SCM1 „SYNTHESECHEMIE“
Aktuelle katalytische Synthesemethoden
Teil 2: Photoredoxkatalyse

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Fridays 8.15-9.45

WiSe

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„Modern (Homogeneous) Catalysis?“
Outline

I. C-H Activation
II. Photoredox Catalysis
2. Introduction

2.1. What is it?

- Which reactions promoted by light do you know?
2. Introduction

2.1. What is it?

- Photoredox catalysis:
  - the energy of light accelerates a chemical reaction
  - the catalyst is a light-sensitive compound that after excitation mediates the transfer of electrons (SET = single electron transfer) between chemical compounds that otherwise would react more slowly or not at all.
  - visible light is usually used

\[
\text{Photocatalyst} \quad \xrightarrow{h\nu} \quad \text{Photocatalyst}^* \quad \xrightarrow{\pm e^-} \quad \text{Substrate} \quad \text{or} \quad \text{Substrate}^* \\
\text{Visible light}
\]
2. Introduction

2.1. What is it?

- Typical catalysts:

  **Ru(bpy)₃(II)**
  - $E_{1/2} (M^+/M^{*}) = -0.81$
  - $E_{1/2} (M^{*}/M) = +0.77$
  - $E_{1/2} (M^+/M) = +1.29$
  - $E_{1/2} (M/M^*) = -1.33$

  **Ru(bpz)₃(II)**
  - $E_{1/2} (M^+/M^{*}) = -0.26$
  - $E_{1/2} (M^{*}/M) = +1.45$
  - $E_{1/2} (M^+/M) = +1.86$
  - $E_{1/2} (M/M^*) = -0.80$

  **Ir(ppy)₃(III)**
  - $E_{1/2} (M^+/M^{*}) = -1.73$
  - $E_{1/2} (M^{*}/M) = +0.31$
  - $E_{1/2} (M^+/M) = +0.77$
  - $E_{1/2} (M/M^*) = -2.19$

- absorption of visible light (452 nm for Ru(bpy)₃(II))
- stable, long lived excited state ($\tau = 1100$ ns for Ru(bpy)₃(II))
- powerful oxidants and reductants in excited state
2. Introduction

2.1. What is it?

- Redox potential: what was it again?
2. Introduction

2.1. What is it?

- Typical catalytic cycles:

\[
\begin{align*}
&\text{A} 
\xrightarrow{\text{Ru(bpy)}_3(II)} \text{Ru(bpy)}_3(III) \\
&\text{A} 
\xrightarrow{\text{Oxidative Quenching Cycle}} \text{D} \\
&\text{D} 
\xrightarrow{\text{Reducive Quenching Cycle}} \text{A} \\
&\text{D} 
\xrightarrow{h\nu} \text{Ru(bpy)}_3(II) \\
&\text{A} 
\xrightarrow{\text{Oxidative Quenching Cycle}} \text{D} \\
&\text{D} 
\xrightarrow{\text{Reducive Quenching Cycle}} \text{A} \\
&\text{A} = \text{electron acceptor} \\
&\text{D} = \text{electron donor}
\end{align*}
\]
2. Introduction

2.1. What is it?

- **Ru(bpy)_3(II):**
  - absorption and emission spectrum:

  ![Absorption and emission spectrum diagram](image)


  MLCT = metal-to-ligand charge transfer
2. Introduction

2.1. What is it?

- Ru(bpy)$_3$(II):
  - Orbitals (simplified):

$$\text{Ru(bpy)}_3^{2+} \rightarrow \text{light} \rightarrow \text{oxidation} \rightarrow \text{E}_{1/2} = -0.81 \text{ V}$$

$$\text{E}_{1/2} = +0.77 \text{ V}$$

$$\text{π}^* \rightarrow \text{π}^*$$

$$\text{t}_{2g} \rightarrow \text{t}_{2g}$$

$$\text{e}_g^* \rightarrow \text{e}_g^*$$

$$\text{Ru(bpy)}_3^{2+} \rightarrow \text{*Ru(bpy)}_3^{2+} \rightarrow \text{E}_{1/2} = +0.77 \text{ V}$$

$$\text{E}_{1/2} = -0.81 \text{ V}$$

$$\text{π}^* \rightarrow \text{π}^*$$

$$\text{t}_{2g} \rightarrow \text{t}_{2g}$$

$$\text{e}_g^* \rightarrow \text{e}_g^*$$

$$\text{Ru(bpy)}_3^{3+*}$$
2. Introduction

2.2. Literature

- Reviews:


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Chemical Photocatalysis
B. König (Ed.), **2013**
ISBN 978-3-11-026916-1
2. Introduction

2.3. History

a) Early works:

**Reduction of electron-deficient alkenes**

\[
\text{CO}_2\text{Me} + \text{CO}_2\text{Me} + \text{BNAH} \xrightarrow{\text{Ru(bpy)}_3\text{Cl}_2 (2 \text{ mol\%}) \text{ pyridine, MeOH \ visible light}} \text{MeO}_2\text{C-CH} = \text{CHCO}_2\text{Me} \quad 96\%
\]


**Reductive dehalogenation**

\[
\text{Ph} = \text{CHBr} + \text{N-Me} \xrightarrow{\text{Ru(bpy)}_3\text{Cl}_2 (2 \text{ mol\%}) \text{ MeCN \ visible light}} \text{Ph-CH}_2\text{H} \quad 74\%
\]

2. Introduction

2.3. History

a) Early works:

**Photocatalytic oxidation**

\[
\text{ArOH} + \text{PhN}_2^+ \xrightarrow{\text{Ru(L)}_3\text{Cl}_2 (2 \text{ mol\%})} \text{Ar} = \text{H} \quad 28-100\%
\]


**Cycloaddition of oxygen**

\[
\text{Acridinium cat.} \quad \text{MeCN, O}_2 \quad \text{visible light} \quad \text{acridinium cat.}
\]

2. Introduction

b) Seminal works:

Combination of photo- and organocatalysis

\[
\ce{\text{HCHO \ + \ Br\text{-EWG} \ \rightarrow \ \text{HCO\text{-EWG}}} \ 
\text{Me} \quad \text{Me} \quad \text{tBu} \quad \text{tBu} \quad \text{Me} \quad \text{Me} \quad \text{TfOH}}
\]

20 mol%

0.5 mol% \( \text{Ru(bpy)}_3\text{Cl}_2 \)

2,6-lutidine, DMF

visible light

2. Introduction

b) Seminal works:

**Intramolecular [2+2] cycloaddition**

\[
\begin{align*}
\text{Ru(bpy)}_3\text{Cl}_2 \text{ (5 mol\%)} \\
i\text{Pr}_2\text{NEt}, \text{LiBF}_4, \text{MeCN} \\
\text{visible light}
\end{align*}
\]

\[
\begin{align*}
&\text{R}_1 \\
&\text{O} \\
&\text{R}_2 \\
\text{R}_1 &\text{H} \\
\text{R}_2 &\text{H}
\end{align*}
\]

2. Introduction

2.3. History

b) Seminal works:

**Reductive dehalogenation**

\[
\begin{align*}
&\text{Hal} \\
&\text{R}_1\text{R}_2 \\
\rightleftharpoons \\
&\text{H} \\
&\text{R}_1\text{R}_2
\end{align*}
\]

\[
\text{[Ru(bpy)_3]Cl}_2 \text{ (2.5 mol\%)} \\
\text{HCOOH, iPr}_2\text{NEt, DMF} \\
\text{visible light}
\]

1. Introduction

2. Key Players

D. W. C. MacMillan  T. Yoon  C. Stephenson  R. Knowles

From Germany...

B. König  T. Bach  A. Griesbeck  K. Zeitler

D. Niciewicz  P. Melchiorre  L. Fensterbank  W. Xiao

and many more

……..
2. Ru, Ir Complexes

2.1. Net oxidative reactions

2.1.1. Formation and functionalization of iminium ions

**Photoredox aza-Henry reaction**

\[
\text{Ir(ppy)}_2(\text{dtbby})\text{PF}_6 \text{ (1 mol\%)} \quad \text{MeNO}_2, \text{O}_2 \quad \text{visible light} \quad 92\%
\]

2. Ru, Ir Complexes

2.1. Net oxidative reactions

2.1.1. Formation and functionalization of iminium ions

Further nucleophiles

\[ \text{KCN} \]

\[ \text{OTMS} \]

\[ \text{Ir or Ru photocat. O}_2 \text{ or BrCCl}_3 \]

\[ \text{L-proline (10 mol\%)} \]

\[ \text{TMSCF}_3 \]

2. Ru, Ir Complexes

2.2. Net reductive reactions

2.2.1. Alkene reduction

2. Ru, Ir Complexes

2.2. Net reductive reactions

2.2.2. Reductive dehalogenation

\[
\begin{align*}
[Ru(bpy)_3Cl_2 (2.5 \text{ mol\%})] & \rightarrow \text{HCOOH, iPr}_2\text{NEt, DMF} \\
\text{visible light} & \rightarrow \\
\text{HCOOH} & \rightarrow \text{iPr}_2\text{NEt} \\
\text{visible light} & \rightarrow \\
\text{reductive quenching cycle} & \rightarrow \\
\text{Ru(I)} & \rightarrow \\
\text{Ru(II)} & \rightarrow \\
\text{Ru(II)} & \rightarrow \\
\text{Ru(I)} & \rightarrow \\
\text{R}_1 \text{R}_2 & \rightarrow \\
\text{H} & \rightarrow \\
\text{R}_1 \text{R}_2 & \rightarrow \\
\end{align*}
\]

Limitation: only activated halides

2. Ru, Ir Complexes

2.2. Net reductive reactions

2.2.2. Reductive dehalogenation

Dehalogenation of unactivated halides

Ir-catalyst has greater reduction potential!!!


Combination with C-C bond formation

2. Ru, Ir Complexes

2.3. Redox neutral reactions

- The substrates participate in both the reductive and oxidative steps of the photocatalytic cycle, with no change to the overall oxidation state from starting materials to product.
- The ability to have both oxidation and reduction processes occurring simultaneously for one overall reaction can enable reaction pathways that would otherwise not be possible.

2.3.1. Cycloadditions

Diels-Alder reaction: two electron-rich partners

2. Ru, Ir Complexes

2.3. Redox neutral reactions

2.3.1. Cycloadditions

\[
\begin{align*}
*\text{Ru(bpz)}_3^{2+} & \xrightarrow{\text{light}} \text{Ru(bpz)}_3^{2+} \\
\text{Ru(bpz)}_3^{2+} & \xrightarrow{O_2} \text{O}_2 \xrightarrow{O_2} \text{O}_2 \\
\text{O}_2 & \xrightarrow{O_2} \text{Ru(bpz)}_3^{+} \\
\text{Ru(bpz)}_3^{+} & \xrightarrow{O_2} \text{MeO}^{+} + \text{Me} \\
\text{MeO}^{+} + \text{Me} & \xrightarrow{[4+2]} \text{MeO}^{+} + \text{Me}
\end{align*}
\]

2. Ru, Ir Complexes

2.3. Redox neutral reactions

2.3.2. C-H arylation of amines

\[ \text{Ar} + \text{CN} \xrightarrow{\text{Ir(ppy)_3 (1 mol\%)}} \text{EWG} \]

NaOAc, DMA, RT

visible light

\[
\begin{align*}
\text{Ar} & \quad \text{EWG} \\
\text{Ph} & \quad \text{CN} \\
\text{Ph} & \quad \text{CO}_2\text{Et} \\
\text{Ph} & \quad \\
\text{Ph} & \quad \text{Boc} \\
\end{align*}
\]

96 %

54 %

72 %

92 %

2. Ru, Ir Complexes

2.3. Redox neutral reactions

2.3.3. Trifluoromethylation

Trimethylfluoronation of Lipitor

2. Ru, Ir Complexes

2.3. Redox neutral reactions

2.3.4. Decarboxylative couplings

\[
\begin{align*}
R' & \text{COOH} + \text{NRBoc} & \xrightarrow{\text{Ir(III) cat.}} & \text{NRBoc} \quad \text{visible light} \\
\text{RCN} & \xrightarrow{X = C, N} & \text{R''} \\
\text{R'COOH} & + \text{NC-RCN} & \xrightarrow{\text{Ir(III) cat.}} & \text{NC-PhOMe} \quad \text{visible light} \\
\text{MeO-Ph-COOH} & + \text{NC-CPh} & \xrightarrow{\text{Ir(III) cat.}} & \text{Ph-NC-PhOMe} \quad \text{visible light} \\
\end{align*}
\]

2. Ru, Ir Complexes

2.3. Redox neutral reactions

2.3.4. Decarboxylative couplings

2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.1. Enamine catalysis

a) $\alpha$-Functionalization

Combination of photo- and organocatalysis

\[
\text{Me} - \text{N} - \text{tBu} \quad \text{•TfOH}
\]

\[
\begin{align*}
\text{H} & \quad + \quad \text{Br}_{\text{EWG}} \\
\text{H} & \quad \text{R} \\
\text{H} & \quad \text{EWG}
\end{align*}
\]

\[
\text{20 mol\%} \quad \text{0.5 mol\% Ru(bpy)$_3$Cl$_2$} \\
\text{2,6-lutidine, DMF} \\
\text{visible light}
\]

\[
\begin{align*}
\text{H} & \quad \text{CO$_2$Et} \\
\text{hex} & \quad \text{CO$_2$Et} \\
\text{93\%, 90\% ee} \\
\text{H} & \quad \text{CO$_2$Et} \\
\text{hex} & \quad \text{Ph} \\
\text{92\%, 90\% ee} \\
\text{H} & \quad \text{O} \\
\text{hex} & \quad \text{O} \\
\text{84\%, 96\% ee} \\
\text{H} & \quad \text{O} \\
\text{hex} & \quad \text{O} \\
\text{80\%, 92\% ee}
\end{align*}
\]

2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.1. Enamine catalysis

a) α-Functionalization

2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.1. Enamine catalysis

b) β-Functionalization

\[
\text{[Ir(p-MeO-ppy)\textsubscript{3}] (1 mol\%) + [Ir(ppy)\textsubscript{3} (1 mol%) + DABCO, DMPU, RT visible light]}
\]

\[
\text{43-61%}
\]

2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.1. Enamine catalysis

b) β-Functionalization

2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.2. Metal catalysis

Cross-coupling of amines with halides

\[
\begin{align*}
\text{R}_1\text{CO}_2\text{H} & \quad \text{NHBOc} \\
\text{or} & \quad \text{or} \\
\text{or} & \quad \text{or} \\
\text{R} & \quad \text{CO}_2\text{H} \\
\text{X} & \quad \text{Ar} \\
\text{X} & \quad \text{R}_2
\end{align*}
\]

Ir photocatalyst (1 mol%)  
Ni catalyst (2-10 mol%)  
Blue LEDs

\[
\begin{align*}
\text{R}_1\text{Ar} & \quad \text{NHBOc} \\
\text{or} & \quad \text{or} \\
\text{R}_1 & \quad \text{NHBOc}
\end{align*}
\]

\(X = \text{halide}\)


Cross-coupling of boronates with halides

\[
\begin{align*}
\text{R}_1\text{BF}_3\text{K} & \quad \text{Br} \\
\text{R}_1 & \quad \text{Br} \\
\text{Br} & \quad \text{R}_2
\end{align*}
\]

Ir photocatalyst (2 mol%)  
Ni catalyst (3 mol%)  
26W CFL

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_2 \\
\text{R}_1 & \quad \text{R}_2
\end{align*}
\]

2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.2. Metal catalysis

Mechanism

Nickel cycle

Photoredox cycle

oxidative addition

visible light

SET
2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.3. Hydrogen atom transfer catalysis

\[ \text{R}_1\text{N} = \text{H} + \text{HO} \cdot \text{R}_2 \xrightarrow{\text{Irt catalyst (1 mol\%)} \atop \text{thiol catalyst (5 mol\%)} \atop \text{TsOH, DMSO, 23 °C} \atop \text{Blue LEDs}} \xrightarrow{} \text{R}_1\text{N} \cdot \text{R}_2 \]

Thiol catalysts

2. Ru, Ir Complexes

2.4. Dual catalysis

2.4.3. Hydrogen atom transfer catalysis

For methylation of pyridine:

3. Organic Catalysts

3.1. Catalyst structures

- Often cheaper and better available than metal-based catalysts
- Good properties (see review above)

**XANTHENES**

- X, Y, Z = H *Fluorescein*
- X, Y = Br, Z = H *Eosin Y*
- X, Y = I, Z = Cl *Rose Bengal*

**PYRYLIUMS**

- Y, R\(^{-}\) = H, R, R\(^{-}\) = Et *Rhodamine B*
- Y = Me, R\(^{+}\) = H, R, R\(^{+}\) = Et *Rhodamine 6G*

**ACRIDINIUMS**

**PERYLENES**

**CYANOARENES**
3.2.1. With Eosin Y

**Photoredox/enamine catalysis**

\[
\begin{align*}
\text{hex-CHO} + \text{Br-} & \quad \text{Br-} \quad \text{CO}_2\text{Et} \quad \text{CO}_2\text{Et} \\
\text{hex} & \quad \text{Br} & \quad \text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

20 mol\% eosin Y (0.5 mol\%) 2,6-lutidine, DMF, visible light

\[
\begin{align*}
\text{hex-CHO} \quad \text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{hex} & \quad \text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

85\%, 88\% ee


**Diaryl coupling**

\[
\begin{align*}
\text{Ph-N}_2\text{BF}_4 & \quad + \quad \text{C}_5 \quad \text{X} \\
\text{R}_2 & \quad \text{C}_5 & \quad \text{X} \\
\end{align*}
\]

 eosin Y (1 mol\%) DMSO, 530 nm LED

\[
\begin{align*}
\text{Ph} & \quad \text{X} \\
\end{align*}
\]

X = O, NBoc, S

40-86\%

3. Organic Catalysts

3.2. Examples

3.2.1. With Eosin Y

Mechanism

\[
\text{N}_2\text{BF}_4 \rightarrow \text{eosin Y} \rightarrow \text{X} \rightarrow \text{X}^- \rightarrow \text{N}_2 + \text{BF}_4^- + \text{C}_6\text{H}_5^-
\]

Photoredox cycle

3. Organic Catalysts

3.2. Examples

3.2.2. With Acridinium Salts

Intramolecular hydroetherification

3. Organic Catalysts

3.2. Examples

3.2.2. With Acridinium Salts

Intermolecular hydrofunctionalization

\[ R_2CH\equiv CHMe + HX \xrightarrow{\text{Cat.}} R_2CHMeX \quad \text{anti-Markovnikov} \]

Cat.: \[ ^{+}\text{N}^\text{Me}\text{ClO}_4^- \]

HX = HF, HCl, HR\text{2}PO\text{4}, HRSO\text{3}

3. Organic Catalysts

3.2. Examples

3.2.3. With Perylenes

Challenge:
• aryl radical generation: only from electron-poor substrates:

• common photocatalysts cannot provide enough energy for:

Solution:
• consecutive photoelectron transfer: conPET = two excitations of the catalyst

3.2.3. With Perylenes

conPET: principle

3. Organic Catalysts

3.2. Examples

3.2.3. With Perylenes

• Applications:

Photoreduction

\[
\begin{align*}
\text{Cl, Br, I} & \quad \text{PDI (5 mol\%)} \\
\text{Et}_3\text{N} & \quad \text{Et}_3\text{N} \\
\text{DMSO, 455 nm LED} & \quad \text{DMSO, 455 nm LED} \\
\text{35-98\%} & \quad \text{35-98\%}
\end{align*}
\]

Arylation

\[
\begin{align*}
\text{Cl, Br} & \quad \text{X} \\
\text{R}_1 & \quad \text{X = O, NR} \\
\text{PDI (10 mol\%)} & \quad \text{PDI (10 mol\%)} \\
\text{Et}_3\text{N} & \quad \text{Et}_3\text{N} \\
\text{DMSO, 455 nm LED} & \quad \text{DMSO, 455 nm LED} \\
\text{28-72\%} & \quad \text{28-72\%}
\end{align*}
\]

4. Total Syntheses