



铜催化自由基参与C-C/X键构建机制的 DFT理论计算研究

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张雪 副研究员(有机所)

汇报时间：2024.09.27



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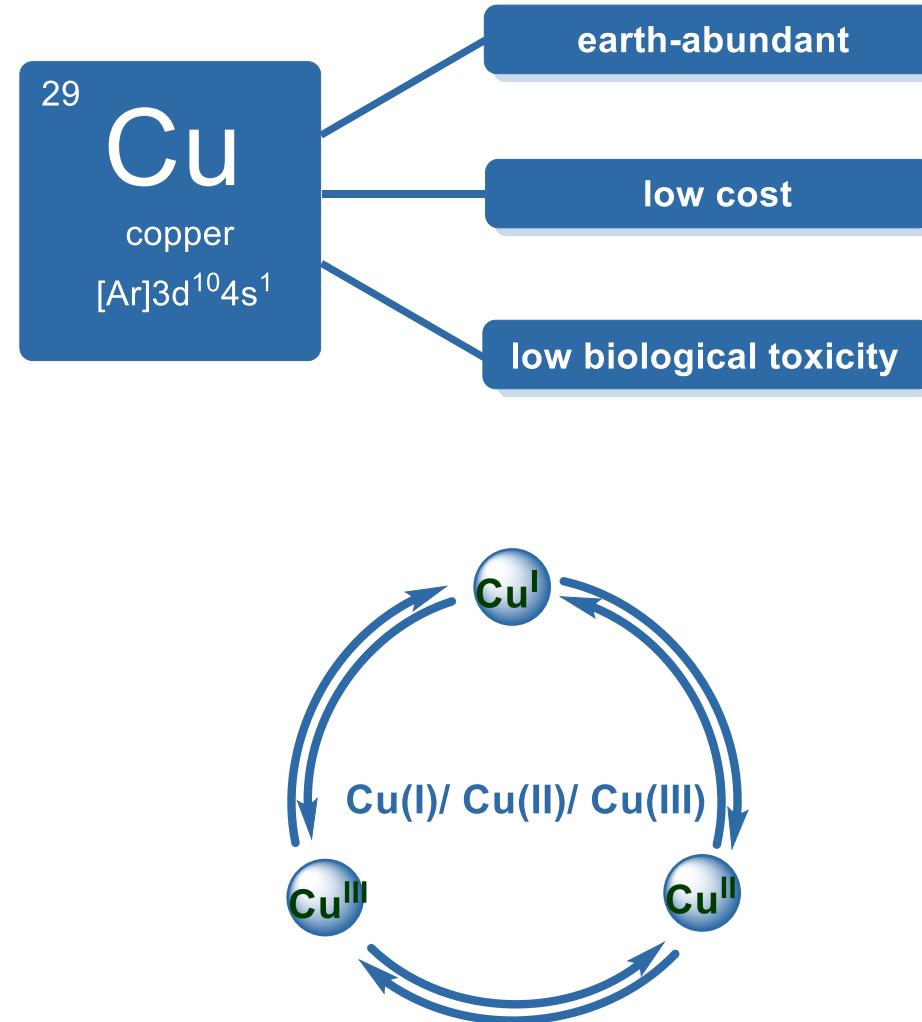
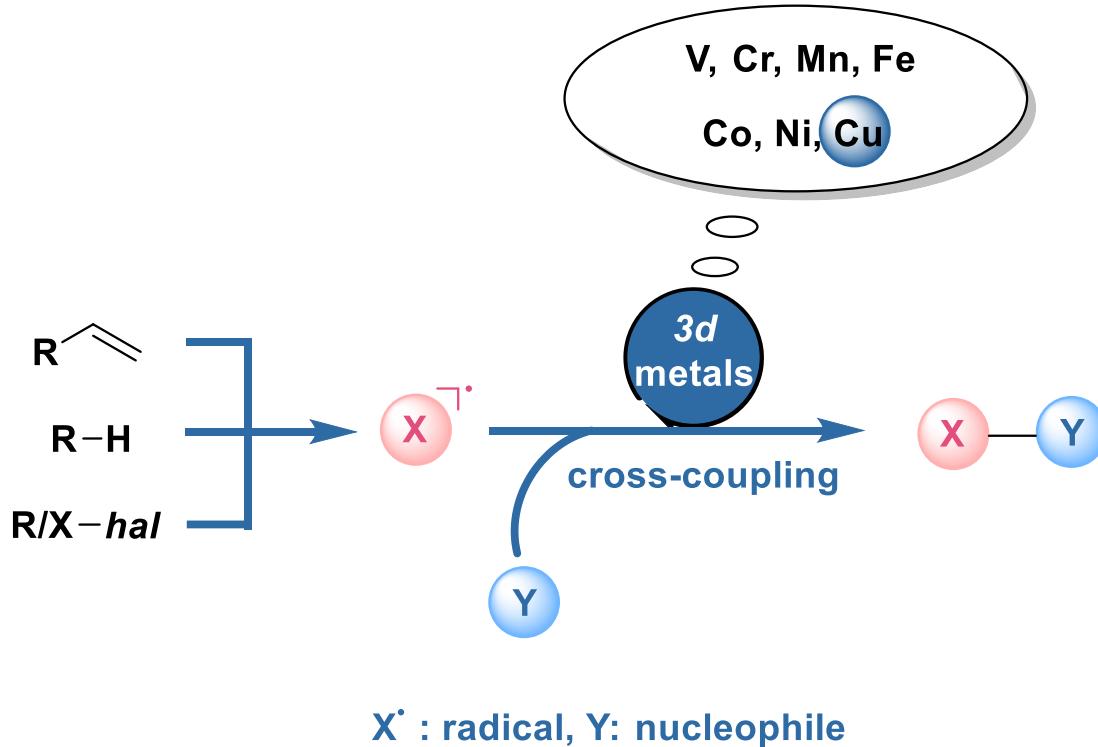
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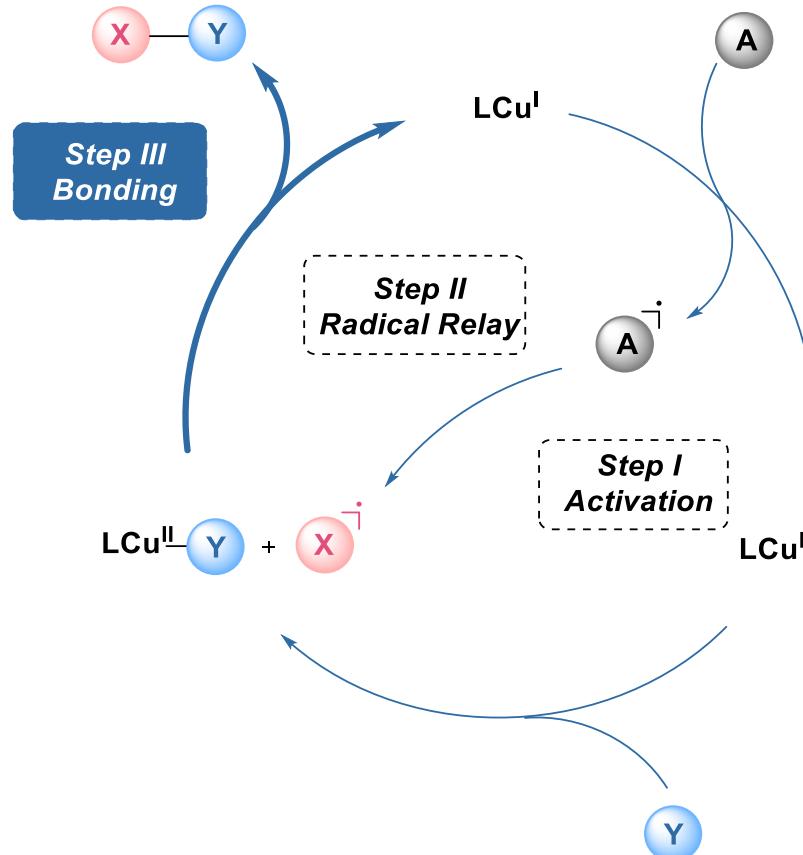
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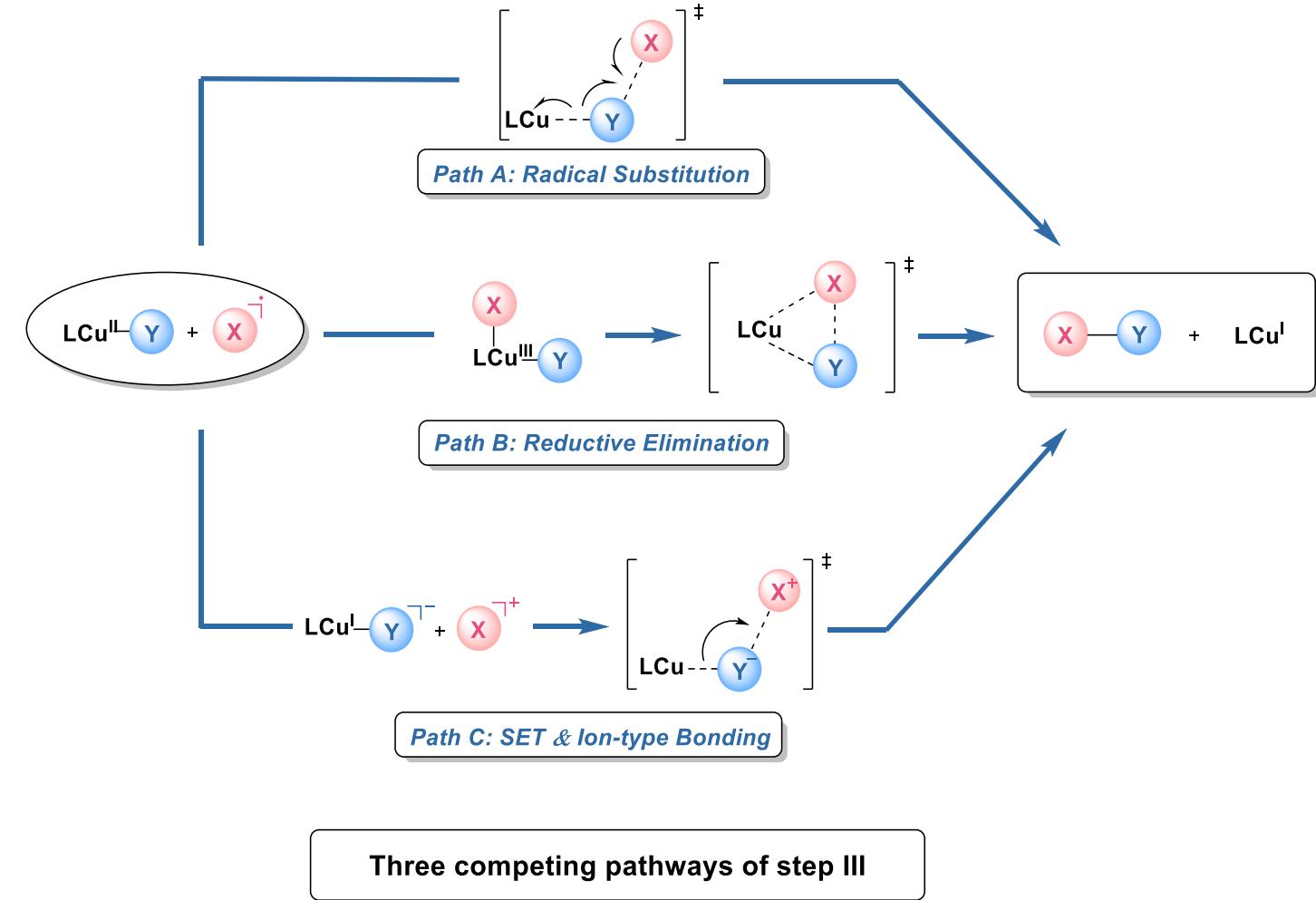
1 背景介绍



1 背景介绍

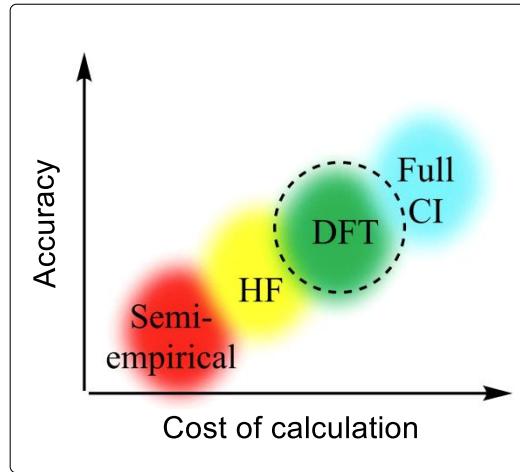


General Mechanistic Proposal for Copper Catalyzed Radical Transformation Reactions

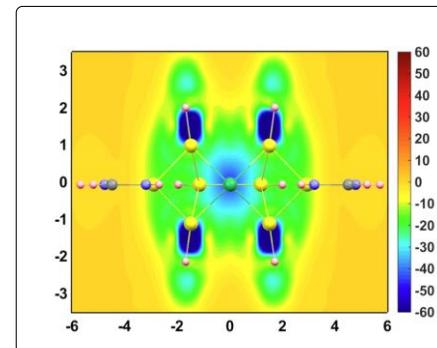


Three competing pathways of step III

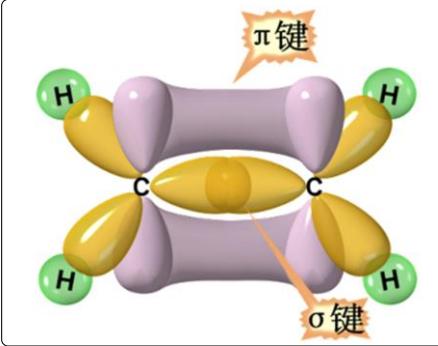
1 背景介绍



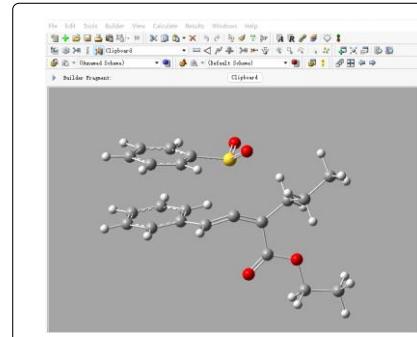
电子性质



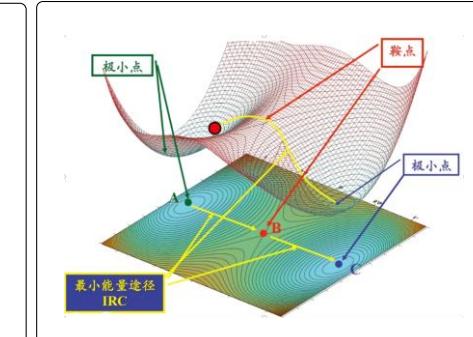
轨道分析



获取关键中间体和过渡态



反应机理



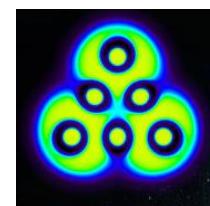
常用计算与分析软件



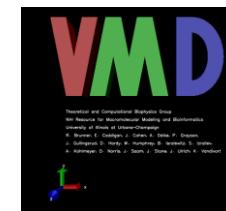
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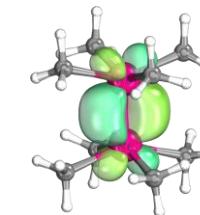
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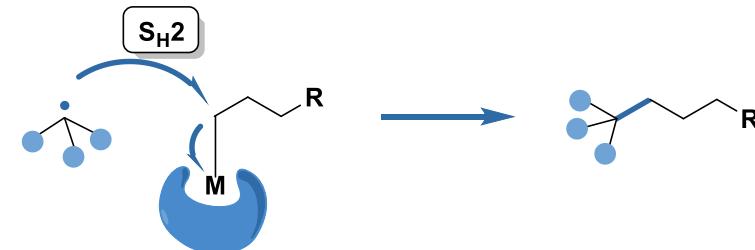
2.2 基于还原消除机制

2.3 基于离子型成键机制

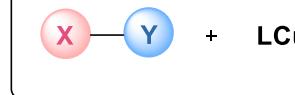
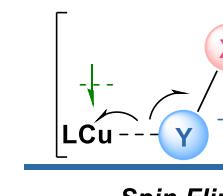
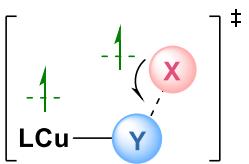
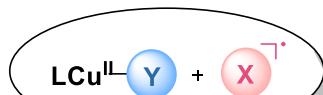
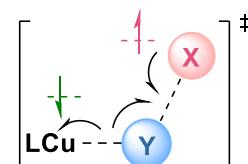
☞ 3 总结与展望

2.1 基于自由基取代机制

Path A: Radical Substitution

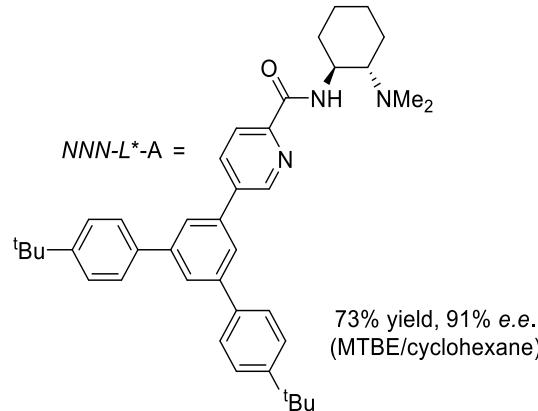
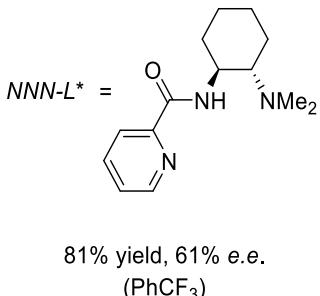
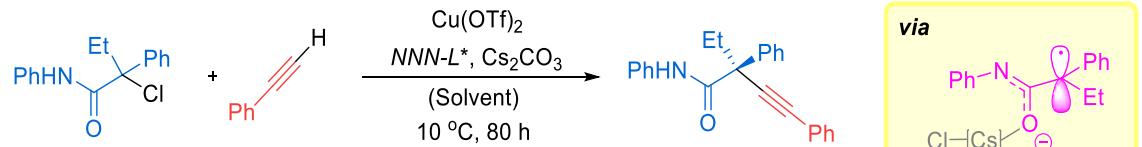


S_{H2} Substitution

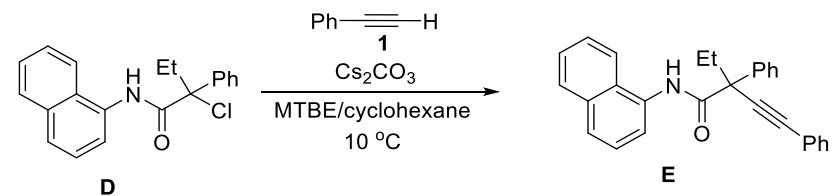
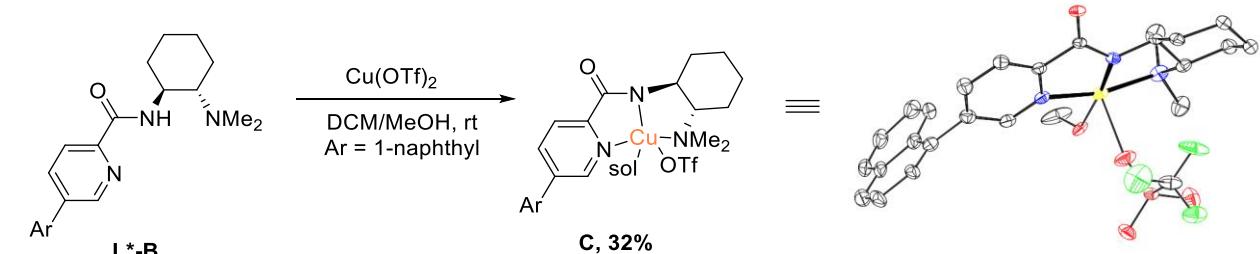


2.1 基于自由基取代机制

C-C

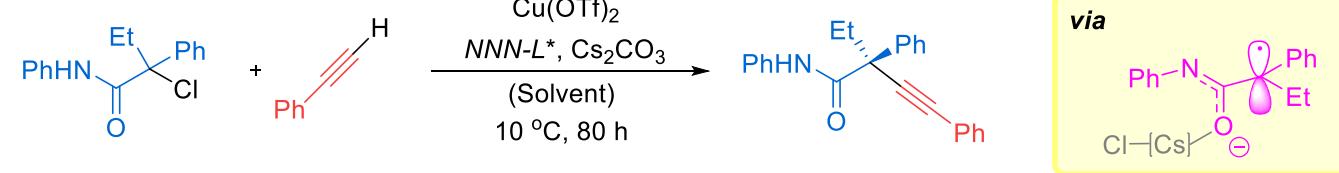


机理实验

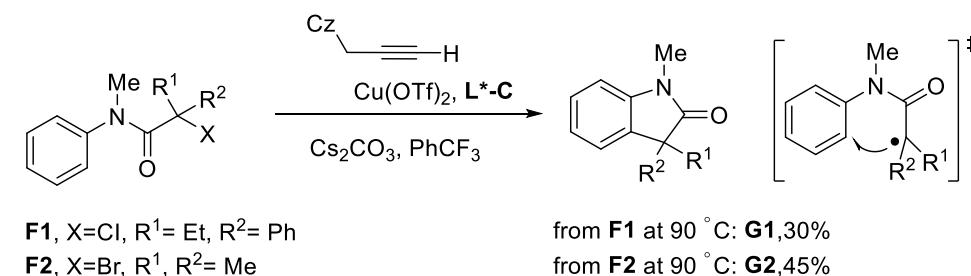
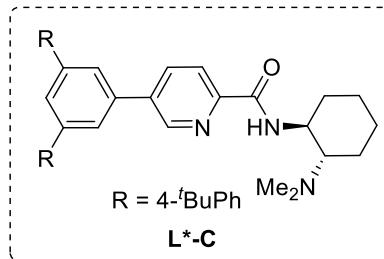
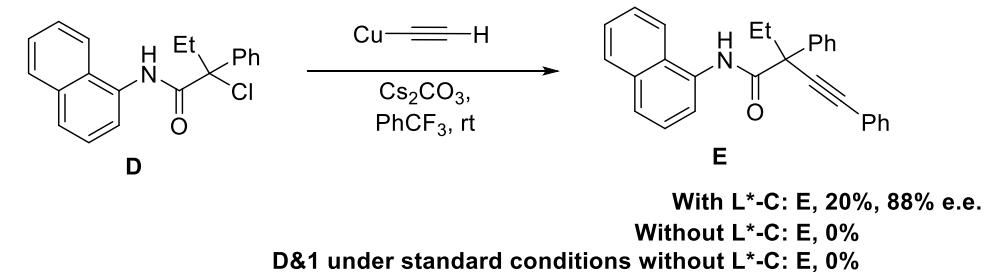
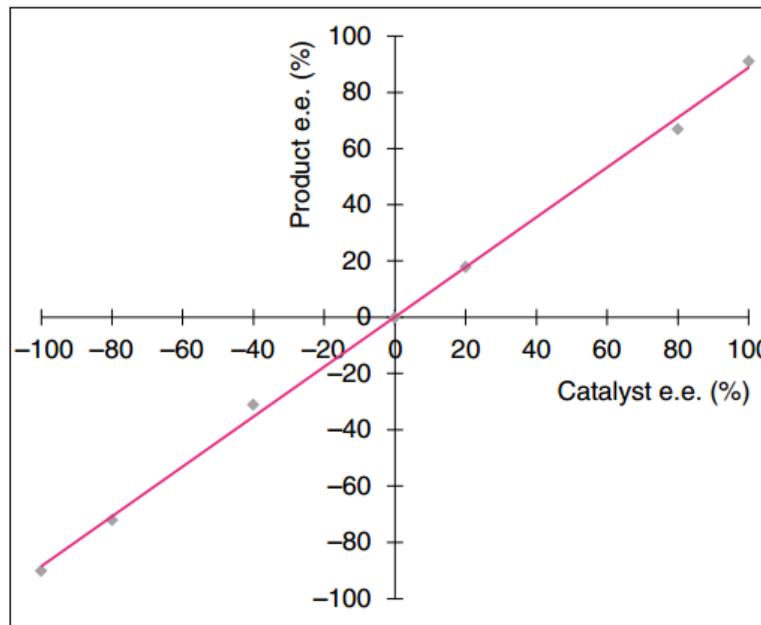


With C : E , 75%, 89% e.e.
With $\text{Cu}(\text{OTf})_2/L^*-B$: E , 50%, 88% e.e.

2.1 基于自由基取代机制

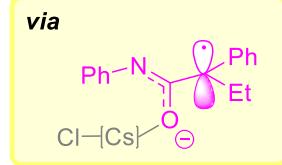
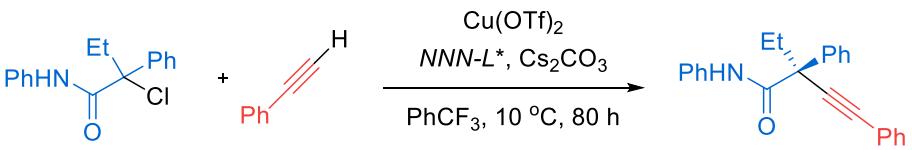


机理实验

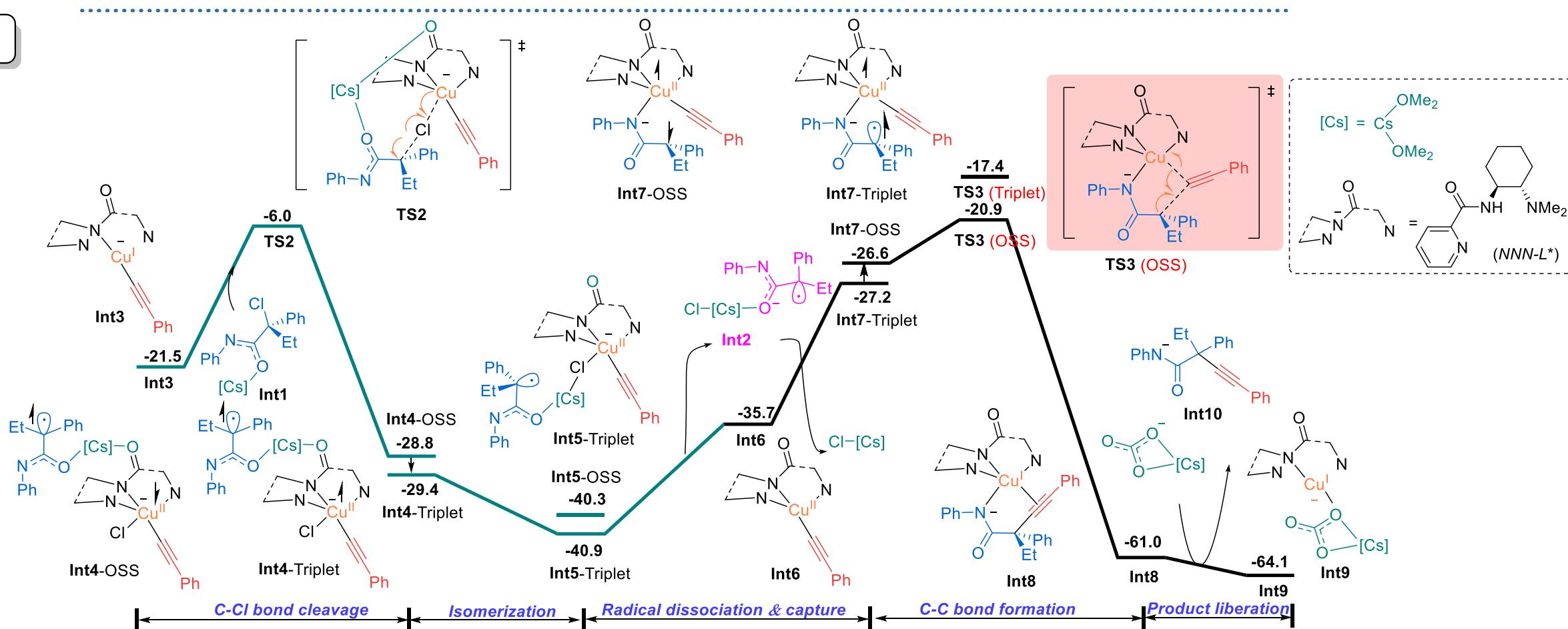


Relationship between ee values of ligand and product.

2.1 基于自由基取代机制



势能面

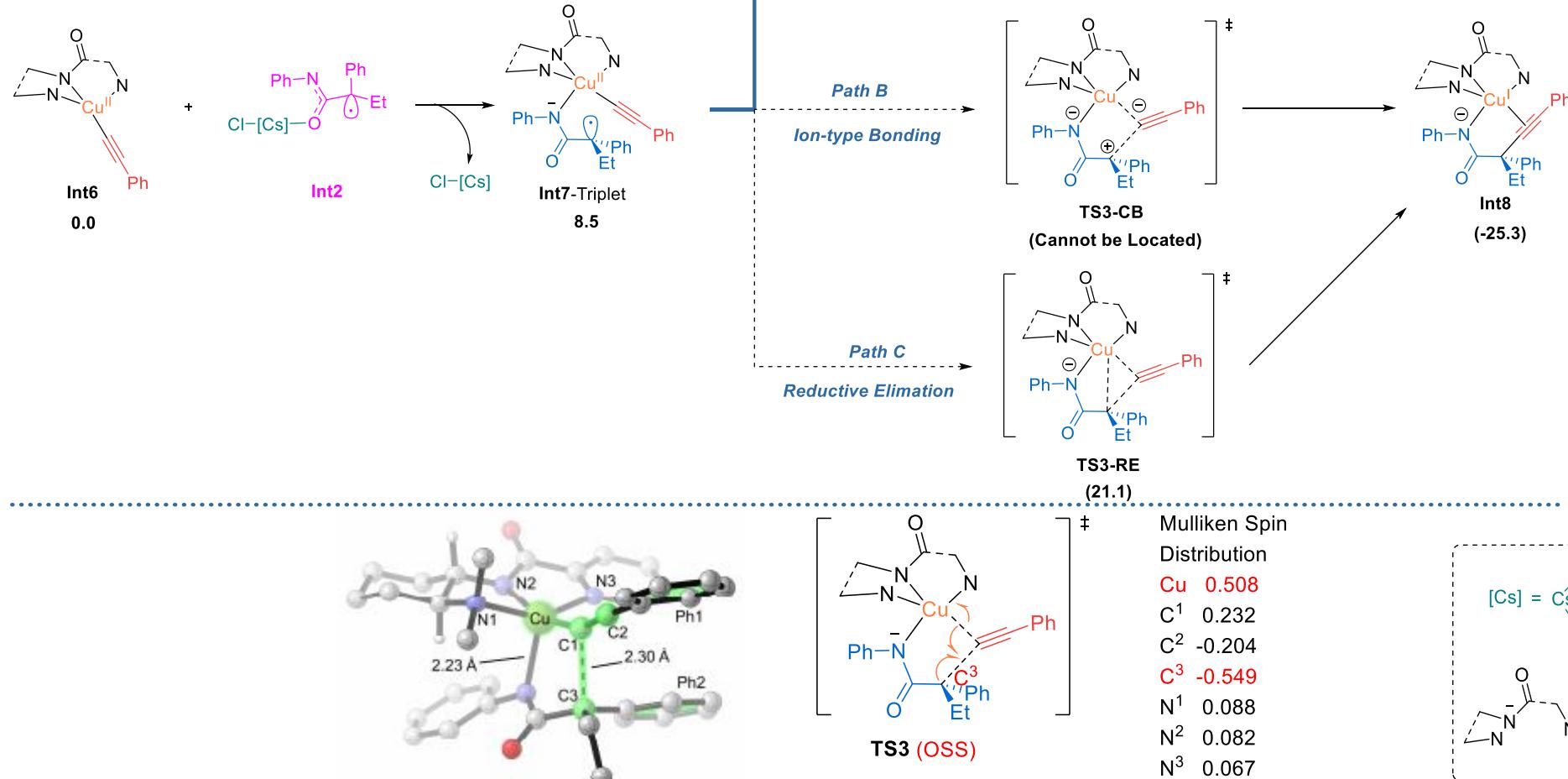


ΔG_{sol} in kcal/mol, B3LYP-D3(BJ)/6-311+G(d,p)-SDD-SMD(Cyclohexane)//B3LYPD3(BJ)/6-31G(d)-LANL2DZ

Liu, X.-Y. et.al., *Nat. Chem.* 2022, 14, 949–957.

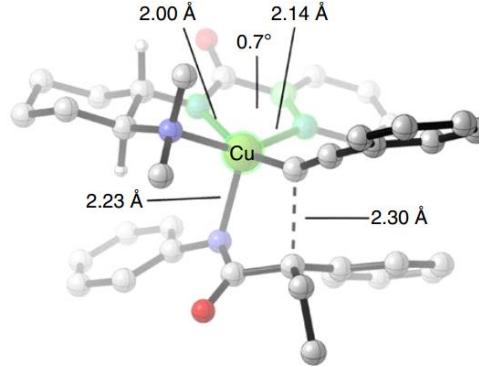
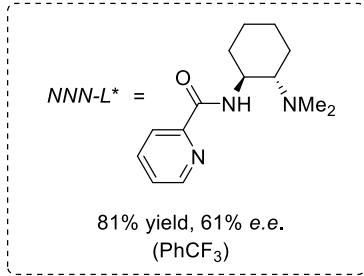
2.1 基于自由基取代机制

竞争路径

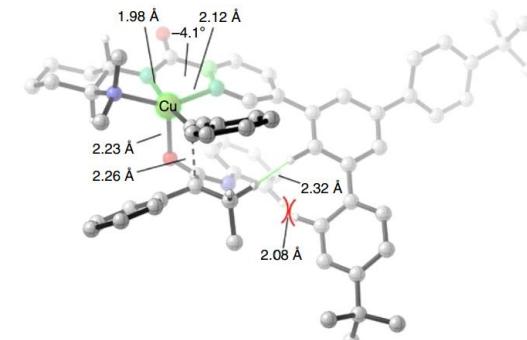
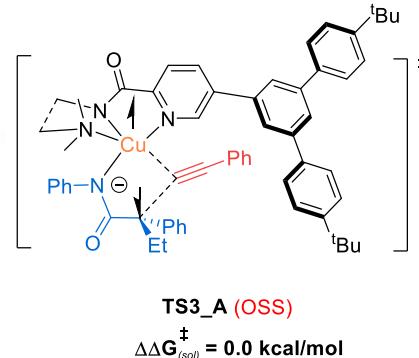
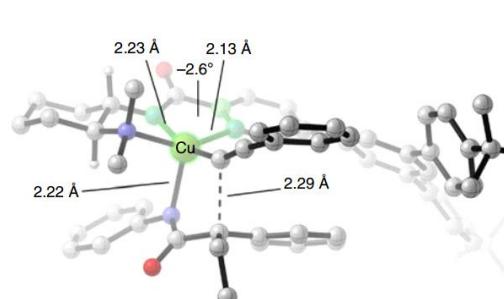
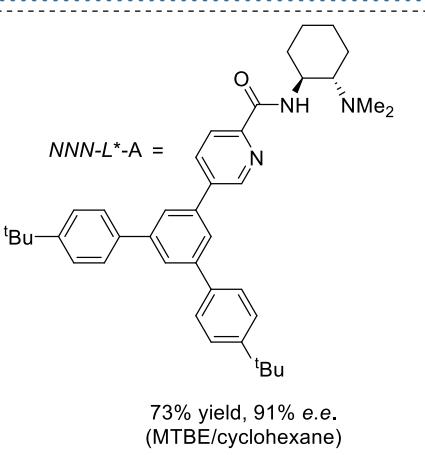
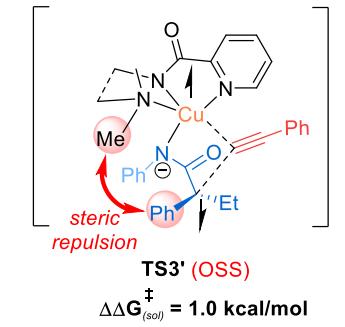
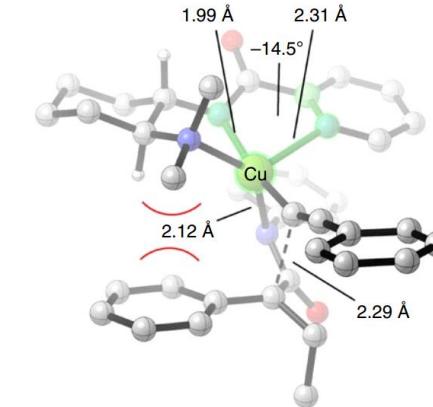
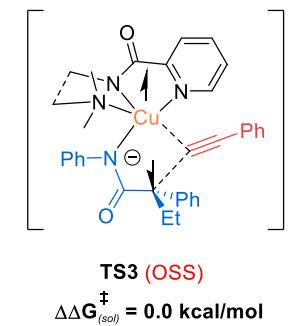


2.1 基于自由基取代机制

对映选择性



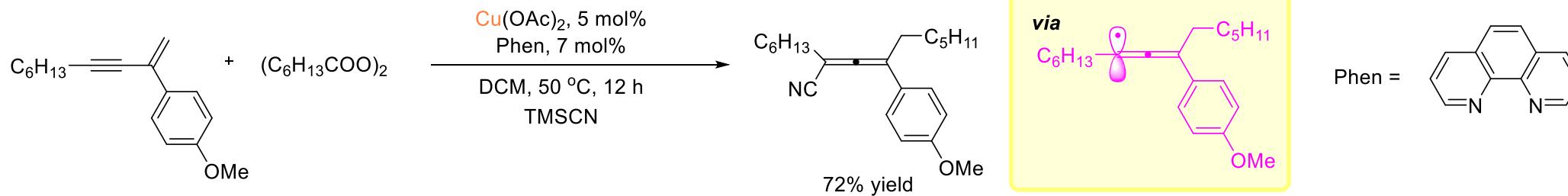
实验结果ee: 61%
计算结果ee: 68%



实验结果ee: 91%
计算结果ee: 94%

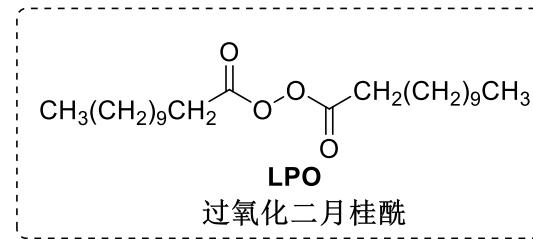
2.1 基于自由基取代机制

C-C



机理实验

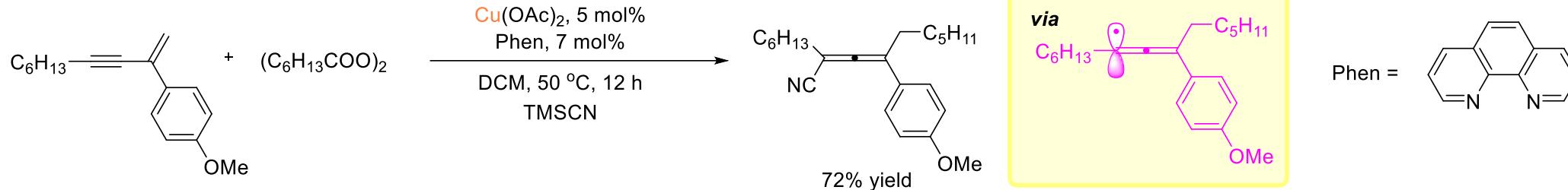
Radical Trapping



Ring-Opening Experiments

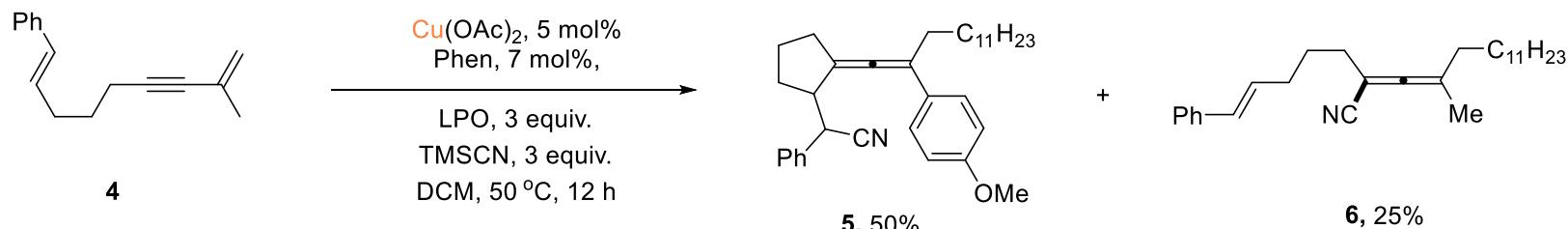


2.1 基于自由基取代机制

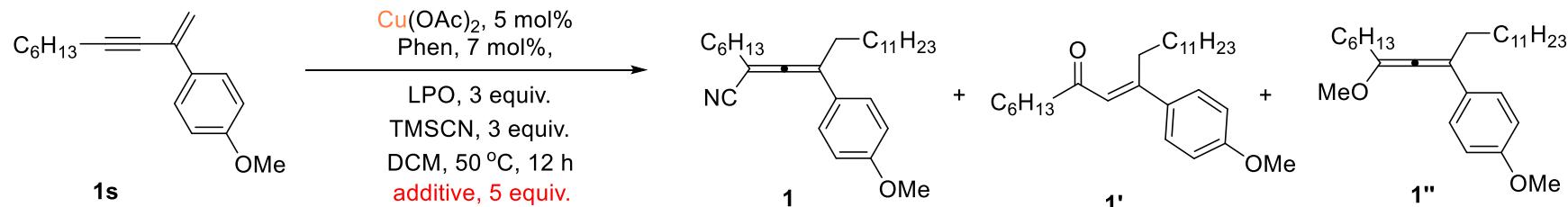


机理实验

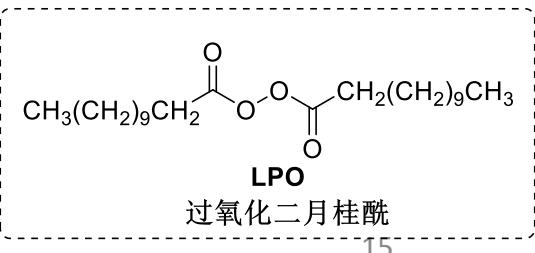
Ring-Closing Experiments



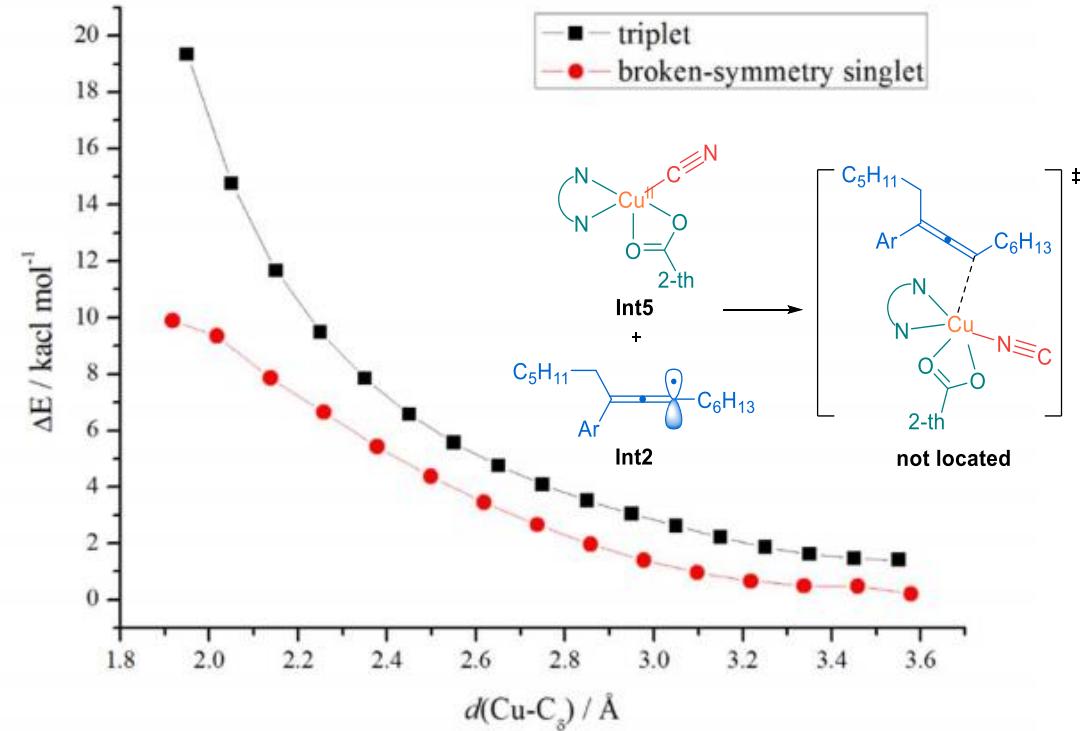
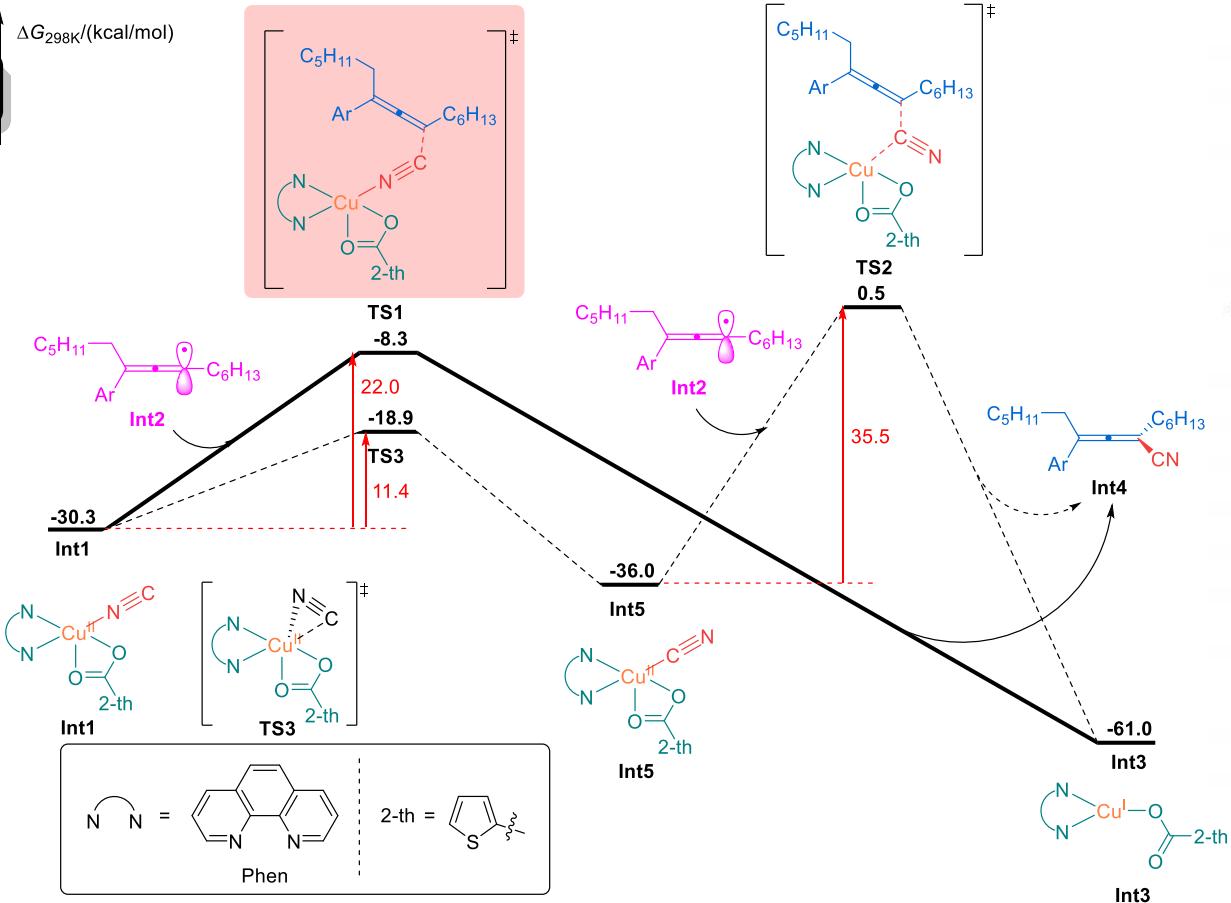
Probe Experiments for the Allenyl Cation with LPO



entry	additive	1	1'	1''
1	none	73%	/	/
2	H ₂ O	71%	0	/
3	MeOH	69%	/	0

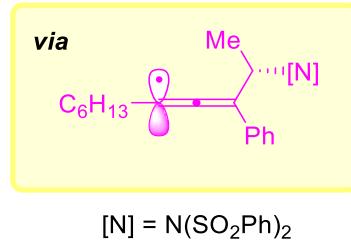
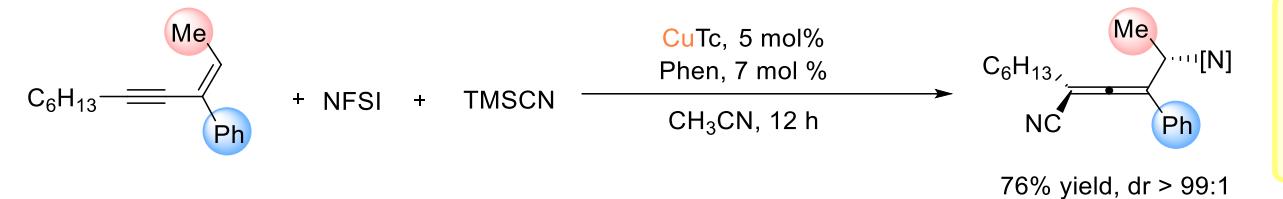


2.1 基于自由基取代机制

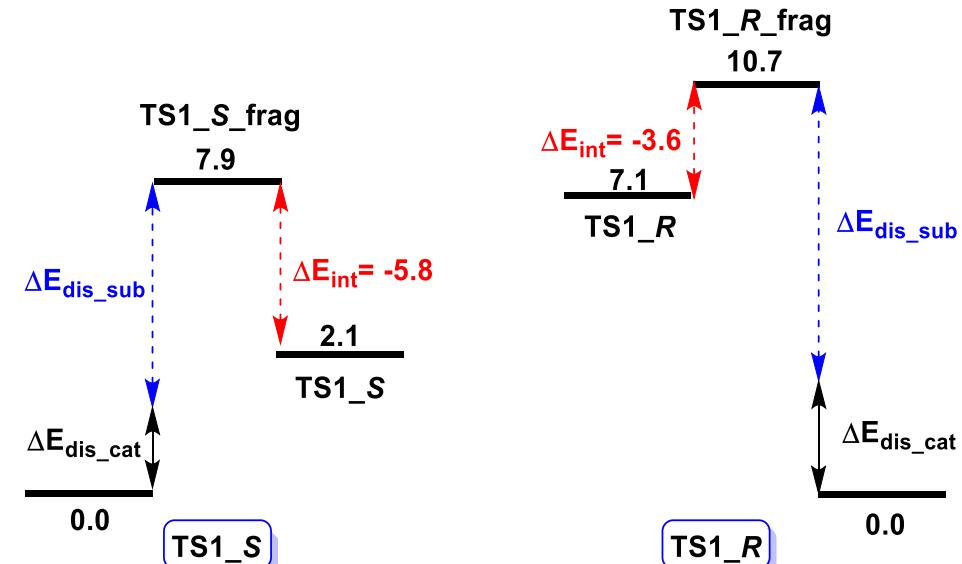
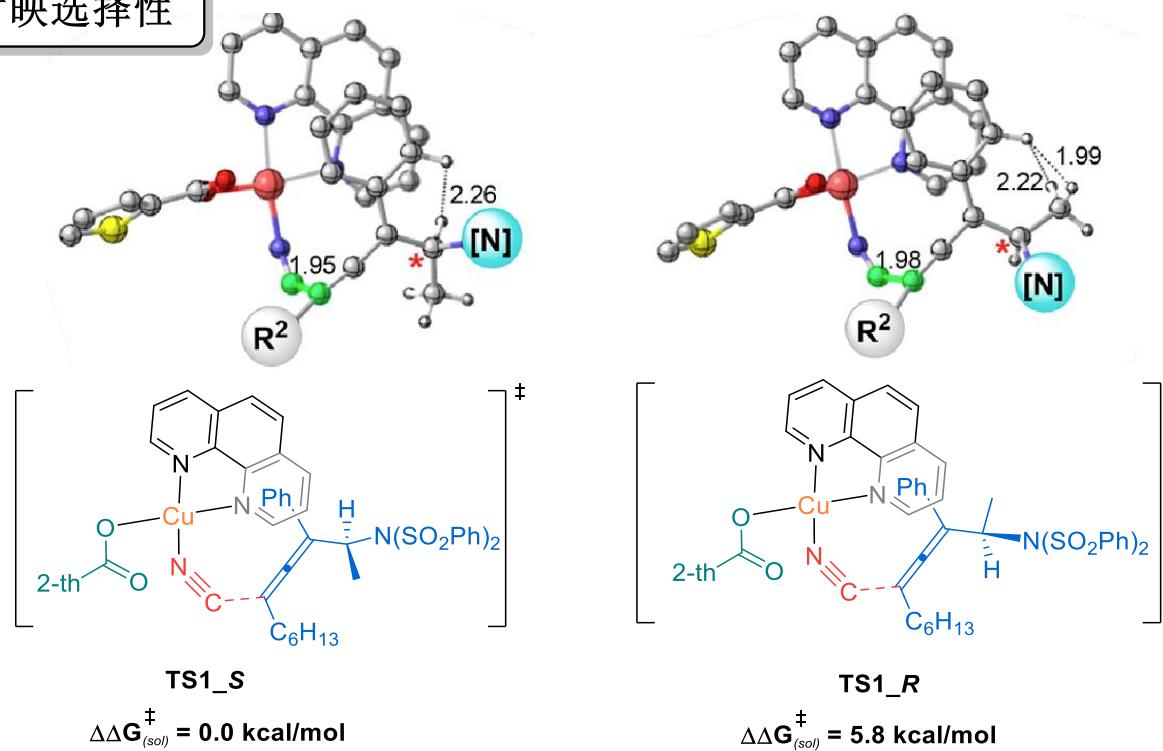


The relaxed potential energy surfaces corresponding to Cu-C δ bond coupling between **INT5** with **INT2** on triplet (black line) and broken-symmetry singlet state (red line) surfaces.

2.1 基于自由基取代机制



非对映选择性



Distortion and interaction analyses for TS1S (left) and TS1R (right).
 Abbreviations at the subscript of ΔE are defined as following. "dis" and "int" denote the distortion energy and interaction energy, respectively. "sub" and "cat" indicate the electronic energy contributed from the substrate (radical) and catalyst, respectively.



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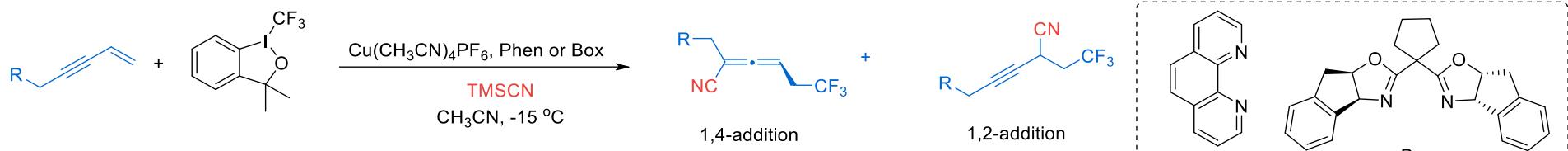
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2.3 基于离子型成键机制

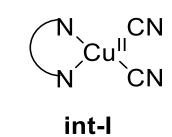
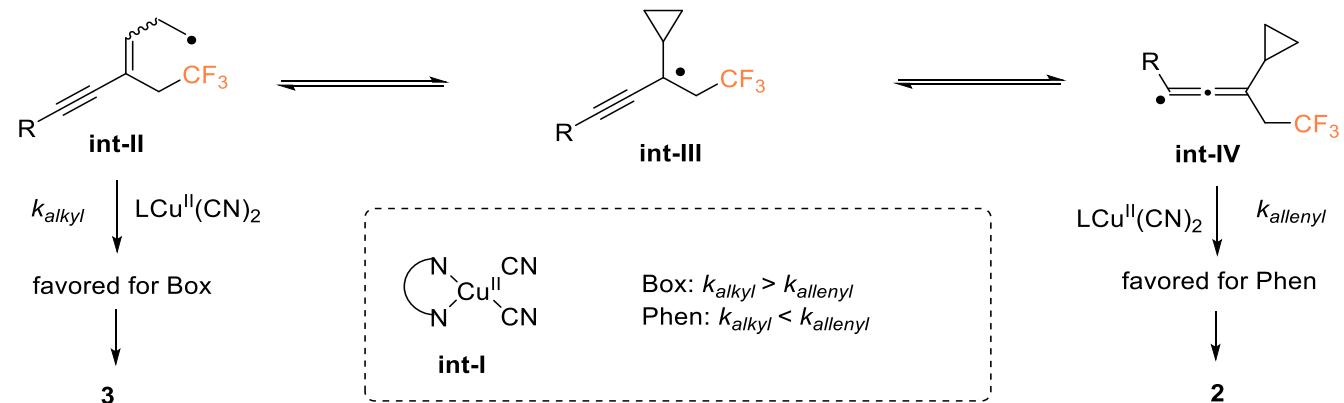
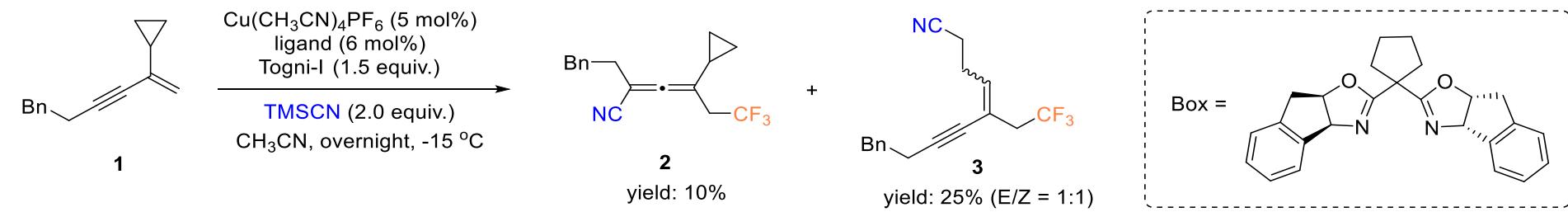
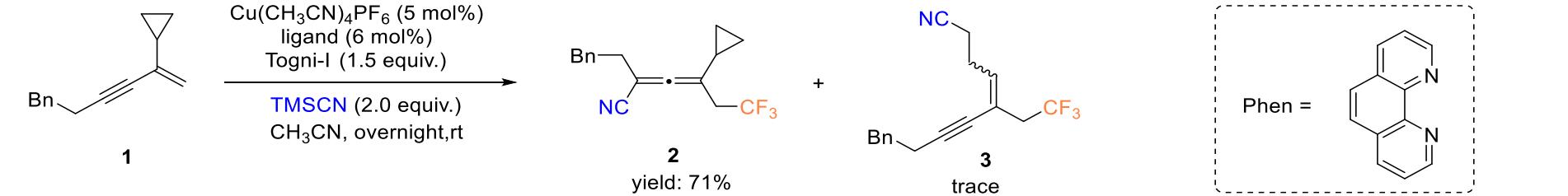
☞ 3 总结与展望

2.2 基于还原消除机制

C-C



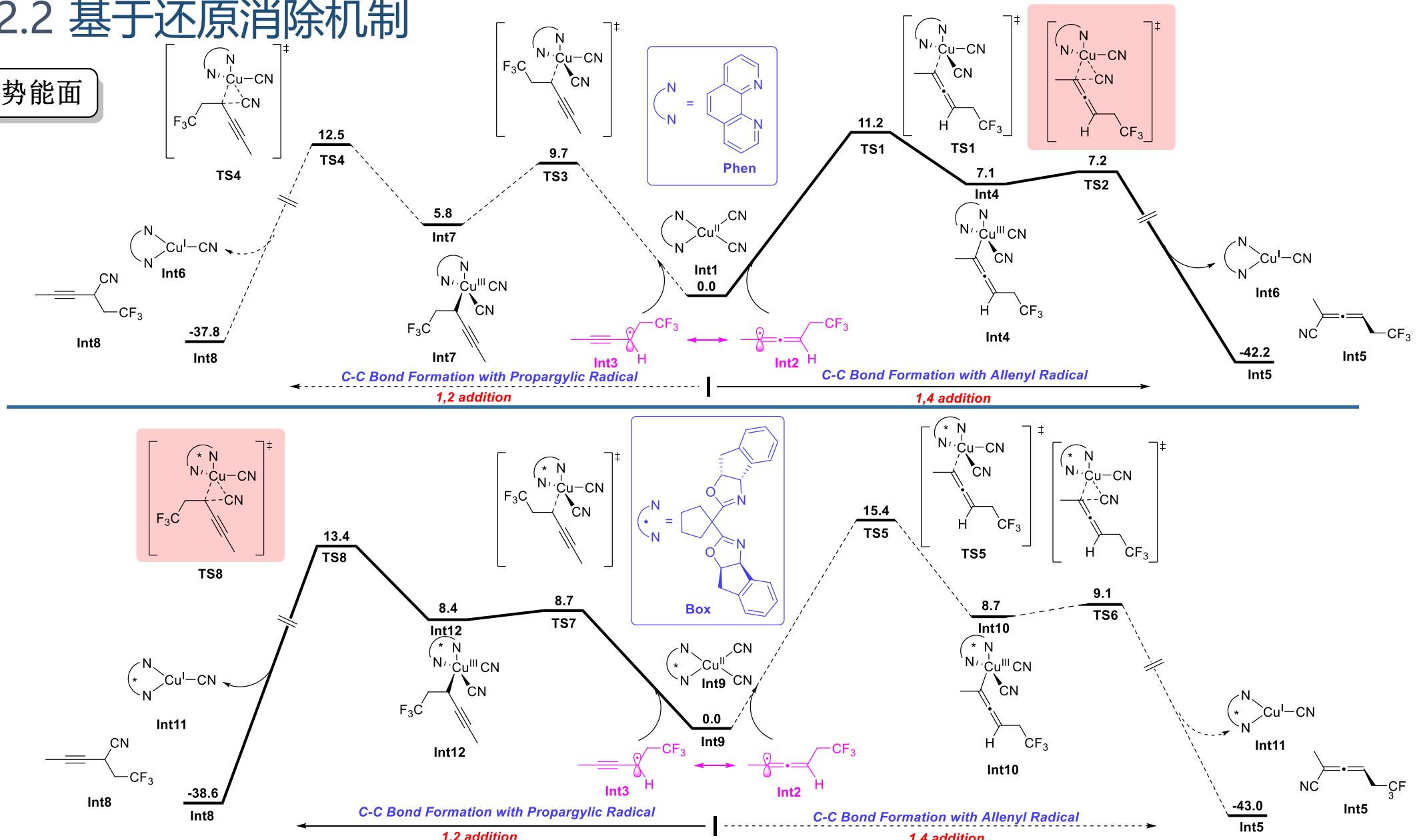
机理实验



Box: $k_{\text{alkyl}} > k_{\text{allenyl}}$
Phen: $k_{\text{alkyl}} < k_{\text{allenyl}}$

2.2 基于还原消除机制

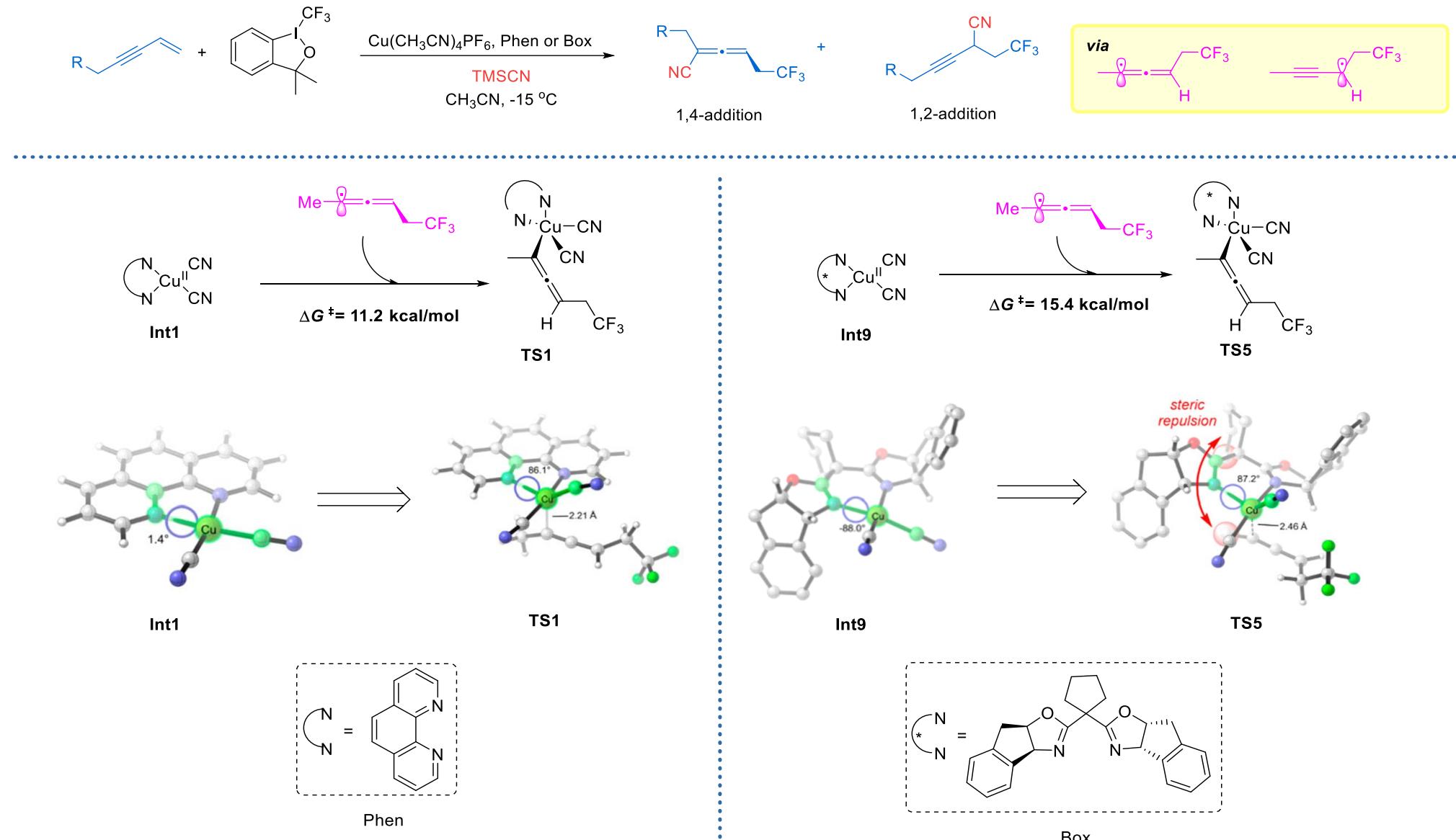
势能面



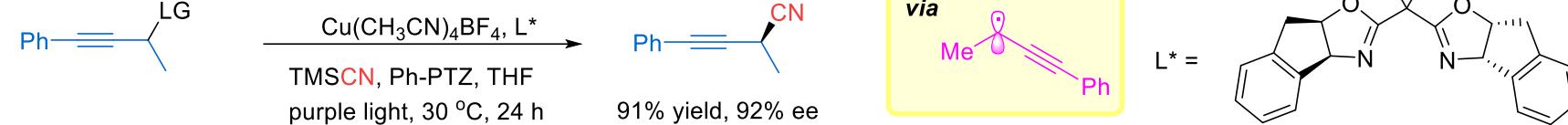
ΔG_{sol} in kcal/mol, M06/6-311++G(d,p)-CPCM(Acetonitrile)//M06/6-31G(d)-6-311G(d)-CPCM

Liu, G. et.al., Angew.Chem. Int. Ed. 2018, 57, 7140–7145.

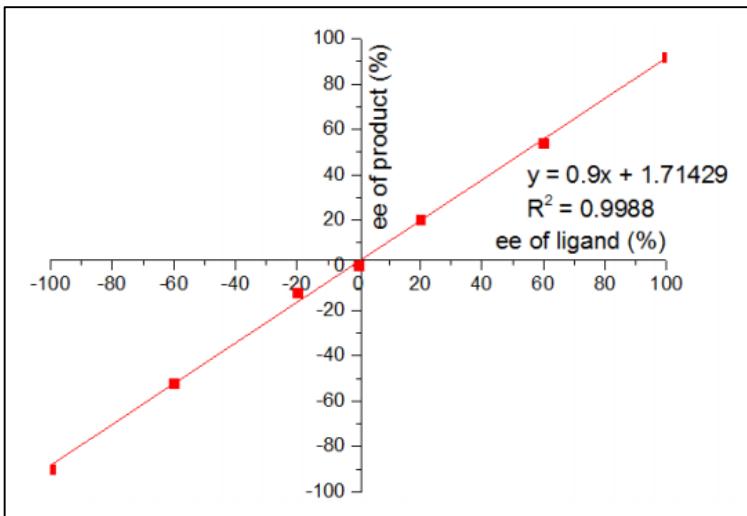
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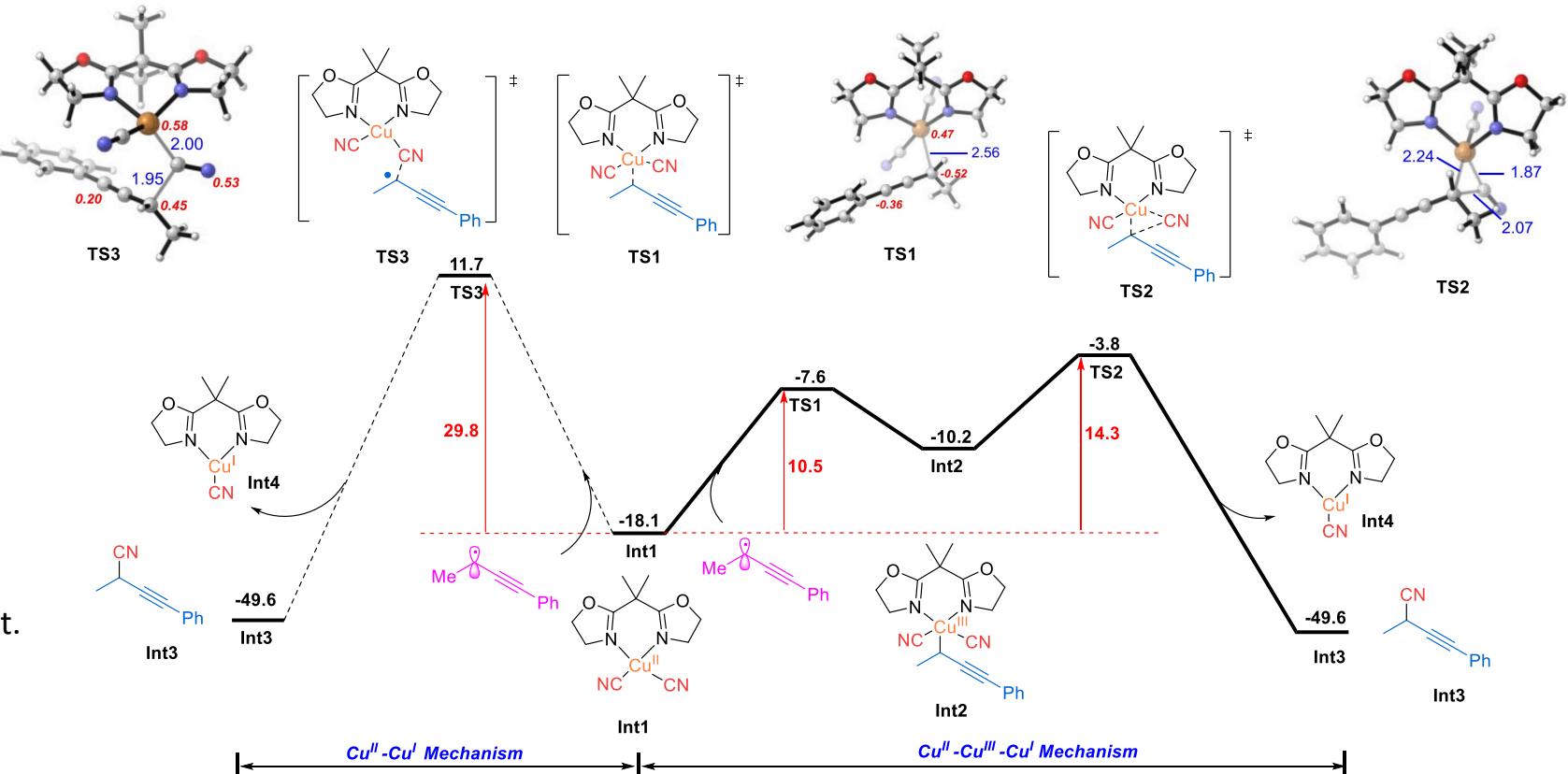
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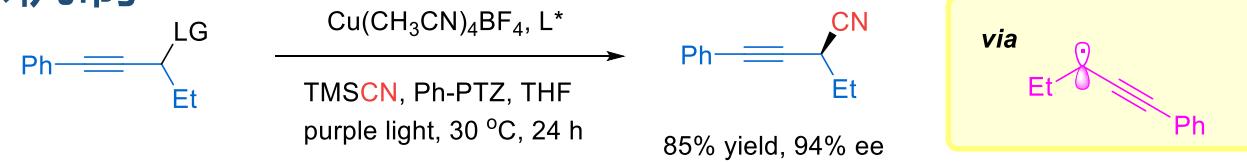
机理实验



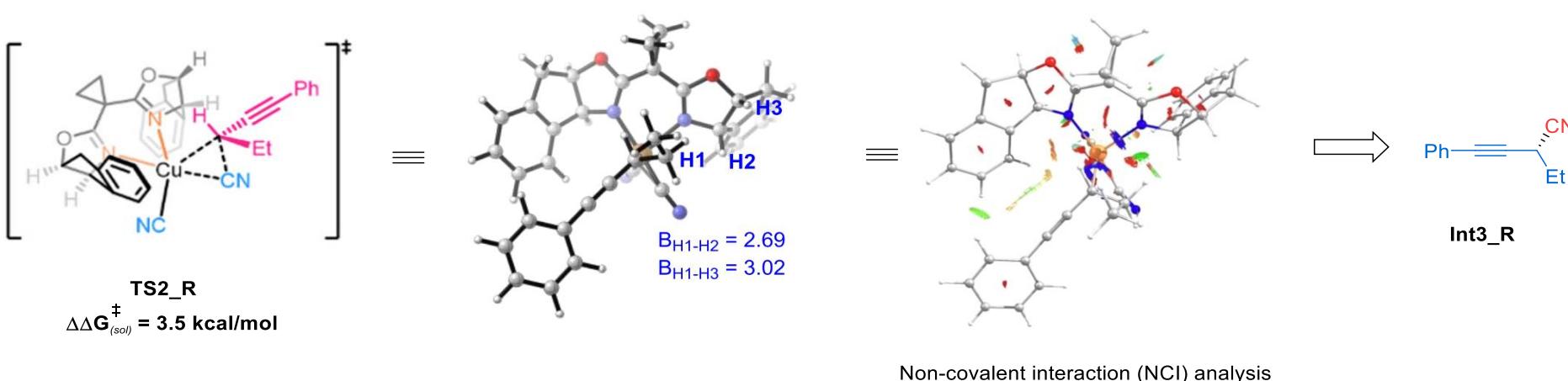
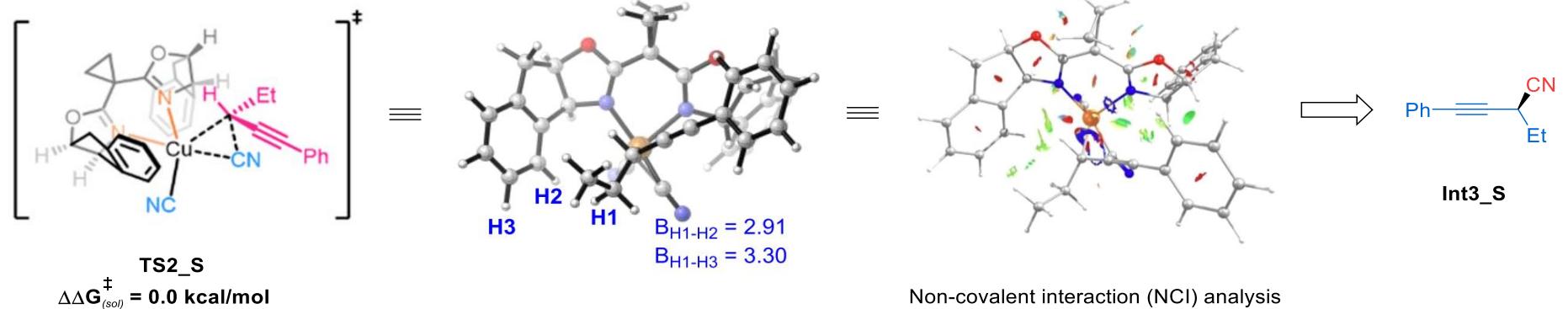
势能面



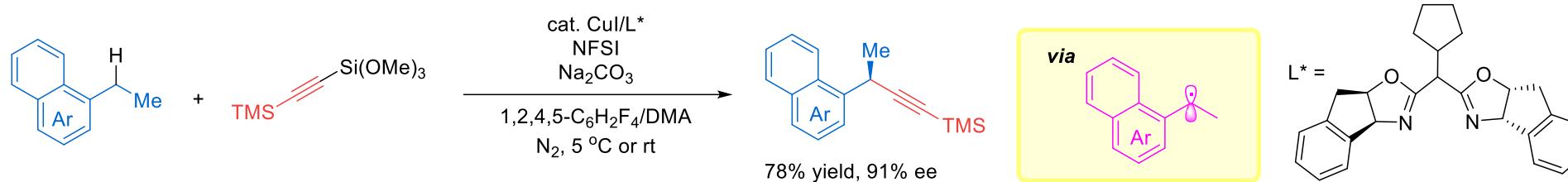
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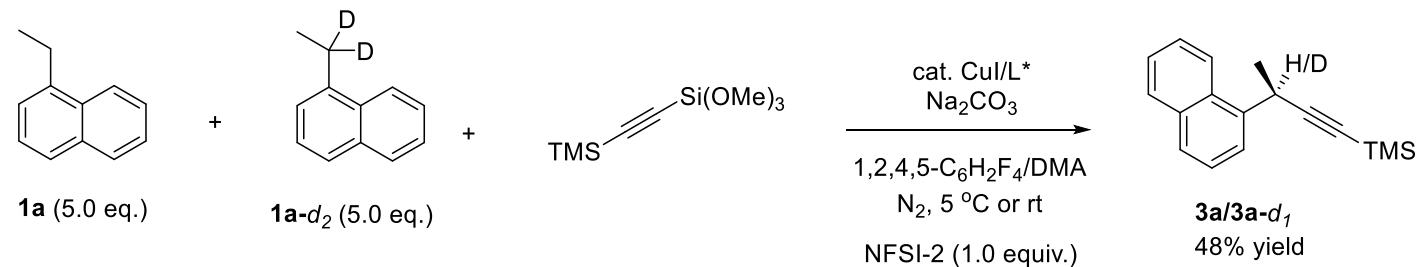
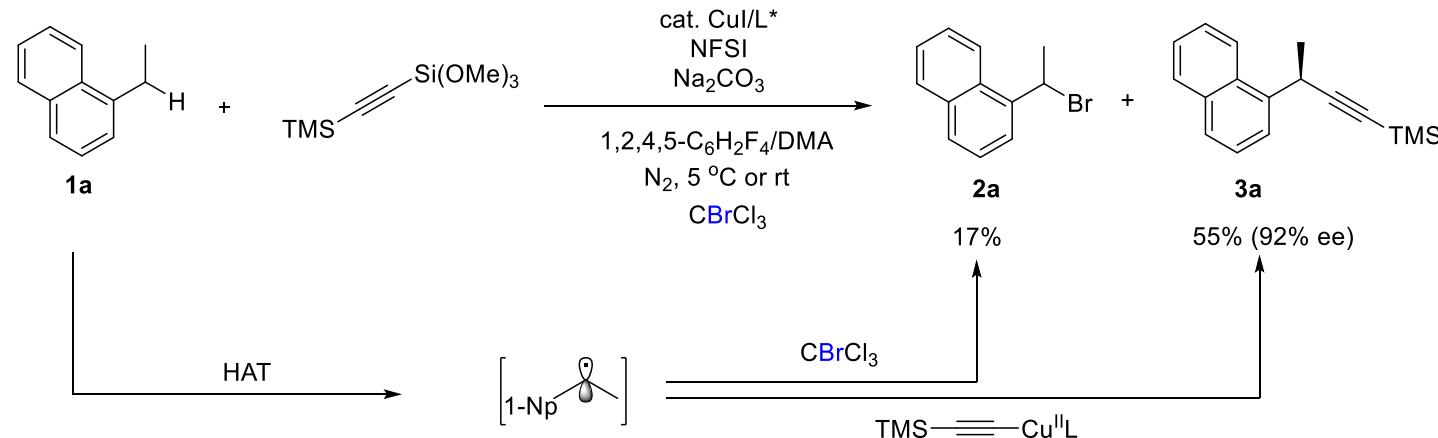
对映选择性



2.2 基于还原消除机制



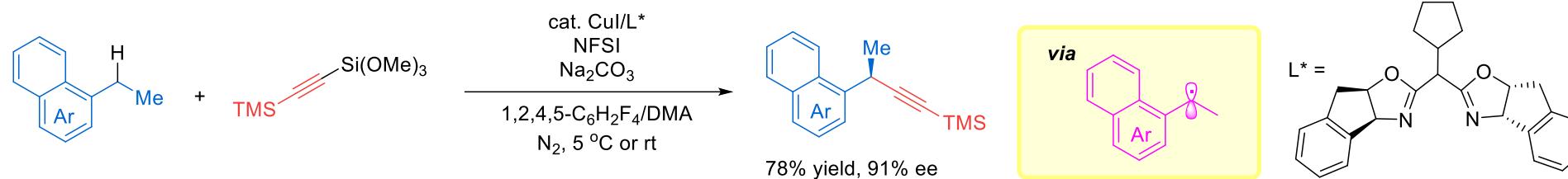
机理实验



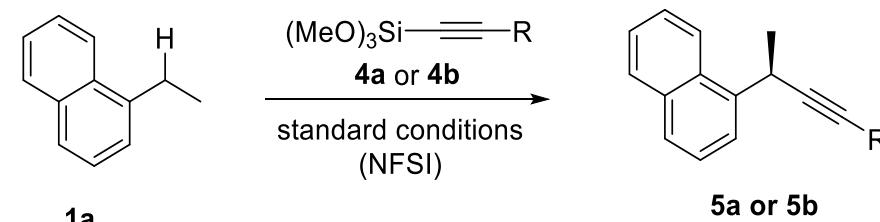
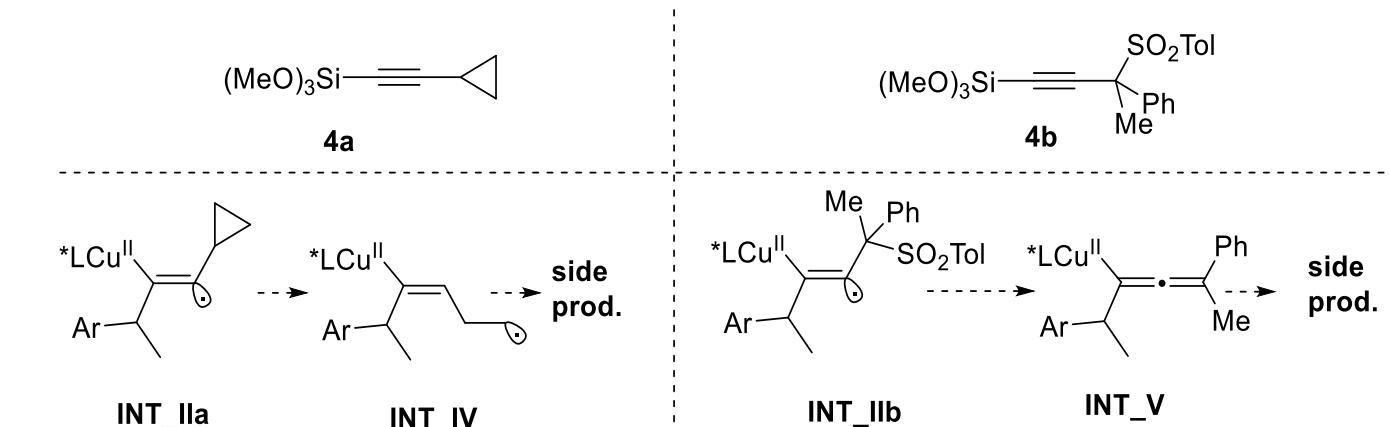
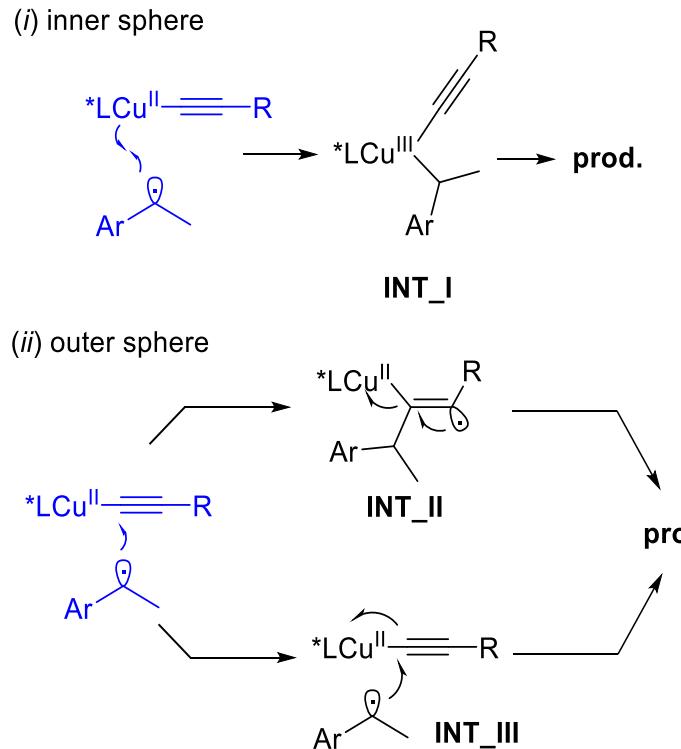
Competition reaction : $\text{KIE} = K_{\text{H}} / K_{\text{D}} = 5.0$

Parallel reaction : $\text{KIE} = K_{\text{H}} / K_{\text{D}} = 2.27$

2.2 基于还原消除机制

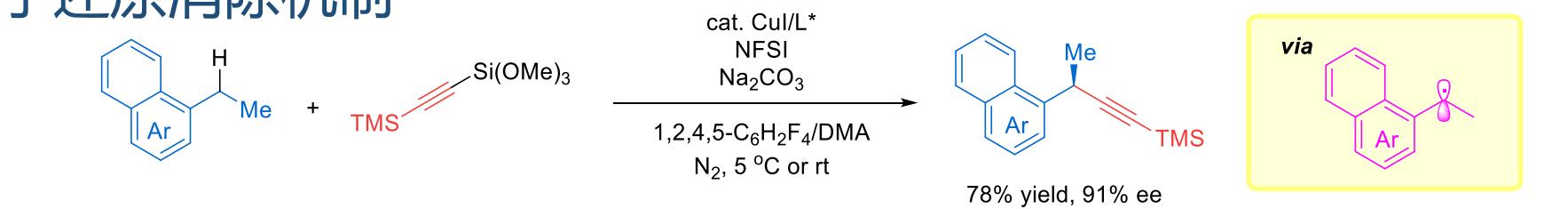


机理实验

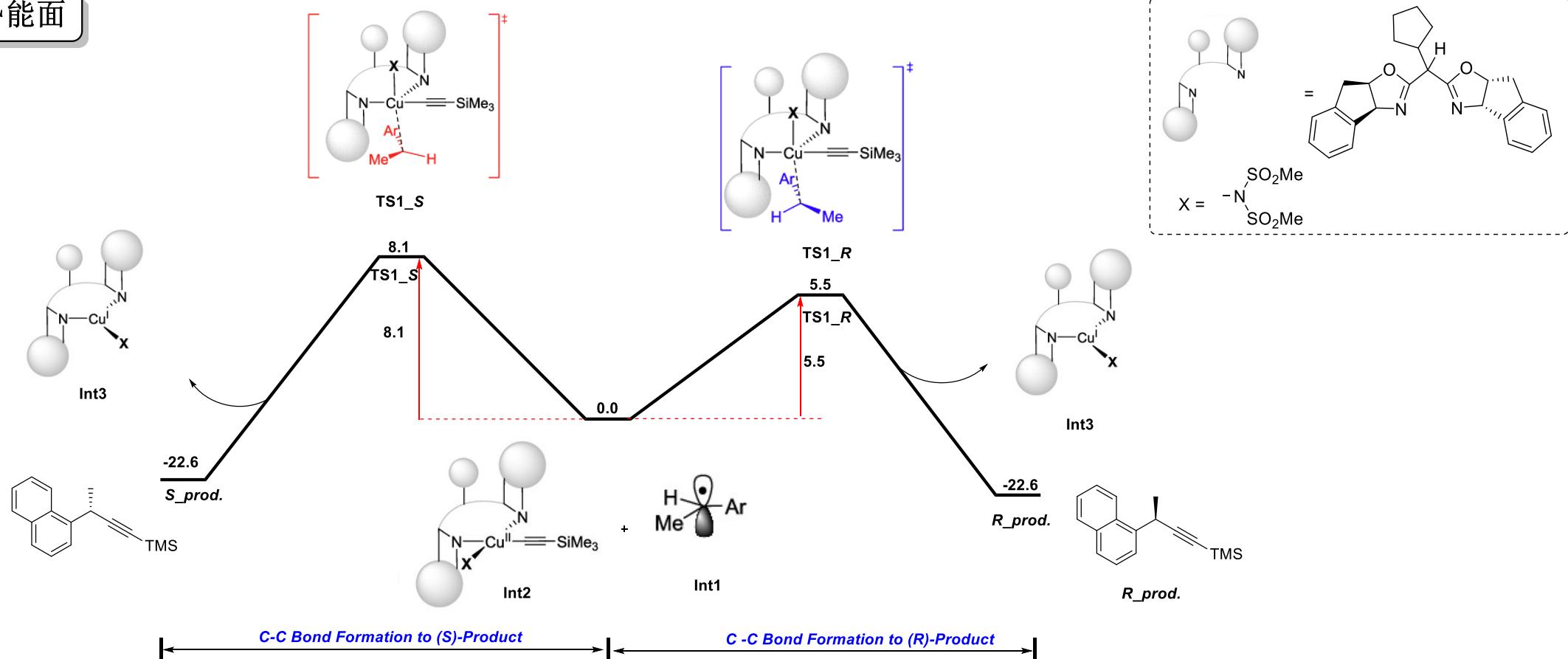


from **4a**: **5a** 31% (87% ee); 41% conversion
 from **4b**: **5b** 44% (d.r. = 1.1:1, 74% ee/75% ee); 51% conversion

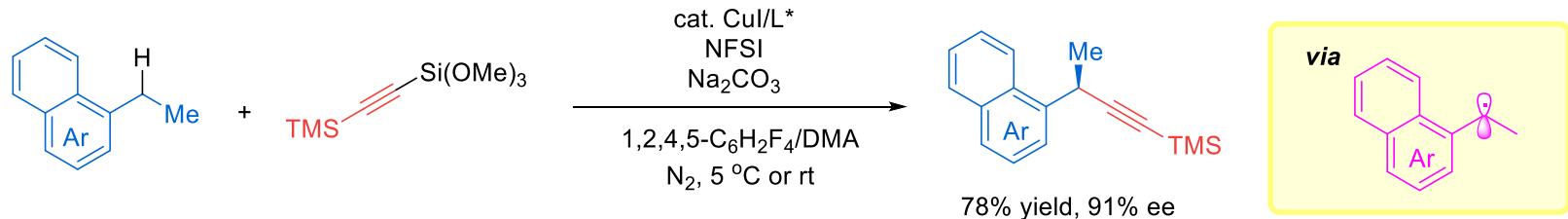
2.2 基于还原消除机制



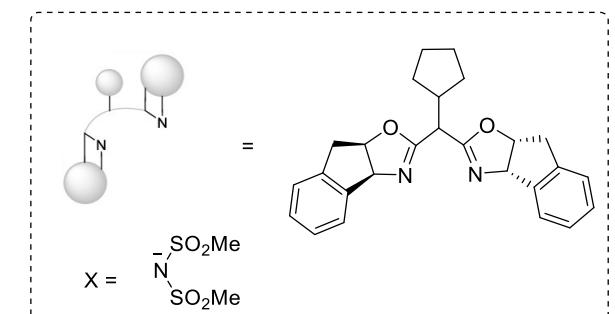
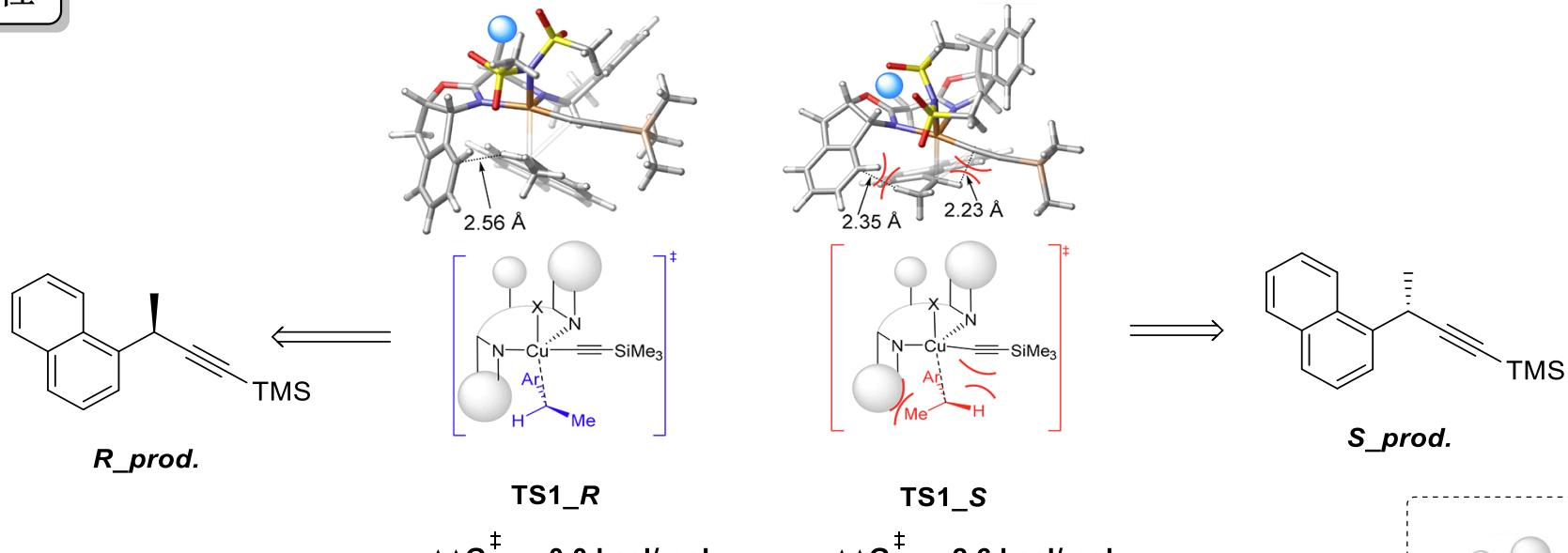
势能面



2.2 基于还原消除机制



对映选择性





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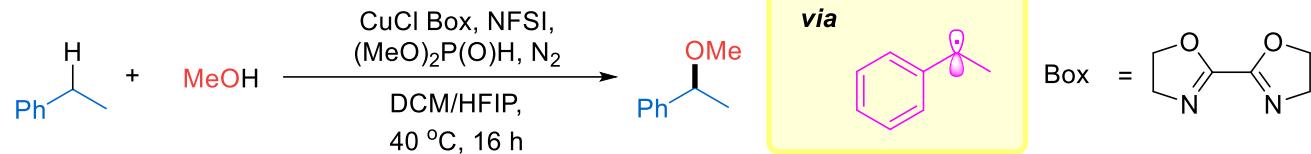
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☞ 2.3 基于离子型成键机制

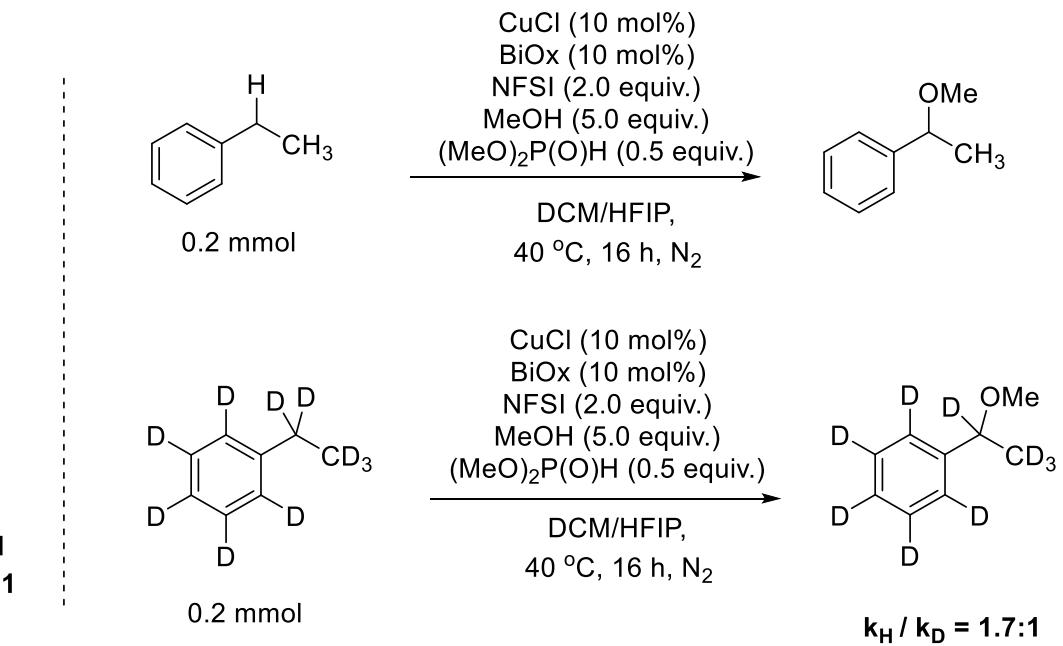
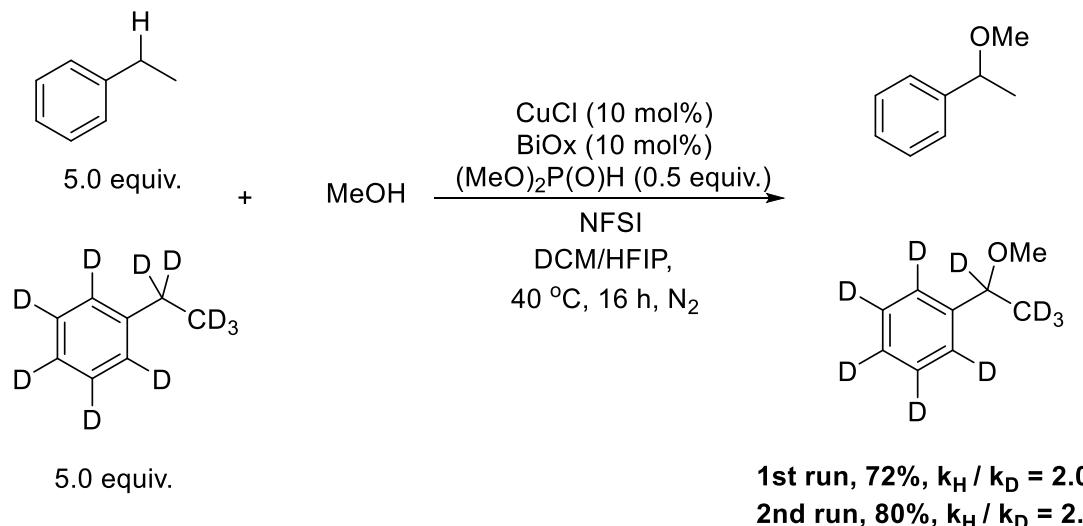
☞ 3 总结与展望

2.3 基于离子型成键机制

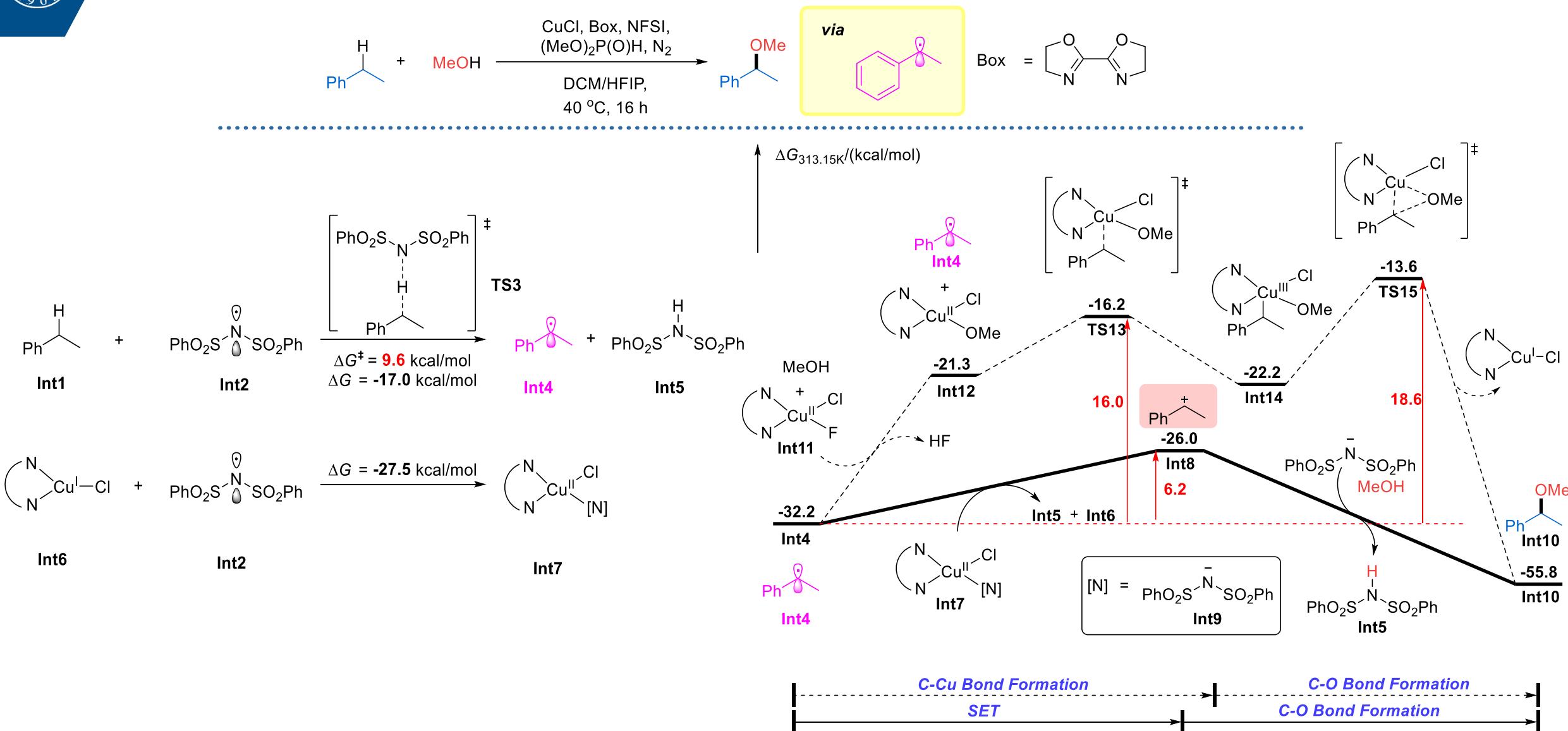
C-O



机理实验

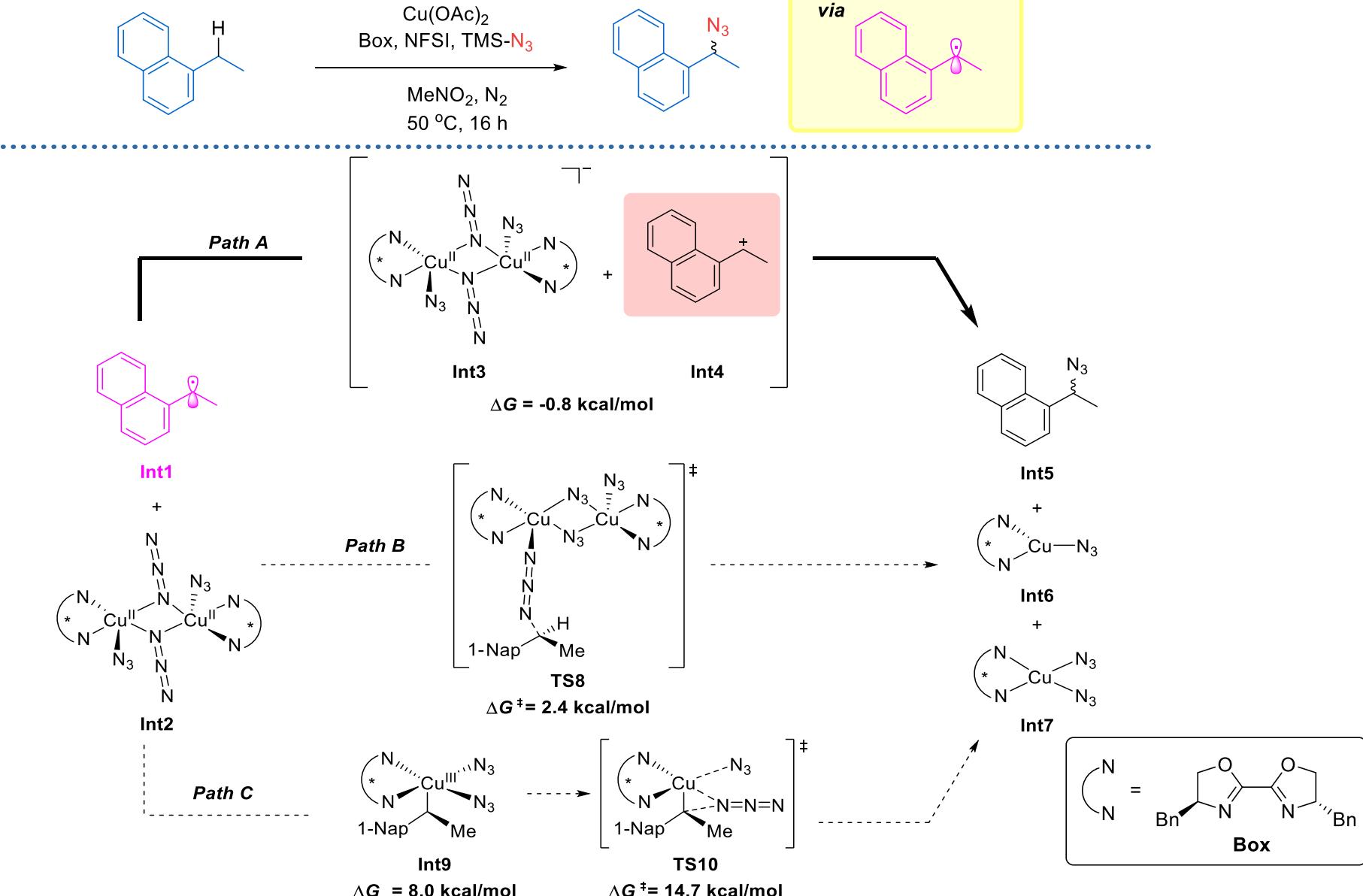


2.3 基于离子型成键机制



2.3 基于离子型成键机制

C-N



ΔG_{sol} in kcal/mol, M06-L/def2-TZVP-SDD-SMD(MeNO₂)//B3LYP-D3(BJ)/6-31G(d,p)-SDD

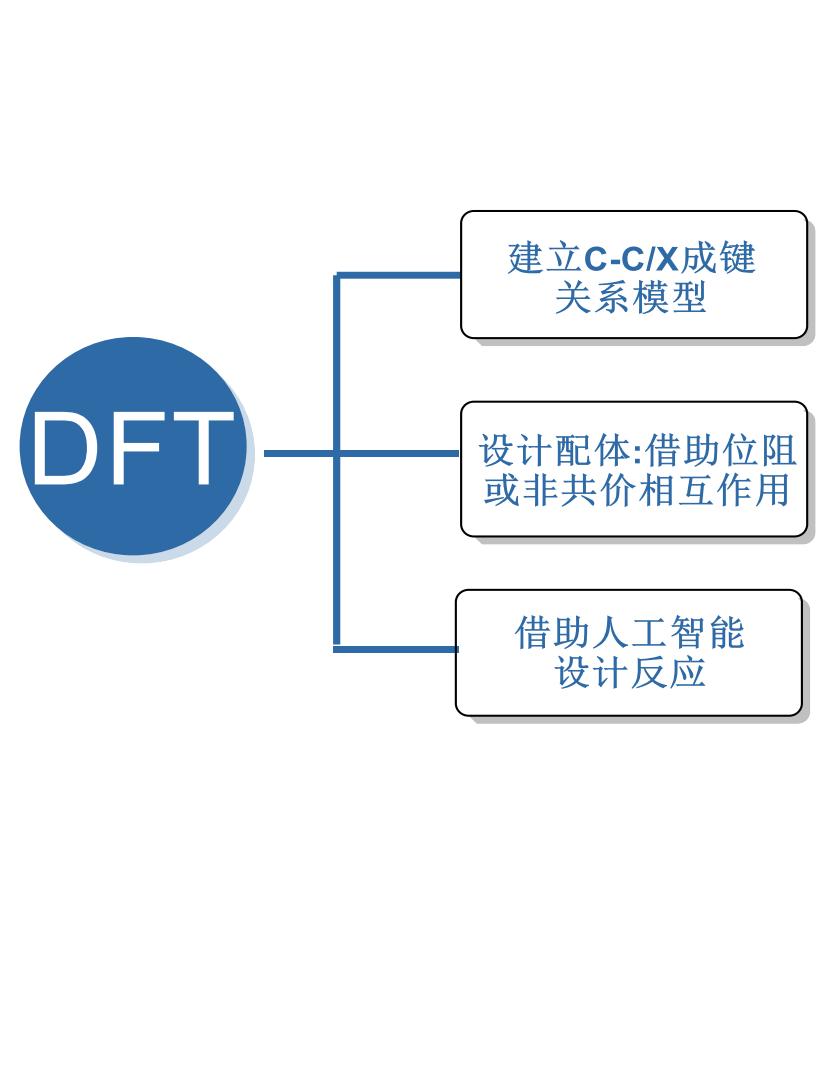
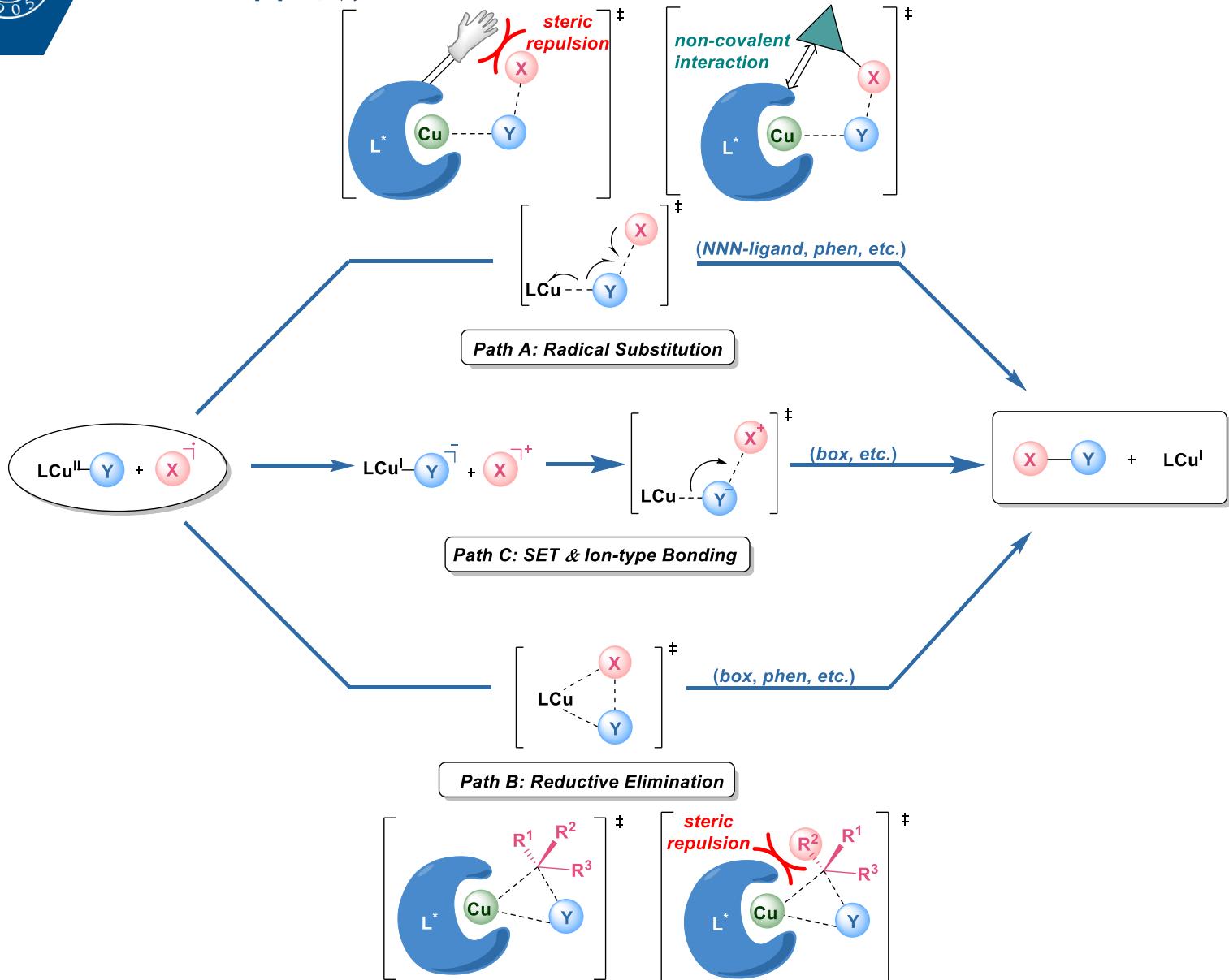
Stahl, S. S. et.al., J. Am. Chem. Soc. 2020, 142, 11388–11393.



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3 总结与展望





THANKS