Photoredox Catalyst in Organic Chemistry
~Toward Green & Efficient Reaction~

$Ru(bpy)_3^{2+}$ $Ir(ppy)_2(dtb-bpy)^+$
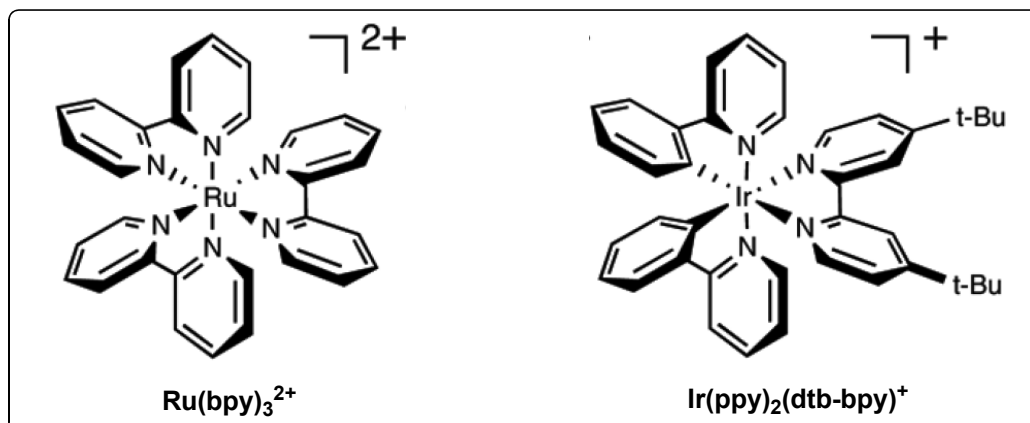
Photochemical reaction has a large potential in green chemistry. In various areas, photochemical energy was used. Nature's ability to convert solar energy to chemical energy in photosynthesis has inspired the development of a host of photoredox systems in efforts to mimic this process.

Today's theme "Photoredox Catalyst" is discovery and development with a lot of potential of such Nature-mimic system in all area of science, including organic chemistry.

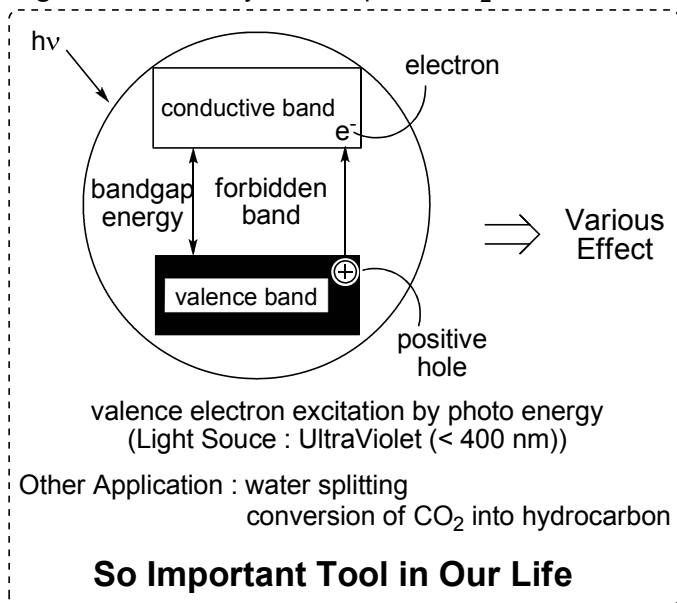**Contents**

1. Introduction -Photochemistry-

Photocatalyst   (ref. Itano's Lit. (M2 Part))

・Inorganic Photocatalyst

Photocatalyst is applied to many fields;

antibacterial, sterilization, deodorization, antifouling, antifogging, water / air purification...

$\Longrightarrow$ TiO_2 is employed in most area.
(Semiconductor)

Figure. Photocatalysis Principle of TiO_2

valence electron excitation by photo energy
(Light Souce : UltraViolet (< 400 nm))

Other Application : water splitting
conversion of CO_2 into hydrocarbon

So Important Tool in Our Life

・Organic Photocatalyst (Sensitizer)

Most of photo reactions of organic compound undergo in Triplet Excited State.

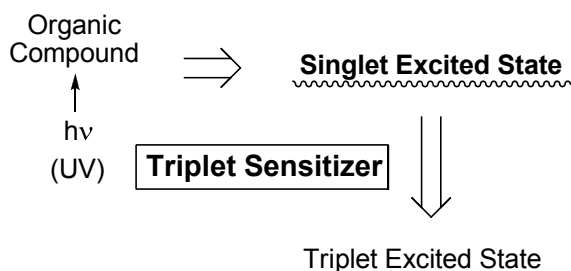Organic Compound $\Longrightarrow$ **Singlet Excited State**

$h\nu$ (UV) → [**Triplet Sensitizer**] $\Downarrow$

Triplet Excited State

Figure. Example of Triplet Sensitizer

Examples;

Benzophenone (BP)   Anthraquinone (AQ)
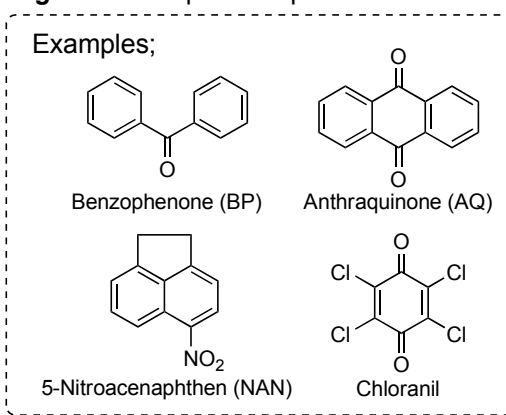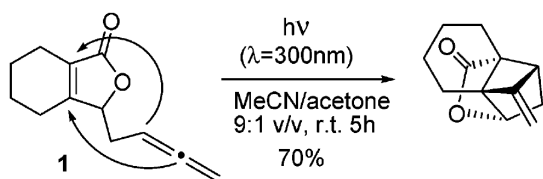
5-Nitroacenaphthen (NAN)   Chloranil

Photo Reaction (Photochemistry in Organic Reaction)

Chem. Rev., **2007**, *107*, 2725.
Chem. Rev., **2008**, *108*, 1052.

Scheme. Example of Photo Reaction

・[2+2] Photocycloaddition

$h\nu$
(λ=300nm)
MeCN/acetone
9:1 v/v, r.t. 5h
70%

1

・Intermolecular Addition onto Unsaturated C-C Bond

3

BP, $h\nu$
C_6H_6

90%

Ad = 1-Adamantyl
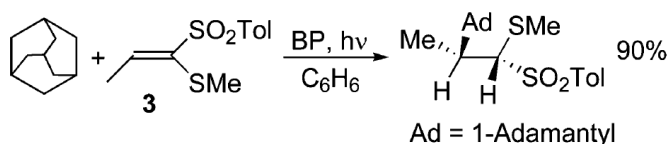
・Electron-Transfer Reaction

131   +   **132**
$h\nu$
(λ=350nm)
sens.
94%

sens. : **134**

133a   **133b**

1   :   1.2

(-)-Isoretronecanol   (+)-Laburnine
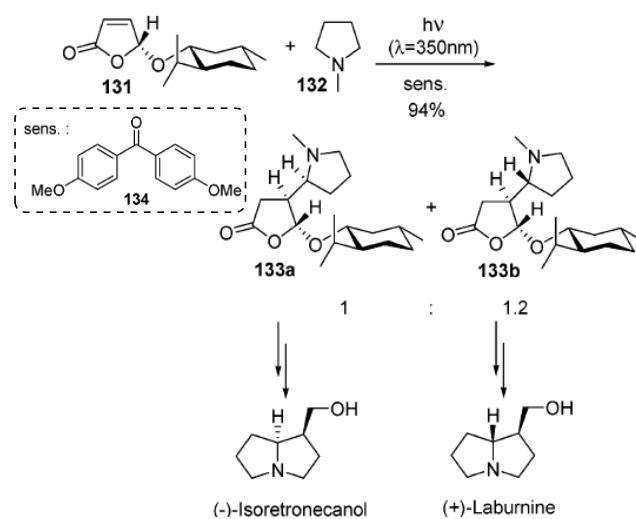
These reactions' "reagent" is light source. **These are high atom economy and green reaction.**

But, Most light source is ultraviolet, which is reactive for unsaturated bond and some functional group, and is not Nature's light.

‖
Visible light

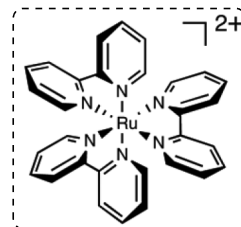# 2. Photoredox Catalyst

Catalyst that shows oxidative and reductive property by absorbing <u>visible</u>-photoenergy

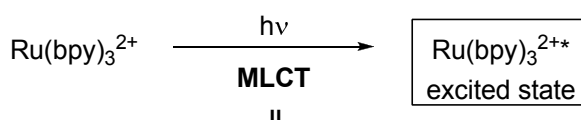Most of photoredox catalyst is metal-ligand complex molecules.
Metal : Ru, Ir, Cr, Rh, Co...   Ligand : 2,2'-bipyridine (bpy), 1,10-phenanthroline (phen)...

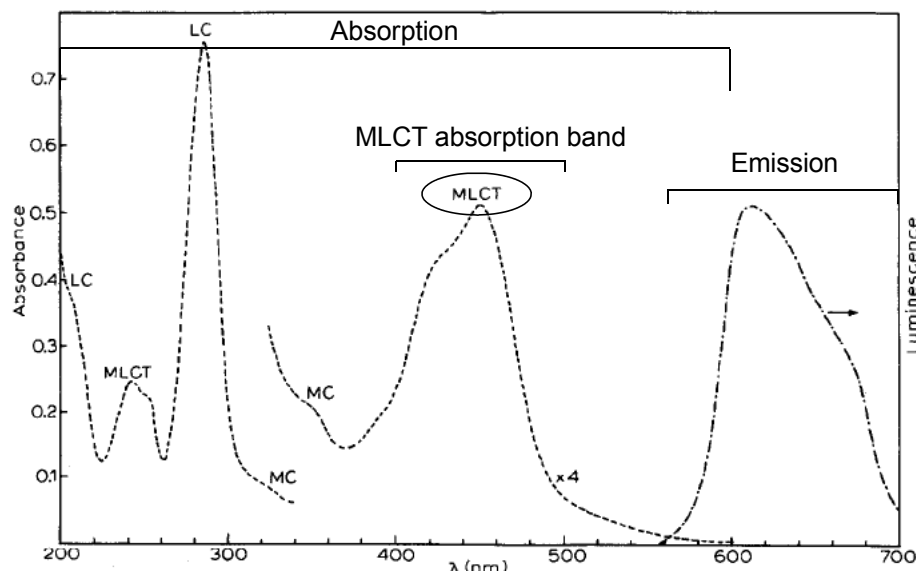Among them, **Ru(bpy)$_3$$^{2+}$** is most studied <u>one-electron</u> <u>photoredox</u> <u>catalyst</u>.

$$[Ru(bpy)_3]^{2+}$$

2-1. Photophysical Property of Ru(bpy)$_3$$^{2+}$

K. Kalyanasundaram, *Coord. Chem. Rev*., **1982**, *46*, 159.
A. Julis *et al*., *Coord. Chem. Rev*., **1988**, *84*, 85.

<u>Photoabsorption</u> <u>and</u> <u>Excited</u> <u>State</u>

$$Ru(bpy)_3^{2+} \xrightarrow[\textbf{MLCT}]{h\nu} \boxed{\begin{array}{c} Ru(bpy)_3^{2+*} \\ \text{excited state} \end{array}}$$

Metal-to-Ligand Charge Transfer —— 2+ charge of Ruthenium is transferred to Ligand (trisbipyridine) by photoenergy. so high energy state, triplet excited state.

Figure. Absorption and emission spectrum for Ru(bpy)$_3$$^{2+}$ in aqueous solution at room temperature along with the assignments for the various bands.

MLCT excited state absorption;
λ_{max} = 452 nm

Visible Light

⇓

By irradiated with visible light, Ru(bpy)$_3$$^{2+}$ is excited high energy state.

Excited state energy was computed;
$E_0[Ru(bpy)_3^{2+/2+*}]$ = -2.10 V
(*vs.* SCE in MeCN)

<u>Energetics</u> <u>of</u> <u>Various</u> <u>Redox</u> <u>State</u>

A.J. Bard *et al.*, *JACS*, **1973**, *95*, 6582.

Ox + e- → Re , E(V)
E > 0 : potent oxidant
E < 0 : potent reductant

+2 state : stable ground state;

+3 <u>state</u> : <u>good</u> <u>oxidant</u>
+1 <u>state</u> : <u>good</u> <u>reductant</u>

cf) oxidising water to O$_2$ ($E_0(O_2/H_2O)$ = +1.23 V

Table. Oxidation and Reduction Potential evaluated by Cyclic Voltammetry.

| Ru-complex and medium	Midpoint potential (V)				
	(3+/2+)	(2+/+)	(1+/0)	(0/−1)	(−1/−2)
Ru(bpy)$_3^{2+}$, H$_2$O (vs. NHE)	1.26	−1.28			
Ru(bpy)$_3^{2+}$, CH$_3$CN (vs. SCE)	+1.29	−1.33	−1.52	−1.76	−2.4
Ru(phen)$_3^{2+}$, CH$_3$CN (vs. SCE)	+1.36	−1.44	−1.54	−1.84	−2.24

SCE : Saturated Calomel Electrode
a reference electrode based on the reaction between elemental mercury and mercury(I) chloride in KCl sat. aq.; use mesurement of Redox potential
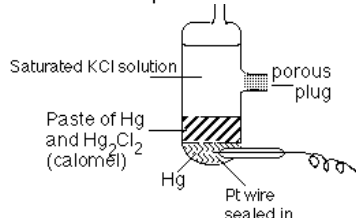
NHE : Normal Hydrogen Electrode (= SHE)
a redox electrode which forms the basis of the thermodynamics scale of oxidation - reduction potentials; use mesurement of Redox potential
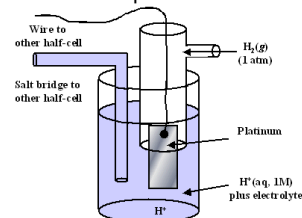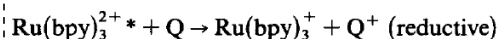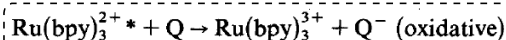
The excited state redox potentials are obtainable from the redox potentials of the corresponding ground state. (Probably, the excited state energy is all available as free energy for the excited state redox processes.)

Calculated (*vs.* SCE);

C. Creutz, N. Sutin, *Inorg. Chem.*, **1976**, *15*, 496
T. J. Meyer *et al.*, *JACS*, **1979**, *101*, 4815

$Ru(bpy)_3^{2+}* + Q \rightarrow Ru(bpy)_3^{3+} + Q^-$ (oxidative)

$Ru(bpy)_3^{2+}* + Q \rightarrow Ru(bpy)_3^{+} + Q^+$ (reductive)

$E_0[Ru(bpy)_3^{2+*/3+}] = E_0[Ru(bpy)_3^{2+/2+*}] - E_0[Ru(bpy)_3^{2+/3+}]$
$= -2.10 + 1.29 = -0.81$ V

Similarly

$E_0[Ru(bpy)_3^{2+*/+}] = E_0[Ru(bpy)_3^{2+/+}] - E_0[Ru(bpy)_3^{2+/2+*}]$
$= -1.33 - (-2.12) = +0.77$ V

Figure. Redox potential diaglam

$Ru(bpy)_3^{3+} \xrightarrow[\text{reductant}]{-0.81} Ru(bpy)_3^{2+*} \xrightarrow[\text{oxidant}]{+0.78} Ru(bpy)_3^{+}$

ΔG_{ES}

$Ru(bpy)_3^{3+} \xrightarrow[\text{oxidant}]{1.29} Ru(bpy)_3^{2+} \xrightarrow[\text{reductant}]{-1.33} Ru(bpy)_3^{+}$

volts vs. SCE in CH_3CN, $\mu = 0.1$ M

Table. Formal Reduction Potentials at Room Temperature ($\mu = 0.1$ M)

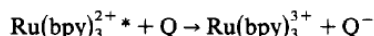| couple	E, V (CH_3CN vs. SCE)	E, V (H_2O vs. NHE)[a]	
$Ru(bpy)_3^{3+/2+}$	1.29 ± 0.07	1.26	potent oxidant
$Ru(bpy)_3^{2+*/+}$	0.77 ± 0.07	0.84	
$Ru(bpy)_3^{3+/2+*}$	-0.81 ± 0.07	-0.84	
$Ru(bpy)_3^{2+/+}$	-1.33 ± 0.07	-1.26	potent reductant
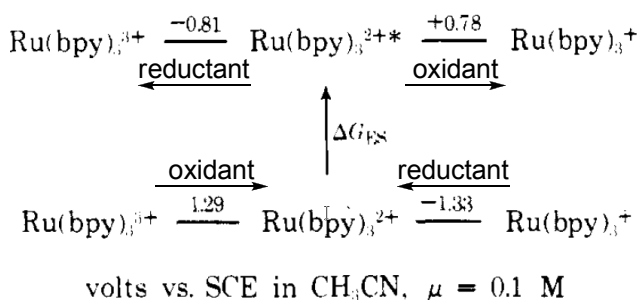
Excited state $Ru(bpy)_3^{2+*}$ is **good oxidant** and **good reductant**

Redox Quenching of excited state

(a) excited state acts as an energy donor
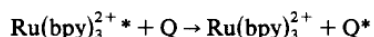
$Ru(bpy)_3^{2+}* + Q \rightarrow Ru(bpy)_3^{2+} + Q*$

(b) excited state acts as a reductant (oxidative quenching)

$Ru(bpy)_3^{2+}* + Q \rightarrow Ru(bpy)_3^{3+} + Q^-$

(c) excited state acts as an oxidant (reductive quenching)

$Ru(bpy)_3^{2+}* + Q \rightarrow Ru(bpy)_3^{+} + Q^+$

$Ru(bpy)_3^{2+}* + O_2 \rightarrow (Ru(bpy)_3^{3+} \cdots O_2^-) \rightarrow Ru(bpy)_3^{3+} + O_2^-$

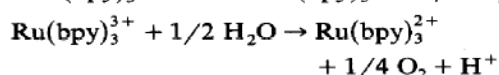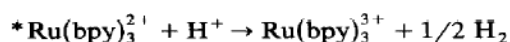$Ru(bpy)_3^{3+} + O_2^- \rightarrow Ru(bpy)_3^{2+} + O_2(^1\Delta_2)$
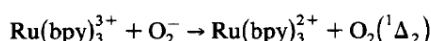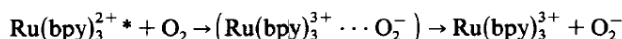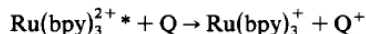
generation of singlet oxigen

Table. Rate parameters in the quenching of $Ru(bpy)_3^{2+*}$ by inorganic ions and molecules (k_q ; quenching rate constant, k_2 :decrease rate constant of $Ru(bpy)_3^{2+*}$)

Quencher	Medium	k_q ($M^{-1} s^{-1}$)	k_2 ($M^{-1} s^{-1}$)	Mechanism
Fe^{3+}	H_2SO_4 (0.5 M)	2.7×10^9	5.2×10^6	Oxid.
Fe^{2+}	$HClO_4$ (0.5 M)	1.6×10^7		
Cu^{2+}	H_2SO_4 (0.5 M)	6.2×10^7	9.7×10^8	Oxid.
Eu^{2+}	H_2O	2.8×10^7	4.5×10^7	Reduc.
Eu^{3+}	H_2O	$<0.8 \times 10^5$	3.0×10^9	Oxid.
Cr^{3+}	H_2O	1.2×10^7		Energy transfer
Tl^{3+}	$HClO_4$ (0.5 M)	1.1×10^8	Irrev.	Oxid.
Tl^{3+}	HCl (1.0 M)	3.3×10^9		
Tl^{+}	$HClO_4$ (0.5 M)	$<10^6$		
Ti^{3+}	HCl (1.0 M)	6.0×10^6		Energy transfer
Ag^{+}	H_2O	3.5×10^6	1.2×10^{10}	Oxid.
Ag^{+}	CH_3CN	1.1×10^5	5.5×10^9	Oxid.
$S_2O_8^{2-}$	H_2SO_4 (0.5 M)	5.6×10^8	Irrev.	Oxid.
$S_2O_4^{2-}$	Acetate buffer (0.02 M)	2.4×10^9		
O_2	H_2O	3.3×10^9		Energy/oxid.
SO_3^{2-}	H_2O	3.0×10^5	$<10^6$	Reduc.
Ascorbate	H_2O	2.0×10^7	1.0×10^9	Reduc.
Hg^{2+}	$HClO_4$ (0.1 M)	1.5×10^8	2.0×10^9	Oxid.
$HgCl_2$	$HClO_4$ (0.1 M)	3.8×10^8		
Sb^{3+}	H_2SO_4	$<10^6$		

Several Application (Using Visible Light)

· Water split

$*Ru(bpy)_3^{2+} + H^+ \rightarrow Ru(bpy)_3^{3+} + 1/2\ H_2$

$Ru(bpy)_3^{3+} + 1/2\ H_2O \rightarrow Ru(bpy)_3^{2+}$
$+ 1/4\ O_2 + H^+$

H₂ & O₂ Production

· Reduction of Carbon Dioxide

$Ru(bpy)_3^{2+} + CO_2 \xrightarrow[\text{N(CH}_2\text{CH}_2\text{OH)}_3\text{-DMF}]{h\nu\ (400\ nm)} HCO_2H$

$CO_2 + 2H^+ + 2e^-\ HCO_2H\ \ E = -0.61$ V

$Ru(bpy)_3Cl_2 \xrightarrow[\text{photosensitizer}]{h\nu\ (400\ nm)} Ru(bpy)_3^{2+*}$ proton source

$Ru(bpy)_3^{2+*} + N(CH_2CH_2OH)_3$
$\longrightarrow Ru(bpy)_3^{+} + N(CH_2CH_2OH)_3^{\cdot+}$ reductant

$Ru(bpy)_3^{+} + 1/2\ CO_2 \xrightarrow{\text{proton source}} \begin{array}{l}1/2\ HCO_2H \\ Ru(bpy)_3^{2+}\end{array}$

G. Christou *et al.*, *J. Chem. Soc., Chem. Comm.*, **1985**, 56.
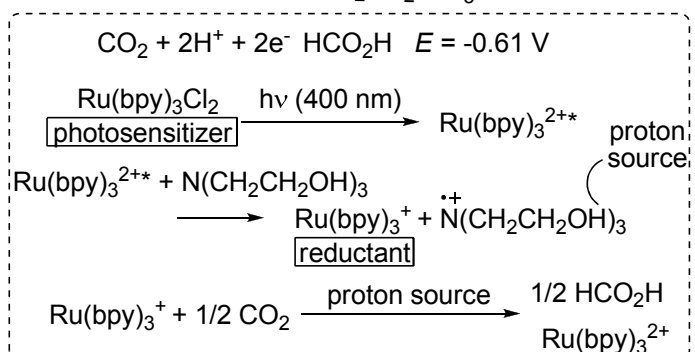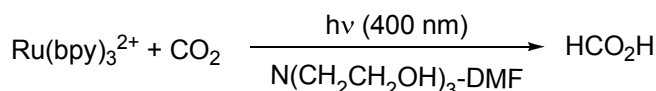
3. Photoredox Catalyst in Organic Reaction

3-1. Early Important Report (MacMillan's Work)

Background and Consideration

Many fundamental organic reactions rely on the generation and use of **radicals or single-electron intermediates**; metal-mediated reaction, photoreaction, polymerization, etc...

← Ru(bpy)$_3$$^{2+}$: **one-electron photoredox catalyst**, important development of H$_2$, O$_2$, energy storage, etc...

Application as initiator of single-electron intermediates??

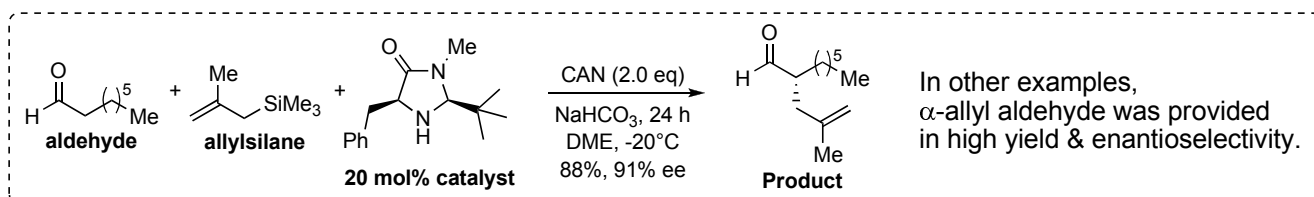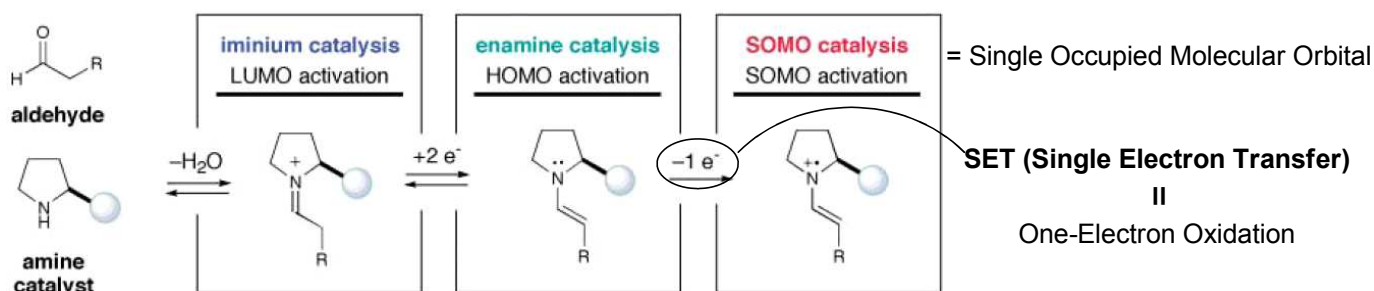- -

On the other hand....

Previous MacMillan's work : organo-HOMO, LUMO, SOMO-activation catalysis (ref. Mihara's Lit. (D1 Part))

D. W. C. MacMillan *et al.*, *Science*, **2007**, *316*, 582.

iminium catalysis LUMO activation   **enamine catalysis** HOMO activation   **SOMO catalysis** SOMO activation = Single Occupied Molecular Orbital

aldehyde / amine catalyst / −H$_2$O / +2 e$^-$ / −1 e$^-$

SET (Single Electron Transfer)

∥

One-Electron Oxidation

aldehyde + allylsilane + 20 mol% catalyst (Ph, Me, ^{t}Bu imidazolidinone)

CAN (2.0 eq)
NaHCO$_3$, 24 h
DME, -20°C
88%, 91% ee

Product

In other examples, α-allyl aldehyde was provided in high yield & enantioselectivity.
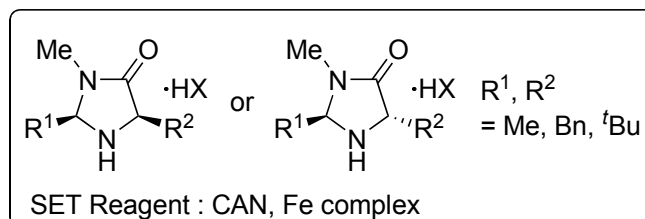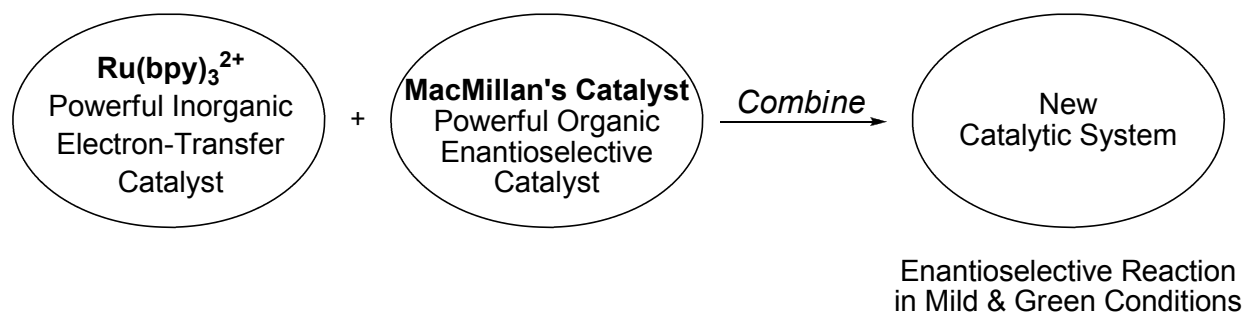
In later report...

Many Applications of SOMO catalysis via SET;
Aldol, Friedel-Crafts, Vinylation, Allylation,
Arylation, Enolation, Enal Reduction, ...

See these literature;

JACS, **2007**, *129*, 7004.	*JACS*, **2008**, *130*, 398.
JACS, **2008**, *130*, 16494.	*JACS*, **2009**, *131*, 11640.
JACS, **2009**, *131*, 11332.	*ACIE*, **2009**, *48*, 5121.
JACS, **2010**, *132*, 5027.	et cetera...

R^1, R^2 = Me, Bn, ^{t}Bu

SET Reagent : CAN, Fe complex

- -

· Suggestion of New Catalytic System

Ru(bpy)$_3$$^{2+}$
Powerful Inorganic
Electron-Transfer
Catalyst

+

MacMillan's Catalyst
Powerful Organic
Enantioselective
Catalyst

Combine →

New
Catalytic System

Enantioselective Reaction
in Mild & Green Conditions

Merging photoredox catalysis with organocatalysis

α-Alkylation of Aldehyde Using New Catalytic System   D. W. C. MacMillan *et al.*, *Science*, **2008**, *322*, 77.

· Proposed Mechanism (Theoretical Hypothesis)

Figure. Merging Photoredox Cataysis with Organocatalyis. Proposed Mechanism.

aldehyde **7**

H$_2$O

8   DFT–8
SOMOphile

catalyst **6**

Organocatalytic Cycle

Si-face open

radical **5**
SOMO

E = -0.92 ~ -1.12 V *vs.* SCE in MeCN
a low barrier to oxidation
Chem. Phys. Lett., **1986**, *131*, 189

10   **9**

H$_2$O

enantioenriched α-alkylated aldehyde

E = -1.33 V *vs.* SCE in MeCN
(potent reductant)
JACS, **1979**, *101*, 4815

SET

Ru(bpy)$_3^+$ (**3**)
reductant

*Ru(bpy)$_3^{2+}$ (**2**)
oxidant

MLCT excited state
potent oxidant or reductant

alkyl halide   FG⌒Br
4

Phenacyl bromide was reduced in this reductant.
(Half-reduction potential;
$E_{1/2}$ = -4.9 V *vs.* SCE in MeCN)
J. Phy.Chem, **1990**, *94*, 722

SET

Photoredox Catalytic Cycle

light

(photosensitizer)
Ru(bpy)$_3^{2+}$
photoredox catalyst 1

Photon Source

electron-deficient radical **5**

· Start of cycle : **2** (MLCT exited state, **high energy intermediate**) removes a single electron from a trace quantify of enamine **(slowly)**. Generated radical amine quenched in photoredox cycle.
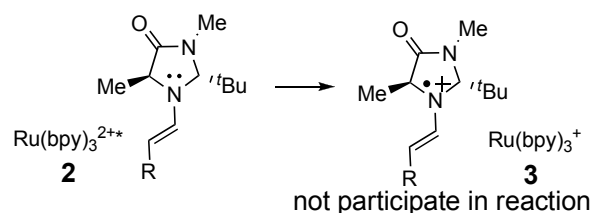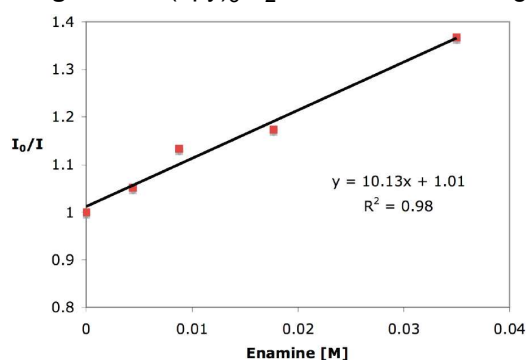
Ru(bpy)$_3^{2+*}$ **2**   →   Ru(bpy)$_3^+$ **3**
not participate in reaction

y = 10.13x + 1.01
R^2 = 0.98

I$_0$/I

Enamine [M]

I_0 = Emission intensity of Ru(bpy)$_3^{2+}$.
I = Emission intensity of Ru(bpy)$_3^{2+}$ in the presence of quencher.

Small decrease of emission intensity in presence of enamine.

⟹ **2** behaves as an oxidant, and enamine can be reacted with Ru(bpy)$_3^{2+}$ (but so slowly).

· Electron-deficient radical **5** is reactive, so it reacts with enamine **8** **(fast).**

· Stereocontrol and reaction surfice control of enamine **8**;
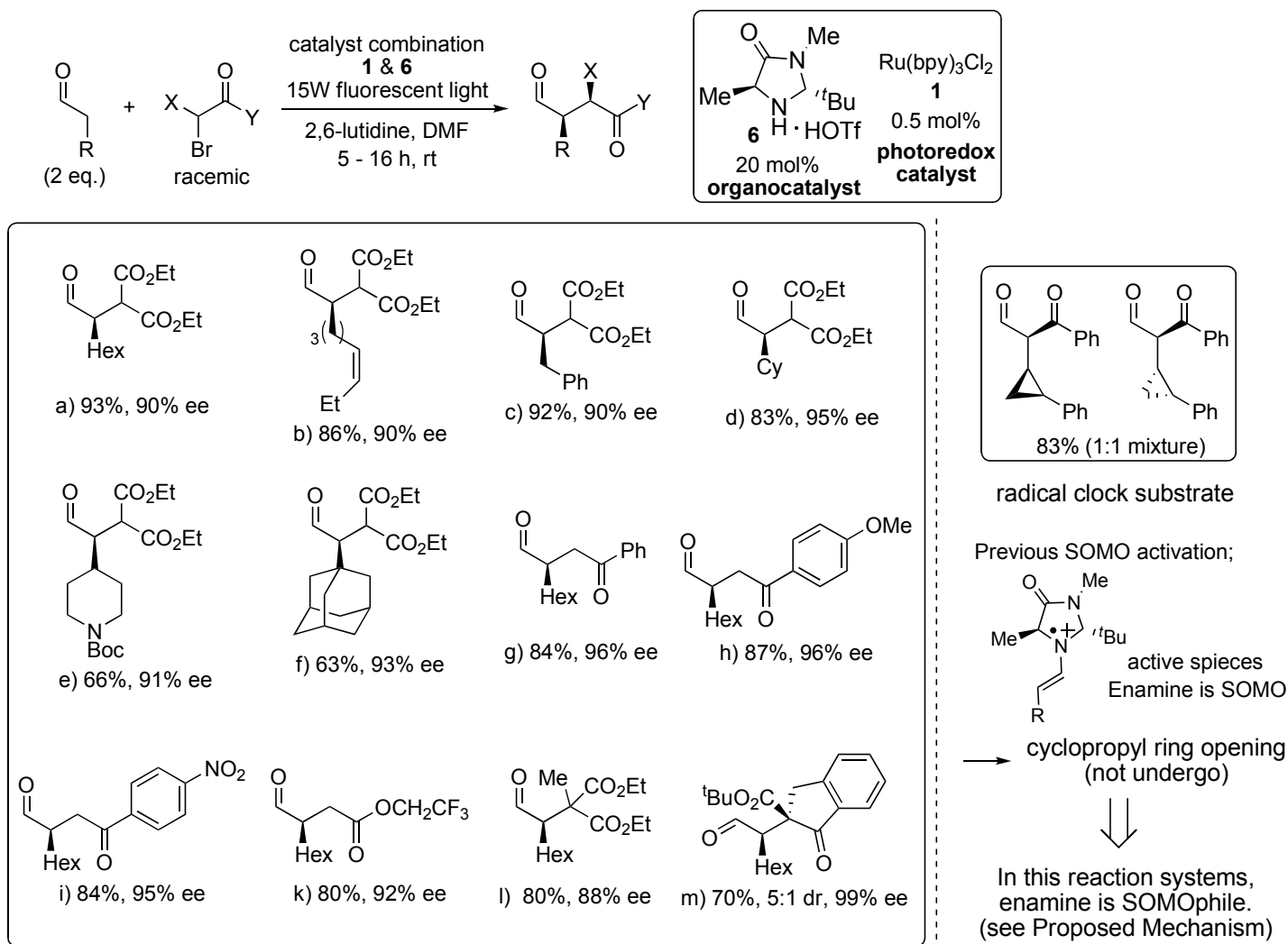
R   *Re* face covered
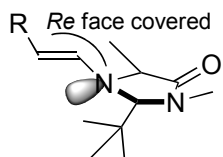
Substituent on N is away from vulky *tert*-butyl group.

To minimize with non-bonding electron pair, (*E*)-configuration.

Methyl group effectively shields the *Re* face.
→ Enantioselective radical addition from *Si* face

· Result

Reaction scheme: aldehyde (R, 2 eq.) + α-bromo carbonyl (X, Y, Br, racemic) → product, catalyst combination **1 & 6**, 15W fluorescent light, 2,6-lutidine, DMF, 5 – 16 h, rt.

Organocatalyst **6** (20 mol%), Ru(bpy)$_3$Cl$_2$ **1** (0.5 mol%, photoredox catalyst).

a) 93%, 90% ee

b) 86%, 90% ee

c) 92%, 90% ee

d) 83%, 95% ee

e) 66%, 91% ee

f) 63%, 93% ee

g) 84%, 96% ee

h) 87%, 96% ee

i) 84%, 95% ee

k) 80%, 92% ee

l) 80%, 88% ee

m) 70%, 5:1 dr, 99% ee

radical clock substrate: 83% (1:1 mixture)

Previous SOMO activation; active spieces Enamine is SOMO

cyclopropyl ring opening (not undergo)

In this reaction systems, enamine is SOMOphile. (see Proposed Mechanism)

· Chemical functionalities that are prone to redox (olefins, esters, carbamates, and arenes) were inert to these mild redox conditions (**b-f**). **Chemoselective Reaction.**

· Vulkiness of R has little impact of yield & ee.

· Electron-deficient α-bromo carbonyls effectively serve as alkylating agents (**g-m**).

· **Tertiary bromo-substituted alkylating agents are readily employed (l, m).**

· A 2g alkylation was readily accomplished (**g**).

· Exclusion of light failed to produce even trace quantities of the coupling adduct.

· Removal of Ru(bpy)$_3^{2+}$ resulted in small quantities of product (24 h).

· Light source tuned to the Ru(bpy)$_3^{2+}$ MLCT absorption band resulted in a acceleration (90 min).

Participation of the Ru(bpy)$_3^{2+}$* excited state

· It does not require any heating or cooling, all of the components are commercially available and inexpensive.

· Simple household 15-W fluorescent light bulb can be employed as a suitable light source → **Visible Light**

Chemoselective Reaction, and Decrease of Side Reaction

∗ diastereoselectivity of **m**;
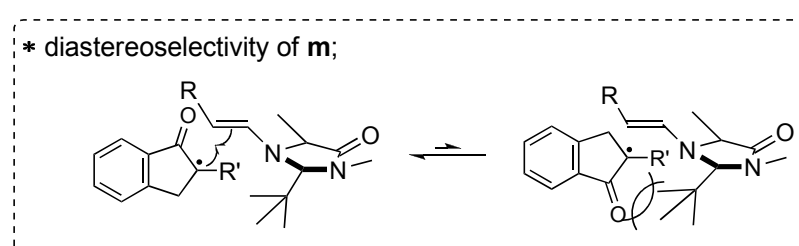
3-2. Various Reactions Using Photoredox Catalysis

Reductive Dehalogenation

· Classical Method

$$\text{Bu}_3\text{SnH, AIBN},\ \text{C}_6\text{H}_6,\ \text{reflux},\ 99\%$$
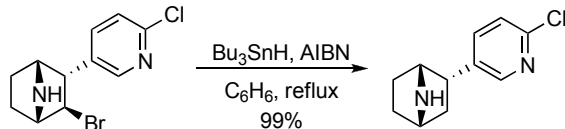
Org. Lett., **2005**, *7*, 2965.

Using trialkyltin, toxic and environmental pollutants.

· Using Photoredox Catalyst (Tin-Free Method))

C. R. J. Stephenson *et al.*, *J. Am. Chem. Soc.*, **2009**, *131*, 8756.
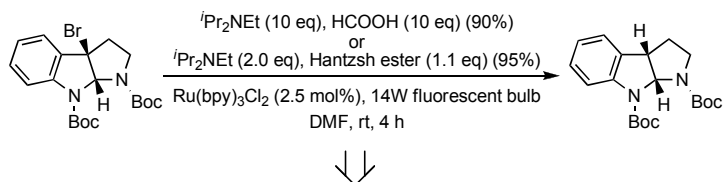
Scheme. Reductive Debromination

$^i\text{Pr}_2\text{NEt}$ (10 eq), HCOOH (10 eq) (90%) or $^i\text{Pr}_2\text{NEt}$ (2.0 eq), Hantzsh ester (1.1 eq) (95%) Ru(bpy)$_3$Cl$_2$ (2.5 mol%), 14W fluorescent bulb DMF, rt, 4 h

Table. Reductive Dehalogenation Using Photoredox Catalysis

entry	substrate	product	yield[a]
1			95[b]
2			92[b]
3			91[b]
4			99[b]
5			79[b]
6			80[b]
7			78[c]
8			88[c]
9			81[c]
10			89[c]

[a] Isolated yield after purification by chromatography on SiO$_2$. [b] Ru(bpy)$_3$Cl$_2$·6H$_2$O (2.5 mol %), $^i\text{Pr}_2$NEt (10 equiv), HCO$_2$H (10 equiv), DMF, *hν*, r.t., 4 h. [c] Ru(bpy)$_3$Cl$_2$·6H$_2$O (2.5 mol %), $^i\text{Pr}_2$NEt (2 equiv), **3** (1.1 equiv), DMF, *hν*, r.t., 4−24 h. **3** : Hantzsh ester
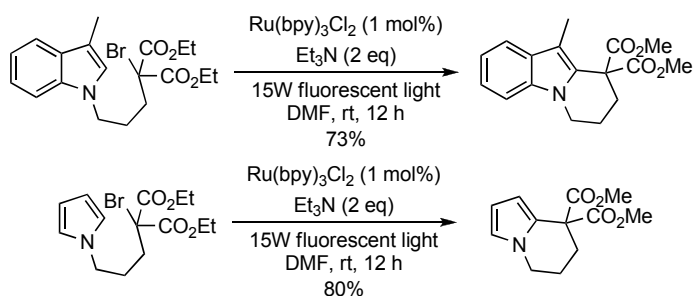
Scheme. Proposed Mechanism
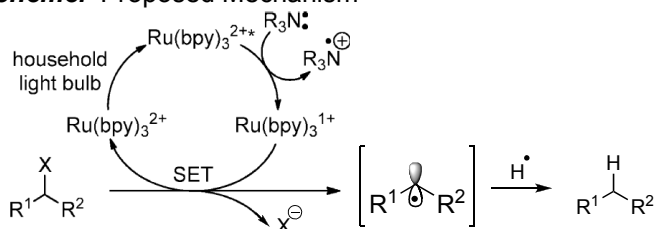
Intramolecular Radical Addition (Tin-Free)

C. R. J. Stephenson *et al.*, *Org. Lett.*, **2010**, *12*, 368.

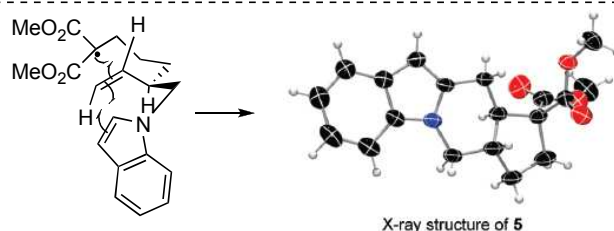**Scheme.** Intramolecular Radical Addition of Indole and pyrrole

Ru(bpy)$_3$Cl$_2$ (1 mol%), Et$_3$N (2 eq), 15W fluorescent light DMF, rt, 12 h, 73%

Ru(bpy)$_3$Cl$_2$ (1 mol%), Et$_3$N (2 eq), 15W fluorescent light DMF, rt, 12 h, 80%

Other several examples was performed, in moderate - high yields.

Scheme 3. Cascade Radical Cyclization

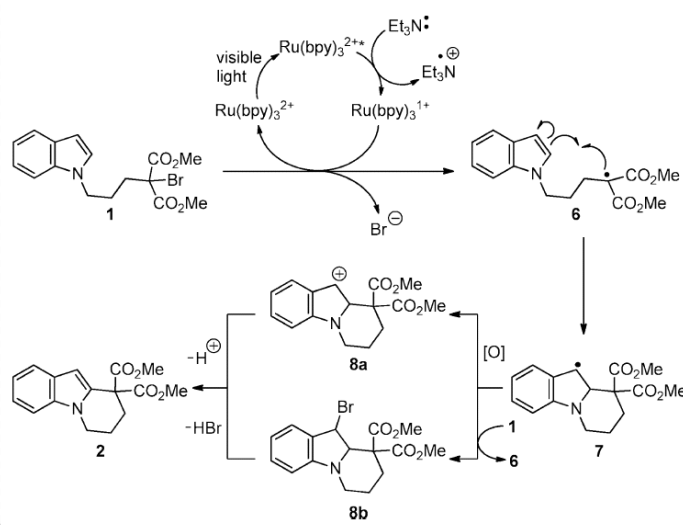Ru(bpy)$_3$Cl$_2$ (1 mol %), Et$_3$N (2 equiv), DMF, visible light, rt, 16 h, 79%
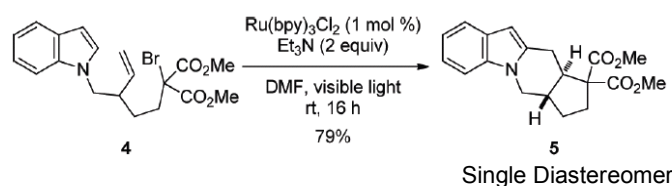
Single Diastereomer
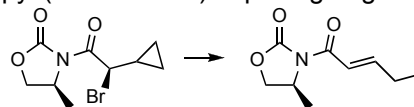

X-ray structure of **5**

Scheme 4. Proposed Mechanism

· Various chemical functionalities were inert to these redox conditions.
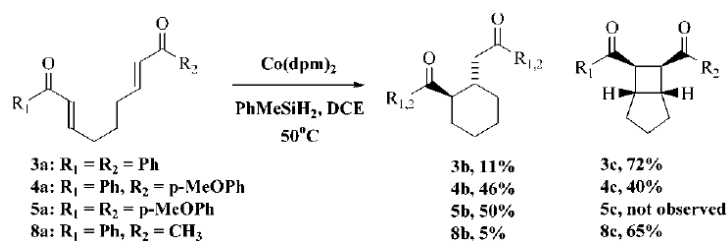
· **Tin-Free, and mild conditions**
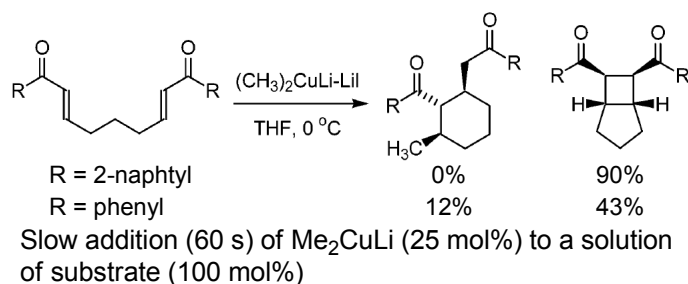
· cyclopropyl (radical clock) : opening ring

· Ru* - Amine electron transfer was reported; *JACS*, **1979**, *101*, 4007

$$\text{RuL}_3{}^{2+*} + \text{Et}_3\text{N} \rightarrow \text{RuL}_3{}^{+} + \text{Et}_3\text{N}^{+\bullet}$$

[2+2] Cycloaddition (Enone Cycloaddition)

・ Previous Method (Kirsche)

Co(dpm)$_2$
PhMeSiH$_2$, DCE
50°C

3a: R$_1$ = R$_2$ = Ph
4a: R$_1$ = Ph, R$_2$ = p-MeOPh
5a: R$_1$ = R$_2$ = p-MeOPh
8a: R$_1$ = Ph, R$_2$ = CH$_3$

3b, 11%
4b, 46%
5b, 50%
8b, 5%

3c, 72%
4c, 40%
5c, not observed
8c, 65%

J. Am. Chem. Soc, **2002**, *124*, 9448.

(CH$_3$)$_2$CuLi-LiI
THF, 0 °C

R = 2-naphtyl
R = phenyl

0%   90%
12%   43%

Slow addition (60 s) of Me$_2$CuLi (25 mol%) to a solution of substrate (100 mol%)

J. Org. Chem, **2004**, *69*, 7979.

Problem of these reaction systems; Chemoselectivity, Yield, Narrowness of sabstrate scope

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・ New Method Using Photoredox Catalyst   T. P. Yoon *et al.*, *J. Am. Chem. Soc.*, **2008**, *130*, 12886.
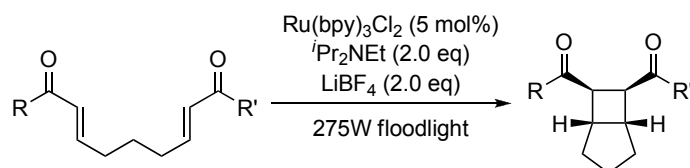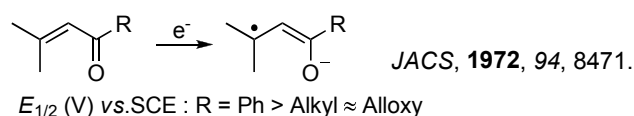

Ru(bpy)$_3$Cl$_2$ (5 mol%)
^{i}Pr$_2$NEt (2.0 eq)
LiBF$_4$ (2.0 eq)
275W floodlight

Table. Visible Light Photocatalysis of Enone Cycloaddition[a]

entry[a]	substrate	cycloadduct	time	yield[b]	dr[b]
1	R = Ph		50 min	89%	>10:1
2	R = 4-MeOPh		20 min	98%	10:1
3	R = 4-ClPh		10 min	96%	>10:1
4	R = 2-furyl		30 min	89%	>10:1
5	R = Me		22 h	0%	--
6	R = OEt		17 h	0%	--
7	X = O		10 min	90%	5:1
8	X = CMe$_2$		10 min	68%	4:1
9			2 h	54%	6:1
10	R = Me		75 min	85%	>10:1
11	R = OEt		45 min	88%	>10:1
12	R = NEt$_2$		30 min	74%	>10:1
13			1 h	84%	10:1
14[c]	R = Ph		2 h	82%	>10:1
15[c]	R = 4-ClPh		1 h	93%	>10:1

Yoon, *JACS*, **2009**, *131*, 14604

・Aliphatic enone and enoate do not cyclize (**entries 5, 6**)
→ because of more negative reduction potential

$E_{1/2}$ (V) *vs*.SCE : R = Ph > Alkyl ≈ Alloxy

JACS, **1972**, *94*, 8471.

・ no reaction in the absence of ^{i}Pr$_2$NEt
⇒ Cycloaddition is not directly initiated by Ru(bpy)$_3$$^{2+*}$, Ru(bpy)$_3$$^+$ formed by reductive quenching of amine.

・ no reaction occurs in the absence of LiBF$_4$
・ Ru(bpy)$_3$Cl$_2$: sparingly soluble → Ru(bpy)$_3$(BF$_4$)$_2$: soluble
・ Na$^+$, Bu$_4$N$^+$: low reactivity → Li$^+$ is involved in reaction.

cf.

$E_{1/2}$ = -1.58 V (*vs.* SCE)
Ru(bpy)$_3$$^+$: lack of reductive power
So, Li$^+$ is essential

Scheme.

5 mol%
Ru(bipy)$_3$Cl$_2$,
i-Pr$_2$NEt, LiBF$_4$
sunlight
1 h

PMP = 4-MeOPh   gram scale

3   4

94% yield, 10:1 d.r.

Scheme. Proposed Mechanism

---

[a] Reactions conducted using Ru(bipy)$_3$Cl$_2$·6H$_2$O (5 mol%), LiBF$_4$ (2 equiv), and *i*-Pr$_2$NEt (2 equiv) in degassed MeCN (0.1 M) under irradiation by a 275 W floodlight at a distance of 20 cm. [b] Isolated yields and diastereomer ratios are averaged from two reproducible experiments. [c] Molar ratios for intermolecular dimerizations calculated with respect to theoretical yield of product (e.g., 2.5 mol% catalyst with respect to enone).
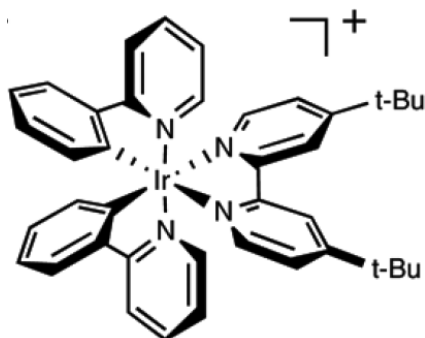
3-3. Reaction Using Ir Catalyst

Ir(ppy)₂(dtb-bpy)⁺
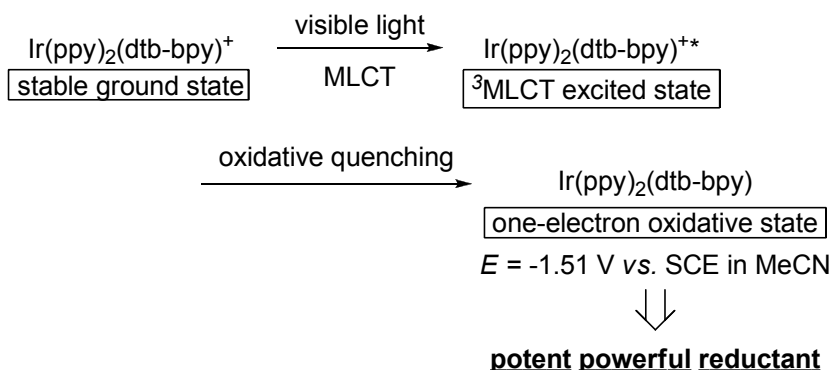
S. Bernhard *et al.*, *J. Am. Chem. Soc.*, **2004**, *126*, 2763.
S. Bernhard *et al.*, *J. Am. Chem. Soc.*, **2004**, *126*, 14219.

Various **Ir** photoredox catalyst was synthesized and investigated property;
· It readily accepts a photon from a visible light, and excites.
· high reductive ability of one-electron oxidative state

Ir(ppy)₂(dtb-bpy)⁺

$$Ir(ppy)_2(dtb\text{-}bpy)^+ \xrightarrow[\text{MLCT}]{\text{visible light}} Ir(ppy)_2(dtb\text{-}bpy)^{+*}$$

stable ground state → ³MLCT excited state

$$\xrightarrow{\text{oxidative quenching}} Ir(ppy)_2(dtb\text{-}bpy)$$

one-electron oxidative state

E = -1.51 V *vs*. SCE in MeCN

⇓

potent powerful reductant

Aza-Henry Reaction via C-H Activation

C. R. J. Stephenson *et al.*, *J. Am. Chem. Soc.*, **2010**, *132*, 1464.

Table. Oxidative Iminium Ion Generation and Trapping

entry	conditions[a]	conversion[b] (yield[c])
1	3 (2 mol %), (EtO₂C)₂CHBr (5, 1.5 equiv) DMF, 2 h; X = OCH₃	100 (73)[d]
2	3 (1 mol %), 5 (1.5 equiv), CH₃OH, 2 h; X = OCH₃	100
3	3 (1 mol %), *no additive*, CH₃OH, 16 h; X = OCH₃	100
4	3 (1 mol %), CH₃NO₂, 20 h; X = CH₂NO₂	100 (81)
5	3 (1 mol %), CH₃NO₂, 20 h; X = CH₂NO₂; *reaction was degassed*	76
6	4 (1 mol %), CH₃NO₂, 10 h; X = CH₂NO₂	100 (92)
7	4 (1 mol %), *no light*, CH₃NO₂, 48 h; X = CH₂NO₂	0
8	*no catalyst*, CH₃NO₂, 180 h; X = CH₂NO₂	83

[a] With the exception of entry 5, the reactions were not rigorously degassed. [b] Calculated on the basis of crude ¹H NMR analysis. [c] Isolated yield after purification by chromatography on SiO₂. [d] Purified on SiO₂ using CH₃OH as a cosolvent. **3**: Ru(bpy)₃Cl₂.

Reactivity : Ru cat. < Ir cat.
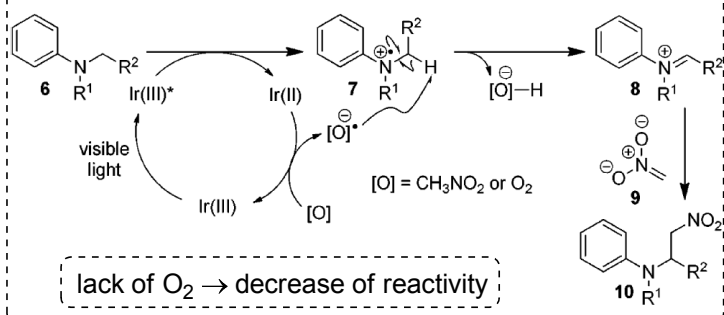
Scheme. Plausible Mechanism

$$[O] = CH_3NO_2 \text{ or } O_2$$

lack of O₂ → decrease of reactivity

Table. Oxidative Aza-Henry Reaction

| entry	substrate[f]	product	time (h)	yield (%)[a]
1			10	92[b]
2			16	96[b,c]
3			18	96[b]
4			18	92[b,d]
5			16	90[b]
6			13	93[b]
7			13	92[b]
8			18	95[b]
9			72	27[b,e]

[a] Isolated yield after purification on SiO₂. [b] Conditions: **4** (1.0 mol %), visible light, CH₃NO₂, rt. [c] dr = 2:1. [d] dr = 2.3:1. [e] Conversion = 40% as determined by crude ¹H NMR analysis. open to air.

· Although the process was slowly, C-H oxidation of a nonbenzylic amine afforded (entry 9).

· Although reaction using Cu(I) and TBHP is faster than these reactions (ref. *JACS*, **2005**, *127*, 3672), these reactions provide desired products in higher yields.

α-Trifluoromethylation of Aldehyde

Table. Enantioselective α-Trifluoromethylation: Initial Studies
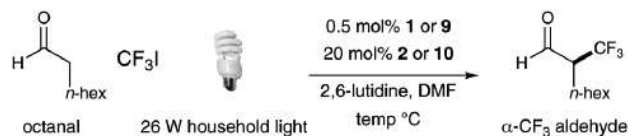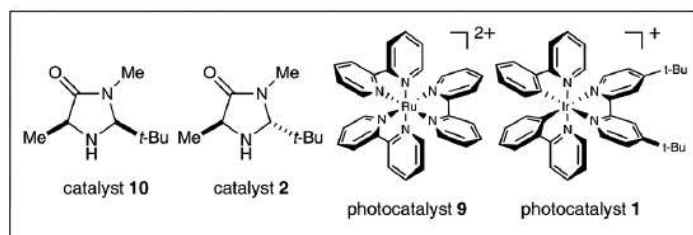
entry	organocat.	photocat.	light	temp (°C)	% yield	% ee[a]
1	10	9	yes	23	51	0
2	10	9	no	23	<5	0
3	10	1	yes	23	85	0
4	10	1	yes	−20	92	52
5	2	9	yes	−20	67	87
6	2	1	yes	−20	79	99

[a] Enantiomeric excess by chiral GC analysis of the corresponding alcohol. Yield of the corresponding alcohol.

· Racemization was detected in room temperature, but in low temperature, racemization was not detected.

· Reactivity and selectivity : Ru cat. < Ir cat.

Table. Enantioselective α-Trifluoromethylation: Aldehyde Scope
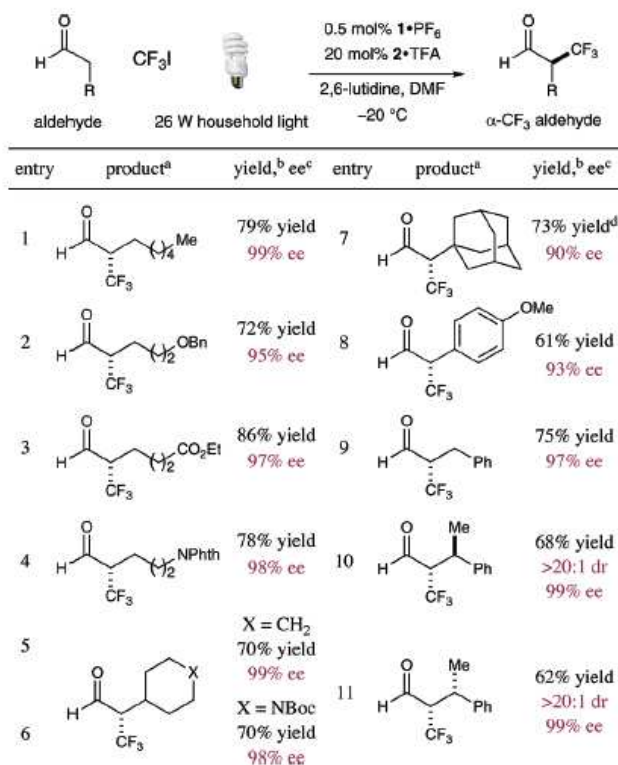
entry	product[a]	yield,[b] ee[c]	entry	product[a]	yield,[b] ee[c]
1		79% yield, 99% ee	7		73% yield[d], 90% ee
2		72% yield, 95% ee	8		61% yield, 93% ee
3		86% yield, 97% ee	9		75% yield, 97% ee
4		78% yield, 98% ee	10		68% yield, >20:1 dr, 99% ee
5	X = CH₂ 70% yield, 99% ee		11		62% yield, >20:1 dr, 99% ee
6	X = NBoc 70% yield, 98% ee				

[a] Stereochemistry assigned by chemical correlation or by analogy. [b] Isolated yields of the corresponding alcohol. [c] Enantiomeric excess determined by chiral SFC or HPLC analysis. [d] Using catalyst 11;

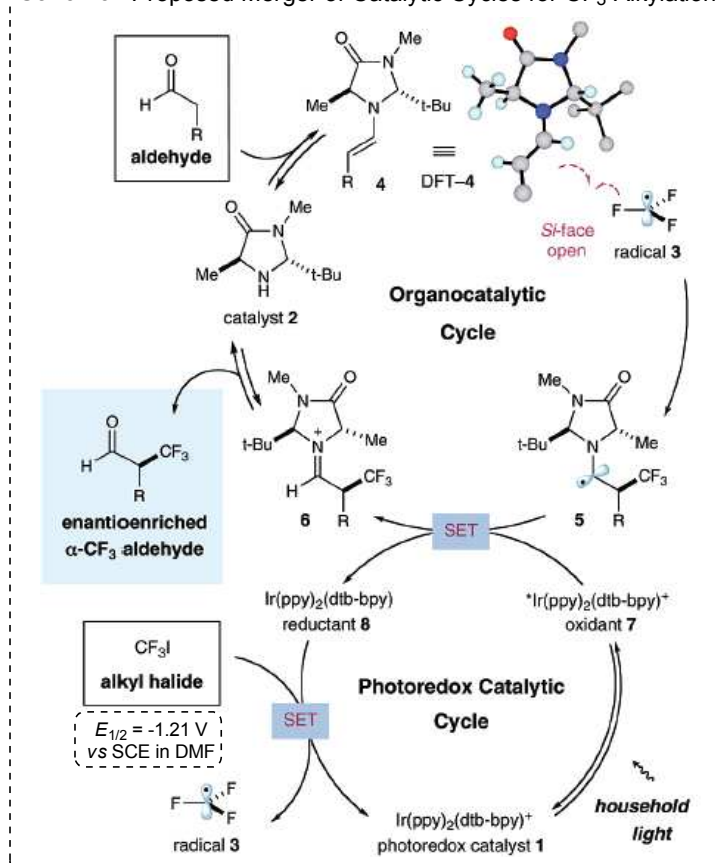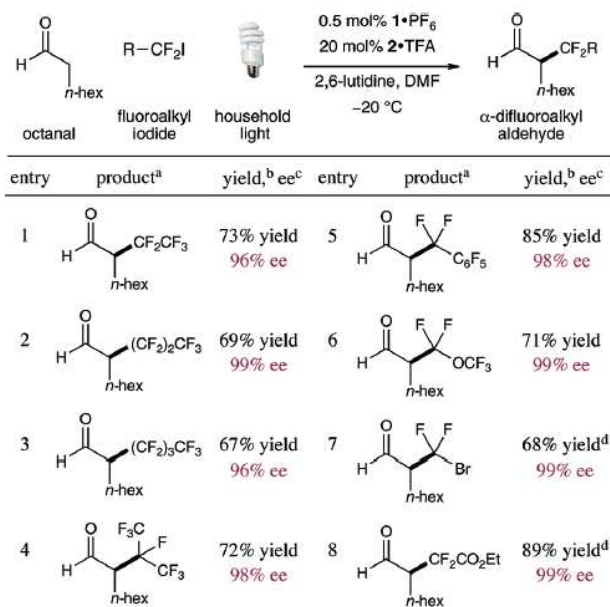**Scheme.** Proposed Merger of Catalytic Cycles for CF₃-Alkylation

Table. Enantioselective α-Perfluoroalkylation: Alkyl Iodide Scope

entry	product[a]	yield,[b] ee[c]	entry	product[a]	yield,[b] ee[c]
1	CF₂CF₃	73% yield, 96% ee	5	C₆F₅	85% yield, 98% ee
2	(CF₂)₂CF₃	69% yield, 99% ee	6	OCF₃	71% yield, 99% ee
3	(CF₂)₃CF₃	67% yield, 96% ee	7	Br	68% yield[d], 99% ee
4		72% yield, 98% ee	8	CF₂CO₂Et	89% yield[d], 99% ee

[a] Stereochemistry assigned by chemical correlation or by analogy. [b] Isolated yields of the corresponding alcohol. [c] Enantiomeric excess determined by chiral HPLC analysis of corresponding 2-naphthoyl ester. [d] The perfluoroalkyl bromide was employed as starting material.
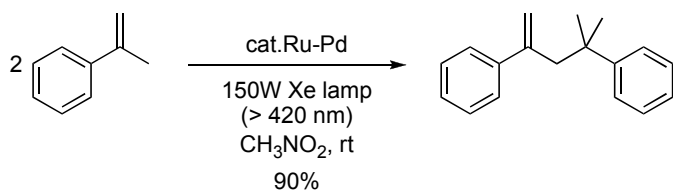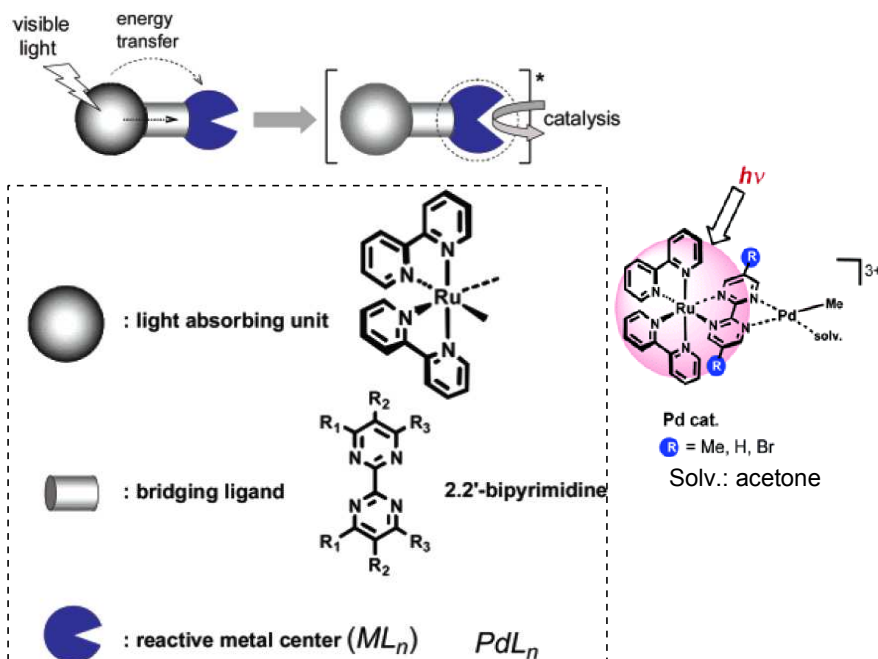
4. Other Catalysts (Other Recent Applications)

Ru-Pd complex (Dimerization of Methystyrene)

M. Akita *et al.*, *Chem. Comm.*, **2005**, 5468.
M. Akita *et al.*, *Inorg. Chem.*, **2007**, *46*, 2432.

Scheme . Transition-metal complex containing a visible-light-absorning unit
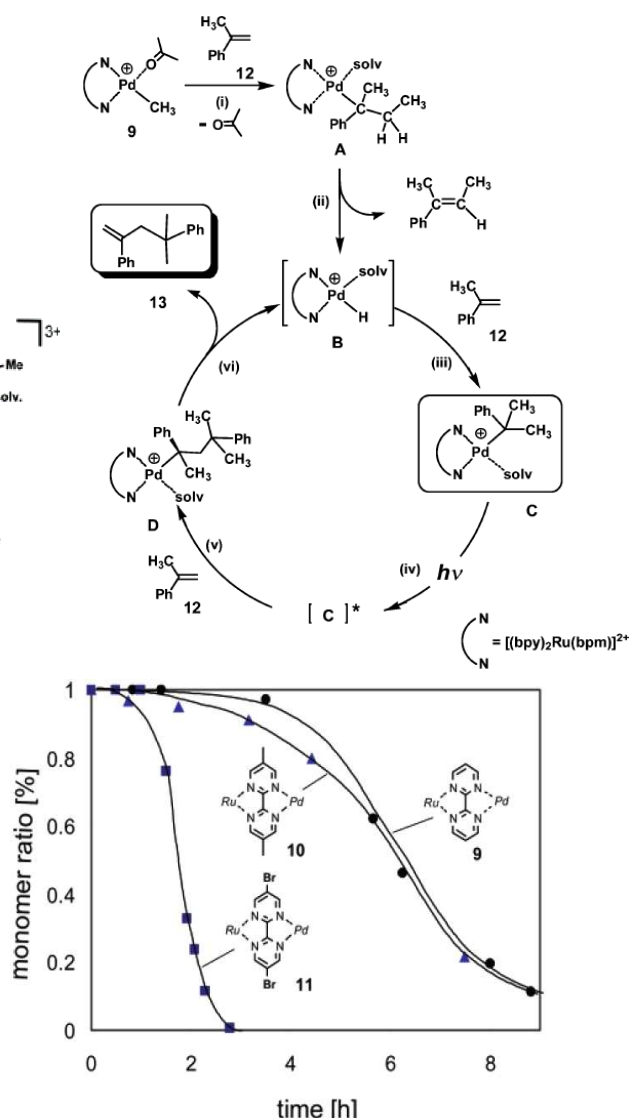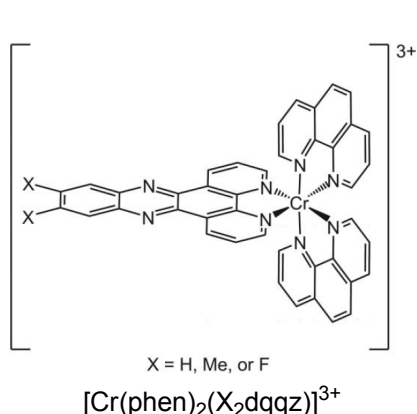
Scheme . Proposed Mechanism

Figure . Consumption rate of the monomer in the reaction of 9-11 under irradiated conditions.

2 → cat.Ru-Pd, 150W Xe lamp (> 420 nm), CH_3NO_2, rt, 90%

- ● : light absorbing unit
- ▬ : bridging ligand   2.2'-bipyrimidine
- ◖ : reactive metal center (ML_n) PdL_n

Pd cat.
R = Me, H, Br
Solv.: acetone

Cr Complex

J. M. Kelly *et al.*, *Dalton Trans.*, **2010**, 3990.

strongly binding and interact with DNA
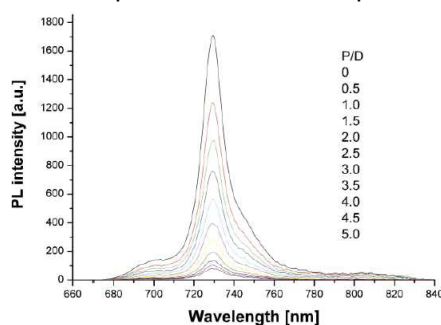→ Phosphorescence of complex is efficiently quenched.

$[Cr(phen)_2(X_2dqqz)]^{3+}$

X = H, Me, or F

Fig. 6 Phosphorescence spectra of *rac*-[Cr(phen)₂(F₂dppz)](CF₃SO₃)₃ (*rac*-**3**) (50 μM in 100 mM phosphate buffer solution) in the presence of increasing concentration of CT-DNA (λ_ex = 308 nm).

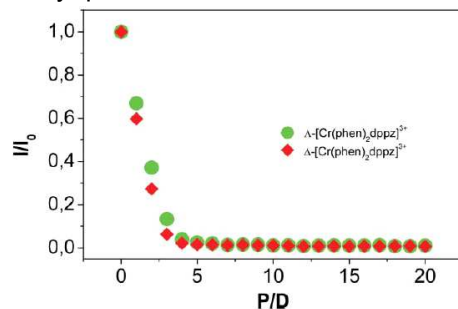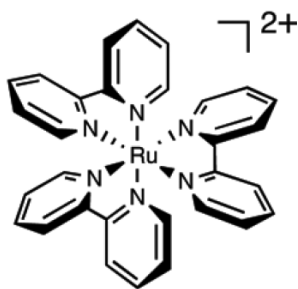Fig. 8 Comparison of the intensity of phosphorescence (*I*) of Δ- and Λ-[Cr(phen)₂(dppz)](Cl)₃ in the presence of CT-DNA compared to that in its absence (*I₀*) (25 mM phosphate buffer solution, pH = 7; P/D = nucleotide:Cr; λ_ex = 370 nm).

When it binds with DNA, it shows property to photoenergy.

⟹ **Potential as nucleic acid probes**

5. Summary & Future

conserves energy in absorbing visible light, and functions development in the field related to the environment.

⇓ After that

In organic chemistry, using this catalyst, radical-mediated efficient and green reaction was developed. However, application examples is still few.

Next study

· Development of more efficient catalyst (Metal, Ligand, ...)

· Expand of this catalytic system in many fields (In organic reaction, new radical-reaction)

And...

Thess "efficient and chemoselective" methodology represents a potential means for accessing a variety of medicinally and biologically active natural or non-natural products.

⟹ Synthesis of Complex Molecules