

# Ligand-to-Metal Charge Transfer via [M—O]\* Intermediate in Organic Photochemistry

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**1. Introduction** 

2. LMCT via [M—O]\* Intermediate in Organic Synthesis
 2.1. LMCT via [M—OR]\* Intermediate: Alkoxy Radicals
 2.2. LMCT via [M—O<sub>2</sub>CR]\* Intermediate: Carboxylic Radicals

**3. Summary and Outlook** 





### Photocatalytic Synthesis via MLCT & LMCT



[1] Z. Zuo, et al. Chem. Rev. 2022, 122, 2429; [2] K. Fu, et al. Eur. J. Org. Chem. 2023, 26, 1.





## **Comparison Between MLCT and LMCT**





- Bimolecular quenching: requires long-lived excited state
- Photoredox: requires matching redox-potentials
- Metal-complex: [Ru(bpy)<sub>3</sub>]<sup>2+</sup>, *fac*-[lr(ppy)<sub>3</sub>], etc.



- Electronic transition:  $\pi_{(L)} \rightarrow d^*_{(M)}$
- Pre-coordination avoids the need for long-lived excited states
- Independent from individual redox-potentials
- Metal-complex: CuCl<sub>2</sub>, FeCl<sub>3</sub>, Ce(OMe)Cl<sub>5</sub><sup>2-</sup>, etc.





## Ligand-to-Metal Charge Transfer (LMCT)



Electrophilic, high-valent metal: the empty metal orbital (d\*) must be relatively low in energy. Electron-rich  $\sigma$  or  $\sigma$ + $\pi$ -donor ligands: the internal source of electrons.

## Introduction





via [M—C]\* Intermediate: Co(III)-C Homolysis





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## LMCT via [M—OR]\* Intermediate: Alkoxy Radicals



General mechanism diagram and generation of radicals



## LMCT via [M—OR]\* Intermediate: Selected Examples



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#### Zuo, 2018: δ-Functionalization of Alkanols



[1] Z. Zuo, et al. J. Am. Chem. Soc. 2018, 140, 1612;
 [2] R. Zeng, Y. Li, et al. Org. Lett. 2021, 23, 8968;
 [3] Z. Zuo, et al. J. Am. Chem. Soc. 2020, 142, 6216;
 [4] Z. Zuo, et al. Chem. 2020, 6, 266.

## LMCT via [M—OR]\* Intermediate: Selected Examples

Zuo, 2018: Cycloaddition of Cycloalkanols with Alkenes



## LMCT via [M—OR]\* Intermediate: Alkoxy Radical or Chlorine Radical ?



Homoleptic Metal Complexes [MX<sub>n</sub>]



Comfired by transient absorption spectroscopy and photocrystallography

Heteroleptic Metal Complexes [M(OR)X<sub>n</sub>]



### For HAT process :



[CI-ROH]<sup>•</sup>: Proposed by Walsh and Schelter to explain the changing regioselectivities with different alcohol co-catalysts.



A. Investigating the Possibility of Chlorine Radical–Alcohol Complexes as Selective HAT Agents



- Alcohol co-catalysts give varying degrees of regiocontrol.
- Precluing CI radical as selective HAT agent by varing selectivities.

 Precluing CI radical–ROH complexes as selective HAT agent by identical selectivities.

B. EPR Studies to Investigate the Identity of Ligand Centered Radicals





- The spectrum of chlorine radical spin adduct is distinguishable from the PBN adduct of alkoxy radicals, precluding the generation of chlorine radical in the LMCT of Ce(OR)Cl<sub>5</sub><sup>2-</sup>.
- Most plausible LMCT pathway: release of alkoxy radicals.

C. Transient Absorption Spectroscopy (TAS) Studies to Probe the Generation of Ligand-Centered Radicals

**Principle of TAS:** 



- Chlorine radical showcased charge-transfer absorption in the 320–360 nm region.
- Chlorine radical and benzene could form a chlorine radical-benzene complex with a strong absorption band centered at 490 nm.
- Chlorine radical and CH<sub>3</sub>OH couldn't form a chlorine radical–alcohol complex since only the chlorine-radical absorption band was observed.

C. Transient Absorption (TA) Spectroscopy Studies to Probe the Generation of Ligand-Centered Radicals



- [CeCl<sub>6</sub>]<sup>2-</sup> showcased chlorine charge transfer band in the range of 320–360 nm, while the same absorption was not detected in [Ce(OR)Cl<sub>5</sub>]<sup>2-</sup>.
- Addition of alkoxy radicals to PPh<sub>3</sub> could enable the confirmation of alkoxy radicals via detection of [ROPPh<sub>3</sub>]<sup>•</sup>

D. Kinetic Study with Premade Ce(IV) Methoxide Pentachloride Complex to Probe the Rate-Limiting Step



 Ce<sup>III</sup>/TBACI/MeOH: exhibits an induction period. Ce<sup>III</sup> can be activated by a photoinduced singleelectron oxidation with DBAD.

 $(E_{1/2}(Ce^{III}/Ce^{IV}) = 0.41 V vs SCE)$ DBAD ( $E^* = 1.66 V vs SCE$ )

 Methoxy radical-mediated HAT is the rate-limiting step in the reaction mediated by [Ce(OMe)Cl<sub>5</sub>]<sup>2-</sup>

D. Kinetic Study with Premade Ce(IV) Methoxide Pentachloride Complex to Probe the Rate-Limiting Step



• The identical KIE of entry 1 and 3 validates the alkoxy radical as the exclusive HAT agent, as the coexistence of chlorine radical would lead to a declined ratio.

E. Regioselectivity Study to Probe the Identity of the Selective HAT Agent



F. Density Functional Theory Calculations on Photoexcitation and Radical-Mediated HAT

### Hole-electron Analysis of [Ce(OMe)Cl<sub>5</sub>]<sup>2-</sup> by TD-DFT Calculations



Confirming a typical LMCT process:

- The electrons are excited mainly from the O atom (38.2%) and the trans-Cl atom (24.9%) to the Ce atom (93.6%).
- Structural relaxation of this excited state reveals Ce–O bond was significantly elongated during the relaxation.

F. Density Functional Theory Calculations on Photoexcitation and Radical-Mediated HAT



Regiochemical divergence of C-H amination of DMB with methoxy and trichloroethoxy radical



G. Selectivity of Radical Generation from the LMCT Homolysis of Ce(IV)-Alkoxide Complexes



## Summary:



- Ce(IV) alkoxide complexes: isolated and XRD characterizaed
- EPR (with DMPO, PBN): DMPO-OR, PBN-OR detected
- TA spectrosopy: alkoxy radical comfired, chlorine radical precluded

- HAT identified an RDS: X = OMe, primary KIE:  $k_H/k_D = 5.5$
- DFT calculations: X = OMe,  $\triangle G^{\neq}$  (1° vs. 3°)= 3.6 kcal/mol
- chloride-free and chloride-containing conditions: identical regioselectivity obtained





#### Horeau principle

Multiplicative nature of stereoinduction lead to amplification of the enantiodifferentation ability of the catalyst.



enantiodifferention in bond formation



### **Reaction scope:**





#### **Mechanistic investigations:**



B. Enantioconvergent transformation: Same prochiral intermediate generated by the C–C bond scission





C. Steady state photolysis experiments:





#### D. Spin-trapping EPR experiments:



![](_page_29_Picture_1.jpeg)

![](_page_29_Figure_2.jpeg)

#### Z. Zuo, et al. Science. 2023, 382, 458.

![](_page_30_Picture_0.jpeg)

![](_page_30_Picture_1.jpeg)

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## LMCT via [M—O<sub>2</sub>CR]\* Intermediate: Carboxylic Radicals

![](_page_31_Picture_1.jpeg)

General mechanism diagram and generation of radicals

![](_page_31_Figure_3.jpeg)

![](_page_32_Figure_1.jpeg)

**Mechanistic Investigations:** 

![](_page_33_Figure_2.jpeg)

C. Radical trapping experiments: TBAF·(<sup>t</sup>BuOH)₄ (2.5 equiv.) Cu(OTf)<sub>2</sub> (2.5 equiv.), Cu(MeCN)<sub>4</sub>BF<sub>4</sub> (2.5 equiv.) MeO. COOH 2 3 1 + + MeCN/benzene (1:1) MeO. MeO MeO. 1 2 3 yield (%) reaction condition 2 3 1 w/ Cu(MeCN)<sub>4</sub>BF<sub>4</sub> 36 14 4 w/o Cu(MeCN)<sub>4</sub>BF<sub>4</sub> 25 21 9

UV-vis absorption spectra of reaction components

#### D. Radical cyclization experiment:

#### Proposed mecchanism

![](_page_34_Figure_3.jpeg)

MacMillan, 2022:

![](_page_35_Figure_2.jpeg)

[1] W. MacMillan, et al. J. Am. Chem. Soc. 2022, 144, 6163; [2] T. Yoon, et al. Nat. Chem. 2022, 14, 94; [3] O. Reiser, et al. Chem. Commun., 2022, 58, 4456;
 [4] J. Jin, et al. Org. Lett. 2019, 21, 4259.

## Content

![](_page_36_Picture_1.jpeg)

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## Summary and Outlook

![](_page_37_Picture_1.jpeg)

![](_page_37_Figure_2.jpeg)

## Summary and Outlook

![](_page_38_Picture_1.jpeg)

![](_page_38_Figure_2.jpeg)

[1] H. Bamford, et al. J. Chem. Soc. Faraday Trans. 1 Phys. Chem. Condens. Phases 1975, 71, 1733; [2] S. Soo, et al. Chem. Sci. 2015, 6, 7130.

![](_page_39_Picture_0.jpeg)

# Thanks for your attention

![](_page_40_Picture_0.jpeg)

![](_page_40_Picture_1.jpeg)

## Alkoxy Radical & Carboxylic Radical: Versatile Intermediates

![](_page_40_Figure_3.jpeg)

[1] Z. W. Zuo, et al. Chem. Rev. 2022, 122, 2429.

# Appendix

![](_page_41_Figure_1.jpeg)

Figure 6. Mechanistic Investigations and Proposed Mechanism

# Appendix

![](_page_42_Picture_1.jpeg)

#### 4.6 The investigations on the diastereoselectivity

![](_page_42_Figure_3.jpeg)

Figure S18. The investigations on the diastereoselectivity.

# Appendix

![](_page_43_Picture_1.jpeg)

## Investigation on the enantioselective C-C bond scission step of amino alcohol

![](_page_43_Figure_3.jpeg)

$$\frac{k_{\rm -S}}{k_{\rm -R}} = \frac{50 \times 100\% - 29 \times 65\%}{50 \times 100\% - 71 \times 65\%} = 8.1$$