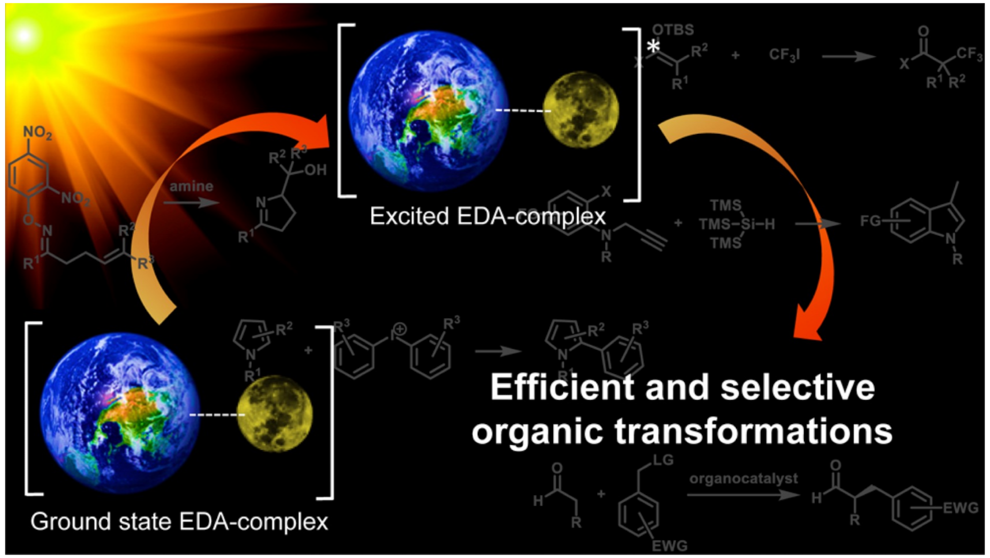
Innovative catalytic EDA complex

Literature seminar _ 2023,2,2

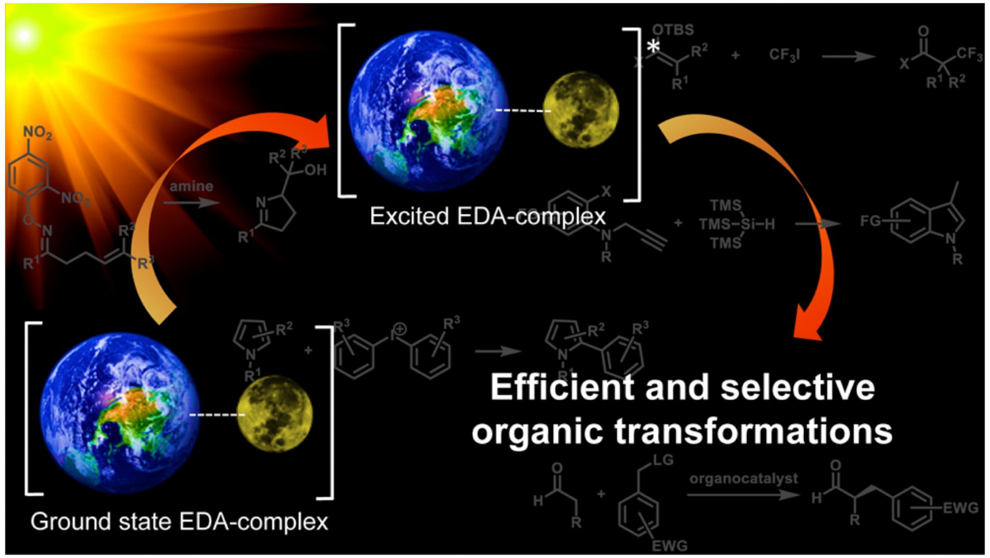
B4, Takeshi Inoue

Contents



Excited EDA-complex
Ground state EDA-complex
Efficient and selective organic transformations
amine
organocatalyst

Contents

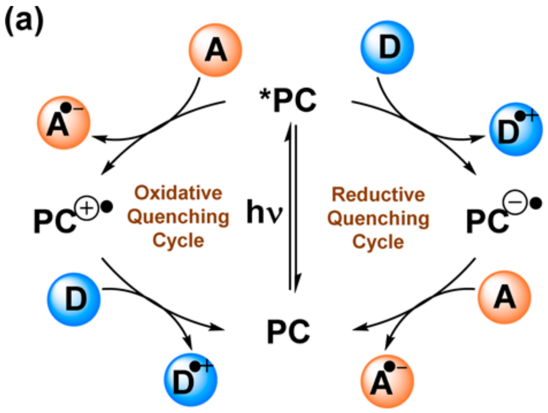


Excited EDA-complex
Ground state EDA-complex
Efficient and selective organic transformations
amine
organocatalyst

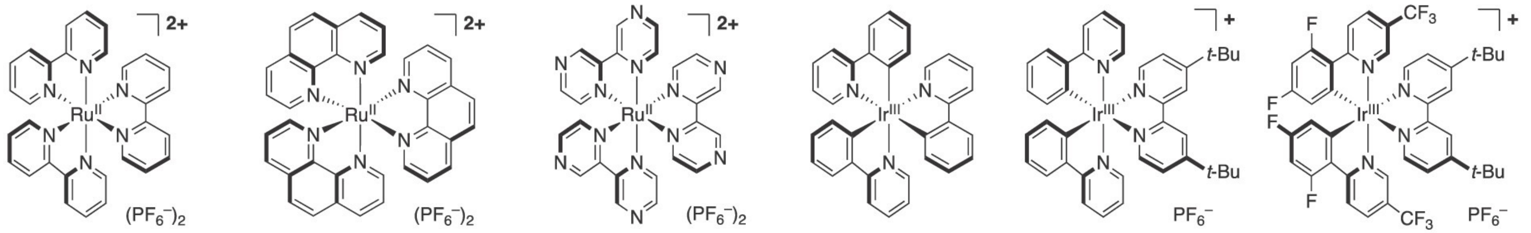
Photo-redox chemistry

- Photo-redox catalysts

(a)

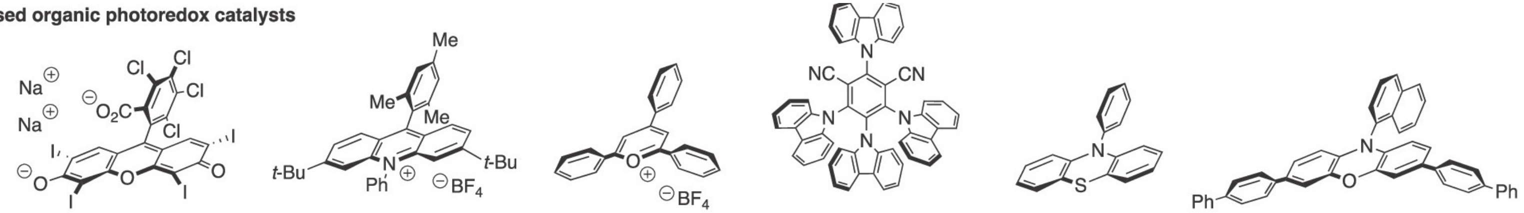


A. Commonly-used transition metal centered photoredox catalysts



	11.1 Ru(bpy)$_3$(PF$_6$)$_2$	**11.2** Ru(phen)$_3$(PF$_6$)$_2$	**11.3** Ru(bpz)$_3$(PF$_6$)$_2$	**11.4** *fac*-Ir(ppy)$_3$	**11.5** Ir(tbbpy)(ppy)$_2$PF$_6$	**11.6** Ir[dF(CF$_3$)ppy]$_2$(dtbpy)PF$_6$
E^*_{red}	+0.77 V	+0.82 V	+1.45 V	+0.31 V	+0.66 V	+1.21 V
E^*_{ox}	–0.81 V	–0.87 V	–0.26 V	–1.73 V	–0.96 V	–0.89 V

B. Commonly-used organic photoredox catalysts

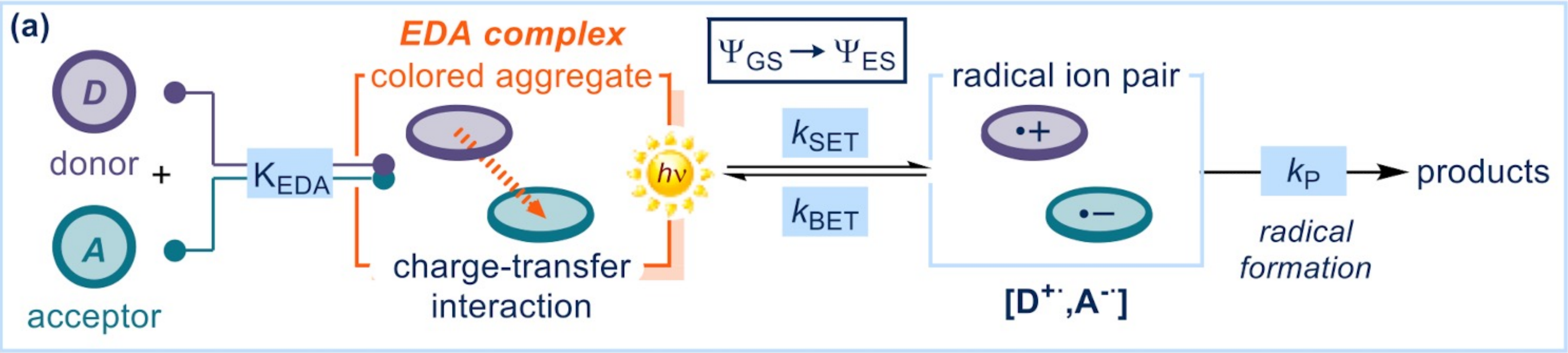


	11.7 Rose Bengal	**11.8** (Mes-3,6-dtb-Ph-Acr)BF$_4$	**11.9** TPPBF$_4$	**11.10** 4CzIPN	**11.11** PTH	**11.12** Phenox O-PC™ A0202
E^*_{red}	+0.81 V	+2.18 V	+2.09 V	+1.35 V	N/A	N/A
E^*_{ox}	–0.96 V	N/A	N/A	–1.04 V	–2.10 V	–1.70 V

- Synthetically elaborated organic dyes.
- Metal complexes with polyheteroaryl ligands.
- Exogenous compounds.

Paixao *et al. ACS Catal.* **2016**, *6*, 1389-1407.

Electron donor-acceptor complex (EDA complex)



donor

; Electron rich,
Low ionization potential
(i.e., reductant, nucleophile)

acceptor

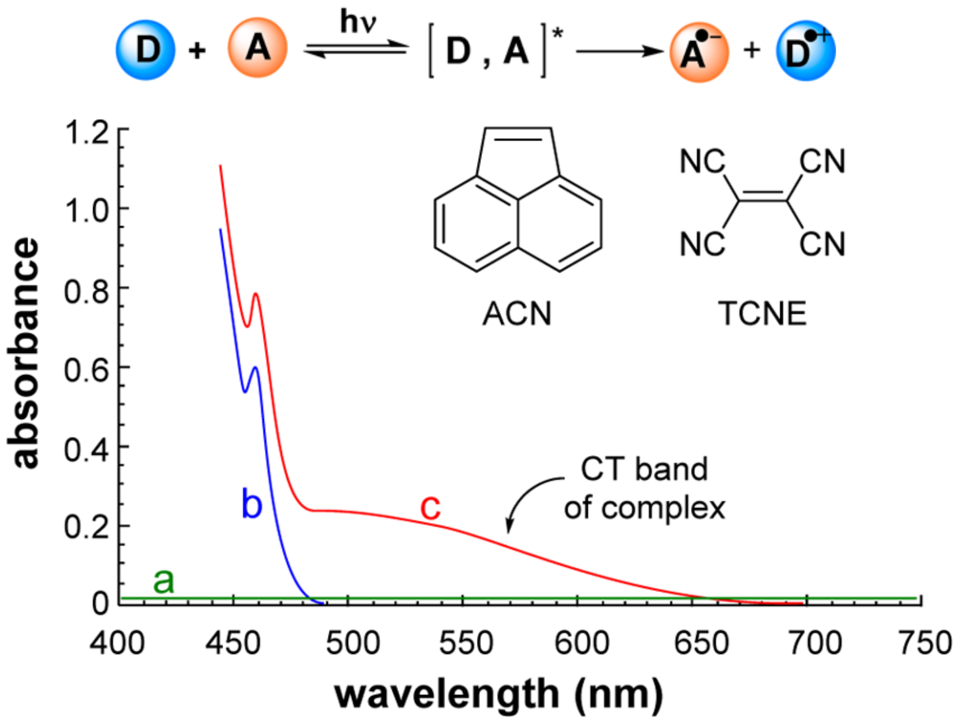
; Electron poor,
high electron affinity
(i.e., oxidant, electrophile)

- Generating radical species without exogenous photo-redox catalysts or metals.
- Induce various radical reaction under mild condition.
- Expand the chemical space. (new selectivity and substrate scope, etc)

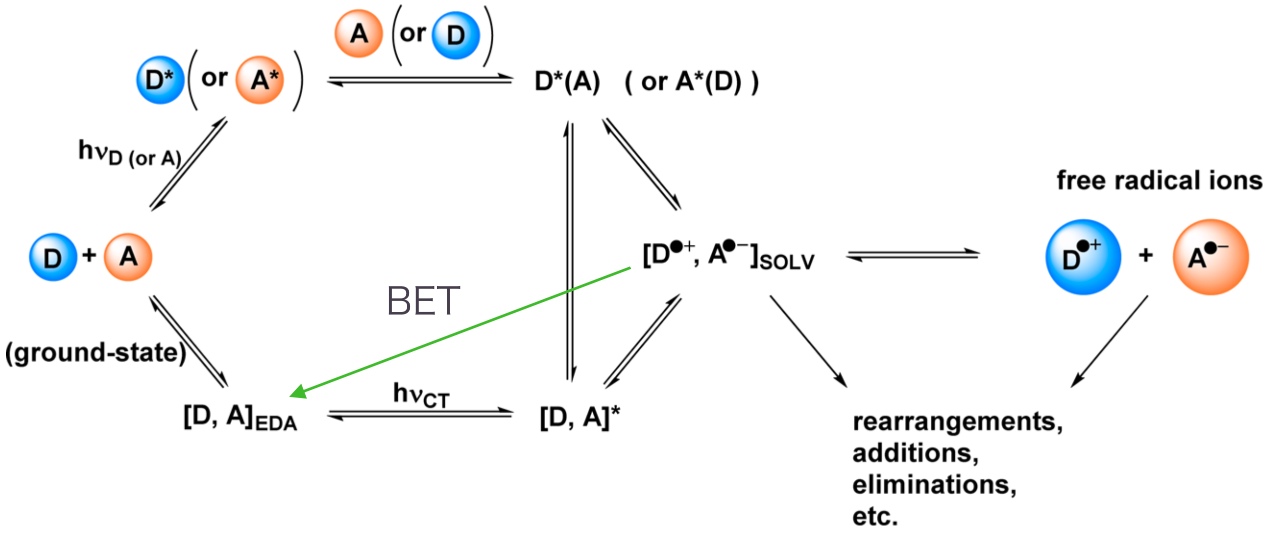
Melchiorre *et al. J. Am. Chem. Soc.* **2020**, *142*, 5461-5476.

Theoretical background

[Charge transfer band of EDA complex]



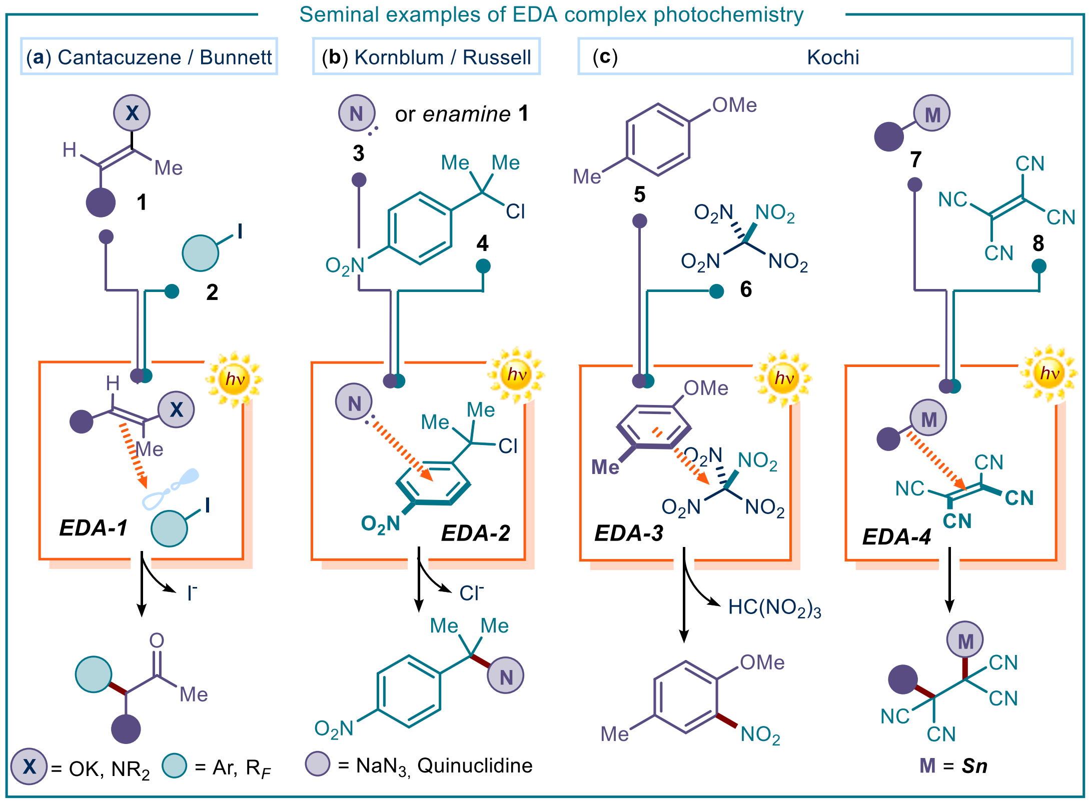
[Back electron transfer (BET)]



- EDA complex exhibits new absorption band in longer wavelength.
- Competition with BET is unavoidable problem in EDA complex.

Paixao *et al.* *ACS Catal.* **2016**, *6*, 1389-1407.

Pioneering synthetic applications



Irreversible fragmentation

(Leaving groups)

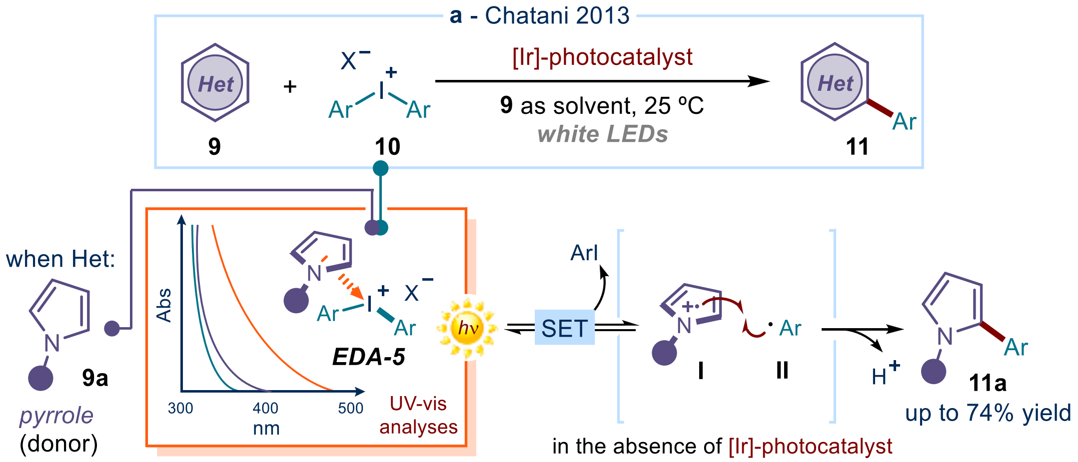
→ Avoid unproductive BET.

Electron donor ;	Enamine, Enolate	Enamine, Amine	Anisole	Alkyl stannene
Acceptor;	Organo iodide	Nitroarene	Tetranitro methane	TCNE

(a) Cantacuzene *et al.* *J. Chem. Soc., Perkin Trans. 1* **1977**, 1365-1371.
Bunnett. *Acc. Chem. Res.* **1978**, *11*, 413-420.
(b) Russell *et al.* *J. Org. Chem.* **1987**, *52*, 3102-3107.
Kornblum *et al.* *J. Org. Chem.* **1991**, *56*, 3475-3479.
(c) Kochi *et al.* *J. Am. Chem. Soc.* **1987**, *109*, 7824-7838.
Kochi *et al.* *J. Am. Chem. Soc.* **1979**, *101*, 5961-5972.

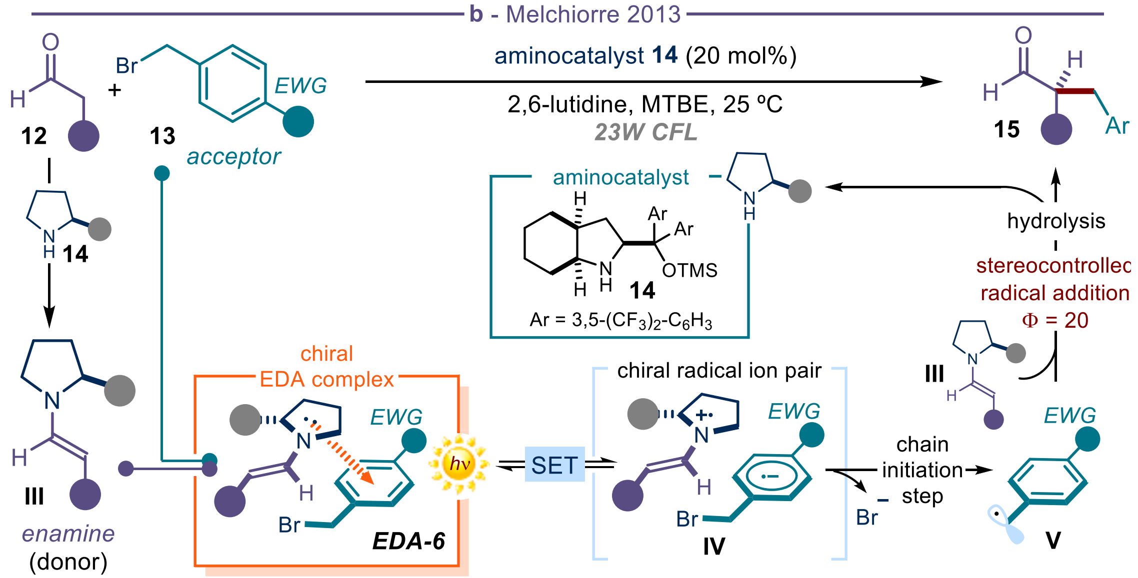
Synthetic renaissance of EDA complex photochemistry

- Pyrrole and iodonium cation



Chatani *et al. Chem. Lett.* **2013**, *42*, 1203-1205.

- Enamine and benzyl bromide



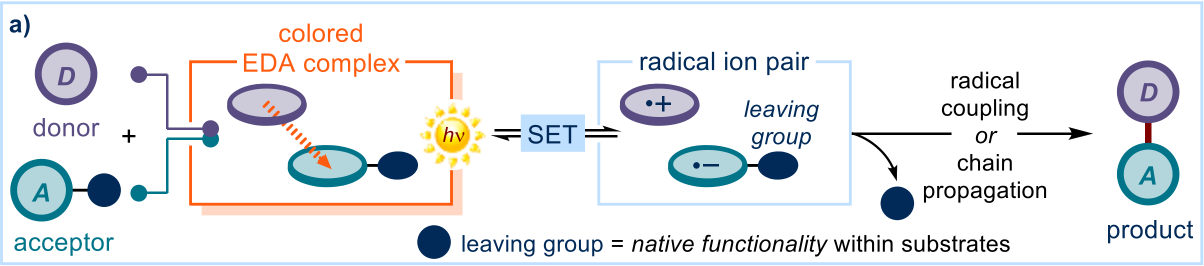
Melchiorre *et al. Nat. Chem.* **2013**, *5*, 750-756.

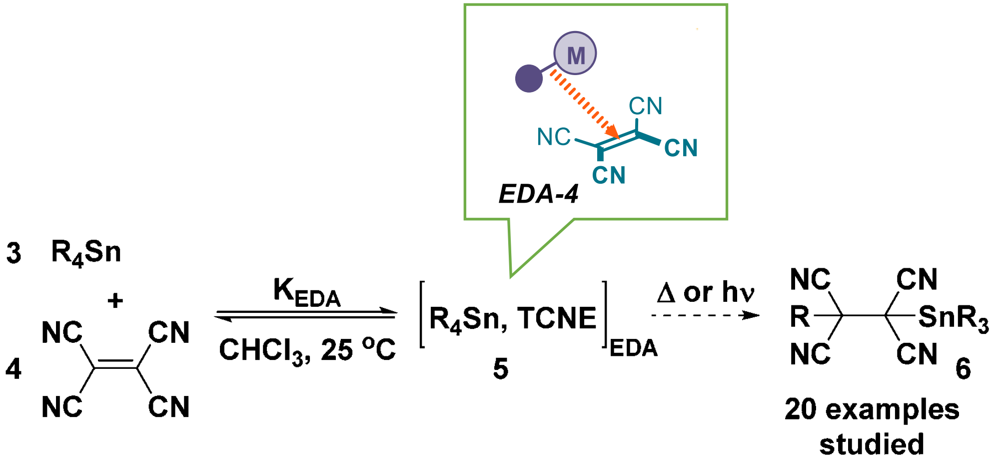
Serendipitous observation (linked to control experiment).

→ Reintroduced EDA complex photochemistry.

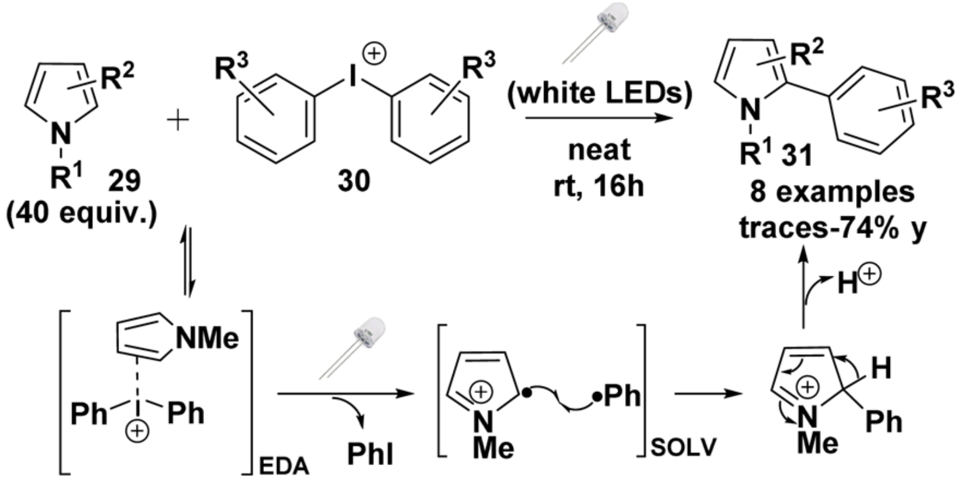
Stoichiometric EDA complex

[Coupling of stoichiometric donor and acceptor]





Kochi *et al. J. Am. Chem. Soc.* **1979**, *101*, 5961-5972.

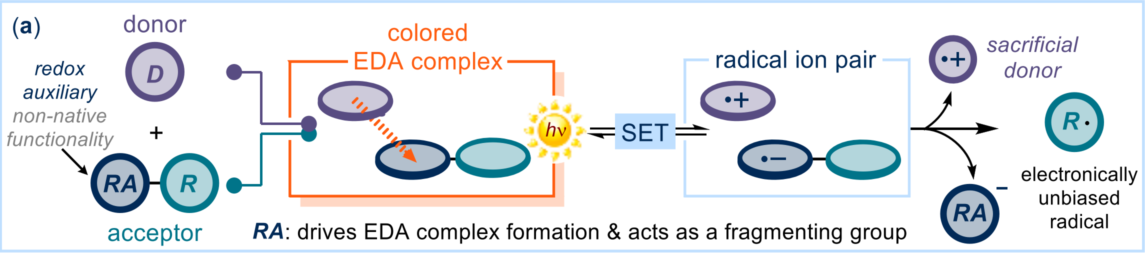


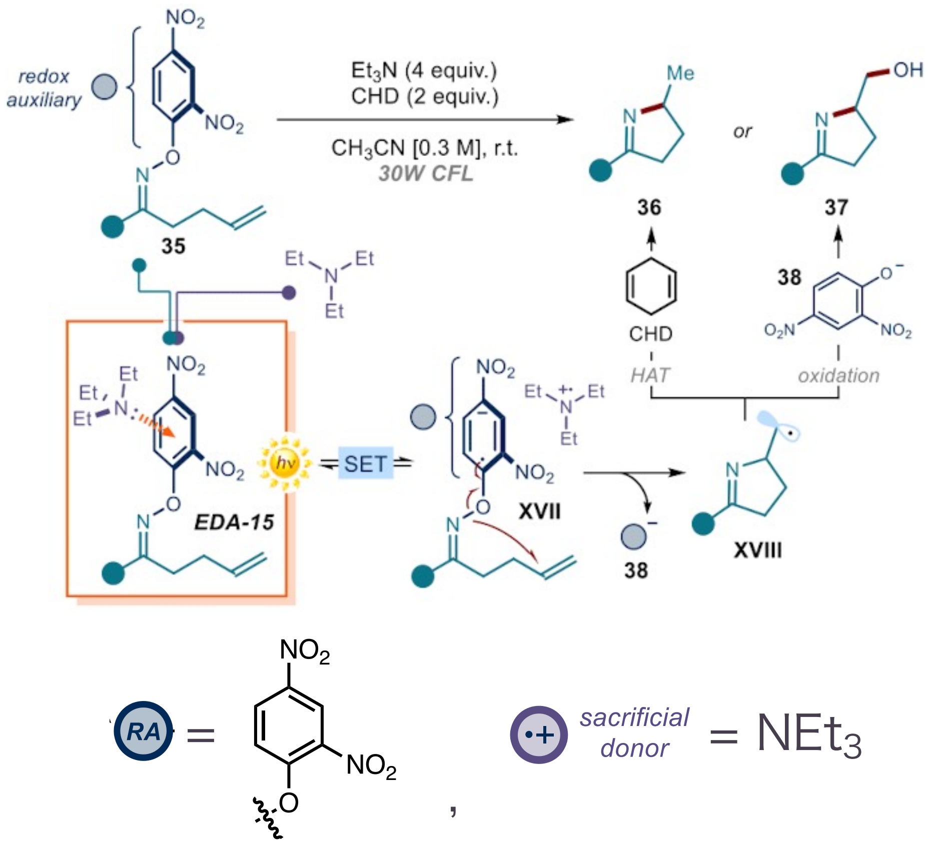
Chatani *et al. Chem. Lett.* **2013**, *42*, 1203-1205.

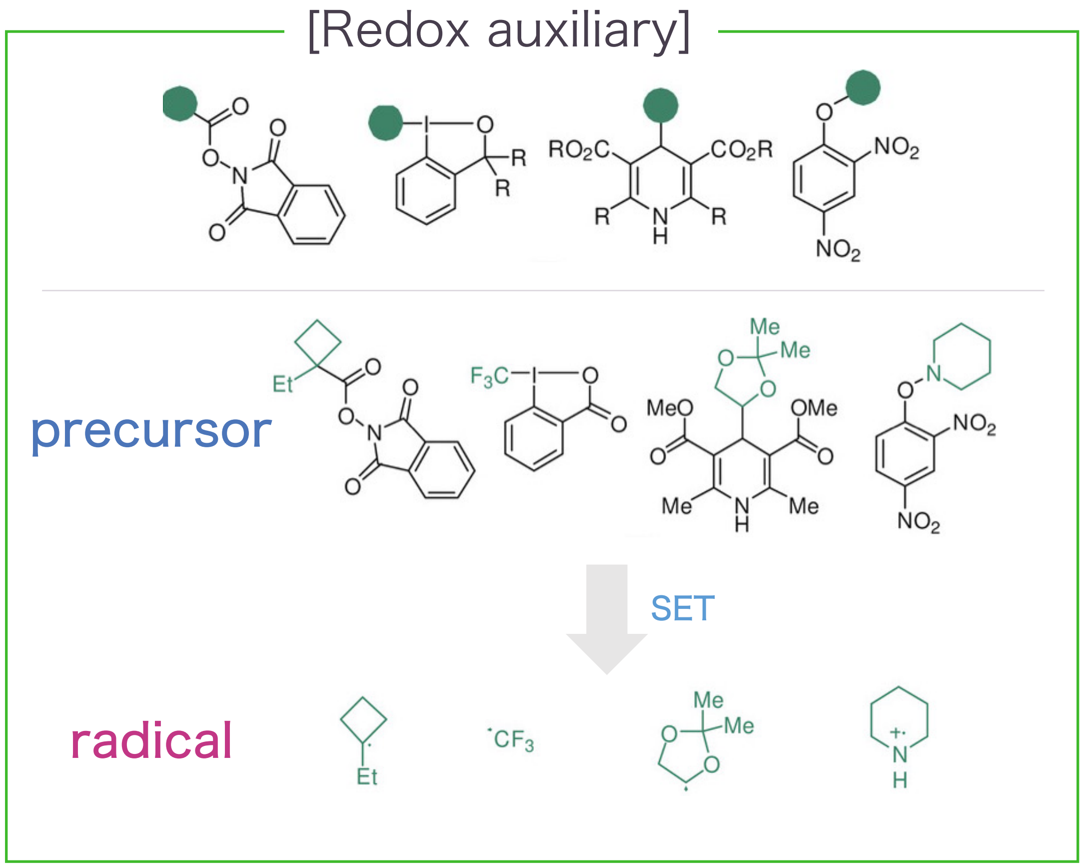
- Electron donor and acceptor finally end up in product scaffold.
- Electronically biased substrates.

→ Low applicability in synthesis.

Sacrificial donor and redox auxiliary



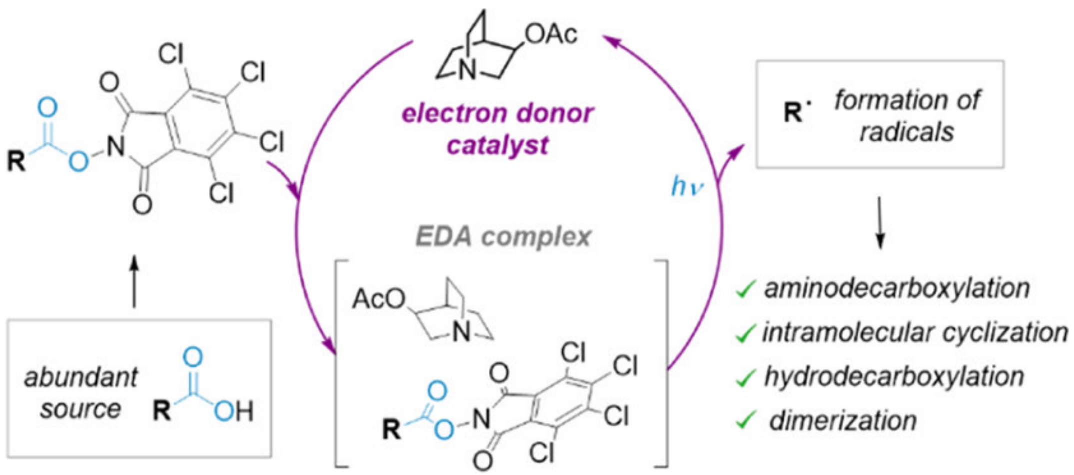




Leonori *et al. Angew. Chem., Int. Ed.* **2015**, *54*, 14017-14021.

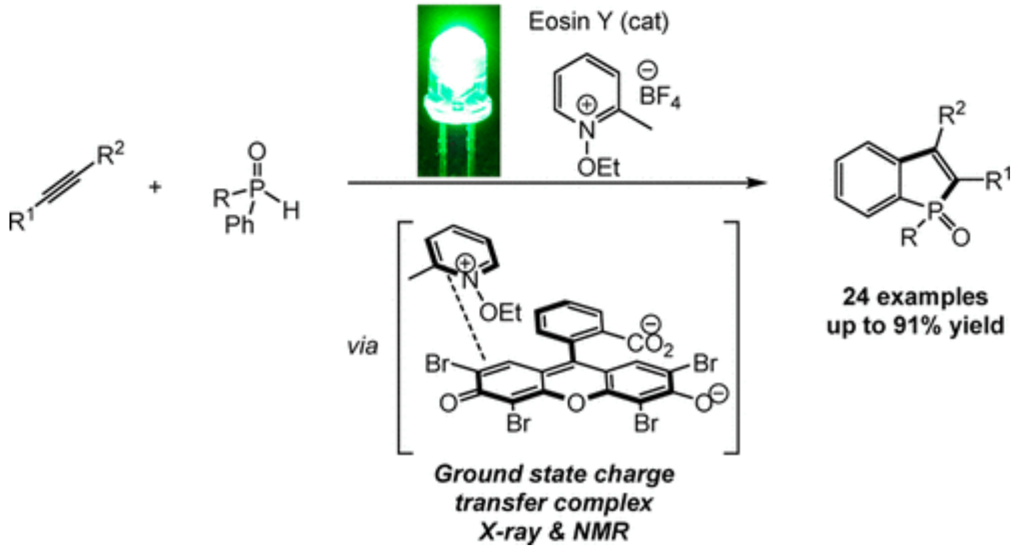
Catalytic EDA complex

- Quinuclidine + Tetrachlorophthalimide



Bach *et al. ACS Catal.* **2019**, *9*, 9103–9109.

- Eosin Y + Pyridinium



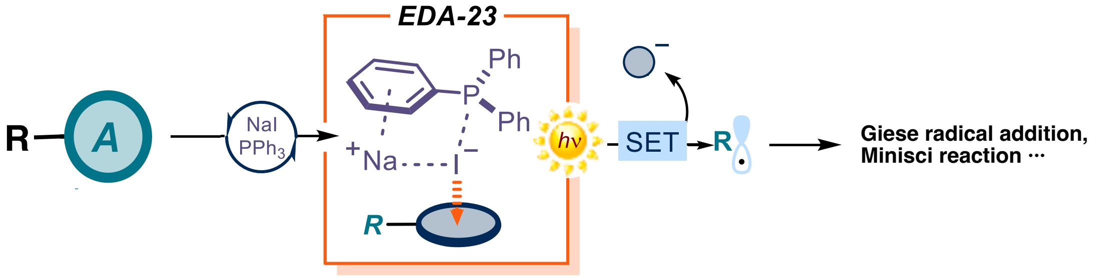
Lakhdar *et al. J. Am. Chem. Soc.* **2016**, *138*, 7436–7441.

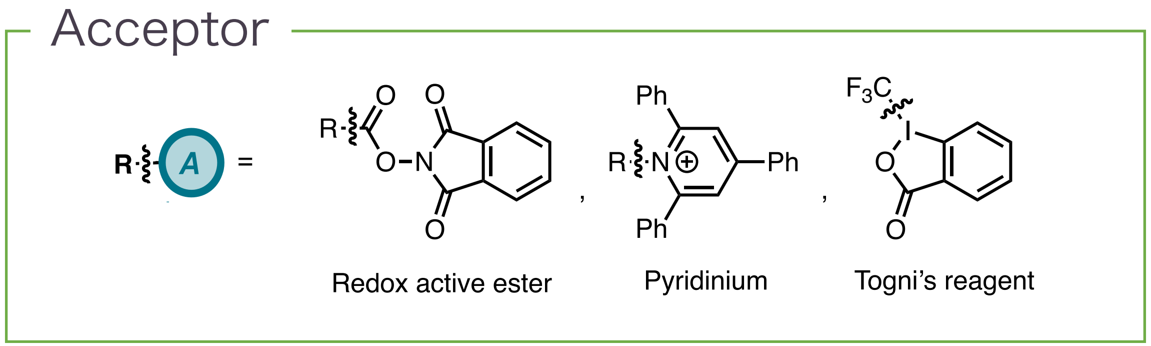
- Specific pair of electron donor and acceptor.

⟺ Limited to selected substrates.

Contents

Catalytic electron donor ; NaI + PPh_3



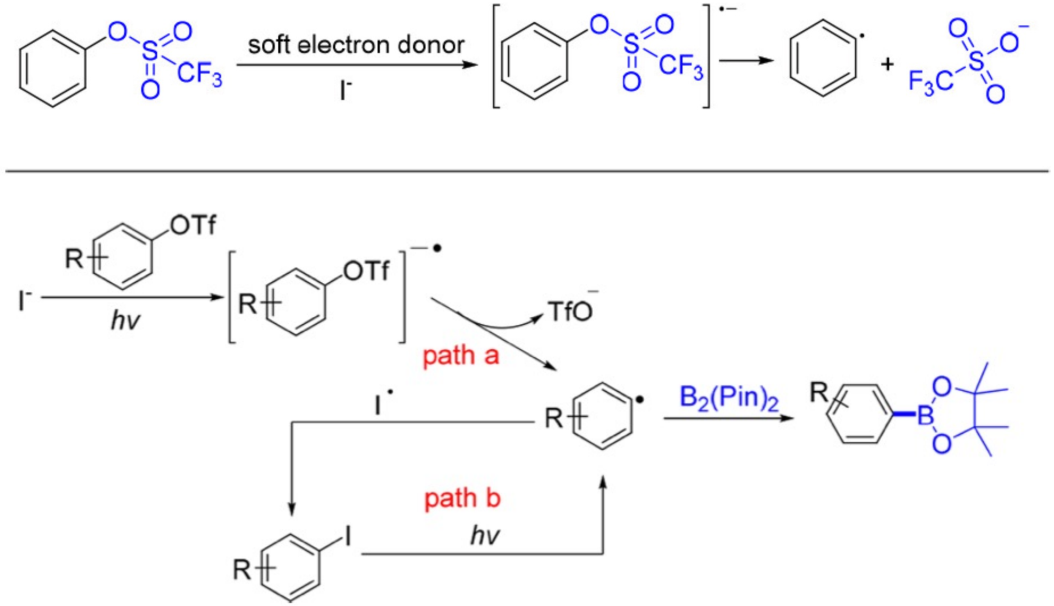


- Combination of simple compound (PPh_3 + NaI) warks as catalytic donor.
- EDA complex formation with several acceptors.
- Visible light.

Fu *et al. Science*. **2019**, *363*, 1429–1434.

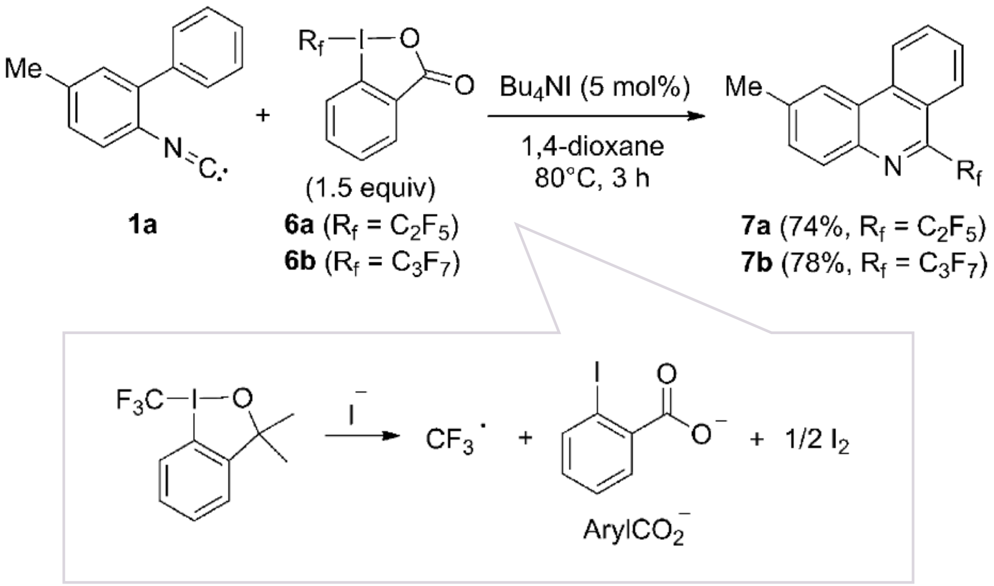
Background

[Aryl triflate]



Li *et al. J. Am. Chem. Soc.* **2017**, *139*, 8621–8627.

[Hypervalent iodine]



Studer *et al. Angew. Chem. Int. Ed.* **2013**, *52*, 10792-10795.

- Iodide is known to reduce various organic molecules.

× UV irradiation or high temperature is required.

This work

→ Reduction of RAE via EDA complex.

→ Visible light excitation with PPh_3.

Delocalized radical between iodide and PPh_3

[Observation of Ph_3P–I· by ESR]

$$R_3P \rightarrow R_3P^{\cdot +} + e^-$$
$$R_3P^{\cdot +} + hal^- \rightarrow R_3P^{\cdot}\text{—}hal,$$

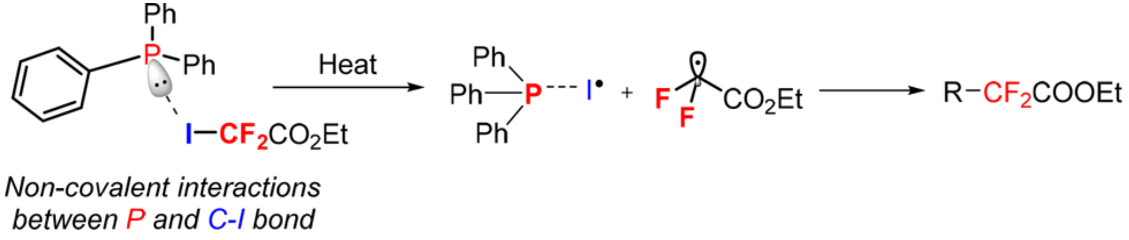
$$hal^- \rightarrow hal\cdot + e^-$$
$$R_3P + hal\cdot \rightarrow R_3P^{\cdot}\text{—}hal.$$

TABLE 3.—ORBITAL POPULATIONS ESTIMATED FROM E.S.R. PARAMETERS[a, b]

radical	atom	a_s^2	a_p^2	total
$R_3P\cdot$—Cl	P	0.164	0.58	0.744
	Cl	0.0131	0.26	0.291
$R_3P\cdot$—Br	P	0.136	0.46	0.596
	Br	0.026	0.36	0.386
$(MeO)_2P(S)\cdot$—Br	P	0.180	0.59	0.77
	Br	0.022	0.32	0.34
$R_3P\cdot$—I	P	0.148	0.48	0.468
	I	0.030	0.38	0.410
$R_2S\cdot$—Cl	Cl	0.050	0.30	0.35
$R_2S\cdot$—Br	Br	0.026	0.43	0.456
$R_2S\cdot$—I	I	0.033	0.43	0.463

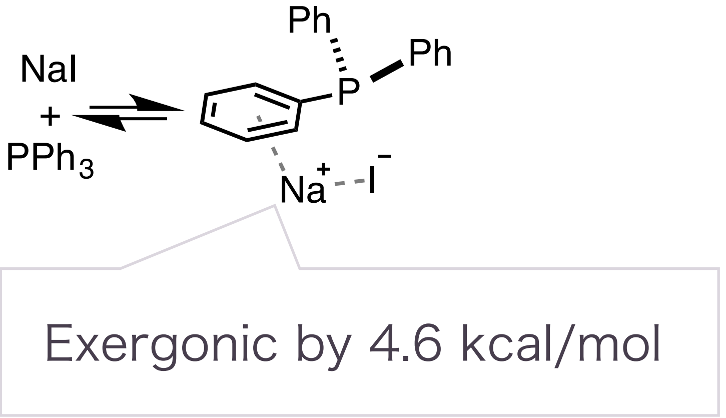
Petersen *et al.* *J. Chem. Soc. Faraday Trans. II.* **1979**, *75*, 210–219.

[Reaction example]

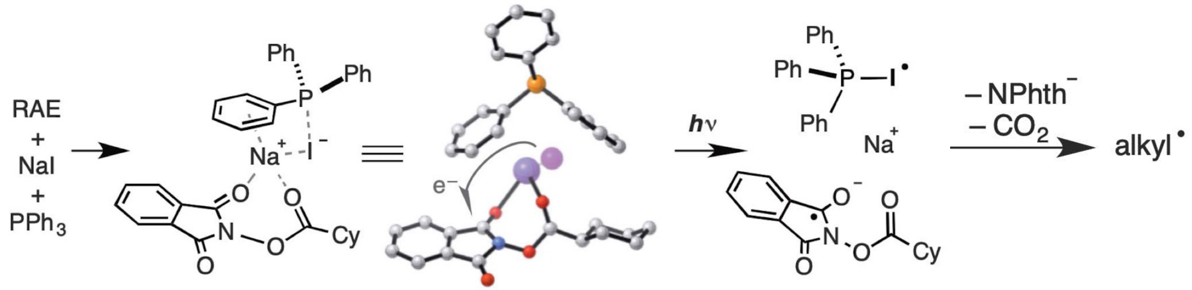


He *et al.* *Org. Lett.* **2019**, *21*, 6705–6709.

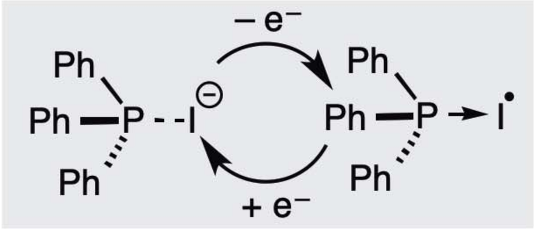
[Complexation of NaI and PPh_3]



Simulations of charge transfer energetics

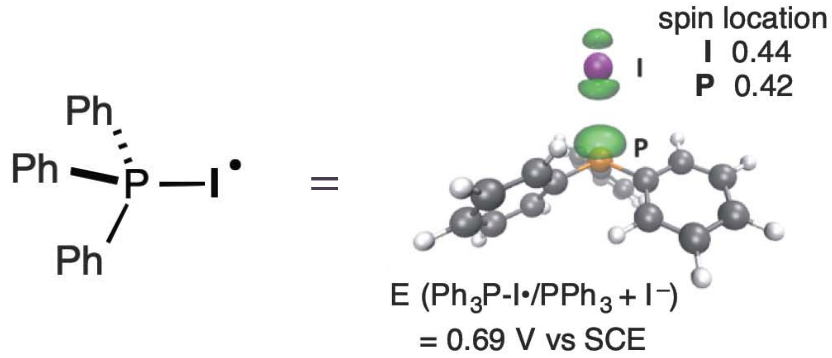


[DFT calculation]



D	ΔG
NaI	56.2 kcal/mol
$NaI•PPh_3$	44.3 kcal/mol
	(alkyl = cyclohexyl)

[Spin delocalization]

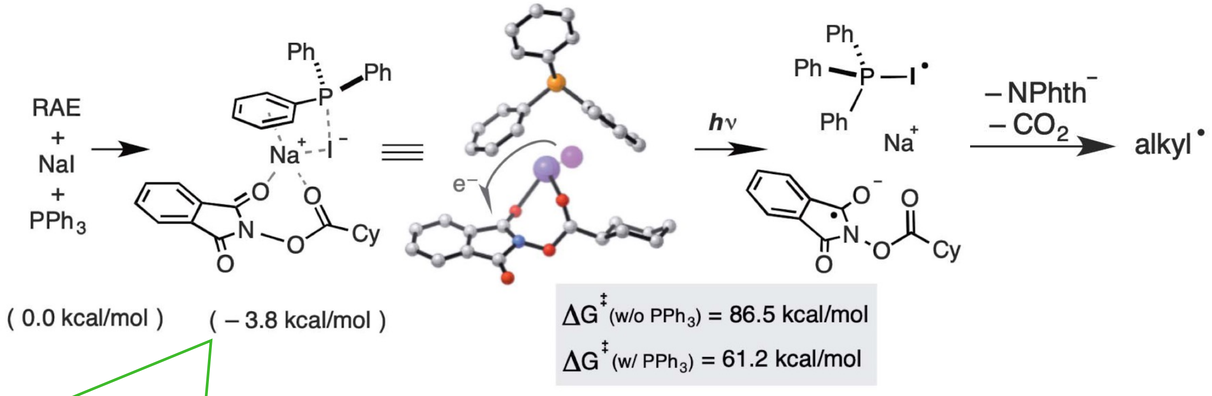


PPh_3 stabilizes the iodide radical.

→ Relatively favorable formation of PhP_3–I· radical.

Simulations of charge transfer energetics

[The energy barrier of charge transfer]



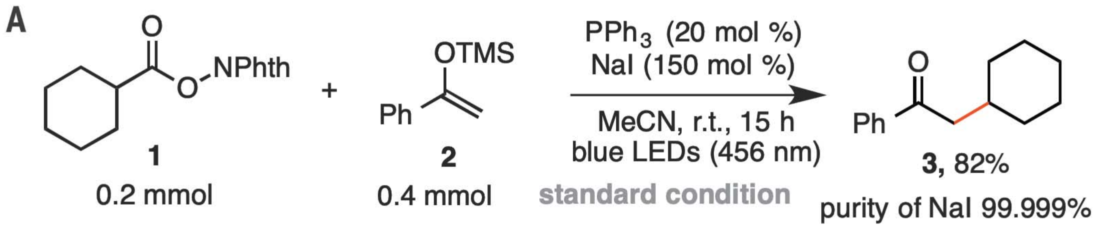
Coulombic interaction
+
Cation-π interaction

(w/ LiI ; −1.1kcal/mol, w/ KI ; −2.9kcal/mol)

PPh_3 lowers energy barrier of charge transfer.

→ SET with visible light.

Investigation of key reaction parameters



different alkali halides instead of NaI

LiI	KI	*n*-Bu_4NI	NaF	NaCl	NaBr
74%	50%	< 1%	0%	< 1%	< 1%

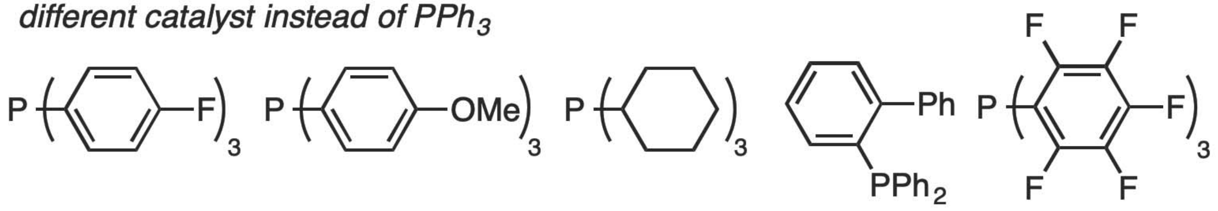
× Cation interaction with RAE.

control experiments

w/o PPh_3	w/o NaI	w/o blue LEDs	addition of 10 mol% I_2
< 5%	< 1%	0%	0%

green LEDs (520 nm)	< 5%
blue LEDs (440 nm)	81%
purple LEDs (427 nm)	80%
purple LEDs (390 nm)	71%
UV (365 nm)	36%
white LEDs	47%

different catalyst instead of PPh_3

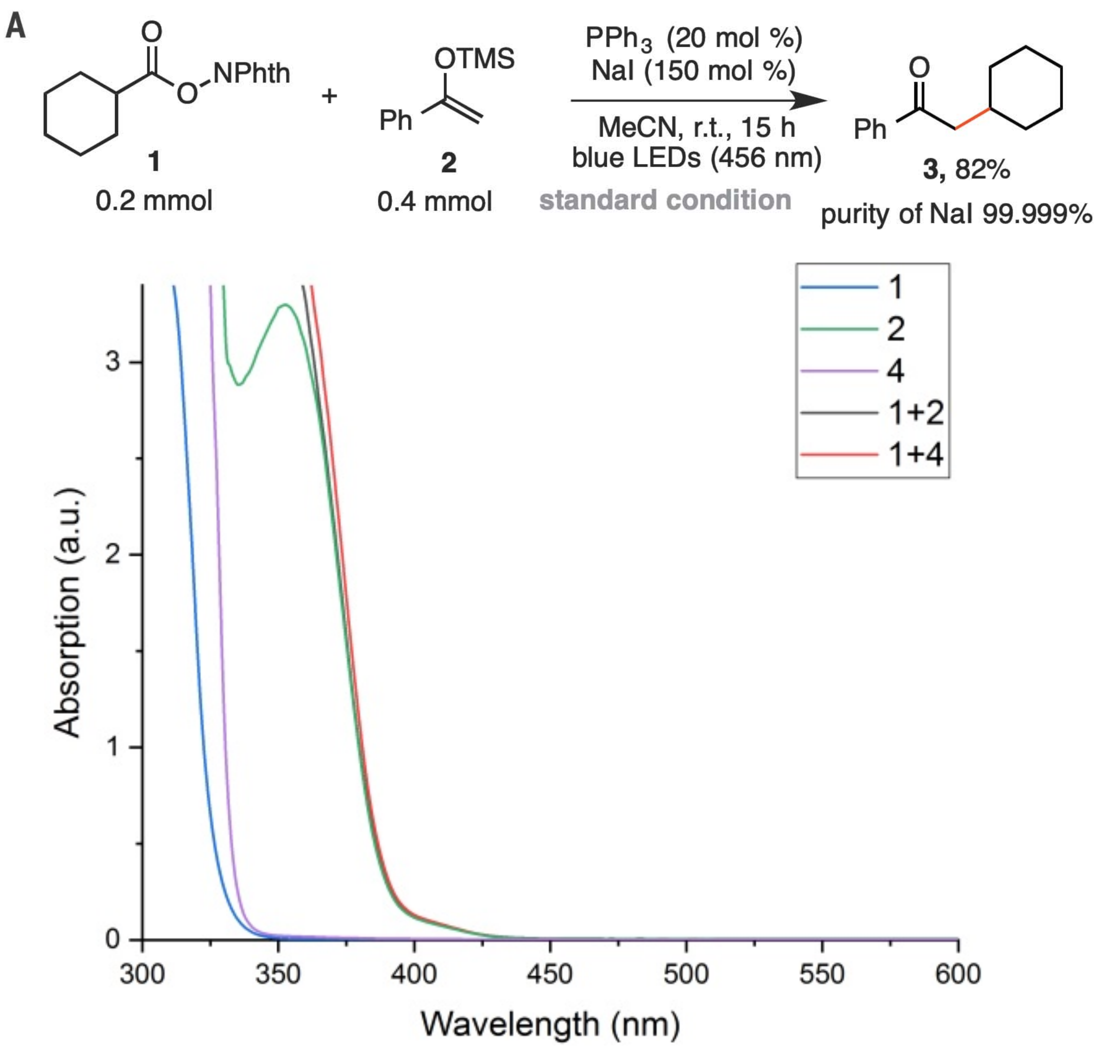


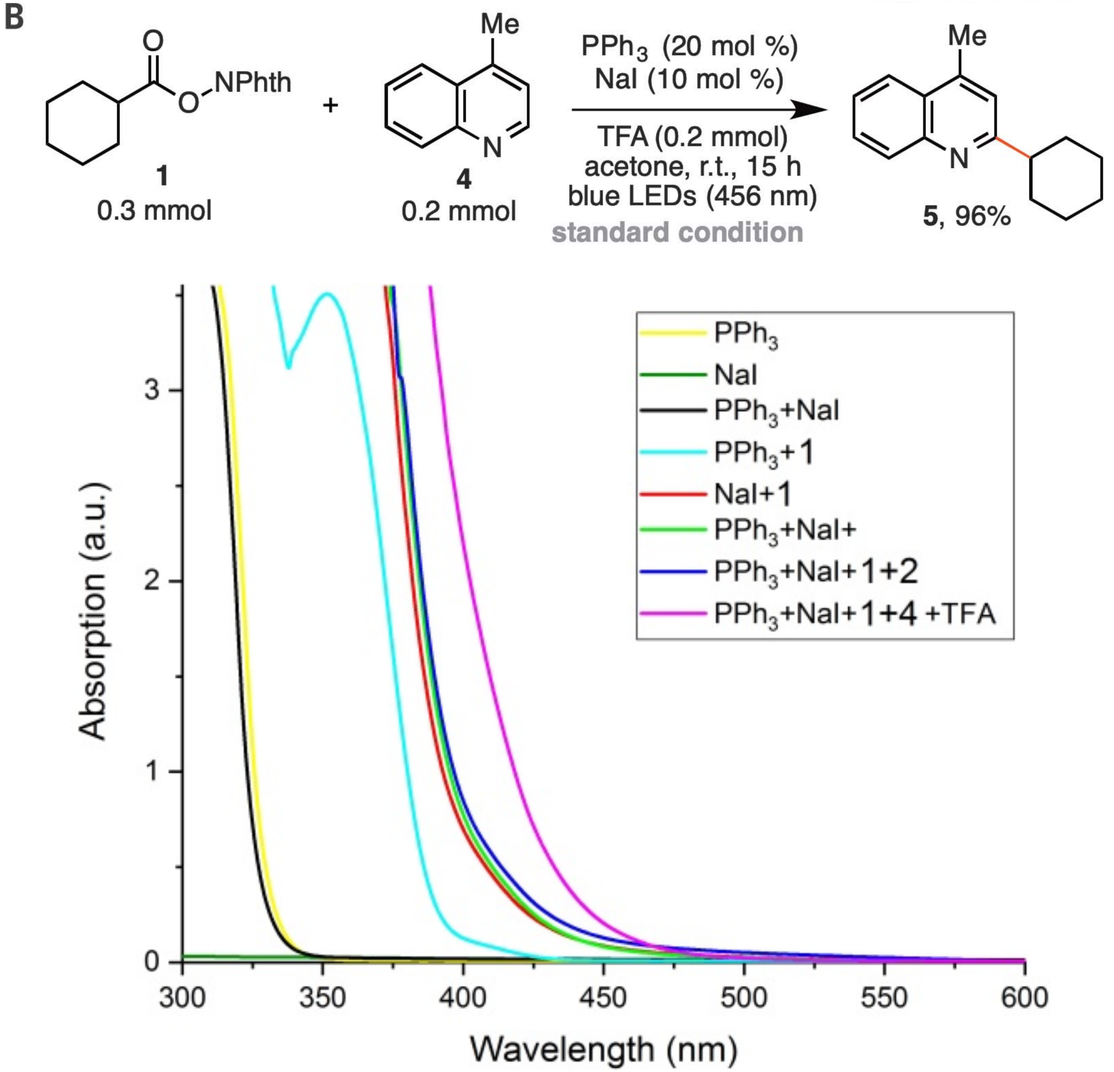
90%	85%	32%	27%	< 5%

Steric hinderance.

× Electron donating capacity.

UV-vis spectroscopy

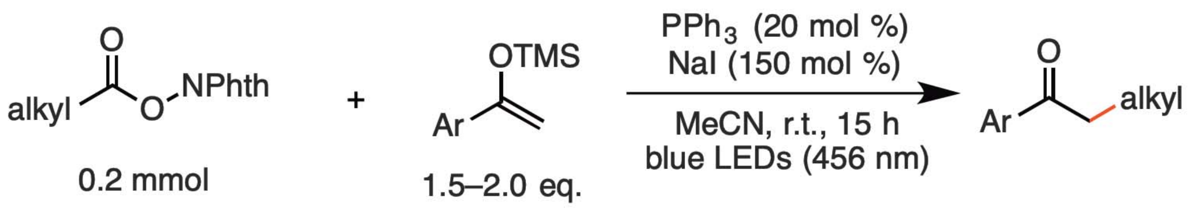


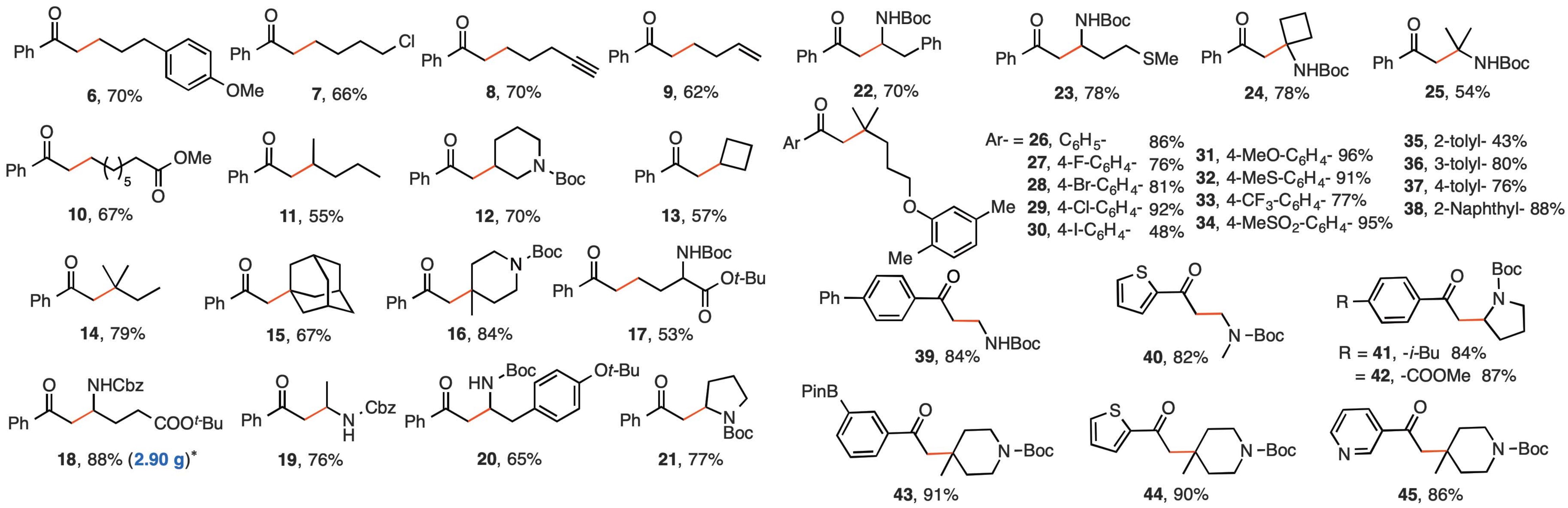


Red shift was observed.

→ Formation of EDA complex between NaI/PPh_3 and RAE.

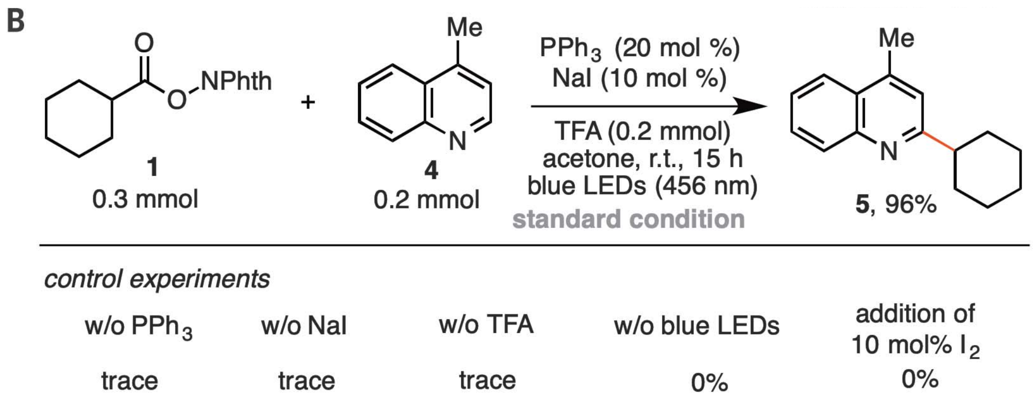
Substrate scope of decarboxylative alkylation of silyl enol ether





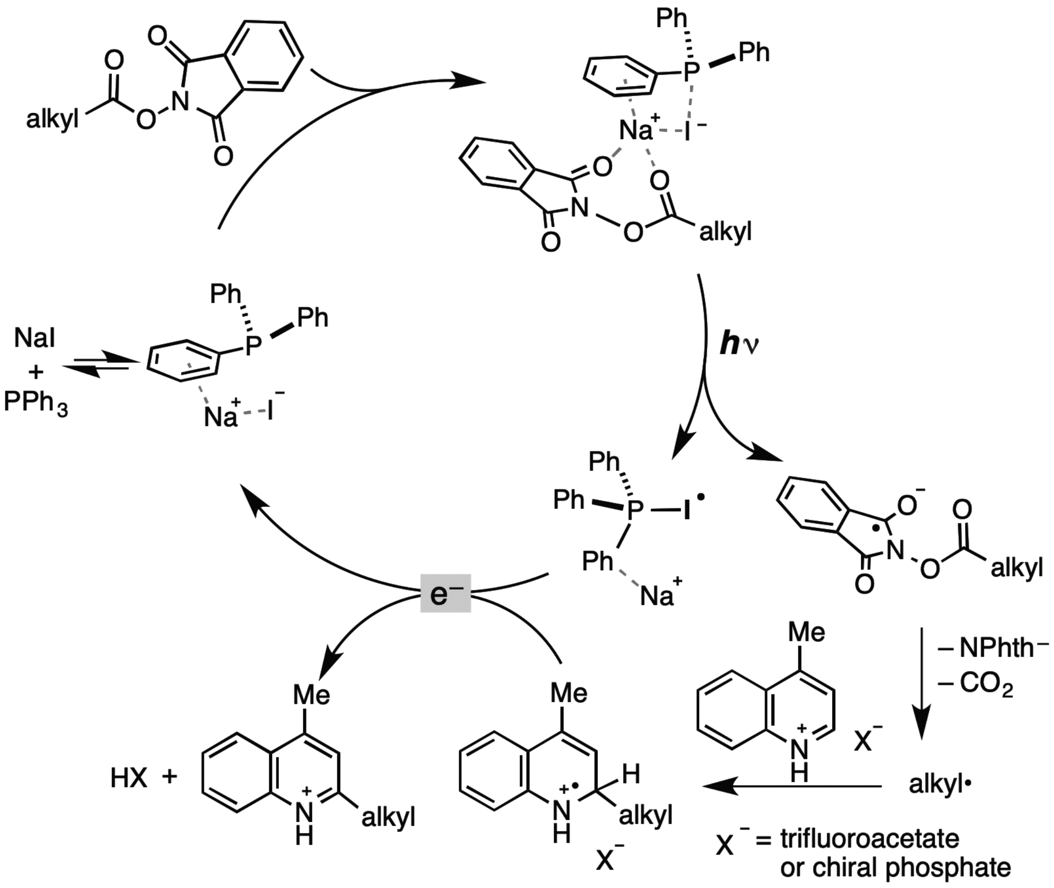
Minisci-type addition to heterocycle

Control experiment.

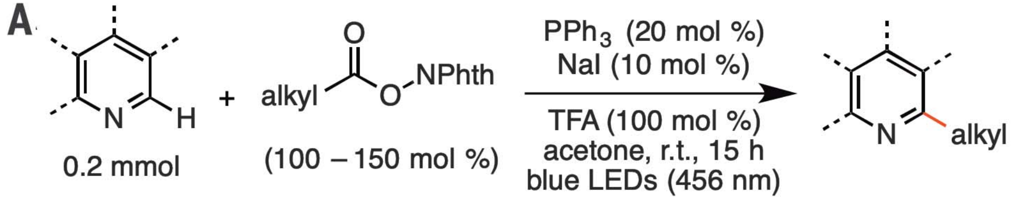


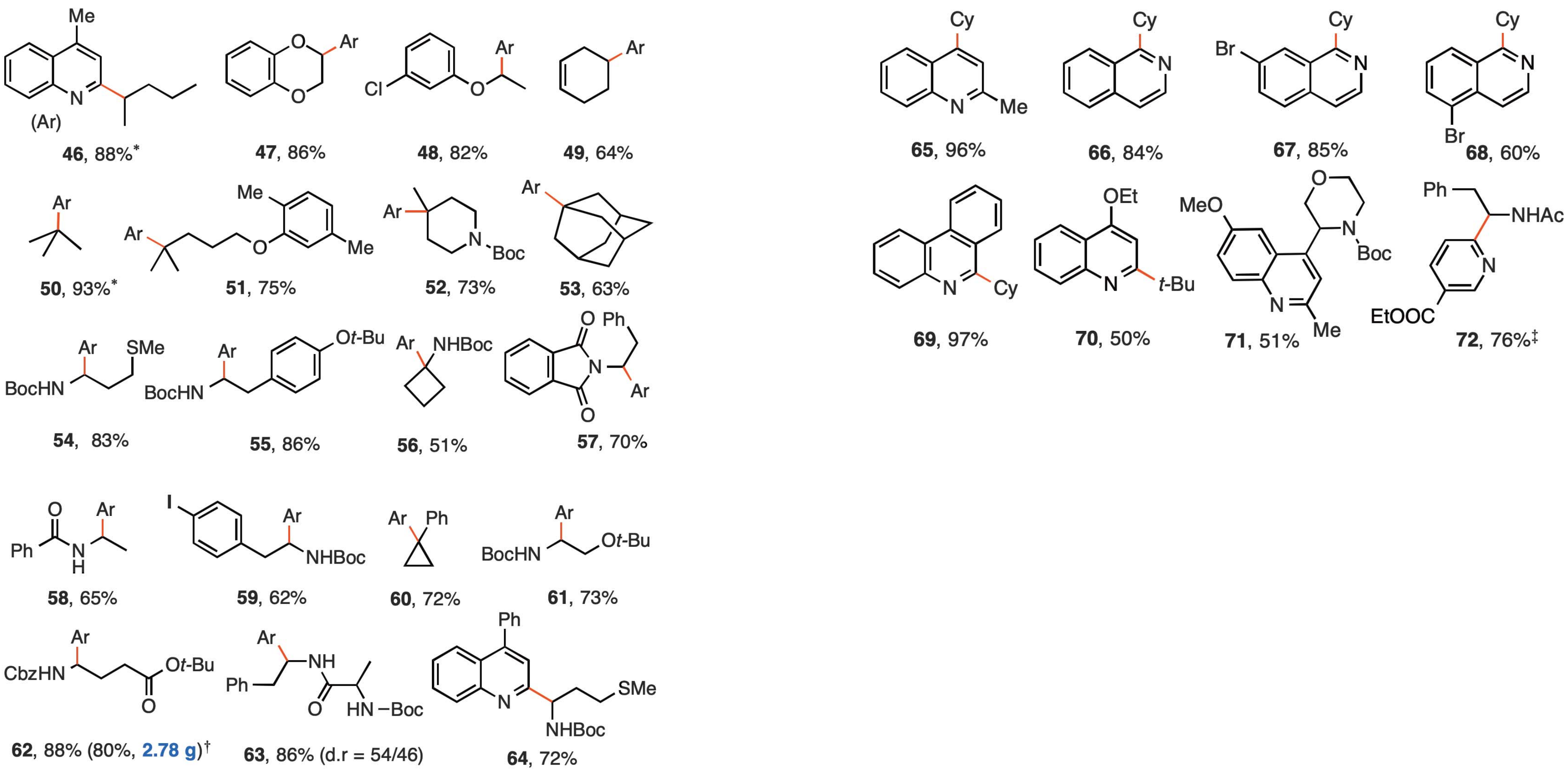
Quantum yield = 0.15
→ Closed catalytic cycle rather than radical chain process

Proposed mechanism

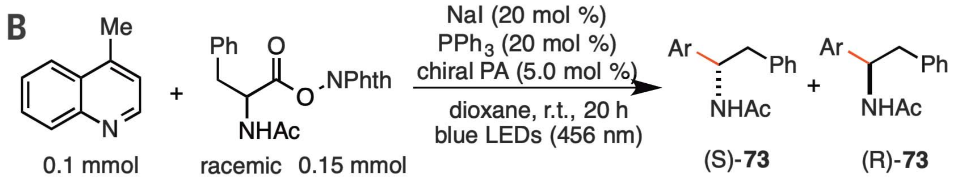


Substrate scope of minisci-type radical addition

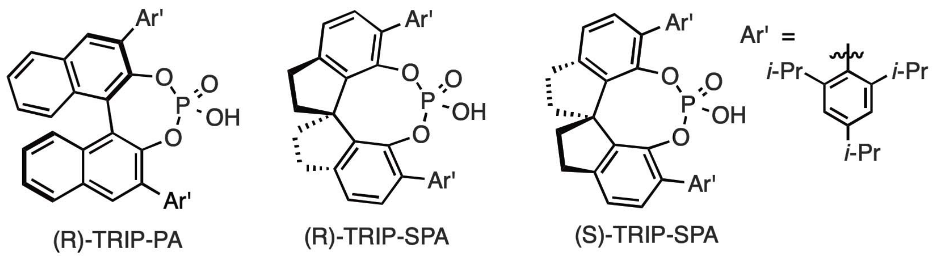




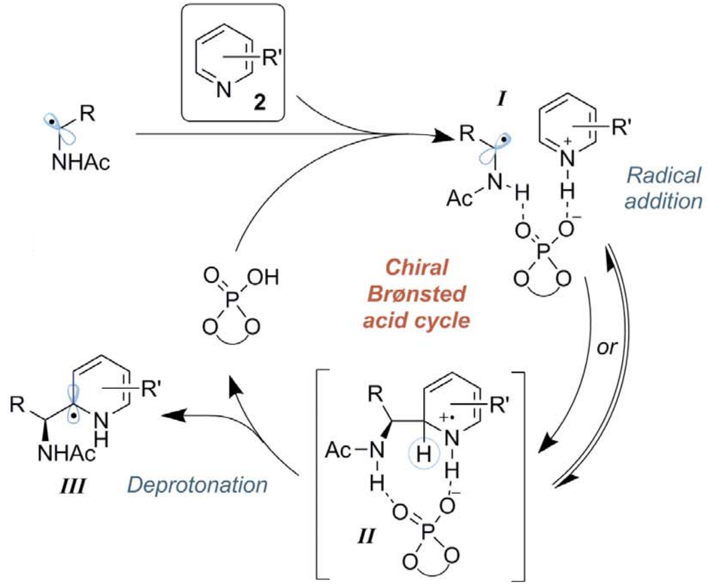
Enantioselective minisci-type reaction



chiral phosphoric acids	yield of (R+S) (%)	*ee* of (S)- (%)	*ee* of (R)- (%)
(R)-TRIP-PA	97	95	–
(R)-TRIP-SPA	96	–	94
(S)-TRIP-SPA	95	94	–

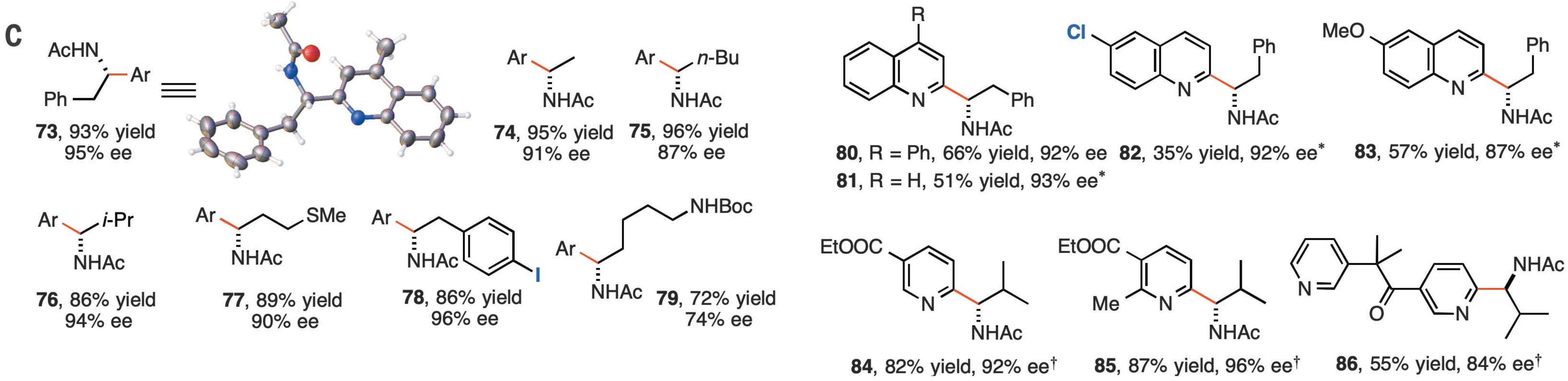


[Reaction mechanism]



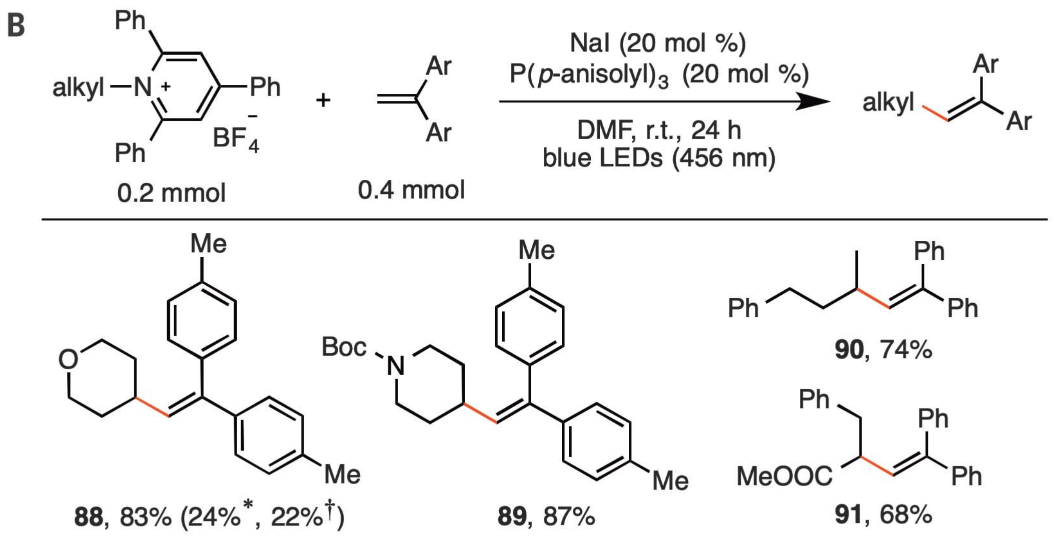
Phipps *et al. Science*. 2018, *360*, 419–422.

[Substrate scope]

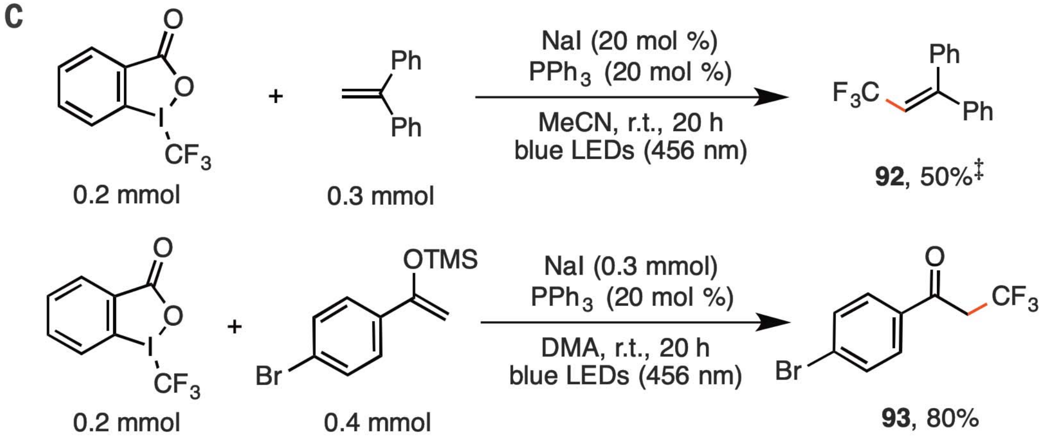


EDA complex formation with other acceptors

EDA complex with pyridinium



EDA complex with Togni's reagent

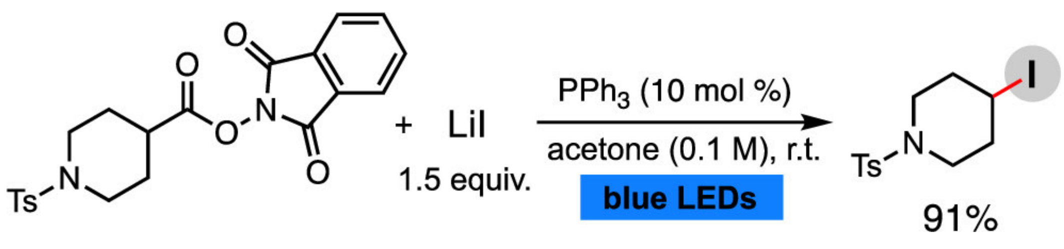


- Applicable to various electron acceptors.

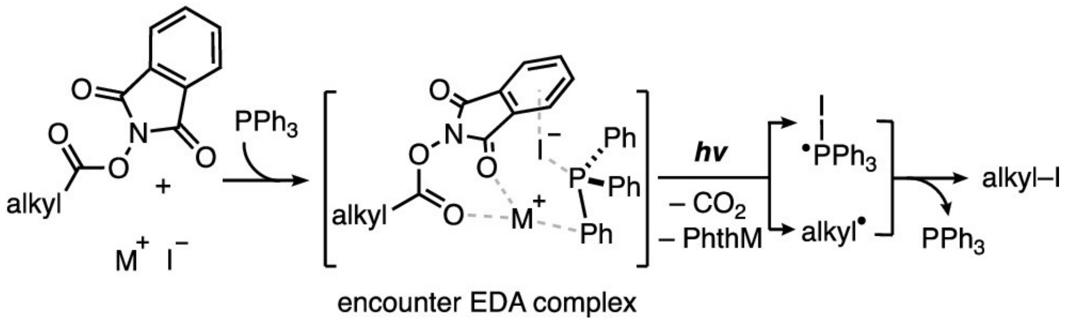
→ Wide substrate activation.

Other applications of NaI/PPh_3 system

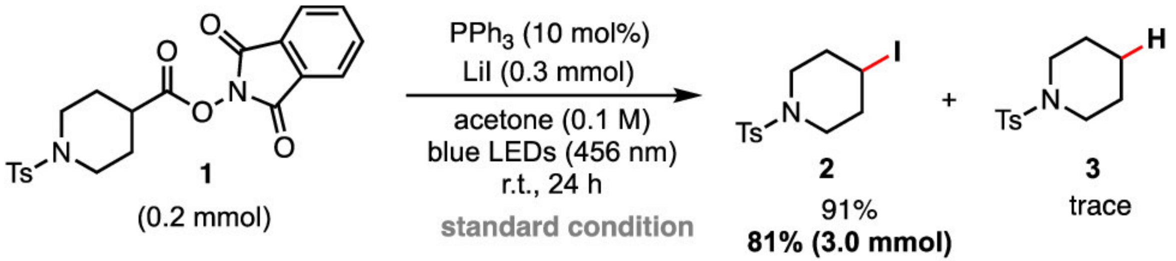
1. Iododecarboxylation using LiI/PPh_3



[Reaction mechanism]



[Investigation of key reaction parameters]

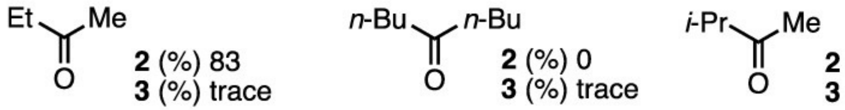


different iodides instead of LiI

	NaI	KI	RbI	CsI	CaI_2	ZnI_2	n-Bu_4NI
2 (%)	72	64	56	10	46	trace	trace
3 (%)	trace	trace	40	40	trace	trace	trace

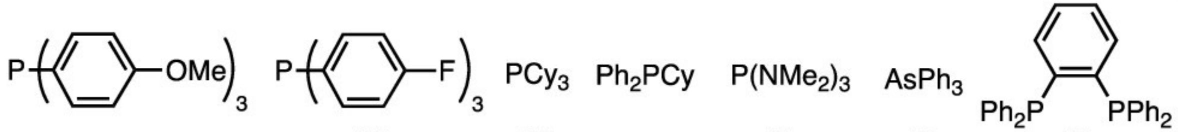
different solvents instead of acetone

	DMF	DMA	MeCN	EtOAc	DCM	$PhCF_3$	THF	dioxane	acetone/THF (v/v = 1/1)
2 (%)	trace	15	8	16	0	0	81	0	92
3 (%)	60	50	trace	trace	0	trace	trace	trace	trace



	Et(C=O)Me	n-Bu(C=O)n-Bu	i-Pr(C=O)Me
2 (%)	83	0	0
3 (%)	trace	trace	trace

different catalysts instead of PPh_3

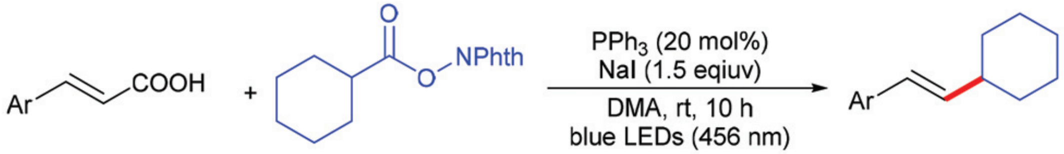


	$P(C_6H_4\text{-}OMe)_3$	$P(C_6H_4\text{-}F)_3$	PCy_3	Ph_2PCy	$P(NMe_2)_3$	$AsPh_3$	1,2-bis(diphenylphosphino)benzene
2 (%)	54	65	39	70	42	16	52
3 (%)	11	trace	trace	8	trace	trace	trace

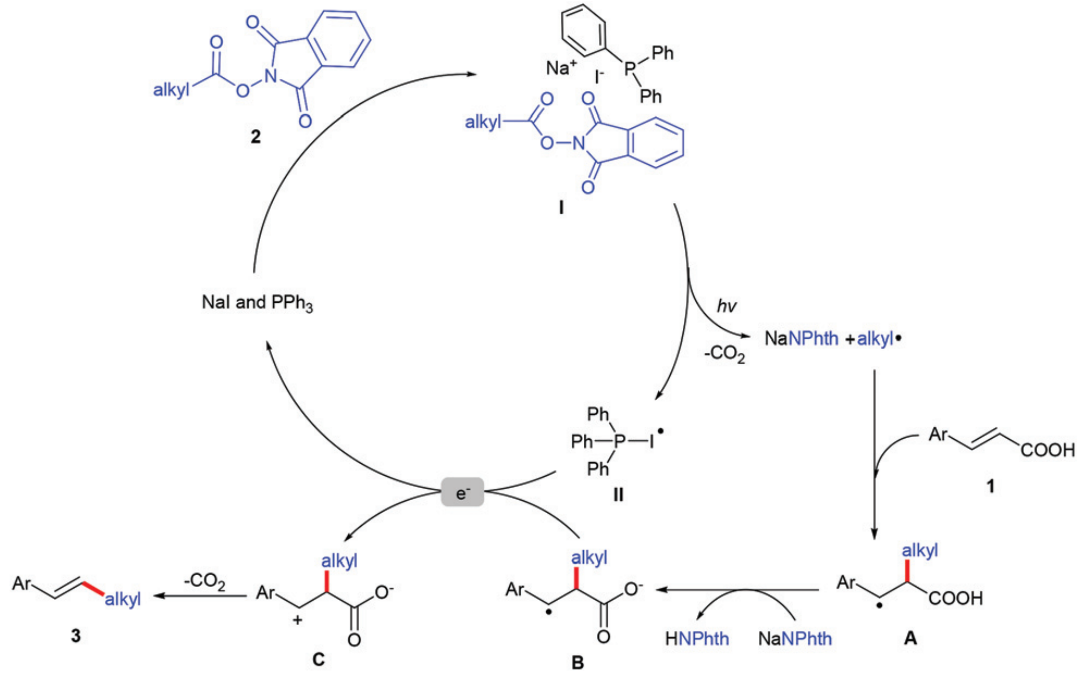
Shang *et al. Org. Lett.* **2020**, *22*, 8572–8577.

Other applications of NaI/PPh_3 system

2. Decarboxylative cross-coupling

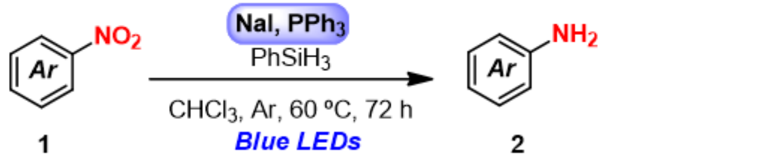


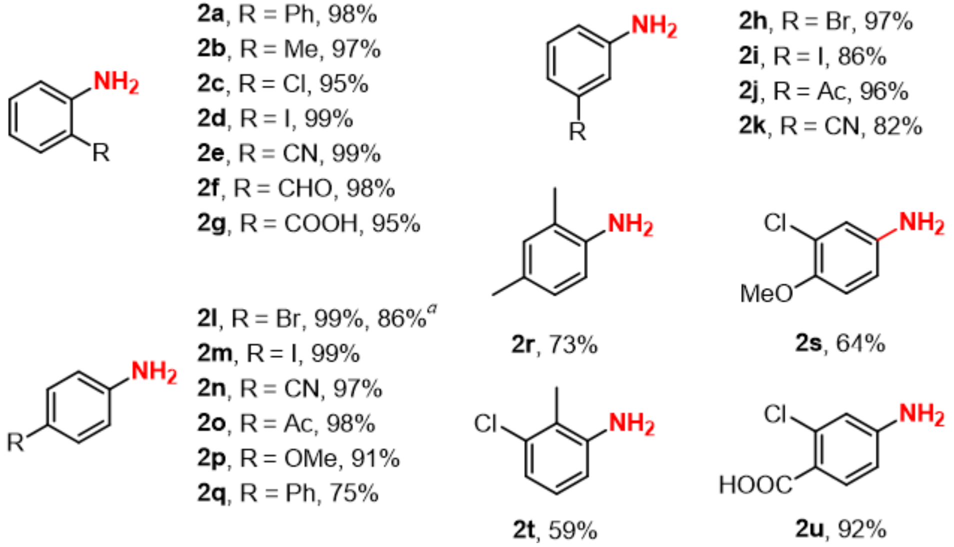
Reaction mechanism

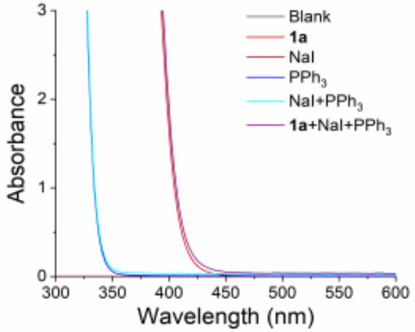


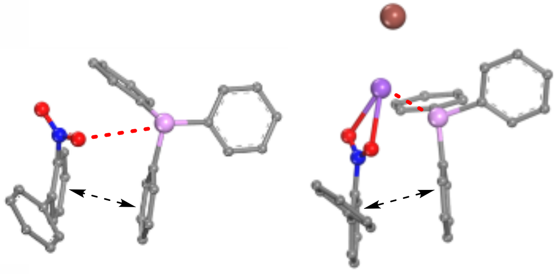
Li *et al. Org. Biomol. Chem.* **2020**, *18*, 5589–5593.

3. Reduction of nitroarene









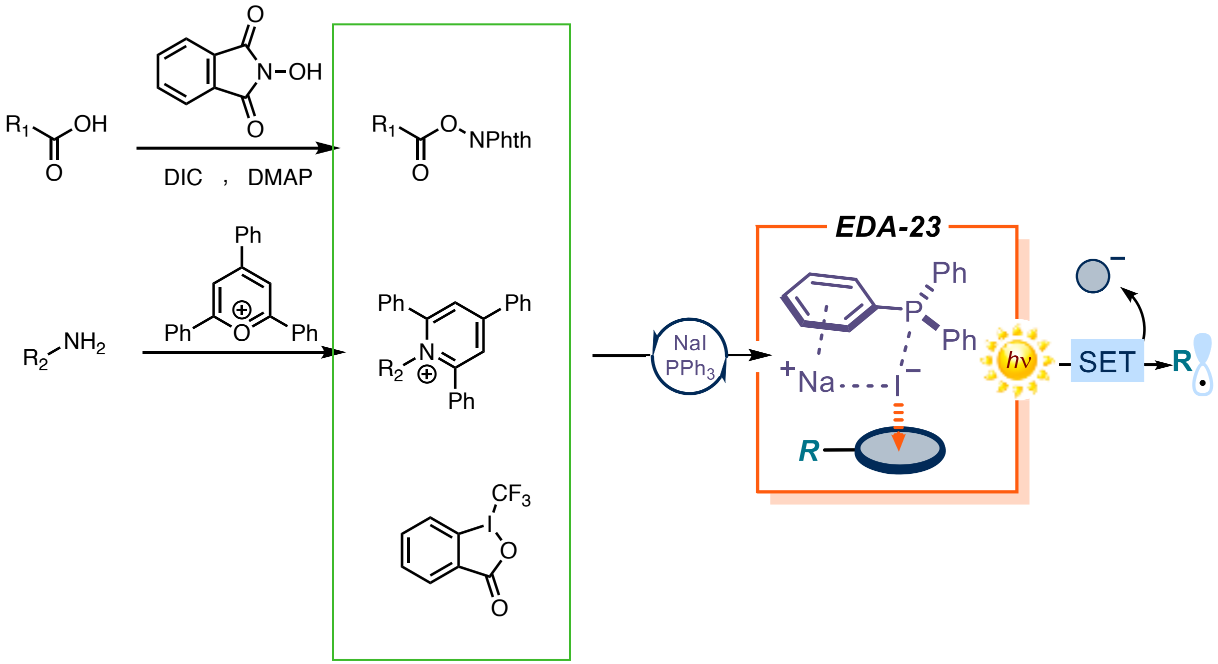
Int-1 (2.2 kcal/mol)

Int-2 (1.7 kcal/mol)

Huang *et al. Org. Lett.* **2021**, *23*, 5349–5353.

Short summary

Catalytic electron donor; NaI + PPh_3

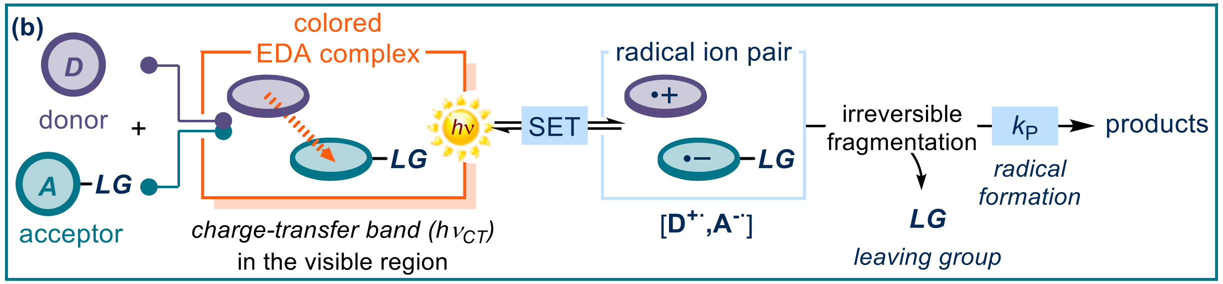


- Combination of the simple compounds (NaI + PPh_3).
  → Application to large-scale synthesis.
- PPh_3 enables SET from iodide to acceptors by visible light irradiation.
- Wide substrate activation.

Contents

General strategy to suppress back electron transfer

[General strategy]

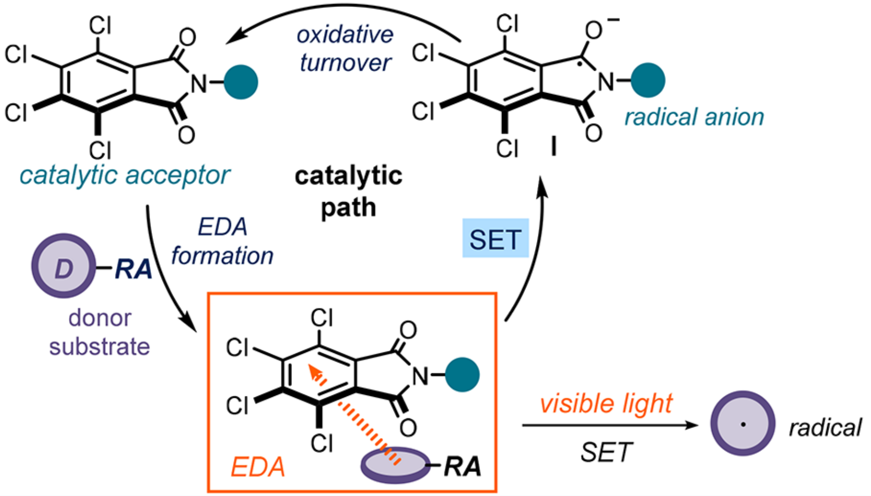


Incorporation of leaving groups in electron acceptor to suppress BET.

→ Requires equivalent amount of electron acceptor.

⇔ Few examples of catalytic electron acceptor.

This work ; Tetrachlorophthalimide as a catalytic electron acceptor.



✓ Catalytic acceptor

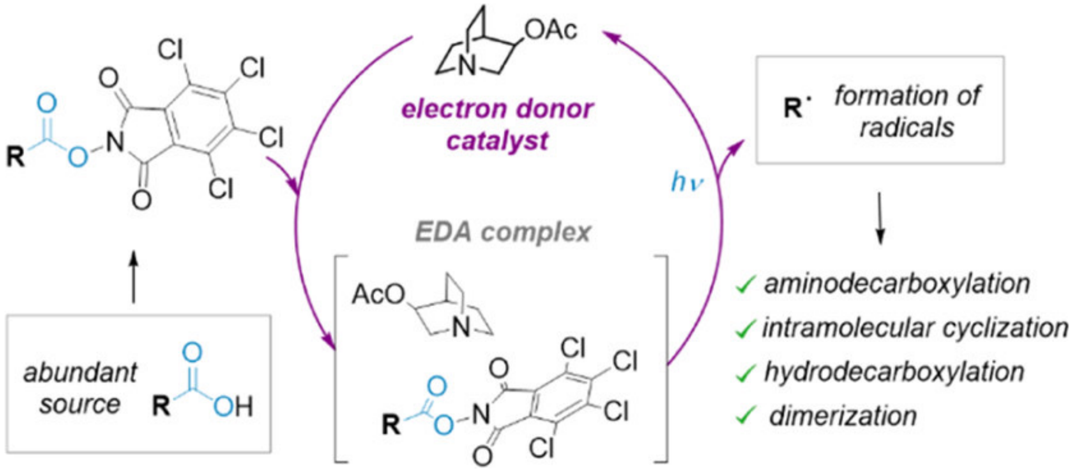
✓ Effective turnover

✓ Wide substrate activation

Melchiorre *et al. J. Am. Chem. Soc.* **2022**, *144*, 8914–8919.

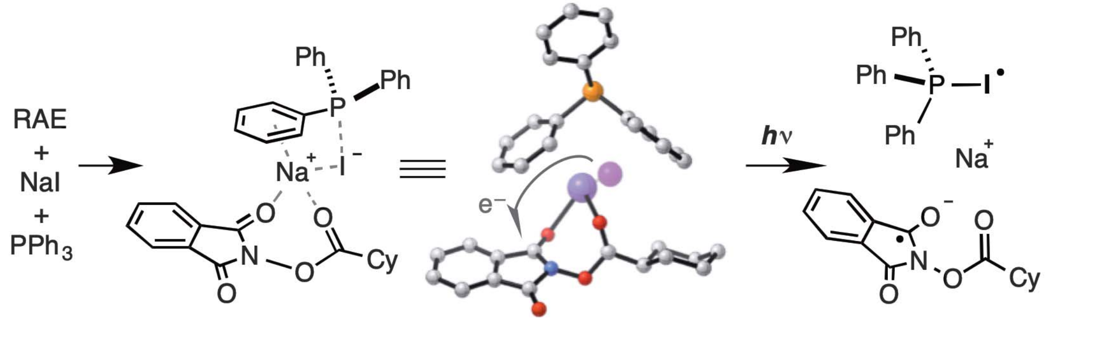
Background

- Quinuclidine + Tetrachlorophthalimide



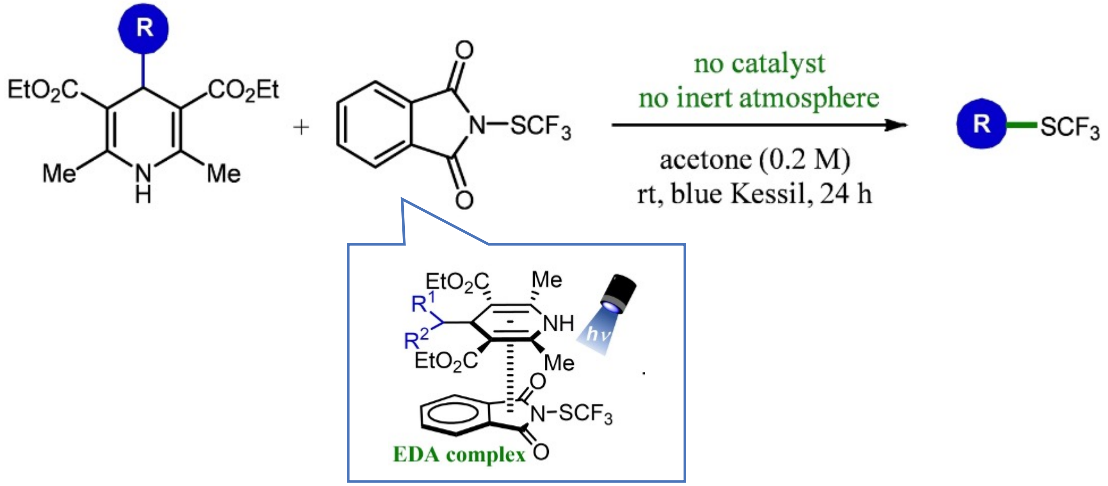
Bach *et al. ACS Catal.* **2019**, *9*, 9103–9109.

- NaI/PPh_3 and Phthalimide



Fu *et al. Science.* **2019**, *363*, 1429–1434.

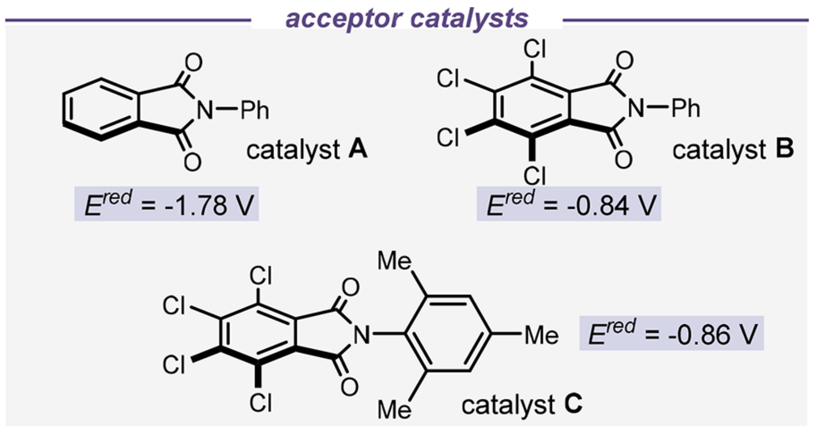
- DHP and Phthalimide

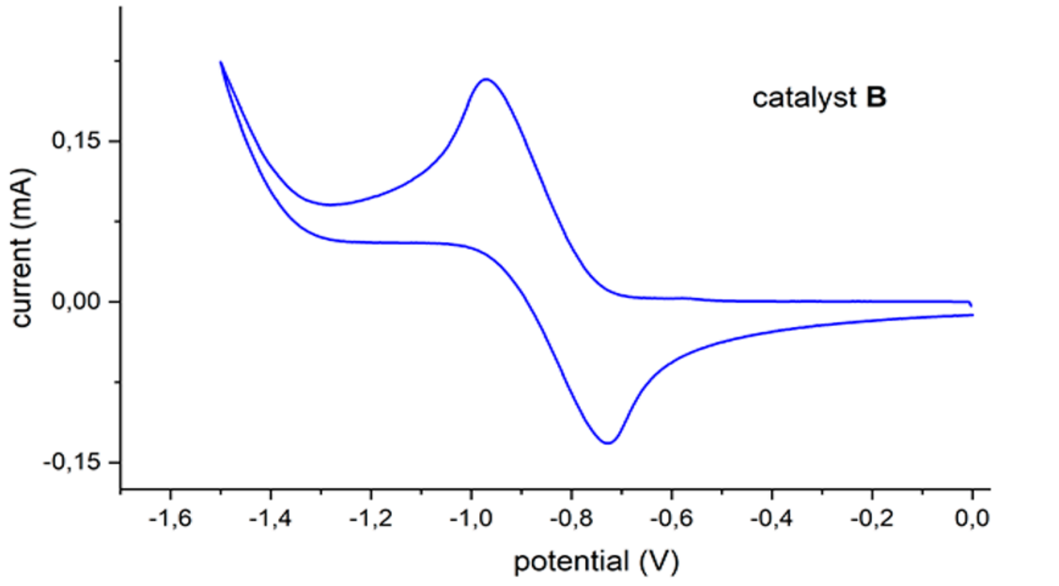


Molander *et al. Adv. Synth. Catal.* **2021**, *363*, 3507–3535.

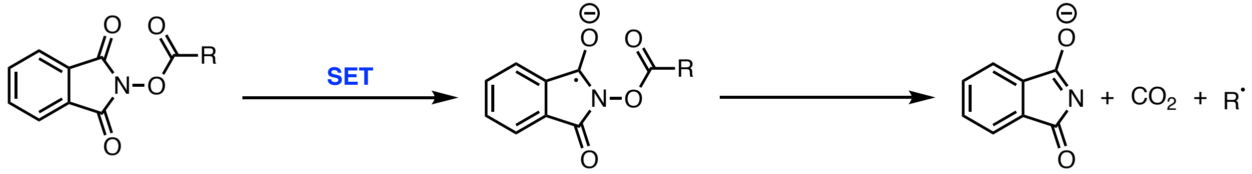
Phthalimide effectively forms EDA complex with various electron donors.

Properties of acceptor catalysts

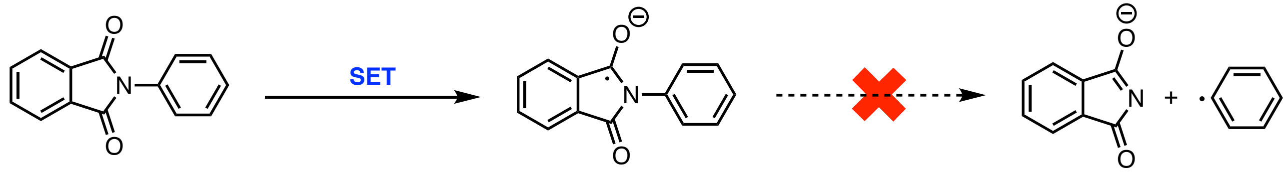




[Redox active ether]



[acceptor catalysts]

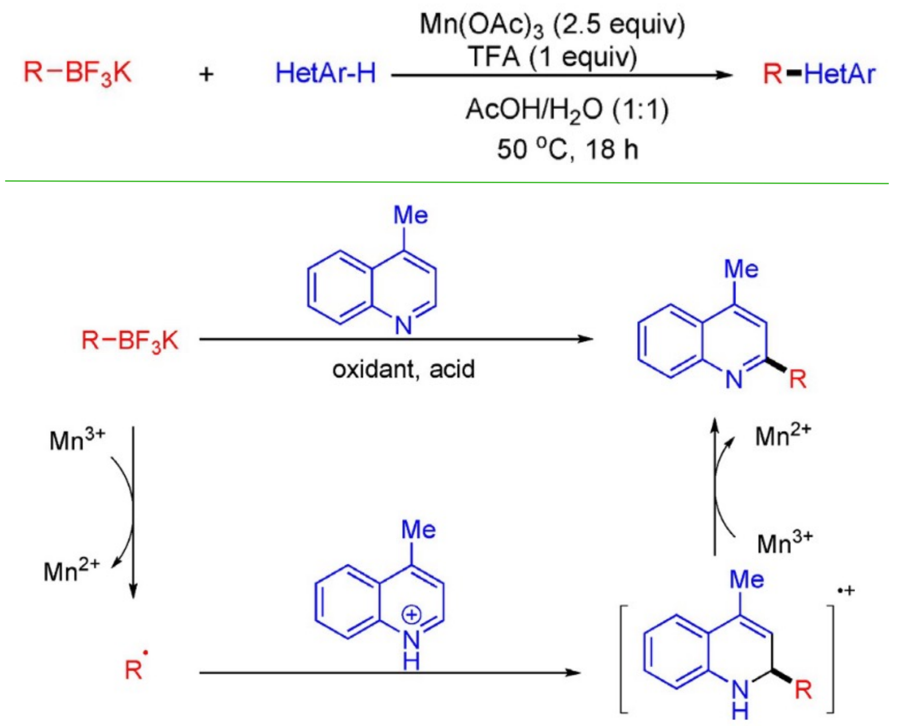


Reduced catalyst B is kinetically stable.

→ Effective turn over.

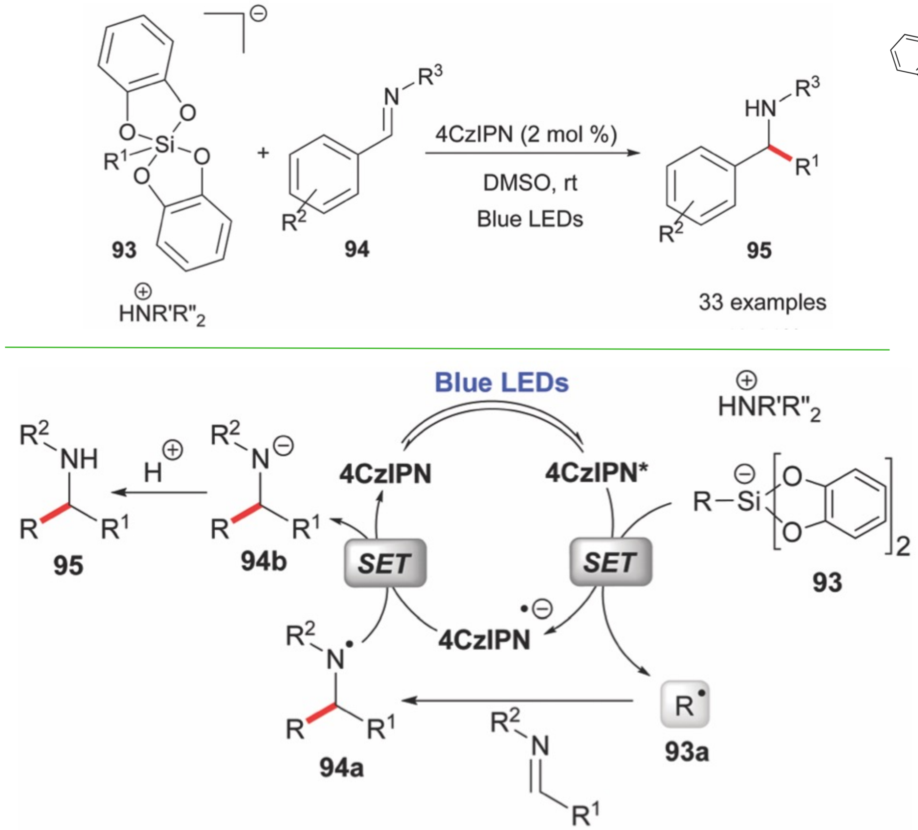
Electron donors as radical source

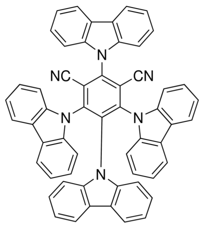
[Trifluoroborate]



Li *et al. Adv. Synth. Catal.* **2018**, *360*, 2781–2795.

[silicate]

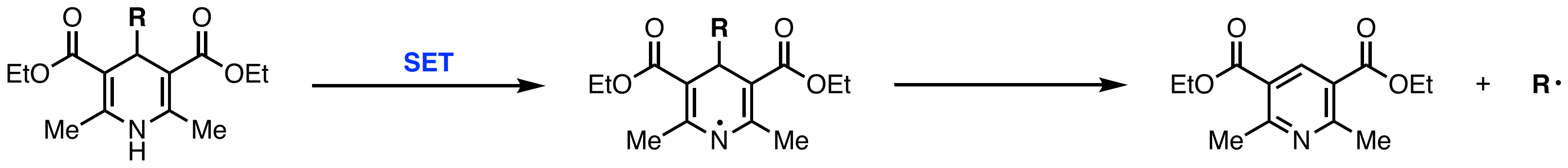




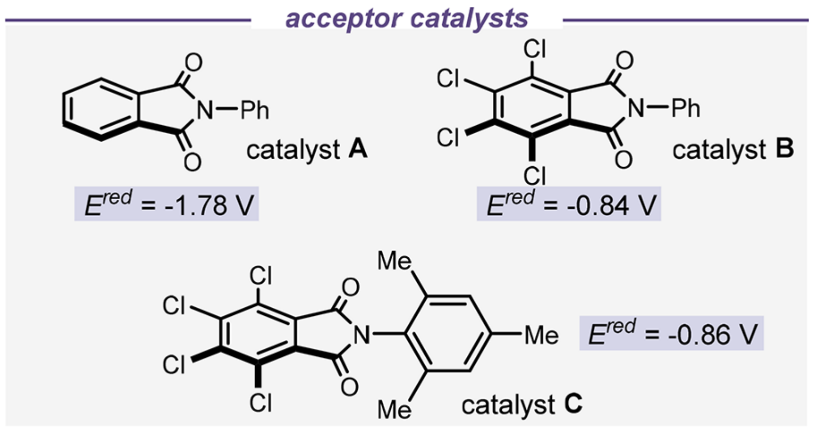
4CzIPN

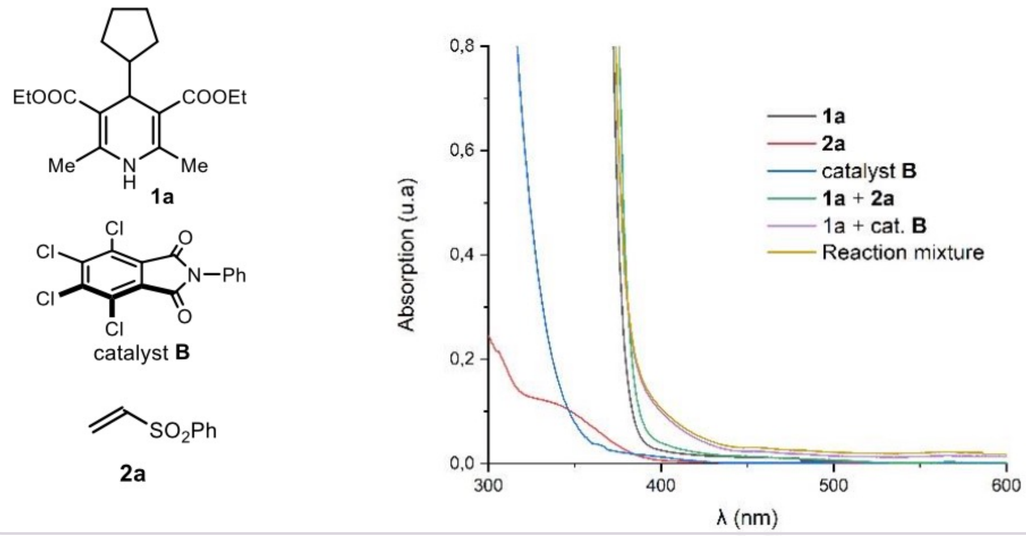
Fensterbank *et al. Chem. Soc. Rev.*, **2022**, *51*, 1470–1510.

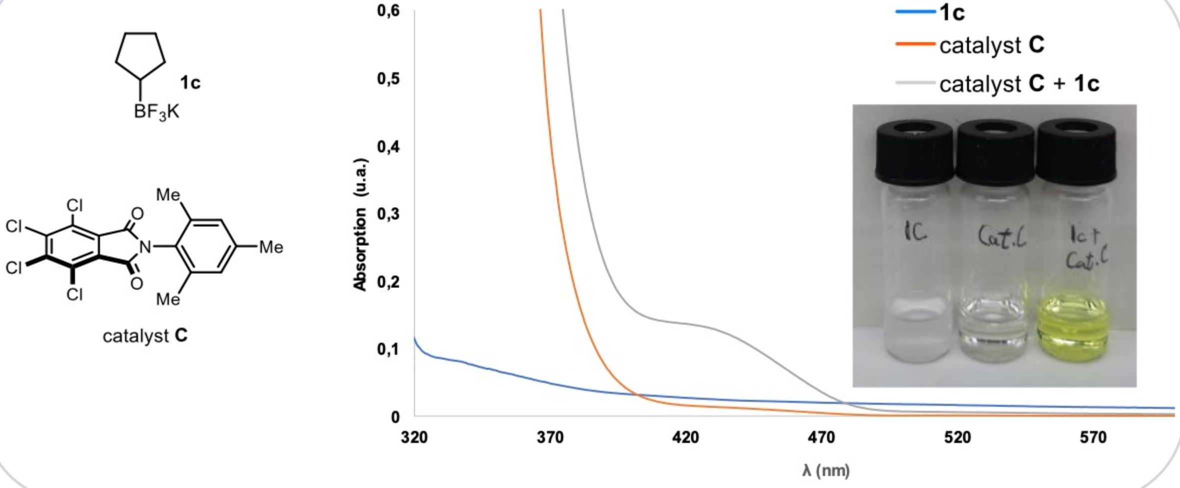
[Dihydropyridine]

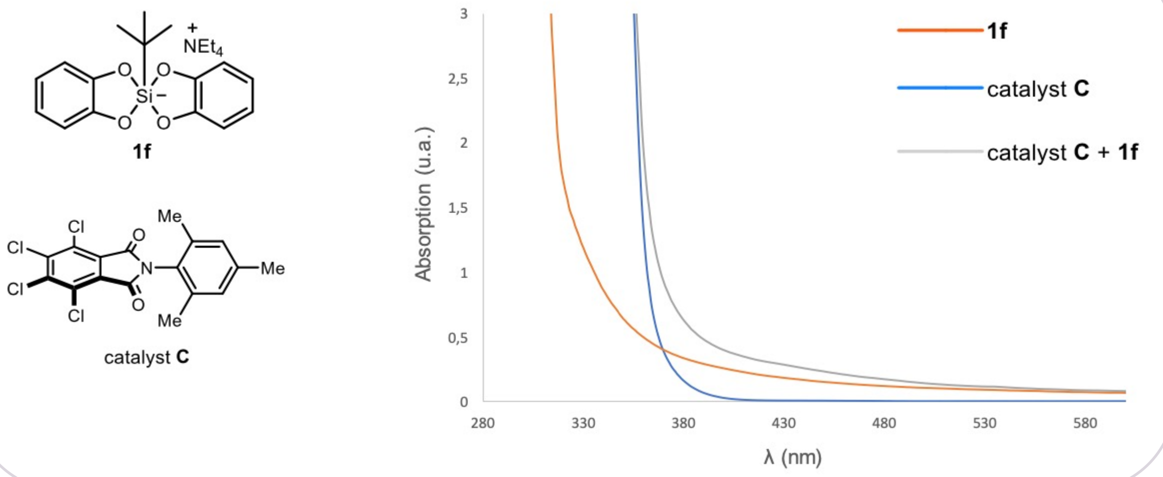


UV-vis spectroscopy







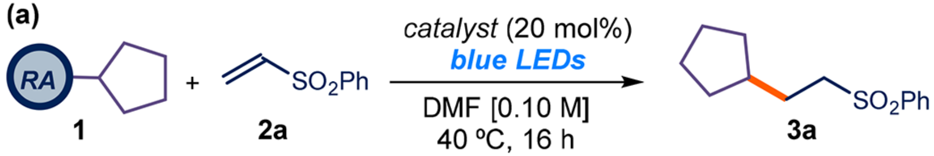


Red shift was observed. → EDA complex formation.

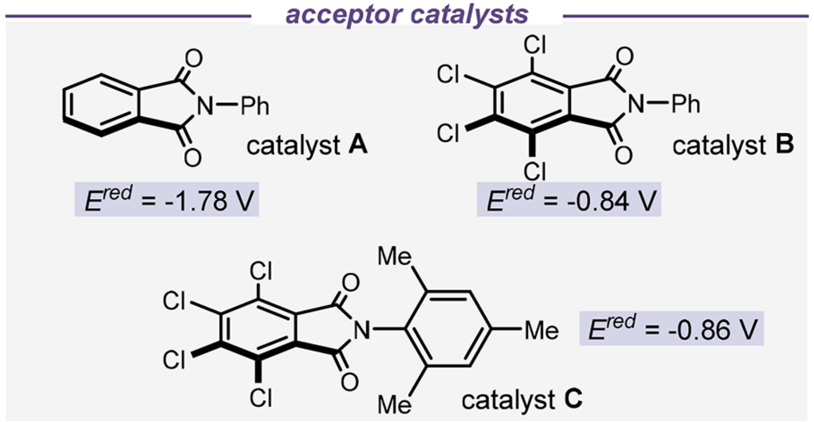
Screening of acceptor catalysts

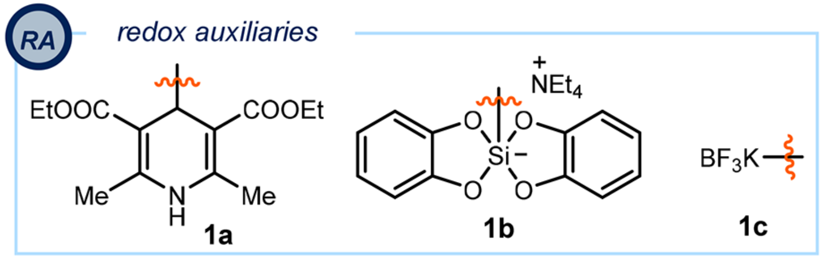
[Giese-type radical addition]

(a)



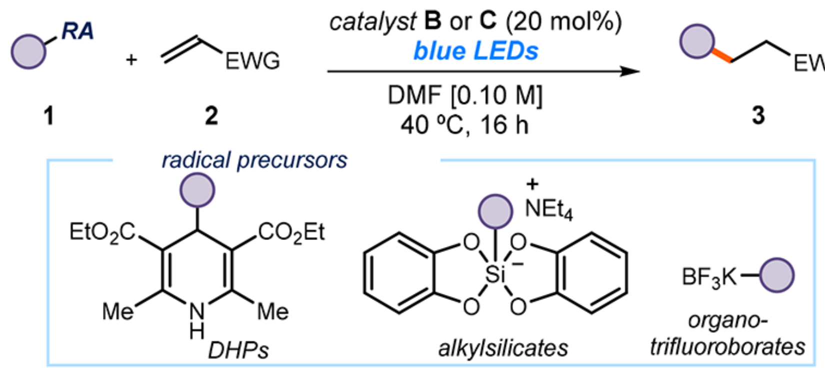
entry	catalyst	1	deviation	yield **3a** (%)
1	**A**	**1a**	none	0
2	**B**	**1a**	none	89(87)*
3	**C**	**1a**	none	85
4	**B**	**1b**	none	52
5	**C**	**1b**	none	74 (70)*
6	**B**	**1c**	none	41
7	**C**	**1c**	none	64 (63)*
8	**B**	**1a**	green light	39
9	**C**	**1b**	green light	55
10	**B**	**1c**	green light	27
11	**C**	**1a-c**	no light	0
12	none	**1a-c**	none	0



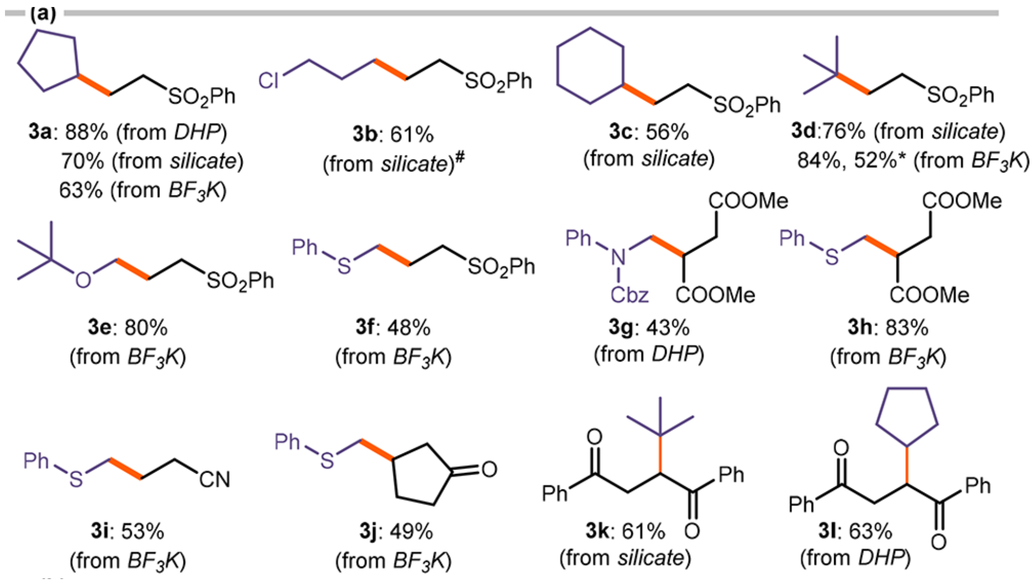


- Catalyst B and C afforded product in high yield.
- Radical generation via EDA complex. (entry 8~10)

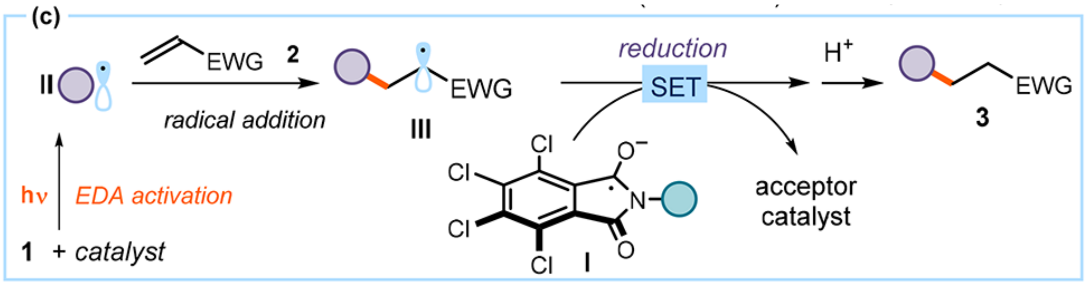
Substrate scope of Giese-type radical addition



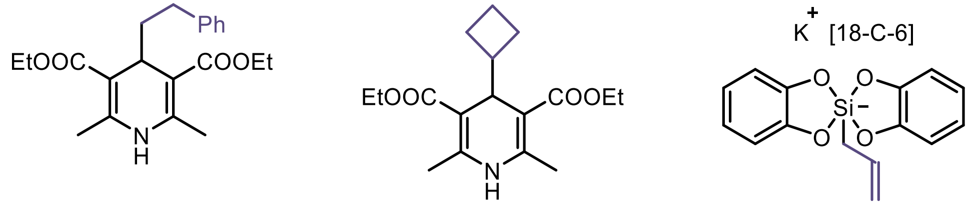
[Substrate scope]



[Reaction mechanism]



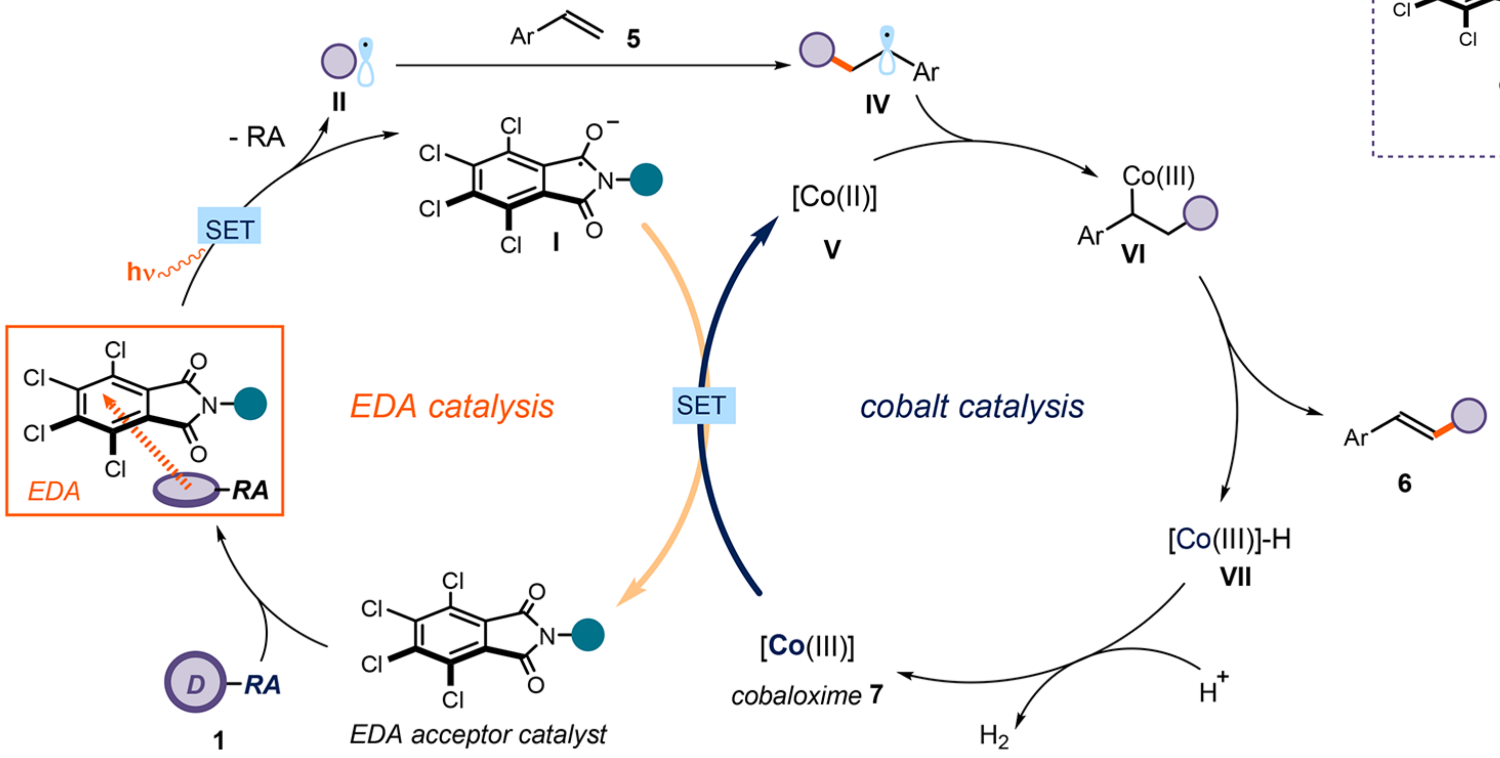
Unsuccessful substrates

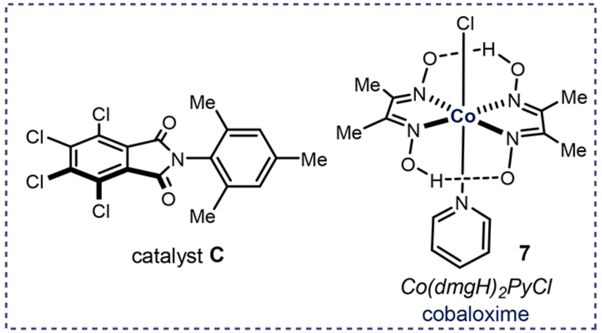


Quantum yield = 0.04

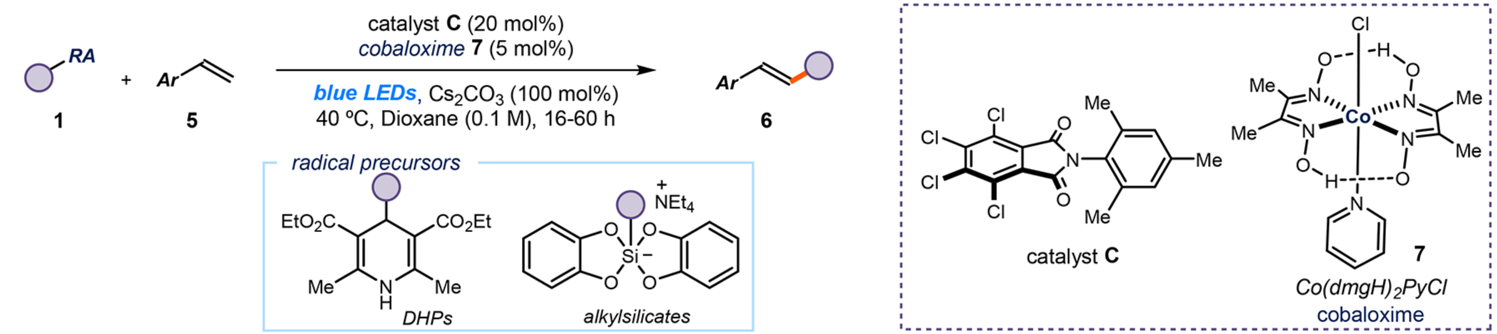
Heck-type reaction with cobaloxime

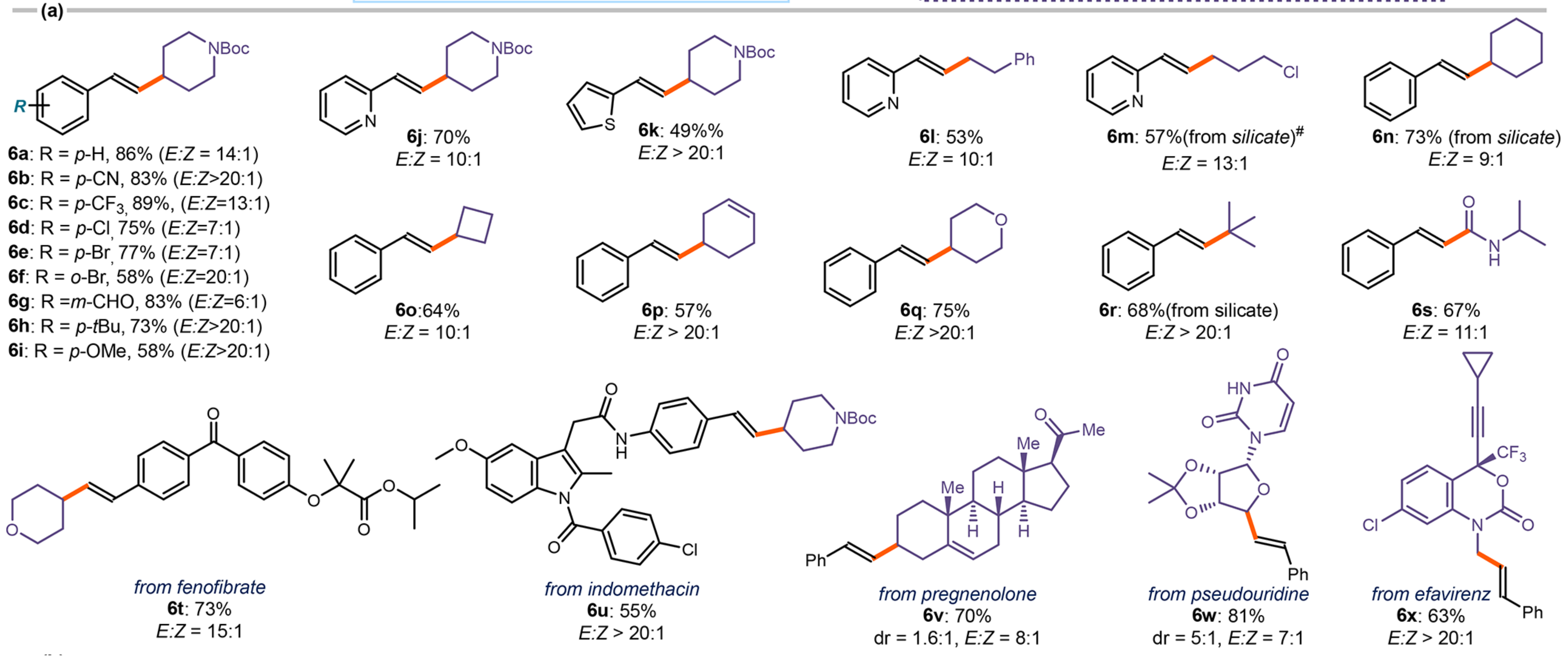
[Reaction design]



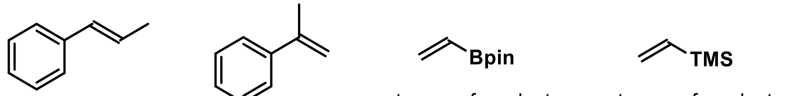


Substrate scope of Heck-type reaction





Unsuccessful substrates



traces of product　　traces of product

Quantum yield = 0.01

Contents

Summary & perspective

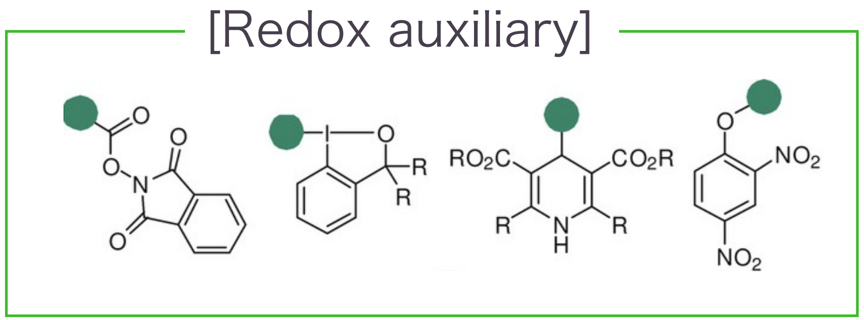
[NaI and PPh_3]

- Tricomponent EDA complex.
- Industrial application to large-scale synthesis.
- Applicable to wide range of electron acceptor.

[Tetrachlorophthalimide]

- One of the few examples of catalytic acceptors.
- Applicable to wide range of electron donors.
- Combination with metal-based catalytic system.

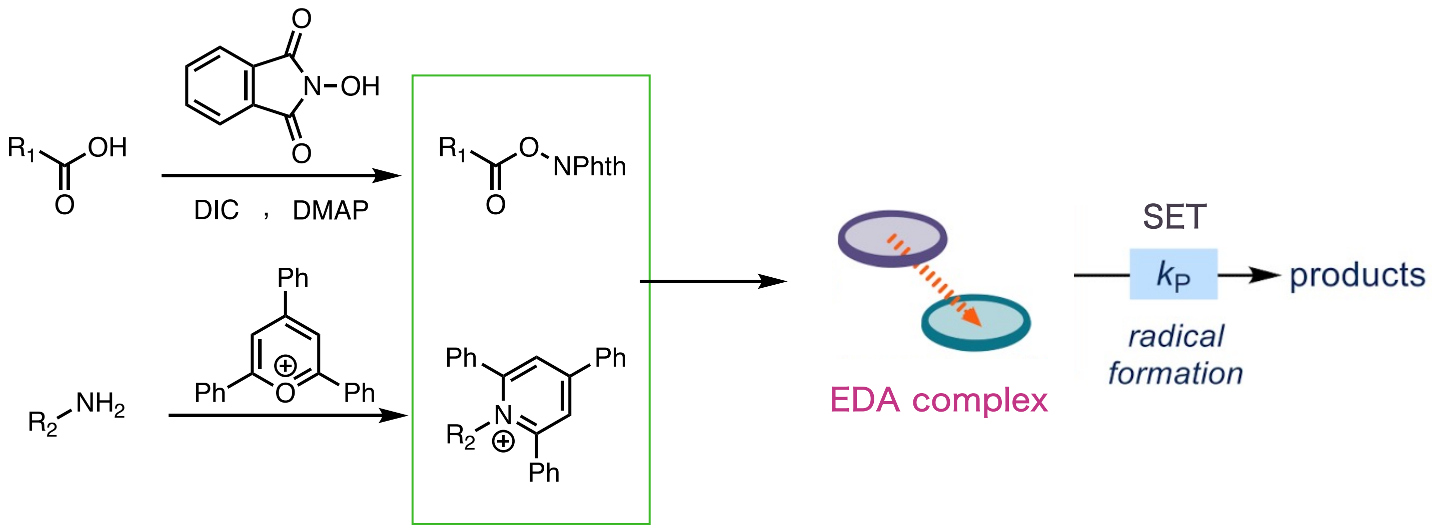
Perspective



- Relying on existing redox auxiliaries.

→ Investigation of new EDA-active structure(redox auxiliary).

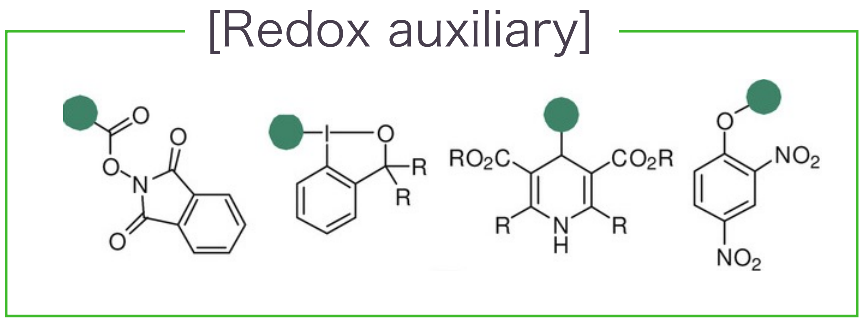
- Radical generation without conversion to redox auxiliary.



Perspective

- Relying on existing redox auxiliaries.

→ Investigation of new EDA-active structure(redox auxiliary).



- Radical generation without conversion to redox auxiliary.