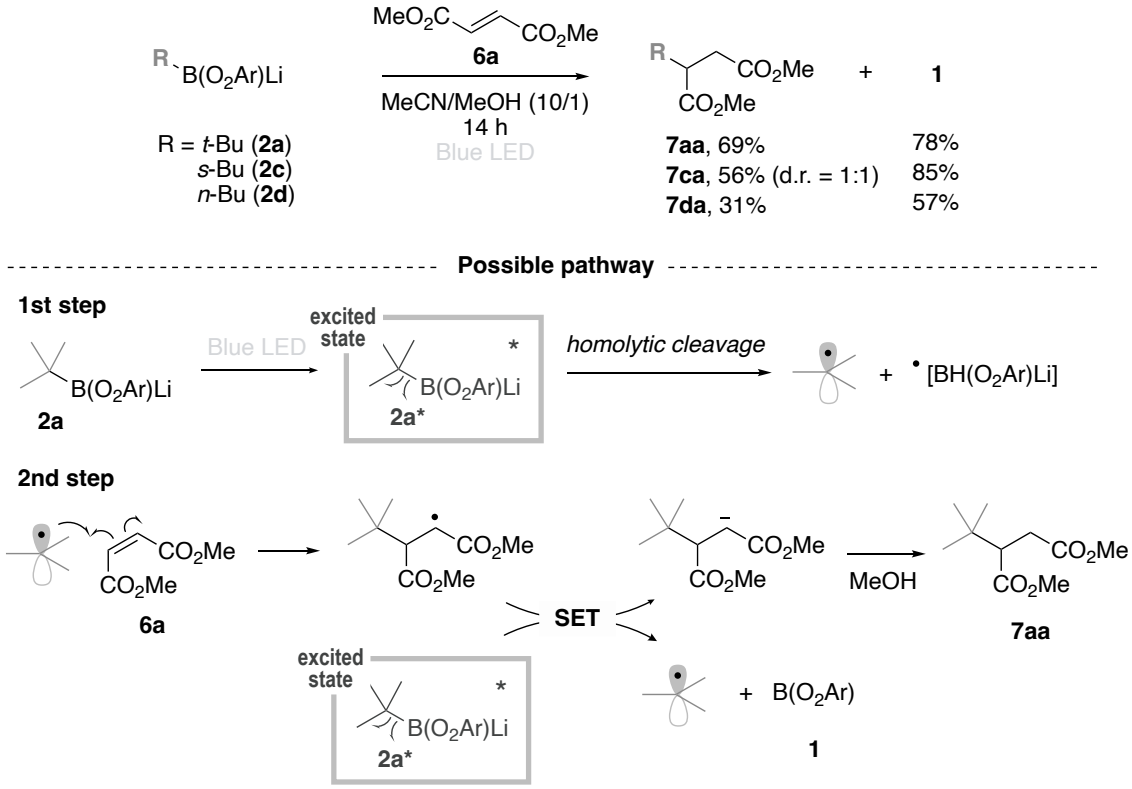
続いて、ホウ素アート錯体 **2a** の一電子移動能を評価するべく 4-シアノピリジン **4**（$E_{1/2}$ = −1.75 V vs. SCE in MeCN）との光反応を行った[4,5]。可視光照射下、アセトニトリル溶媒中でホウ素アート錯体 **2a** と 4-シアノピリジン **4** を反応させたところ、脱シアノアルキル化体 **5a** を 80%の収率で与え、ボラセン **1** が定量的に回収された（**Scheme 1-3**）。すなわち、光励起されたホウ素アート錯体 **2a** から 4-シアノピリジン **4** に対して一電子移動が進行し、それぞれ長寿命なシアノピリジルラジカルアニオン種と短寿命な *t*-ブチル



Scheme 1-3. Decyanoalkylation of 4-cyanopyridine.

ラジカルが生じ、それらのラジカル同士でラジカル–ラジカルカップリングが進行することで、生成物 **5a** を与えたと推定される [6]。

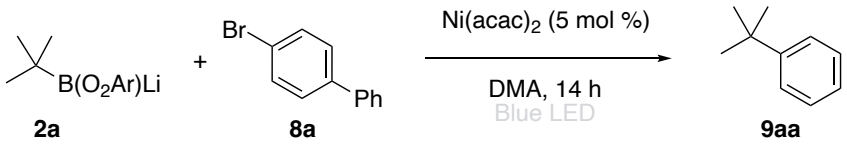
また、このアルキルホウ素アート錯体を Giese 付加反応へと適用した [7]。可視光照射下、*t*-ブチル **2a**、*s*-ブチル **2c**、*n*-ブチルホウ素アート錯体 **2d** をそれぞれフマル酸ジメチル **6a** と反応させたところ、対応する 1,4-付加体が高い収率およびボラセン回収率で得られた（**Scheme 1-4**）。したがって、このホウ素アート錯体からのアルキルラジカルの生成には、一電子酸化あるいは光分解を介して進行することが示唆された。



Scheme 1-4. Giese addition.

第 4 節　Ni 触媒によるクロスカップリング反応への適用

上記の測定および実験結果に基づき、可視光照射下、ホウ素アート錯体 **2** を Ni 触媒によるハロゲン化アリールとのクロスカップリング反応へと展開した。可視光照射下、DMA 溶媒中で $Ni(acac)_2$（5 mol %）存在下、ホウ素アート錯体 **2a**（0.3 mmol）、4-ブロモビフェニル **8a**（0.2 mmol）を反応させたところ、目的の *t*-ブチル化体 **9aa** が単離収率 76%で得られた（**Table 1-1**, **Entry 1**）。本反応において、照射する光源としてより短波長の 390 nm の光源を用いた場合には収率が低下し、可視光を照射しない条件では全く反応が進行しなかった（**Table 1-1**, **Entries 2** and **3**）。また、用いるラジカル源を *t*-ブチルトリフルオロボレート塩やビスピナコラートボランから誘導したホウ素アート錯体を用



Entry	Deviation from standard conditions[a]	Yield (%)
1	none	76
2	**390 nm light** instead of 440 nm	40[b]
3	**no light**	0
4	***tert*-BuBF$_3$K** instead of **2a**	0
5	***tert*-BuBF$_3$K** instead of **2a**[c]	0
6	**[*tert*-Bu(Ph)Bpin]Li**[d], instead of **2a**	0
7	**Ni(cod)$_2$** instead of Ni(acac)$_2$	trace
8	**Ni(cod)$_2$**, **acetylacetone**[e], **KOtBu**[e], instead of Ni(acac)$_2$	59[b]
9	**Ni(HFPD)$_2$**[f] instead of Ni(acac)$_2$	9[b]
10	**Ni(TMHD)$_2$**[g] instead of Ni(acac)$_2$	74[b]
11	**Fe(acac)$_2$** instead of Ni(acac)$_2$	0
12	**Pd(acac)$_2$** instead of Ni(acac)$_2$	0
13	**Co(acac)$_2$** instead of Ni(acac)$_2$	0
14	**Cu(acac)$_2$** instead of Ni(acac)$_2$	0

[a]Reaction was carried out with **2a** (0.12 mmol), **8a** (0.1 mmol), catalyst (5.0 μmol) in DMA (1 mL) under Kessil PR160L 440 nm irradiation for 14 h. [b]^{1}H NMR yield based on **8a**. [c]10 mol % of Ni(TMHD)$_2$, ZnBr$_2$, and, 1.0 equiv of K_2HPO_4 were used. [d]The borate was prepared from precomplexation of *tert*-BuBpin with PhLi. [e]10 mol % was used. [f]HFPD = 1,1,1,5,5,5-hexafluoropentane-2,4-dione. [g]TMHD = 2,2,6,6-tetramethyl-3,5-heptanedione.

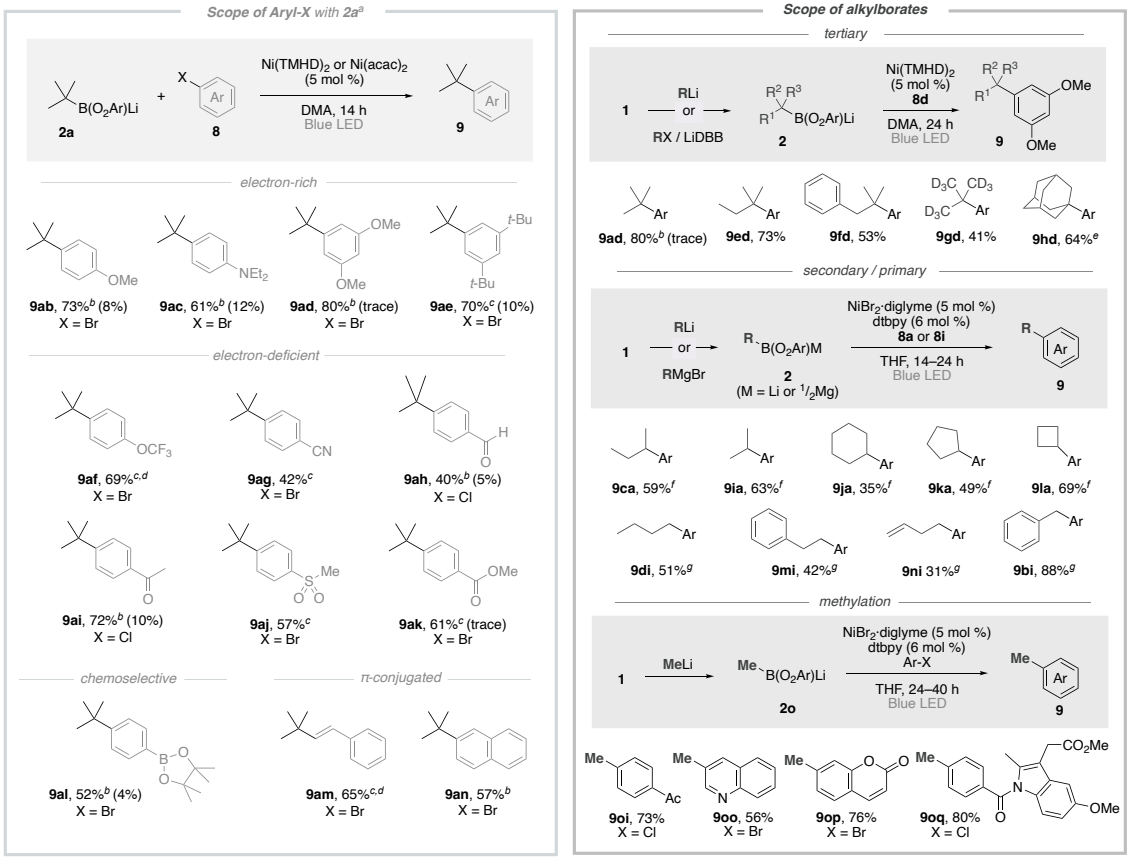
Table 1-1. Optimization of Ni-catalyzed alkylation.

いた場合には、全く反応が進行しなかった（**Table 1-1**, **Entries 4−6**）。Ni 触媒として他の Ni 錯体に変更した場合、Ni(cod)$_2$ や Ni(acac)$_2$ 系中調製、より電子不足な Ni(HFPD)$_2$ を用いた際には収率が低下した（**Table 1-1**, **Entries 7−9**）。一方で、Ni(TMHD)$_2$ を用いた際には、最適条件と同等の収率で目的のカップリング反応が進行した（**Table 1-1**, **Entry 10**）。触媒としてその他の遷移金属錯体を用いた際には目的のアルキル化体が全く得られなかった（**Table 1-1**, **Entries 11−14**）。

上記の条件検討で得られた最適条件に基づき、Ni 触媒によるアルキル–アリールクロスカップリング反応における、ハロゲン化アリールおよびアルキルホウ素アート錯体の基質適用範囲の検討を行った（**Table 1-2**）。まず、電子豊富および電子不足なハロゲン化アリールを用いて検討を行った。基質によっては *t*-ブチル基がイソブチル基に異性化

して導入されたカップリング体が低収率ながら副生成物として得られる。Ni 触媒に $Ni(TMHD)_2$ を用いることで、この副反応が抑制されるため、副生成物が有意に観測される基質については、$Ni(TMHD)_2$ を適用している[8]。これまでに Molander らは、Ni/Ir 光酸化還元協働触媒系によるアルキル–アリールクロスカップリング反応を報告している[9]。本反応は、Ni/Ir 光酸化還元協働触媒では適用困難であった電子豊富なハロゲン化アリールに対しても、高収率で目的のアルキル化体が得られた（**9ab**–**9ae**）。また、ピナコールボリル基を有する場合には炭素–臭素結合選択的に目的のカップリング反応が進行した（**9al**）。さらに、β-ブロモスチレンや 2-ブロモナフタレンの場合でも問題なく目的のアルキル化が進行した（**9am**–**9an**）。

続いて、種々のアルキル基を有するホウ素アート錯体の適用範囲について検討を行った。ボラセン **1** と市販の有機リチウム試薬を反応させることで、対応する第三級、二級および一級のアルキル基を有するアルキルホウ素アート錯体が調製可能であった。また

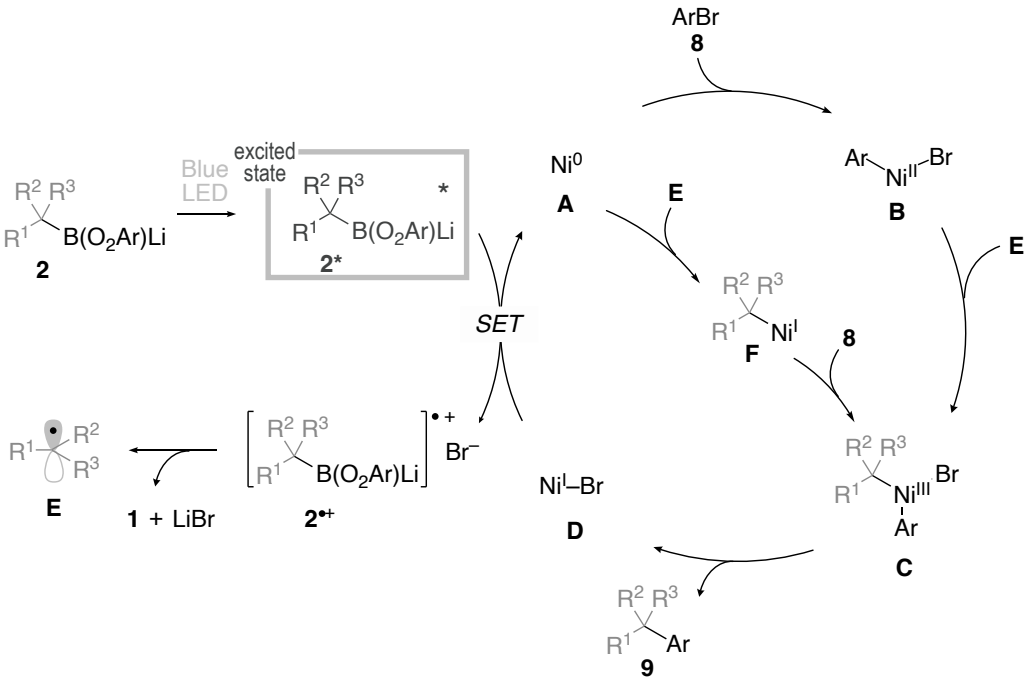


[a]Number in parentheses is NMR yield of isobutylated arenes. [b]$Ni(TMHD)_2$ was used as a catalyst. TMHD = 2,2,6,6-tetramethyl-3,5-heptanedionate. [c]$Ni(acac)_2$ was used as a catalyst. [d]NMR yield. [e]$NiBr_2$·diglyme (5 mol %), 4,4'-di-*tert*-butyl-2,2'-bipyridyl (dtbpy) (6 mol %) and THF solvent were used. [f]Ar = 4-biphenyl. [g]Ar = 4-acetylphenyl.

Table 1-2. Substrate scope of Ni-catalyzed alkylation.

市販で入手困難なアルキルリチウム試薬の場合は、対応するハロゲン化アルキルとリチウム 4,4'-ジ-*t*-ブチルビフェニリド（LiDBB）により調製されるリチウム試薬とボラセン **1** を反応させることで調製できた[10]。これらの単離もしくは用時調製した第三級アルキルホウ素アート錯体を用いることで、対応する非環状および環状の三級炭素が導入可能であった（**9ed**–**9hd**）。また、第二級および第一級アルキルホウ素アート錯体においては、ボラセン **1** と対応するアルキルグリニャール反応剤を反応させることで調製可能であった。それらの第二級および第一級のアルキルホウ素アート錯体を用いた際には、触媒として $NiBr_2$(diglyme)と 4,4'-ジ-*tert*-ブチル-2,2'-ビピリジル（dtbpy）を組み合わせることで、効率よく対応するアルキル化体が得られた（**9ca**–**9bi**）。さらに、本反応系では一般には発生が困難なメチルラジカルが効率よく生成できる。したがって、創薬において重要なユニットであるメチル基を、蛍光分子であるクマリンや医薬品関連物質であるインドメタシンメチルエステルなどのヘテロアレーンに対しても効率よく導入可能であった（**9oi**–**9oq**）[11]。

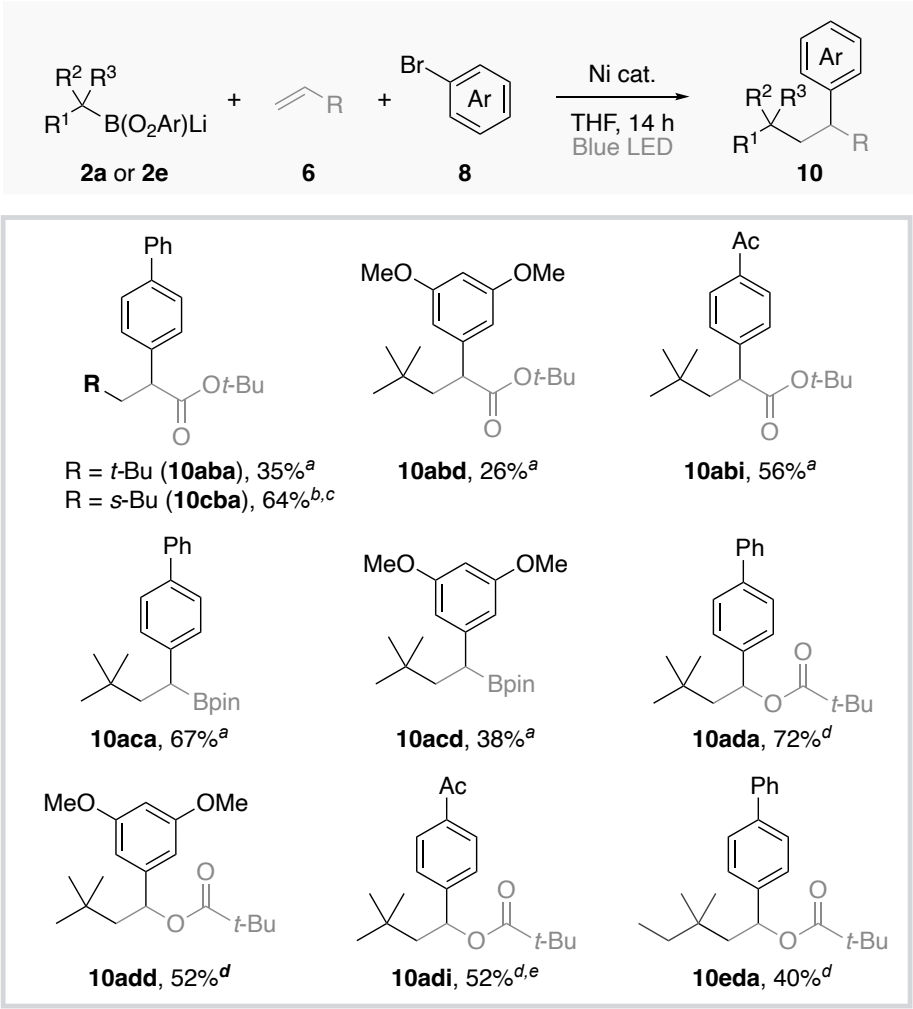
ホウ素アート錯体 **2** の可視光直接励起に基づく Ni 触媒によるアルキル–アリールクロスカップリング反応の推定反応機構を示す（**Scheme 1-5**）。光励起されたホウ素アート錯体 **2***はラジカル前駆体だけでなく一電子還元剤としても機能するため、反応開始段階の Ni^{II} 錯体および Ni^{I} 錯体 **D** を還元するのに十分な一電子移動能を有している（[E(**2a**$^{\bullet+}$/**2a***)] = −2.2 V vs. SCE in MeCN）[12,13]。したがって、励起状態のホウ素アート錯体 **2***からの一電子移動により、活性種 Ni^{0} 錯体 **A** を生じるとともに、ホウ素アート錯体



Scheme 1-5. Possible pathway.

のラジカルカチオン種 **2**$^{\bullet+}$が形成し、続くフラグメント化により炭素中心ラジカル **E** が生じるとともに、ボラセン **1** が再生する。Ni 触媒サイクルとしては、以下の二つの反応機構を推定している。1）Ni^0 錯体 **A** に対する臭化アリール **8** の酸化的付加により、Ni^{II} 錯体 **B** が生じ、続くアルキルラジカル **E** が付加する、2）先に炭素中心ラジカル **E** が Ni^0 錯体 **A** に対して付加し、Ni^{I} 錯体 **F** を形成したのちに、臭化アリール **8** の酸化的付加が進行する。どちらの反応経路においても Ni^{III} 錯体 **C** が生じ、還元的脱離により目的のクロスカップリング体 **9** と Ni^{I} 錯体 **D** が得られる。

Ni 触媒によるクロスカップリング反応と Giese 付加反応の結果（**Scheme 1-4**）を踏まえ、ホウ素アート錯体 **2** をアルケンへの三成分ビシナルアルキルアリール化反応へと適用した（**Table 1-3**）[14]。可視光照射下、THF 溶媒中にて、Ni 触媒を用い、ホウ素アート錯体 **2** とアルケン **6**、臭化アリール **8** を反応させたところ、目的の三成分カップリング体 **10** が得られた。本手法は、第三級および第二級のアルキル基とアリール基を炭素–炭素二重結合に対してそれぞれ位置選択的に導入できるため、複雑な骨格を一挙に構築できる。すなわち、ホウ素アート錯体 **2** から生じた炭素中心ラジカルがアルケン **6** にラジカル付加し、新たに形成した炭素中心ラジカルが Ni 触媒サイクルに移行することで、目的のカップリング体が得られる。アルケンとして、アクリル酸 *t*-ブチル **6b** を用いた際には対応するアルキルアリール化体が問題なく得られた（**10aba**, **10cba**, **10abd**, and **10abi**）。ビニルボロン酸ピナコールエステル **6c** を用いた際には、炭素–ホウ素結合を損なうことなく、対応する三成分カップリング体が得られた（**10aca** and **10acd**）。これは中間体として生じる α-ボリルラジカルの超共役に基づく安定化のため、ラジカル付加が効率よく進行したものと考えられる。同様に、アルケンとして電子豊富なピバル酸ビニル **6d** を用いた際には、β-アルコキシ脱離を伴うことなく、三成分カップリングに適用できた（**10ada**, **10add**, **10adi**, and **10eda**）。残念ながら、第一級アルキルホウ素アート錯体は適用困難であった。



[a]$NiBr_2$ (5 mol %) and bipyridine (6 mol %) were used as catalysts. [b]$NiBr_2$·diglyme (5 mol %) and dtbpy (6 mol %) were used as catalysts. [c]Diastereomeric ratio (1:1). [d]$Ni(cod)_2$ (5 mol %) and 1,10-phenanthroline (6 mol %) were used as catalysts. [e]4'-Chloroacetophenone was used.

Table 1-3. Substrate scope of three-component alkylarylation of alkenes.

第 5 節　結論

広いπ-共役構造を有する有機ホウ素化合物、ボラセンから誘導されるアルキルホウ素アート錯体の可視光直接励起により、光酸化還元触媒やその他の添加剤を必要とすることなく、第三級、二級および一級のアルキルラジカルの発生・制御を可能にした。このアルキルホウ素アート錯体の直接励起法は、励起状態のホウ素アート錯体の一電子移動能あるいは炭素中心ラジカル発生能に基づき、脱シアノアルキル化反応、Giese付加反応、およびNi触媒によるアルキル–アリールクロスカップリング反応やアルケンの三成分ビシナルアルキルアリール化反応などの種々の炭素–炭素結合反応へと適用可能であった。さらに、反応後にボラセンは回収・再利用が可能であるため、環境調和性に優れ

た手法といえる。このボラセン構造に基づく反応基質の直接励起法は、有機合成における炭素−炭素結合形成の更なる発展への寄与が期待される。

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第 1 章の実験項

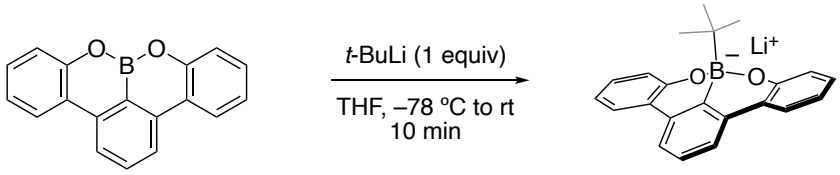
■ Instrumentation and Chemicals ■

NMR spectra were recorded on a JNM-ECS400 or a JEOL 400SS, operating at 400 MHz for ^{1}H NMR, 100.5 MHz for ^{13}C NMR, and, 127 MHz for ^{11}B NMR, and JNM-ECA600, operating at 600 MHz for ^{1}H NMR and 150.9 MHz for ^{13}C NMR. Chemical shift values for ^{1}H, ^{13}C, and, ^{11}B NMR are referenced to Me_4Si, the residual solvent resonances, and $BF_3{\cdot}OEt_2$ (δ 0.0 ppm in $CDCl_3$), respectively. Chemical shifts are reported in δ ppm. Mass spectra were obtained with a Thermo Scientific Exactive Plus Orbitrap or JMS-T100TD (DART). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Kanto Chemical Co., Silica gel 60 N, spherical, neutral) was used for column chromatography. 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 Yanaco MP-500D apparatus. CV measurements were recorded with a CH Instruments: BAS Model 600E Series Electrochemical Analyzer. UV-Vis absorption spectra were recorded on a Shimadzu UV-1900. Fluorescence spectra were recorded on a Shimadzu RF-6000. Kessil PR160L 440 nm (highest blue and intensity setting) was used as a light source. Single-crystal X-ray diffraction data were collected on a Rigaku AFC-8 diffractometer equippted with Saturn70 CCD detector. The structures were solved by dual space method (SHELXT-2018)[1] and refined by the full-matrix least-squares on F^2 (SHELXL-2018)[2]. CCDC 1871613 (compounds **2a**) contain the supplementary crystallographic data for these structures. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC) via www.ccdc.cam.ac.uk/data_request/cif.

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers stored under nitrogen, and used as received or prepared according to standard procedures unless otherwise noted. 8,9-Dioxa-8a-borabenzo[*fg*]tetracene (boracene) **1** was prepared by the reported procedure[3, 4] or purchased by Sumika Technoservice Corporation, and used as received. Dimethylacetoamide was purchased from Nacalai Tesque Inc. Dehydrated tetrahydrofuran, acetonitrile, and methanol were purchased from FUJIFILM Wako Pure Chemical Co. *tert*-Butyllithium (in *n*-pentane, 1.6 mol/L) was purchased from Kanto Chemical Co. Inc. $Ni(acac)_2$, $Ni(TMHD)_2$, NiBr·diglyme, 4,4′-di-*tert*-butylbiphenyl, lithium wire (in mineral oil, diam. 3.2 mm, 99.9% trace metals basis), and dtbpy, were purchased from Sigma-Aldrich. THF-d_8 was purchased from Eurisotop. 2-Chloro-2-methylpropane-d_9 (99.3%D) was purchased from CDN isotopes.

■ Characterization Data for 2a ■

tert-Butylborate 2a



1 **2a**

To a suspension of boracene (270 mg, 1.00 mmol) in THF (10 mL) was added *t*-butyllithium (1.6 M in *n*-pentane, 0.6 mL, 1.0 mmol) at –78 °C. After warming to room temperature, the mixture was stirred for 10 min at the same temperature. The mixture was concentrated under reduced pressure to give **2a** (475 mg, 993 μmol, 99.3%) as a colorless solid.

The molecular weight of **2a** was calculated as [*t*-Bu(boracene)]Li·2THF (MW: 478.36) determined from ^{1}H NMR and the X-ray structure, for the use of the experiments.

M.p. 163 °C (decomp.).

IR (ZnSe, cm^{-1}): 731, 754, 899, 918, 947, 1042, 1130, 1234, 1290, 1406, 1447, 1578, 2843, 2884, 2920; The number of coordinated THF was determined from the integral value of ^{1}H NMR.

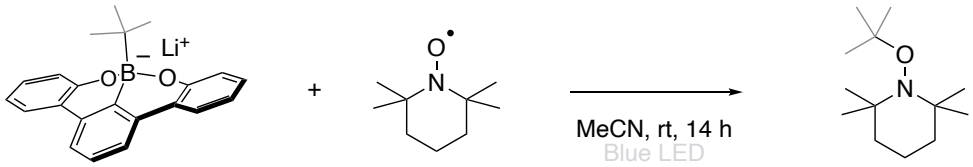
^{1}H NMR (400 MHz, CD_2Cl_2) δ 0.46 (s, 9H), 1.61–1.72 (m, THF), 3.54–3.65 (m, THF), 6.80–6.89 (m, 4H), 7.10 (ddd, J = 1.6, 8.0, 8.0 Hz, 2H), 7.31 (t, J = 8.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.76 (dd, J = 1.6, 8.0 Hz, 2H)

^{13}C NMR (100 MHz, CD_2Cl_2) δ 25.6 (THF), 27.3 (3C), 68.6 (THF), 119.0 (2C), 119.5 (2C), 120.4 (2C), 124.0 (2C), 127.1, 128.4 (2C), 128.6 (2C), 135.7 (2C), 156.7 (2C). The signals for the carbons attached to the boron atom were not observed.

^{11}B NMR (127 MHz, CD_2Cl_2) δ 7.49 (br).

HRMS (ESI$^-$ *m*/*z*): [M–(Li+2THF)]$^-$ calcd for $C_{22}H_{20}BO_2^-$, 327.1562; found, 327.1564.

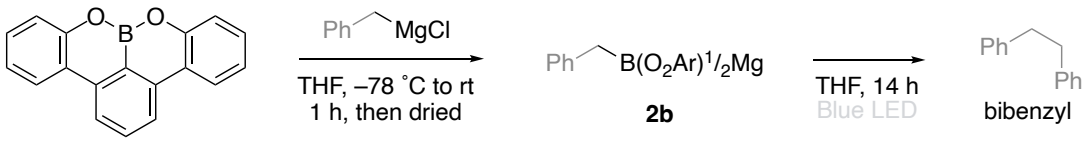
■ Procedure for Radical Trap Experiment (Scheme 1-1) ■



2a TEMPO **3a**

In a glovebox, to an oven-dried vial with a stirring bar was added *tert*-butylborate **2a** (95.7 mg, 0.20 mmol), 2,2,6,6-tetramethylpiperidine 1-oxyl, (TEMPO, 15.6 mg, 0.20 mmol) and MeCN (400 μl). After sealing the vial with parafilm, the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 14 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 gave the **3a** (27.5 mg, 64% isolated yield) with the recovery of boracene **1** as a colorless solid.

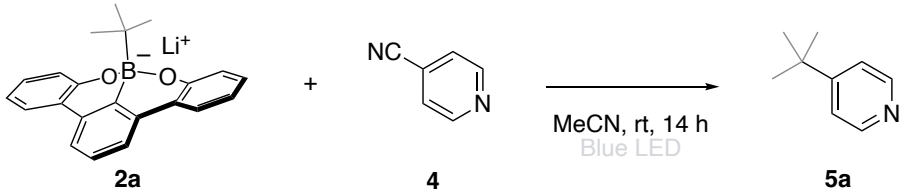
■ Dimerization via direct excitaion (Scheme 1-2) ■



1 **2b** bibenzyl

To a suspension of boracene **1** (54 mg, 0.2 mmol) in THF (200 μl) was added benzyl magnesium chloride solution (300 μl, 0.22 mmol) in THF (0.75 M) prepared by conventional method at –78 ºC and then allowed to warm up to room temperature. After stirred for 2 h, passed through a short plug of N–H silica gel to give benzyl borate **2b** in THF solution. the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 14 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, the residue was dissolved in $CDCl_3$ (500 μL) and added 1,1,2,2-tetrachloroethane (11 μL, 10.5 μmol) as an internal standard. ^{1}H NMR (400 MHz) yield (quantitative) was obtained by comparing the relative value of integration for the doublet peak observed at 2.92 ppm of bibenzyl with that of 1,1,2,2-tetrachloroethane observed at 5.95 ppm.

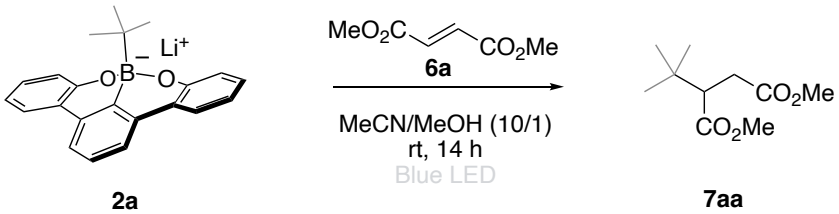
■ Procedure for Decyanoalkylation (Scheme 1-3) ■



2a **4** **5a**

In a glovebox, to an oven-dried vial with a stirring bar was added *tert*-butyl borate **2a** (71.8 mg, 0.15 mmol), 4-cyanopyridine **4** (10.4 mg, 0.1 mmol) and MeCN (100 μl). After sealing the vial with parafilm, the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 14 h, the reaction was quenched with a short plug of silica gel using ethyl acetate. After volatiles were removed under reduced pressure, the residue was dissolved in $CDCl_3$ (500 μL) and added 1,1,2,2-tetrachloroethane (11 μL, 10.5 μmol) as an internal standard. ^{1}H NMR (400 MHz) yield (80%) was obtained by comparing the relative value of integration for the doublet peak observed at 8.40 ppm of **5a** with that of 1,1,2,2-tetrachloroethane observed at 5.96 ppm. The generation of **5a** was also confirmed by observation of the corresponding molecular ion peak with GC-MS analysis.

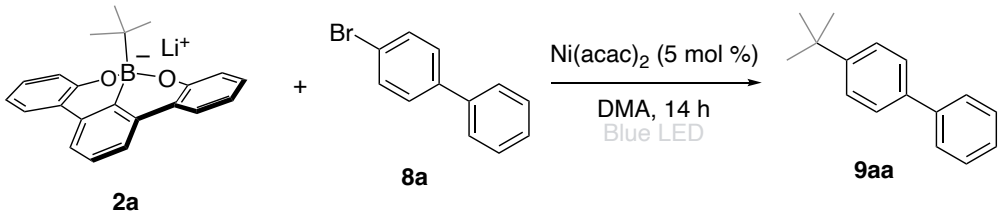
■ Procedure for Giese Addition (Scheme 1-4) ■



2a **7aa**

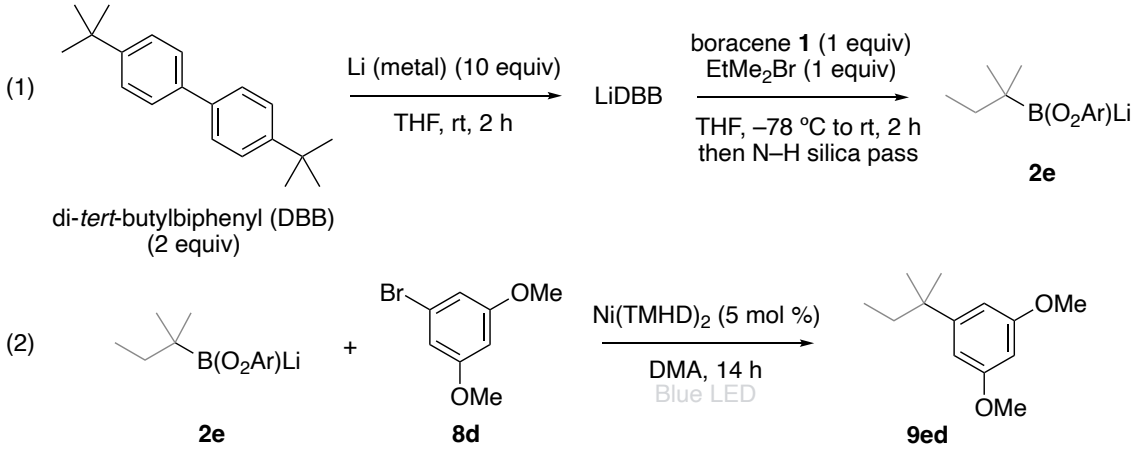
In a glovebox, to an oven-dried vial with a stirring bar was added *tert*-butyl borate **2a** (71.8 mg, 0.15 mmol), dimethyl fumarate **6a** (14.4 mg, 0.1 mmol) and MeCN/MeOH (9/1, 100 μl). After sealing the vial with parafilm, the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 14 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 gave the **7aa** (14.0 mg, 69% isolated yield) with the recovery of boracene **1** as a colorless solid.

■ Protocols for Ni-Catalyzed Alkylation (Table 1-1 and **1-2) ■**



2a **8a** **9aa**

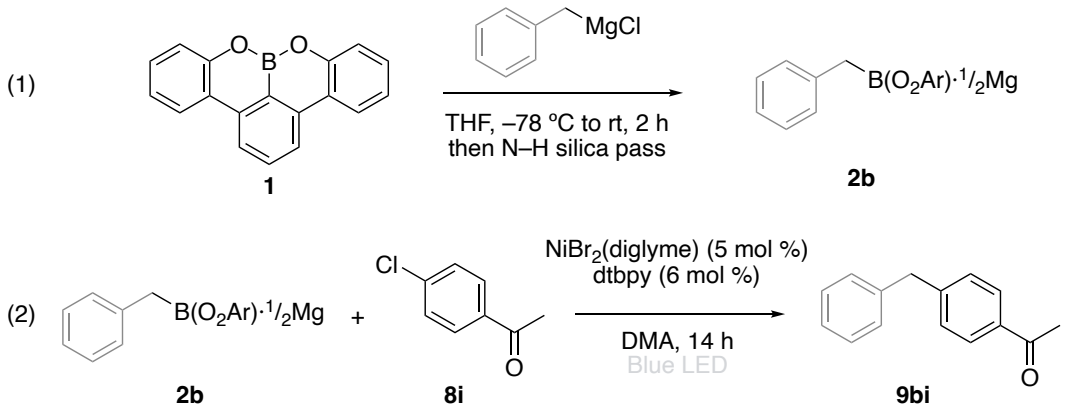
Method A (synthesis of **9aa** as a representative): In a glovebox, to an oven-dried vial with a stirring bar was added $Ni(acac)_2$ (2.6 mg, 0.01 mmol), pre-prepared *tert*-butyl borate **2a** (143.5 mg, 0.3 mmol), aryl bromide **8a** (46.6 mg, 0.2 mmol) and DMA (500 µl). After sealing the vial with parafilm, the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 14 h, the reaction was quenched with water and extracted with diethyl ether (ca. 2 mL × 3). The combined organic extract was dried over Na_2SO_4 and after filtration, the filtrate was concentrated under reduced pressure. The residue was washed with MeOH to remove most of boracene and after MeOH were removed under reduced pressure, purified by flash column chromatography on silica gel gave **9aa** (32.0 mg, 76%) as a white solid.



Method B (synthesis of **9ed** as a representative): To a suspension of boracene **1** (54 mg, 0.2 mmol) and 2-bromo-2-methylbutane (25 µl, 0.2 mmol) in THF (1.0 ml) was added LiDBB solution in THF (0.4 M), prepared from 4,4′-di-*tert*-butylbiphenyl (DBB, 107 mg, 0.4 mmol, 4 equiv) and lithium wire (13.9 mg, 2.0 mmol, 20 equiv) by according to the literature[5], at –78 °C and then allowed to warm up to room temperature. After stirred for 2 h, passed through a short plug of N–H silica gel and THF was removed by spraying nitrogen gas to give *tert*-pentyl borate **2e**. The borate was used without further purification.

In a glovebox, to an oven-dried vial with a stirring bar was added $Ni(TMHD)_2$ (2.1 mg, 5.0 µmol) and 1-bromo-3,5-dimethoxybenzene **8d** (21.7 mg, 0.100 mmol). To the mixture was added

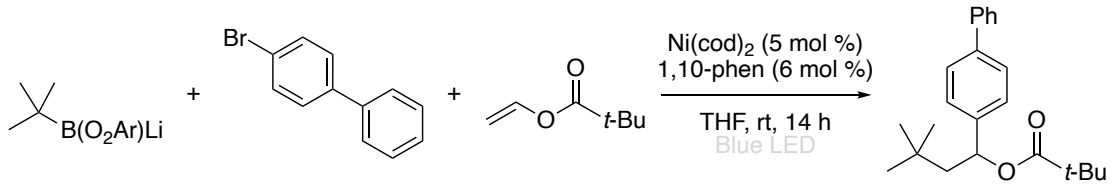
tert-pentyl borate **2e** dissolved in DMA (1.0 ml). After sealing the vial with parafilm, the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 24 h, the reaction was quenched with water and extracted with diethyl ether (ca. 2 mL × 3). The combined organic extract was dried over Na_2SO_4 and after filtration, the filtrate was concentrated under reduced pressure. The residue was washed with MeOH to remove most of boracene and after MeOH were removed under reduced pressure, purified by flash column chromatography on silica gel gave **9ed** (15.3 mg, 73%) as a colorless oil.



Method C (synthesis of **9bi** as a representative): To a suspension of boracene **1** in THF (1.0 ml) was added benzylmagnesium chloride solution in THF (1.0 M) prepared by conventional method at –78 °C and then allowed to warm up to room temperature. After stirred for 2 h, passed through a short plug of N–H silica gel to give benzyl borate **2b** in THF solution. The mixture was used without further purification.

In a glovebox, to an oven-dried vial with a stirring bar was added $NiBr_2$·diglyme (1.5 mg, 5.0 μmol), dtbpy (4,4'-di-*tert*-butyl-2,2'-bipyridyl) (1.6 mg, 6.0 μmol) and 4'-chloroacetophenone **8i** (15.5 mg, 0.1 mmol). To the mixture was added benzyl borate **2b** in THF solution (1.0 mL). After sealing the vial with parafilm, the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 24 h, the reaction was quenched with water and extracted with diethyl ether (ca. 2 mL × 3). The combined organic extract was dried over Na_2SO_4 and after filtration, the filtrate was concentrated under reduced pressure. The residue was washed with MeOH to remove most of boracene and after MeOH were removed under reduced pressure, purified by flash column chromatography on silica gel gave **9bi** (18.8 mg, 89%) as a colorless oil.

■ Procedure for Ni-Catalyzed Three-Cmponent Coupling (Table 1-3) ■

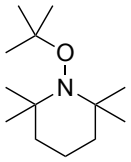


2a **8a** **6d** **10ada**

In a glovebox, to an oven-dried vial with a stirring bar was added $Ni(cod)_2$ (1.4 mg, 5.0 μmol) and 1,10-phenanthroline (1.1 mg, 6.0 μmol). To the mixture was added *tert*-butylborate **2a** (71.8 mg, 0.15 mmol), vinyl pivalate **6d** (25.6 mg, 29.1 μl, 0.2 mmol), 4-bromo-1,1'-biphenyl **8a** (23.3 mg, 0.1 mmol) and THF (1.0 ml). After sealing the vial with parafilm, the reaction was placed in EvoluChem photoreactor (PhotoRedOx Duo) equiped with a 45W blue LED. After stirred for 14 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 gave the **10ada** (24.5 mg, 72%) with the recovery of boracene **1** as a colorless solid.

■ Characterization Data for Alkylation Products ■

1-(*tert*-Butoxy)-2,2,6,6-tetramethylpiperidine (3a)



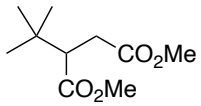
The product **3a** was purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Scheme 1-1**; 27.5 mg, 0.129 mmol, 64% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (s, 6H), 1.12 (s, 6H), 1.26 (s, 9H), 1.23–1.28 (m, 1H), 1.30–1.61 (m, 5H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 17.2, 20.4 (2C), 29.4 (3C), 34.8 (2C), 40.8 (2C), 59.0 (2C), 77.1.

The ^{1}H and ^{13}C NMR spectra data of **3a** were consistent with the literature.[6]

Dimethyl 2-(*tert*-Butyl)succinate (7aa)



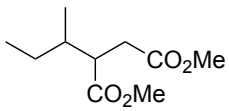
The product **7aa** was purified by flash chromatography on silica gel (100:0–10:1, hexane/EtOAc) (**Scheme 1-4**; 14.0 mg, 0.069 mmol, 69% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 9H), 2.48 (dd, J = 2.0, 11.2 Hz, 1H), 2.65 (dd, J = 2.0, 8.0 Hz, 1H), 2.80 (dd, J = 8.0, 11.2 Hz, 1H), 3.66 (s, 3H), 3.70 (s, 3H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 27.8 (4C), 32.6, 51.2, 51.4, 51.8, 173.2, 174.7.

The ^{1}H and ^{13}C NMR spectra data of **7aa** were consistent with the literature.[7]

Dimethyl 2-(*sec*-Butyl)succinate (7ca)



The product **7ca** (1:1 mixture of diastereomers) was purified by flash chromatography on silica gel (100:0–10:1, hexane/EtOAc) (**Scheme 1-4**; 11.3 mg, 0.056 mmol, 56% isolated yield). Colorless oil.

IR (neat) 754, 845, 1005, 1165, 1253, 1347, 1437, 1734, 2961 cm^{-1}.

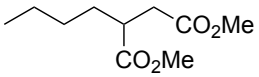
^{1}H NMR (600 MHz, $CDCl_3$) δ 0.85–0.93 (m, 3H), 1.14–1.46 (m, 5H), 1.70 (m, 0.5H), 1.83 (m, 0.5H), 2.35 (dd, J = 3.6, 16.8 Hz, 0.5H), 2.40 (dd, J = 3.6, 16.8 Hz, 0.5H), 2.75 (m, 1H), 2.88 (m,

1H), 3.67 (d, J = 1.2 Hz, 3H), 3.70 (d, J = 3.0 Hz, 3H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 11.6, 11.7, 15.8, 16.4, 26.7, 27.2, 31.4, 33.4, 36.3, 36.9, 45.5, 45.8, 51.6, 51.7, 51.8 (2C), 173.0, 173.1, 174.7, 175.2.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{10}H_{19}O_4^+$, 203.1283; found, 203.1286.

Dimethyl 2-Butylsuccinate (7da)



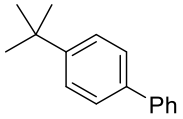
The product **7da** was purified by flash chromatography on silica gel (100:0–10:1, hexane/EtOAc) (**Scheme 1-4**; 6.3 mg, 0.031 mmol, 31% isolated yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3H), 1.14–1.38 (m, 4H), 1.51 (m, 1H), 1.64 (m, 1H), 2.44 (dd, J = 4.8, 16.8 Hz, 1H), 2.72 (dd, J = 9.0, 16.8 Hz, 1H), 2.84 (m, 1H), 3.67 (s, 3H), 3.70 (s, 3H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 13.8, 21.0, 29.1, 31.6, 35.8, 41.1, 51.7, 51.8, 172.5, 175.5.

The ^{1}H and ^{13}C NMR spectra data of **7da** were consistent with the literature.[8]

4-(*tert*-Butyl)-1,1'-biphenyl (9aa)



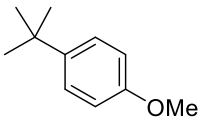
The product **9aa** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 32.0 mg, 0.15 mmol, 76% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 9H), 7.32 (m, 1H), 7.41–7.48 (m, 4H), 7.53–7.55 (m, 2H), 7.58–7.60 (m, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.4 (3C), 34.5, 125.7 (2C), 126.8 (2C), 127.0, 127.0 (2C), 128.7 (2C), 138.3, 141.0, 150.2.

The ^{1}H and ^{13}C NMR spectra data of **9aa** were consistent with the literature.[9]

1-(*tert*-Butyl)-4-methoxybenzene (9ab)



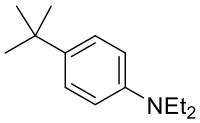
The product **9ab** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 23.9 mg, 0.15 mmol, 73% isolated yield, including isomerization product).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 9H), 3.80 (s, 3H), 6.85 (d, J = 9.2 Hz, 2H), 7.31 (d, J = 9.2 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.5 (3C), 34.0, 55.2, 113.3 (2C), 126.2 (2C), 143.3, 157.3.

The ^{1}H and ^{13}C NMR spectra data of product **9ab** were consistent with the literature.[9]

4-(*tert*-Butyl)-*N*,*N*-diethylaniline (9ac)



The product **9ac** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 25.2 mg, 0.12 mmol, 61% isolated yield, including isomerization product). Pale orange oil.

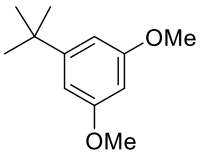
IR (neat) 812, 1205, 1263, 1361, 1373, 1518, 1614, 2962 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ 1.15 (t, J = 7.2 Hz, 6H), 1.28 (s, 9H), 3.32 (q, J = 7.2 Hz, 4H), 6.64 (d, J = 9.0 Hz, 2H), 7.24 (d, J = 9.0 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.7 (2C), 31.6 (3C), 33.6, 44.3 (2C), 111.5 (2C), 126.0 (2C), 137.9, 145.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{24}N^+$, 206.1903; found, 206.1907.

1-(*tert*-Butyl)-3,5-dimethoxybenzene (9ad)



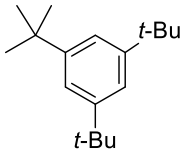
The product **9ad** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 31.0 mg, 0.16 mmol, 80% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 9H), 3.80 (s, 6H), 6.31 (t, J = 2.0 Hz, 1H), 6.55 (d, J = 2.0 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.2 (3C), 34.9, 55.2 (2C), 96.7, 104.0 (2C), 153.8, 160.5 (2C).

The ^{1}H and ^{13}C NMR spectra data of product **9ad** were consistent with the literature.[9]

1,3,5-Tri-*tert*-butylbenzene (9ae)



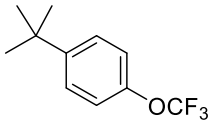
The product **9ae** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 34.3 mg, 0.14 mmol, 70% isolated yield, including isomerization product).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 27H), 7.26 (s, 3H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.6 (9C), 35.0 (3C), 119.5 (3C), 149.9 (3C).

The ^{1}H and ^{13}C NMR spectra data of product **9ae** were consistent with the literature.[10]

1-(*tert*-Butyl)-4-(trifluoromethoxy)benzene (9af)



The product **9af** synthesized according to **Method A** (**Table 1-2**; 69% ^{1}H NMR yield).

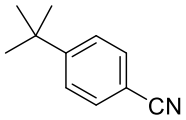
^{1}H NMR (600 MHz, $CDCl_3$) δ 1.32 (s, 9H), 7.13 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 31.3, (3C), 34.5, 120.4 (2C), 120.4 (q, J = 270.0 Hz), 126.6 (2C), 146.9, 149.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ –56.6.

The ^{1}H, ^{13}C, and, ^{19}F NMR spectra data of product **9af** were consistent with the literature.[11]

4-(*tert*-Butyl)benzonitrile (9ag)



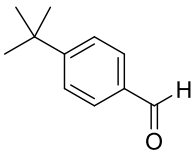
The product **9ag** was syntheesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 13.3 mg, 0.084 mmol, 42% isolated yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 1.33 (s, 9H), 7.48 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 30.9 (3C), 35.3, 109.3, 119.2, 126.2 (2C), 132.0 (2C), 156.6.

The ^{1}H and ^{13}C NMR spectra data of product **9ag** were consistent with the literature.[12]

4-(*tert*-Butyl)benzaldehyde (9ah)



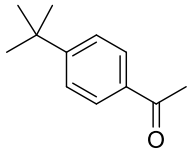
The product **9ah** was synthesized according to **Method A**, and purified by flash chromatography on silica gel (100:0–80:20, hexane/CH_2Cl_2)) (**Table 1-2**; 13.0 mg, 0.080 mmol, 40% isolated yield, including isomerization product and inseparable impurity).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 9H), 7.56 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.4 Hz, 2H), 9.99 (s, 1H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.1 (3C), 35.3, 126.0 (2C), 129.7 (2C), 134.1, 158.4, 192.1.

The ^{1}H and ^{13}C NMR spectra data of product **9ah** were consistent with the literature.[12]

1-[4-(*tert*-Butyl)phenyl]ethan-1-one (9ai)



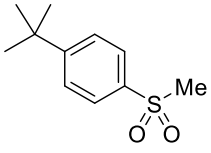
The product **9ai** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 25.4 mg, 0.14 mmol, 72% isolated yield, including isomerization product).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 9H), 2.59 (s, 3H), 7.48 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 26.5, 31.1 (3C), 35.1, 125.5 (2C), 128.3 (2C), 134.6, 156.8, 197.9.

The ^{1}H and ^{13}C NMR spectra data of product **9ai** were consistent with the literature.[12]

1-(*tert*-Butyl)-4-(methylsulfonyl)benzene (9aj)



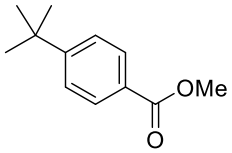
The product **9aj** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 24.1 mg, 0.11 mmol, 57% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 9H), 3.05 (s, 3H), 7.58 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.0 (3C), 35.2, 44.6, 126.3 (2C), 127.2 (2C), 137.6, 157.6.

The ^{1}H and ^{13}C NMR spectra data of product **9aj** were consistent with the literature.[11]

Methyl 4-(*tert*-Butyl)benzoate (9ak)



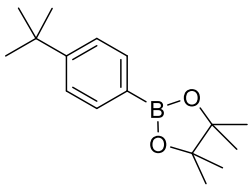
The product **9ak** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 23.5 mg, 0.12 mmol, 61 % isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.90 (s, 3H), 7.45 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 8.8 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.1 (3C), 35.0, 51.9, 125.3 (2C), 127.3, 129.4 (2C), 156.5, 167.1.

The ^{1}H and ^{13}C NMR spectra data of product **9ak** were consistent with the literature.[13]

2-[4-(*tert*-Butyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9al)



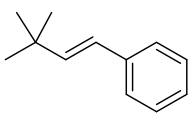
The product **9al** was synthesized according to **Method A**, and purified by flash chromatography on silica gel (100:0–85:15, hexane/toluene) (**Table 1-2**; 27.0 mg, 0.10 mmol, 52 % isolated yield, including isomerization product).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 9H), 1.33 (s, 12H), 7.41 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 8.0 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 24.8 (4C), 31.2 (3C), 34.9, 83.6 (2C), 124.7 (2C), 134.7 (2C), 154.5. The signal for the carbon attached to the boron atom was not observed.

The ^{1}H and ^{13}C NMR spectra data of product **9al** were consistent with the literature.[14]

(*E*)-(3,3-Dimethylbut-1-en-1-yl)benzene (9am)



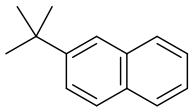
The product **9am** synthesized according to **Method A** (**Table 1-2**; 65 % ^{1}H NMR yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (s, 9H), 6.25 (d, J = 16.4 Hz, 1H), 6.31 (d, J = 16.4 Hz, 1H), 7.19 (m, 1H), 7.24–7.31 (m, 2H), 7.36 (d, J = 7.6 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 29.6 (3C), 33.3, 124.5, 126.0 (2C), 126.7, 128.5 (2C), 138.0, 141.8.

The ^{1}H and ^{13}C NMR spectra data of product **9am** were consistent with the literature.[15]

2-(*tert*-Butyl)naphthalene (9an)



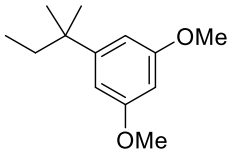
The product **9an** was synthesized according to **Method A**, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 21.1 mg, 0.11 mmol, 57 % isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (s, 9H), 7.41– 7.45 (m, 2H), 7.58 (m, 1H), 7.76–7.82 (m, 4H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.2 (3C), 34.8, 122.8, 124.8, 125.2, 125.8, 127.3, 127.5, 127.9, 131.6, 133.3, 148.5.

The ^{1}H and ^{13}C NMR spectra data of product **9an** were consistent with the literature.[9]

1,3-Dimethoxy-5-(*tert*-pentyl)benzene (9ed)



The product **9ed** was synthesized according to **Method B** using 2-bromo-2-methylbutane with LiDBB, and purified by flash chromatography on silica gel (100:0–80:20, hexane/CH_2Cl_2) (**Table 1-2**; 15.2 mg, 0.073 mmol, 73 % isolated yield). Colorless oil.

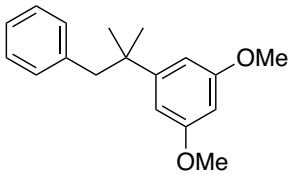
IR (neat) 831, 1155, 1205, 1422, 1456, 1595, 2835, 2962 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.69 (t, J = 7.2 Hz, 3H), 1.25 (s, 6H), 1.61 (q, J = 7.2 Hz, 2H), 3.80 (s, 6H), 6.30 (t, J = 2.4 Hz, 1H), 6.49 (d, J = 2.4 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 9.1, 28.4 (2C), 36.8, 38.2, 55.2 (2C), 96.6, 104.8 (2C), 152.2, 160.4 (2C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{13}H_{21}O_2^+$, 209.1536; found, 209.1545.

1,3-Dimethoxy-5-(2-methyl-1-phenylpropan-2-yl)benzene (9fd)



The product **9fd** was synthesized according to **Method B** using 2-bromo-2-methyl-1-phenylpropane with LiDBB, and purified by flash chromatography on silica gel (100:0–80:20, hexane/CH_2Cl_2) (**Table 1-2**; 14.4 mg, 0.053 mmol, 53 % isolated yield). Colorless oil.

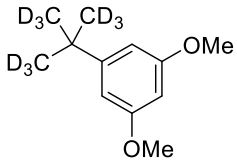
IR (neat) 702, 831, 1056, 1155, 1204, 1341, 1422, 1455, 1495, 2961 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ 1.28 (s, 6H), 2.84 (s, 2H), 3.77 (s, 6H), 6.33 (s, 1H), 6.45 (s, 2H), 6.87–6.89 (m, 2H), 7.14–7.17 (m, 3H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 28.2 (2C), 39.0, 50.8, 55.2 (2C), 97.1, 105.0 (2C), 125.9, 127.5 (2C), 130.4 (2C), 138.8, 151.8, 160.3 (2C).

HRMS–DART (*m/z*): $[M]^+$ calcd for $C_{18}H_{22}O_2^+$, 270.1614; found, 270.1616.

1,3-Dimethoxy-5-[2-(methyl-*d*$_3$)propan-2-yl-1,1,1,3,3,3-*d*$_6$]benzene (9gd)



The product **9gd** was synthesized according to **Method B** using 2-chloro-2-methylpropane-*d*$_9$ (99.3%D) with LiDBB, and purified by flash chromatography on silica gel (100:0–80:10, hexane/CH_2Cl_2) (**Table 1-2**; 8.3 mg, 0.041 mmol, 41 % isolated yield, 98.9%D). Colorless oil.

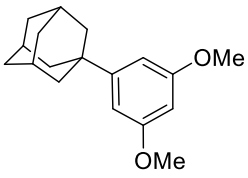
IR (neat) 852, 1072, 1154, 1204, 1456, 1595, 2215, 2937 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 6H), 6.31 (t, J = 2.4 Hz, 1H), 6.54 (t, J = 2.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 55.2 (2C), 96.7, 104.1 (2C), 160.5 (2C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{12}H_{10}D_9O_2^+$, 204.1944; found, 204.1951.

(3r,5r,7r)-1-(3,5-Dimethoxyphenyl)adamantane (9hd)



The product **9hd** was synthesized according to **Method B** using 1-bromoadamantane with LiDBB, and purified by flash chromatography on silica gel (100:0–80:10, hexane/CH_2Cl_2) (**Table 1-2**; 17.5 mg, 0.064 mmol, 64 % isolated yield). Pale yellow oil.

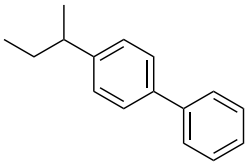
IR (neat) 694, 1150, 1203, 1453, 1593, 2846, 2899 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72–1.80 (m, 6H), 1.90 (s, 6H), 2.08 (s, 3H), 3.80 (s, 6H), 6.31 (t, J = 2.4 Hz, 1H), 6.53 (d, J = 2.4 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 28.9 (3C), 36.5, 36.8 (3C), 43.1 (3C), 55.2 (2C), 97.0, 103.5 (2C), 154.1, 160.5 (2C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{25}O_2^+$, 273.1849; found, 273.1850.

4-(*sec*-Butyl)-1,1'-biphenyl (9ca)



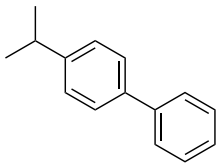
The product **9ca** was synthesized according to **Method A** using *sec*-butyllithium, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 12.4 mg, 0.059 mmol, 59% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, J = 7.8 Hz, 3H), 1.27 (d, J = 7.3 Hz, 3H), 1.63 (dq, J = 6.9, 7.8 Hz, 2H), 2.64 (tq, J = 6.9, 7.3 Hz, 1H), 7.26 (d, J = 8.2 Hz, 2H), 7.32 (dd, J = 7.3, 7.3 Hz, 1H), 7.43 (dd, J = 7.3, 7.8 Hz, 2H), 7.52 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.2 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 12.3, 21.8, 31.2, 41.3, 126.9, 127.0 (4C), 127.4 (2C), 128.7 (2C), 138.7, 141.2, 146.8.

The ^{1}H and ^{13}C NMR spectra data of product **9ca** were consistent with the literature.[16]

4-Isopropyl-1,1'-biphenyl (9ia)



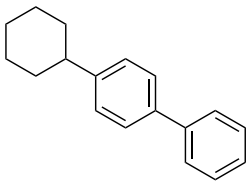
The product **9ia** was synthesized according to **Method C** using *iso*-propyl magnesium bromide, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 12.3 mg, 0.063 mmol, 63% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (d, J = 6.9 Hz, 6H), 2.96 (sep, J = 6.9 Hz, 1H), 7.28–7.35 (m, 3H), 7.43 (dd, J = 7.3, 7.8 Hz, 2H), 7.53 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 24.0 (2C), 33.8, 126.8 (2C), 126.9 (2C), 127.0 (2C), 127.1, 128.7 (2C), 138.7, 141.2, 148.0.

The ^{1}H and ^{13}C NMR spectra data of product **9ia** were consistent with the literature.[16]

4-Cyclohexyl-1,1'-biphenyl (9ja)



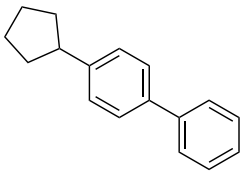
The product **9ja** was synthesized according to **Method C** using cyclohexyl magnesium bromide, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 8.3 mg, 0.035 mmol, 35% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22–1.48 (m, 5H), 1.77 (m, 1H), 1.82–195 (m, 4H), 2.55 (m, 1H), 7.28 (d, J = 8.2 Hz, 2H), 7.32 (dd, J = 7.3, 7.3 Hz, 1H), 7.42 (dd, J = 7.3, 7.8 Hz, 2H), 7.52 (d, J = 7.3 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 26.2, 26.9 (2C), 34.4 (2C), 44,2, 126.9, 127.0 (4C), 127.2 (2C), 128.7 (2C), 138.7, 141.2, 147.2.

The ^{1}H and ^{13}C NMR spectra data of product **9ja** were consistent with the literature.[17]

4-Cyclopentyl-1,1'-biphenyl (9ka)



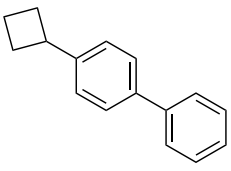
The product **9ka** was synthesized according to **Method C** using cyclopentyl magnesium chloride, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 10.9 mg, 0.049 mmol, 49% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58–1.75 (m, 4H), 1.78–1.85 (m, 2H), 2.05–2.30 (m, 2H), 3.03 (quint., J = 7.8 Hz, 1H), 7.30–7.34 (m, 3H), 7.39 (dd, J = 7.8, 7.8 Hz, 2H), 7.54 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 7.3 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 25.5 (2C), 34.6 (2C), 45.6, 126.97, 126.99 (4C), 127.5 (2C), 128.7 (2C), 138.6, 141.2, 145.7.

The ^{1}H and ^{13}C NMR spectra data of product **9ka** were consistent with the literature.[17]

4-Cyclobutyl-1,1'-biphenyl (9ia)



The product **9ia** was synthesized according to **Method C** using cyclobutyl magnesium bromide, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**;

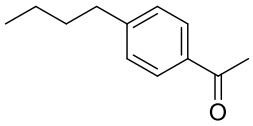
14.3 mg, 0.069 mmol, 69% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88 (m, 1H), 2.04 (m, 1H), 2.15–2.25 (m, 2H), 2.34–2.44 (m, 2H), 3.59 (quint., J = 8.7 Hz, 1H), 7.30–7.34 (m, 3H), 7.39 (dd, J = 7.8, 7.8 Hz, 2H), 7.54 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 7.3 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 18.3, 29.8 (2C), 40.1, 126.7, 126.95 (2C), 126.99 (2C), 127.0 (2C), 128.7 (2C), 138.7, 141.2, 145.4.

The ^{1}H and ^{13}C NMR spectra data of product **9ia** were consistent with the literature.[17]

1-(4-Butylphenyl)ethan-1-one (9di)



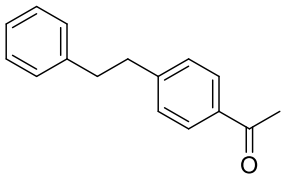
The product **9di** was synthesized according to **Method A** using *n*-butyl lithium, and purified by flash chromatography on NH–silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 18.0 mg, 0.10 mmol, 51% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3H), 1.31–1.40 (m, 2H), 1.58–1.65 (m, 2H), 2.58 (s, 3H), 2.66 (t, J = 7.2 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 13.9, 22.3, 26.6, 33.2, 35.7, 128.5 (2C), 128.6 (2C), 134.9, 148.8, 197.9.

The ^{1}H and ^{13}C NMR spectra data of product **9di** were consistent with the literature.[18]

1-(4-Phenethylphenyl)ethan-1-one (9mi)



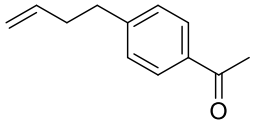
The product **9mi** was synthesized according to **Method C** using phenylethyl magnesium bromide, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 9.4 mg, 0.042 mmol, 42% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (s, 3H), 2.91– .01 (m, 4H), 7.15–7.30 (m, 7H), 7.87 (d, J = 8.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 26.6, 37.4, 37.8, 126.1, 128.39 (2C), 128.42 (2C), 128.5 (2C), 128.7 (2C), 135.1, 141.1, 147.5, 197.9.

The ^{1}H and ^{13}C NMR spectra data of product **9mi** were consistent with the literature.[19]

1-[4-(But-3-en-1-yl)phenyl]ethan-1-one (9ni)



The product **9ni** was synthesized according to **Method C** using 3-buten-1-ylmagnesium bromide, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 5.4 mg, 0.031 mmol, 31% isolated yield, including inseparable isomerization product). Colorless oil.

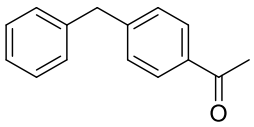
IR (neat) 818, 956, 1268, 1358, 1607, 1683, 2358, 2926 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (q, J = 7.2 Hz, 2H), 2.59 (s, 3H), 2.77 (t, J = 7.2 Hz, 2H), 4.98–5.05 (m, 2H), 5.83 (m, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 26.5, 35.0, 35.3, 115.4, 128.5 (2C), 128.6 (2C), 135.0, 137.5, 147.6, 197.9.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{12}H_{15}O^+$, 175.1117; found, 175.1121.

1-(4-Benzylphenyl)ethan-1-one (9bi)



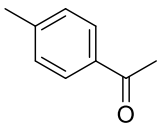
The product **9bi** was synthesized according to **Method C**, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 18.8 mg, 0.089 mmol, 89% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (s, 3H), 4.04 (s, 2H), 7.18–7.30 (m, 7H), 7.89 (d, J = 8.0 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 26.6, 41.9, 126.4 (2C), 128.6 (2C), 128.9 (2C), 129.0, 129.1 (2C), 135.2, 140.0, 146.8, 197.9.

The ^{1}H and ^{13}C NMR spectra data of product **9bi** were consistent with the literature.[19]

1-(*p*-Tolyl)ethan-1-one (9oi)



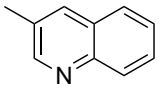
The product **9oi** was synthesized according to **Method C** using methyl lithium, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 9.8 mg, 0.073 mmol, 73% isolated yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (s, 3H), 2.58 (s, 3H), 7.26 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.0 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 22.1, 26.9, 128.8 (2C), 129.6, 129.7, 135.1, 144.3, 198.3.

The ^{1}H and ^{13}C NMR spectra data of product **9oi** were consistent with the literature.[20]

3-Methylquinoline (9oo)



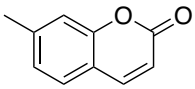
The product **9oo** was synthesized according to **Method C** using methyl lithium, and purified by flash chromatography on silica gel (100:0–90:10, hexane/CH_2Cl_2) (**Table 1-2**; 16.0 mg, 0.112 mmol, 56% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 3H), 7.51 (m, 1H), 7.65 (m, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.93 (s, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.78 (d, J = 2.0 Hz, 1H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 18.8, 126.5, 127.1, 128.1, 128.4, 129.2, 130.5, 134.7, 146.6, 152.4.

The ^{1}H and ^{13}C NMR spectra data of product **9oo** were consistent with the literature.[21]

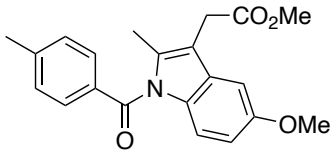
7-Methyl-2*H*-chromen-2-one (9op)



The product **9op** was synthesized according to **Method C** using methyl lithium, and purified by flash chromatography on silica gel (100:0–95:5, CH_2Cl_2/MeOH) (**Table 1-2**; 24.3 mg, 0.152 mmol, 76% isolated yield, including impurity).

The ^{1}H spectra data of product **9op** was consistent with the literature.[22]

Methyl 2-[5-Methoxy-2-methyl-1-(4-methylbenzoyl)-1*H*-indol-3-yl]acetate (9op)



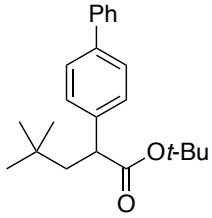
The product **9op** was synthesized according to **Method C** using methyl lithium, and purified by flash chromatography on silica gel (100:0–90:10, hexane/EtOAc) (**Table 1-2**; 28.2 mg, 0.08 mmol, 80% isolated yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.47 (s, 3H), 3.68 (s, 2H), 3.71 (s, 3H), 3.85 (s, 3H), 6.66 (dd, J = 2.4, 8.9 Hz, 1H), 6.89 (d, J = 8.9 Hz, 1H), 6.97 (d, J = 2.4 Hz, 1H), 7.29 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 13.2, 21.7, 30.2, 52.1, 55.7, 101.0, 111.4, 111.8, 115.0, 129.4 (2C), 130.0 (2C), 130.4, 131.0, 132.7, 136.1, 143.7, 155.8, 169.4, 171.5.

The ^{1}H and ^{13}C NMR spectra data of product **9op** were consistent with the literature.[21]

***tert*-Butyl 2-[(1,1'-Biphenyl)-4-yl]-4,4-dimethylpentanoate (9aba)**



The product **9aba** was purified by flash chromatography on silica gel (100:0–10:1, hexane/CH_2Cl_2) (**Table 1-3**; 11.7 mg, 0.035 mmol, 35% isolated yield). White solid.

M.p. :84–86 °C

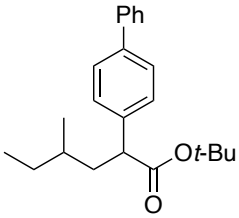
IR (neat) 669, 1142, 1731, 2341, 2957, 3734 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 9H), 1.39 (s, 9H), 1.53 (dd, J = 3.6, 14.4 Hz, 1H), 2.30 (dd, J = 9.2, 14.4 Hz, 1H), 3.58 (dd, J = 3.6, 9.2 Hz, 1H), 7.33 (t, J = 7.2 Hz, 1H), 7.37 (d, J = 8.4 Hz, 2H), 7.43 (dd, J = 7.2, 7.8 Hz, 2H) 7.53 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 27.9 (3C), 29.5 (3C), 31.1, 47.3, 48.9, 80.4, 127.0 (4C), 128.0 (4C), 128.7 (2C), 139.5, 140.7, 173.9.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{31}O_2^+$, 339.2319; found, 339.2317.

***tert*-Butyl 2-[(1,1'-Biphenyl)-4-yl]-4-methylhexanoate (10cba)**



The product **10cba** was purified by flash chromatography on silica gel (100:0–10:1, hexane/CH_2Cl_2) (**Table 1-3**; 21.8 mg, 0.64 mmol, 64% isolated yield, 1:1 diastereomixture and including impurity). Colorless oil.

IR (neat) 506, 561, 648, 697, 732, 759, 843, 908, 1145, 1258, 1367, 1457, 1487, 1726, 2874, 2928, 2961 cm^{-1}.

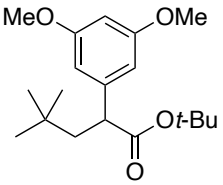
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82–0.95 (m, 7H), 1.12–1.35 (m, 1.5H), 1.37–1.51 (m, 1H), 1.41 (s, 4.5H), 1.42 (s, 4.5H), 1.83 (t, J = 6.7 Hz, 1H), 2.11–2.17 (m, 0.5H), 3.57–3.64 (m, 1H), 7.31–7.46 (m, 5H), 7.55 (d, J = 8.2 Hz, 2H), 7.60 (dd, J = 1.8, 6.0 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 11.13 (0.5C), 11.14 (0.5C), 18.9 (0.5C), 19.1 (0.5C), 27.97 (1.5C), 27.99 (1.5C), 29.4 (0.5C), 29.5 (0.5C), 32.0 (0.5C), 32.4 (0.5C), 40.2 (0.5C), 40.9 (0.5C), 50.09 (0.5C), 50.14 (0.5C), 80.50 (0.5C), 80.54 (0.5C), 127.00 (2C), 127.09 (2C), 127.12 (1C),

128.2 (1C), 128.3 (1C), 128.7 (1C), 138.9 (1C), 139.4 (1C), 139.64 (0.5C), 139.66 (0.5C), 140.8 (1C), 173.4 (0.5C), 173.7 (0.5C).

HRMS–DART (*m/z*): $[M]^+$ calcd for $C_{23}H_{30}O_2^+$, 338.2252; found, 338.2240.

***tert*-Butyl 2-(3,5-Dimethoxyphenyl)-4,4-dimethylpentanoate (10abd)**



The product **10abd** was purified by flash chromatography on silica gel (100:0–10:1, hexane/CH_2Cl_2) (**Table 1-3**; 8.3 mg, 0.026 mmol, 26% isolated yield, including inseparable impurity). Colorless oil.

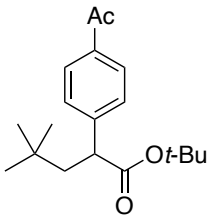
IR (neat) 669, 1142, 1206, 1596, 1729, 2341, 2928 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (s, 9H), 1.39 (s, 9H), 1.46 (dd, J = 2.8, 15.6 Hz, 1H), 2.23 (dd, J = 9.2, 14.2 Hz, 1H), 3.45 (dd, J = 3.2, 9.6 Hz, 1H), 3.78 (s, 6H), 6.33 (t, J = 1.8 Hz, 1H), 6.46 (d, J = 2.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 27.9 (3C), 29.5 (3C), 29.7, 31.0, 47.2, 55.3 (2C), 80.4, 98.7, 105.7 (2C), 139.4, 160.7 (2C), 173.5.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{31}O_4^+$, 323.2222; found, 323.2214.

***tert*-Butyl 2-(4-Acetylphenyl)-4,4-dimethylpentanoate (10abi)**



The product **10abi** was purified by flash chromatography on silica gel (100:0–10:1, hexane/CH_2Cl_2) (**Table 1-3**; 16.9 mg, 0.056 mmol, 56% isolated yield). Pale orange solid.

M.p. :54–56 °C

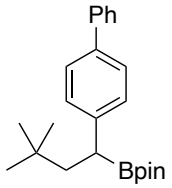
IR (neat) 669, 1144, 1685, 1732, 2341, 2957, 3733 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (s, 9H), 1.37 (s, 9H), 1.50 (dd, J = 3.6, 14.0 Hz, 1H), 2.28 (dd, J = 8.8, 14.0 Hz, 1H), 2.59 (s, 3H), 3.60 (dd, J = 3.6, 8.8 Hz, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 26.6, 27.8 (3C), 29.5 (3C), 31.1, 47.0, 49.4, 80.8, 127.9 (2C), 128.6 (2C), 135.7, 147.1, 173.1, 197.8.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{29}O_3^+$, 305.2111; found, 305.2106.

2-{1-[(1,1'-Biphenyl)-4-yl]-3,3-dimethylbutyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (10aca)



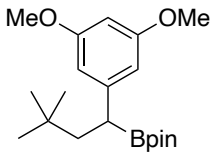
The product **10aca** was purified by flash chromatography on silica gel (100:0–10:1, hexane/CH_2Cl_2) (**Table 1-3**; 24.4 mg, 0.067 mmol, 67% isolated yield, including inseparable impurity).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (s, 9H), 1.157 (s, 6H), 1.160 (s, 6H), 1.53 (dd, J = 3.6, 13.6 Hz, 1H), 2.04 (dd, J = 3.2, 6.8 Hz, 1H), 2.44 (dd, J = 3.6, 10.0 Hz, 1H), 7.29–7.32 (m, 3H), 7.41 (t, J = 7.6 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 7.2 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 24.4 (2C), 24.6 (2C), 29.7 (3C), 30.2, 46.6, 83.3 (2C), 127.07, 127.12 (2C), 127.3 (2C), 128.6 (2C), 128.8 (2C), 137.7, 141.2, 144.1.

The ^{1}H and ^{13}C NMR spectra data of product **10aca** were consistent with the literature[23].

2-[1-(3,5-Dimethoxyphenyl)-3,3-dimethylbutyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (10acd)



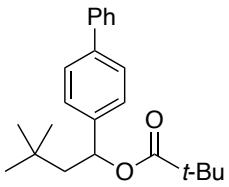
The product **10acd** was purified by flash chromatography on silica gel (100:0–1:1, hexane/CH_2Cl_2) (**Table 1-3**; 13.3 mg, 0.038 mmol, 38% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (s, 9H), 1.165 (s, 6H), 1.168 (s, 6H), 1.47 (dd, J = 3.6, 13.2 Hz, 1H), 1.98 (dd, J = 10.0, 13.2 Hz, 1H), 2.32 (dd, J = 3.2, 10.0 Hz, 1H), 3.77 (s, 6H), 6.24 (t, J = 2.4 Hz, 1H), 6.41 (d, J = 2.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 24.4 (2C), 24.7 (2C), 29.6 (3C), 31.3, 46.6, 55.2 (2C), 83.2 (2C), 97.4, 106.1 (2C), 147.3, 160.5 (2C).

The ^{1}H and ^{13}C NMR spectra data of product **10acd** were consistent with the literature.[23]

1-[(1,1'-Biphenyl)-4-yl]-3,3-dimethylbutyl Pivalate (10ada)



The product **10ada** was purified by flash chromatography on silica gel (100:0–10:1, hexane/CH_2Cl_2) (**Table 1-3**; 24.5 mg, 0.072 mmol, 72% isolated yield). White solid.

M.p. :93–95 °C

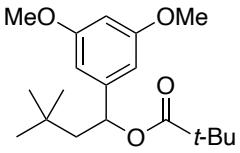
IR (neat) 405, 669, 1151, 1728, 1978, 2342, 2359, 2959 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (s, 9H), 1.20 (s, 9H), 1.61 (dd, J = 2.8, 14.8 Hz, 1H), 2.01 (dd, J = 9.2, 14.8 Hz, 1H), 5.85 (dd, J = 2.8, 9.2 Hz, 1H), 7.31–7.37 (m, 3H), 7.34 (t, J = 7.6 Hz, 2H), 7.55–7.58 (m, 4H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 27.1 (3C), 30.0 (3C), 30.5, 38.6, 50.4, 73.7, 126.3, 127.1 (2C), 127.2 (4C), 128.7 (2C), 140.3, 140.8, 142.1, 177.6.

HRMS–DART (*m/z*): $[M+NH_4]^+$ calcd for $C_{23}H_{34}N_1O_2^+$, 356.2590; found, 356.2593.

1-(3,5-Dimethoxyphenyl)-3,3-dimethylbutyl Pivalate (10add)



The product **10add** was purified by flash chromatography on silica gel (100:0–7:3, hexane/CH_2Cl_2) (**Table 1-3**; 16.7 mg, 0.052 mmol, 52% isolated yield). Pale yellow oil.

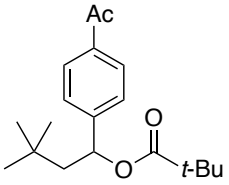
IR (neat) 669, 1155, 1205, 1598, 1729, 2341, 2957 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 9H), 1.20 (s, 9H), 1.55 (dd, J = 2.4, 14.8 Hz, 1H), 1.92 (dd, J = 9.6, 14.8 Hz, 1H), 3.77 (s, 6H), 5.72 (dd, J = 2.4, 9.6 Hz, 1H), 6.33 (t, J = 2.4 Hz, 1H), 6.43 (d, J = 2.4 Hz, 2H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 27.1 (3C), 29.9 (3C), 30.5, 38.6, 50.5, 55.3 (2C), 73.8, 99.2, 103.6 (2C), 145.7, 160.8 (2C), 177.5.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{31}O_4^+$, 323.2217; found, 323.2219.

1-(4-Acetylphenyl)-3,3-dimethylbutyl Pivalate (10adi)



The product **10adi** was purified by flash chromatography on silica gel (100:0–7:3,

hexane/CH_2Cl_2) (**Table 1-3**; 15.8 mg, 0.052 mmol, 52% isolated yield). Colorless oil.

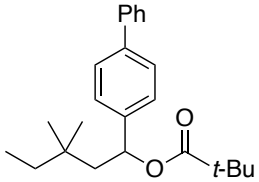
IR (neat) 669, 1151, 1267, 1689, 1729, 2340, 2958 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ 0.97 (s, 9H), 1.19 (s, 9H), 1.55 (dd, J = 2.4, 7.2 Hz, 1H), 1.97 (dd, J = 9.0, 15.0 Hz, 1H), 2.58 (s, 3H), 5.82 (dd, J = 3.0, 9.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 2H).

^{13}C NMR (150.9 MHz, $CDCl_3$) δ 26.6, 27.0 (3C), 29.9 (3C), 30.5, 38.5, 50.1, 73.5, 125.9 (2C), 128.7 (2C), 136.3, 148.3, 177.5, 197.6.

HRMS–DART (*m/z*): $[M+NH_4]^+$ calcd for $C_{19}H_{32}N_1O_3^+$, 322.2382; found, 322.2376.

1-[(1,1'-Biphenyl)-4-yl]-3,3-dimethylpentyl Pivalate (10bda)



The product **10bda** was purified by flash chromatography on silica gel (100:0–10:1, hexane/CH_2Cl_2) (**Table 1-3**; 14.0 mg, 0.040 mmol, 40% isolated yield). Pale yellow solid.

M.p. :54–56 °C

IR (neat) 697, 836, 1280, 1487, 1727, 2360, 2961 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, J = 7.6 Hz, 3H), 0.93 (d, J = 9.2 Hz, 6H), 1.20 (s, 9H), 1.23–1.39 (m, 2H), 1.59 (dd, J = 2.8, 15.2 Hz, 1H), 2.00 (dd, J = 9.2, 14.8 Hz, 1H), 5.84 (dd, J = 2.8, 9.2 Hz, 1H),7.31–7.37 (m, 3H), 7.43 (t, J = 7.6 Hz, 2H), 7.44–7.58 (m, 4H).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ 8.5, 27.0 (3C), 27.1 (2C), 33.0, 34.7, 38.6, 47.8, 73.5, 126.2, 127.1 (2C), 127.2 (4C), 128.7 (2C), 140.3, 140.8, 142.3, 177.6.

HRMS–DART (*m/z*): $[M]^+$ calcd for $C_{24}H_{32}O_2^+$, 352.2402; found, 352.2407.

■ Reference ■

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[2] Sheldrick, G. M. *Acta Crystallogr. Sect. C*. **2015**, *71*, 3-8.

[3] Sumida, Y.; Harada, R.; Kato-Sumida, T.; Johmoto, K.; Uekusa, H.; Hosoya, T. *Org. Lett.* **2014**, *16*, 6240–6243.

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第２章　可視光励起ホウ素アート錯体を用いた N-ヘテロ環カルベン触媒反応

第１節　着想背景および作業仮説

立体的に嵩高いユニット同士の結合形成反応は、創薬研究やケミカルスペースの拡大の観点から重要な方法論ではあるものの、有機合成においては依然として挑戦的な課題である。異なる 2 つのラジカル種が反応する“ラジカル–ラジカルカップリング”は、本課題を解決しうるプロセスである [1, 2]。異なる 2 つのラジカル種が同じ速度でそれぞれ形成する場合、長寿命なラジカル（persistent radical）と短寿命なラジカル（transient radical）のラジカル–ラジカルカップリングが、高選択的に進行する（Persistent Radical Effect = PRE）[3]。この PRE に基づくラジカル–ラジカルカップリングを活用した、可視光駆動型の結合形成反応が、近年数多く報告されている。しかし、そのほとんどが、光酸化還元触媒あるいは電荷移動錯体形成を必要とするため、多段階の電子移動もしくはエネルギー移動が起こり、反応プロセスを複雑化する。したがって、基質同士での一電子授受によって、2 つのラジカル種を形成させ、ラジカル–ラジカルカップリングを起こすことができれば、直截的かつ効率的な反応プロセスの開発に繋がる（**Figure 2-1**）。

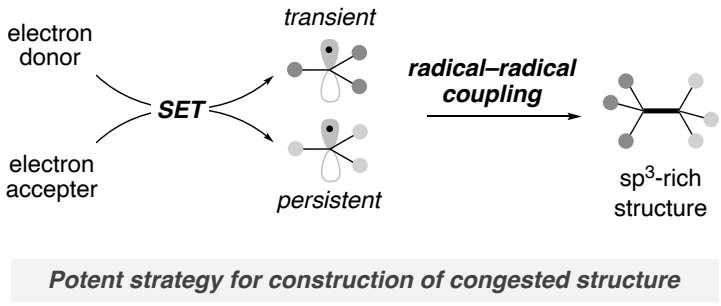


Figure 2-1. Radical−radical coupling based on the persistent radical effect.

2019 年以降、当研究室は、PRE に基づくラジカル–ラジカルカップリングを活用した、N-ヘテロ環カルベン（NHC）触媒反応を開発してきた（**Figure 2-2**, 上段）[4–8]。本手法では、アルデヒドと第 3 級および第 2 級脂肪族カルボン酸誘導体（酸化還元活性エステル）の脱炭酸型クロスカップリング反応が進行し、嵩高いケトンを与える。塩基存在下、NHC 触媒とアルデヒドより形成される Breslow 中間体 [9] のエノラート体から、電子受容体である酸化還元活性エステルに対して一電子移動が起こることで、長寿命なケチルラジカルと短寿命なアルキルラジカルがそれぞれ形成される。これらラジカル種のラジカル–ラジカルカップリングによりケトンを与えるとともに NHC 触媒が再生する。また、最近、相補的な手法として、光酸化還元触媒を用いたカルボン酸誘導体（アシルイミダゾールなど）とラジカル前駆体のクロスカップリング反応が、他のグループによって報告された（**Figure 2-2**, 下段）[10–18]。NHC 触媒とカルボン酸誘導体より形成されるアシル

アゾリウム中間体[19]に対して一電子移動が起こり、同様にケチルラジカルとアルキルラジカルが生じ、ラジカル–ラジカルカップリングに導かれる。しかし、本協働触媒では、光酸化還元触媒とラジカル前駆体との一電子移動による炭素中心ラジカルが生じるため、導入可能な有機基に制限がある。

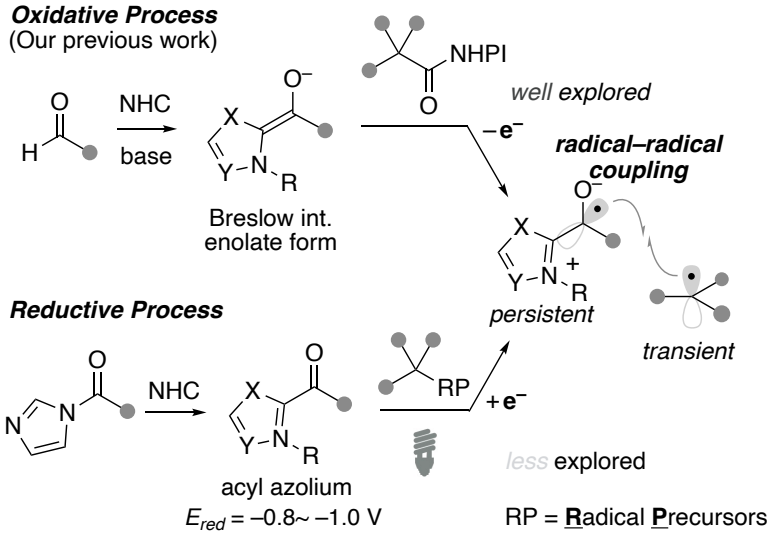


Figure 2-2. Radical NHC catalysis. Oxidative process (upper) and reductive process (bottom).

このような背景を踏まえ、反応基質間での一電子授受を介した還元的ラジカル NHC 触媒反応を達成できれば、上記の課題を克服できると想定した。具体的には、電子供与体として、広く入手容易かつ電子豊富な化学種である有機ホウ素化合物に着目した[20]。しかしながら、これまで報告された有機ホウ素化合物は、一般により電子豊富な 4 配位ホウ素アート錯体の状態においても、アシルアゾリウム中間体（$E_{1/2}$ = ca. −0.8〜−1.0 V vs. SCE in MeCN）に対する一電子移動を起こすのに十分な還元電位に達しない（**Figure 2-3**）[21–26]。一方で、本論第 1 章でも述べた通り、直接光励起可能なボラセン由来のホウ素アート錯体 **1a** は励起状態において、強力な一電子還元剤（[E(**2a**$^{\bullet+}$/**2a***)] = –2.2 V vs. SCE in MeCN）として機能する。また、当研究室では、有機ホウ素化合物と 2,2'-(**p**yridine-2,6-diyl)**dip**henol（PDP）より得られるホウ素アート錯体 **2a** も可視光励起可能であり、励起状態において **1a** と同様の反応性を示すことを見出している[27,28]。この PDP 由来のホウ素アート錯体は、対応するボロン酸またはトリフルオロボレート塩から調製可能であるため、官能基を有するような複雑な有機ラジカル種の生成が可能である。したがって、還元的ラジカル NHC 触媒反応に対して、これらホウ素アート錯体を一電子還元剤かつ有機ラジカル前駆体として適用することで、網羅的なケトン化合物構築法を提供できると想定した（**Figure 2-4**）。

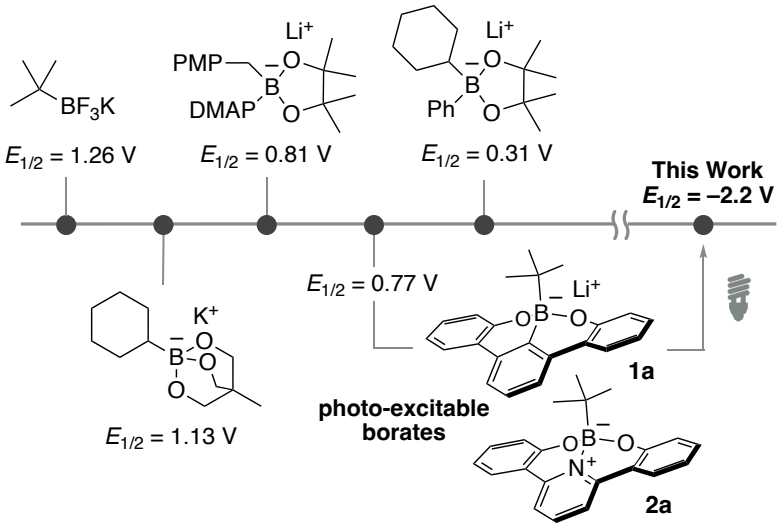


Figure 2-3. Redox potential of the reported alkylborates.

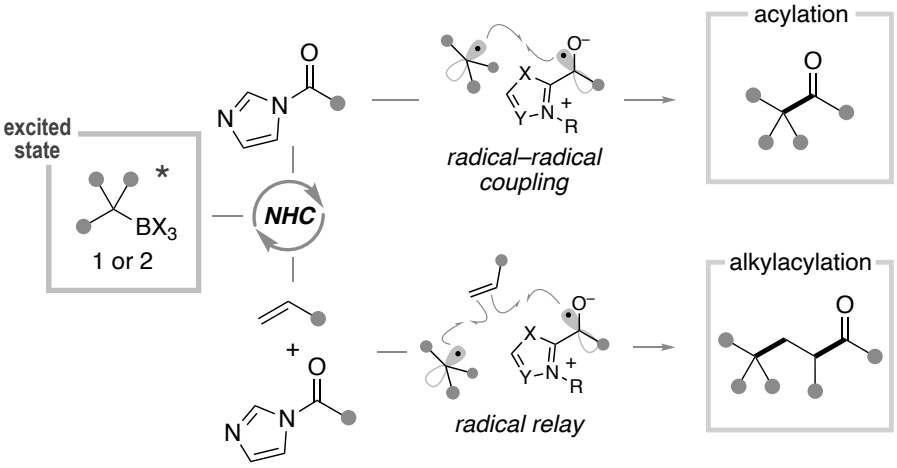
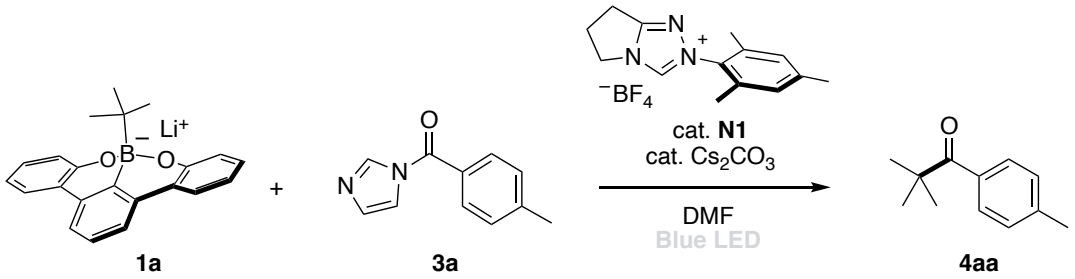


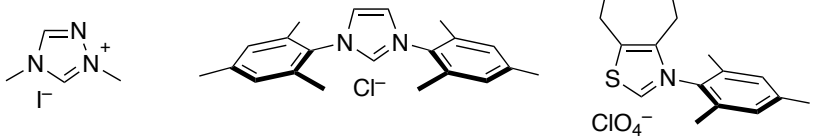
Figure 2-4. Merging radical N-heterocyclic carbene catalysis with direct photoexcitation of alkylborates.

第 2 節　ホウ素アート錯体とアシルイミダゾールの二成分クロスカップリング反応

上述の作業仮説に基づき、ホウ素アート錯体とアシルイミダゾールとのラジカルクロスカップリングを検討した。可視光照射下、DMF 溶媒中で、トリアゾール型 NHC 触媒 **N1** と炭酸セシウム（15 mol %）存在下、ホウ素アート錯体 **1a**（0.12 mmol）、アシルイミダゾール **3a**（0.2 mmol）を反応させたところ、目的のケトン **4aa** が NMR 収率 58%で得られた（**Table 2-1**, **Entry 1**）。NHC 触媒として、立体障害のより小さな **N2**、またはより高い求核性を有するイミダゾール型 **N3** およびチアゾール型 **N4** を用いた際には、アシル化体の収率は低下した（**Table 2-1, Entries 2−4**）。これは、アシルアゾリウム中間体の形成速度のミスマッチやケチルラジカルの安定性に起因すると推測される。アシルドナーとして、アシルフッカ物 **A1** やアシルトリアゾール **A2** を用いた際にはわずかながら収率は低下し、ペンタフルオロフェニルエステル **A3** の場合には大幅に収率を低下させた（**Table 2-1**, **Entries 5−7**）。溶媒としては、DMF の代わりに MeCN を用いた際にも、多少収率は低下するものの目的のアシル化が進行した（**Table 2-1**, **Entry 8**）。アルキルラジカル前駆体として、広く用いられているトリフルオロボレート塩を用いた際には、目的のケトン体が全く得られなかった（**Table 2-1**, **Entry 9**）。可視光を照射しない条件では全く反応が進行しなかった一方で、NHC 触媒を添加しない場合には、わずかながら目的のアシル化体が得られた（**Table 2-1**, **Entries 10** and **11**）。ボラセン由来のホウ素アート錯体 **1a** の代わりに PDP 由来のホウ素アート錯体 **2a** を用いた際には、わずかながら収率は低下するものの、同様に目的のクロスカップリング体を与えた（**Table 2-1**, **Entry 12**）。

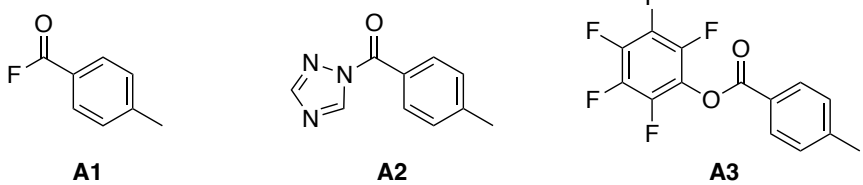


NHC catalyst



N2　　**N3**　　**N4**

acyl donor



A1　　**A2**　　**A3**

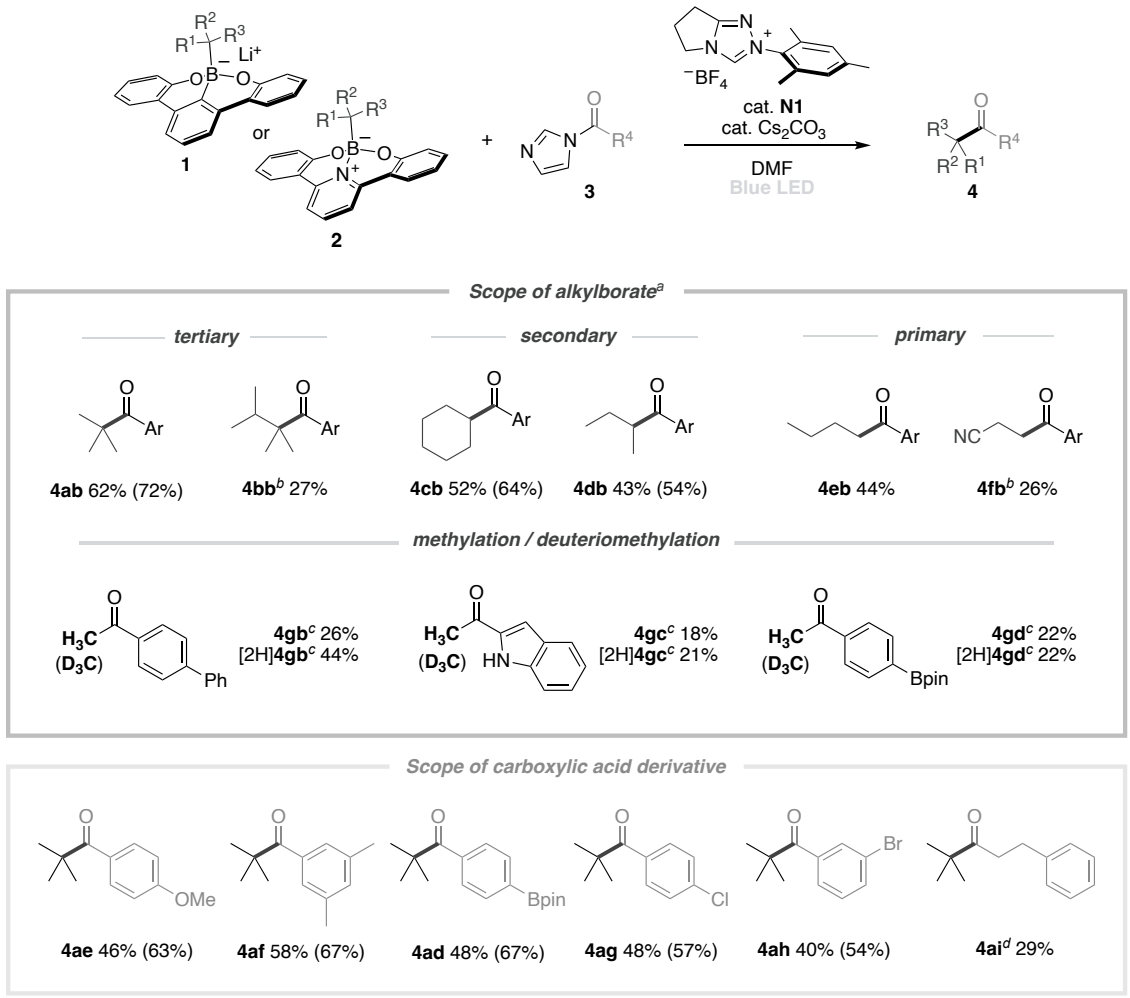
Entry	Deviation from standard conditions[a]	Yield (%)[b] of **4aa**
1	none	58
2	**N2** instead of **N1**	14
3	**N3** instead of **N1**	17
4	**N4** instead of **N1**	15
5	**A1** instead of **3a**	39
6	**A2** instead of **3a**	39
7	**A3** instead of **3a**	10
8	MeCN instead of DMF	44
9	*t*-$BuBF_3K$ instead of **1a**	0
10	no light irradiation	0
11	without **N1**	16
12[c]	**2a** instead of **1a**	35

[a]Reaction was carried out with **1a** (0.12 mmol), **3a** (0.1 mmol), **N1** (0.015 mmol), and Cs_2CO_3 (0.015 mmol) in DMF (1 mL) under Kessil PR160L 440 nm irradiation at ambient temperature for 6 h. [b]^{1}H NMR yield. [c]MeCN was used as a solvent.

Table 2-1. Screening of reaction conditions.

上記の条件検討で得られた最適条件に基づき、アルキルホウ素アート錯体（**1** and **2**）およびアシルイミダゾール **3** の基質適用範囲の検討を行った（**Table 2-2**）。まず、ボラセン由来のホウ素アート錯体 **1** および PDP 由来のアート錯体 **2** をそれぞれ用いて検討を行った。本クロスカップリング反応において、第三級、第二級および第一級アルキルラジカルの適用が可能であった（**4ab**–**4eb**）。またニトリル基を有するアルキルホウ素アート錯体 **2f** も収率は低下するものの、目的のアシル化体 **4fb** を与えた。この収率の低下は、PDP 由来のアート錯体 **2** にラジカル発生効率の低さに起因すると推測される。本ホウ素アート錯体は、その有機ラジカル生成能の高さゆえ、可視光照射下、メチルラジカルおよび重水素メチルラジカルの発生が可能である。したがって、ラジカル介在型 NHC 触媒反応に適用することで、対応するカルボン酸からアセチル（**4gb**–**4gd**）および重水素アセチル（[2H]**4gb**–[2H]**4gd**）ユニットを構築可能であった。

続いて、アシルイミダゾールの適用範囲についても検討を行った。安息香酸誘導において、芳香環上に電子供与基あるいは電子求引基有する場合、どちらにおいても目的のアシル化体が得られた（**4ae**–**4ah**）。特に、一般に遷移金属触媒に対して化学選択性の低いピナコールボリル基やハロゲン基は、問題なくアルキル化が進行した（**4ad**, **4ag**, and **4ah**）。安息香酸誘導体とはケチルラジカル中間体でのスピン密度が異なる脂肪族カルボン酸 **3i** においても、収率は低いもののアシル化生成物 **4ai** を与えた [12]。



Reaction was carried out with **1** or **2** (0.12 mmol), **3** (0.1 mmol), **N1** (0.015 mmol), and Cs_2CO_3 (0.015 mmol) in DMF (1 mL) for 6 h under Kessil PR160L 440 nm irradiation. [a]Ar = 4-biphenyl. ^{1}H NMR yield in parentheses. [b]Borate **2** and MeCN were used instead of **1** and DMF. [c]The reaction time was 24 h for methylation and deuteriomethylation. was used as a solvent. [d]**N2** was used instead of **N1.**

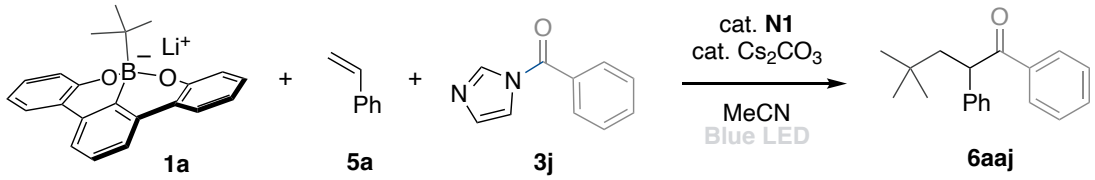
Table 2-2. Substrate scope of radical cross-coupling.

第 3 節　アルケンのビシナルアルキルアシル化反応

本反応の有用性を高めるため、アルケンの三成分ビシナル二炭素結合形成反応に着目した [29, 30]。アルケンのビシナル二炭素結合形成反応は、二つの炭素–炭素結合を一挙に形成できるため、入手容易な原料から複雑な骨格を構築可能とする魅力的な手法である。これまで遷移金属触媒を用いた、カルボメタル化を基点とした化学変換が広く開発されてきた [31]。しかしながら、その反応の性質上、β-水素脱離やアルケンの異性化などの副反応が競合することが問題であった。近年、連続的なラジカル機構を経由する、“ラジカルリレー型反応”に基づく合成戦略は、遷移金属触媒プロセスの問題点を回避できるため、非常に注目が集まっている。当研究室での NHC 触媒を用いたアルケンのアシル

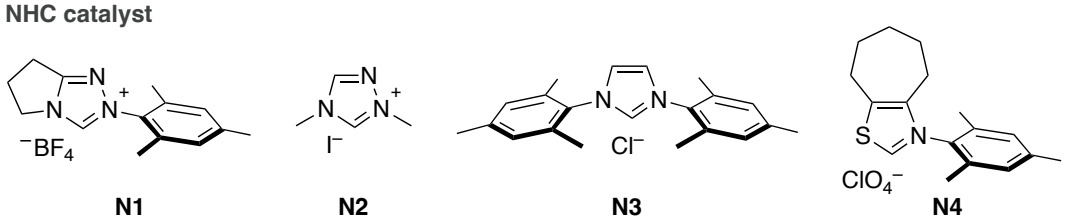
アルキル化反応の報告を皮切りに、酸化的ラジカル NHC 触媒反応に基づく三成分カップリング反応は広く開発が進んでいる[5−8, 32, 33]。一方で、還元的ラジカル NHC 触媒反応に基づくラジカルリレーを介したビシナルの二炭素官能基化はほとんど報告されていない。

このような背景を踏まえ、アルケンに対するホウ素アート錯体とアシルイミダゾールを用いたアルキルアシル化反応を検討した。可視光照射下、DMF 溶媒中で、トリアゾール型 NHC 触媒 **N1** と炭酸セシウム（15 mol %）存在下、ホウ素アート錯体 **1a**（0.12 mmol）、スチレン **5a**（0.2 mmol）、アシルイミダゾール **3j**（0.2 mmol）を反応させたところ、目的の三成分カップリング体 **6aaj** が NMR 収率 51%で得られた（**Table 2-3**, **Entry 1**）。NHC 触媒として、立体障害のより小さな **N2**、またはより高い求核性を有するイミダゾール型 **N3** およびチアゾール型 **N4** を用いた際には、アシルアルキル化体の収率は低下した（**Table 2-3**, **Entries 2−4**）。溶媒としては、DMF の代わりに DMSO や DMA を用いた際には収率は低下した（**Table 2-3**, **Entries 5** and **6**）。DMF の反応濃度はあまり反応影響を与えなかった（**Table 2-3**, **Entry 7**）。ボラセン由来のホウ素アート錯体 **1a** の代わりに PDP 由来のホウ素アート錯体 **2a** を用いた際には、同等の収率で目的のクロスカップリング体を与えた（**Table 2-3**, **Entry 8**）。さらに、この PDP 由来のホウ素アート錯体 **2a** を用いた条件において、二成分カップリングの条件検討を参考に、用いる溶媒を MeCN に変更した際に収率が改善し（**Table 2-3**, **Entry 9**）、スチレンの添加量を 5 当量まで増加した際に 79%で目的の三成分カップリング体が得られた（**Table 2-3**, **Entry 10**）。



1a **5a** **3j** **6aaj**

NHC catalyst



N1 **N2** **N3** **N4**

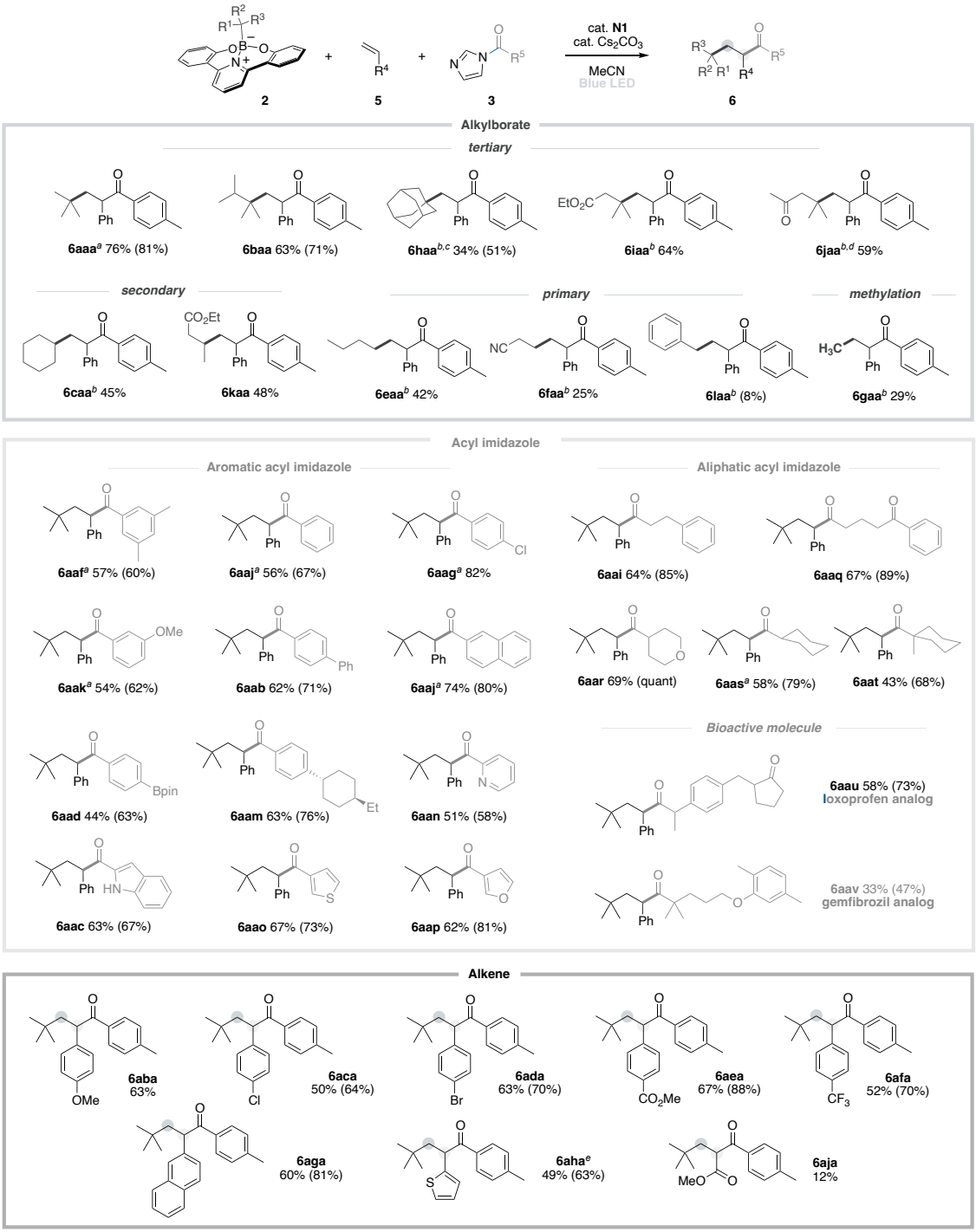
Entry	Deviation from standard conditions[a]	Yield (%)[b] of **6aaj**
1	none	51
2	**N2** instead of **N1**	29
3	**N3** instead of **N1**	14
4	**N4** instead of **N1**	17
5	DMSO instead of DMF	13
6	DMA instead of DMF	41
7	DMF (0.33 M)	50
8[c]	**2a** instead of **1a**	45
9[d]	**2a** instead of **1a**	68
10[e]	**2a** instead of **1a**	79

[a]Reaction was carried out with **1a** (0.12 mmol), **3j** (0.1 mmol), **5a** (0.2 mmol), catalyst (0.015 mmol) in DMF (1 mL) under Kessil PR160L 440 nm irradiation equiped with PhotoRedOx Duo for 14 h. [b]^{1}H NMR yield. [c]Reaction was carried out in DMF (300 μL) for 6 h. [d]Reaction was carried out with **2a** (0.12 mmol), styrene (**5a**) (0.2 mmol), **3j** (0.10 mmol), **N1** catalyst (0.015 mmol) in MeCN (300 μL) under blue LED (440 nm) irradiation for 6 h. [e]5 equiv of styrene was used.

Table 2-3. Optimization of reaction conditions.

上記の条件検討で得られた最適条件に基づき、アルキルホウ素アート錯体 **2**、アルケン **5**、アシルイミダゾール **3** の基質適用範囲の検討を行った（**Table 2-4**）。まず、PDP 由来のアート錯体 **2** を用いて検討を行った（**Table 2-4**, 上段）。PDP 由来のホウ素アート錯体は、対応するボロン酸およびトリフルオロボレート塩から調製可能であるため、官能基を有する種々のアルキル基の導入が可能であった。ヒドロホウ素化および 1,4-共役ホウ素化により、対応する有機ホウ素化合物が容易に得られ、本手法に適用することで、第三級アルキル化が進行した（**6aaa**–**6jaa**）。一般に、第二級および第一級アルキルラジカルは二成分カップリングが競合するため、ラジカルリレー型反応への適用は困難である。一方で、本手法の場合には、それらの二成分カップリング体やアルキルラジカルのホモカップリング体がほとんど形成せずに、第二級、第一級およびメチルラジカルの適用が可能であった（**6caa**–**6gaa**）。本プロセスのアルキルラジカルの広範な適用範囲は、光励起可能なホウ素アート錯体の反応性に起因すると推測される。

続いて、アシルイミダゾールの適用範囲についても検討を行った（**Table 2-4**, 中段）。安息香酸誘導体において、芳香環上に電子供与基あるいは電子求引基を有する場合、ど



Reaction was carried out with **2** (0.24 mmol), **5** (1 mmol), **3** (0.2 mmol), **N1** (0.03 mmol), and Cs_2CO_3 (0.03 mmol) in MeCN (0.6 mL) for 6 h under Kessil PR160L 440 nm irradiation equipped with a PhotoRedOx Duo. ^{1}H NMR yield in parentheses. [a]2 equiv of styrene was used. [b]The reaction was carried out in a 0.1 mmol scale of acyl imidazole. [c]The reaction time was 43 h. [d]Borate (0.15 mmol) and MeCN (1 mL) were used. [e]4 equiv of styrene was used.

Table 2-4. Substrate scope of radical relay-type alkylacylation of alkenens.

ちらにおいても目的の三成分カップリング体が得られた（**6aaf**, **6aaj**, **6aag**, and **6aak**）。ケチルラジカル中間体の反応性が異なる、より広い π 共役構造を有する基質においても、アルキルアシル化体が高い収率で得られた（**6aab** and **6aaj**）本手法の化学選択性の高さゆえ、ピナコールボリル基や不斉炭素中心を有する基質の場合にも、問題なく適用可能であった（**6aad** and **6aam**）。また、脂肪族カルボン酸由来のアシルイミダゾール（**3i** and **3q**−**3t**）も、本触媒系において適用可能であった（**6aai** and **6aaq**−**6aat**）。特に、これまで報告されているラジカル NHC 触媒反応では適用できなかった立体障害の大きい第三級カルボン酸由来のアシル基の導入も可能であった（**6aat**）。第三級および第二級脂肪族カルボン酸を有するロキソプロフェンやゲムフィブロジルなどの生理活性分子も適用可能であった（**6aau** and **6aav**）。この適用範囲拡大の要因は、現状明確にはなっていないが、本手法のホウ素アート錯体の高い一電子移動能や適切な NHC 触媒の選択に起因すると推測される。

次に、アルケンの適用範囲についても検討を行った（**Table 2-4**, 下段）。本手法は、スチレンの芳香環上に種々の置換基を有する場合にも、良好な収率で目的のアルキルアシル化体が得られた（**6aba**−**6aga**）。5 当量のアルケンを用いることで、十分な収率で目的の三成分カップリング体が得られるものの、副生成物として精製困難な二成分カップリング体が混在する結果となった。チオフェンを有するビニルヘテロアレーンの適用も可能であった（**6aha**）。スチレン類縁体以外にも、アクリル酸メチル **5i** も適用可能であり、1,3-ケトエステル **6aia** が低収率ながら得られた。

第 4 節　反応機構解析

ホウ素アート錯体 **1a**、アシルイミダゾール **3a**、および反応中間体であるアシルアゾリウム中間体 **INT-I**[34] に対して光物性解析を行った。このホウ素アート錯体を用いた還元的ラジカル介在型 NHC 触媒反応は、作業仮説で想定した、ホウ素アート錯体の光励起を基点とした反応経路と異なるプロセスが想定されうる。すなわち、アシルアゾリウム錯体 **INT-I** が可視光により励起状態に至り、ホウ素アート錯体に対して一電子酸化を起こし、それぞれケチルラジカルおよびアルキルラジカルを生成する反応経路である。しかし、紫外可視吸光スペクトルにおいて、アシルアゾリウム錯体 **INT-I** の吸収強度は、ホウ素アート錯体 **1a** の吸収強度と比較して、極めて弱いことから、ホウ素アート錯体が優先的に光励起されることが推測される（**Figure 2-5**）。さらに、ホウ素アート錯体 **1a** とアシルアゾリウム中間体 **INT-I** またはアシルイミダゾール **3a** それぞれの混合溶液において、溶液の変色および紫外可視吸光スペクトルのピークの形状が未変化なことを考慮すると、EDA 錯体の形成による反応経路も否定された（**Figure 2-6**）。

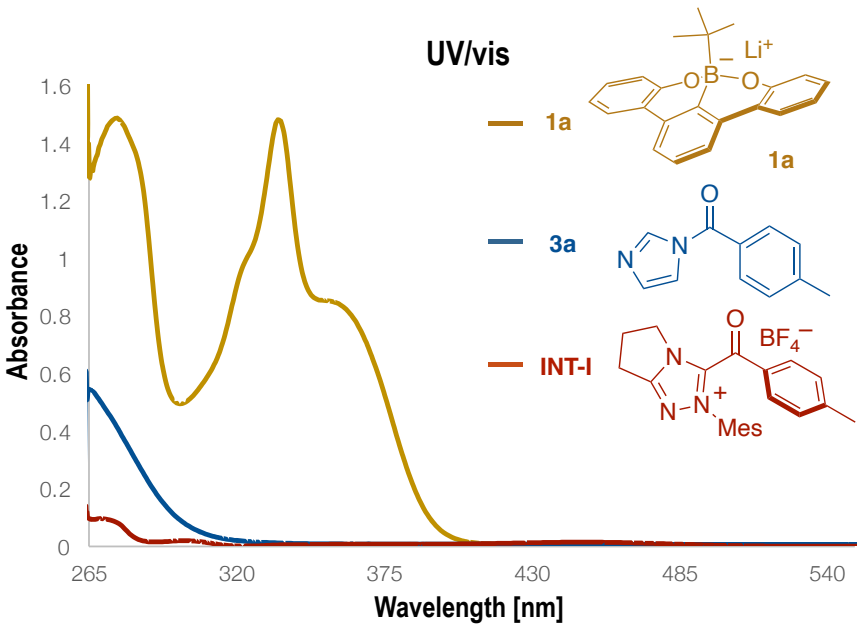


Figure 2-5. Overlaid UV/visible spectra of borate **1a**, acyl imidazole **3a**, and acyl azolium intermediate **INT-I** were measured 0.1 mM DMF solution.

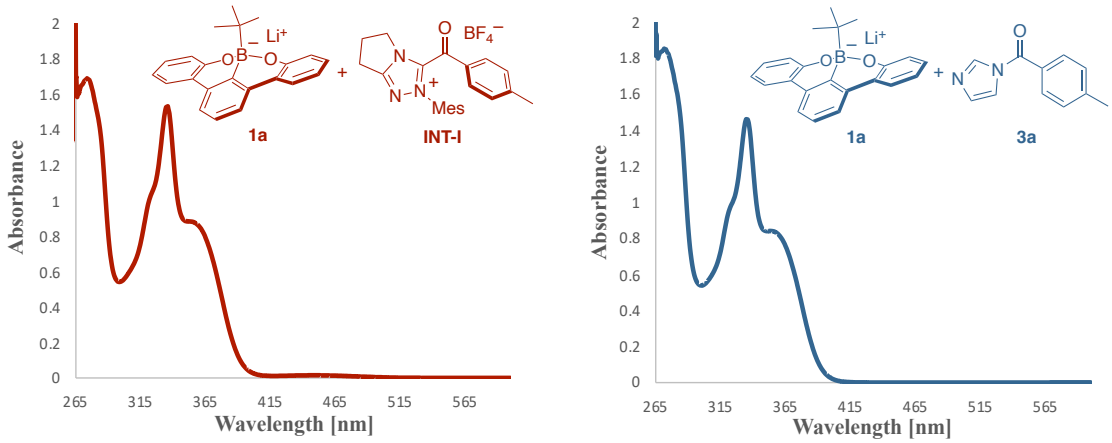


Figure 2-6. UV/vis absorption spectra of mixed solution (borate **1a** : acyl azolium **INT-I** = 1:1 or borate **1a** : acyl imidazole **3a** = 1:1). Red line: mixed solution (borate **1a** : acyl azolium **INT-I** = 1:1) in 0.1 mM DMF. Blue line: mixed solution (borate **1a** : acyl imidazole **3a** = 1:1) in 0.1 mM DMF.

ホウ素アート錯体からの一電子移動段階における詳細を調査するべく、光消光実験も行った（**Figure 2-7**）。ホウ素アート錯体 **1a** に対して、消光剤としてアシルアゾリウム中間体 **INT-I** およびアシルイミダゾール **3a** を添加した際の、Stern-Volmer プロット

を得た。下図の結果から、アシルアゾリウム中間体 **INT-I** がホウ素アート錯体 **1a** を効率的に消光することが示唆された。一方、アシルイミダゾール **3a** の場合、効率は低いものの、ホウ素アート錯体 **1a** が消光されることが確認された。これらの結果から、励起状態のホウ素アート錯体から反応系中で形成したアシルアゾリウム中間体への一電子移動の関与が支持された。また、NHC 触媒を添加せずに反応基質 **3a** のみで低収率ながら目的のアルキル化体が得られた実験結果は、観測されたプロットの結果とも一致した（**Table 2-1**, **Entry 11**）。

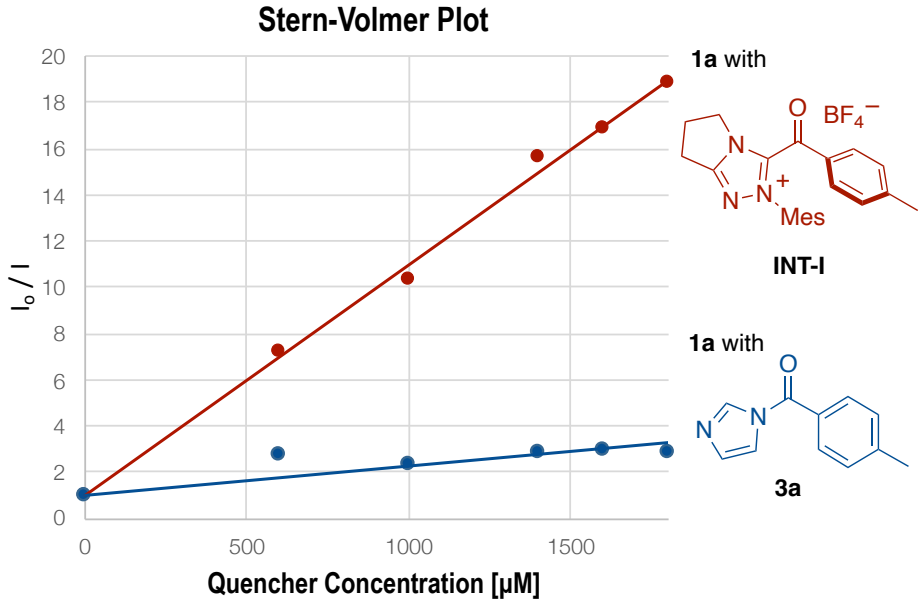
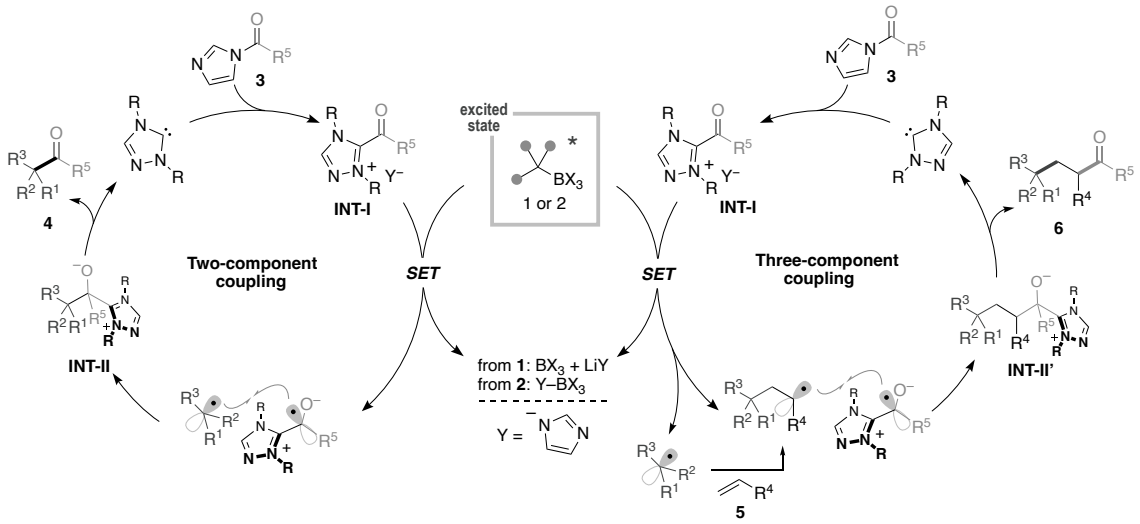


Figure 2-7. Photoquenching experiment of borate **1a** (in 2mM MeCN) with acyl azolium **INT-I** or acyl imidazole **3a**.

これらの機構実験に基づき、推定される反応機構を示す（**Scheme 2-1**）。ホウ素アート錯体とアシルイミダゾールとの二成分クロスカップリングでは、NHC 触媒とアシルイミダゾール **3** が反応し、アシルアゾリウム中間体 **INT-I** が形成する。この中間体 **INT-I** に対して、可視光により励起されたホウ素アート錯体 **1** または **2** から一電子移動が進行し、長寿命なケチルラジカルと短寿命なアルキルラジカルがそれぞれ生じる。これら二つのラジカル種のラジカル–ラジカルカップリングにより、目的のケトン化合物 **4** を与えるとともに、NHC 触媒が再生する（**Scheme 2-1**, 左サイクル）。アルケンに対する三成分アルキルアシル化反応においては、アルケン **5** の添加により、ホウ素アート錯体由来のアルキルラジカルがアルケン **5** にラジカル付加し、新たな炭素中心ラジカルが形成する。この炭素中心ラジカルとケチルラジカルとのラジカル–ラジカルカップリングが

進行する、すなわちラジカルリレー型プロセスにより、アルキルアシル化生成物 **6** を与える（**Scheme 2-1**, 右サイクル）。



Scheme 2-1. Possible reaction pathways.

第 5 節　結論

有機ホウ素アート錯体の直接光励起を活用した、ラジカル介在型 NHC 触媒反応を開発した。本プロセスでは、可視光照射下、光励起状態のホウ素アート錯体とアシルアゾリウム中間体との間での、一電子授受を起点として、PRE に基づく選択的なラジカル–ラジカルカップリングが進行する。この光駆動型ラジカル NHC 触媒系により、ホウ素アート錯体とアシルイミダゾールとのクロスカップリング、およびホウ素アート錯体とアシルイミダゾールによるアルケンのラジカルリレー型アルキルアシル化が可能となった。特に、アルケンのアルキルアシル化は、これまで適用が困難であった幅広い基質適用範囲を実現した。本手法は、ケトン合成における網羅的な合成プロセスを提供し、還元的ラジカル NHC 触媒反応における新たな反応形式を示した。

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第 2 章の実験項

■ Instrumentation and Chemicals ■

NMR spectra were recorded on Bruker AVANCE NEO 400N spectrometer, operating at 400 MHz for ^{1}H NMR, 61.4 MHz for ^{2}H NMR, 100.6 MHz for ^{13}C NMR, 376.5 MHz for ^{19}F NMR and 128.4 MHz for ^{11}B NMR. Chemical shifts were reported in δ ppm. Chloroform-d_1 ($CDCl_3$) containing 0.03% tetramethylsilane (TMS) (>99.8%D, Cambridge Isotope Laboratories, Inc., Cat. No. DLM-7), acetone-d_6 (99.96%D, Cambridge Isotope Laboratories, Inc., Cat. No. DLM-38) and dimethyl sulfoxide-d_6 (99.9%D, Cambridge Isotope Laboratories, Inc., Cat. No. DLM-10) were used as solvents for NMR measurements at ambient temperature. Chemical shifts (δ) for ^{1}H NMR are given in parts per million (ppm) relative to relative to TMS (δ 0.00 ppm in $CDCl_3$), or residual acetone (δ 2.07 ppm). Chemical shifts (δ) for ^{13}C NMR are given in ppm relative to $CDCl_3$ (δ 77.0 ppm), or residual acetone (δ 30.6 ppm) or residual dimethyl sulfoxide (δ 39.5 ppm). Chemical shifts (δ) for ^{19}F NMR are given in ppm relative to α,α,α-trifluorotoluene (δ –63.0 ppm in $CDCl_3$) used as the external standard. Chemical shifts (δ) for ^{11}B NMR are given in ppm relative to $BF_3{\cdot}OEt_2$ (δ 0.0 ppm in $CDCl_3$) used as the external standard. Chemical shifts (δ) for ^{2}H NMR are given in ppm relative to $CHCl_3$ (δ 7.26 ppm). The abbreviations s, d, t, q, br s, and m signify singlet, doublet, triplet, quartet, heptet, broad singlet, and multiplet, respectively.

DART-Mass (HRMS) were measured with JMS-T100TD (JEOL Ltd.).

TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Kanto Chemical Co., Silica gel 60 N, spherical, neutral) was used for column chromatography.

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 an OptiMelt MPA100 automated melting point apparatus (Stanford Research Systems).

CV measurements were recorded with a CH Instruments: BAS Model 600E Series Electrochemical Analyzer.

UV-Vis absorption spectra were recorded on a Shimadzu UV-1900.

Fluorescence spectra were recorded on a Shimadzu RF-6000.

Reaction set-up and materials

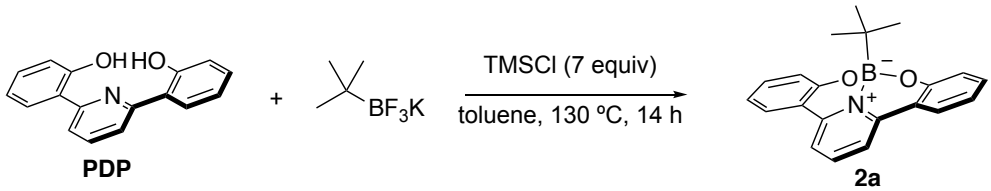
Kessil PR160L 440 nm (highest blue and intensity setting) was used as a light source. TEKNOS MG9 was used as a fan.

All reactions were carried out under nitrogen atmosphere. Materials were obtained from commercial suppliers listed as below and stored under nitrogen, and used as received or prepared according to standard procedures unless otherwise noted. 8,9-Dioxa-8a-borabenzo[*fg*]tetracene

(boracene) was prepared by the reported procedure[1,2] Triazolium salts (**N1, N5**–**N11**) were prepared according to the literature.[3] Imidazolium salt **N3** was prepared according to tha literature.[4] Thiazolium salt **N4** was prepared according to tha literature.[5] Acyl donors (**A1**[6] and **A3**[7]) were prepared according to the literatures. Alkenes (**5e**, **5f** and **5g**) were prepared according to the literature.[8]

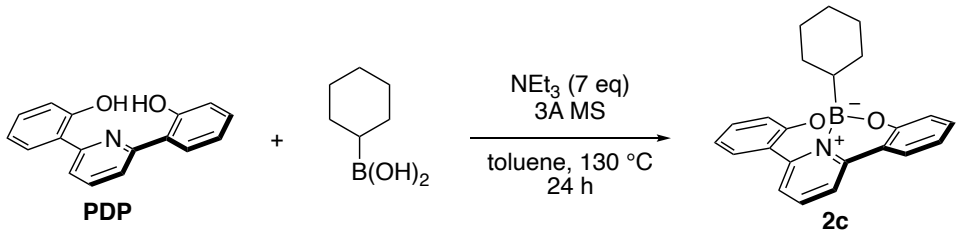
■ General Procedure for Synthesis of PDP-Alkylborates ■

Method A (synthesis of 2a as a representative)[9]



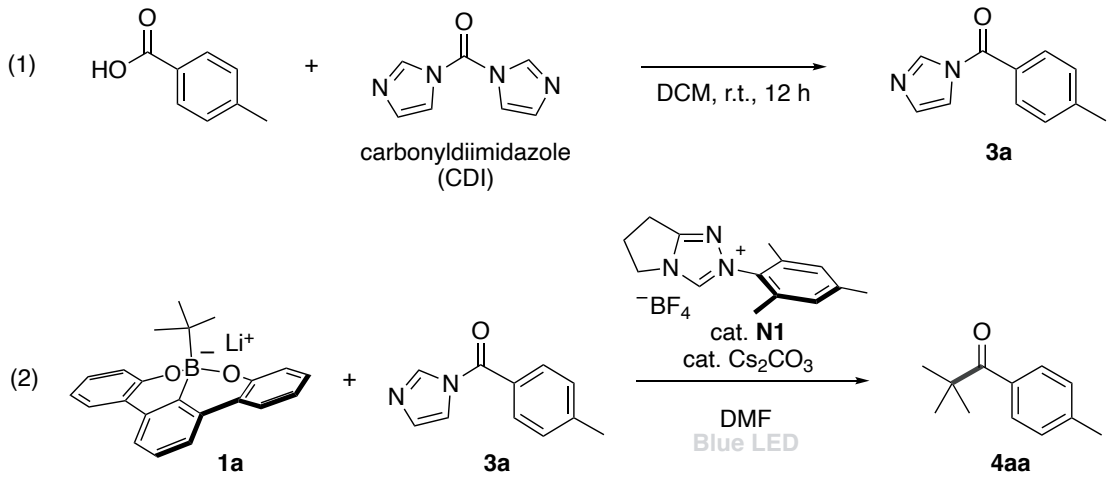
Under an ambient atmosphere, to an oven-dried screw-top 20 mL vial with a stirring bar was added 2,2'-(pyridine-2,6-diyl)diphenol (263.3 mg, 1.0 mmol), *t*-BuBF_3K (164.0 mg, 1.0 mmol). The vial was brought to a globebox, and added toluene (10 mL) and TMSCl (884 μL, 7.0 mmol). After the vial was removed from the glovebox and sealed with Teflon tape, the vial was placed in aluminum heating block at 130 °C and stirred for 14 h. After cooling to room temperature, the reaction crude was passed through a short pad of N–H silica gel with toluene followed by evaporation and vacuum pump to remove the solvent to give PDP-borate **2a** as a yellow solid (315.9 mg, 0.960 mmol, 96% yield).

Method B (synthesis of 2c as a representative)[9]



Under an ambient atmosphere, to an oven-dried screw-top 20 mL vial with a stirring bar was added 2,2'-(pyridine-2,6-diyl)diphenol (263.3 mg, 1.0 mmol), cyclohexylboronic acid (114.0 mg, 1.0 mmol). The vial was brought to a globebox, and added molecular sieve 3A (100 mg), toluene (3.3 mL) and triethylamine (976 μL, 7.0 mmol). After the vial was removed from the glovebox and sealed with Teflon tape, the vial was placed in aluminum heating block at 130 °C and stirred for 24 h. After cooling to room temperature, the reaction crude was passed through a short pad of Celite followed by evaporation and vacuum pump remove the solvent to give PDP-borate **2c** as a yellow solid (344 mg, 0.968 mmol, 97%).

■ General Procedure for Two-Component Coupling ■

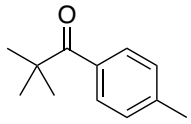


The reaction to produce 4aa in Table 2-1 is representative. According to the literature,[10] acyl imidazole **3a** was prepared. To a suspension of *p*-toluic acid (13.6 mg, 0.1 mmol) in dry dichloromethane (333 μL) was added slowly carbonyldiimidazole (CDI, 24.3 mg, 0.15 mmol, 1.5 equiv) (caution, exothermic). After stirring for 12 h at room temperature, the resulting solution was transferred to separatory funnel and washed with deionized water (ca. 5 mL). The organic extract was dried over Na_2SO_4 and after filtration, the filtrate was concentrated under reduced pressure to afford the acyl imidazole **3a** (18.6 mg, 0.1 mmol, quantitative). The acyl imidazole was used without further purification.

Triazolium salt **N1** (4.7 mg, 15 μmol), borate **1a** (57.4 mg, 0.12 mmol), Cs_2CO_3 (4.9 mg, 15 μmol), and acyl imidazole **3a** (18.6 mg, 0.1 mmol) were placed in an oven-dried screw-top 5 mL vial containing a magnetic stirring bar. The vial was sealed by a hole cap with rubber septum, and then sparged with nitrogen, followed by addition of degassed DMF (1 mL). After 6 h stirring at ambient temperature under photoirradiation (440 nm), the reaction mixture was quenched with water (1 mL), then extracted with diethyl ether (4 times) and dried over sodium sulfate. After filtration was evaporated under reduced pressure. After the volatiles were removed under reduced pressure, flash column chromatography on silica gel (100:0–98:2, hexane/Et_2O) gave **4aa** (9.2 mg, 0.052 mmol) in 52% yield.

■ Characterization Data for Acylation Products ■

2,2-Dimethyl-1-(*p*-tolyl)propan-1-one (4aa)



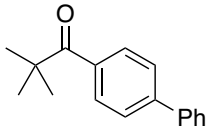
The product **4aa** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-1**; 9.2 mg, 0.052 mmol, 52% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 7.6 Hz, 2H), 2.38 (s, 3H), 1.35 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 208.3, 141.4, 135.4, 128.7 (2C), 128.3 (2C), 44.0, 28.1 (3C), 21.4.

The ^{1}H and ^{13}C NMR spectra data of product **4aa** were consistent with the literature.[11]

1-[(1,1'-Biphenyl)-4-yl]-2,2-dimethylpropan-1-one (4ab)



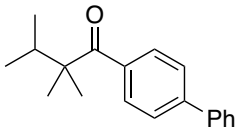
The product **4ab** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-2**; 14.8 mg, 0.062 mmol, 62% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 2H), 7.63–7.61 (m, 4H), 7.46 (t, J = 7.2 Hz, 2H), 7.38 (m, 1H), 1.39 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 208.3, 143.7, 140.0, 136.9, 128.9 (2C), 128.7 (2C), 127.9, 127.1 (2C), 126.7 (2C), 44.2, 28.1 (3C).

The ^{1}H and ^{13}C NMR spectra data of product **4ab** were consistent with the literature.[12]

1-[(1,1'-Biphenyl)-4-yl]-2,2,3-trimethylbutan-1-one (4bb)



The product **4bb** was purified by flash chromatography on silica gel (100:0–80:20, hexane/Et_2O) (**Table 2-2**; 7.3 mg, 0.027 mmol, 27% isolated yield). Yellow solid.

M.p. 64–66 °C.

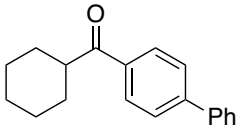
IR (neat) 669, 751, 970, 1172, 1260, 1395, 1464, 1603, 1670, 2360, 2966 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 7.6 Hz, 4H), 7.46 (t, J = 7.6, 2H), 7.38 (m, 1H), 2.42 (m, 1H), 1.26 (s, 6H), 0.90 (d, J = 6.4 Hz, 6H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 209.2, 143.5, 140.1, 137.9, 128.9 (2C), 128.5 (2C), 127.9, 127.2 (2C), 126.7 (2C), 51.3, 34.1, 22.0 (2C), 17.7 (2C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{23}O^+$, 267.1743; found, 267.1742.

(1,1'-Biphenyl)-4-yl(cyclohexyl)methanone (4cb)



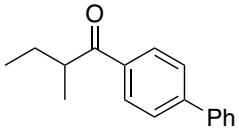
The product **4cb** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-2**; 13.8 mg, 0.052 mmol, 52% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.68 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.47 (t, J = 7.2 Hz, 2H), 7.40 (m, 1H), 3.30 (m, 1H), 1.94–1.85 (m, 4H), 1.76 (m, 1H), 1.55–1.26 (m, 5H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 203.5, 145.4, 140.0, 135.0, 128.93 (2C), 128.86 (2C), 128.1, 127.2 (2C × 2), 45.7, 29.5 (2C), 26.0, 25.9 (2C).

The ^{1}H and ^{13}C NMR spectra data of product **4cb** were consistent with the literature.[13]

1-[(1,1'-Biphenyl)-4-yl]-2-methylbutan-1-one (4db)



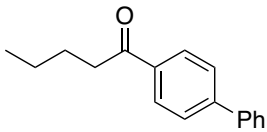
The product **4db** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-2**; 10.1 mg, 0.042 mmol, 42% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.47 (t, J = 7.2 Hz, 2H), 7.40 (m, 1H), 3.44 (m, 1H), 1.87 (m, 1H), 1.52 (m, 1H), 1.22 (d, J = 6.8 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 204.0, 145.5, 139.9, 135.5, 128.9 (2C), 128.8 (2C), 128.1, 127.2 (2C × 2), 42.1, 26.7, 16.8, 11.8.

The ^{1}H and ^{13}C NMR spectra data of product **4db** were consistent with the literature.[14]

1-[(1,1'-Biphenyl)-4-yl]pentan-1-one (4eb)



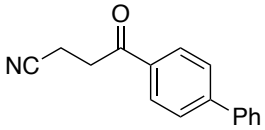
The product **4eb** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-2**; 10.5 mg, 0.044 mmol, 44% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.68 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.47 (t, J = 7.2 Hz, 2H), 7.40 (m, 1H), 3.00 (t, J = 7.2 Hz, 2H), 1.75 (m, 2H), 1.48–1.41 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 200.2, 145.5, 139.9, 135.8, 128.9 (2C), 128.7 (2C), 128.2, 127.3 (2C), 127.2 (2C), 38.4, 26.6, 22.5, 14.0.

The ^{1}H and ^{13}C NMR spectra data of product **4eb** were consistent with the literature.[15]

4-[(1,1'-Biphenyl)-4-yl]-4-oxobutanenitrile (4fb)



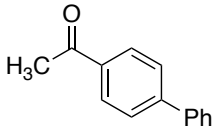
The product **4fb** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 2-2**; 6.1 mg, 0.026 mmol, 26% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 7.2 Hz, 2H), 7.49 (t, J = 7.2 Hz, 2H), 7.42 (m, 1H), 3.42 (t, J = 7.2 Hz, 2H), 2.81 (t, J = 7.2 Hz, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 194.9, 146.6, 139.5, 134.3, 129.0 (2C), 128.6 (2C), 128.5, 127.5 (2C), 127.3 (2C), 119.2, 34.3, 11.8.

The ^{1}H and ^{13}C NMR spectra data of product **4fb** were consistent with the literature.[16]

1-[(1,1'-Biphenyl)-4-yl]ethan-1-one (4gb)



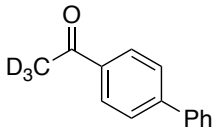
The product **4gb** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-2**; 5.0 mg, 0.026 mmol, 26% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.41 (m, 1H), 2.65 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.8, 145.8, 139.9, 135.8, 128.95 (2C), 128.91 (2C), 128.2, 127.3 (2C), 127.2 (2C), 26.7.

The ^{1}H and ^{13}C NMR spectra data of product **4gb** were consistent with the literature.[17]

1-[(1,1'-Biphenyl)-4-yl]ethan-1-one-2,2,2-*d*$_3$ ([2H]4gb)



The product [2H]**4gb** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-2**; 5.0 mg, 0.026 mmol, 26% isolated yield, 93%D). Pale yellow solid.

M.p. 113–115 °C.

IR (neat) 690, 760, 827, 1117, 1269, 1405, 1602, 1677, 2359, 2922 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.2 Hz, 2H), 7.40 (m, 1H).

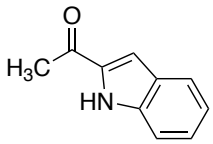
^{2}H NMR (61.4 MHz, $CDCl_3$) δ 2.62.

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.9, 145.8, 139.9, 135.8, 128.94 (2C), 128.89 (2C), 128.2, 127.3 (2C), 127.2 (2C), 29.7 (m).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{10}D_3O^+$, 200.1149; found, 200.1150.

The ^{1}H and ^{2}H NMR spectra data of product [2H]**4gb** were consistent with the literature.[18]

1-(1*H*-Indol-2-yl)ethan-1-one (4gc)



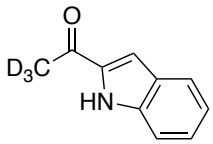
The product **4gc** was purified by flash chromatography on silica gel (100:0–80:20, hexane/Et_2O) (**Table 2-2**; 2.9 mg, 0.018 mmol, 18% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (br s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.35 (t, J = 7.2 Hz, 1H), 7.21 (s, 1H), 7.16 (t, J = 7.2 Hz, 1H), 2.60 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 190.4, 137.2, 135.4, 127.6, 126.4, 123.1, 121.0, 112.1, 109.8, 25.8.

The ^{1}H and ^{13}C NMR spectra data of product **4gc** were consistent with the literature.[19]

1-(1*H*-Indol-2-yl)ethan-1-one-2,2,2-*d*$_3$ ([2H]4gc)



The product [2H]**4gc** was purified by flash chromatography on silica gel (100:0–80:20, hexane/Et_2O) (**Table 2-2**; 3.8 mg, 0.025 mmol, 25% isolated yield, containing 93%D). Pale yellow solid.

M.p. 140–142 °C.

IR (neat) 692, 754, 813, 1230, 1344, 1523, 1681, 2924, 3335 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (br s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.4 Hz,

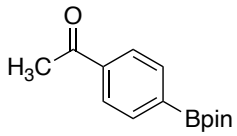
1H), 7.35 (t, J = 7.2 Hz, 1H), 7.21 (s, 1H), 7.16 (d, J = 7.2 Hz, 1H).

^{2}H NMR (61.4 MHz, $CDCl_3$) δ 2.57.

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 190.5, 137.2, 135.4, 127.6, 126.4, 123.1, 121.0, 112.1, 109.8, 30.9 (m).

HRMS–DART (*m/z*): $[M]^+$ calcd for $C_{10}H_6D_3NO^+$, 162.0867; found, 162.0867.

1-[4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethan-1-one (4gd)



The product **4gd** was purified by flash chromatography on silica gel (100:0–90:10, hexane/Et_2O) (**Table 2-2**; 5.3 mg, 0.022 mmol, 22% isolated yield).

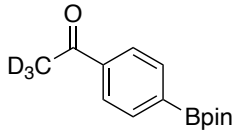
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 2H), 2.62 (s, 3H), 1.36 (s, 12H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.5, 139.0, 134.9 (2C), 127.3 (2C), 84.2 (2C), 26.8, 24.9 (4C). A signal connected directly to boron was not observed.

^{11}B NMR (128.4 MHz, $CDCl_3$) δ 30.9.

The ^{1}H, ^{13}C and ^{11}B NMR spectra data of product **4gd** were consistent with the literature.[15]

1-[4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethan-1-one-2,2,2-d_3 ([2H]4gd)



The product [2H]**4gd** was purified by flash chromatography on silica gel (100:0–90:10, hexane/Et_2O) (**Table 2-2**; 5.5 mg, 0.022 mmol, 22% isolated yield, containing 93%D). Orange oil.

IR (neat) 653, 857, 1086, 1144, 1266, 1360, 1398, 1684, 2360, 2979 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 2H), 1.36 (s, 9H).

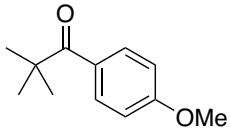
^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.6, 139.0, 134.9 (2C), 127.3 (2C), 84.2 (2C), 29.7 (m), 24.9 (4C). A signal connected directly to boron was not observed.

^{11}B NMR (128.4 MHz, $CDCl_3$) δ 31.1.

^{2}H NMR (61.4 MHz, $CDCl_3$) δ 2.59.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{17}D_3BO_3^+$, 250.1688; found, 250.1683.

1-(4-Methoxyphenyl)-2,2-dimethylpropan-1-one (4ae)



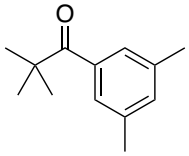
The product **4ae** was purified by flash chromatography on silica gel (100:0–90:10, hexane/Et_2O) (**Table 2-2**; 8.8 mg, 0.046 mmol, 46% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.0 Hz, 2H), 3.85 (s, 3H), 1.37 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 206.3, 162.0, 130.9 (2C), 130.1, 113.2 (2C), 55.3, 43.9, 28.4 (3C).

The ^{1}H and ^{13}C NMR spectra data of product **4ae** were consistent with the literature.[11]

1-(3,5-Dimethylphenyl)-2,2-dimethylpropan-1-one (4af)



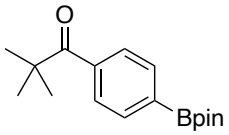
The product **4af** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-2**; 11.0 mg, 0.058 mmol, 58% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (s, 2H), 7.08 (s, 1H), 2.34 (s, 6H), 1.33 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 210.1, 139.0, 137.6, 132.2 (2C), 125.3 (2C), 44.2, 28.0 (3C), 21.3 (2C).

The ^{1}H and ^{13}C NMR spectra data of product **4af** were consistent with the literature.[20]

2,2-Dimethyl-1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]propan-1-one (4ad)



The product **4ad** was purified by flash chromatography on silica gel (100:0–90:10, hexane/Et_2O) (**Table 2-2**; 13.8 mg, 0.048 mmol, 48% isolated yield). Pale yellow solid.

M.p. 148–151 °C.

IR (neat) 661, 858, 955, 1087, 1143, 1326, 1357, 1396, 1685, 2359, 2972 cm^{-1}.

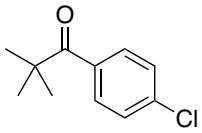
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 1.35 (s, 12H), 1.33 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 209.9, 141.2, 134.4 (2C), 126.6 (2C), 84.1 (2C), 44.2, 27.8 (3C), 24.9 (4C). A signal connected directly to boron was not observed.

^{11}B NMR (128.4 MHz, $CDCl_3$) δ 30.3.

HRMS–DART (*m/z*): $[M]^+$ calcd for $C_{17}H_{25}BO_3^+$, 288.1891; found, 288.1893.

1-(4-Chlorophenyl)-2,2-dimethylpropan-1-one (4ag)



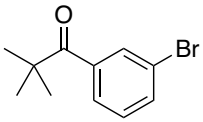
The product **4ag** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-2**; 9.5 mg, 0.048 mmol, 48% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 1.34 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 207.7, 137.2, 136.5, 129.5 (2C), 128.3 (2C), 44.2, 28.0 (3C).

The ^{1}H and ^{13}C NMR spectra data of product **4ag** were consistent with the literature.[11]

1-(3-Bromophenyl)-2,2-dimethylpropan-1-one (4ah)



The product **4ah** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-2**; 9.6 mg, 0.040 mmol, 40% isolated yield). Orange oil.

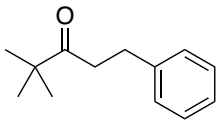
IR (neat) 722, 750, 977, 1181, 1279, 1476, 1562, 1677, 2968 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.28 (t, J = 8.0 Hz, 1H), 1.37 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 207.9, 140.5, 133.7, 130.8, 129.6, 126.2, 122.4, 44.3, 27.8 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{11}H_{14}BrO^+$, 241.0223; found, 241.0223.

4,4-Dimethyl-1-phenylpentan-3-one (4ai)



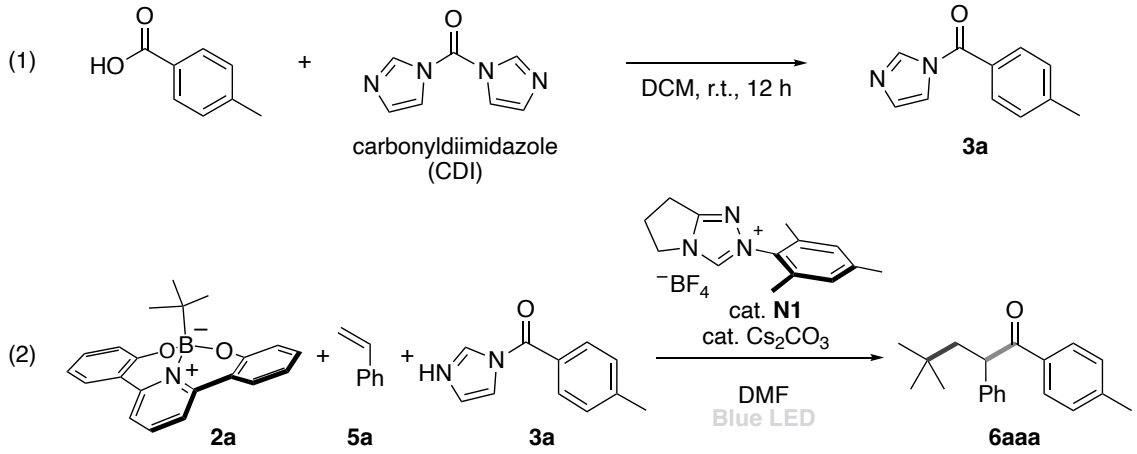
The product **4ai** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-2**; 5.5 mg, 0.029 mmol, 29% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2H), 7.20–7.18 (m, 3H), 2.88 (d, J = 7.2 Hz, 2H), 2.79 (d, J = 7.2 Hz, 2H), 1.11 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 214.9, 141.6, 128.41 (2C), 128.38, 126.0 (2C), 44.1, 38.5, 30.1, 26.3 (3C).

The ^{1}H and ^{13}C NMR spectra data of product **4ai** were consistent with the literature.[21]

■ General Procedure for Three-Component Coupling ■

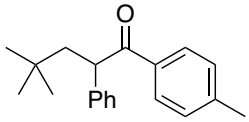


(**The reaction to produce 6aaa in Table 2-4 is representative.**) To a suspension of 4-toluic acid (27.2 mg, 0.2 mmol) in dry dichloromethane (667 μL) was added slowly carbonyldiimidazole (CDI, 48.6 mg, 0.30 mmol, 1.5 equiv) (caution, exothermic). After stirring for 12 h at room temperature, the resulting solution was transferred to separatory funnel and washed with deionized water (ca. 5 mL). The organic extract was dried over Na_2SO_4 and after filtration, the filtrate was concentrated under reduced pressure to afford the acyl imidazole **3a**. The acyl imidazole was used without further purification.

Triazolium salt **N1** (9.5 mg, 30 μmol), borate **2a** (79.0 mg, 0.24 mmol), Cs_2CO_3 (9.8 mg, 30 μmol), and acyl imidazole **3a** (37.2 mg, 0.2 mmol) were placed in an oven-dried screw-top 5 mL vial containing a magnetic stirring bar. The vial was sealed by a hole cap with rubber septum, and then sparging with nitrogen, followed by addition of alkene **5a** (46.0 μL, 41.7 mg, 0.4 mmol) and degassed MeCN (600 μL). After 6 h stirring at ambient temperature under photoirradiation (440 nm), the reaction mixture was evaporated under reduced pressure. After the volatiles were removed under reduced pressure, flash column chromatography on silica gel (100:0–96.5:3.5, hexane/Et_2O) gave **6aaa** (42.4 mg, 0.15 mmol) in 76% yield.

■ Characterization Data for Alkylacylation Products ■

4,4-Dimethyl-1-(4-methylphenyl)-2-phenylpentan-1-one (6aaa)



The product **6aaa** was purified by flash chromatography on silica gel (100:0–96.5:3.5, hexane/Et_2O) (**Table 2-4**; 42.4 mg, 0.15 mmol, 76% isolated yield, containing 2% impurity of two component coupling product). White solid.

M.p. 90–93 °C.

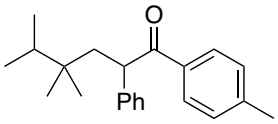
IR (neat) 699, 731, 1176, 1222, 1281, 1365, 1456, 1474, 1558, 1606, 1681, 2954 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 7.25 (dd, J = 7.2, 7.2 Hz, 2H), 7.20 (d, J = 7.2 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 4.70 (d, J = 9.2 Hz, 1H), 2.62 (dd, J = 14.0, 9.2 Hz, 1H), 2.36 (s, 3H), 1.57 (d, J = 14.0 Hz, 1H), 0.88 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.5, 143.5, 141.3, 134.4, 129.3 (2C), 128.8 (2C), 128.7 (2C), 128.1 (2C), 126.6, 49.4, 47.5, 31.2, 29.8 (3C), 21.5.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{25}O^+$, 281.1900; found, 281.1898.

4,4,5-Trimethyl-2-phenyl-1-(*p*-tolyl)hexan-1-one (6baa)



The product **6baa** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (**Table 2-4**; 38.7 mg, 0.13 mmol, 63 % isolated yield). Colorless oil.

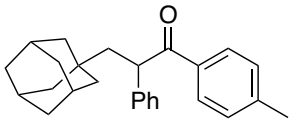
IR (neat) 702, 750, 809, 1175, 1269, 1452, 1605, 1678, 2873, 2959 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 2H), 7.33–7.14 (m, 7H), 4.71 (d, J = 8.8 Hz, 1H), 2.65 (dd, J = 14.0, 8.8 Hz, 1H), 2.36 (s, 3H), 1.60–1.48 (m, 2H), 0.85–0.81 (m, 9H), 0.72 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.6, 143.5, 141.6, 134.5, 129.3 (2C), 128.8 (2C), 128.7 (2C), 128.1 (2C), 126.6, 48.7, 43.5, 36.3, 36.0, 24.7, 24.2, 21.5, 17.6, 17.5.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{29}O^+$, 309.2213; found, 309.2222.

3-[(3r,5r,7r)-Adamantan-1-yl]-2-phenyl-1-(*p*-tolyl)propan-1-one (6haa)



The product **6haa** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (**Table 2-4**; 12.1 mg, 0.034 mmol, 34 % isolated yield). White solid.

M.p. 98–100 °C.

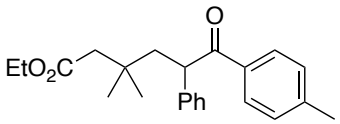
IR (neat) 699, 807, 966, 1176, 1232, 1450, 1605, 1679, 2844, 2898 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.30–7.13 (m, 7H), 4.75 (d, J = 9.2 Hz, 1H), 2.52 (dd, J = 13.6, 9.2 Hz, 1H), 2.36 (s, 3H), 1.89 (s, 3H), 1.66–1.53 (m, 10H), 1.42–1.36 (m, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.4, 143.5, 141.5, 134.3, 129.3 (2C), 128.8 (2C + 1C), 128.1 (2C), 126.5 (2C), 48.3, 47.3, 42.7 (3C), 36.9 (3C), 33.1, 28.6 (3C), 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{31}O^+$, 359.2369; found, 359.2369.

Ethyl 3,3-Dimethyl-6-oxo-5-phenyl-6-(*p*-tolyl)hexanoate (6iaa)



The product **6iaa** was purified by flash chromatography on silica gel (100:0–50:50, hexane/EtOAc) (**Table 2-4**; 22.5 mg, 0.064 mmol, 64 % isolated yield). Colourless oil.

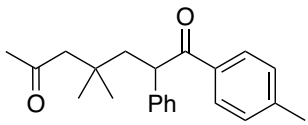
IR (neat) 700, 1036, 1175, 1224, 1368, 1452, 1605, 1677, 1727, 2959 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.33–7.14 (m, 7H), 4.75 (d, J = 8.4 Hz, 1H), 4.07 (q, J = 6.8 Hz, 2H), 2.68 (dd, J = 14.4, 8.4 Hz, 1H), 2.36 (s, 3H), 2.22 (s, 2H), 1.74 (d, J = 14.4 Hz, 1H), 1.20 (t, J = 6.8 Hz, 3H), 0.97 (s, 6H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.2, 172.0, 143.7, 140.8, 134.2, 129.3 (2C), 128.9 (2C), 128.8 (2C), 128.2 (2C), 126.8, 60.0, 49.0, 46.4, 45.5, 34.0, 27.8, 27.7, 21.6, 14.2.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{29}O_3^+$, 353.2111; found, 353.2115.

4,4-Dimethyl-2-phenyl-1-(*p*-tolyl)heptane-1,6-dione (6jaa)



The product **6jaa** was purified by flash chromatography on silica gel (100:0–50:50, hexane/EtOAc) (**Table 2-4**; 18.9 mg, 0.059 mmol, 59 % isolated yield). Pale yellow solid.

M.p. 71–73 °C.

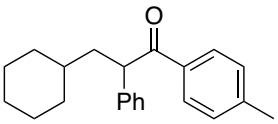
IR (neat) 701, 733, 974, 1175, 1362, 1605, 1677, 1712, 2871, 2956 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 2H), 7.31–7.14 (m, 7H), 4.73 (d, J = 8.8 Hz, 1H), 2.63 (dd, J = 14.0, 8.8 Hz, 1H), 2.36 (s, 3H), 2.34 (d, J = 15.2 Hz, 1H), 2.23 (d, J = 15.2 Hz, 1H), 2.05 (s, 3H), 1.77 (d, J = 14.0 Hz, 1H), 1.01 (s, 3H), 0.98 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 208.5, 199.2, 143.7, 140.8, 134.2, 129.3 (2C), 128.9 (2C), 128.7 (2C), 128.2 (2C), 126.8, 54.3, 49.0, 45.7, 34.1, 32.4, 27.6, 27.5, 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{27}O_2^+$, 323.2006; found, 323.2012.

3-Cyclohexyl-2-phenyl-1-(*p*-tolyl)propan-1-one (6caa)



The product **6caa** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (**Table 2-4**; 13.9 mg, 0.045 mmol, 45 % isolated yield). White solid.

M.p. 89–91 °C.

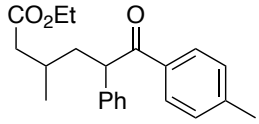
IR (neat) 700, 739, 940, 1176, 1448, 1493, 1606, 1677, 2850, 2920 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 2H), 7.31–7.26 (m, 4H), 7.19 (d, J = 7.6 Hz, 3H), 4.69 (t, J = 7.2 Hz, 1H), 2.36 (s, 3H), 2.13 (m, 1H), 1.82 (d, J = 12.4 Hz, 1H), 1.72–1.60 (m, 5H), 1.26–1.06 (m, 4H), 0.95–0.84 (m, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.6, 143.6, 140.2, 134.4, 129.2 (2C), 128.78 (2C), 128.76 (2C), 128.2 (2C), 126.8, 50.3, 41.7, 35.3, 33.6, 33.3, 26.5, 26.14, 26.13, 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{27}O^+$, 307.2056; found, 307.2053.

Ethyl 3-Methyl-6-oxo-5-phenyl-6-(*p*-tolyl)hexanoate (6kaa)



The product **6kaa** was purified by flash chromatography on silica gel (100:0–60:40, hexane/EtOAc) (**Table 2-4**; 32.2 mg, 0.095 mmol, 48 % isolated yield). The diastereomeric ratio is 1:1 determined by ^{1}H NMR. Pale orange oil.

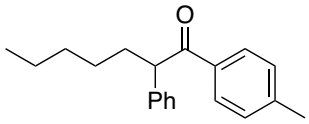
IR (neat) 701, 741, 1030, 1175, 1265, 1453, 1605, 1676, 1728, 2959 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.0 Hz, 2H), 7.29–7.26 (m, 4H), 7.19 (d, J = 7.6 Hz, 3H), 4.69–4.63 (m, 1H), 4.14–4.03 (m, 2H), 2.35 (s, 3H), 2.40–2.24 (m, 0.5 × 3H), 2.17–2.12 (m, 1H), 2.04 (m, 0.5 × 1H), 1.94–1.86 (m, 0.5 × 3H), 1.68 (m, 0.5 × 1H), 1.25–1.18 (m, 3H), 1.00 (d, J = 6.0 Hz, 0.5 × 3H), 0.94 (d, J = 7.2 Hz, 0.5 × 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.1, 198.9, 172.74, 172.68, 143.69, 143.66, 139.8, 139.4, 134.2, 134.1, 129.22 (2C), 129.21 (2C), 128.91 (2C), 128.89 (2C), 128.8 (2C × 2), 128.2 (2C), 128.1 (2C), 127.00, 126.97, 60.2, 60.1, 50.9, 50.8, 42.0, 41.7, 40.9, 40.4, 28.5, 28.2, 21.6 (2C), 20.0, 19.7, 14.23, 14.19.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{27}O_3^+$, 339.1955; found, 339.1959.

2-Phenyl-1-(*p*-tolyl)heptan-1-one (6eaa)



The product **6eaa** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (**Table 2-4**; 11.8 mg, 0.042 mmol, 42 % isolated yield). Colorless oil.

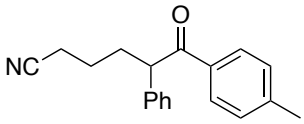
IR (neat) 700, 799, 1030, 1176, 1453, 1493, 1606, 1677, 2857, 2926 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 2H), 7.31–7.26 (m, 4H), 7.18 (d, J = 6.8 Hz, 3H), 4.51 (t, J = 7.2 Hz, 1H), 2.35 (s, 3H), 2.17 (m, 1H), 1.79 (m, 1H), 1.28–1.24 (m, 6H), 0.84–0.83 (m, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.7, 143.5, 140.1, 134.5, 129.2 (2C), 128.8 (2C + 1C), 128.2 (2C), 126.8 (2C), 53.5, 34.0, 31.8, 27.4, 22.5, 21.6, 14.0.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{25}O^+$, 281.1900; found, 281.1905.

6-Oxo-5-phenyl-6-(*p*-tolyl)hexanenitrile (6faa)



The product **6faa** was purified by flash chromatography on silica gel (95:5–60:40, hexane/EtOAc) (**Table 2-4**; 6.9 mg, 0.025 mmol, 25 % isolated yield). Pale yellow oil.

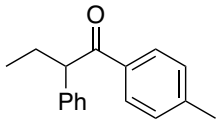
IR (neat) 701, 755, 1176, 1230, 1453, 1605, 1675, 2360, 2850, 2921 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.6 Hz, 2H), 7.32–7.26 (m, 4H), 7.23–7.12 (m, 3H), 4.53 (t, J = 6.8 Hz, 1H), 2.40–2.24 (m, 6H), 1.99 (m, 1H), 1.73–1.58 (m, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.5, 144.0, 139.0, 133.9, 129.3 (2C), 129.1 (2C), 128.8 (2C), 128.0 (2C), 127.3, 119.4, 52.9, 32.9, 23.6, 21.6, 17.3.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{20}NO^+$, 278.1539; found, 278.1537.

2-Phenyl-1-(*p*-tolyl)butan-1-one (6gaa)



The product **6gaa** was purified by flash chromatography on silica gel (100:0–80:20, hexane/EtOAc) (**Table 2-4**; 6.9 mg, 0.029 mmol, 29 % isolated yield).

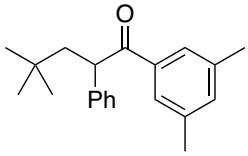
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 2H), 7.29–7.25 (m, 4H), 7.18 (d, J = 7.6 Hz, 3H), 4.42 (t, J = 7.2 Hz, 1H), 2.35 (s, 3H), 2.19 (m, 1H), 1.85 (m, 1H), 0.90 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.7, 143.5, 139.9, 134.5, 129.2 (2C), 128.8 (3C), 128.2 (2C),

126.8 (2C), 55.3, 27.1, 21.5, 12.3.

The ^{1}H and ^{13}C NMR spectra data of product **6gaa** was consistent with the literature.[22]

1-(3,5-Dimethylphenyl)-4,4-dimethyl-2-phenylpentan-1-one (6aaf)



The product **6aaf** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (**Table 2-4**; 33.3 mg, 0.11 mmol, 57 % isolated yield). White solid.

M.p. 31–33 °C.

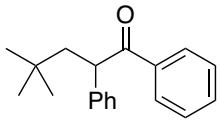
IR (neat) 700, 832, 1153, 1297, 1452, 1492, 1605, 1681, 2866, 2952 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 2H), 7.32–7.24 (m, 4H), 7.18–7.13 (m, 2H), 4.70 (dd, J = 8.8, 2.4 Hz, 1H), 2.61 (dd, J = 14.0, 8.8 Hz, 1H), 2.33 (s, 6H), 1.56 (m, 1H), 0.89 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 200.3, 141.3, 138.1, 137.1, 134.5 (2C), 128.8 (2C), 128.1 (2C), 126.6, 126.4 (2C), 49.6, 47.7, 31.2, 29.8 (3C), 21.3 (2C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{21}H_{27}O^+$, 295.2056; found, 295.2054.

4,4-Dimethyl-1,2-diphenylpentan-1-one (6aaj)



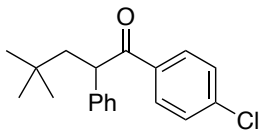
The product **6aaj** was purified by flash chromatography on silica gel (100:0–85:15, hexane/EtOAc) (**Table 2-4**; 30.0 mg, 0.11 mmol, 56 % isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.2 Hz, 2H), 7.50 (m, 1H), 7.43–7.39 (m, 2H), 7.33–7.25 (m, 4H), 7.17 (m, 1H), 4.72 (dd, J = 8.8, 3.2 Hz, 1H), 2.63 (dd, J = 14.0, 8.8 Hz, 1H), 1.58 (dd, J = 14.0, 3.2 Hz, 1H), 0.89 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 200.0, 141.1, 137.0, 132.8, 128.9 (2C), 128.6 (2C), 128.5 (2C), 128.1 (2C), 126.7, 49.6, 47.6, 31.2, 29.8 (3C).

The ^{1}H and ^{13}C NMR spectra data of product **6aa** was consistent with the literature.[23]

1-(4-Chlorophenyl)-4,4-dimethyl-2-phenylpentan-1-one (6aag)



The product **6aag** was purified by flash chromatography on silica gel (100:0–90:10,

hexane/EtOAc) (**Table 2-4**; 50.4 mg, 0.164 mmol, 82% isolated yield, containing 3% impurity of two component coupling product). Pale yellow solid.

M.p. 106–109 °C.

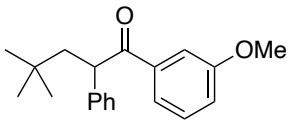
IR (neat) 698, 974, 1093, 1217, 1280, 1365, 1399, 1588, 1683, 2954 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.28–7.26 (m, 4H), 7.18 (m, 1H), 4.64 (d, J = 8.8 Hz, 1H), 2.61 (dd, J = 14.0, 8.8 Hz, 1H), 1.57 (d, J = 14.0 Hz, 1H), 0.88 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.7, 140.8, 139.2, 135.3, 130.0 (2C), 129.0 (2C), 128.9 (2C), 128.0 (2C), 126.9, 49.7, 47.4, 31.2, 29.8 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{22}ClO^+$, 301.1354; found, 301.1349.

1-(3-Methoxyphenyl)-4,4-dimethyl-2-phenylpentan-1-one (6aak)



The product **6aak** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (**Table 2-4**; 31.5 mg, 0.102 mmol, 54% isolated yield, containing 7% impurity). Pale yellow solid.

M.p. 65–67 °C.

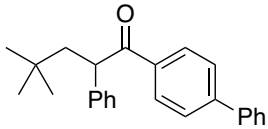
IR (neat) 700, 729, 774, 1044, 1259, 1429, 1489, 1596, 1684, 2359, 2955 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.6 Hz, 1H), 7.43 (s, 1H), 7.26–7.17 (m, 5H), 7.09 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 4.62 (d, J = 8.8 Hz, 1H), 3.74 (s, 3H), 2.55 (dd, J = 14.0, 8.8 Hz, 1H), 1.50 (d, J = 14.0 Hz, 1H), 0.81 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.8, 159.8, 141.1, 138.4, 129.5, 128.9 (2C), 128.1 (2C), 126.7, 121.1, 119.1, 113.1, 55.3, 49.7, 47.6, 31.2, 29.8 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{25}O_2^+$, 297.1849; found, 297.1849.

1-[(1,1'-Biphenyl)-4-yl]-4,4-dimethyl-2-phenylpentan-1-one (6aab)



The product **6aab** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-4**; 41.7 mg, 0.120 mmol, 62% isolated yield, containing 1% impurity). White solid.

M.p. 138–141 °C.

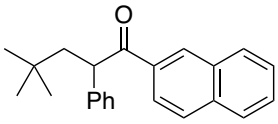
IR (neat) 697, 719, 734, 762, 1218, 1281, 1365, 1602, 1676, 2953 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.6Hz, 2H), 7.58 (d, J = 7.6 Hz, 2H), 7.44 (t, J =7.2 Hz, 2H), 7.39–7.34 (m, 3H), 7.30–7.16 (m, 3H), 4.75 (d, J = 9.2 Hz, 1H), 2.66 (dd, J = 14.0, 9.2 Hz, 1H), 1.60 (d, J = 14.0 Hz, 1H), 0.91 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.5, 145.5, 141.2, 139.9, 135.6, 129.2 (2C), 128.9 (2C × 2), 128.1 (2C + 1C), 127.25 (2C), 127.21 (2C), 126.7, 49.6, 47.5, 31.2, 29.8 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{27}O^+$, 343.2056; found, 343.2058.

4,4-Dimethyl-1-(naphthalen-2-yl)-2-phenylpentan-1-one (6aal)



The product **6aal** was purified by flash chromatography on silica gel (100:0–95:5, hexane/EtOAc) (**Table 2-4**; 46.9 mg, 0.15 mmol, 74 % isolated yield). White solid.

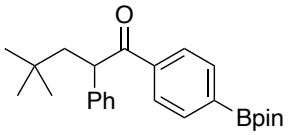
M.p. 106–108 °C.

IR (neat) 698, 726, 821, 1171, 1280, 1393, 1467, 1677, 2953, 3060 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 7.6 Hz, 1H), 7.84 (t, J = 7.2 Hz, 2H), 7.58–7.50 (m, 2H), 7.38 (d, J = 7.6 Hz, 2H), 7.29–7.25 (m, 2H), 7.16 (m, 1H), 4.88 (d, J = 8.8 Hz, 1H), 2.69 (dd, J = 14.0, 8.8 Hz, 1H), 1.63 (d, J = 14.0 Hz, 1H), 0.92 (s, 9H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 199.9, 141.2, 135.4, 134.3, 132.5, 130.0, 129.6, 128.9 (2C), 128.4, 128.3, 128.1 (2C), 127.7, 126.7, 126.6, 124.5, 49.7, 47.6, 31.2, 29.8 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{25}O^+$, 317.1900; found, 317.1901.

4,4-Dimethyl-1-[4-(4,4,5,5-tetramethy-1,3,2-dioxaborolan-2-yl)phenyl]-2-phenylpentan-1-one (6aad)



The product **6aad** was purified by flash chromatography on silica gel (100:0–90:10, hexane/Et_2O) (**Table 2-4**; 34.2 mg, 0.0872 mmol, 44% isolated yield). Pale yellow solid.

M.p. 157–161 °C.

IR (neat) 651, 696, 858, 1090, 1144, 1215, 1364, 1399, 1675, 2950 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.6 Hz, 2H), 7.84 (d, J = 7.6 Hz, 2H), 7.31–7.23 (m, 4H), 7.15 (t, J = 7.2 Hz, 1H), 4.72 (d, J = 8.8 Hz, 1H), 2.62 (dd, J = 13.6 Hz, 8.8 Hz, 1H), 1.58 (d, J = 13.6 Hz, 1H), 1.33 (s, 12H), 0.88 (s, 9H).

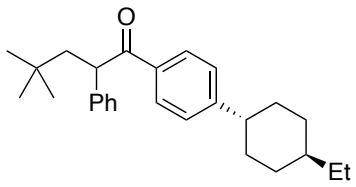
^{13}C NMR (100.6 MHz, $CDCl_3$) δ 200.3, 141.0, 138.9, 134.9 (2C), 128.8 (2C), 128.2 (2C), 127.6 (2C), 126.7, 84.1 (2C), 49.7, 47.4, 31.2, 29.8 (3C), 24.84 (2C), 24.82 (2C). A signal

connected directly to boron was not observed.

^{11}B NMR (128.4 MHz, $CDCl_3$) δ 30.8.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{34}BO_3^+$, 393.2596; found, 393.2601.

1-[4-(*trans*-4-Ethylcyclohexyl)phenyl]-4,4-dimethyl-2-phenylpentan-1-one (6aam)



The product **6aam** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-4**; 47.8 mg, 0.126 mmol, 63% isolated yield). White solid.

M.p. 77–80 °C.

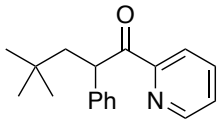
IR (neat) 700, 1176, 1218, 1281, 1365, 1448, 1474, 1605, 1681, 2851, 2922, 2956 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.6 Hz, 2H), 7.32 (d, J = 7.2 Hz, 2H), 7.28–7.23 (m, 4H), 7.16 (t, J = 7.2 Hz, 1H), 4.71 (d, J = 8.8 Hz, 1H), 2.62 (dd, J = 13.6, 8.8 Hz, 1H), 2.48 (t, J = 11.6 Hz, 1H), 1.86 (d, J = 10.0 Hz, 4H), 1.56 (d, J = 13.6 Hz, 1H), 1.42 (q, J = 11.6 Hz, 2H), 1.25 (q, J = 7.2 Hz, 2H), 1.18 (m, 1H), 1.02 (q, J = 11.6 Hz, 2H), 0.90 (t, J = 7.2 Hz, 3H), 0.88 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.5, 153.2, 141.4, 134.8, 128.82 (2C), 128.79 (2C), 128.1 (2C), 127.1 (2C), 126.6, 49.4, 47.6, 44.7, 39.0, 33.9 (2C), 33.0 (2C), 31.2, 29.9, 29.8 (3C), 11.5.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{37}O^+$, 377.2839; found, 377.2842.

4,4-Dimethyl-2-phenyl-1-(pyridin-2-yl)pentan-1-one (6aan)



The product **6aan** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-4**; 27.6 mg, 0.103 mmol, 51% isolated yield, containing trace inpurity of two component coupling product). Pale yellow solid.

M.p. 64–66 °C.

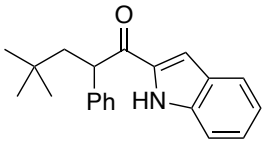
IR (neat) 703, 739, 978, 995, 1218, 1365, 1493, 1582, 1697, 2954 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 4.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.74 (dd, J = 8.0, 8.0 Hz, 1H), 7.41–7.39 (m, 3H), 7.22 (dd, J = 7.2, 7.2 Hz, 2H), 7.13 (t, J = 7.2 Hz, 1H), 5.66 (d, J = 9.2 Hz, 1H), 2.59 (dd, J = 13.6, 9.2 Hz, 1H), 1.66 (d, J = 13.6 Hz, 1H), 0.89 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.5, 152.9, 148.9, 141.0, 136.7, 128.9 (2C), 128.4 (2C), 126.8, 126.4, 122.9, 46.9, 46.4, 31.3, 29.8 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{22}NO^+$, 268.1696; found, 268.1703.

1-(1*H*-Indol-2-yl)-4,4-dimethyl-2-phenylpentan-1-one (6aac)



The product **6aac** was purified by flash chromatography on silica gel (100:0–88:12, hexane/Et_2O) (**Table 2-4**; 38.8 mg, 0.127 mmol, 63% isolated yield, containing trace impurity of two component coupling product). Pale yellow solid.

M.p. 145–147 °C.

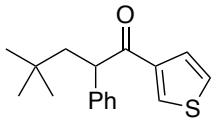
IR (neat) 698, 739, 752, 1137, 1166, 1343, 1520, 1647, 2954, 3317 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (br s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.40–7.26 (m, 7H), 7.19–7.13 (m, 2H), 4.63 (d, J = 9.2 Hz, 1H), 2.61 (dd, J = 13.6, 9.2 Hz, 1H), 1.65 (d, J = 13.6 Hz, 1H), 0.92 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 192.9, 141.2, 137.4, 134.9, 128.8 (2C), 128.0 (2C), 127.6, 126.8, 126.3, 123.1, 120.9, 112.1, 109.3, 50.2, 47.0, 31.2, 29.7 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{21}H_{24}NO^+$, 306.1852; found, 306.1854.

4,4-Dimethyl-2-phenyl-1-(thiophen-3-yl)pentan-1-one (6aao)



The product **6aao** was purified by flash chromatography on silica gel (100:0–97:3, hexane/Et_2O) (**Table 2-4**; 36.8 mg, 0.133 mmol, 67% isolated yield, containing 1% impurity of two component coupling product). White solid.

M.p. 132–134 °C.

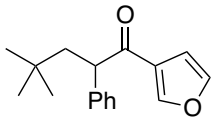
IR (neat) 698, 865, 1178, 1226, 1453, 1508, 1660, 2865, 2956, 3092 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.56 (d, J = 4.8 Hz, 1H), 7.32–7.26 (m, 5H), 7.18 (t, J = 7.2 Hz, 1H), 4.49 (d, J = 8.8 Hz, 1H), 2.58 (dd, J = 14.0, 8.8 Hz, 1H), 1.56 (d, J = 14.0 Hz, 1H), 0.89 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 194.2, 142.1, 141.2, 132.2, 128.9 (2C), 128.1 (2C), 127.5, 126.8, 126.2, 51.7, 47.1, 31.1, 29.7 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{21}OS^+$, 273.1308; found, 273.1312.

1-(Furan-3-yl)-4,4-dimethyl-2-phenylpentan-1-one (6aap)



The product **6aap** was purified by flash chromatography on silica gel (100:0–96.5:3.5, hexane/Et_2O) (**Table 2-4**; 31.9 mg, 0.124 mmol, 62% isolated yield). White solid.

M.p. 123–126 °C.

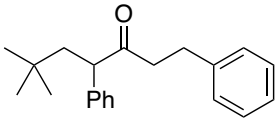
IR (neat) 600, 697, 713, 727, 745, 872, 1154, 1452, 1514, 1666, 2959, 3131 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.37 (s, 1H), 7.28–7.27 (m, 4H), 7.20 (m, 1H), 6.75 (s, 1H), 4.22 (d, J = 8.8 Hz, 1H), 2.56 (dd, J = 14.0, 8.8 Hz, 1H), 1.54 (d, J = 14.0 Hz, 1H), 0.88 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 194.7, 147.1, 144.1, 141.1, 128.9 (2C), 128.0 (2C), 127.5, 126.9, 109.2, 52.8, 46.7, 31.1, 29.7 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{21}O_2^+$, 257.1536; found, 257.1536.

6,6-Dimethyl-1,4-diphenylheptan-3-one (6aai)



The product **6aai** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-4**; 38.4 mg, 0.129 mmol, 64% isolated yield, containing 2% impurity of two component coupling product). White solid.

M.p. 71–74 °C.

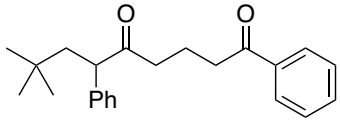
IR (neat) 699, 747, 1030, 1090, 1365, 1453, 1475, 1494, 1714, 2865, 2953 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2H), 7.23–7.12 (m, 6H), 7.05 (d, J = 7.2 Hz, 2H), 3.71 (dd, J = 7.6, 4.0 Hz, 1H), 2.86–2.73 (m, 4H), 2.34 (dd, J = 14.0, 7.6 Hz, 1H), 1.49 (dd, J = 14.0, 4.0 Hz, 1H), 0.81 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 209.1, 141.0, 140.6, 128.8 (2C), 128.3 (2C), 128.2 (2C × 2) 126.9, 125.9, 55.7, 45.3, 43.3, 30.9, 29.9, 29.7 (3C).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{21}H_{27}O^+$, 295.2056; found, 295.2054.

8,8-Dimethyl-1,6-diphenylnonan-1,5-dione (6aaq)



The product **6aaq** was purified by flash chromatography on silica gel (100:0–90:10, hexane/Et_2O) (**Table 2-4**; 45.8 mg, 0.134 mmol, 67% isolated yield, containing 2% impurity of

two component coupling product). Pale yellow solid.

M.p. 62–66 °C.

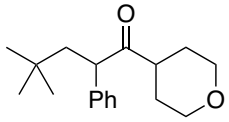
IR (neat) 691, 701, 732, 753, 1225, 1365, 1449, 1684, 1712, 2952 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.42 (dd, J = 7.2, 7.2 Hz, 2H), 7.28–7.15 (m, 5H), 3.76 (d, J = 7.6 Hz, 1H), 2.83 (m, 1H), 2.74 (m, 1H), 2.57 (t, J = 6.8 Hz, 2H), 2.36 (dd, J = 14.0, 7.6 Hz, 1H), 1.96–1.88 (m, 2H), 1.50 (d, J = 14.0 Hz, 1H), 0.83 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 209.8, 199.7, 140.5, 136.7, 132.9, 128.8 (2C), 128.5 (2C), 128.2 (2C), 128.0 (2C), 127.0, 55.7, 45.3, 40.6, 37.2, 30.9, 29.7 (3C), 18.2.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{29}O_2^+$, 337.2162; found, 337.2167.

4,4-Dimethyl-1-(oxan-4-yl)-2-phenylpentan-1-one (6aar)



The product **6aar** was purified by flash chromatography on silica gel (100:0–85:15, hexane/Et_2O) (**Table 2-4**; 37.9 mg, 0.138 mmol, 69% isolated yield). Pale yellow solid.

M.p. 77–81 °C.

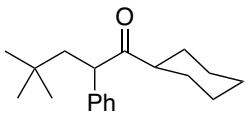
IR (neat) 700, 723, 1023, 1093, 1115, 1240, 1365, 1708, 2846, 2951 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.26 (m, 2H), 7.24–7.19 (m, 3H), 3.97 (d, J = 11.2 Hz, 1H), 3.90 (dd, J = 7.6, 4.0 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 3.37 (t, J = 11.6 Hz, 1H), 3.25 (t, J = 11.6 Hz, 1H), 2.63 (m, 1H), 2.35 (dd, J = 14.0, 7.6 Hz, 1H), 1.77–1.58 (m, 3H), 1.45 (dd, J = 14.0, 4.0 Hz, 1H), 1.29 (d, J = 13.6 Hz, 1H), 0.84 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 211.0, 140.6, 128.9 (2C), 128.3 (2C), 127.0, 67.3, 67.1, 53.5, 47.1, 45.9, 30.9, 29.7 (3C), 29.1, 28.4.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{27}O_2^+$, 275.2006; found, 275.2004.

1-Cyclohexyl-4,4-dimethyl-2-phenylpentan-1-one (6aas)



The product **6aas** was purified by flash chromatography on silica gel (100:0–97.5:2.5, hexane/EtOAc) (**Table 2-4**; 32.3 mg, 0.117 mmol, 58% isolated yield, containing 1% impurity of two component coupling product). Pale yellow solid.

M.p. 55–56 °C.

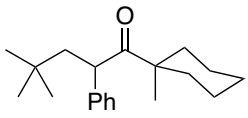
IR (neat) 699, 721, 989, 1365, 1451, 1474, 1492, 1708, 2855, 2931 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.22–7.19 (m, 3H), 3.89 (dd, J = 7.2, 4.0 Hz, 1H), 2.41 (t, J = 10.8 Hz, 1H), 2.32 (dd, J = 14.0, 7.2 Hz, 1H), 1.87 (d, J = 10.8 Hz, 1H), 1.76 (d, J = 10.8 Hz, 1H), 1.65–1.57 (m, 2H), 1.45–1.06 (m, 7H), 0.83 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 212.9, 141.0, 128.7 (2C), 128.4 (2C), 126.7, 53.8, 50.4, 46.0, 31.0, 29.7 (3C), 29.6, 28.7, 25.9, 25.7, 25.4.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{29}O^+$, 273.2213; found, 273.2218.

4,4-Dimethyl-1-(1-methylcyclohexyl)-2-phenylpentan-1-one (6aat)



The product **6aat** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-4**; 24.4 mg, 0.0852 mmol, 43% isolated yield, containing inpurity). White solid.

M.p. 40–43 °C.

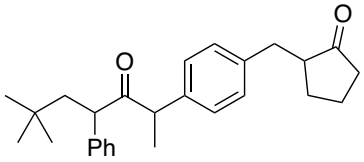
IR (neat) 700, 730, 1012, 1364, 1456, 1493, 1558, 1699, 2864, 2933 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 7.2 Hz, 2H), 7.25 (dd, J = 7.2, 7.2 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 4.28 (dd, J = 8.4, 4.4 Hz, 1H), 1.94–1.86 (m, 2H), 1.82–1.74 (m, 2H), 1.45–1.41 (m, 2H), 1.34–1.21 (m, 6H), 1.05 (s, 3H), 0.79 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 215.6, 141.1, 128.8 (2C), 128.4 (2C), 126.5, 49.3, 49.0, 48.3, 34.8, 34.5, 31.3, 30.0 (3C), 25.8, 23.8, 22.5, 22.4.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{31}O^+$, 287.2369; found, 287.2380.

6,6-Dimethyl-2-{4-[(2-oxocyclopentan-1-yl)methyl]phenyl}-4-phenylheptan-3-one (6aau)



The product **6aau** was purified by flash chromatography on silica gel (100:0–85:15, hexane/Et_2O) (**Table 2-4**; 45.6 mg, 0.117 mmol, 58% isolated yield). Yellow oil.

IR (neat) 700, 1154, 1366, 1453, 1474, 1492, 1511, 1713, 1739, 2868, 2956 cm^{-1}.

Signals for two diastereomers (54:46) were given:

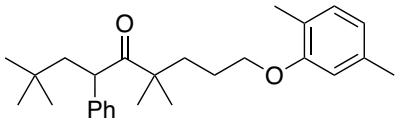
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.08 (m, 6H), 6.93–6.91 (m, 2H), 6.84 (m, 1H), 3.89–3.70 (m, 2H), 3.08 (m, 1H), 2.61–1.41 (m, 10H), 1.37 (d, J = 6.8 Hz, 0.54 × 3H), 1.22 (d, J = 6.8 Hz, 0.46 × 3H), 0.81 (s, 0.54 × 9H), 0.53 (s, 0.46 × 9H).

Signals for diastereomers were given:

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 220.1, 210.7, 209.3, 141.25, 141.22, 140.7, 139.0, 138.9, 138.6, 138.5, 138.34, 138.32, 137.75, 137.72, 129.5, 129.4, 129.0, 128.8, 128.5, 128.28, 128.26, 128.1, 126.9, 126.4, 126.3, 54.1, 54.0, 53.2, 52.61, 52.58, 50.99, 50.94, 50.89, 50.87, 47.00, 46.95, 45.2, 38.3, 38.23, 38.21, 38.18, 35.11, 35.07, 35.04, 31.1, 30.9, 30.8, 29.7, 29.3, 29.10, 29.06, 28.9, 28.8, 25.0, 20.5, 18.12, 18.08, 17.51, 17.46 (only observed peaks).

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{35}O_2^+$, 391.2632; found, 391.2628.

4,4,8,8-Tetramethyl-1-(2,5-dimethylphenoxy)-6-phenylnonan-5-one (6aav)



The product **6aav** was purified by flash chromatography on silica gel (95:5, hexane/Et_2O) (**Table 2-4**; 26.0 mg, 0.0659 mmol, 33% isolated yield). Colourless oil.

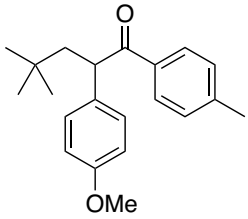
IR (neat) 700, 732, 1028, 1130, 1157, 1265, 1365, 1472, 1509, 1699, 2954 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 7.2 Hz, 2H), 7.25 (dd, J = 7.2, 7.2 Hz, 2H), 7.17 (t, J = 7.2 Hz, 1H), 6.99 (d, J = 7.2 Hz, 1H), 6.65 (d, J = 7.2 Hz, 1H), 6.54 (s, 1H), 4.27 (dd, J = 7.2, 4.8 Hz, 1H), 3.77–3.69 (m, 2H), 2.30 (s, 3H), 2.14 (s, 3H), 1.99 (dd, J = 14.4, 4.8 Hz, 1H), 1.71 (dd, J = 14.4, 7.2 Hz, 1H), 1.65–1.52 (m, 3H), 1.33 (m, 1H), 1.13 (s, 6H), 0.80 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 214.9, 156.9, 140.8, 136.4, 130.2, 128.7 (2C), 128.5 (2C), 126.6, 123.6, 120.6, 112.0, 68.0, 49.3, 48.6, 48.2, 36.5, 31.3, 29.9 (3C), 25.2, 24.74, 24.69, 21.4, 15.8.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{39}O_2^+$, 395.2945; found, 395.2940.

2-(4-Methoxyphenyl)-4,4-dimethyl-1-(4-methylphenyl)pentan-1-one (6aba)



The product **6aba** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-4**; 39.3 mg, 0.126 mmol, 63% isolated yield, containing trace inpurity of two component coupling product). Pale yellow solid.

M.p. 78–82 °C.

IR (neat) 1177, 1251, 1457, 1473, 1508, 1541, 1558, 1607, 1653, 1683, 2953 cm^{-1}.

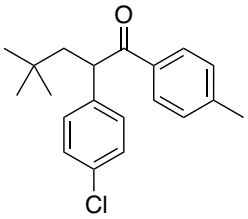
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 2H), 7.23–7.20 (m, 4H), 6.79 (d, J = 7.6 Hz, 2H), 4.65 (d, J = 9.2 Hz, 1H), 3.74 (s, 3H), 2.57 (dd, J = 14.0, 9.2 Hz, 1H), 2.36 (s, 3H), 1.54

(d, J = 14.0 Hz, 1H), 0.87 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.8, 158.3, 143.5, 134.5, 133.3, 129.2 (2C), 129.1 (2C), 128.7 (2C), 114.2 (2C), 55.2, 48.4, 47.5, 31.1, 29.8 (3C), 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{21}H_{27}O_2^+$, 311.2006; found, 311.2003.

2-(4-Chlorophenyl)-4,4-dimethyl-1-(4-methylphenyl)pentan-1-one (6aca)



The product **6aca** was purified by flash chromatography on silica gel (100:0–95:5, hexane/Et_2O) (**Table 2-4**; 31.5 mg, 0.0993 mmol, 50% isolated yield, containing trace impurity of two component coupling product). Pale yellow solid.

M.p. 96–97 °C.

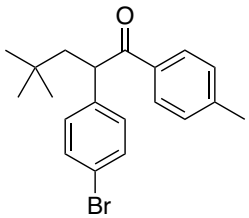
IR (neat) 753, 828, 1015, 1092, 1175, 1365, 1489, 1607, 1681, 2955 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 2H), 7.24–7.21 (m, 6H), 4.68 (d, J = 8.8 Hz, 1H), 2.57 (dd, J = 14.0, 8.8 Hz, 1H), 2.37 (s, 3H), 1.54 (d, J = 14.0 Hz, 1H), 0.87 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.3, 143.8, 139.8, 134.2, 132.5, 129.5 (2C), 129.4 (2C), 128.9 (2C), 128.7 (2C), 48.7, 47.5, 31.2, 29.8 (3C), 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{24}ClO^+$, 315.1510; found, 315.1508.

2-(4-Bromophenyl)-4,4-dimethyl-1-(4-methylphenyl)pentan-1-one (6ada)



The product **6ada** was purified by flash chromatography on silica gel (100:0–97.5:2.5, hexane/Et_2O) (**Table 2-4**; 45.7 mg, 0.126 mmol, 63% isolated yield, containing 1% impurity of two component coupling product). White solid.

M.p. 91–93 °C.

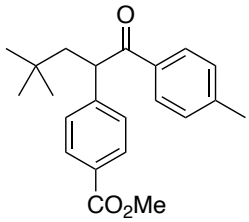
IR (neat) 1011, 1175, 1487, 1507, 1540, 1558, 1607, 1653, 1683, 2955 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.23–7.18 (m, 4H), 4.67 (d, J = 8.8 Hz, 1H), 2.57 (dd, J = 14.0, 8.8 Hz, 1H), 2.37 (s, 3H), 1.54 (d, J = 14.0 Hz, 1H), 0.87 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.2, 143.9, 140.3, 134.1, 131.9 (2C), 129.8 (2C), 129.4 (2C), 128.7 (2C), 120.6, 48.7, 47.4, 31.2, 29.8 (3C), 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{24}BrO^+$, 359.1005; found, 359.1009.

2-[4-(Methoxycarbonyl)phenyl]-4,4-dimethyl-1-(4-methylphenyl)pentan-1-one (6aea)



The product **6aea** was purified by flash chromatography on silica gel (100:0–85:15, hexane/Et_2O) (**Table 2-4**; 45.6 mg, 0.135 mmol, 67% isolated yield). White solid.

M.p. 103–105 °C.

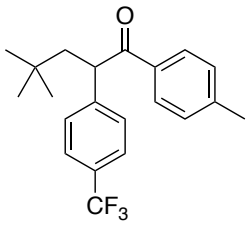
IR (neat) 741,1112, 1180, 1250, 1280, 1435, 1607, 1682, 1722, 2952 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 4.76 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 2.61 (dd, J = 14.0, 8.4 Hz, 1H), 2.37 (s, 3H), 1.57 (d, J = 14.0 Hz, 1H), 0.88 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.9, 166.8, 146.5, 143.9, 134.2, 130.1 (2C), 129.4 (2C), 128.7 (2C), 128.6, 128.2 (2C), 52.0, 49.5, 47.4, 31.3, 29.8 (3C), 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{27}O_3^+$, 339.1955; found, 339.1965.

2-[4-(Trifluoromethyl)phenyl]-4,4-dimethyl-1-(4-methylphenyl)pentan-1-one (6afa)



The product **6afa** was purified by flash chromatography on silica gel (100:0–98:2, hexane/Et_2O) (**Table 2-4**; 36.0 mg, 0.103 mmol, 52% isolated yield, containing trace amount of impurity of two component coupling product). White solid.

M.p. 80–83 °C.

IR (neat) 1019, 1069, 1110, 1126, 1165, 1325, 1607, 1615, 1681, 2958 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 4.78 (d, J = 9.2 Hz, 1H), 2.62 (dd, J = 13.6, 9.2 Hz, 1H), 2.38 (s, 3H), 1.56 (d, J = 13.6 Hz, 1H), 0.89 (s, 9H).

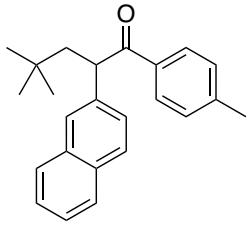
^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.9, 145.3, 144.1, 134.0, 129.4 (2C), 129.0 (q, $J_{C–F}$ = 32.3

Hz, 1C), 128.7 (2C), 128.4 (2C), 125.7 (q, $J_{C–F}$ = 3.5 Hz, 2C), 124.1 (q, $J_{C–F}$ = 272.0 Hz, 1C), 49.1, 47.5, 31.3, 29.8 (3C), 21.6.

^{19}F NMR (376.5 MHz, $CDCl_3$) δ –62.5.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{21}H_{24}F_3O^+$, 349.1774; found, 349.1768.

4,4-Dimethyl-1-(4-methylphenyl)-2-(2-naphthyl)pentan-1-one (6aga)



The product **6aga** was purified by flash chromatography on silica gel (100:0–97:3, hexane/Et_2O) (**Table 2-4**; 39.5 mg, 0.120 mmol, 60% isolated yield). Pale pink solid.

M.p. 118–121 °C.

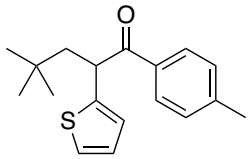
IR (neat) 755, 818, 975, 1181, 1222, 1282, 1365, 1475, 1606, 1678, 2954 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.6 Hz, 2H), 7.77–7.75 (m, 3H), 7.72 (s, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.44–7.38 (m, 2H), 7.19 (d, J = 7.6 Hz, 2H), 4.86 (d, J = 8.8 Hz, 1H), 2.71 (dd, J = 14.0, 8.8 Hz, 1H), 2.34 (s, 3H), 1.64 (d, J = 14.0 Hz, 1H), 0.91 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.5, 143.6, 138.8, 134.5, 133.6, 132.3, 129.3 (2C), 128.8 (2C), 128.6, 127.7, 127.6, 126.7, 126.3, 126.1, 125.6, 49.6, 47.5, 31.3, 29.8 (3C), 21.5.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{27}O^+$, 331.2056; found, 331.2053.

4,4-Dimethyl-1-(4-methylphenyl)-2-(thiophen-2-yl)pentan-1-one (6aha)



The product **6aha** was purified by flash chromatography on silica gel (100:0–97:3, hexane/Et_2O) (**Table 2-4**; 28.1 mg, 0.0977 mmol, 49% isolated yield, containing trace amount of impurity of two component coupling product). Pale yellow solid.

M.p. 65–67 °C.

IR (neat) 695, 1181, 1228, 1280, 1365, 1475, 1606, 1682, 2865, 2954 cm^{-1}.

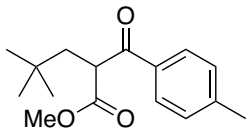
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.6 Hz, 2H), 7.25 (d, J = 7.6 Hz, 2H), 7.13 (m, 1H), 6.86 (s, 2H), 5.00 (d, J = 8.8 Hz, 1H), 2.58 (dd, J = 14.0, 8.8 Hz, 1H), 2.39 (s, 3H), 1.72 (d, J = 14.0 Hz, 1H), 0.89 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.4, 143.92, 143.91, 133.8, 129.4 (2C), 128.8 (2C), 126.8,

125.0, 124.4, 48.2, 43.9, 31.1, 29.7 (3C), 21.6.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{23}OS^+$, 287.1464; found, 287.1471.

Methyl 4,4-Dimethyl-2-(4-methylbenzoyl)pentanoate (6aia)



The product **6aia** was purified by flash chromatography on silica gel (85:15, hexane/Et_2O) (**Table 2-4**; 6.2 mg, 0.024 mmol, 12% isolated yield, containing unidentified impurity). Colourless oil.

IR (neat) 1077, 1155, 1182, 1230, 1284, 1367, 1608, 1683, 1740, 2953 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 4.40 (t, J = 6.0 Hz, 1H), 3.67 (s, 3H), 2.42 (s, 3H), 2.03 (d, J = 6.0 Hz, 2H), 0.90 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 195.0, 171.1, 144.4, 133.5, 129.5 (2C), 128.9 (2C), 52.5, 50.5, 42.0, 30.9, 29.3 (3C), 21.7.

HRMS–DART (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{23}O_3^+$, 263.1642; found, 263.1641.

■ Cyclic Voltammetry of Acyl Azolium Intermediates ■

The preparation of INT-I is representative. In a glovebox, to an oven-dried vial with a stirring bar was added acyl imidazole **3a** (1.86 mg, 10 μmol), **N1** (3.15 mg, 10 μmol) and Cs_2CO_3 (3.26 mg, 10 μmol). To the vial, 5.0 mL of MeCN with tetrabutylammonium hexafluorophosphate ($[N(nBu)]_4PF_6$) (193.7 mg, 0.5 mmol, 0.1 M) dissolved as a supporting electrolyte was added, and the mixture was stirred for 2 h at room temperature. Then, the ressulting solution was transffered to the measuring vessel, and the electrochemical property of the ground state acyl azolium **INT-I** was mesured.

Measurements used a glassy carbon working electrode (area = 0.07 cm^2), a Ag/AgCl reference electrode (SCE), and a Pt wire counter electrode. The concentration of the sample solution was fixed at 2 mM and the sweep rates were set to 100 mV/s.

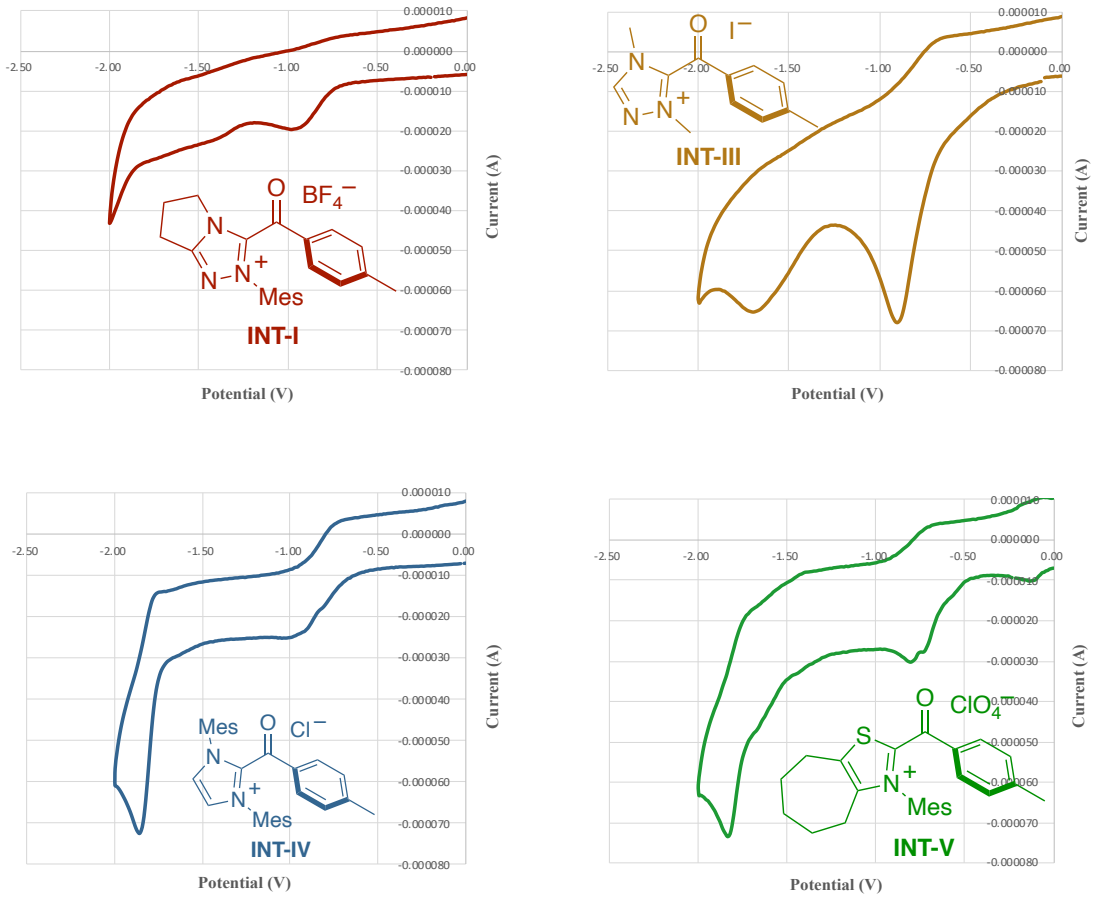


Figure 2-8. Cyclic voltammogram of acyl azolium intermediates.

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第３章　可視光励起ホウ素アート錯体を用いた N-ヘテロ環カルベン触媒反応

第１節　着想背景および作業仮説

含窒素有機化合物は、生理活性物質に多く含まれ、機能性有機分子の創出の観点からも重要視されている[1–4]。その中でも環状または非環状の β-アミドケトンは、生理活性発現において重要な部分構造であり、天然物や医薬品に多く見られる骨格である。さらに還元することで、同様に生理活性を有するβ-アミノアルコールへと容易に変換できる（**Figure 3-1**）[5–7]。特に、sp^3 炭素に富んだ骨格は、ケミカルスペース拡大の観点から、精力的に合成法の開発が進められてきた。これまでの β-アミドケトン合成法としては、反応系中で形成したイミンに対してエノラート種を求核付加させる立体選択的 Mannich 反応は、最も直截的なアプローチの一つであるが、高いジアステレオ選択性を実現するためには、反応基質への配向基の導入や反応系中でのエノール化によるラセミ化など、課題が残されていた[8–10]。

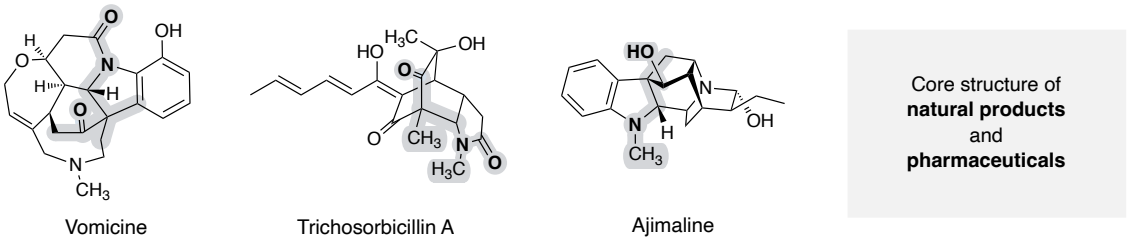


Figure 3-1. Natural products and pharmaceuticals including β-amido ketones and alcohols.

窒素中心ラジカルの発生およびその利用は、sp^3 炭素に富んだ含窒素化合物を合成する魅力的な手法として注目されている[11,12]。近年、アミジルラジカルやイミニルラジカルの生成は、精巧に設計された窒素中心ラジカル前駆体を調製することによって、効率化がなされてきた[13–22]。ごく最近、光駆動型酸化的プロトン共役電子移動（PCET）は、より網羅的な窒素中心ラジカル生成法として盛んに開発が進められている。この光駆動型 PCET プロセスは、光酸化還元触媒とリン酸アニオン種などの弱塩基を用いる非常に温和な条件下で、一般に弱酸性（pKa ≈ 32 in MeCN）かつ高い酸化電位（$E_{1/2}$ = 1.78 V vs. SCE in MeCN）を有するアリールアミドの窒素–水素結合の均等開裂を起こし、対応する窒素中心ラジカルへのアクセスを可能とする（**Figure 3-2**）[23–30]。しかしながら、ほとんどの PCET プロセスを基点とした反応は、HAT を介したプロトン化、Giese 付加、遷移金属とのクロスカップリングなどのラジカル捕捉を介した化学変換に適用が制限されている[23–30]。これは PCET プロセスが、塩基の酸性度、反応基質の窒素–水素結合の結合解離エネルギー、分子内環化あるいは分子内 HAT などの後続反応の反応速度、触媒の酸化還元電位など、多くの要因に支配されるためである。このように非常に高度な

反応設計が必要となるものの、PCET プロセスに基づくラジカル–ラジカルカップリングは、立体的に混み合ったユニットを構築する強力な手法を提供でき、新たなケミカルスペースの拡大につながる。

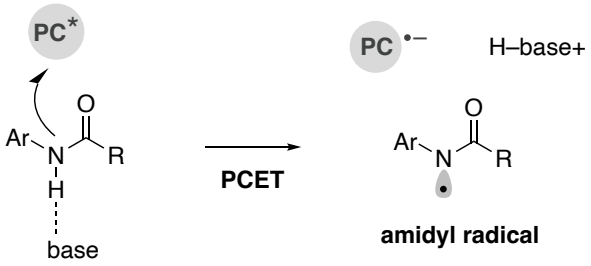
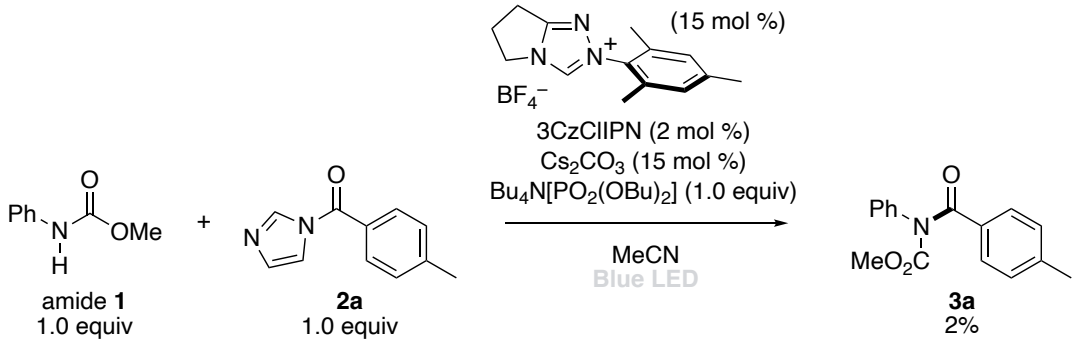


Figure 3-2. Photoredox-catalysis-promoted oxidative concerted PCET.

本論第2章でも述べたとおり、一電子移動を介したラジカル介在型NHC触媒反応は、立体的に混んだユニットを構築するための強力な合成戦略である。そこで、初期検討として、可視光駆動型 PCET に基づく NHC 触媒系を用いたアミド化合物のアシル化反応を試みた（**Scheme 3-1**）。トリアゾール型 NHC 触媒および高い酸化力を有する光酸化還元触媒存在下、窒素中心ラジカル前駆体としてアミド **1**、アシル供与体としてアシルイミダゾール **2a** を用いて反応を行なったが、目的のアシル化体 **3a** がほとんど得られなかった。その原因として、酸化的 PCET により生じたアミジルラジカルと NHC 触媒由来のケチルラジカルの反応性、発生濃度や速度のミスマッチが想定された。



Scheme 3-1. Preliminary study for merging photoredox PCET with NHC Catalysis.

そこで、これらの問題点を解決するべくアミジルラジカル前駆体として、分子内にオレフィンを有するアミド化合物を選択し、可視光駆動型 PCET に基づく NHC 触媒系を用いた、アルケンのアミドアシル化反応を着想した。可視光照射下、酸化的 PCET プロセスにより、分子内にアルケンを有するアミド化合物の窒素中心にラジカルが発生し、速やかな分子内環化を経て、アルキルラジカルを与える。この短寿命ラジカル種が NHC

触媒由来の長寿命なケチルラジカルと選択的にラジカル–ラジカルカップリングを起こすことで、かさ高いβ-アミドケトン体が得られる。また、形成されるかさ高いアルキルラジカルとケチルラジカルとの間の立体的相互作用により、ジアステレオ選択的なラジカルカップリングが実現できると想定した。（**Figure 3-3**）。

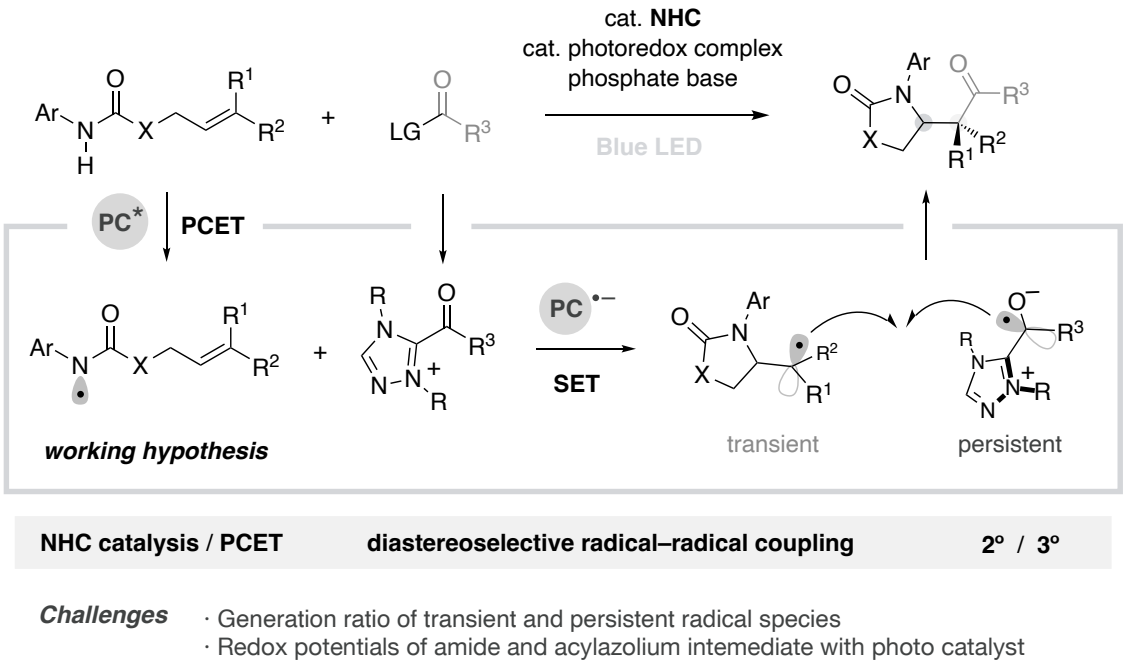


Figure 3-3. NHC-catalyzed radical−radical coupling incorporating PCET.

この協奏的 PCET プロセスに基づくラジカル–ラジカルカップリングの実現のためには、短寿命なラジカルと長寿命なラジカルの生成比率の精密制御が必要である上、反応を阻害する以下の経路が想定される（**Figure 3-4**）。

1) 窒素中心ラジカルの形成効率は、塩基の酸性度と光酸化還元触媒の酸化還元電位に依存する。用いる塩基の塩基性度が高すぎる場合には、反応性の高いアミドアニオン種が形成され、アシルイミダゾールまたはアシルアゾリウム中間体の分解を引き起こす。

2) 窒素中心ラジカルと分子内のアルケン部位との速やかな分子内環化により、炭素中心ラジカルが生成する。しかし、このアルキルラジカルとケチルラジカルのラジカル–ラジカルカップリングが効率的に進行しない場合、分子内環化は可逆的なプロセスであるため、開環が起こって元の窒素中心ラジカルが再生する、もしくは炭素中心ラジカルがさらに一電子還元されて、炭素アニオン種が生じ、副生成物であるプロトン化体に変換される。

3) 用いる光酸化還元触媒は、窒素中心ラジカルを発生するために十分な酸化力を有し、アシルアゾリウム中間体（$E_{1/2}$ = ca. −0.8〜−1.0 V vs. SCE in MeCN）[31] を還元できる一方で、上述した副生成物の形成につながる炭素アニオン種を形成しない適切な還元力を有

する必要がある。光酸化還元触媒は、還元的消光と酸化的消光の両方を起こす可能性があり、光酸化還元触媒の酸化還元電位と反応経路に大きく依存する。還元的消光では、開始段階で酸化的 PCET が起こり、窒素中心ラジカルが生成する。同時に生じた還元状態の光酸化還元触媒は、ケチルラジカルを形成するアシルアゾリウム中間体の還元剤として機能する（**Figure 3-4**, 左サイクル）。酸化的消光はアシルアゾリウム中間体の一電子還元によって開始される（**Figure 3-4**, 右サイクル）。どちらの触媒サイクルにおいても、同様の中間体および生成物を与えるものの、両サイクルが共存する場合、反応系中で生じる短寿命なラジカルと長寿命なラジカルの生成比率の制御が困難となる。したがって、酸化的 PCET プロセスに基づくラジカルカップリングを達成するためには、酸化還元電位を精密に制御することが鍵となる。

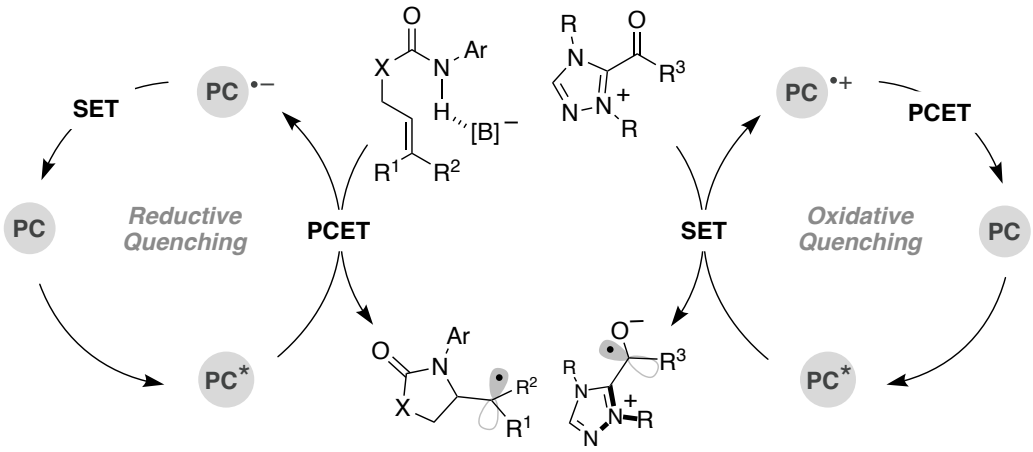
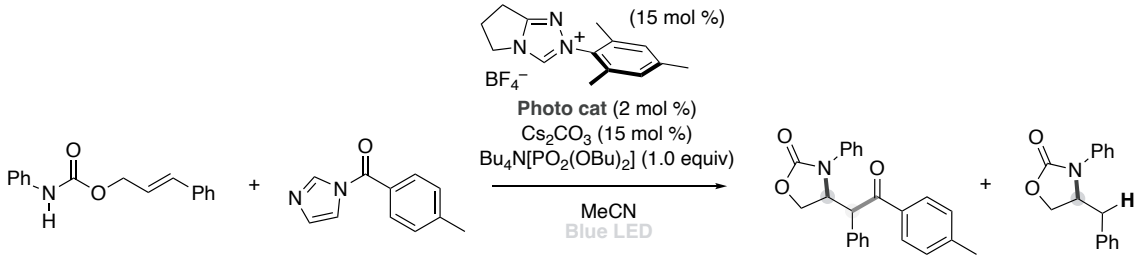


Figure 3-4. Two possible pathways for radical−radical coupling.

第 2 節　反応条件の最適化

上述の作業仮説に基づき、可視光駆動型 PCET に基づく NHC 触媒系を用いた、アルケンのアミドアシル化反応を検討した。トリアゾール型 NHC 触媒の存在下、窒素中心ラジカル前駆体としてシンナミルカルバマート **1a**、ケチルラジカル前駆体としてアシルイミダゾール **2a** を用いた際に、種々の酸化還元電位を有する光酸化還元触媒の反応性を評価した（**Table 3-1**）。光酸化還元触媒として頻用される、高い還元電位を有する $Ir(dFppy)_3$（**PC1**）[32] を用いた反応では、所望の生成物 **3aa** は得られず、副生成物のプロトン化体 **4aa** のみが得られた（**Table 3-1**, **Entry 1**）。還元電位が **PC1** よりもわずかに低い有機光酸化還元触媒 3DPA2FBN（**PC2**）を用いたところ、目的生成物 **3aa** は得られたが、副生成物 **4aa** が優先的に得られた（**Table 3-1**, **Entry 2**）[33]。より酸化力の高い有機光酸化還元触媒である **PC3** や **PC4** は、アミドアシル化体 **3aa** の収率は低下した（**Table 3-1**, **Entries 3** and **4**）[33, 34]。Ir 光酸化還元触媒 **PC5** と **PC6** は、生成物 **3aa** の収率を向上させたものの、プロトン化体 **4aa** が高い収率で得られた（**Table 3-1**, **Entries 5** and **6**）[36]。

リン酸塩基存在下でのアミドの酸化電位が（$E_{1/2}$ = 1.27 V vs. SCE in MeCN）であることを考慮すると、**PC6** による収率の改善は妥当であった [31]。幅広い酸化還元電位を有する 4CzIPN（**PC7**）を用いた場合、目的物 **3aa** の収率は **PC6** と同等であったが、副生成物 **4aa** の形成が大幅に抑制された（**Table 3-1**, **Entry 7**）[36]。結果として、酸化電位がより高く、還元電位が中程度の光酸化還元触媒 3CzClIPN（**PC8**）を用いた際に、最も高い収率で β-アミドケトン体を与えた（**Table 3-1**, **Entries 8** and **9**）[32]。



Entry	Photoredox catalyst	Redox potential (E_{red}^* / E_{red})	Yield (%)[a, b] of **3aa** (dr) / **4aa**
1	$Ir(dFppy)_3$ (**PC1**)	0.77 / –2.0	N. D. / 85
2	3DPA2FBN (**PC2**)	0.92 / –1.92	15 (3.3/1) / 54
3	3DPAFIPN (**PC3**)	1.09 / –1.59	11 (1/1.1) / 48
4	4DPAIPN (**PC4**)	1.10 / –1.52	5 (1/1.5) / 68
5	$[Ir\{dF(CF_3)ppy\}_2dtbpy]PF_6$ (**PC5**)	1.21 / –1.37	21 (2.5/1) / 59
6	$[Ir\{dF(CF_3)ppy\}_2bpy]PF_6$ (**PC6**)	1.32 / –1.37	51 (2.4/1) / 44
7	4CzIPN (**PC7**)	1.43 / –1.24	48 (2.7/1) / 13
8	3CzClIPN (**PC8**)	1.56 / –1.16	**72 (2.8/1) / 15**
9	3CzClIPN (**PC8**)	1.56 / –1.16	**80 (2.8/1) / trace**[c]

[a]Reaction was carried out with **1a** (0.1 mmol), acyl imidazole **2a** (0.1 mmol), Photoredox catalyst (2 mol %), NHC catalyst (15 mol %), Cs_2CO_3 (0.015 mmol), and $Bu_4N[PO_2(OBu)_2]$ (0.1 mmol) in MeCN (1.0 mL) under 440 nm (Kessil lamp equipped with PhotoRedOx Duo) irradiation for 12 h. [b]^{1}H NMR yield. [c]**2a** (1.5 equiv), NHC catalyst (30 mol %), and Cs_2CO_3 (0.03 mmol) were used.

Table 3-1. Optimization of photoredox catalysts.

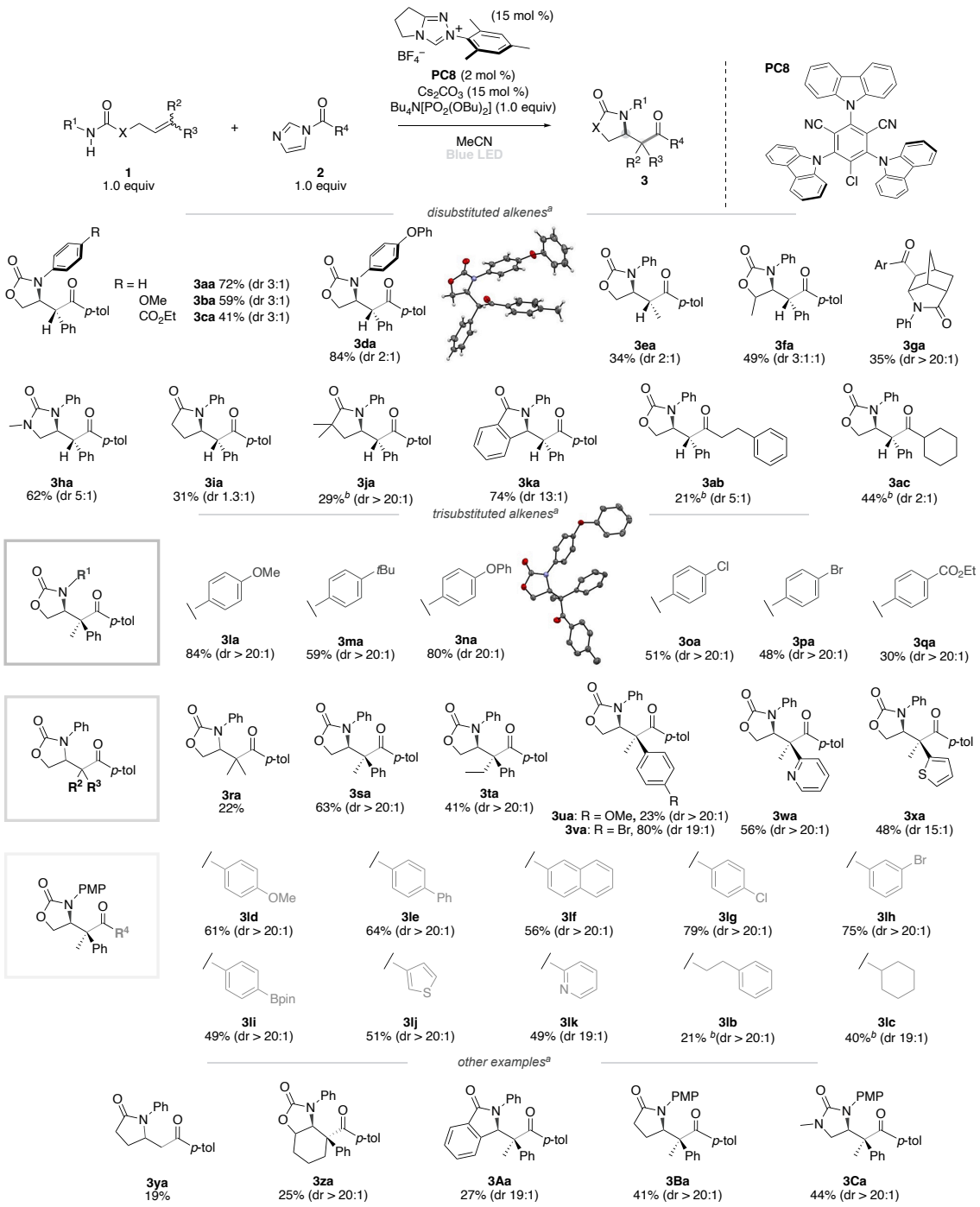
第 3 節　基質適用範囲および生成物の誘導化

上記の条件検討で得られた最適条件に基づき、分子内にアルケンを有するアミド **1** とアシルイミダゾール **2** の基質適用範囲の検討を行った（**Table 3-2**）。まず、二置換アルケンを有するアミド **2** を用いて検討を行った。分子内ラジカル環化反応によりベンジルラジカルを形成するカルバマート（**1a–d**）は、アシルイミダゾール **2a** と反応し、対応する α 位に第 3 級炭素を有する β-アミドケトン生成物を良好な収率で得た（**3aa–3da**）。生成物の立体化学は、生成物 **3da** のジアステレオマーをカラムクロマトグラフィーで単離精製し、再結晶を行うことで X 線結晶構造解析により確認した。また生成物の相対配置は、先行研究として報告された NHC 触媒によるジアステレオ選択的なラジカル–ラジカルカップリングの生成物の立体化学と一致した[23]。したがって、本プロセスにおいても、ラジカル–ラジカルカップリングの段階でジアステレオ選択性が発現すると推測される。第二級アルキルラジカルを形成する **1e** では収率が低下した（**3ea**）。アリル位にメチル基を持つ **1f** ではジアステレオ選択性の向上は見られなかった一方で、架橋構造を有する **1g** では高いジアステレオ選択性で目的の環化生成物 **3ga** を与えた。尿素 **1h**、脂肪族アミド（**1i** and **1j**）、アリールアミド **1k** でも問題なく反応が進行し、高いジアステレオ選択性で目的物（**3ha–3ka**）がそれぞれ得られた。本手法は、脂肪族カルボン酸から誘導されるアシルイミダゾール **2b** および **2c** に対しても適用可能であった（**3ab** and **3ac**）。

続いて、三置換アルケンを有するアミジルラジカル前駆体 **1** を用いた際の反応性も評価した。**1l** と **2a** を反応させると、α 位に 4 級炭素を有する β-アミドケトン化合物 **3la** が優れたジアステレオ選択性かつ高収率で得られた。窒素原子上のアリール基の電子状態は酸化的 PCET プロセスの反応性に影響すると推測されるが、芳香環の電子状態に関わらず、高いジアステレオ選択性で生成物を与えた（**3ma–3qa**）。生成物の立体化学は生成物 **3na** の X 線結晶構造解析より確認できた。同様に、アルケン上置換基においては、メチル基よりもかさ高いエチル基を有する **1t**、アリール基上に種々の官能基が置換した（**1u** and **1v**）、ヘテロアリール基（**1w** and **1x**）を有する場合にも良好な結果が得られたが（**3ta–3xa**）、ジメチル基が置換した **1r** では収率が低下した。

安息香酸誘導体由来のアシルイミダゾールにおいては、電子供与基を有する基質（**2d–2f**）や電子求引基を有する基質（**2g** and **2h**）、ボロン酸ピナコールエステル **2i** でも反応は効率よく進行した（**3ld–3li**）。ヘテロアリールカルボン酸としてチオフェン **2j** やピリジン **2k** や、脂肪族カルボン酸から誘導した基質（**2b** and **2c**）においても、高いジアステレオ選択性で所望の β-アミドケトン体を与えた（**3lj–3lc**）。

分子内環化により不安定な第一級アルキルラジカル種が形成する、一置換アルケン **1y** の場合には収率は低いものの、目的のカップリング体 **3ya** が得られた。二置換アルケンの場合と同様に、縮環生成物を与える（**1z** and **1A**）やカルバマート以外のアミド化合物 **1B** やウレア化合物 **1C** においても、対応する生成物を高いジアステレオ選択性で与え

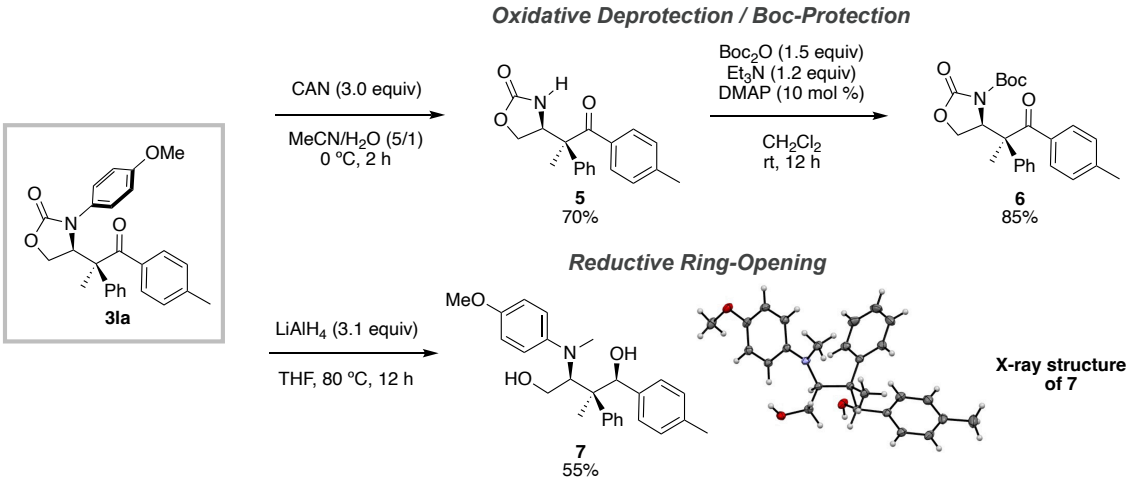


[a]Reaction was carried out with **1** (0.1 mmol), acyl imidazole **2** (0.1 mmol), **PC8** (2 mol %), NHC catalyst (15 mol %), Cs_2CO_3 (0.015 mmol), and $Bu_4N[PO_2(OBu)_2]$ (0.1 mmol) in MeCN (1.0 mL) under 440 nm (Kessil lamp equipped with PhotoRedOx Duo) irradiation for 12 h. [b]**2** (1.5 equiv), NHC catalyst (30 mol %), and Cs_2CO_3 (0.03 mmol) were used.

Table 3-2. Scope of NHC-catalyzed radical−radical coupling incorporating PCET.

た（**3za**–**3Ca**）。これらの α 位に 4 級炭素を有するようなかさ高い複雑な β-アミドケトン化合物は、古典的な合成法や最近報告された Ni/Ir 光酸化還元協働触媒系による合成法[31]では構築困難であり、本手法の有用性が示された。

次に、生成物の誘導化を検討した（**Scheme 3-2**）。β-アミドケトン **3la** に対して、硝酸セリウムアンモニウム（CAN）で酸化すると、窒素上の *p*-メトキシフェニル基が脱保護された化合物 **5** が得られた[37]。**3la** を水素化リチウムアルミニウムで還元すると、連続する 3 つの不斉炭素中心を有する β-アミノアルコール体 **7** が高いジアステレオ選択性で得られ[38]、その相対配置は X 線結晶構造解析によって確認された。



Scheme 3-2. Transformation of the synthesized product of **3la**.

第 4 節　反応機構解析

光酸化還元触媒の酸化還元電位と反応収率の関係は、触媒選択の指針として重要である。そこで、このラジカル–ラジカルカップリングにおける触媒活性を評価するために、還元的クエンチングと酸化的クエンチングそれぞれの酸化還元電位に対する生成物の収率をプロットした（**Figure 3-5**）。x 軸は励起状態の光触媒の還元電位または酸化電位、z 軸は消光後の酸化還元電位である。還元的消光に対するプロットは、光酸化還元触媒の酸化還元電位と生成物 **3aa** の収率の間に良い相関が得られた（**Figure 3-5**, 左図）。一方で、酸化的消光に対するプロットは、ある程度の相関が見られたものの、異常値も確認された（**Figure 3-5**, 右図）。これらの結果から、励起状態の光酸化還元触媒がアミジルラジカル前駆体に対する酸化的 PCET プロセスが先行する、還元的消光サイクルで進行していることが示唆された。一方、励起状態での還元電位が低い光触媒 **PC2** と **PC3** は、生成物の収率をわずかに増加させた（$E_{red}^{*} = 0.92 \sim 1.10$ V）[33]。高い酸化電位を有する光酸化還元触媒の場合には、酸化的消光サイクルが優先的に進行すると推測される。

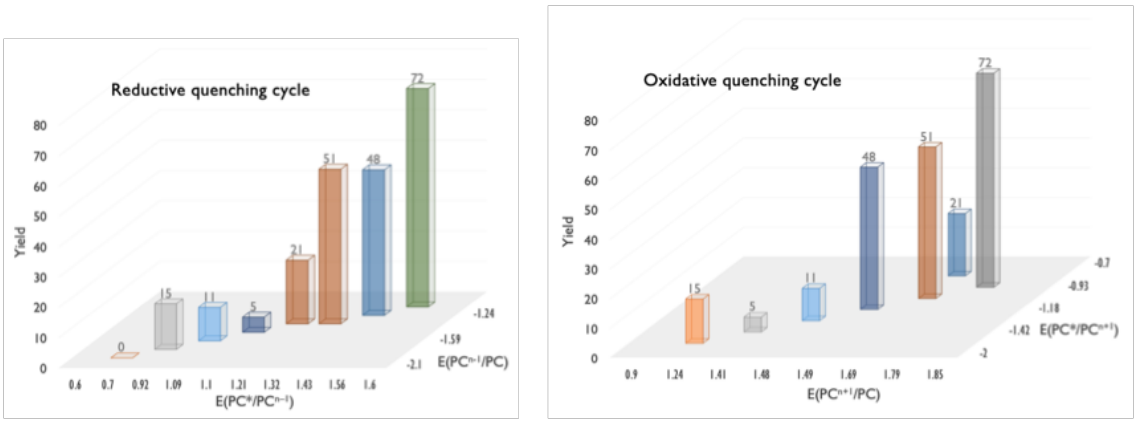


Figure 3-5. Correlation of reaction yield of **3aa** with redox potential of photoredox catalysts.

高い触媒活性を示す光酸化還元触媒 **PC6** と **PC8** に対して消光実験を行い、還元的消光と酸化的消光のどちらの反応経路で進行するかを調査した（**Figure 3-6**）。**PC6** に対して、反応基質 **1a** とリン酸塩基（$Bu_4N[PO_2(OBu)_2]$）の反応物、あるいはアシルアゾリウム中間体を消光剤として添加した際の、Stern-Volmer プロットの結果は、どちらの場合も励起状態の **PC6** を効率的に消光することが示唆された。一方、**PC8** は最も高い収率で生成物 **3aa** を与える光酸化還元触媒であるにもかかわらず、**1a** と $Bu_4N[PO_2(OBu)_2]$の反応物による消光は穏やかであり、アシルアゾリウム中間体に対してはほとんど消光が見られなかった。Stern-Volmer プロットは、**PC6** と **PC8** の両触媒において、**1a** と $Bu_4N[PO_2(OBu)_2]$の混合物による消光がアシルアゾリウム中間体による消光よりも効率的に起こる、すなわち酸化的 PCET プロセスが先行することかが支持された。特に **PC6** ではアシルアゾリウム中間体による消光も効率的に起こるが、**PC8** では起こらない。このアシルアゾリウム中間体に対する一電子移動の効率の違いが、生成物 **3aa** と副生成物 **4aa** の生成比率につながったと考えられる。有機光酸化還元触媒 **PC8** は、励起寿命は短

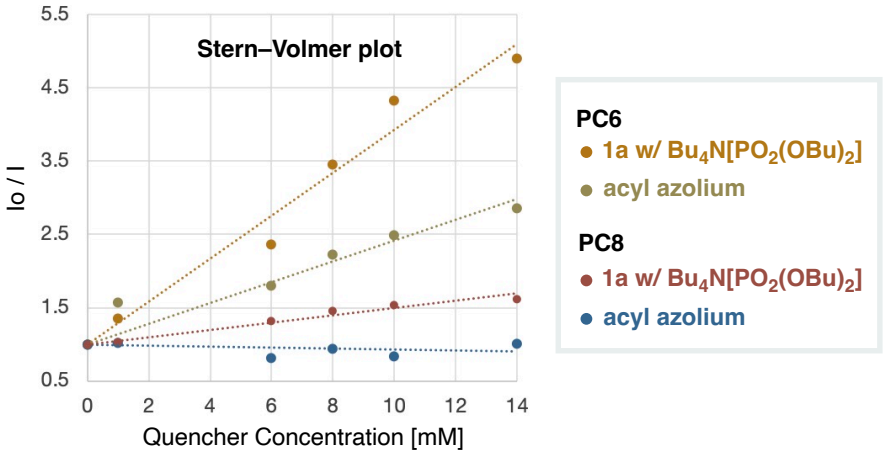
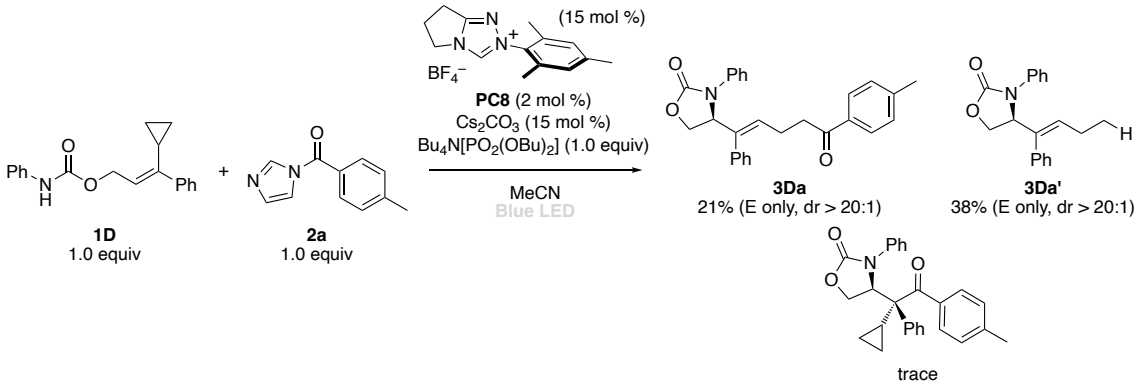


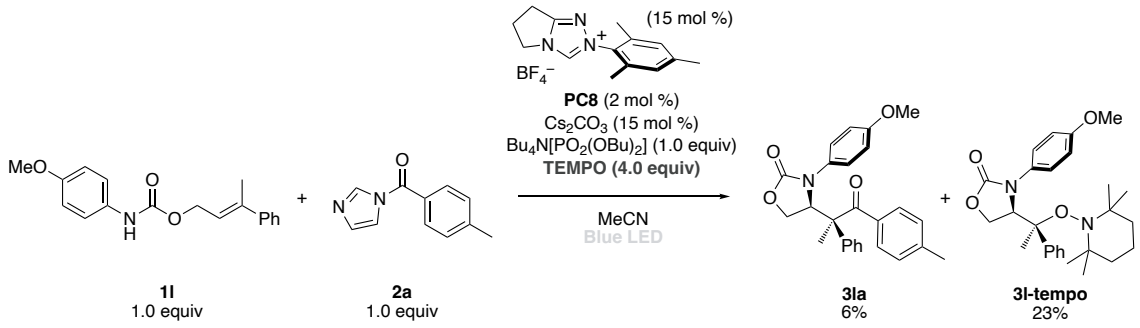
Figure 3-6. Photo-quenching analysis.

いものの、Stern-Volmer 式（$I_0/I = 1+kqt_0[Q]$）から、大きな消光定数を持ち、電子またはエネルギー移動の効率が高いことが示唆された。

一電子機構の関与を裏付けるべく、以下に示すいくつかの実験を行った。アルケン上にシクロプロピル基を有する **1D** に対して反応を行ったところ、シクロプロピル基が開環した生成物 **3Da** およびプロトン化体 **3Da'**が主生成物として得られた（**Scheme 3-3**）。また最適条件にラジカル捕捉剤である TEMPO を添加し、反応を行った際には、目的のβ-アミドケトン化合物 **3la** はほとんど得られず、ラジカル環化で生じたベンジルラジカル種が捕捉された生成物 **3l-tempo** を与えた（**Scheme 3-4**）。これらの実験結果から本反応はラジカル種の形成を経由して反応が進行していることが示唆された。

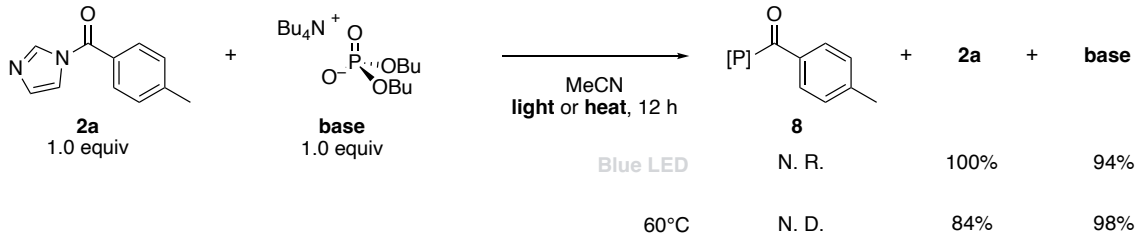


Scheme 3-3. Radical clock experiment.



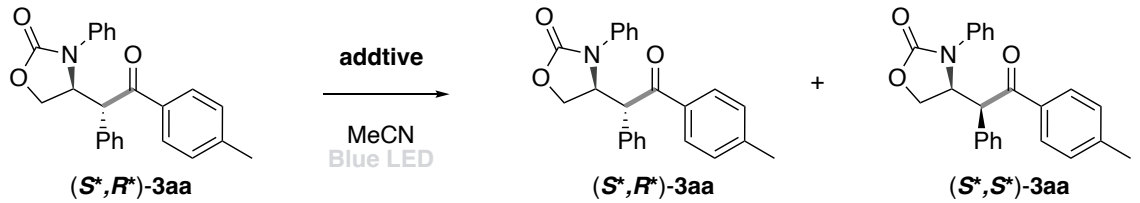
Scheme 3-4. TEMPO trappinig experiment.

Molander らの報告した Ni/Ir 光酸化還元協働触媒系による β-アミドケトン合成では、カルボン酸誘導体とリン酸塩基が反応し、より反応性の高いアシル供与体が形成することが知られている[31]。本反応において、リン酸塩基が酸化的 PCET プロセス以外にも関与しているかを調査するべく、以下に示すアシルイミダゾール **2a** との反応を検討した（**Scheme 3-5**）。可視光照射下もしくは加熱条件下で、反応を行ったところ、新たなアシルドナー**8** が形成していないことが確認された。



Scheme 3-5. Elucidation of the role of phosphate base.

本手法で得られる α 位に第 3 級炭素を有する β-アミドケトン化合物のジアステレオ選択性の低さの要因を探究するべく、生成物 **3aa** の安定性を評価した（**Table 3-3**）。生成物 **3aa** のジアステレオマーをカラムクロマトグラフィーで単離精製し、種々の反応条件に付したところ、加熱条件のみでも容易にエピメリ化が起こることが確認された（**Table 3-3**, **Entry 6**）。したがって、結合形成段階の選択性よりも過小評価されている可能性が示唆された。



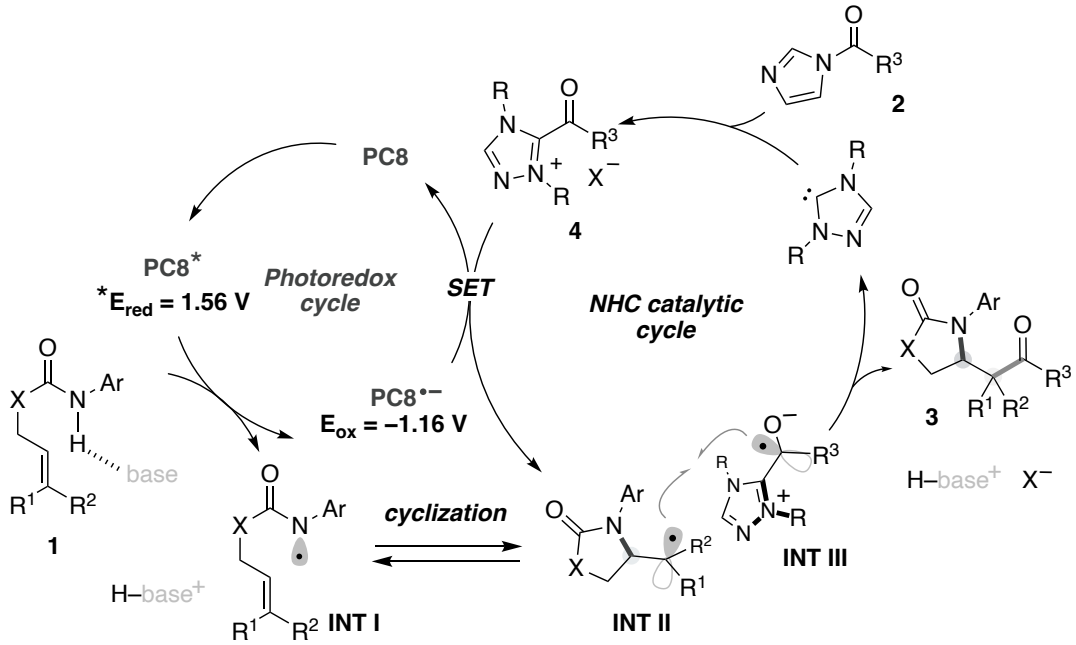
Entry	Additive	Yield (%)[a] of **3aa** (dr)
1	**2a** (1.0 equiv), **PC8** (2 mol %), **N1** (15 mol %), Cs_2CO_3 (15 mol %) and $Bu_4N[OP(O)(OBu)_2]$ (1.0 equiv)	100 (3.1/1)
2	Cs_2CO_3 (1.0 equiv)	100 (3.5/1)
3	$Bu_4N[OP(O)(OBu)_2]$ (1.0 equiv)	100 (3.4/1)
4	**2a** (1.0 equiv.), **N1** (1.0 equiv.) and Cs_2CO_3 (1.0 equiv)	100 (3.1/1)
5	none	100 (24/1)
6[b]	none	100 (11/1)
7[c]	none	100 (> 20/1)

[a]Reaction was carried out with **3aa** (0.10 mmol) and additive in MeCN (1 mL) under Kessil PR160L 440 nm irradiation at ambient temperature for 12 h. [b]Reaction was carried out at 60°C for 12 h. [c]Reaction was carried out at room temperature for 12 h.

Table 3-3. Epimerization experiment of product **3aa**.

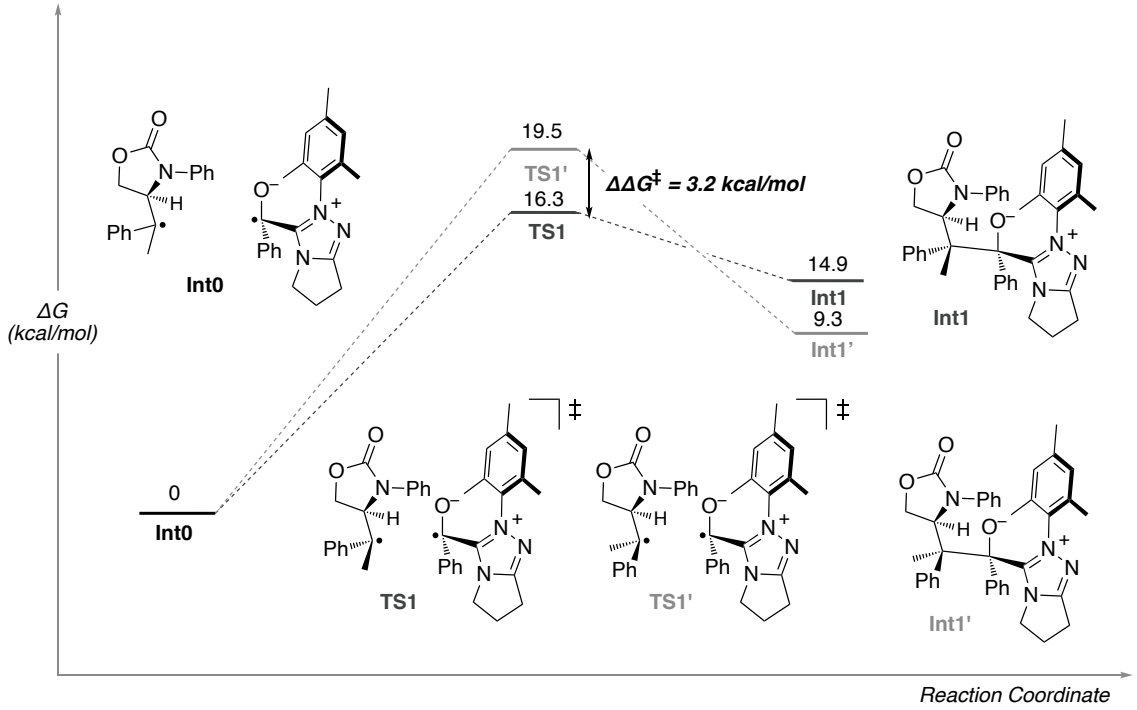
上記の反応機構解析の結果に基づき、推定される反応機構を以下に示した（**Scheme 3-6**）。励起状態で比較的高い酸化電位（$E_{red}^* = 1.56$ V vs. SCE）[33] を有する **PC8** とリン酸塩

基により、酸化的 PCET プロセスを介してアミド **1** から窒素中心ラジカル **INT I** が生じるとともに、還元状態の光酸化還元触媒（E_{ox} = −1.16 V vs. SCE）[33] が形成する。窒素中心ラジカル **INT I** が分子内のアルケンと速やかに環化反応を進行し、炭素中心ラジカル **INT II** が形成する。NHC 触媒サイクルでは、NHC とアシルイミダゾール **2** が反応し、アシルアゾリウム中間体 **4** が形成し、先ほど生じた還元状態の **PC8**$^{\bullet-}$から一電子還元が起こり、長寿命なケチルラジカル **INT III** が得られる。**INT II** と **INT III** の間で選択的なラジカル–ラジカルカップリングが進行し、アミドアシル化生成物 **3** を与える。



Scheme 3-6. Plausible mechanism.

本反応のジアステレオ選択性についての知見を得るべく、ラジカル–ラジカルカップリング段階に対して DFT 計算を行った（**Figure 3-7**）。短寿命なアルキルラジカル **INT II** と長寿命ケチルラジカル **INT III** とのラジカル–ラジカルカップリングの際に、遷移状態 **TS1** では実際に得られた生成物の立体構造を与え、遷移状態 **TS1'**ではもう一方の立体構造を与える。**TS1** と **TS1'**の活性化エネルギーの差は 3.2 kcal/mol であり、この高いジアステレオ選択性の発現に対する十分なエネルギー差が得られた。したがって、このラジカル–ラジカルカップリング段階において、ジアステレオ選択性を決定することが示唆された。



(U)B3LYP/6-31G // (U)B3LYP-D3/6-311G+(d,p) _SMD(MeCN) (hartree)

Figure 3-7. Reaction coordinate of the radical−radical coupling.

第 5 節　結論

可視光駆動型 PCET プロセスに基づく NHC 触媒系を用いた、不活性アルケンのアミドアシル化を達成した。本手法は、ラジカル−ラジカルカップリング段階を触媒的に精密に制御することで、高いジアステレオ選択性で α 位に 3 級または 4 級炭素中心を有する環状 β-アミドケトンを構築できた。本触媒系は、窒素中心ラジカルの分子内環化反応による短寿命なアルキルラジカルの生成と、アシルアゾリウム中間体の一電子還元による長寿命なケチルラジカルの生成を引き起こす。このジアステレオ選択的なラジカル−ラジカルカップリングを達成するためには、2 種のラジカル生成における一電子移動の精密な制御が鍵となる。本プロセスは、従来法では合成困難なかさ高い β-アミドケトンの構築を可能とし、新たなケミカルスペースの創出につながる。さらに、合成した β-アミドケトンは、酸化・還元することで、立体環境を損なうことなく、脱保護されたカルバマートと鎖状のアミノブタンジオールがそれぞれ得られた。

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第 3 章の実験項

■ Instrumentation and Chemicals ■

NMR spectra were recorded on Bruker AVANCE NEO 400N spectrometer, operating at 400 MHz for ^{1}H NMR, 100.6 MHz for ^{13}C NMR and 128.4 MHz for ^{11}B NMR. Chemical shifts were reported in δ ppm. Chloroform-d_1 ($CDCl_3$) containing 0.03% tetramethylsilane (TMS) (>99.8%D, Cambridge Isotope Laboratories, Inc., Cat. No. DLM-7) and acetone-*d*6 (99.96%D, Cambridge Isotope Laboratories, Inc., Cat. No. DLM-38) were used as solvents for NMR measurements at ambient temperature. Chemical shifts (δ) for ^{1}H NMR are given in parts per million (ppm) relative to relative to TMS (δ 0.00 ppm in $CDCl_3$), or residual acetone (δ 2.07 ppm). Chemical shifts (δ) for ^{13}C NMR are given in ppm relative to $CDCl_3$ (δ 77.0 ppm), or residual acetone (δ 30.6 ppm). Chemical shifts (δ) for ^{11}B NMR are given in ppm relative to $BF_3{\cdot}OEt_2$ (δ 0.0 ppm in $CDCl_3$) used as the external standard. The abbreviations s, d, t, q, quin, br s, and m signify singlet, doublet, triplet, quartet, quintet, broad singlet, and multiplet, respectively.

ESI-Mass (HRMS) were measured with a Bruker Impact HD mass spectrometer, a Bruker micrOTOF mass spectrometer or Bruker solari X mass spectrometer.

TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Kanto Chemical Co., Silica gel 60 N, spherical, neutral) was used for column chromatography.

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 an OptiMelt MPA100 automated melting point apparatus (Stanford Research Systems).

UV-Vis absorption spectra were recorded on a Shimadzu UV-1900.

Fluorescence spectra were recorded on a Shimadzu RF-6000.

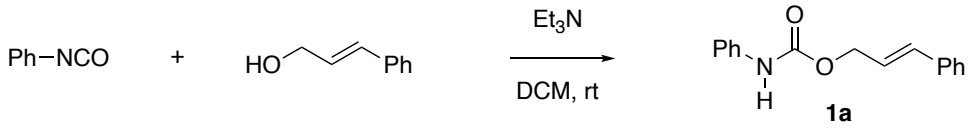
Reaction set-up and materials

Kessil PR160L 440 nm (highest blue and intensity setting) was used as a light source. The light was equipped with PhotoRedOx Box Duo (EvoluChem).

All reactions were carried out under nitrogen atmosphere. Materials were obtained from commercial suppliers listed as below and stored under nitrogen and used as received or prepared according to standard procedures unless otherwise noted. Photoredox catalysts (**P1**–**P8**) were prepared according to the literature.[1–3] Triazolium salts (**N1**–**N5**) were prepared according to the literature.[4] Imidazolium salt **N6** was prepared according to the literature.[5] Thiazolium salt **N7** was prepared according to the literature.[6] $Bu_4N[PO_2(OBu)_2]$[7] and $Bu_4N[PO_2(OBn)_2]$[8] were prepared according to the literatures. Acyl donors (**A2**–**A4**) were prepared according to the literatures.[9–11]

■ General Procedure for Synthesis of Amidyl Radical Precursors ■

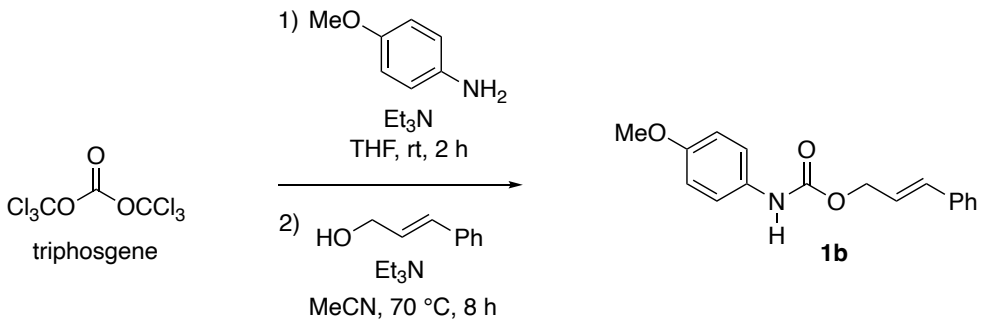
Method A (synthesis of phenyl carbamate/urea)[12]



1a

Synthesis of 1a as a representative. An oven-dried round-bottomed flask with a stirring bar was degassed, flushed with nitrogen, and was added phenyl isocyanate (543 μL, 5.0 mmol, 1.0 equiv), DCM (5.0 mL, 1.0 M), Et_3N (2.09 mL, 15 mmol, 3.0 equiv) and (*E*)-3-phenylprop-2-en-1-ol (642.5 μL, 5.0 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature until the alcohol was fully consumed by TLC. The reaction mixture was then diluted with DCM (10 mL), washed with 1M HCl (10 mL), water (10 mL), and brine (10 mL), and then dried by Na_2SO_4 and concentrated. The crude product was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) to afford **1a** (1.153 g, 4.55 mmol) in 91% yield.

Method B (synthesis of aryl carbamate/urea)[12]

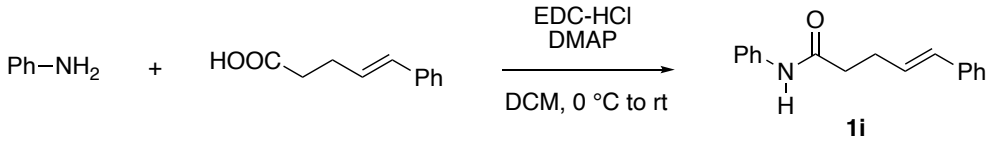


1b

Synthesis of 1b as a representative. An oven-dried round-bottomed flask was degassed, flushed with nitrogen, and was added triphosgene (593.5 mg, 2.0 mmol, 1.0 equiv) in THF (4.0 mL). Then, a solution of 4-methoxyaniline (246.3 mg, 2.0 mmol, 1.0 equiv) dissolved in THF (16 mL) was slowly dripped into the triphosgene solution. Et_3N (585 μL, 4.2 mmol, 2.1 equiv) was then added slowly to the reaction mixture after the aniline was added. The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was then concentrated and the flask containing the resulting residue was degassed and acetonitrile (32 mL, 0.125 M), Et_3N (585.4 μL, 4.2 mmol, 2.1 equiv), and (*E*)-3-phenylprop-2-en-1-ol (322 mg, 2.4 mmol, 1.2 equiv) were added.

The reaction mixture was then stirred at 70 ºC for 8 hours. The crude product was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) to afford **1b** (510 mg, 1.80 mmol) in 90% yield.

Method C (synthesis of amide)[12]

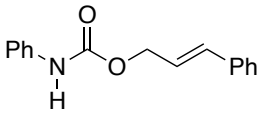


1i

Synthesis of 1i as a representative. An oven-dried round-bottomed flask was degassed, flushed with nitrogen, and was added DCM (2.8 mL, 0.4 M), EDC-HCl (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride; 281.1 mg, 1.47 mmol, 1.3 equiv.), and DMAP (193.0 mg, 1.58 mmol, 1.4 equiv). The reaction flask was cooled to 0 ℃ in an ice bath and (*E*)-5-phenylpent-4-enoic acid (200 mg, 1.13 mmol, 1.0 equiv) was added. After five minutes of stirring, aniline (124.2 μL, 1.36 mmol, 1.2 equiv) was added. The ice bath was then removed, and the reaction allowed to stir until the carboxylic acid was consumed by TLC. The reaction was quenched with 1M HCl (5.0 mL) and the organics separated. The aqueous layer was then extracted with DCM (2 × 5.0 mL). The organic layers were combined and dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) to afford **1i** (240.5 mg, 0.957 mmol) in 87% yield (dr = 9:1).

■ Characterization Data for Amidyl Radical Precursors ■

Cinnamyl Phenylcarbamate (1a)



Synthesized using **Method A** starting from (*E*)-3-phenylprop-2-en-1-ol on a 5.0 mmol scale with respect to the alcohol.

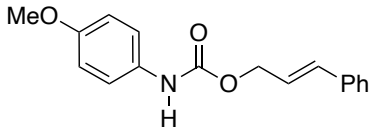
The product **1a** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (1.153 g, 4.55 mmol, 91% isolated yield). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.2 Hz, 4H), 7.34–7.24 (m, 5H), 7.09–7.05 (m, 2H), 6.33 (dt, J = 15.6, 6.4 Hz, 1H), 4.83 (dd, J = 6.4, 0.8 Hz, 2H) (the signal for the proton of N–H was not observed).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.3, 137.8, 136.2, 134.2, 129.1 (2C), 128.6 (2C), 128.1 (2C), 126.6 (2C), 123.5, 123.3, 118.7, 65.8.

The ^{1}H and ^{13}C NMR spectra data of product **1a** were consistent with the literature.[12]

Cinnamyl (4-Methoxyphenyl)carbamate (1b)



Synthesized using **Method B** starting from (*E*)-3-phenylprop-2-en-1-ol and 4-methoxyaniline on a 2.0 mmol scale with respect to the amine.

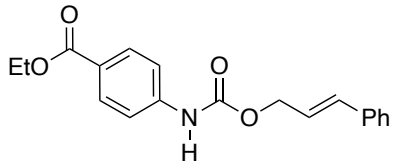
The product **1b** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (510.0 mg, 1.80 mmol, 90% isolated yield). Pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.39 (m, 2H), 7.34–7.24 (m, 5H), 6.87–6.83 (m, 2H), 6.68 (d, J = 16.0 Hz, 1H), 6.56 (br s, 1H), 6.33 (dt, J = 16.0, 6.4 Hz, 1H), 4.81 (dd, J = 6.4, 1.2 Hz, 2H), 3.78 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.0, 153.7, 136.2, 134.1 (2C), 130.8, 128.6 (2C), 128.0, 126.6 (2C), 123.5, 120.7, 114.2 (2C), 65.7, 55.5.

The ^{1}H and ^{13}C NMR spectra data of product **1b** were consistent with the literature.[13]

Ethyl 4-{[(Cinnamyloxy)carbonyl]amino}benzoate (1c)



Synthesized using **Method B** starting from (*E*)-3-phenylprop-2-en-1-ol and ethyl 4-aminobenzoate on a 2.0 mmol scale with respect to the amine.

The product **1c** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (553.1 mg, 1.70 mmol, 85% isolated yield). Pale yellow solid.

M.p. 114–116 °C.

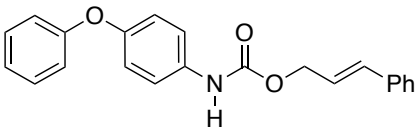
IR (neat) 770, 1050, 1108, 1276, 1412, 1532, 1692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.8 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.8 Hz, 2H), 7.35–7.31 (m, 2H), 7.27 (m, 1H), 6.94 (br s, 1H), 6.70 (d, J = 16.0 Hz, 1H), 6.32 (dt, J = 16.0, 6.4 Hz, 1H), 4.84 (dd, J = 6.4, 1.2 Hz, 2H), 4.36 (q, J = 7.2 Hz, 2H), 1.38 (d, J = 7.2 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.2, 152.8, 142.0, 136.0, 134.6, 130.9 (2C), 128.6 (2C), 128.2, 126.6 (2C), 125.2, 122.9 (2C), 117.6, 66.3, 60.8, 14.3.

HRMS–ESI (*m/z*): $[M+NH_4]^+$ calcd for $C_{18}H_{23}N_2O_4^+$, 343.1652; found, 343.1633.

Cinnamyl (4-Phenoxyphenyl)carbamate (1d)



Synthesized using **Method B** starting from (*E*)-3-phenylprop-2-en-1-ol and 4-phenoxyaniline on a 2.0 mmol scale with respect to the amine.

The product **1d** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (601.0 mg, 1.74 mmol, 87% isolated yield). White solid.

M.p. 121–123 °C.

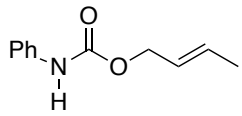
IR (neat) 691, 741, 972, 1227, 1488, 1508, 1590, 1696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.25 (m, 9H), 7.07 (t, J = 7.6 Hz, 1H), 7.00–6.97 (m, 4H), 6.70 (d, J = 16.0 Hz, 1H), 6.60 (br s, 1H), 6.33 (dt, J = 16.0, 6.4 Hz, 1H), 4.83 (dd, J = 6.4, 0.8 Hz, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.7, 153.5, 153.0, 136.2, 134.3 (2C), 133.3, 129.7 (2C), 128.6 (2C), 128.1, 126.6 (2C), 123.3, 123.0, 120.6, 119.9 (2C), 118.3 (2C), 65.8.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{20}NO_3^+$, 346.1438; found, 346.1451.

(*E*)-But-2-en-1-yl Phenylcarbamate (1e)



Synthesized using **Method A** starting from (*E*)-but-2-en-1-ol on a 1.0 mmol scale with respect to the alcohol.

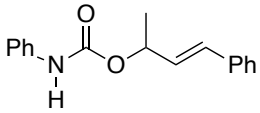
The product **1e** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (79.8 mg, 0.94 mmol, 94% isolated yield). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 7.6 Hz, 2H), 7.31–7.28 (m, 2H), 7.05 (m, 1H), 6.65 (br s, 1H), 5.84 (m, 1H), 5.64 (m, 1H), 4.59 (d, J = 6.8 Hz, 2H), 1.74 (dd, J = 6.8, 1.2 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.4, 137.9, 131.6, 129.0 (2C), 125.3 (2C), 123.4, 118.6, 65.9, 17.8.

The ^{1}H and ^{13}C NMR spectra data of product **1e** were consistent with the literature.[14]

(*E*)-4-Phenylbut-3-en-2-yl Phenylcarbamate (1f)



Synthesized using **Method A** starting from (*E*)-pent-3-en-2-ol[15] on a 2.0 mmol scale with respect to the alcohol.

The product **1f** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (465.2 mg, 1.74 mmol, 87% isolated yield). Orange solid.

M.p. 83–86 °C.

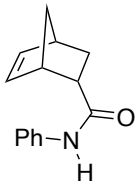
IR (neat) 691, 747, 1048, 1312, 1442, 1599, 1700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.37 (m, 4H), 7.32–7.22 (m, 5H), 7.05 (t, J = 7.2 Hz, 1H), 6.68–6.63 (m, 2H), 6.23 (dd, J = 16.0, 6.8 Hz, 1H), 5.54 (m, 1H), 1.47 (d, J = 6.8 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.9, 137.9, 136.3, 131.6 (2C), 129.0 (2C), 128.8, 128.5 (2C), 127.9, 126.6 (2C), 123.3, 118.6, 71.9, 20.6.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{18}NO_2^+$, 268.1332; found, 268.1332.

(1*S*,2*S*,4*S*)-*N*-Phenylbicyclo[2.2.1]hept-5-ene-2-carboxamide (1g)



Synthesized using **Method C** starting from bicyclo[2.2.1]hept-5-ene-2-carboxylic acid and aniline on a 2.0 mmol scale with respect to the carboxylic acid.

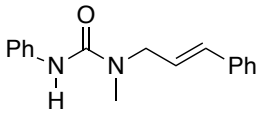
The product **1g** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (Figure 3; 302.9 mg, 1.42 mmol, 71% isolated yield). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.0 Hz, 2H), 7.30 (t, J = 7.6 Hz, 2H), 7.12–7.06 (m, 2H), 6.30 (m, 1H), 6.05 (m, 1H), 3.24 (s, 1H), 3.04–2.98 (m, 2H), 2.02 (m, 1H), 1.52–1.46 (m, 2H), 1.35 (d, J = 8.0 Hz, 1H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 172.5, 138.1, 132.1 (2C), 128.9 (× 2), 124.0, 119.6 (2C), 50.2, 46.5, 45.9, 42.8, 30.0.

The ^{1}H and ^{13}C NMR spectra data of product **1g** were consistent with the literature.[12]

1-Cinnamyl-1-methyl-3-phenylurea (1h)



Synthesized using **Method A** starting from (*E*)-*N*-methylbut-2-en-1-amine[16] on a 1.2 mmol scale with respect to the amine.

The product **1h** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (258.9 mg, 0.972 mmol, 81% isolated yield). White solid.

M.p. 122–123 °C.

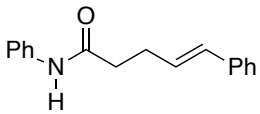
IR (neat) 692, 750, 1240, 1440, 1478, 1595, 1641 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.31 (m, 6H), 7.29–7.24 (m, 3H), 7.02 (t, J = 7.2 Hz, 1H), 6.58 (t, J = 16.0 Hz, 1H), 6.42 (br s, 1H), 6.23 (dt, J = 16.0, 1.2 Hz, 1H), 4.14 (dd, J = 6.0, 1.2 Hz, 2H), 3.05 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 155.5, 139.1, 136.2, 132.3, 128.8 (2C), 128.7 (2C), 127.9, 126.4 (2C), 124.8, 123.0, 119.8 (2C), 51.0, 34.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{19}N_2O^+$, 267.1492; found, 267.1477.

(*E*)-*N*,5-Diphenylpent-4-enamide (1i)



Synthesized using **Method C** starting from (*E*)-5-phenylpent-4-enoic acid[17] and aniline on a 1.1 mmol scale with respect to the carboxylic acid.

The product **1i** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (240.5 mg, 0.957 mmol, 87% isolated yield, dr = 9:1). Pale yellow solid.

M.p. 108–110 °C.

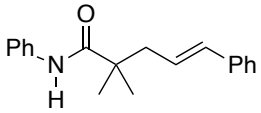
IR (neat) 692, 759, 966, 1253, 1441, 1498, 1599, 1700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.46 (m, 2H), 7.34–7.25 (m, 7H), 7.21 (m, 1H), 7.10 (t, *J* = 7.2 Hz, 1H), 6.49 (m, 1H), 6.25 (m, 0.9H), 5.69 (m, 0.1H), 2.77 (m, 0.2H), 2.67–2.62 (m, 1.8H), 2.54–2.46 (m, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.4 (× 2), 137.8 (× 2), 137.2 (× 2), 131.3 (× 2), 130.5, 130.3, 129.0 (2C), 128.7, 128.52 (2C × 2), 128.48 (2C), 128.3, 127.2 (2C), 126.9, 126.1 (2C), 124.3, 119.9 (2C × 2), 37.6, 37.3, 28.8, 24.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{18}NO_2^+$, 252.1383; found, 252.1364.

(*E*)-2,2-Dimethyl-*N*,5-diphenylpent-4-enamide (1j)



Synthesized using **Method C** starting from (*E*)-2,2-dimethyl-5-phenylpent-4-enoic acid[18] and aniline on a 2.5 mmol scale with respect to the carboxylic acid.

The product **1j** was purified by flash chromatography on silica gel (100:0–95:5, hexane/AcOEt) (475.0 mg, 1.70 mmol, 68% isolated yield). Brown solid.

M.p. 92–94 °C.

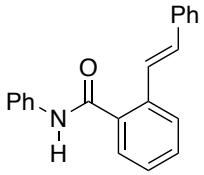
IR (neat) 691, 747, 967, 1313, 1437, 1497, 1597, 1654, 1701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.0 Hz, 2H), 7.38 (br s, 1H), 7.34–7.22 (m, 6H), 7.19 (m, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.47 (d, *J* = 16.0 Hz, 1H), 6.21 (m, 1H), 2.52 (dd, *J* = 7.6, 0.8 Hz, 2H), 1.34 (s, 6H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 175.4, 137.8, 137.1, 133.5, 128.9 (2C), 128.5 (2C), 127.3, 126.1 (2C), 125.8, 124.3, 120.1 (2C), 44.3, 43.3, 25.4 (2C).

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{22}N_2O_4^+$, 280.1696; found, 280.1679.

(*E*)-*N*-Phenyl-2-styrylbenzamide (1k)



Synthesized using **Method C** starting from (*E*)-2-styrylbenzoic acid[19] and aniline on a 2.8 mmol scale with respect to the carboxylic acid.

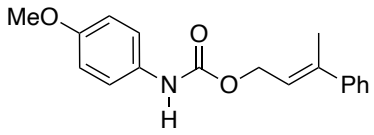
The product **1k** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (Figure. 3; 762.8 mg, 2.55 mmol, 91% isolated yield). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.61–7.46 (m, 8H), 7.37–7.31 (m, 5H), 7.25 (m, 1H), 7.17–7.08 (m, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.4, 137.9, 136.8, 135.8, 135.4, 132.1, 130.7, 129.1 (2C), 128.7 (2C), 128.1, 127.8, 127.6, 126.8 (2C), 126.5, 125.6, 124.7, 119.9 (2C).

The ^{1}H and ^{13}C NMR spectra data of product **1k** were consistent with the literature.[20]

(*E*)-3-Phenylbut-2-en-1-yl (4-Methoxyphenyl)carbamate (1l)



Synthesized using **Method B** starting from (*E*)-3-phenylbut-2-en-1-ol[20] and 4-methoxyaniline on a 10 mmol scale with respect to the amine.

The product **1l** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (2.589 g, 8.70 mmol, 87% isolated yield). pale yellow solid.

M.p. 74–76 °C.

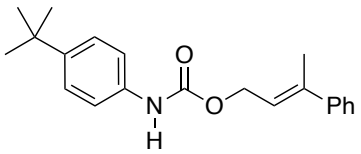
IR (neat) 702, 758, 830, 1030, 1135, 1220, 1247, 1412, 1729 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.2 Hz, 2H), 7.34–7.25 (m, 5H), 6.85 (d, J = 8.8 Hz, 2H), 6.55 (br s, 1H), 5.94 (t, J = 6.8 Hz, 1H), 4.87 (d, J = 6.8 Hz, 2H), 3.76 (s, 3H), 2.14 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.0, 142.5, 140.2, 130.9, 128.3 (2C), 127.7, 127.5 (2C), 125.8 (2C), 121.6, 120.7, 114.2 (2C), 62.2, 55.5, 16.2.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{19}NNaO_3^+$, 320.1257; found, 320.1251.

(*E*)-3-Phenylbut-2-en-1-yl [4-(*tert*-Butyl)phenyl]carbamate (1m)



Synthesized using **Method B** starting from (*E*)-3-phenylbut-2-en-1-ol[20] and 4-(*tert*-butyl)aniline on a 1.5 mmol scale with respect to the amine.

The product **1m** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (407.5 mg, 1.26 mmol, 84% isolated yield). Orange solid.

M.p. 85–86 °C.

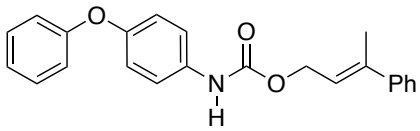
IR (neat) 696, 835, 1048, 1220, 1318, 1495, 1597, 1704 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.6 Hz, 2H), 7.35–7.27 (m, 7H), 6.58 (br s, 1H), 5.94 (t, J = 6.8 Hz, 1H), 4.88 (d, J = 6.8, 2H), 2.14 (s, 3H), 1.30 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.6, 146.4, 142.6, 140.3, 135.2, 128.3 (2C), 127.5 (2C), 125.87 (2C), 125.86, 121.5 (2C), 118.6, 62.2, 34.3, 31.4 (3C), 16.2.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{21}H_{26}NO_2^+$, 324.1958; found, 324.1955.

(*E*)-3-Phenylbut-2-en-1-yl (4-Phenoxyphenyl)carbamate (1n)



Synthesized using **Method B** starting from (*E*)-3-phenylbut-2-en-1-ol[20] and 4-phenoxyaniline on a 1.5 mmol scale with respect to the amine.

The product **1n** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (463.7 mg, 1.29 mmol, 86% isolated yield). Orange oil.

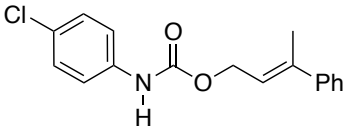
IR (neat) 691, 750, 849, 1045, 1166, 1411, 1487, 1507, 1699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.6 Hz, 2H), 7.36–7.24 (m, 7H), 7.06 (d, J = 7.2 Hz, 1H), 6.97 (d, J = 8.8 Hz, 4H), 6.68 (br s, 1H), 5.94 (t, J = 7.2 Hz, 1H), 4.88 (d, J = 7.2 Hz, 2H), 2.14 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.7, 153.7, 152.8, 142.5, 140.4, 133.4, 129.7 (2C), 128.3 (2C), 127.5 (2C), 125.8 (2C), 122.9, 121.4 (2C), 120.5, 119.8, 118.2 (2C), 62.3, 16.2.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{22}NO_3^+$, 360.1594; found, 360.1581.

(*E*)-3-Phenylbut-2-en-1-yl (4-Chlorophenyl)carbamate (1o)



Synthesized using **Method B** starting from (*E*)-3-phenylbut-2-en-1-ol[20] and 4-chloroaniline on a 1.5 mmol scale with respect to the amine.

The product **1o** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (366.7 mg, 1.21 mmol, 81% isolated yield). Orange solid.

M.p. 84–87 °C.

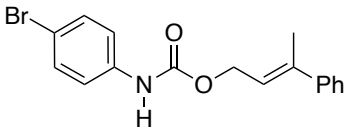
IR (neat) 695, 827, 1046, 1119, 1306, 1401, 1493, 1522, 1700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.6 Hz, 2H), 7.35–7.31 (m, 4H), 7.29–7.25 (m, 3H), 6.65 (br s, 1H), 5.93 (t, J = 6.8 Hz, 1H), 4.88 (d, J = 6.8 Hz, 2H), 2.15 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.4, 142.4, 140.6, 136.5, 129.0 (2C), 128.4, 128.3 (2C), 127.6, 125.8 (2C), 121.2 (2C), 119.9, 62.4, 16.2.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{16}ClNNaO_2^+$, 324.0762; found, 324.0755.

(*E*)-3-Phenylbut-2-en-1-yl (4-Bromophenyl)carbamate (1p)



Synthesized using **Method B** starting from (*E*)-3-phenylbut-2-en-1-ol[20] and 4-bromoaniline on a 1.5 mmol scale with respect to the amine.

The product **1p** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (399.9 mg, 1.16 mmol, 77% isolated yield). Pale orange solid

M.p. 92–94 °C.

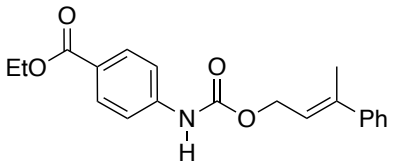
IR (neat) 695, 823, 1045, 1074, 1306, 1398, 1490, 1520, 1700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.39 (m, 4H), 7.35–7.25 (m, 5H), 6.67 (br s, 1H), 5.93 (t, J = 6.8 Hz, 1H), 4.88 (d, J = 6.8 Hz, 2H), 2.14 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.3, 142.4, 140.7, 137.0, 132.0 (2C), 128.3 (2C), 127.6, 125.8 (2C), 121.2 (2C), 120.2, 115.9, 62.5, 16.2.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{16}BrNNaO_2^+$, 368.0257; found, 368.0250.

Ethyl (*E*)-4-({[(3-Phenylbut-2-en-1-yl)oxy]carbonyl}amino)benzoate (1q)



Synthesized using **Method B** starting from (*E*)-3-phenylbut-2-en-1-ol[20] and ethyl 4-aminobenzoate on a 2.0 mmol scale with respect to the amine.

The product **1q** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (556.6 mg, 1.64 mmol, 82% isolated yield). Pale yellow solid.

M.p. 120–121 °C.

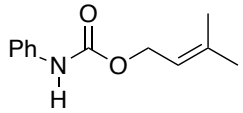
IR (neat) 770, 1108, 1175, 1277, 1412, 1532, 1596, 1693, 1710 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 7.2 Hz, 2H), 7.36–7.32 (m, 2H), 7.29 (d, J = 7.2 Hz, 2H), 6.85 (br s, 1H), 5.94 (t, J = 7.2 Hz, 1H), 4.90 (d, J = 7.2 Hz, 2H), 4.36 (q, J = 7.2 Hz, 2H), 2.16 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H),.

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.2, 153.0, 142.4, 142.0, 140.8, 130.9 (2C), 128.3 (2C), 127.6 (2C), 125.9 (2C), 125.2, 121.0, 117.5, 62.6, 60.8, 16.3, 14.3.

HRMS–ESI (*m/z*): $[M+NH_4]^+$ calcd for $C_{20}H_{25}N_2O_4^+$, 357.1809; found, 357.1807.

3-Methylbut-2-en-1-yl Phenylcarbamate (1r)



Synthesized using **Method A** starting from 3-methylbut-2-en-1-ol on a 1.0 mmol scale with respect to the alcohol.

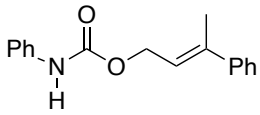
The product **1r** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (188.8 mg, 0.92 mmol, 92% isolated yield). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.0 Hz, 2H), 7.32–7.26 (m, 2H), 7.05 (t, J = 7.2 Hz, 1H), 6.63 (br s, 1H), 5.40 (m, 1H), 4.67 (d, J = 7.2 Hz, 2H), 1.78 (s, 3H), 1.75 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.6, 139.4, 137.9, 129.0 (2C), 123.3, 118.7 (2C), 118.6, 62.0, 25.8, 18.0.

The ^{1}H and ^{13}C NMR spectra data of product **1r** were consistent with the literature.[15]

(*E*)-3-Phenylbut-2-en-1-yl Phenylcarbamate (1s)



Synthesized using **Method A** starting from (*E*)-3-phenylbut-2-en-1-ol[20] on a 4.2 mmol scale with respect to the alcohol.

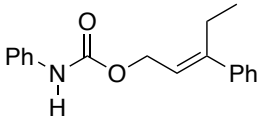
The product **1s** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (Figure 3; 999.3 mg, 3.73 mmol, 89% isolated yield). pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.35 (m, 4H), 7.33–7.27 (m, 5H), 7.06 (t, J = 7.2 Hz, 1H), 6.23 (br s, 1H), 5.95 (t, J = 6.8 Hz, 1H), 4.89 (d, J = 6.8 Hz, 2H), 2.15 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.5, 142.5, 140.4, 137.8, 129.1 (2C), 128.3 (2C), 127.5, 125.9 (2C), 123.5, 121.4 (2C), 118.7, 62.3, 16.2.

The ^{1}H and ^{13}C NMR spectra data of product **1s** were consistent with the literature.[14]

(*E*)-3-Phenylpent-2-en-1-yl Phenylcarbamate (1t)



Synthesized using **Method A** starting from (*E*)-3-phenylpent-2-en-1-ol[20] on a 1.0 mmol scale with respect to the alcohol.

The product **1t** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (227.9 mg, 0.81 mmol, 81% isolated yield, dr = 13:1). Pale yellow solid.

M.p. 68–70 °C.

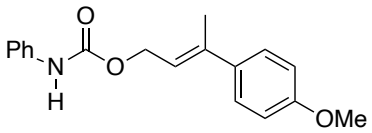
IR (neat) 650, 907, 1209, 1311, 1443, 1524, 1728 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (m, 0.07H), 7.39–7.27 (m, 8.79H), 7.16 (d, J = 7.2 Hz, 0.14H), 7.16 (t, J = 7.2 Hz, 1H), 6.61 (m, 1H), 5.81 (t, J = 7.2 Hz, 0.93H), 5.67 (t, J = 7.2 Hz, 0.07H), 4.88 (d, J = 7.2 Hz, 1.86H), 4.57 (d, J = 7.2 Hz, 0.14H), 2.61 (q, J = 7.6 Hz, 1.86H), 2.42 (q, J = 7.6 Hz, 0.14H), 1.03–0.99 (m, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.5 (× 2), 147.3 (× 2), 141.6 (× 2), 137.8 (× 2), 129.0 (2C), 128.3 (2C), 128.2 (2C), 128.0 (2C), 127.5, 127.3, 126.5 (2C × 2), 123.4, 123.3, 121.1 (2C × 2), 119.5, 118.7, 62.0, 61.5, 31.9, 23.4, 13.8, 12.6.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{19}NNaO_2^+$, 304.1308; found, 304.1305.

(*E*)-3-(4-Methoxyphenyl)but-2-en-1-yl Phenylcarbamate (1u)



Synthesized using **Method A** starting from (*E*)-3-(4-methoxyphenyl)but-2-en-1-ol[20] on a 1.4 mmol scale with respect to the alcohol.

The product **1u** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (353.9 mg, 1.19 mmol, 85% isolated yield). Yellow solid.

M.p. 86–87 °C.

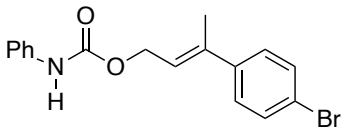
IR (neat) 755, 1047, 1181, 1313, 1443, 1518, 1601, 1704 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.35 (m, 4H), 7.32–7.28 (m, 2H), 7.06 (t, J = 7.2 Hz, 1H), 6.88–6.83 (m, 2H), 6.64 (br s, 1H), 5.89 (td, J = 7.2, 1.2 Hz, 1H), 4.87 (d, J = 7.2 Hz, 2H), 3.81 (s, 3H), 2.12 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.2, 153.5, 140.0, 137.9, 134.9, 129.0 (2C), 126.9 (2C), 123.4, 119.7 (2C), 118.7, 113.6 (2C), 62.3, 55.3, 16.2.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{19}NNaO_3^+$, 320.1257; found, 320.1255.

(*E*)-3-(4-Bromophenyl)but-2-en-1-yl Phenylcarbamate (1v)



Synthesized using **Method A** starting from (*E*)-3-(4-bromophenyl)but-2-en-1-ol[21] on a 2.5 mmol scale with respect to the alcohol.

The product **1v** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (683.8 mg, 1.98 mmol, 79% isolated yield). White solid.

M.p. 121–122 °C.

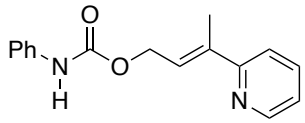
IR (neat) 734, 910, 1047, 1089, 1378, 1446, 1701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.33–7.26 (m, 4H), 7.07 (t, J = 7.2 Hz, 1H), 6.63 (br s, 1H), 5.93 (t, J = 6.8 Hz, 1H), 4.86 (d, J = 6.8 Hz, 2H), 2.11 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.4, 141.4, 139.2, 137.8, 131.4 (2C), 129.1 (2C), 127.5 (2C), 123.5, 122.1 (2C), 121.5, 118.7, 62.1, 16.1.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{16}BrNNaO_2^+$, 368.0257; found, 368.0249.

(*E*)-3-(Pyridin-2-yl)but-2-en-1-yl Phenylcarbamate (1w)



Synthesized using **Method A** starting from (*E*)-3-(pyridin-2-yl)but-2-en-1-ol[22] on a 1.3 mmol scale with respect to the alcohol.

The product **1w** was purified by flash chromatography on silica gel (100:0–84:16, hexane/AcOEt) (326 mg, 1.21 mmol, 92% isolated yield). White solid.

M.p. 56–59 °C.

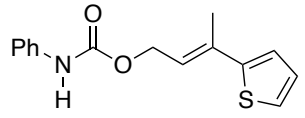
IR (neat) 692, 753, 1028, 1046, 1313, 1444, 1541, 1597, 1705 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (m, 1H), 7.63 (td, J = 7.8, 2.0 Hz, 1H), 7.43–7.38 (m, 3H), 7.30–7.26 (m, 2H), 7.15 (m, 1H), 7.09 (br s, 1H), 7.04 (m, 1H), 6.50 (td, J = 6.8, 1.2 Hz, 1H), 4.93 (d, J = 6.8 Hz, 2H), 2.18 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.6, 153.6, 148.8, 138.8, 137.9, 136.4, 128.9 (2C), 124.7, 123.3, 122.2, 120.0 (2C), 118.6, 62.1, 14.6.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{16}H_{16}N_2NaO_2^+$, 291.1104; found, 291.1106.

(*E*)-3-(Thiophen-2-yl)but-2-en-1-yl Phenylcarbamate (1x)



Synthesized using **Method A** starting from (*E*)-3-(thiophen-2-yl)but-2-en-1-ol[23] on a 4.0 mmol scale with respect to the alcohol.

The product **1x** was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) (869 mg, 3.16 mmol, 79% isolated yield, dr = 6:1). Orange solid.

M.p. 80–82 °C.

IR (neat) 691, 1046, 1212, 1313, 1444, 1501, 1527, 1600, 1701 cm^{-1}.

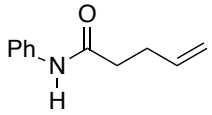
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.0 Hz, 1.68H), 7.31–7.27 (m, 2.32H), 7.17 (dd, J

= 5.0, 1.2 Hz, 0.84H), 7.12–6.96 (m, 3.16H), 6.73 (br s, 1H), 6.08 (td, *J* = 7.2, 1.2 Hz, 0.84H), 4.71 (td, *J* = 6.8, 1.2 Hz, 0.16H), 4.88–4.84 (m, 2H), 2.17–2.15 (m, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.4 (× 2), 146.2, 141.8, 137.8, 134.2, 133.9, 132.5, 129.3 (2C), 129.0 (2C), 128.1 (2C), 127.3 (2C), 127.0, 126.2, 125.5, 124.4 (× 2), 123.7, 123.4, 122.1, 119.5, 118.7, 62.8, 61.8, 25.8, 16.0.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{15}H_{15}NNaO_2S^+$, 296.0716; found, 296.0718.

_N_-Phenylpent-4-enamide (1y)



Synthesized using **Method C** starting from pent-4-enoic acid and aniline on a 2.0 mmol scale with respect to the carboxylic acid.

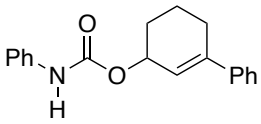
The product **1y** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (318.9 mg, 1.82 mmol, 91% isolated yield). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.6 Hz, 2H), 7.41 (br s, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 5.87 (m, 1H), 5.14–5.04 (m, 2H), 2.05–2.43 (m, 4H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.6, 137.8, 136.8, 128.9 (2C), 124.2, 119.9 (2C), 115.9, 36.8, 29.4.

The ^{1}H and ^{13}C NMR spectra data of product **1y** were consistent with the literature.[14]

3,4,5,6-Tetrahydro-[1,1'-biphenyl]-3-yl Phenylcarbamate (1z)



Synthesized using **Method A** starting from 3,4,5,6-tetrahydro-[1,1'-biphenyl]-3-ol[24] on a 2.4 mmol scale with respect to the alcohol.

The product **1z** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (612.5 mg, 2.09 mmol, 87% isolated yield). Pale yellow solid.

M.p. 138–140 °C.

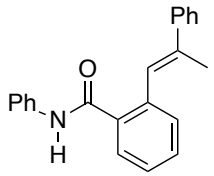
IR (neat) 696, 752, 1230, 1316, 1441, 1488, 1597, 1690 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.38 (m, 4H), 7.35–7.27 (m, 5H), 7.06 (m, 1H), 6.62 (br s, 1H), 6.17 (m, 1H), 5.48 (m, 1H), 2.54 (m, 1H), 2.40 (m, 1H), 2.03–1.78 (m, 4H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.3, 142.3, 141.0, 138.0, 129.0 (2C), 128.3 (2C), 127.7, 125.4 (2C), 123.3, 122.3 (2C), 118.6, 69.7, 28.2, 27.4, 19.3.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{19}NNaO_2^+$, 316.1308; found, 316.1302.

(*E*)-*N*-Phenyl-2-(2-phenylprop-1-en-1-yl)benzamide (1A)



Synthesized using **Method C** starting from (*E*)-2-(2-phenylprop-1-en-1-yl)benzoic acid[25] and aniline on a 1.0 mmol scale with respect to the carboxylic acid.

The product **1A** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (285.2 mg, 0.91 mmol, 91% isolated yield). Orange oil.

M.p. 132–134 °C.

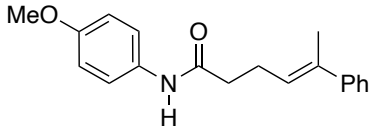
IR (neat) 648, 794, 906, 1045, 1091, 1259, 1443, 1530, 1660,1699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.91 (m, 2H), 7.54–7.49 (m, 5H), 7.44–7.26 (m, 7H), 7.12–7.08 (m, 2H), 2.22 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.5, 142.2, 140.1, 137.9, 135.8, 135.0, 130.6, 130.5, 129.2, 129.0 (2C), 128.5 (2C), 127.9, 127.5, 125.9 (2C), 125.5, 124.4, 119.7 (2C), 17.4.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{20}NO^+$, 314.1539; found, 314.1530.

(*E*)-*N*-(4-Methoxyphenyl)-5-phenylhex-4-enamide (1B)



Synthesized using **Method C** starting from (*E*)-5-phenylhex-4-enoic acid[26] and 4-methoxyaniline on a 2.0 mmol scale with respect to the carboxylic acid.

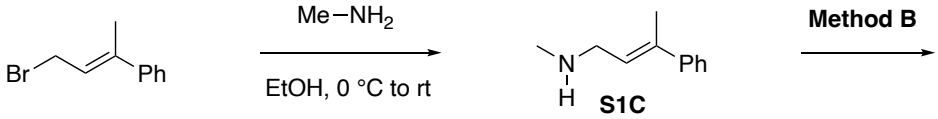
The product **1B** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (490.3 mg, 1.66 mmol, 83% isolated yield). White solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.21 (m, 8H), 6.84 (d, J = 8.4 Hz, 2H), 5.79 (t, J = 7.2 Hz, 1H), 3.77 (s, 3H), 2.64–2.61 (m, 2H), 2.47 (d, J = 7.2 Hz, 2H), 2.07 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.5, 156.4, 143.5, 136.6, 131.0, 128.2 (2C), 126.8, 126.1, 125.6 (× 2), 121.7 (2C), 114.1 (2C), 55.4, 37.2, 24.9, 15.9.

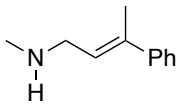
The ^{1}H and ^{13}C NMR spectra data of product **1B** were consistent with the literature.[27]

Synthesis of Amine S1C[16]



An oven-dried round-bottomed flask was degassed, flushed with nitrogen, and was added methylamine in ethanol (33 wt%, 4.663 mL, 37.3 mmol, 10 equiv). The reaction flask was cooled to 0 °C in an ice bath and (*E*)-(4-bromobut-2-en-2-yl)benzene (839.1 mg, 3.73 mmol, 1.0 equiv) was added in one portion with rapid stirring. The reaction was stirred for 1 hour at 0 °C then warmed to room temperature for 2 hours. The reaction was quenched with 1M sodium hydroxide and the aqueous layer was then extracted with Et_2O (2 × 10 mL). The organic layers were combined and washed with brine (10 mL), and then dried by Na_2SO_4 and concentrated. The crude product was purified by flash chromatography on silica gel (80:20–0:100, hexane/AcOEt) to afford **S1C** (589.4 mg, 3.66 mmol) in 98% yield.

(*E*)-*N*-Methyl-3-phenylbut-2-en-1-amine (S1C)



The product **S1C** was purified by flash chromatography on silica gel (80:20–0:100, hexane/AcOEt) (589.4 mg, 3.66 mmol, 98% isolated yield). Orange oil.

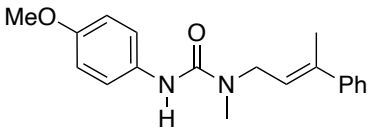
IR (neat) 697, 757, 881, 924, 1048, 1093, 1327, 1445 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.0 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.24 (m, 1H), 5.87 (td, J = 6.4, 1.2 Hz, 1H), 3.42 (d, J = 6.4 Hz, 2H), 2.49 (s, 3H), 2.07 (s, 3H) (the signal for the proton of N–H was not observed).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 143.2, 137.1, 128.2 (2C), 126.9, 125.8, 125.7 (2C), 49.6, 35.9, 16.1.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{11}H_{16}N^+$, 162.1277; found, 162.1286.

(*E*)-3-(4-Methoxyphenyl)-1-methyl-1-(3-phenylbut-2-en-1-yl)urea (1C)



Synthesized using **Method B** starting from (*E*)-*N*-methyl-3-phenylbut-2-en-1-amine (**S1C**) and 4-methoxyaniline on a 1.8 mmol scale with respect to the aniline derivative.

The product **1C** was purified by flash chromatography on silica gel (100:0–91:9,

hexane/AcOEt) (402.3 mg, 1.30 mmol, 72% isolated yield). Pale orange solid.

M.p. 107–110 °C.

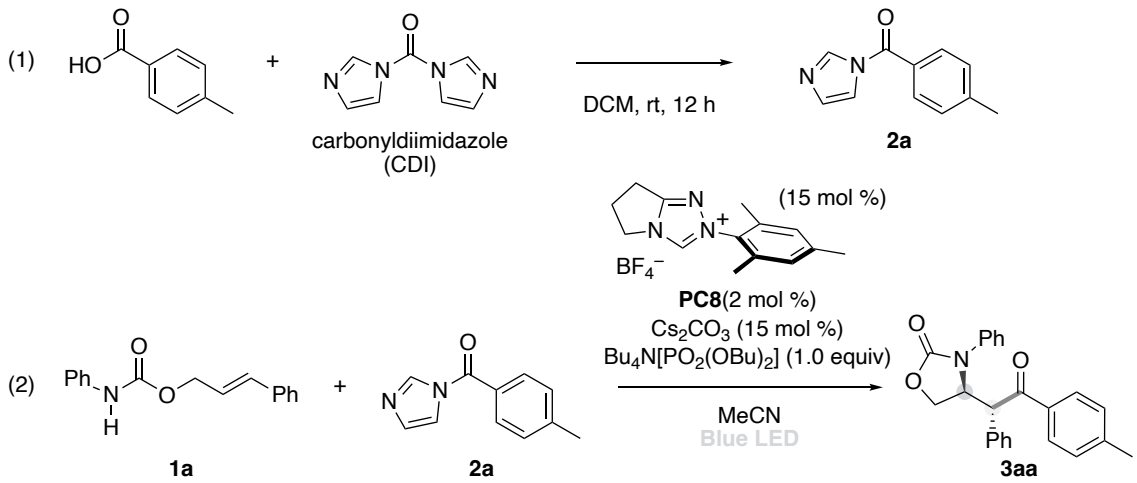
IR (neat) 756, 825, 1029, 1229, 1412, 1464, 1508, 1634, 1705 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.0 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.25 (d, J = 8.0 Hz, 3H), 6.81 (d, J = 8.4 Hz, 2H), 6.37 (br s, 1H), 5.81 (t, J = 6.4 Hz, 1H), 4.16 (d, J = 6.4 Hz, 2H), 3.75 (s, 3H), 3.00 (s, 3H), 2.13 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.0, 155.6, 142.6, 138.3, 132.2, 128.3 (2C), 127.3, 125.7 (2C), 123.6, 122.1 (2C), 114.0 (2C), 55.4, 47.1, 34.4, 15.9.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{23}N_2O_2^+$, 311.1754; found, 311.1741.

■ General Procedure for Amidoacylation of Alkenes ■

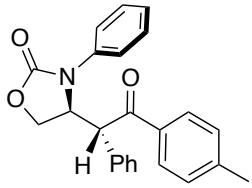


The reaction to produce 3aa in Table 3-2 is representative. According to the literature,[28] acyl imidazole was prepared. To a suspension of *p*-toluic acid (13.6 mg, 0.1 mmol) in dry dichloromethane (333 μL) was added slowly carbonyldiimidazole (CDI, 24.3 mg, 0.15 mmol, 1.5 equiv) (caution, exothermic). After stirring for 12 h at room temperature, the resulting solution was transferred to separatory funnel and washed with deionized water (ca. 5 mL). The organic extract was dried over Na_2SO_4 and after filtration, the filtrate was concentrated under reduced pressure to afford the acyl imidazole **2a** (18.6 mg, 0.1 mmol, quantitative). The acyl imidazole was used without further purification.

Under an ambient atmosphere, to an oven-dried screw-top 5 mL vial with a stirring bar was added Photo catalyst **PC8** (1.32 mg, 2 μmol), triazolium salt NHC (4.73 mg, 15 μmol), carbamate **1a** (35.3 mg, 0.10 mmol) and acyl imidazole **2a** (18.6 mg, 0.1 mmol). The vial was brought to a globebox, and added MeCN (1.0 mL), Cs_2CO_3 (4.89 mg, 15 μmol) and $Bu_4N[PO_2(OBu)_2]$ (45.2 mg, 0.10 mmol). After the vial was removed from the glovebox and sealed with Teflon tape, the vial was placed in Photoreodox Duo. After 12 h stirring at ambient temperature under photoirradiation (440 nm), the reaction mixture was passed through a short pad of silica gel with AcOEt followed by evaporation and flash column chromatography on silica gel (100:0–75:25, hexane/AcOEt) gave **3aa** (26.7 mg, 0.72 mmol) in 72% yield (dr = 3:1).

■ Characterization Date for Amidoacylation Products ■

(*S**)-4-[(*R**)-2-Oxo-1-phenyl-2-(*p*-tolyl)ethyl]-3-phenyloxazolidin-2-one (3aa)



The product **3aa** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 26.7 mg, 0.72 mmol, 72% isolated yield, dr = 3:1). Pale yellow solid. The stereochemistry of **3aa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 159–161 °C.

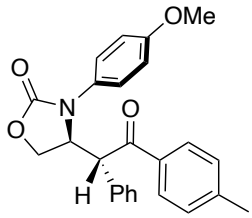
IR (neat) 666, 734, 753, 879, 1046, 1087, 1380, 1704 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 0.48H), 7.62 (d, J = 8.4 Hz, 1.52H), 7.56 (d, J = 7.6 Hz, 1.52H), 7.44 (t, J = 7.6 Hz, 1.52H), 7.33–7.26 (m, 2.28H), 7.22 (t, J = 7.6 Hz, 0.76H), 7.14–6.96 (m, 5.68H), 6.92 (m, 0.24H), 5.24 (m, 1H), 5.03 (d, J = 3.2 Hz, 0.76H), 4.92 (d, J = 8.4 Hz, 0.24H), 4.66 (m, 1H), 4.44 (dd, J = 9.6, 4.0 Hz, 0.76H), 4.31 (dd, J = 9.6, 4.0 Hz, 0.24H), 2.31 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.1, 197.2, 156.2, 155.5, 144.7 (× 2), 136.9, 136.6, 134.3, 133.1, 132.8, 132.7, 129.5 (2C), 129.4 (2C), 129.31 (2C), 129.27 (2C), 129.1 (2C), 129.0 (2C), 128.94 (2C), 128.87 (2C), 128.8 (2C), 128.4, 127.8 (2C), 125.2, 125.0, 123.3, 121.6 (2C × 2), 67.1, 64.1, 59.6, 57.4, 56.5, 52.8, 21.6 (× 2).

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{22}NO_3^+$, 372.1594; found, 372.1587.

(*S**)-3-(4-Methoxyphenyl)-4-[(*R**)-2-oxo-1-phenyl-2-(*p*-tolyl)ethyl]oxazolidin-2-one (3ba)



The product **3ba** was purified by flash chromatography on silica gel (100:0–85:15, hexane/AcOEt) (**Table 3-2**; 23.7 mg, 0.59 mmol, 59% isolated yield, dr = 3:1). Pale orange solid. The stereochemistry of **3ba** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 118–120 °C.

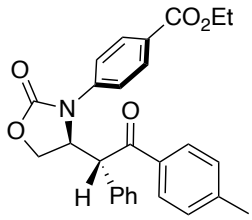
IR (neat) 665, 756, 880, 1087, 1273, 1326, 1701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 0.50H), 7.60 (d, J = 8.0 Hz, 1.50H), 7.41–7.37 (m, 1.50H), 7.34–7.29 (m, 2.25H), 7.14 (d, J = 8.0 Hz, 0.50H), 7.10–7.00 (m, 4.25H), 6.96–6.91 (m, 2H), 6.58 (m, 0.50H), 5.18 (quin, J = 4.4 Hz, 0.75H), 5.12 (m, 0.25H), 4.96 (d, J = 4.0 Hz, 0.75H), 4.88 (d, J = 8.4 Hz, 0.25H), 4.64 (m, 1H), 4.37 (dd, J = 9.6, 4.8 Hz, 0.75H), 4.30 (dd, J = 9.6, 4.8 Hz, 0.25H), 3.82 (s, 2.25H), 3.69 (s, 0.75H), 2.33 (s, 0.75H), 2.32 (s, 2.25H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.9, 197.2, 157.3, 157.1, 156.6, 155.9, 144.64, 144.56, 134.5, 133.2, 132.92, 132.86, 129.7, 129.4 (2C), 129.32 (2C), 129.28 (2C), 129.26 (2C), 129.1 (2C), 129.0 (2C), 128.9 (2C), 128.87 (2C), 128.76, 128.4, 127.7, 125.4 (2C), 124.2 (2C), 114.7 (2C), 113.9 (2C), 67.0, 64.2, 60.3, 57.4, 57.3, 55.5, 55.4, 53.4, 21.6 (× 2).

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{24}NO_4^+$, 402.1700; found, 402.1694.

Ethyl 4-{(*S)-2-Oxo-4-[(*R**)-2-oxo-1-phenyl-2-(*p*-tolyl)ethyl]oxazolidin-3-yl}benzoate (3ca)**



The product **3ca** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 18.2 mg, 0.41 mmol, 41% isolated yield, dr = 3:1). Pale yellow solid. The stereochemistry of **3ca** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 138–140 °C.

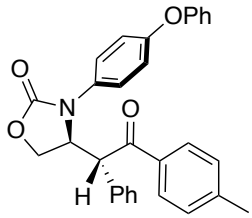
IR (neat) 669, 878, 909, 1046, 1215, 1392, 1706 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16–8.12 (m, 1.50H), 7.74–7.68 (m, 2.50H), 7.62 (d, J = 8.0 Hz, 1.50H), 7.32–7.28 (m, 2.25H), 7.19 (m, 0.50H), 7.15–7.08 (m, 2.50H), 7.01 (m, 0.75H), 6.96–6.92 (m, 1.50H), 5.32 (td, J = 8.8, 3.6 Hz, 0.25H), 5.26 (m, 0.75H), 5.06 (d, J = 2.8 Hz, 0.75H), 4.93 (d, J = 8.8 Hz, 0.25H), 4.72 (t, J = 8.8 Hz, 0.75H), 4.65 (d, J = 8.8 Hz, 0.25H), 4.52 (dd, J = 9.6, 3.6 Hz, 0.75H), 4.40 (q, J = 7.2 Hz, 1.50H), 4.31 (m, 0.75H), 2.32 (s, 3H), 1.42 (t, J = 7.2 Hz, 2.25H), 1.36 (t, J = 7.2 Hz, 0.75H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.1, 197.1, 165.9 (× 2), 155.5, 154.9, 144.9, 144.1, 141.2, 140.8, 134.2, 132.9, 132.53, 132.46, 131.1 (2C), 129.8 (2C), 129.4 (2C × 2), 129.2, 129.14 (2C), 129.08 (2C), 129.0 (2C), 128.9 (2C), 128.6 (2C), 128.1 (2C), 126.6, 126.0, 121.3, 119.9 (2C × 2), 67.3, 64.1, 61.1, 60.9, 59.0, 57.5, 56.1, 52.2, 21.7 (× 2), 14.4, 14.3.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{26}NO_5^+$, 444.1805; found, 444.1795.

(*S)-4-[(*R**)-2-Oxo-1-phenyl-2-(*p*-tolyl)ethyl]-3-(4-phenoxyphenyl)oxazolidin-2-one (3da)**



The product **3da** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 38.9 mg, 0.84 mmol, 84% isolated yield, dr = 2:1). Yellow solid. The stereochemistry for both diastereomers were assigned by X-ray diffraction analysis. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 168–170 °C.

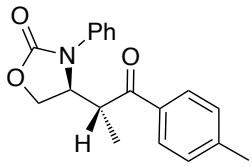
IR (neat) 668, 756, 880, 1087, 1328, 1379, 1701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 0.60H), 7.63 (d, J = 8.0 Hz, 1.40H), 7.44 (d, J = 8.8 Hz, 1.40H), 7.37–7.25 (m, 4.10H), 7.16–7.00 (m, 9.30H), 6.86 (d, J = 8.0 Hz, 0.60H), 6.68 (d, J = 8.8 Hz, 0.60H), 5.23 (m, 1H), 4.98 (d, J = 4.4 Hz, 0.70H), 4.92 (d, J = 8.8 Hz, 0.30H), 4.65 (m, 1H), 4.37 (dd, J = 9.6, 4.0 Hz, 0.70H), 4.26 (dd, J = 9.6, 4.0 Hz, 0.30H), 2.32 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.8, 197.2, 157.4, 156.8, 156.3, 155.8, 154.8, 154.0, 144.7, 144.6, 134.5, 133.0, 132.9, 132.8, 132.3, 131.5, 129.8 (2C), 129.6 (2C), 129.4 (2C × 2), 129.3 (2C × 2), 129.1 (2C), 129.0 (2C), 128.94 (2C), 128.90 (2C), 128.4, 127.7, 125.2 (2C), 124.2 (2C), 123.5, 123.1, 119.5 (2C), 119.2 (2C), 118.9 (2C), 118.3 (2C), 67.3, 64.3, 59.9, 57.9, 57.2, 53.5, 21.6 (× 2).

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{30}H_{26}NO_4^+$, 464.1856; found, 464.1855.

(*S)-4-[(*R**)-1-Oxo-1-(*p*-tolyl)propan-2-yl]-3-phenyloxazolidin-2-one (3ea)**



The product **3ea** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 10.5 mg, 0.34 mmol, 34% isolated yield, dr = 2:1). Colorless oil. The stereochemistry of **3ea** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

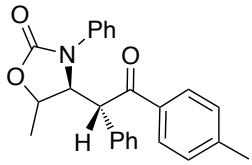
IR (neat) 651, 668, 732, 908, 1214, 1752 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 1.34H), 7.60 (d, J = 8.0 Hz, 0.67H), 7.49–7.35 (m, 4H), 7.24–7.17 (m, 3H), 4.91 (m, 0.67H), 4.83 (m, 0.33H), 4.69 (t, J = 9.2 Hz, 0.67H), 4.53 (m, 1H), 4.40 (dd, J = 9.2, 4.0 Hz, 0.33H), 3.88 (m, 0.33H), 3.86 (qd, J = 7.2, 3.2 Hz, 0.67H), 2.41–2.39 (m, 3H), 1.25 (d, J = 7.2 Hz, 2.0H), 1.12 (d, J = 7.2 Hz, 1.0H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.2, 201.1, 156.0, 155.7, 144.8, 144.6, 137.4, 136.2, 133.4, 132.7, 129.6 (2C), 129.5 (2C), 129.4 (2C), 129.2 (2C), 128.5 (2C), 128.4 (2C), 125.7, 125.5, 122.5 (2C), 122.4 (2C), 65.6, 63.8, 58.8, 56.4, 42.9, 40.6, 21.7, 21.6, 15.2, 10.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{20}NO_3^+$, 310.1438; found, 310.1441.

(4*S)-5-Methyl-4-[(*R**)-2-oxo-1-phenyl-2-(*p*-tolyl)ethyl]-3-phenyloxazolidin-2-one (3fa)**



The product **3fa** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 18.9 mg, 0.49 mmol, 49% isolated yield, dr = 3:1:1). Yellow solid. The stereochemistry of of **3fa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 155–157 °C.

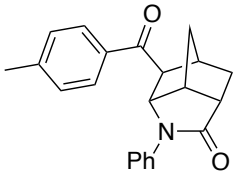
IR (neat) 668, 747, 879, 1047, 1215, 1395, 1457, 1712 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 0.40H), 7.66 (d, J = 8.4 Hz, 0.40H), 7.54–7.42 (m, 2.40H), 7.39–7.29 (m, 1.40H), 7.28–7.20 (m, 1.80H), 7.13 (t, J = 7.6 Hz, 1H), 7.07–6.91 (m, 4.80H), 6.89 (d, J = 4.4 Hz, 0.80H), 6.81 (m, 1H), 5.43 (dd, J = 10.0, 6.4 Hz, 0.20H), 4.97–4.85 (m, 1.20H), 4.73 (m, 0.80H), 4.60 (qd, J = 6.4, 2.4 Hz, 0.60H), 4.49 (qd, J = 6.4, 2.4 Hz, 0.20H), 2.27–2.24 (m, 3H), 1.52 (d, J = 6.4 Hz, 1.80H), 1.40 (d, J = 6.4 Hz, 0.60H), 1.25 (d, J = 6.4 Hz, 0.60H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.3, 197.3, 196.8, 155.9, 155.4, 154.7, 144.7, 144.61, 144.57, 137.6, 137.2, 136.9, 134.1, 133.33, 133.26, 133.2, 132.8, 132.7, 129.52 (2C), 129.48 (2C), 129.4 (2C), 129.3 (2C), 128.94 (2C), 128.92 (2C), 128.89 (2C), 128.83 (2C), 128.80 (2C), 128.6 (2C), 128.4 (2C), 128.1 (2C), 127.8 (2C), 127.7 (2C), 126.9 (2C), 125.0, 124.8, 124.6, 123.5 (2C), 122.9 (2C), 122.1, 121.4 (2C), 121.3, 121.2, 75.2, 75.0, 72.1, 65.7, 63.2, 62.1, 56.9, 53.14, 53.06, 21.6, 21.1, 21.0 (× 2), 18.6, 15.3.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{24}NO_3^+$, 386.1751; found, 386.1743.

6-(4-Methylbenzoyl)-1-phenylhexahydro-3,5-methanocyclopenta[*b*]pyrrol-2(1*H*)-one (3ga)



The product **3ga** was purified by flash chromatography on silica gel (100:0–83:17,

hexane/AcOEt) (**Table 3-2**; 11.6 mg, 0.35 mmol, 35% isolated yield, dr > 20:1). Pale orange solid. The stereochemistry of **3ga** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 216–218 °C.

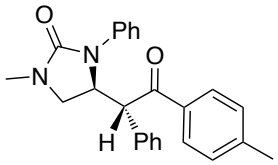
IR (neat) 666, 879, 1047, 1066, 1216, 1394, 1702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.30–7.26 (m, 4H), 7.06 (t, J = 7.6 Hz, 1H), 4.92 (d, J = 5.2 Hz, 1H), 3.32 (s, 1H), 3.17 (t, J = 4.4 Hz, 1H), 2.73–2.69 (m, 2H), 2.42 (s, 3H), 2.10 (m, 1H), 1.87 (d, J = 13.2 Hz, 1H), 1.76 (dd, J = 10.8, 1.2 Hz, 1H), 1.47 (dd, J = 10.8, 1.2 Hz, 1H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.8, 178.1, 144.5, 138.9, 132.7, 129.5 (2C), 129.1 (2C), 128.8 (2C), 123.8, 118.6 (2C), 61.4, 55.7, 44.0, 43.6, 43.1, 35.3, 34.0, 21.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{22}H_{22}NO_2^+$, 332.1645; found, 332.1646.

(*S)-1-Methyl-4-[(*R**)-2-oxo-1-phenyl-2-(*p*-tolyl)ethyl]-3-phenylimidazolidin-2-one (3ha)**



The product **3ha** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 23.8 mg, 0.62 mmol, 62% isolated yield, dr = 5:1). White solid. The stereochemistry of **3ha** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 154–156 °C.

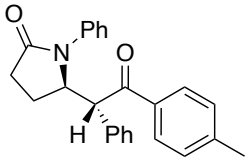
IR (neat) 666, 754, 879, 1087, 1217, 1380, 1449, 1700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4 Hz, 0.34H), 7.63 (d, J = 8.4 Hz, 1.66H), 7.56 (d, J = 8.4 Hz, 1.66H), 7.39–7.35 (m, 1.66H), 7.29–7.22 (m, 3H), 7.16–6.96 (m, 5.51H), 6.83 (t, J = 7.6 Hz, 0.17H), 5.08 (m, 1H), 5.02 (d, J = 3.2 Hz, 0.83H), 4.96 (d, J = 8.4 Hz, 0.17H), 3.74 (t, J = 9.6 Hz, 0.83H), 3.68 (t, J = 9.6 Hz, 0.17H), 3.37 (m, 1H), 2.86 (s, 0.51H), 2.45 (s, 2.49H), 2.32 (s, 2.49H), 2.31 (s, 0.51H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.7, 198.0, 158.6, 157.6, 144.3, 143.8, 139.0, 138.8, 135.1, 133.9, 133.8, 133.1, 129.3 (2C), 129.23 (2C), 129.19 (2C), 129.04 (2C), 128.98 (2C × 2), 128.8 (2C), 128.7 (2C × 2), 128.1 (2C), 127.8, 127.5, 123.4, 123.3, 122.6 (2C), 120.7 (2C), 57.0, 56.6, 53.6, 52.9, 50.3, 46.7, 31.6, 31.1, 30.1, 21.6.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{25}N_2O_2^+$, 385.1911; found, 385.1901.

(*R)-5-[(*R**)-5-(2-Oxo-1-phenyl-2-(*p*-tolyl)ethyl]-1-phenylpyrrolidin-2-one (3ia)**



The product **3ia** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 11.5 mg, 0.31 mmol, 31% isolated yield, dr = 1.3:1). Pale yellow solid. The stereochemistry of **3ia** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 167–169 °C.

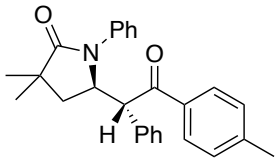
IR (neat) 665, 756, 880, 1046, 1087, 1328, 1379, 1699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 0.86H), 7.59–7.55 (m, 2.28H), 7.42–7.38 (m, 1H), 7.33–7.27 (m, 2H), 7.20 (t, J = 7.6 Hz, 0.57H), 7.16–7.05 (m, 6.86H), 7.00 (m, 0.43H), 5.15 (dt, J = 8.0, 3.2 Hz, 0.57H), 4.99 (td, J = 8.0, 3.2 Hz, 0.43H), 4.85 (d, J = 7.6 Hz, 0.43H), 4.85 (d, J = 7.6 Hz, 0.57H), 2.89 (m, 0.43H), 2.53 (m, 0.43H), 2.45–2.20 (m, 4.43H), 2.19–2.11 (m, 1.14H), 1.44 (m, 0.57H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.3, 197.7, 174.8, 174.7, 144.2, 144.1, 137.7, 137.4, 135.2, 134.6, 134.0, 133.2, 129.33 (2C), 129.26 (2C), 129.2 (2C), 129.13 (2C), 129.11 (2C), 129.0 (2C), 128.9 (2C), 128.8 (2C), 128.62 (2C), 128.57 (2C), 127.9, 127.5, 125.73, 125.68, 124.9 (2C), 123.7 (2C), 70.6, 63.5, 60.3, 55.7, 54.2, 31.0, 30.9, 22.8, 21.6, 21.4.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{24}NO_2^+$, 370.1802; found, 370.1792.

(*R)-3,3-Dimethyl-5-[(*R**)-2-oxo-1-phenyl-2-(*p*-tolyl)ethyl]-1-phenylpyrrolidin-2-one (3ja)**



The product **3ja** was purified by flash chromatography on silica gel (100:0–85:15, hexane/AcOEt) (**Table 3-2**; 9.94 mg, 0.25 mmol, 25% isolated yield, dr > 20:1). Pale yellow solid. The stereochemistry of **3ja** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 171–173 °C.

IR (neat) 666, 734, 879, 1046, 1087, 1217, 1380, 1702 cm^{-1}.

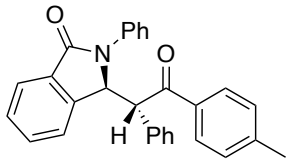
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.4 Hz, 2H), 7.33–7.20 (m, 7H), 7.15–7.07 (m, 3H), 7.04 (d, J = 8.0 Hz, 2H), 5.12 (m, 1H), 4.82 (d, J = 5.2 Hz, 1H), 2.29 (s 3H), 2.09 (dd, J = 13.2, 7.6 Hz, 1H), 1.72 (dd, J = 13.2, 7.6 Hz, 1H), 1.19 (s, 3H), 0.87 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.0, 179.6, 143.8, 137.4, 134.8, 133.5, 129.5 (2C), 129.00

(2C), 128.97 (2C), 128.9 (2C), 128.5 (2C), 127.7, 126.4, 125.8 (2C), 57.3, 55.7, 40.3, 37.5, 25.8, 25.3, 21.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{28}NO_2^+$, 398.2115; found, 398.2102.

(*S)-3-[(*R**)-2-Oxo-1-phenyl-2-(*p*-tolyl)ethyl]-2-phenylisoindolin-1-one (3ka)**



The product **3ka** was purified by flash chromatography on silica gel (100:0–88:12, hexane/AcOEt) (**Table 3-2**; 30.9 mg, 0.74 mmol, 74% isolated yield, dr = 13:1). White solid. The stereochemistry of **3ka** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 184–186 °C.

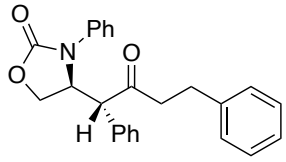
IR (neat) 666, 734, 879, 1046, 1087, 1217, 1380, 1712 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (m, 0.14H), 7.85 (d, J = 8.4 Hz, 0.07H), 7.75 (d, J = 7.6 Hz, 0.93H), 7.69 (d, J = 8.0 Hz, 1.86H), 7.65–7.61 (m, 2.79H), 7.56 (d, J = 8.0 Hz, 0.21H), 7.51–7.39 (m, 3H), 7.33 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.19 (m, 0.35H), 7.11 (m, 0.14H), 7.06 (d, J = 8.4 Hz, 1.86H), 7.01–6.96 (m, 2.79H), 6.75–6.72 (m, 1.86H), 6.18 (d, J = 3.2 Hz, 0.93H), 6.00 (d, J = 7.2 Hz, 0.07H), 5.04 (d, J = 3.2 Hz, 0.93H), 4.99 (d, J = 7.2 Hz, 0.07H), 2.29 (s 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 198.4, 196.7, 167.3 (× 2), 144.4, 144.2, 142.3, 142.0, 137.3, 136.9, 134.3, 133.9, 133.6, 133.1, 132.7, 132.1, 131.7, 131.4, 129.5 (2C), 129.4 (2C), 129.3 (2C), 129.2 (2C), 129.14 (2C), 129.10 (2C), 128.7 (2C), 128.58 (2C), 128.56 (2C), 128.5, 128.3, 128.2 (2C), 127.9, 127.4, 125.7, 125.6, 125.5, 125.1, 124.2 (2C), 123.62 (2C), 123.56, 123.3, 63.9, 61.8, 56.6, 55.7, 21.6, 13.6.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{29}H_{24}NO_2^+$, 418.1802; found, 418.1792.

(*S)-4-[(*R**)-2-Oxo-1,4-diphenylbutyl]-3-phenyloxazolidin-2-one (3ab)**



The product **3ab** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 3-2**; 8.09 mg, 0.21 mmol, 21% isolated yield, including small amount of inpurity, dr = 5:1). White solid. The stereochemistry of **3ab** was assigned by consideration of the

stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 99–101 °C.

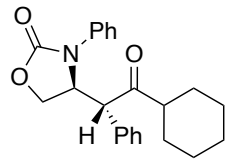
IR (neat) 647, 756, 907, 1046, 1087, 1216, 1380, 1708 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.38 (m, 3H), 7.35–7.14 (m, 6.49H), 7.09–6.94 (m, 3.51H), 6.90–6.85 (m, 2H), 5.10 (m, 0.83H), 4.98 (td, J = 8.4, 4.8 Hz, 0.17H), 4.54 (m, 1H), 4.22 (dd, J = 9.6, 4.8 Hz, 0.83H), 4.17 (dd, J = 9.6, 4.8 Hz, 0.17H), 4.08 (d, J = 4.8 Hz, 0.83H), 4.00 (d, J = 4.8 Hz, 0.17H), 2.85–2.45 (m, 4H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 208.5 (× 2), 155.4 (× 2), 141.4, 140.2, 136.3 (× 2), 131.7 (× 2), 129.4 (2C), 129.3 (2C), 129.2 (2C), 129.0 (2C), 128.9 (2C), 128.7, 128.6 (2C), 128.50 (2C), 128.48 (2C), 128.24 (2C), 128.21 (2C), 128.1, 126.3 (× 2), 125.6, 125.4, 123.7 (2C), 122.4 (2C), 64.0 (× 2), 58.4 (× 2), 56.1 (× 2), 43.6, 43.4, 29.7, 29.6.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{24}NO_3^+$, 386.1751; found, 386.1754.

(*S)-4-[(*R**)-2-Cyclohexyl-2-oxo-1-phenylethyl]-3-phenyloxazolidin-2-one (3ac)**



The product **3ac** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 3-2**; 16.0 mg, 0.44 mmol, 44% isolated yield, dr = 2:1). Orange oil. The stereochemistry of **3ac** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

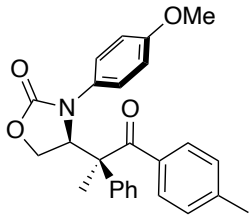
IR (neat) 666, 736, 759, 881, 1089, 1217, 1379, 1454, 1701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.43 (m, 2.66H), 7.36–7.31 (m, 2H), 7.24 (m, 0.66H), 7.10–7.05 (m, 2.34H), 7.00–6.93 (m, 2.34H), 5.09 (m, 0.66H), 5.00 (td, J = 8.8, 4.4 Hz, 0.34H), 4.56 (t, J = 8.8 Hz, 0.34H), 4.49 (t, J = 8.8 Hz, 0.66H), 4.35 (d, J = 4.4 Hz, 0.66H), 4.27–4.20 (m, 1.34H), 2.20 (m, 1H), 1.70–1.50 (m, 5.34H), 1.36–1.22 (m, 1.66H), 1.13–0.99 (m, 4H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 212.3, 211.6, 156.1, 155.5, 136.7, 136.4, 133.3, 131.9, 129.4 (2C), 129.3 (2C), 129.2 (2C), 129.0 (2C), 128.9 (2C), 128.6 (2C), 128.5, 128.0, 125.4, 125.2, 123.4 (2C), 122.2 (2C), 66.7, 64.0, 59.9, 58.5, 56.2, 56.0, 50.2, 49.9, 29.9, 29.2, 27.9, 27.8, 25.7, 25.6, 25.5 (× 2), 25.0, 24.9.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{26}NO_3^+$, 364.1907; found, 364.1915.

(*S)-3-(4-Methoxyphenyl)-4-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]oxazolidin-2-one (3la)**



The product **3la** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 34.9 mg, 0.84 mmol, 84% isolated yield, dr > 20:1). Yellow solid. The stereochemistry of **3la** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 136–138 °C.

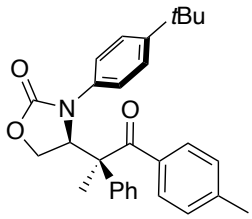
IR (neat) 688, 879, 1046, 1086, 1247, 1472, 1750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.0 Hz, 2H), 7.06–7.00 (m, 7H), 6.80 (d, J = 8.8 Hz, 2H), 6.46 (d, J = 8.8 Hz, 2H), 5.30 (dd, J = 8.8, 4.0 Hz, 1H), 4.87 (t, J = 9.6 Hz, 1H), 4.28 (dd, J = 10.4, 4.0 Hz, 1H), 3.68 (s, 3H), 2.27 (s, 3H), 1.83 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.0, 157.2, 156.6, 143.2, 138.6, 133.1, 130.1, 129.5 (2C), 128.9 (2C), 128.7 (2C), 127.4, 126.8 (2C), 125.4 (2C), 113.6 (2C), 66.8, 64.3, 58.8, 55.4, 21.4, 14.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{26}NO_4^+$, 416.1856; found, 416.1839.

(*S)-3-[4-(*tert*-Butyl)phenyl]-4-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]oxazolidin-2-one (3ma)**



The product **3ma** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 26.1 mg, 0.59 mmol, 59% isolated yield, dr > 20:1). Yellow solid. The stereochemistry of **3ma** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 178–180 °C.

IR (neat) 667, 899, 909, 1047, 1087, 1216, 1380, 1453, 1723 cm^{-1}.

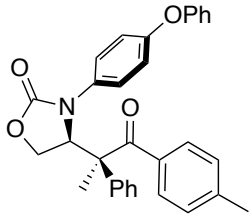
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 7.6 Hz, 2H), 7.00 (d, J = 7.6 Hz, 4H), 6.93–6.91 (m, 5H), 6.80 (d, J = 8.0 Hz, 2H), 5.35 (dd, J = 9.2, 3.6 Hz, 1H), 4.88 (t, J = 9.2 Hz, 1H), 4.28 (dd, J = 10.0, 3.6 Hz, 1H), 2.27 (s, 3H), 1.83 (s, 3H), 1.20 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.1, 157.0, 147.3, 143.2, 138.6, 134.3, 133.1, 129.6 (2C),

128.9 (2C), 128.7 (2C), 127.3, 126.8 (2C), 125.1 (2C), 123.5 (2C), 66.8, 64.0, 58.9, 34.2, 31.1 (3C), 21.4, 14.6.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{29}H_{32}NO_3^+$, 442.2377; found, 442.2396.

(*S)-4-[(*S**)-1-Oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]-3-(4-phenoxyphenyl)oxazolidin-2-one (3na)**



The product **3na** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 3-2**; 38.2 mg, 0.80 mmol, 80% isolated yield, dr > 20:1). Yellow solid. The stereochemistry of **3na** was assigned by X-ray diffraction analysis. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 185–188 °C.

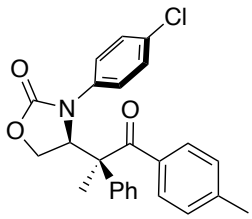
IR (neat) 667, 879, 909, 1046, 1086, 1215, 1381, 1732 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 2H), 7.26 (d, J = 7.6 Hz, 2H), 7.12–7.04 (m, 6H), 7.02 (d, J = 8.0 Hz, 2H), 6.90–6.87 (m, 2H), 6.61–6.57 (m, 2H), 5.35 (dd, J = 9.2, 3.6 Hz, 1H), 4.87 (t, J = 9.2 Hz, 1H), 4.34 (dd, J = 10.4, 3.6 Hz, 1H), 2.28 (s, 3H), 1.85 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.2, 157.3, 157.1, 153.7, 143.3, 138.7, 133.0, 132.6, 129.58 (2C), 129.56 (2C), 128.9 (2C × 2), 127.5, 127.0 (2C), 125.4 (2C), 123.1, 118.9 (2C), 118.4 (2C), 66.9, 64.1, 58.8, 21.4, 14.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{31}H_{28}NO_4^+$, 478.2013; found, 478.2032.

(*S)-3-(4-Chlorophenyl)-4-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]oxazolidin-2-one (3oa)**



The product **3oa** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 3-2**; 21.4 mg, 0.51 mmol, 51% isolated yield, dr > 20:1). White solid. The stereochemistry of **3oa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 152–154 °C.

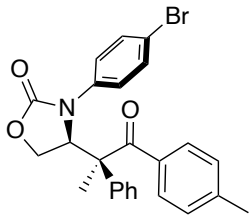
IR (neat) 737, 881, 1050, 1089, 1380, 1454, 1703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 7.6 Hz, 2H), 7.07–7.01 (m, 7H), 6.89–6.83 (m, 4H), 5.33 (dd, J = 8.8, 3.6 Hz, 1H), 4.86 (t, J = 8.8 Hz, 1H), 4.31 (dd, J = 10.4, 3.6 Hz, 1H), 2.28 (s, 3H), 1.82 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.9, 156.7, 143.5, 138.6, 135.9, 132.9, 130.0, 129.6 (2C), 129.0 (2C), 128.9 (2C), 128.1 (2C), 127.7, 126.9 (2C), 124.9 (2C), 66.9, 63.9, 58.9, 21.5, 14.7.

HRMS–ESI (*m/z*): $[M+NH_4]^+$ calcd for $C_{25}H_{26}ClN_2O_3^+$, 437.1626; found, 437.1640.

(*S)-3-(4-Bromophenyl)-4-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]oxazolidin-2-one (3pa)**



The product **3pa** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 3-2**; 22.3 mg, 0.48 mmol, 48% isolated yield, dr > 20:1). White solid. The stereochemistry of **3pa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 171–173 °C.

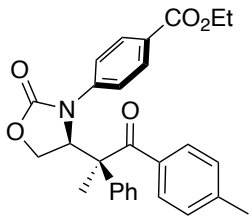
IR (neat) 667, 879, 909, 1046, 1086, 1215, 1381, 1711 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.0 Hz, 2H), 7.10–6.99 (m, 9H), 6.81–6.77 (m, 2H), 5.32 (dd, J = 8.8, 4.0 Hz, 1H), 4.86 (t, J = 8.8 Hz, 1H), 4.30 (dd, J = 10.4, 4.0 Hz, 1H), 2.28 (s, 3H), 1.82 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.9, 156.6, 143.5, 138.6, 136.4, 132.9, 131.1 (2C), 129.6 (2C), 129.0 (2C), 128.9 (2C), 127.6, 126.9 (2C), 125.2 (2C), 117.9, 66.9, 63.8, 58.9, 21.5, 14.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{23}BrNO_3^+$, 464.0856; found, 464.0875.

Ethyl 4-{(*S)-2-Oxo-4-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]oxazolidin-3-yl}benzoate (3qa)**



The product **3qa** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 13.7 mg, 0.30 mmol, 30% isolated yield, dr > 20:1). Pale yellow solid. The stereochemistry of **3qa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 177–179 °C.

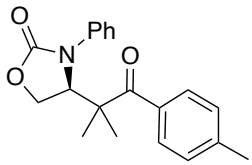
IR (neat) 669, 880, 1046, 1087, 1379, 1457, 1705 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.06–6.93 (m, 9H), 5.42 (dd, J = 8.8, 3.6 Hz, 1H), 4.85 (t, J = 8.8 Hz, 1H), 4.43–4.28 (m, 3H), 2.29 (s, 3H), 1.84 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.0, 165.9, 156.4, 143.5, 141.6, 138.5, 132.8, 129.7 (2C), 129.5 (2C), 128.97 (2C), 128.95 (2C), 127.9, 126.9 (2C), 126.0, 122.5 (2C), 66.9, 63.4, 60.8, 58.9, 21.5, 14.9, 14.3.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{28}H_{28}NO_5^+$, 458.1962; found, 458.1959.

(*S)-4-[2-Methyl-1-oxo-1-(*p*-tolyl)propan-2-yl]-3-phenyloxazolidin-2-one (3ra)**



The product **3ra** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 7.11 mg, 0.22 mmol, 22% isolated yield). Pale yellow oil.

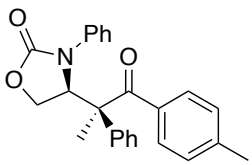
IR (neat) 668, 732, 899, 908, 1047, 1215, 1394, 1653, 1701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.35 (m, 6H), 7.23 (m, 1H), 7.17 (d, J = 8.0 Hz, 2H), 5.20 (dd, J = 9.2, 3.6 Hz, 1H), 4.63 (t, J = 9.2 Hz, 1H), 4.15 (dd, J = 9.6, 3.6 Hz, 1H), 2.38 (s, 3H), 1.45 (s, 3H), 1.17 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 206.5, 142.6, 138.7, 137.9, 134.6, 129.2 (2C), 129.0 (2C), 128.0 (2C), 126.5, 125.0 (2C), 65.8, 61.9, 52.5, 24.0, 21.5, 19.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{20}H_{22}NO_3^+$, 324.1594; found, 324.1607.

(*S)-4-[(*S**)-1-Oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]-3-phenyloxazolidin-2-one (3sa)**



The product **3sa** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 24.3 mg, 0.63 mmol, 63% isolated yield, dr > 20:1) White solid. The

stereochemistry of **3sa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 159–161 °C.

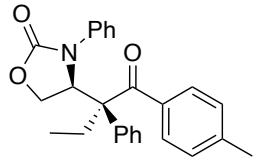
IR (neat) 693, 755, 1214, 1256, 1401, 1500, 1605, 1663, 1735 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.25 (m, 2H), 7.06–7.04 (m, 2H), 7.01 (d, J = 8.0 Hz, 2H), 6.97–6.90 (m, 7H), 6.84 (m, 1H), 5.38 (dd, J = 9.2, 3.6 Hz, 1H), 4.87 (t, J = 9.2 Hz, 1H), 4.30 (dd, J = 10.4, 3.6 Hz, 1H), 2.28 (s, 3H), 1.84 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.1, 157.0, 143.3, 138.5, 137.2, 133.1, 129.6 (2C), 128.9 (2C), 128.8 (2C), 128.2 (2C), 127.6, 126.8 (2C), 124.8, 123.8 (2C), 66.9, 63.8, 58.9, 21.5, 14.8.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{24}NO_3^+$, 386.1751; found, 386.1733.

(*S)-4-[(*S**)-1-Oxo-2-phenyl-1-(*p*-tolyl)butan-2-yl]-3-phenyloxazolidin-2-one (3ta)**



The product **3ta** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 16.4 mg, 0.41 mmol, 41% isolated yield, dr > 20:1). White solid. The stereochemistry of **3ta** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 189–192 °C.

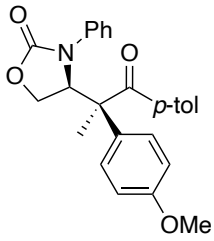
IR (neat) 668, 732, 879, 1087, 1380, 1456, 1757 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.0 Hz, 2H), 7.06–6.88 (m, 12H), 5.33 (dd, J = 9.6, 3.6 Hz, 1H), 4.84 (t, J = 9.6 Hz, 1H), 4.63 (dd, J = 10.4, 3.6 Hz, 1H), 2.66–2.43 (m, 2H), 2.28 (s, 3H), 1.02 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.1, 140.1, 137.3, 134.3, 131.1, 129.3 (2C), 128.9 (2C), 128.6 (2C), 128.2 (2C), 127.4 (2C), 126.0, 124.9, 124.5, 124.0 (2C), 66.7, 64.1, 62.3, 24.5, 21.5, 10.3.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{26}NO_3^+$, 400.1907; found, 400.1907.

(*S)-4-[(*S**)-2-(4-Methoxyphenyl)-1-oxo-1-(*p*-tolyl)propan-2-yl]-3-phenyloxazolidin-2-one (3ua)**



The product **3ua** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 3-2**; 9.56 mg, 0.23 mmol, 23% isolated yield, dr > 20:1). White solid. The stereochemistry of **3ua** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 154–156 °C.

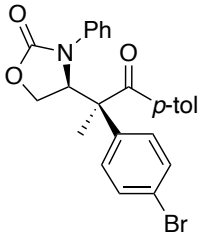
IR (neat) 669, 760, 1036, 1125, 1258, 1507, 1751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.0 Hz, 2H), 7.05–7.01 (m, 2H), 6.99–6.91 (m, 6H), 6.86 (t, J = 7.2 Hz, 1H), 6.47 (d, J = 7.2 Hz, 2H), 5.32 (dd, J = 8.8, 3.6 Hz, 1H), 4.85 (t, J = 9.6 Hz, 1H), 4.28 (dd, J = 9.6, 3.6 Hz, 1H), 3.67 (s, 3H), 2.29 (s, 3H), 1.81 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.3, 158.8, 157.0, 143.2, 137.4, 130.5, 129.6 (2C), 128.9 (2C), 128.1 (2C), 128.0 (2C), 127.5, 124.6, 123.9 (2C), 114.3 (2C), 66.8, 63.9, 58.2, 55.2, 21.5, 14.9.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{26}NO_4^+$, 416.1856; found, 416.1850.

(*S)-4-[(*S**)-2-(4-Bromophenyl)-1-oxo-1-(*p*-tolyl)propan-2-yl]-3-phenyloxazolidin-2-one (3va)**



The product **3va** was purified by flash chromatography on silica gel (100:0–80:20, hexane/AcOEt) (**Table 3-2**; 37.1 mg, 0.80 mmol, 80% isolated yield, dr = 19:1). Pale yellow solid. The stereochemistry of **3va** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material. ^{1}H and ^{13}C NMR data described the major diastereomer.

M.p. 177–179 °C.

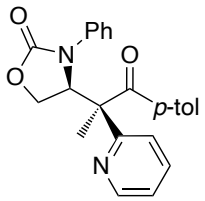
IR (neat) 692, 760, 1087, 1124, 1213, 1400, 1500, 1662, 1741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.0 Hz, 2H), 7.04 (t, J = 8.4 Hz, 4H), 7.01–6.94 (m, 3H), 6.90–6.88 (m, 4H), 5.31 (dd, J = 9.2, 3.6 Hz, 1H), 4.85 (t, J = 9.2 Hz, 1H), 4.28 (dd, J = 10.4, 3.6 Hz, 1H), 2.29 (s, 3H), 1.82 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.5, 156.7, 143.6, 137.9, 137.0, 132.6, 131.8 (2C), 129.6 (2C), 129.0 (2C), 128.4 (2C), 128.3 (2C), 124.7, 123.8 (2C), 121.9, 66.7, 63.8, 58.5, 21.4, 14.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{23}BrNO_3^+$, 464.0856; found, 464.0868.

(*S)-4-[(*R**)-1-Oxo-2-(pyridin-2-yl)-1-(*p*-tolyl)propan-2-yl]-3-phenyloxazolidin-2-one (3wa)**



The product **3wa** was purified by flash chromatography on silica gel (91:9–67:33, hexane/AcOEt) (**Table 3-2**; 21.6 mg, 0.56 mmol, 56% isolated yield, dr > 20:1). Pale yellow solid. The stereochemistry of **3wa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 156–159 °C.

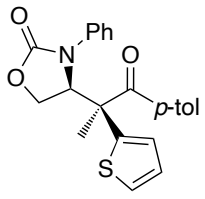
IR (neat) 692, 751, 1123, 1209, 1402, 1501, 1668, 1748 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (m, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.17 (td, J = 7.8, 2.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 7.01–6.96 (m, 2H), 6.95–6.92 (m, 4H), 6.86–6.82 (m, 2H), 5.60 (dd, J = 9.0, 3.6 Hz, 1H), 4.93 (m, 1H), 4.43 (dd, J = 10.4, 3.6 Hz, 1H), 2.26 (s, 3H), 1.91 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.9, 158.8, 156.9, 149.2, 143.1, 137.3, 136.3, 132.4, 129.4 (2C), 128.9 (2C), 128.2 (2C), 124.6, 123.5 (2C), 122.2, 122.1, 66.7, 62.7, 61.1, 21.3, 14.2.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{24}H_{22}N_2NaO_3^+$, 409.1523; found, 409.1535.

(*S)-4-[(*S**)-1-Oxo-2-(thiophen-2-yl)-1-(*p*-tolyl)propan-2-yl]-3-phenyloxazolidin-2-one(3xa)**



The product **3xa** was purified by flash chromatography on silica gel (91:9–75:25, hexane/AcOEt) (**Table 3-2**; 18.8 mg, 0.48 mmol, 48% isolated yield, dr = 15:1). Orange oil. The stereochemistry of **3xa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

IR (neat) 747, 1135, 1214, 1297, 1405, 1446, 1501, 1604, 1627, 1748 cm^{-1}.

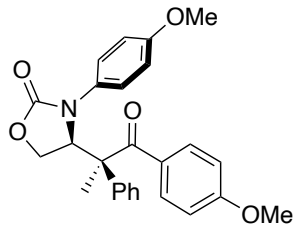
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.73 (m, 1.88H), 7.60 (d, J = 8.0 Hz, 0.12H), 7.56–7.54 (m, 1.88H), 7.47–7.40 (m, 3H), 7.29 (d, J = 8.0 Hz, 2H), 7.21 (m, 1H), 7.15 (m, 0.12H), 7.03 (d,

J = 1.6 Hz, 0.06H), 6.72 (dd, *J* = 3.6, 0.4 Hz, 0.94H), 5.06 (m, 0.06H), 4.73 (m, 0.94H), 4.58 (t, *J* = 9.2 Hz, 0.06H), 4.48 (t, *J* = 9.2 Hz, 0.94H), 4.42 (dd, *J* = 10.2, 4.0 Hz, 0.06H), 4.31 (dd, *J* = 9.2, 4.4 Hz, 0.94H), 3.67 (m, 1H), 2.44 (s, 3H), 1.40 (d, *J* = 7.6 Hz, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 187.4 (× 2), 155.3, 152.9, 151.2 (× 2), 143.6, 143.0, 142.8 (× 2), 136.4, 136.0, 135.1 (× 2), 134.5 (× 2), 129.8 (2C), 129.4 (2C), 129.3 (2C), 129.0 (2C), 128.9 (2C), 128.7 (2C), 126.6, 125.2, 124.9, 122.8, 121.9 (2C), 121.5 (2C), 63.0, 60.6, 59.9, 58.5, 35.4, 23.7, 21.6, 19.5, 17.0, 13.5.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{23}H_{21}NNaO_3S^+$, 414.1134; found, 414.1136.

(*S)-3-(4-Methoxyphenyl)-4-[(*S**)-1-(4-methoxyphenyl)-1-oxo-2-phenylpropan-2-yl]oxazolidin-2-one (3ld)**



The product **3ld** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 26.3 mg, 0.61 mmol, 61% isolated yield, dr > 20:1). Colorless oil. The stereochemistry of **3ld** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

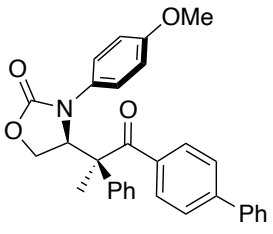
IR (neat) 669, 754, 1047, 1249, 1405, 1541, 1653, 1750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.0 Hz, 2H), 7.05–6.99 (m, 5H), 6.80 (d, *J* = 8.0 Hz, 2H), 6.69 (d, *J* = 8.0 Hz, 2H), 6.46 (d, *J* = 8.4 Hz, 2H), 5.28 (dd, *J* = 9.6, 4.0 Hz, 1H), 4.88 (t, *J* = 9.6 Hz, 1H), 4.30 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 1.85 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 200.7, 162.8, 157.3, 156.6, 139.0, 131.9 (2C), 130.2, 128.7 (2C), 128.1, 127.3, 126.8 (2C), 125.4 (2C), 113.6 (2C), 113.4 (2C), 66.9, 64.4, 58.7, 55.4, 55.3, 14.9.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{26}NO_5^+$, 432.1805; found, 432.1794.

(*S)-4-{(*S**)-1-[(1,1'-Biphenyl)-4-yl]-1-oxo-2-phenylpropan-2-yl}-3-(4-methoxyphenyl)oxazolidin-2-one (3le)**



The product **3le** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 30.6 mg, 0.64 mmol, 64% isolated yield, dr > 20:1). Pale yellow solid. The stereochemistry of **3le** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 203–205 °C.

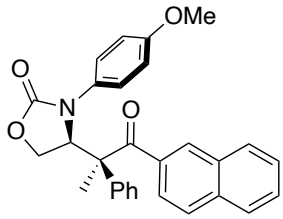
IR (neat) 668, 756, 880, 1087, 1379, 1456, 1741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 2H), 7.45–7.33 (m, 7H), 7.10–7.03 (m, 5H), 6.82 (d, J = 8.4 Hz, 2H), 6.47 (d, J = 8.4 Hz, 2H), 5.33 (dd, J = 9.0, 3.6 Hz, 1H), 4.90 (t, J = 10 Hz, 1H), 4.31 (dd, J = 10.4, 3.6 Hz, 1H), 3.69 (s, 3H), 1.88 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.0, 157.2, 156.6, 145.1, 139.5, 138.5, 134.5, 130.1, 130.0 (2C), 128.9 (2C × 2), 128.2, 127.5, 127.1 (2C), 126.83 (2C), 126.80 (2C), 125.5 (2C), 113.7 (2C), 66.8, 64.3, 59.0, 55.4, 14.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{31}H_{28}NO_4^+$, 478.2013; found, 478.2003.

(*S)-3-(4-Methoxyphenyl)-4-[(*S**)-1-(naphthalen-2-yl)-1-oxo-2-phenylpropan-2-yl]oxazolidin-2-one (3lf)**



The product **3lf** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Figure 3**; 25.3 mg, 0.56 mmol, 56% isolated yield, dr > 20:1). Yellow solid. The stereochemistry of **3lf** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 157–159 °C.

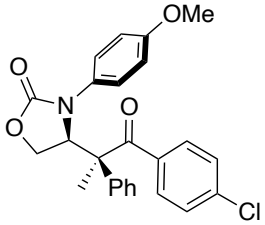
IR (neat) 668, 752, 879, 1045, 1086, 1217, 1457, 1721 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.38 (d, J = 8.8 Hz, 1H), 7.14–7.04 (m, 5H), 6.83 (d, J = 8.8 Hz, 2H), 6.48 (d, J = 8.8 Hz, 2H), 5.37 (dd, J = 9.6, 4.0 Hz, 1H), 4.93 (t, J = 9.6 Hz, 1H), 4.34 (dd, J = 10.4, 4.0 Hz, 1H), 3.70 (s, 3H), 1.89 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.5, 157.3, 156.7, 138.6, 134.8, 133.2, 132.1, 131.1, 130.1, 129.4, 128.9 (2C), 128.5, 127.9, 127.6, 127.5, 126.9 (2C), 126.7, 125.5 (2C), 124.9, 113.7 (2C), 66.8, 64.4, 59.1, 55.4, 14.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{29}H_{26}NO_4^+$, 452.1856; found, 452.1850.

(*S)-4-[(*S**)-1-(4-Chlorophenyl)-1-oxo-2-phenylpropan-2-yl]-3-(4-methoxyphenyl)oxazolidin-2-one (3lg)**



The product **3lg** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 34.4 mg, 0.79 mmol, 79% isolated yield, dr > 20:1). Pale orange solid. The stereochemistry of **3lg** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 158–161 °C.

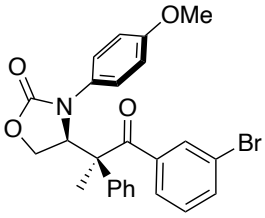
IR (neat) 668, 751, 908, 1046, 1215, 1514, 1669, 1748 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.26 (m, 2H), 7.18 (d, J = 7.2 Hz, 2H), 7.03 (m, 5H), 6.80 (d, J = 8.0 Hz, 2H), 6.46 (d, J = 8.0 Hz, 2H), 5.29 (dd, J = 9.2, 4.0 Hz, 1H), 4.87 (t, J = 9.2 Hz, 1H), 4.26 (dd, J = 10.4, 4.0 Hz, 1H), 3.68 (s, 3H), 1.81 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.2, 157.2, 156.7, 138.8, 138.1, 134.1, 130.8 (2C), 130.0, 129.0 (2C), 128.5 (2C), 127.7, 126.7 (2C), 125.5 (2C), 113.7 (2C), 66.7, 64.2, 58.9, 55.4, 14.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{23}ClNO_4^+$, 436.1310; found, 436.1303.

(*S)-4-[(*S**)-1-(3-Bromophenyl)-1-oxo-2-phenylpropan-2-yl]-3-(4-methoxyphenyl)oxazolidin-2-one (3lh)**



The product **3lh** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 36.0 mg, 0.75 mmol, 75% isolated yield, dr > 20:1). Pale yellow solid. The stereochemistry of **3lh** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 147–149 °C.

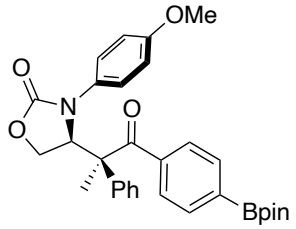
IR (neat) 668, 732, 879, 908, 1046, 1087, 1215, 1753 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.10–7.02 (m, 7H), 6.80 (d, J = 8.4 Hz, 2H), 6.47 (d, J = 8.4 Hz, 2H), 5.30 (dd, J = 9.2, 4.0 Hz, 1H), 4.87 (t, J = 9.2 Hz, 1H), 4.25 (dd, J = 10.0, 4.0 Hz, 1H), 3.69 (s, 3H), 1.81 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.2, 157.1, 156.7, 137.8, 137.7, 135.2, 132.3, 129.9, 129.6, 129.0 (2C), 127.8, 127.6, 126.8 (2C), 125.5 (2C), 122.5, 113.7 (2C), 66.6, 64.1, 59.0, 55.4, 14.4.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{23}BrNO_4^+$, 480.0805; found, 480.0797.

(*S)-3-(4-Methoxyphenyl)-4-{(*S**)-1-oxo-2-phenyl-1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]propan-2-yl}oxazolidin-2-one (3li)**



The product **3li** was purified by flash chromatography on silica gel (100:0–67:33, hexane/AcOEt) (**Table 3-2**; 25.8 mg, 0.49 mmol, 49% isolated yield, dr > 20:1). Yellow solid. The stereochemistry of **3li** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 207–209 °C.

IR (neat) 689, 750, 899, 909, 1046, 1087, 1216, 1381, 1722 cm^{-1}.

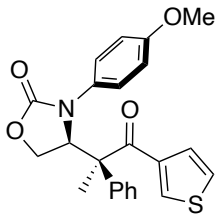
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.4 Hz, 2H), 7.27–7.25 (m, 2H), 7.06–7.00 (m, 5H), 6.82–6.78 (m, 2H), 6.48–6.44 (m, 2H), 5.32 (dd, J = 9.0, 4.0 Hz, 1H), 4.88 (t, J = 9.6 Hz, 1H), 4.27 (dd, J = 9.6, 4.0 Hz, 1H), 3.69 (s, 3H), 1.80 (s, 3H), 1.29 (s, 6H), 1.28 (s, 6H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.9, 157.2, 156.7, 138.2, 138.1, 134.5 (2C), 130.0, 128.8 (2C), 128.2 (2C), 127.5, 126.8 (2C), 125.5 (2C), 113.7 (2C), 84.1, 66.7, 64.2, 59.0, 55.4, 29.7, 24.81 (2C), 24.77 (2C), 14.4. A signal connected directly to boron was not observed.

^{11}B NMR (128.4 MHz, $CDCl_3$) δ 22.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{31}H_{35}BNO_6^+$, 528.2552; found, 528.2545.

(*S)-3-(4-Methoxyphenyl)-4-[(*S**)-1-oxo-2-phenyl-1-(thiophen-3-yl)propan-2-yl]oxazolidin-2-one (3lj)**



The product **3lj** was purified by flash chromatography on silica gel (91:9–70:30, hexane/AcOEt) (**Table 3-2**; 20.8 mg, 0.51 mmol, 51% isolated yield, dr > 20:1). Pale yellow solid. The stereochemistry of **3lj** was assigned by consideration of the stereochemical pathway. The

diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 135–137 °C.

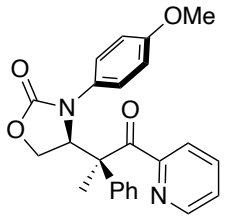
IR (neat) 665, 879, 1046, 1087, 1217, 1327, 1380, 1741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, J = 2.8, 1.2 Hz, 1H), 7.09 (dd, J = 5.2, 2.8 Hz, 1H), 7.04–6.99 (m, 6H), 6.79 (dd, J = 7.0, 2.4 Hz, 2H), 6.46 (dd, J = 7.0, 2.4 Hz, 2H), 5.24 (dd, J = 9.2, 4.4 Hz, 1H), 4.91 (t, J = 9.2 Hz, 1H), 4.38 (dd, J = 10.4, 4.4 Hz, 1H), 3.68 (s, 3H), 1.86 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 196.4, 157.3, 156.7, 138.9, 138.7, 133.4, 130.0, 128.8 (2C), 128.1, 127.6, 127.1 (2C), 125.6 (2C), 125.4, 113.6 (2C), 66.7, 64.0, 58.9, 55.4, 14.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{23}H_{22}NO_4S^+$, 408.1264; found, 408.1265.

(*S)-3-(4-Methoxyphenyl)-4-[(*S**)-1-oxo-2-phenyl-1-(pyridin-2-yl)propan-2-yl]oxazolidin-2-one (3lk)**



The product **3lk** was purified by flash chromatography on silica gel (91:9–70:30, hexane/AcOEt) (**Table 3-2**; 19.7 mg, 0.49 mmol, 49% isolated yield, dr = 19:1). Pale orange solid. The stereochemistry of **3lk** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material. ^{1}H and ^{13}C NMR data described the major diastereomer.

M.p. 130–132 °C.

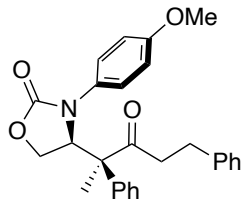
IR (neat) 666, 756, 800, 1088, 1217, 1379, 1454, 1744 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, J = 4.4, 0.8 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.68 (td, J = 9.6, 1.6 Hz, 1H), 7.23 (qd, J = 7.6, 1.2 Hz, 1H), 7.01–6.98 (m, 2H), 6.93–6.86 (m, 3H), 6.82–6.78 (m, 2H), 6.48–6.44 (m, 2H), 5.35 (dd, J = 9.2, 4.0 Hz, 1H), 4.90 (t, J = 9.2 Hz, 1H), 4.36 (dd, J = 10.0, 4.0 Hz, 1H), 3.68 (s, 3H), 2.14 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.2, 157.4, 156.7, 152.6, 148.2, 138.8, 136.5, 129.9, 128.1 (2C), 126.8 (2C), 126.6, 126.2, 125.8 (2C), 124.3, 113.6 (2C), 66.8, 64.2, 58.8, 55.4, 13.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{23}N_2O_4^+$, 403.1652; found, 403.1667.

(*S)-3-(4-Methoxyphenyl)-4-[(*S**)-3-oxo-2,5-diphenylpentan-2-yl]oxazolidin-2-one (3lb)**



The product **3lb** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 9.02 mg, 0.21 mmol, 21% isolated yield, dr > 20:1). Yellow oil. The stereochemistry of **3lb** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

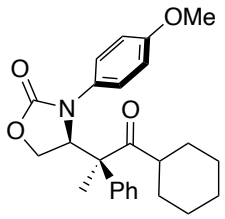
IR (neat) 667, 737, 879, 909, 1047, 1087, 1216, 1381, 1702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.12 (m, 3H), 7.00–6.91 (m, 5H), 6.79 (d, J = 8.0, 1.2 Hz, 2H), 6.73–6.69 (m, 2H), 6.43–6.39 (m, 2H), 5.14 (dd, J = 9.2, 4.4 Hz, 1H), 4.81 (t, J = 9.2 Hz, 1H), 4.17 (dd, J = 10.4, 4.4 Hz, 1H), 3.65 (s, 3H), 2.85 (m, 1H), 2.64 (m, 1H), 2.50 (m, 1H), 2.35 (m, 1H), 1.62 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 210.3, 157.0, 156.8, 140.3, 137.3, 129.5, 128.6 (2C), 128.4 (2C), 128.3 (2C), 127.3, 126.5 (2C), 126.2, 125.8 (2C), 113.6 (2C), 66.4, 63.1, 59.8, 55.4, 39.4, 30.0, 12.3.

HRMS–ESI (*m/z*): $[M+K]^+$ calcd for $C_{27}H_{27}KNO_4^+$, 468.1572; found, 468.1554.

(*S)-4-[(*S**)-1-Cyclohexyl-1-oxo-2-phenylpropan-2-yl]-3-(4-methoxyphenyl)oxazolidin-2-one (3lc)**



The product **3lc** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 16.3 mg, 0.40 mmol, 40% isolated yield, dr = 19:1). Yellow solid. The stereochemistry of **3lc** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material. ^{1}H and ^{13}C NMR data described the major diastereomer.

M.p. 163–165 °C.

IR (neat) 651, 669, 736, 908, 1046, 1215, 1715 cm^{-1}.

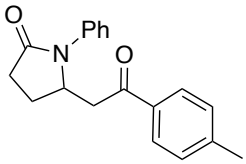
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03–6.99 (m, 3H), 6.93–6.90 (m, 2H), 6.75–6.71 (m, 2H), 6.44–6.40 (m, 2H), 5.17 (dd, J = 9.2, 4.4 Hz, 1H), 4.83 (t, J = 9.2 Hz, 1H), 4.16 (dd, J = 10.4, 4.4 Hz, 1H), 3.66 (s, 3H), 2.02 (tt, J = 12.0, 3.2 Hz, 1H), 1.74–1.70 (m, 4H), 1.55–1.48 (m, 2H), 1.44–

1.24 (m, 3H), 1.15–1.09 (m, 2H), 0.96–0.81 (m, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 214.4, 156.8, 136.7, 129.5, 128.4 (2C), 127.5, 127.0 (2C), 126.0 (2C), 122.5, 113.7 (2C), 66.7, 63.1, 60.4, 55.4, 46.7, 30.7, 30.4, 25.5, 25.4, 25.2, 12.1.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{30}NO_4^+$, 408.2169; found, 408.2158.

5-[2-Oxo-2-(*p*-tolyl)ethyl]-1-phenylpyrrolidin-2-one (3ya)



The product **3ya** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Table 3-2**; 5.57 mg, 0.19 mmol, 19% isolated yield). Pale orange solid.

M.p. 124–126 °C.

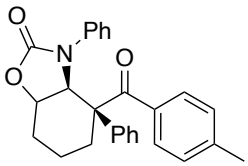
IR (neat) 667, 879, 909, 1046, 1086, 1215, 1727 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.46–7.43 (m, 2H), 7.41–7.37 (m, 2H), 7.26–7.19 (m, 3H), 4.89 (m, 1H), 3.30 (dd, J = 17.4, 2.8 Hz, 1H), 3.07 (dd, J = 17.4, 9.6 Hz, 1H), 2.70–2.55 (m, 3H), 2.40 (s, 3H), 1.84 (m, 1H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 197.2, 174.2, 144.5, 137.2, 134.1, 129.4 (2C), 129.2 (2C), 128.0 (2C), 125.9, 123.7 (2C), 56.2, 42.1, 31.0, 25.0, 21.6.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{20}NO_2^+$, 294.1489; found, 294.1488.

(3a*S,4*S**)-4-(4-Methylbenzoyl)-3,4-diphenylhexahydrobenzo[*d*]oxazol-2(3*H*)-one (3za)**



The product **3za** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 10.3 mg, 0.25 mmol, 25% isolated yield, dr > 20:1). White solid. The stereochemistry of **3za** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 242–244 °C.

IR (neat) 669, 758, 879, 1047, 1394, 1473, 1750 cm^{-1}.

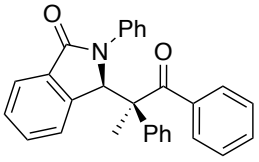
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.26 (m, 4H), 7.01 (d, J = 8.4 Hz, 2H), 6.96–6.89 (m, 4H), 6.86–6.83 (m, 4H), 5.64 (d, J = 7.6 Hz, 1H), 5.16 (m, 1H), 2.70 (m, 1H), 2.47 (m, 1H), 2.29 (s, 3H), 2.05–1.85 (m, 4H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 203.1, 196.0, 143.2, 138.2, 137.1, 133.7, 129.2 (2C), 128.9

(2C), 128.0 (2C), 127.8 (2C), 125.5, 125.0, 124.9 (2C), 124.8 (2C), 75.0, 61.6, 57.4, 24.5, 21.7, 21.5, 15.3.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{26}NO_3^+$, 412.1907; found, 412.1905.

(*R)-3-[(*S**)-1-Oxo-1,2-diphenylpropan-2-yl]-2-phenylisoindolin-1-one (3Aa)**



The product **3Aa** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 11.7 mg, 0.27 mmol, 27% isolated yield, dr = 19:1). White solid. The stereochemistry of **3Aa** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material. ^{1}H and ^{13}C NMR data described the major diastereomer.

M.p. 108–110 °C.

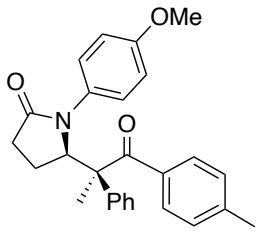
IR (neat) 668, 733, 839, 1046, 1086, 1216, 1456, 1736 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (m, 1H), 7.74 (m, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.54–7.50 (m, 2H), 7.48–7.26 (m, 6H), 7.23–7.15 (m, 3H), 7.12–7.08 (m, 2H), 6.94 (d, J = 7.6 Hz, 1H), 6.80 (s, 1H), 2.28 (s, 3H), 2.22 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 195.0, 166.8, 141.1, 140.6, 138.1, 135.8, 135.0, 131.2, 130.5, 129.10 (2C), 129.06 (2C), 128.5, 128.3 (2C), 128.24 (2C), 128.17, 127.9, 127.2, 125.9 (2C), 124.4, 119.7 (2C), 62.2, 29.7, 26.0, 17.4.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{30}H_{26}NO_2^+$, 432.1958; found, 432.1956.

(*R)-1-(4-Methoxyphenyl)-5-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]pyrrolidin-2-one (3Ba)**



The product **3Ba** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 17.0 mg, 0.41 mmol, 41% isolated yield, dr > 20:1). Yellow solid. The stereochemistry of **3Ba** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 124–126 °C.

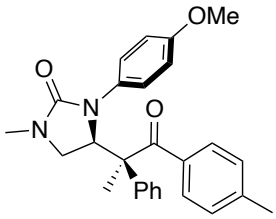
IR (neat) 443, 651, 669, 908, 1047, 1214, 1751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.10 (m, 4H), 7.05–6.92 (m, 5H), 6.82–6.78 (m, 2H), 6.50–6.46 (m, 2H), 5.29 (dd, J = 9.0, 2.4 Hz, 1H), 3.69 (s, 3H), 2.68 (m, 1H), 2.56–2.39 (m, 2H), 2.27 (s, 3H), 2.01 (m, 1H), 1.74 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.9, 175.7, 156.7, 142.3, 138.8, 134.7, 131.3, 128.9 (2C), 128.7 (2C), 128.6 (2C), 127.3 (2C), 127.1, 126.6 (2C), 113.5 (2C), 67.6, 59.4, 55.4, 30.9, 23.7, 21.4, 16.1.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{28}NO_3^+$, 414.2064; found, 414.2064.

(*S)-3-(4-Methoxyphenyl)-1-methyl-4-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]imidazolidin-2-one (3Ca)**



The product **3Ca** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Table 3-2**; 18.9 mg, 0.44 mmol, 44% isolated yield, dr > 20:1). White solid. The stereochemistry of **3Ca** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 150–152 °C.

IR (neat) 647, 757, 907, 1046, 1087, 1217, 1380, 1722 cm^{-1}.

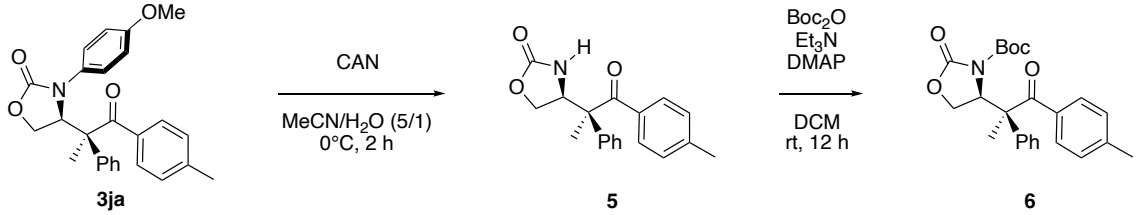
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 2H), 7.20–7.08 (m, 2H), 7.01–6.97 (m, 5H), 6.77–6.73 (m, 2H), 6.44–6.40 (m, 2H), 5.18 (dd, J = 10.0, 4.0 Hz, 1H), 3.96 (t, J = 10.0 Hz, 1H), 3.67 (s, 3H), 3.25 (dd, J = 10.4, 4.0 Hz, 1H), 2.84 (s, 3H), 2.28 (s, 3H), 1.76 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.9, 159.5, 155.7, 142.7, 139.2, 134.0, 132.5, 129.4 (2C), 128.8 (2C), 128.6 (2C), 127.2, 127.1 (2C), 125.5 (2C), 113.4 (2C), 61.3, 59.3, 55.4, 50.0, 30.7, 21.4, 15.0.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{29}N_2O_3^+$, 429.2173; found, 429.2173.

■ Tarnsformation of Products ■

Oxidative Deprotection of 3la / Boc-Protection of 5

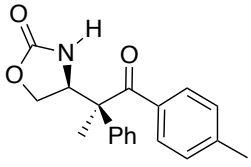


3ja **5** **6**

Oxidative Deprotection of 3la.[29] Under an ambient atmosphere, screw-top 5 mL vial containing a magnetic stirring bar was added **3la** (83.1 mg, 0.20 mmol, 1.0 equiv) and MeCN / H_2O (2.732 mL, 546 μL, 0.061 M). The reaction mixture was cooled to 0 ℃ in an ice bath and diammonium cerium (IV) nitrate (CAN; 328.9 mg, 3.0 mmol, 3.0 equiv) was added. The reaction mixture was stirred at 0 ℃ for 2 h. The reaction was quenched with H_2O (5.0 mL) and extracted with AcOEt (10 mL). The organic layer was washed with sat. $NaHCO_3$ (10 mL × 2), and extracted with AcOEt (10 mL × 3). The organic layers were combined, washed with brine (10 mL) and dried over Na_2SO_4. After filtration was evaporated under reduced pressure and the crude product was purified by flash chromatography on silica gel (100:0–67:33, hexane/AcOEt) to afford **5** (47.0 mg, 0.152 mmol) in 76% yield (dr > 20:1).

Boc-Protection of 5.[30] An oven-dried screw-top 5 mL vial with a stirring bar was degassed, flushed with nitrogen, and was added **5** (47.0 mg, 0.15 mmol, 1.0 equiv) and DCM (2.239 mL, 0.067 M). The reaction mixture was added triethylamine (25.1 μL, 0.18 mmol, 1.2 equiv), 4-dimethylaminopyridine (1.83 mg, 0.015 mmol, 0.10 equiv) and di-*tert*-butyl decarbonate (49.1 mg, 0.225 mmol, 1.5 equiv). The reaction mixture was stirred at room temperature until the carbamoyl **5** was fully consumed by TLC. The reaction mixture was evaporated under reduced pressure and the crude product was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) to afford **6** (52.2 mg, 0.128 mmol) in 85% yield (dr > 20:1).

(*S**)-4-[(*S**)-1-Oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]oxazolidin-2-one (5)



The product **5** was purified by flash chromatography on silica gel (100:0–67:33,

hexane/AcOEt) (**Scheme 3-1**; 47.0 mg, 0.152 mmol, 76% isolated yield, dr > 20:1). Pale orange solid. The stereochemistry of **5** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 197–199 °C.

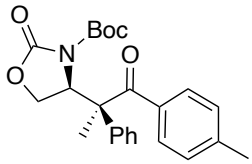
IR (neat) 666, 879, 910, 1046, 1088, 1217, 1379, 1732 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.35 (m, 5H), 7.29 (d, J = 7.2 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 4.83 (br s, 1H), 4.68 (t, J = 9.2 Hz, 1H), 4.49 (dd, J = 9.2, 5.2 Hz, 1H), 4.23 (dd, J = 9.2, 5.2 Hz, 1H), 2.30 (s, 3H), 1.71 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 201.6, 158.7, 143.8, 138.7, 131.9, 130.1 (2C), 129.6 (2C), 129.0 (2C), 128.3, 126.8 (2C), 67.3, 59.5, 57.5, 21.5, 16.7.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{20}NO_3^+$, 310.1438; found, 310.1442.

***tert*-Butyl (*S**)-2-Oxo-4-[(*S**)-1-oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl]oxazolidine-3-carboxylate (6)**



The product **6** was purified by flash chromatography on silica gel (100:0–83:17, hexane/AcOEt) (**Scheme 3-1**; 52.2 mg, 0.128 mmol, 85% isolated yield, dr > 20:1). White solid. The stereochemistry of **6** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

M.p. 128–130 °C.

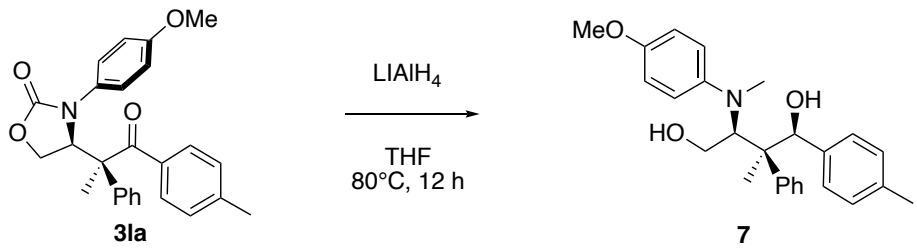
IR (neat) 667, 751, 879, 1046, 1087, 1216, 1380, 1741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.30 (m, 7H), 7.04 (d, J = 8.0 Hz, 2H), 5.21 (d, J = 7.4 Hz, 1H), 4.60 (dd, J = 10.0, 7.4 Hz, 1H), 4.23 (dd, J = 10.0, 1.6 Hz, 1H), 2.30 (s, 3H), 1.74 (s, 3H), 1.19 (s, 9H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.1, 153.5, 149.1, 143.6, 139.1, 132.5, 130.0 (2C), 129.2 (2C), 128.9 (2C), 128.0 (2C), 127.2, 83.6, 67.0, 60.8, 58.5, 27.5 (3C), 21.5, 15.9.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{24}H_{28}NO_5^+$, 410.1962; found, 410.1967.

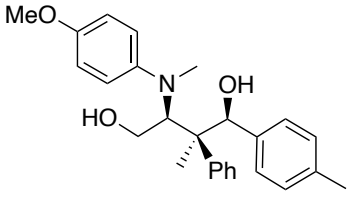
Reductive Ring-Opening of 3la[31]



3la **7**

An oven-dried round-bottomed flask with a stirring bar was degassed, flushed with nitrogen, and was added lithium aluminum hydride (23.9 mg, 0.63 mmol, 3.1 equiv), THF (8.3 mL, 0.024 M) and **3la** (83.1 mg, 0.20 mmol, 1.0 equiv). The reaction mixture was stirred and refluxed at 80 ℃ for 12 h. The reaction was added dropwise H_2O (5.0 mL) and 4.0 M NaOH aq. (5.0 mL) at 0 ℃ and the reaction mixture was stirred vigorously for 15 min at 0 ℃. The reaction mixture was then diluted with Et_2O (10 mL) and dried by Na_2SO_4 and concentrated. The crude product was purified by flash chromatography on silica gel (100:0–91:9, hexane/AcOEt) to afford **7** (38.3 mg, 0.102 mmol) in 51% yield (dr > 20:1).

(1*S*,2*S*,3*S*)-3-[(4-Methoxyphenyl)(methyl)amino]-2-methyl-2-phenyl-1-(*p*-tolyl)butane-1,4-diol (7)



The product **7** was purified by flash chromatography on silica gel (100:0–75:25, hexane/AcOEt) (**Scheme 3-1**; 38.3 mg, 0.102 mmol, 51% isolated yield, dr > 20:1). Pale orange solid. The stereochemistry of **7** was assigned by X-ray diffraction analysis.

M.p. 133–135 °C.

IR (neat) 647, 879, 909, 1046, 1087, 1217, 1380, 1711 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 7.6 Hz, 2H), 7.09 (t, J = 7.2 Hz, 1H), 7.00–6.93 (m, 4H), 6.72–6.68 (m, 4H), 6.54 (d, J = 9.2 Hz, 2H), 4.95 (dd, J = 10.8, 4.0 Hz, 1H), 4.73 (s, 1H), 3.84 (t, J = 10.0 Hz, 1H), 3.75 (s, 3H), 3.65 (dd, J = 10.8, 3.2 Hz, 1H), 2.42 (s, 3H), 2.26 (s, 3H), 2.16–2.04 (m, 2H), 1.31 (s, 3H).

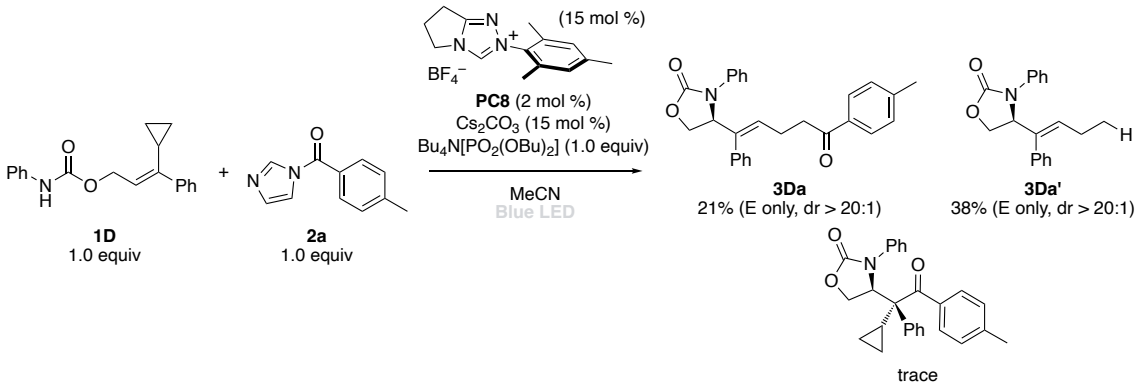
^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.9, 147.4, 140.3, 137.54, 137.47, 128.8 (2C), 128.3 (2C),

128.0 (2C), 126.9 (2C), 126.4, 116.0 (2C), 114.3 (2C), 80.8, 64.8, 59.4, 55.8, 50.4, 32.6, 21.0, 17.5.

HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{32}NO_3^+$, 406.2377; found, 406.2384.

■ Radical Process Experiment ■

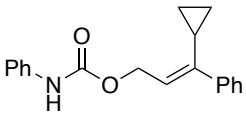
· Radical clock experiment



Protocol

Under an ambient atmosphere, to an oven-dried screw-top 5 mL vial with a stirring bar was added Photo catalyst **PC8** (1.32 mg, 2 μmol), triazolium salt NHC (4.73 mg, 15 μmol), carbamate **1D** (29.3 mg, 0.10 mmol) and acyl imidazole **2a** (18.6 mg, 0.1 mmol). The vial was brought to a globebox, and added MeCN (1.0 mL), Cs_2CO_3 (4.89 mg, 15 μmol) and $Bu_4N[PO_2(OBu)_2]$ (45.2 mg, 0.10 mmol). After the vial was removed from the glovebox and sealed with Teflon tape, the vial was placed in Photoreodox Duo. After 12 h stirring at ambient temperature under photoirradiation (440 nm), the reaction mixture was passed through a short pad of silica gel with AcOEt followed by evaporation and flash column chromatography on silica gel (100:0–83:17, hexane/AcOEt) gave **3Da** (8.63 mg, 0.21 mmol) in 21% yield (dr > 20:1).

(*E*)-3-Cyclopropyl-3-phenylallyl Phenylcarbamate (1D)



Synthesized using **Method A** starting from (*E*)-3-cyclopropyl-3-phenylprop-2-en-1-ol[23] on a 1.2mmol scale with respect to the alcohol.

The product **1D** was purified by flash chromatography on silica gel (100:0–95:5, hexane/AcOEt) (324 mg, 1.10 mmol, 92% isolated yield). White solid

M.p. 48–51 °C.

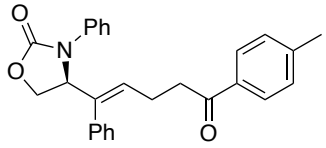
IR (neat) 692, 754, 1028, 1053, 1313, 1444, 1501, 1600, 1702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.21 (m, 9H), 7.05 (tt, J = 7.2, 1.2 Hz, 1H), 6.75 (br s, 1H), 5.85 (td, J = 6.8, 1.6 Hz, 1H), 5.06 (d, J = 6.8 Hz, 2H), 1.80 (m, 1H), 0.87–0.83 (m, 2H), 0.40–0.36 (m, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.6, 145.5, 140.9, 137.9, 129.0 (2C), 127.8 (2C), 127.3 (2C), 127.1 (2C), 124.3, 123.4, 118.6, 62.3, 11.5, 6.6 (2C).

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{19}NNaO_3^+$, 310.1438; found, 310.1442.

(*S,*E*)-4-[5-Oxo-1-phenyl-5-(*p*-tolyl)pent-1-en-1-yl]-3-phenyloxazolidin-2-one (3Da)**



The product **3Da** was purified by flash chromatography on silica gel (100:0–67:33, hexane/AcOEt) (**Scheme 3-2**; 8.63 mg, 0.21 mmol, 21% isolated yield, dr > 20:1). Pale yellow oil. The stereochemistry of **3Ha** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

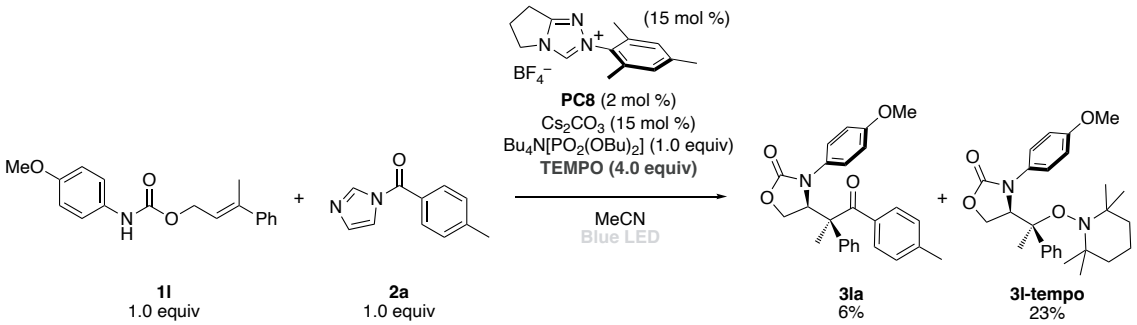
IR (neat) 754, 1214, 1270, 1399, 1501, 1653, 1683, 1735, 1757 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4 Hz, 2H), 7.62 (dd, J = 8.0, 1.6 Hz, 1H), 7.56 (m, 1H), 7.53–7.50 (m, 2H), 7.35–7.30 (m, 7H), 7.11 (m, 1H), 6.09 (t, J = 4.4 Hz, 1H), 5.44 (m, 1H), 4.73 (t, J = 8.4 Hz, 1H), 4.16 (dd, J = 8.4, 4.0 Hz, 1H), 2.85–2.81 (m, 2H), 2.46 (s, 3H), 2.35–2.30 (m, 2H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 195.9, 155.4, 143.4, 141.9, 137.4, 136.5, 134.8, 132.1, 131.7, 130.1 (2C), 129.9, 129.1 (2C), 129.0 (2C), 128.1, 127.6, 124.1, 122.5, 119.1 (2C), 68.1, 56.5, 27.9, 22.3, 21.7.

HRMS–MALDI (*m/z*): $[M+H]^+$ calcd for $C_{27}H_{26}NO_3^+$, 412.1907; found, 412.1907.

· TEMPO trapping experiment

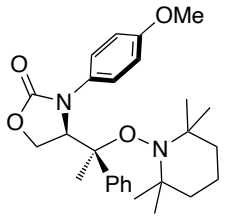


Protocol

Under an ambient atmosphere, to an oven-dried screw-top 5 mL vial with a stirring bar was added Photo catalyst **PC8** (1.32 mg, 2 μmol), triazolium salt NHC (4.73 mg, 15 μmol), carbamate **1l** (29.7 mg, 0.10 mmol) and acyl imidazole **2a** (18.6 mg, 0.1 mmol). The vial was brought to a globebox, and added MeCN (1.0 mL), 2,2,6,6-Tetramethylpiperidine 1-Oxyl Free Radical (TEMPO, 62.5 mg, 0.4 mmol), Cs_2CO_3 (4.89 mg, 15 μmol) and $Bu_4N[PO_2(OBu)_2]$ (45.2 mg, 0.10 mmol). After the vial was

removed from the glovebox and sealed with Teflon tape, the vial was placed in Photoreodox Duo. After 12 h stirring at ambient temperature under photoirradiation (440 nm), the reaction mixture was passed through a short pad of silica gel with AcOEt followed by evaporation and flash column chromatography on silica gel (91:9–75:25, hexane/AcOEt) gave **3l-tempo** (8.59 mg, 0.19 mmol) in 19% yield (dr = 3:1).

(*S)-4-((*S**)-1-Oxo-2-phenyl-1-(*p*-tolyl)propan-2-yl)oxazolidin-2-one (3l-tempo)**



The product **3l-tempo** was purified by flash chromatography on silica gel (91:9–75:25, hexane/AcOEt) (**Scheme 3-3**; 8.59 mg, 0.19 mmol, 19% isolated yield, dr > 20:1). Orange oil. The stereochemistry of **3l-tempo** was assigned by consideration of the stereochemical pathway. The diastereomeric ratio was determined by ^{1}H NMR of the crude material.

IR (neat) 756, 829, 1033, 1132, 1215, 1248, 1403, 1512, 1751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.24 (m, 5H), 7.19–7.15 (m, 2H), 6.93–6.89 (m, 2H), 5.11 (dd, J = 9.6, 2.8 Hz, 1H), 4.88 (dd, J = 9.6, 2.8 Hz, 1H), 4.44 (t, J = 9.6 Hz, 1H), 3.82 (s, 3H), 1.62–1.26 (m, 9H), 1.23–1.22 (m, 6H), 1.15 (s, 3H), 0.49 (s, 3H).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.1, 156.2, 141.5, 130.3, 127.6 (2C), 127.4, 126.5 (2C), 125.3 (2C), 113.8 (2C), 82.1, 64.0, 62.7, 59.8 (× 2), 55.2, 40.8, 40.5, 34.0, 32.8, 22.3, 21.2, 20.8, 16.6.

HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{27}H_{36}N_2NaO_4^+$, 475.2567; found, 475.2581.

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総括

著者は可視光励起を活用した触媒的分子変換反応の開発に関して研究を行い、以下の成果を得た。

第１章　広いπ-共役構造を有する有機ホウ素化合物、ボラセンから誘導されるアルキルホウ素アート錯体の可視光直接励起により、光酸化還元触媒やその他の添加剤を必要とすることなく、第三級、二級および一級のアルキルラジカルの発生・制御を可能にした。このアルキルホウ素アート錯体の直接励起法は、励起状態のホウ素アート錯体の一電子移動能あるいは炭素中心ラジカル発生能に基づき、脱シアノアルキル化反応、Giese付加反応、およびNi触媒によるアルキル–アリールクロスカップリング反応やアルケンの三成分ビシナルアルキルアリール化反応などの種々の炭素–炭素結合反応へと適用可能であった。さらに、反応後にボラセンは回収・再利用が可能であるため、環境調和性に優れた手法といえる。このボラセン構造に基づく反応基質の直接励起法は、有機合成における炭素–炭素結合形成の更なる発展への寄与が期待される。

第２章　有機ホウ素アート錯体の直接光励起を活用した、ラジカル介在型 NHC 触媒反応を開発した。本プロセスでは、可視光照射下、光励起状態のホウ素アート錯体とアシルアゾリウム中間体との間での、一電子授受を起点として、PRE に基づく選択的なラジカル–ラジカルカップリングが進行する。この光駆動型ラジカル NHC 触媒系により、ホウ素アート錯体とアシルイミダゾールとのクロスカップリング、およびホウ素アート錯体とアシルイミダゾールによるアルケンのラジカルリレー型アルキルアシル化が可能となった。特に、アルケンのアルキルアシル化は、これまで適用が困難であった幅広い基質適用範囲を実現した。本手法は、ケトン合成における網羅的な合成プロセスを提供し、還元的ラジカル NHC 触媒反応における新たな反応形式を示した。

第３章　可視光駆動型 PCET プロセスに基づく NHC 触媒系を用いた、不活性アルケンのアミドアシル化を達成した。本手法は、ラジカル–ラジカルカップリング段階を触媒的に精密に制御することで、高いジアステレオ選択性で α 位に 3 級または 4 級炭素中心を有する環状 β-アミドケトンを構築できた。本触媒系は、窒素中心ラジカルの分子内環化反応による短寿命なアルキルラジカルの生成と、アシルアゾリウム中間体の一電子還元による長寿命なケチルラジカルの生成を引き起こす。このジアステレオ選択的なラジカル–ラジカルカップリングを達成するためには、2 種のラジカル生成における一電子移動の精密な制御が鍵となる。本プロセスは、従来法では合成困難なかさ高い β-アミドケトンの構築を可能とし、新たなケミカルスペースの創出につながる。さらに、合成した β-アミドケトンは、酸化・還元することで、立体環境を損なうことなく、脱保護されたカルバマートと鎖状のアミノブタンジオールがそれぞれ得られた。

論文目録

第 1 章

1. Generation of Alkyl Radical through Direct Excitation of Boracene-Based Alkylborate
   Yukiya Sato, Kei Nakamura, Yuto Sumida, Daisuke Hashizume, Takamitsu Hosoya, and Hirohisa Ohmiya
   J. *Am*. *Chem*. *Soc*. **2020**, *142***,** 9938−9943.

第 2 章

2. Light-Driven N-Heterocyclic Carbene Catalysis Using Alkylborates
   Yukiya Sato, Yamoto Goto, Kei Nakamura, Yusuke Miyamoto, Yuto Sumida, and Hirohisa Ohmiya
   ACS Catal. **2021**, *11*, 12886−12892.

第 3 章

3. Diastereoselective Congested β-Amido Ketone Synthesis via NHC-Catalyzed Radical-Radical Coupling
   Yukiya Sato, Yusuke Miyamoto, Takanori Matsi, Yuto Sumida, and Hirohisa Ohmiya
   Chem Catal. **2023**, *3*, 100736.

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