### Contra-thermodynamic Alkene Isomerization via Energy transfer(EnT)

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## **Geometry as Information**



## Geometric isomerization of alkene





- Photochemistry Foundation of Energy Transfer
- Contra-thermodynamic Alkene Isomerization
- Perspective
- Summary

### Jablonski Diagram



## Jablonski Diagram

### Alkene isomerization via photochemistry



## Jablonski Diagram

Alkene isomerization via photochemistry



Common organic molecule UV light Side reaction Safety hazard Low ISC

**Reaction Coordinate** 

## **Triplet-triplet** *EnT*(Energy transfer)

**Steal energy from other excited molecule** 



Photosensitizers bridge the gap between the high energy level of common organic molecule and the lower energy of the visible light

## **Triplet-triplet** *EnT*(Energy transfer)



### How to select a photosensitizer



- ✓ The photocatalyst should have a higher triplet energy than the chosen substrate, but lower than the product
- ✓ The photocatalyst should have high intersystem crossing efficiency (S1 to T1)
- ✓ The photocatalyst should also possess a high extinction coefficient
- ✓ It should not participate in side reactions with any substrate in its excited or ground state: hydrogen atom transfer, competing biradical reactions, or redox process

## **Energy scale of Photosensitizer**



- ✓ The photocatalyst distributed in a very broad spectrum, from 30kcal/mol to about 75 kcal/mol
- ✓ Transition metal complex and phenyl ketone are very common as photosensitizer. Heavy atom effect and El Sayed rule allows these molecules have efficient ISC(S₁-T₁)
- ✓ By changing the substituent on the aromatic ring, the triplet energy can be rationally tuned.
- ✓ Some of the photocatalysts will be discussed later



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## **Reignition of Interest**

### **Cinnamyl amine isomerization via energy transfer**

Weaver(2014)



- Hammond published a very detailed mechanistic study on this type of reaction in 1960s. However, the conditions containing the use of stoichiometric amount of photocatalyst and mercury lamp was not practical for synthesis.
- Weaver is the not first person taking advantage of energy transfer to realize Contra-thermodynamic alkene isomerization. But they are one of the earliest labs to pioneer the rediscovery and optimize it for synthetic use.

## **Reignition of Interest**

### **Cinnamyl amine isomerization via energy transfer**

Weaver(2014)



#### Stern-Volmer Experiment



- Installation of methyl leads to higher Z/E ratio by steric effect
- Stern-Volmer experiment showed large discrepencies of rate of energy transfer between Z and E isomers.



### **Possible mechanisms**





- Because of the peculiarity of the cinnamyl amine, two possible reaction mechanisms has been proposed.
- The reductive quenching mechanism can be excluded by enantioenriched substrate

### **Isomerization of Cinnamonitriles**



### **Isomerization of Cinnamonitriles**

#### **Quantitative relationship**



- Taft parameters is used to evaluate the size of substituent at β position
- Larger the β-substituent, more twist the Z isomer of molecule is and higher the ratio Z/E is

### **Isomerization of Cinnamonitriles**



- Considering steric hindrance in a relatively flexible system can be misleading
- A series of bicyclic systems were selected to minimize the conformational freedom
- Lager ring size force the cyano group closer to H, inducing higher A<sub>1.3</sub> strain and higher ratio

## Summary of styrenyl-based substrate



## Non-styrenyl: Leveraging the $n \rightarrow p$ Interaction



### Styrenyl

- Styrenyl based compound has low triplet energy level
- Deconjugation effect rely on A<sub>1,3</sub> strain
- Limited application

### **Beta-boryl**

- Extend the chromophore, and decrease the triplet energy level of substrate
- C-B would be twisted by 90°, driven by the n<sub>o</sub>-p interaction
- Versatile handle for traceless, stereospecific, coupling

## Non-styrenyl: Leveraging the $n \rightarrow p$ Interaction





#### *Evidence for the n*<sub>o</sub>-*p interaction*

- X-ray structure: 5-membe-ring of BPin is nearly perpendicular to alkene
- <sup>11</sup>B NMR: 17.19 ppm for E-8, indicating stabilizing dative  $(n_0 \rightarrow p)$  interaction

Z-29: indirect evidence, absence of conjugation between B and double systems because of steric hindrance

## Non-styrenyl: Leveraging the $n \rightarrow p$ Interaction





## Non-styrenyl: Leveraging the n- $\pi^*$ Interaction



Di-ester



73%, 94:6







Ester-amide





Di-amide



96%, 95:5

- Deconjugation driven by  $n-\pi^*$  interaction
- n-π\* plays vital structural roles in complex biomolecule, such as collagens.

## Non-styrenyl: Leveraging the n- $\pi^*$ Interaction





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#### Other secondary interactions

On top of allylic strain and dative interaction between non-bonding orbital of O and empty orbital, many other secondary interactions are potential to induce the deconjugation of the Z-isomers, including H-bonding, electrostatic effect and so on. By leveraging various type of interactions, a greater variety of alkene can be isomerized by energy transfer.

#### Cascade transformation

Generally, the photocatalyst is orthogonal to many other downstream transformation, such as crosscoupling. Binding isomerization with stereospecific transformation, stereodivergent catalysis could be achieved

#### Development of new photocatalyst

Finer-tuning the energy level of  $T_1$  of photocatalyst can help to have higher chance to find the optimized conditions of contra-thermodynamic isomerization



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## Summary

- Contra-thermodynamic isomerization via energy transfer
  - Atom economical, efficient, and green
  - Energy transfer provide a milder way to excite the common organic compound to T<sub>1</sub> compared to direct excitation
  - Alkenes on T<sub>1</sub> are able to decay to either E or Z isomers
  - Deconjugation effect is the key reason for the accumulation of Z isomers
- Styrenyl based alkene isomerization
  - Styrenyl based compound has low triplet energy level
  - Deconjugation effect rely on A1,3 strain
- Non-styrenyl based alkene isomerization
  - Boryl unsaturated ester and amide: Leveraging the  $n \rightarrow p$  Interaction
  - 1,4-dicarbonyl coumpound: leveraging n- $\pi^*$  Interaction

## Source

### Review

- Tomáš Neveselý, Max Wienhold, John J. Molloy, and Ryan Gilmour Chemical Reviews 2022 122 (2), 2650-2694
- J. J. Molloy, T. Morack and R. Gilmour Angew. Chem. Int. Ed.2019, 58, 13654-13664.
- Dutta, S.; Erchinger, J. E.; Strieth-Kalthoff, F.; Kleinmans, R.; Glorius, F., Energy transfer photocatalysis: exciting modes of reactivity. Chemical Society Reviews 2024.

#### Website

- <u>https://chemfd.github.io/Photochemistry\_2/index.html</u>
- <u>https://www.youtube.com/watch?v=rHbxqduwc\_E</u>

# **Questions?**