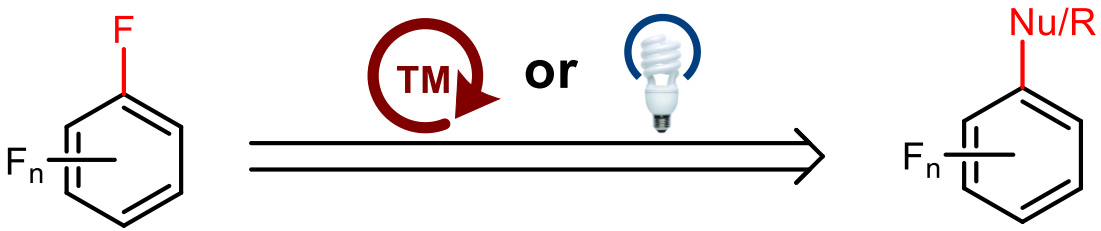
多氟芳烃的脱氟官能团化反应



汇报人：赵佳奥
指导老师：麻生明 教授
钱辉 副教授
汇报时间：2025年10月24日

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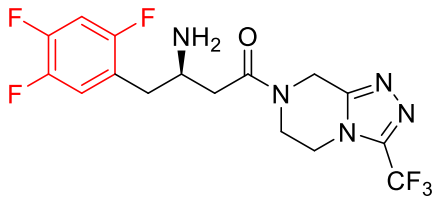
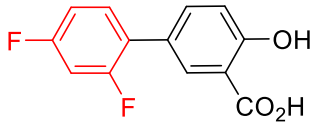


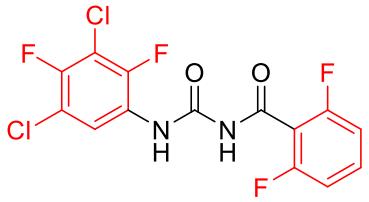
Sitagliptin

用于治疗II型糖尿病



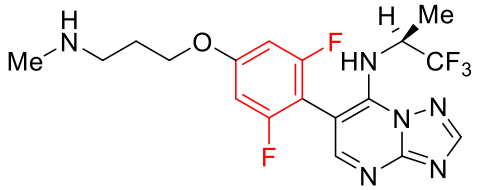
Diflunisal

抗炎药



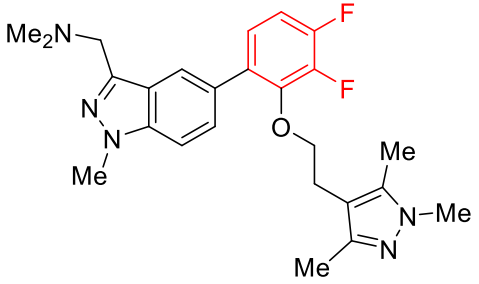
Teflubenzuron

杀虫剂



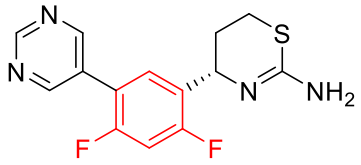
Cevipabulin

具有抗肿瘤活性



IMP-1088

NMT1 、 NMT2 抑制剂



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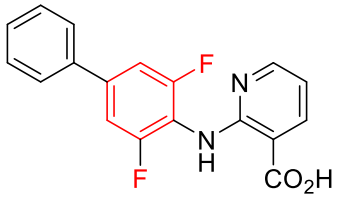
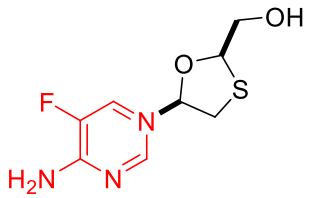
BACE1抑制剂



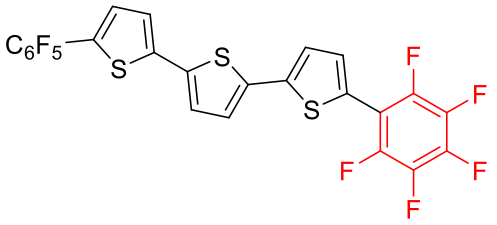
ASLAN003

DHODH抑制剂

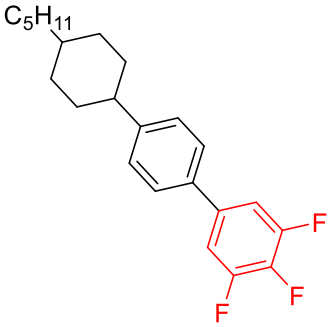


Emtricitabine

抗病毒活性



N-型半导体

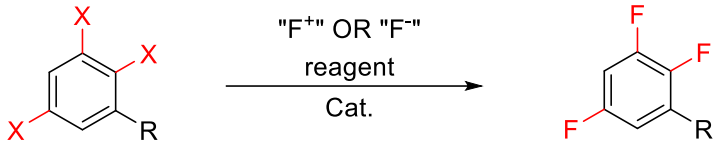


液晶材料

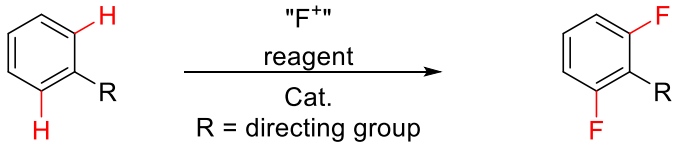
Weaver, J. D. *et, al. Accounts of Chemical Research* **2016**, *49*, 2273-2283.
Chatani, N. *et, al. ACS Catalysis* **2021,** *11*, 12915-12930

1、背景介绍

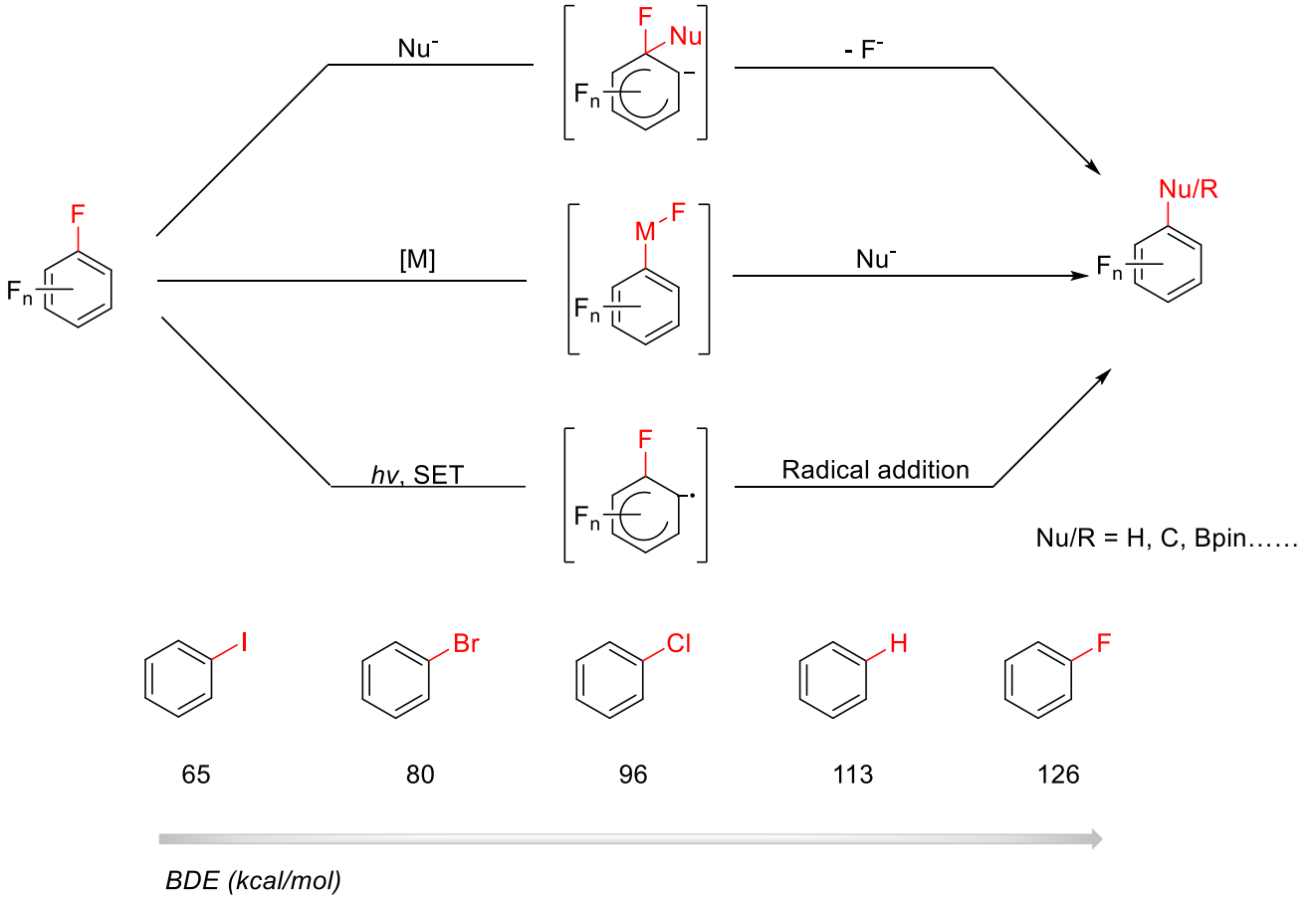
1、采用F^+或F^-实现直接氟化：



For F^-, X = $^-$I, $^-$OTf, IAr. For F^+, X = $B(X)_3$, SnR_3, SIR_4



2、利用多氟芳烃进行脱氟官能团化制备：



Weaver, J. D. *et, al. Accounts of Chemical Research* **2016**, *49*, 2273-2283.
Chatani, N. *et, al. ACS Catalysis* **2021,** *11*, 12915-12930

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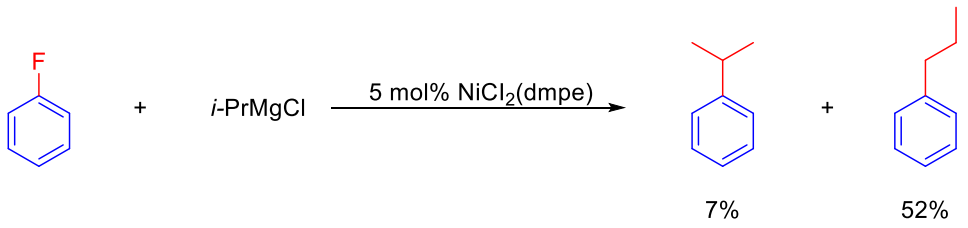
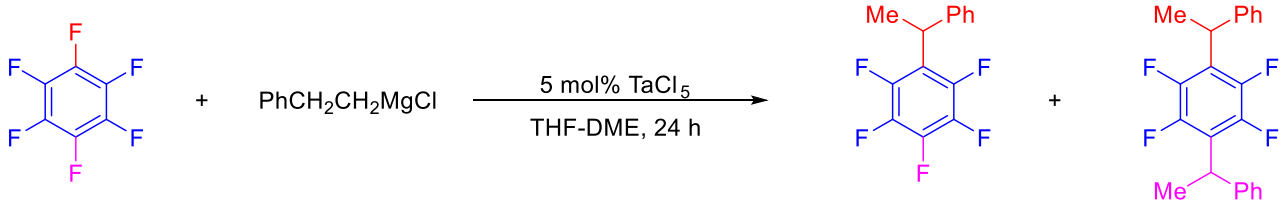
2.1、过渡金属参与的脱氟反应

Kumada, 1973:



7%　　52%

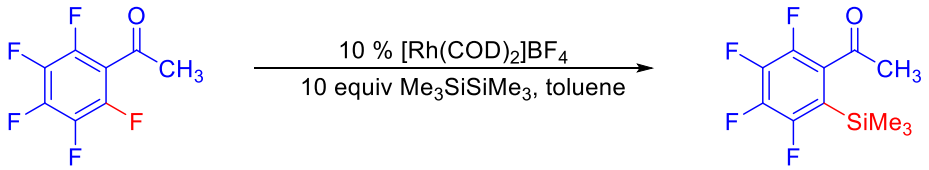
Takahashi, 2006：

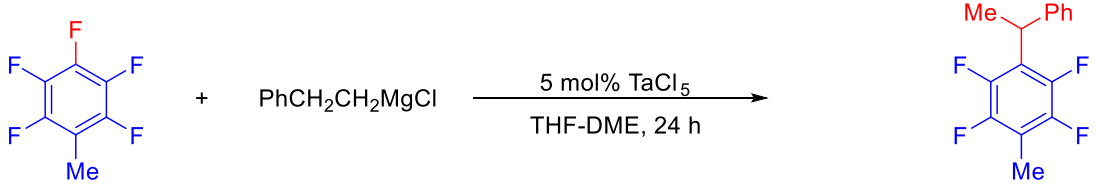


1.5 equiv　　75%　　0%

3.0 equiv　　14%　　57%

Murai, 1998:



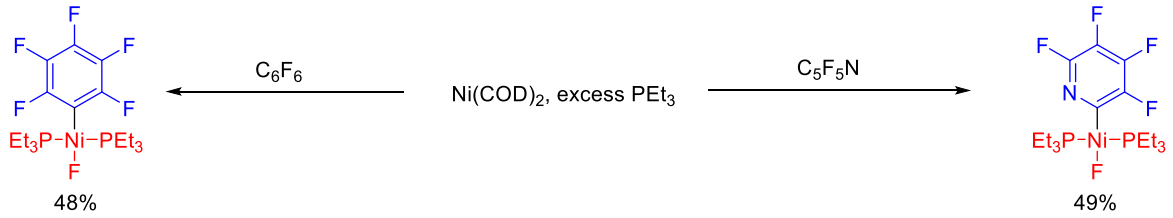


1.5 equiv　　73%

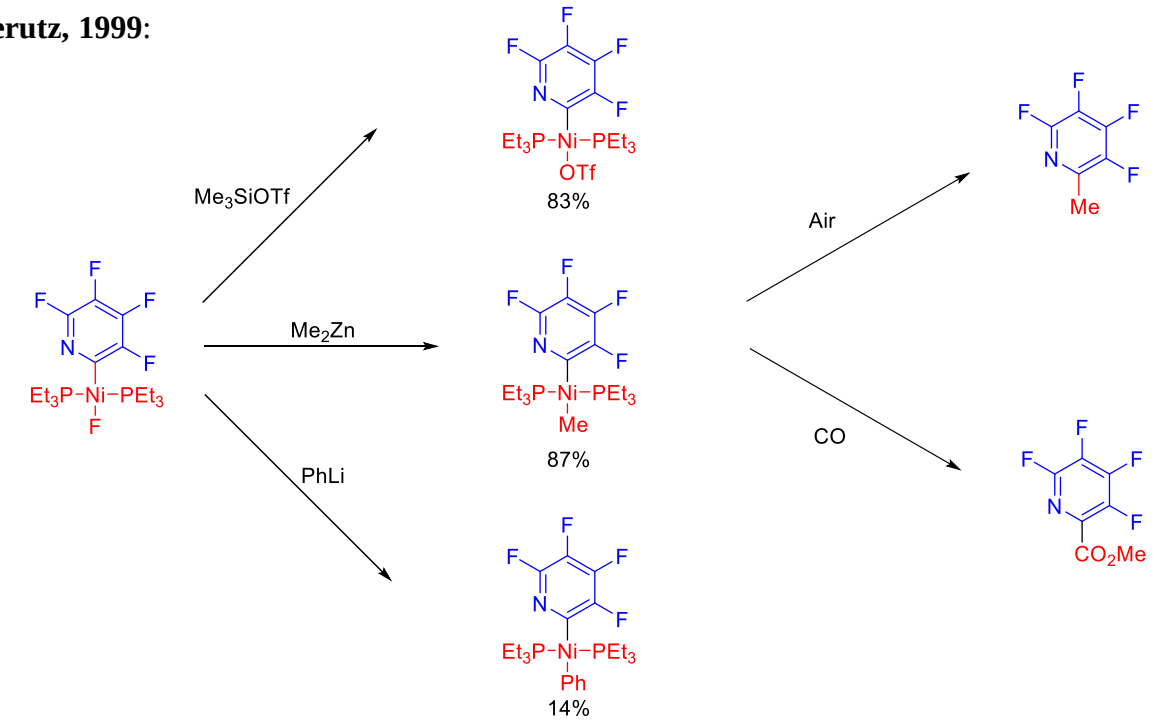
M. Kumada. *et, al. J. Organomet. Chem*., **1973**, *50*, C12–C14.
S. Murai. *et, al. Chem. Lett*., **1998**, 157–158.
T. Takahashi. *et, al. Organometallics*, **2006,** *25*, 2045–2048.

2.1、过渡金属参与的脱氟反应

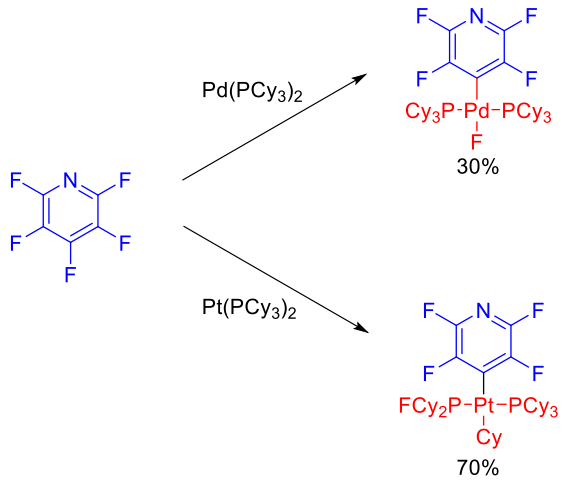
Perutz, 1997:



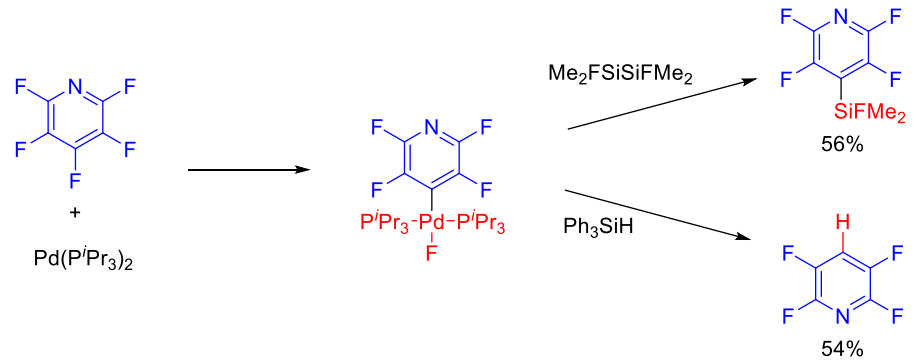
Perutz, 1999:



Peruts, 2004:



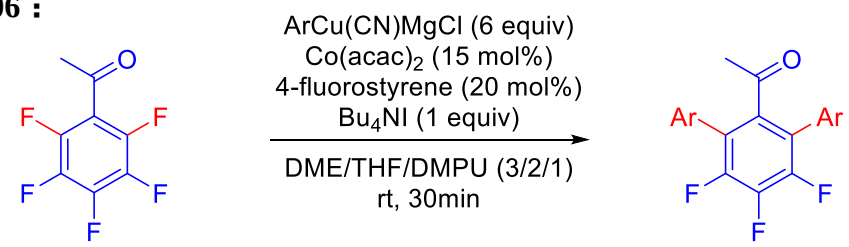
Braun, 2006:



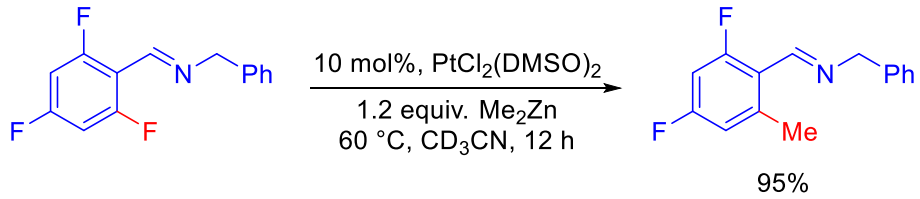
R. Perutz. *et, al. Organometallics*, **1997**, *16*, 4920–4928.
T. Braun R. Perutz. *et, al. Organometallics*, **1999,** *18*, 1710–1716.
R. Perutz. *et, al. Organometallics*, **2004,** *23*, 6140–6149.
T. Braun. *et, al. Dalton Trans*, **2006,** 5118–5123.

2.1、过渡金属参与的脱氟反应

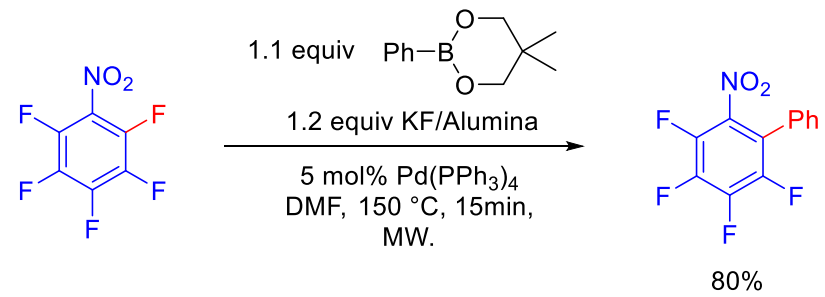
Knochel, 2006：



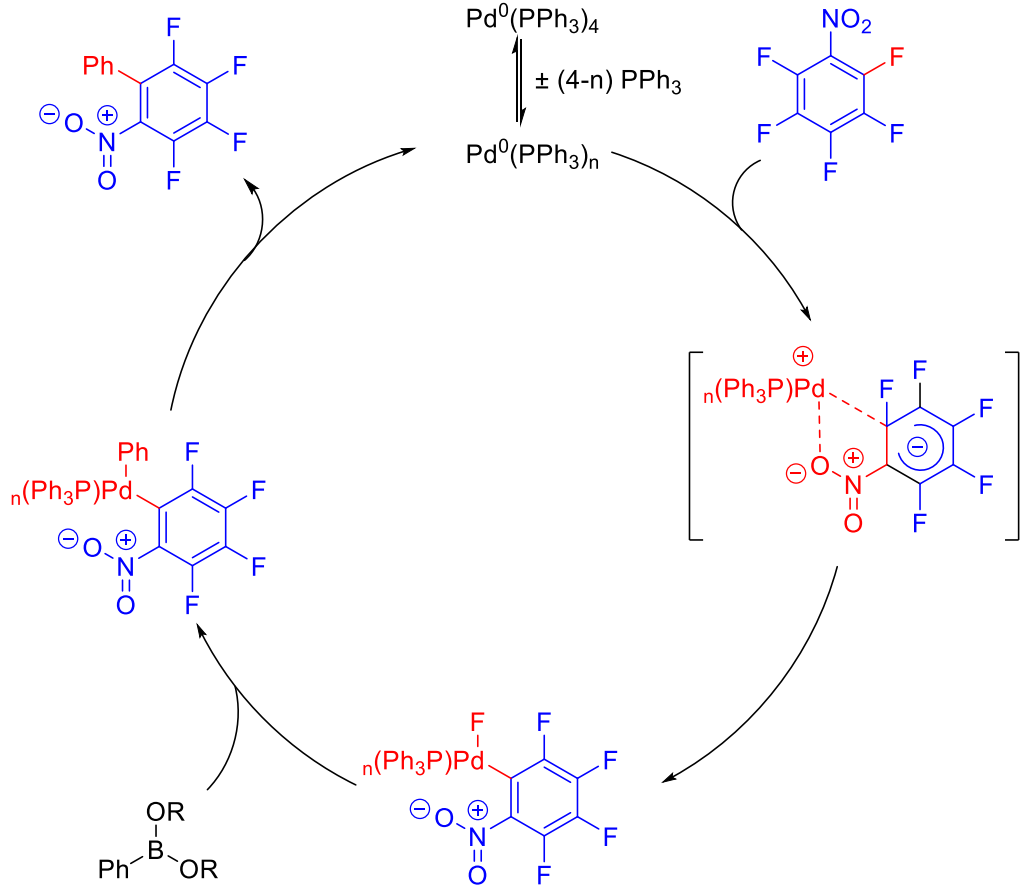
Love, 2010：



Nelles, 2010：



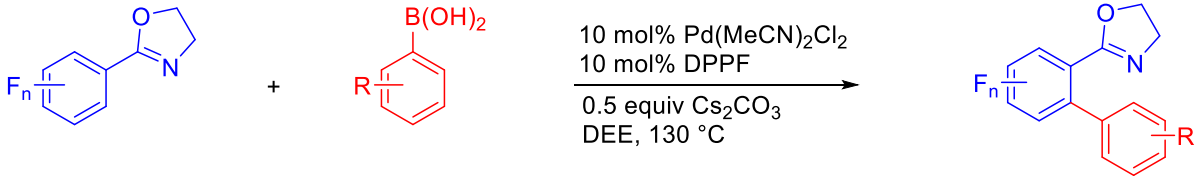
Nelles, 2010：

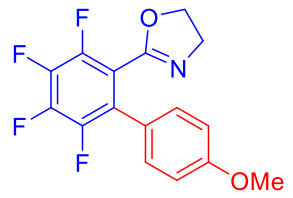


Knochel, P. *et, al. Org. Lett.* **2006,** *8*, 725− 728.
Love, J. A. *et, al. Journal of Fluorine Chemistry* **2010**, *131*, 1237-1240.
Nelles, G. *et, al. J. Org. Chem.* **2010**, *75*, 5860-5866.

2.1、过渡金属参与的脱氟反应

Lu, 2012:

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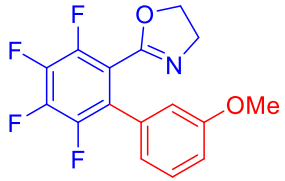
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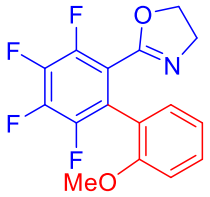
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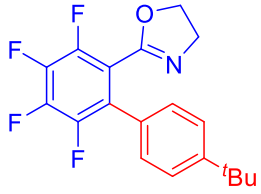
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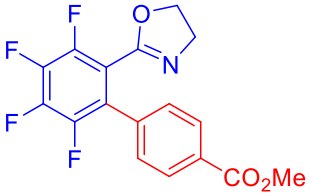
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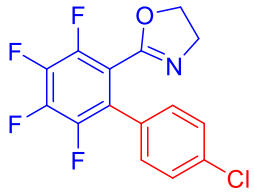
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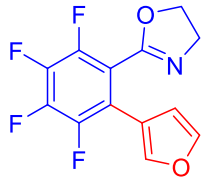
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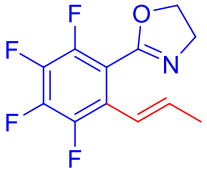
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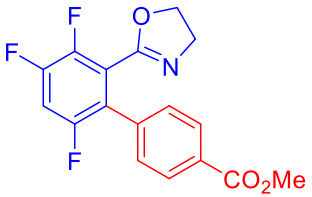
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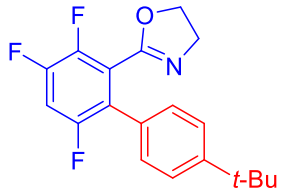
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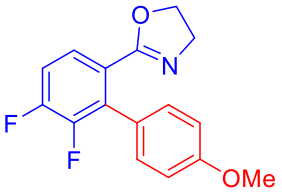
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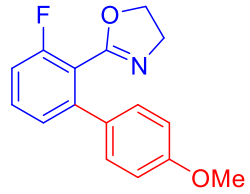
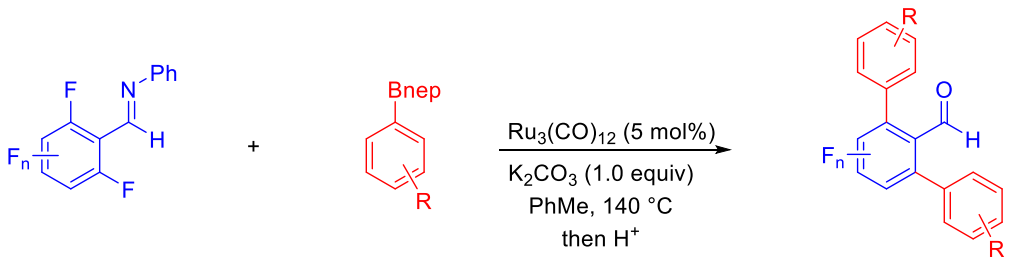
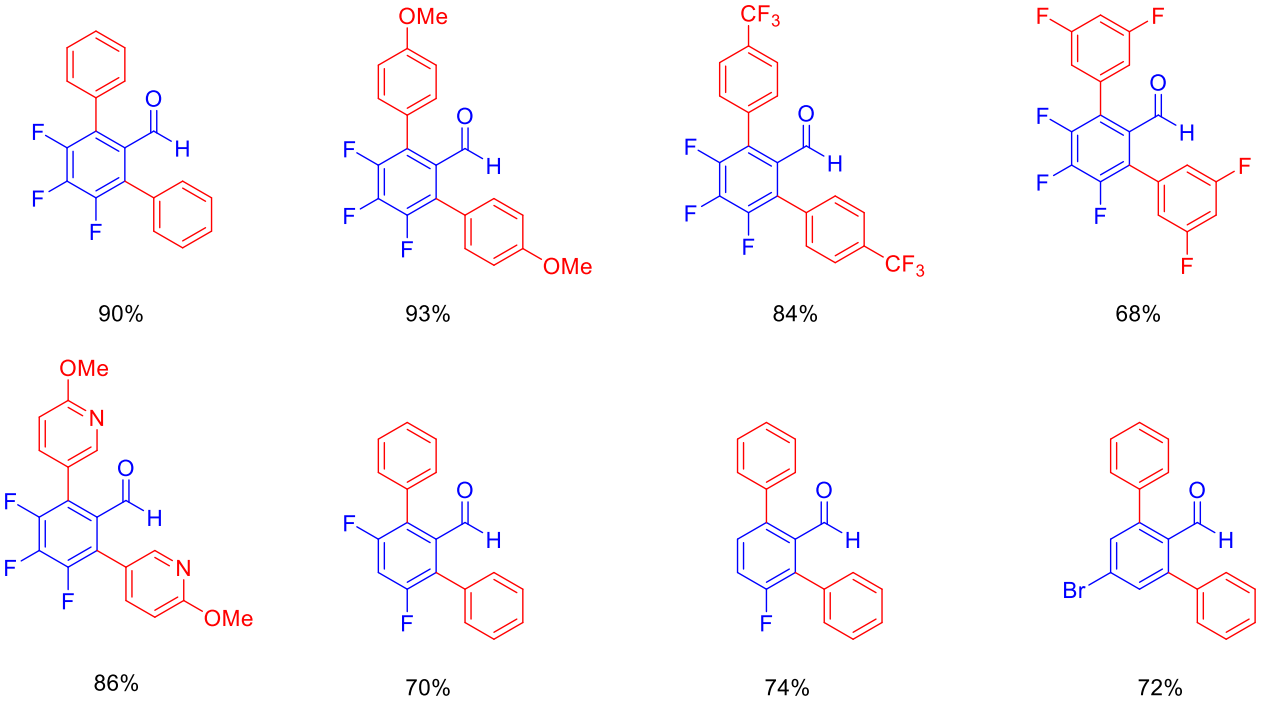

No Reaction

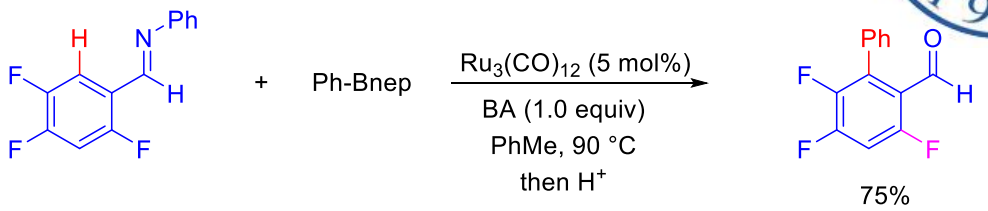
Lu, L. *et, al. J. Org. Chem.* **2012,** *77,* 1798−1804.

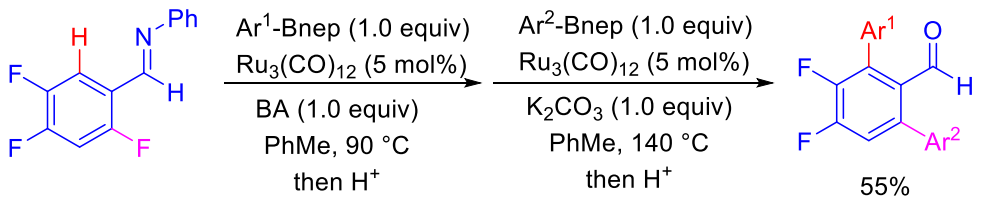
2. 1、过渡金属参与的脱氟反应

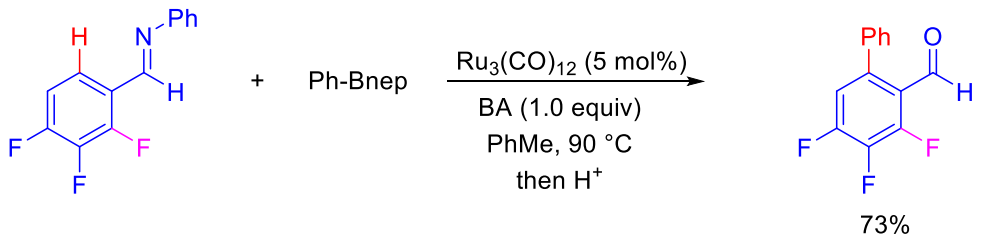
Zhang, 2022:

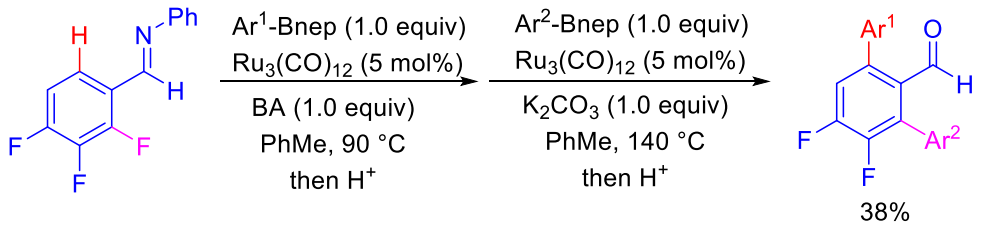










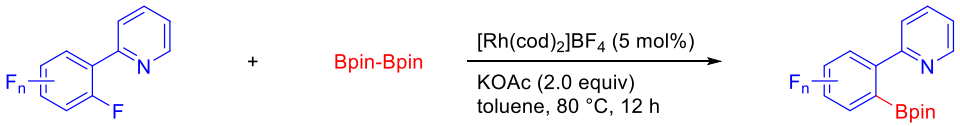


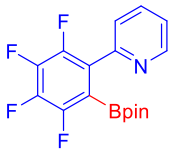
BA= Benzylideneacetone
$Ar^1 = C_6H_5$
Ar^2 = 4-MeO-C_6H_4

Zhang, J. *et, al. ACS Catalysis* **2022**, *12*, 14337-14346

2. 1、过渡金属参与的脱氟反应

Zhang, 2015:

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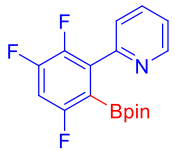
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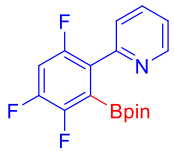
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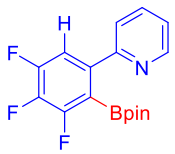
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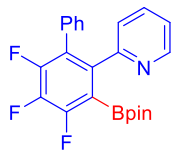
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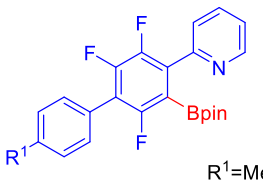
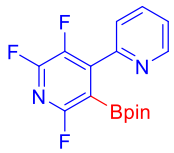

R1=Me,78%
R1=Br, 84%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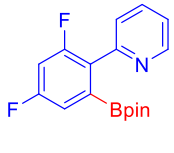
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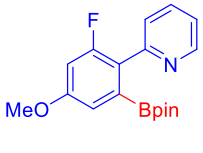
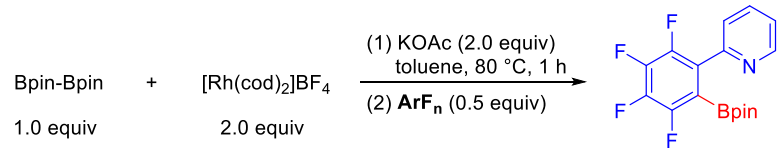
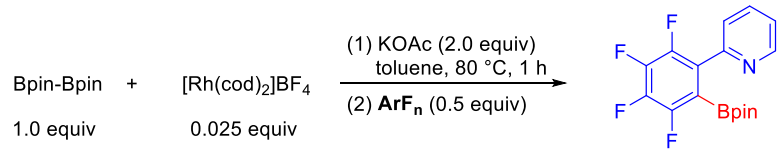

60%

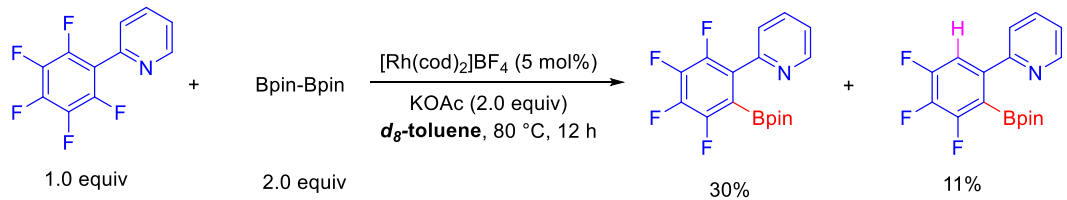
a: 45% yield of C-Hbond borylated product was formed.



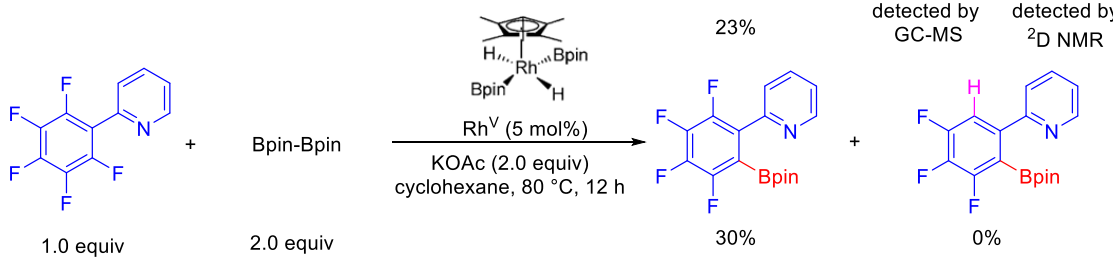
30%



90%

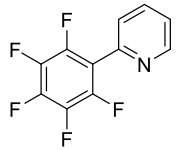


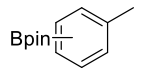
30%
11%
23%
+ 1 and/or 2 +
detected by GC-MS
detected by 2D NMR

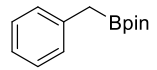


30%
0%

ArFn :



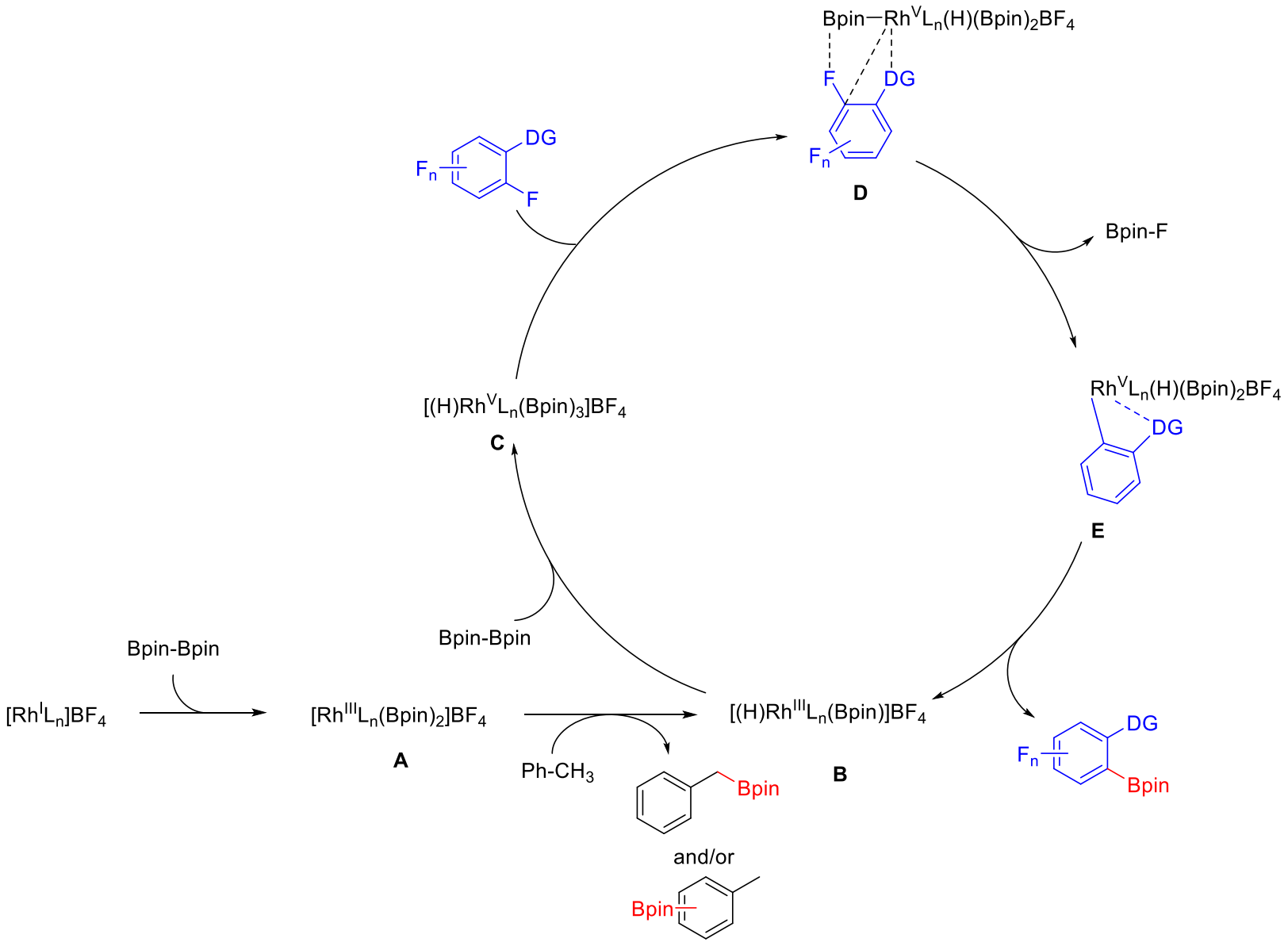
1: 

2: 

Zhang, X. *et, al. Angew.Chem.* **2015**, *127*, 9203–9206

2.1、过渡金属参与的脱氟反应

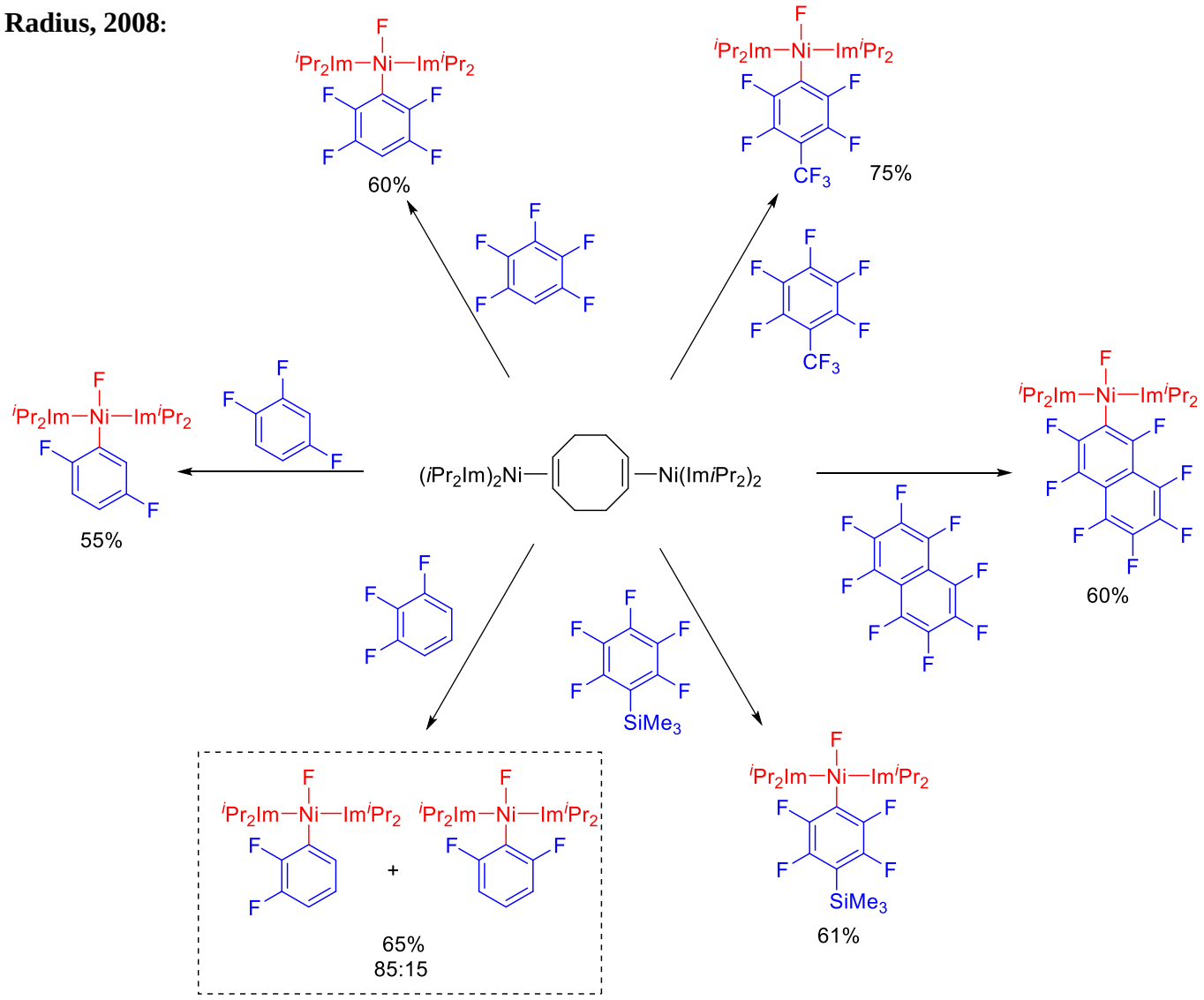
Zhang, 2015:

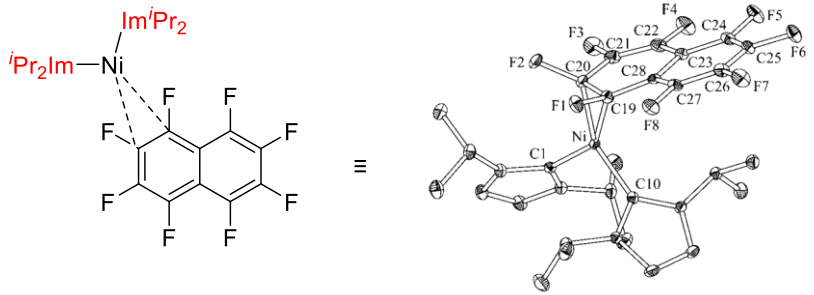


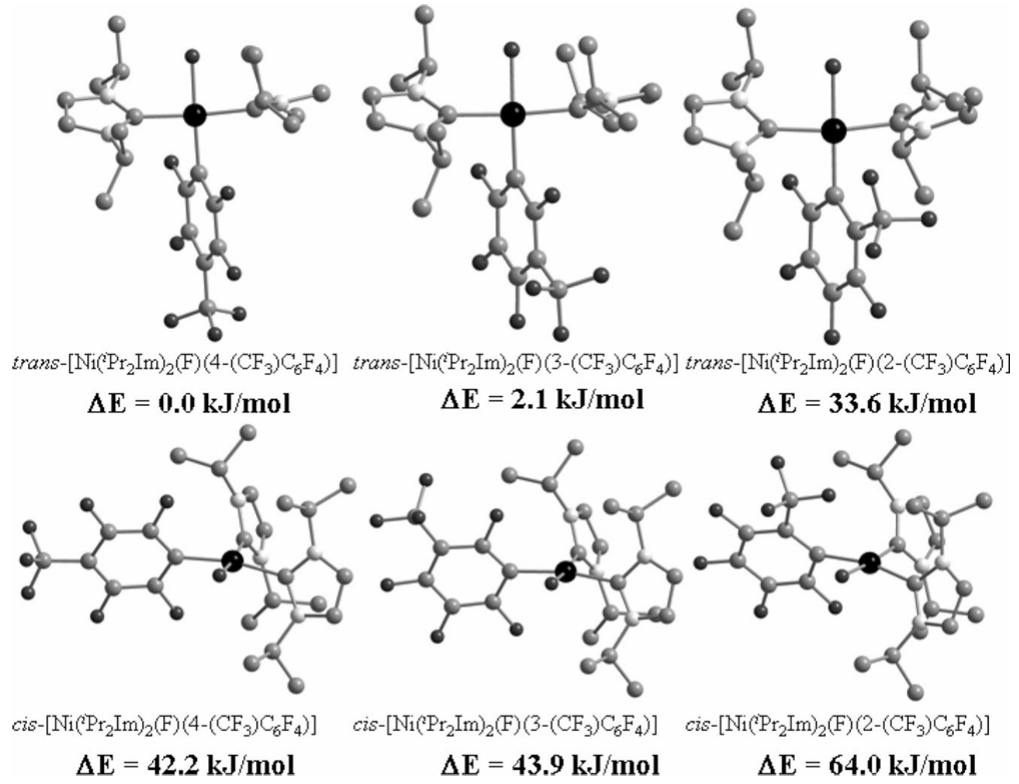
Zhang, X. *et, al. Angew.Chem.* **2015**, *127*, 9203–9206

2.1、过渡金属参与的脱氟反应

Radius, 2008:



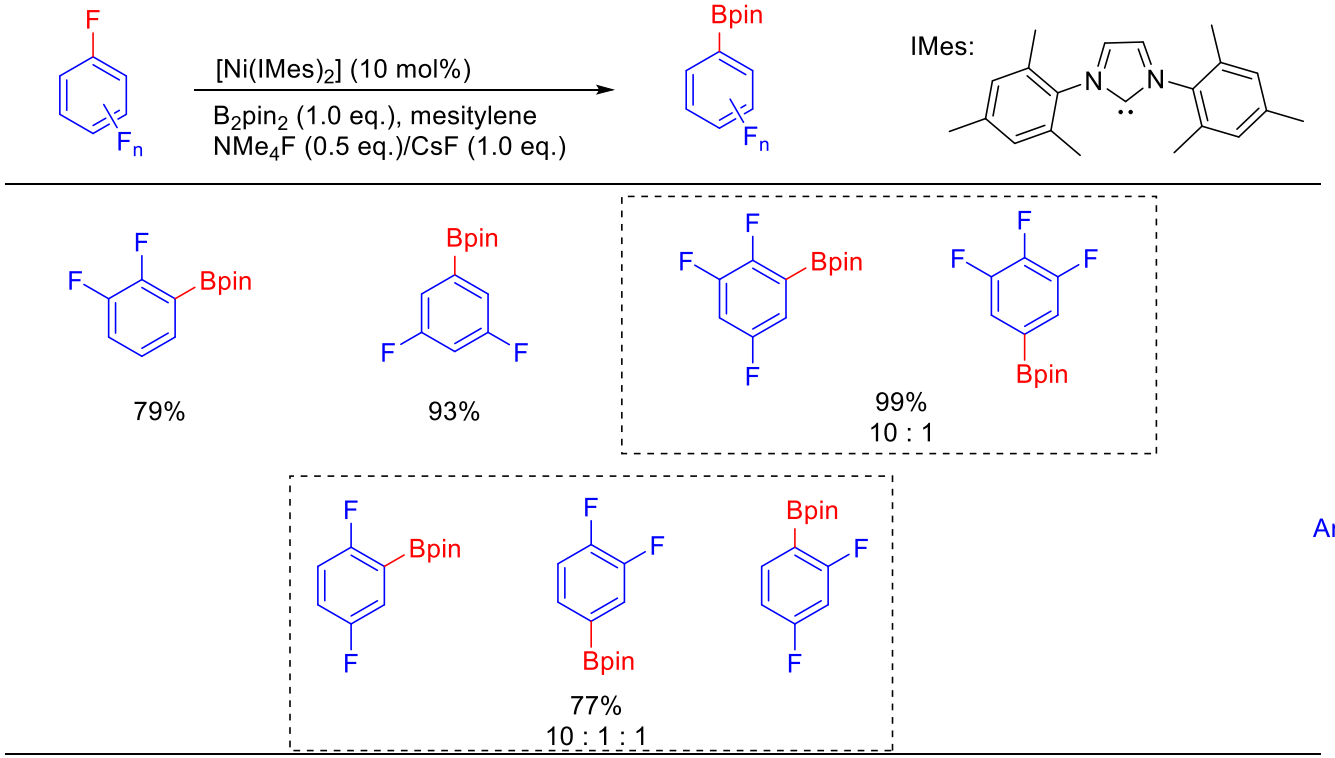


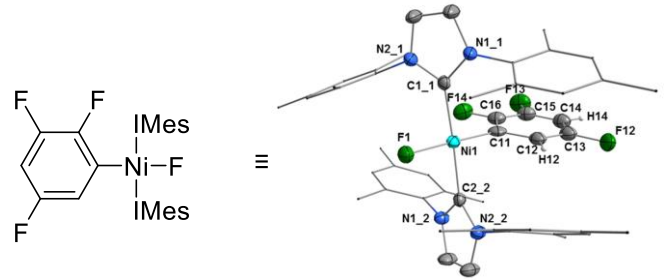


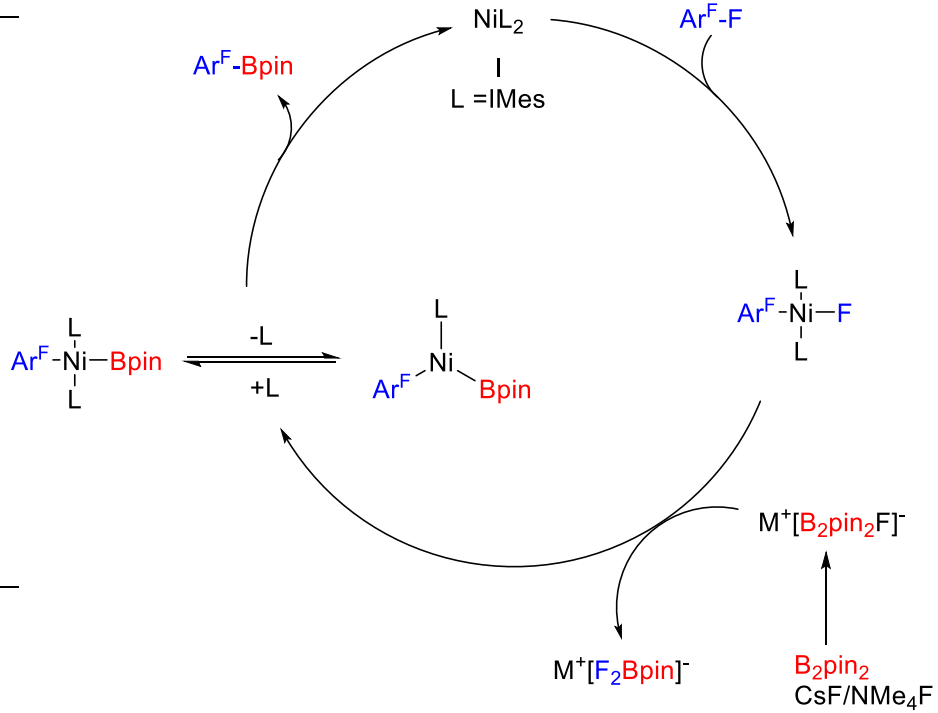
Radius, U. *et. al. J. Am. Chem. Soc* **2008**, *130*, 9304-9317.

2.1、过渡金属参与的脱氟反应

Radius, 2016:



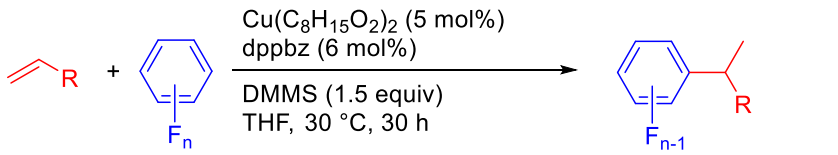


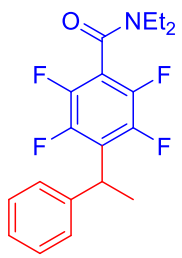


Radius, U. *et. al. J. Am. Chem. Soc.* **2016**, *138*, 5250-5253.

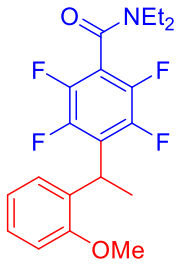
2. 1、过渡金属参与的脱氟反应

Zhang, 2020：





85%



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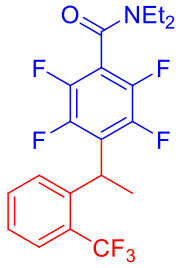

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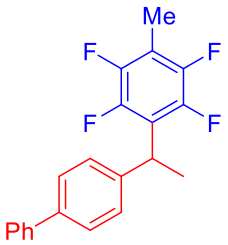
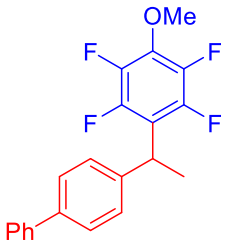


75% *p: m* = 95:5



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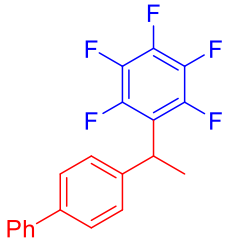

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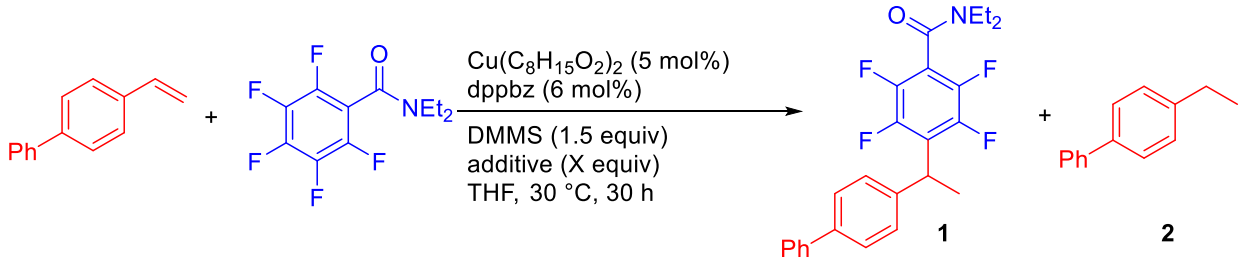
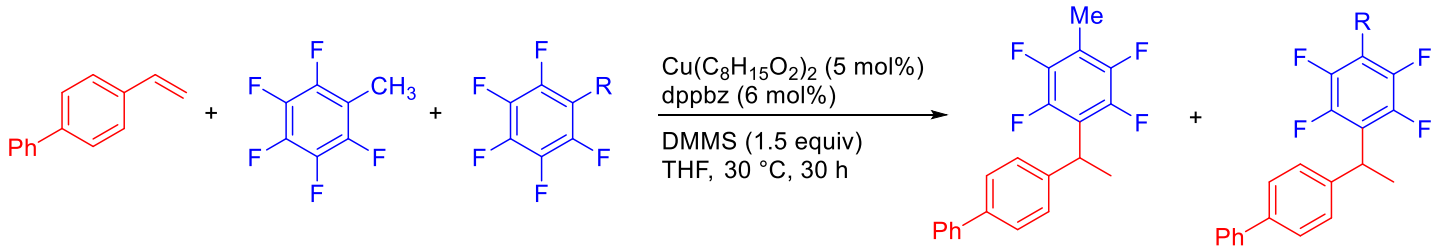


addtive (X equiv)	yield (**1**, %)	addtive (X equiv)	yield (**1**, %)
^{t}BuOH (1.2)	5% (**1**); 17% (**2**)	naphthalene (1.2)	97%
(trifluoromethyl)benzene (1.2)	92%	1,1-diphenylethylene (1.2)	94%

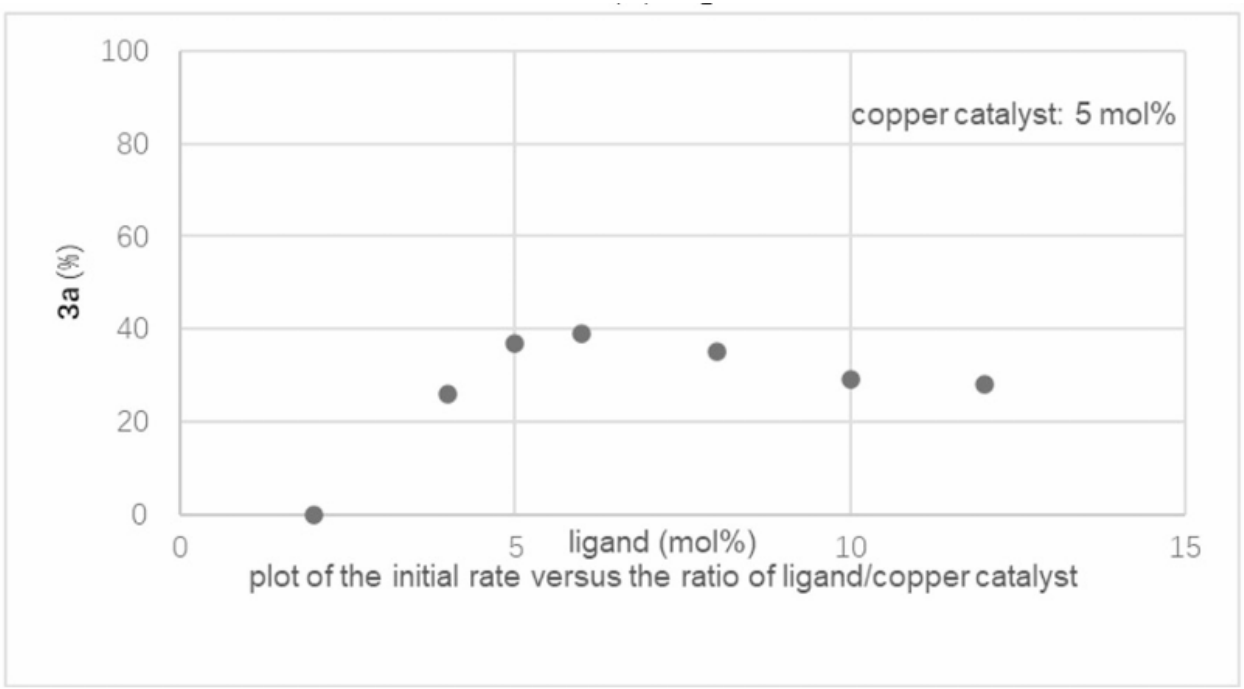


R: Ph	4%	80%
R: -C(O)NEt$_2$	trace	82%

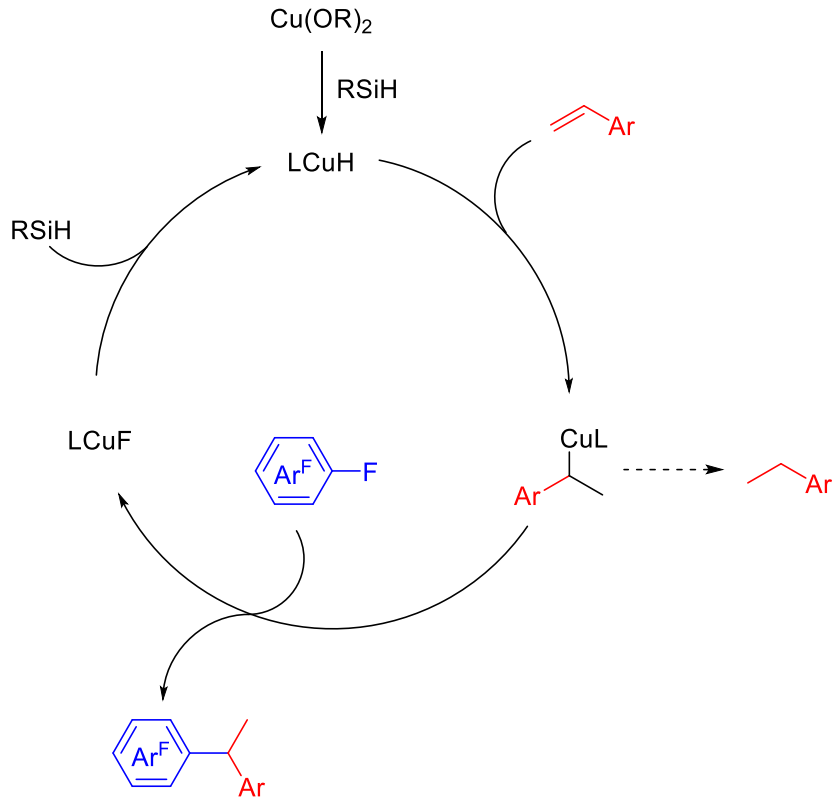
Q. Zhang, *et. al. Angew. Chem. Int. Ed.* **2020**, *59*, 23056.

2.1、过渡金属参与的脱氟反应

Zhang, 2020：



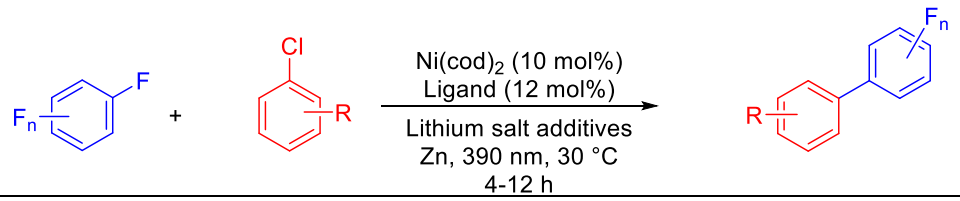
Proposed mechanism：

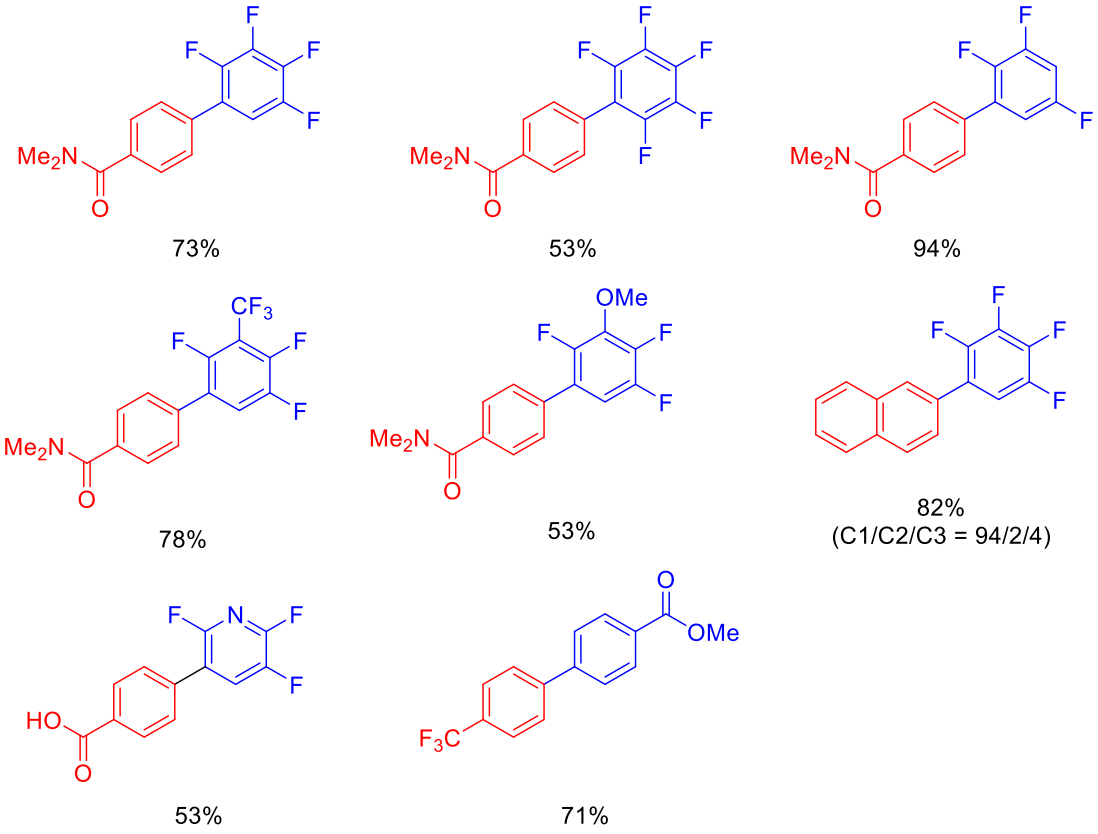


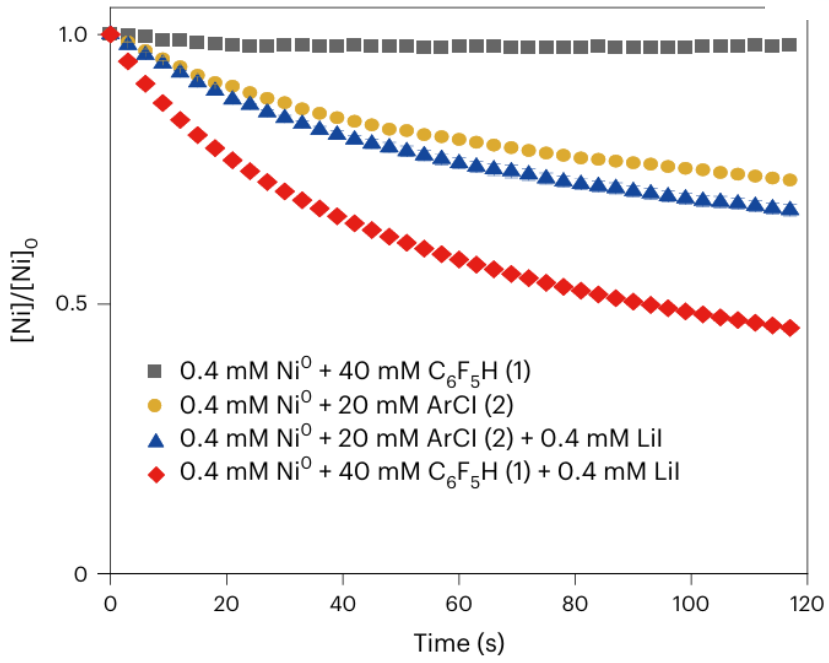
Q. Zhang, *et. al. Angew. Chem. Int. Ed.* **2020**, *59*, 23056.

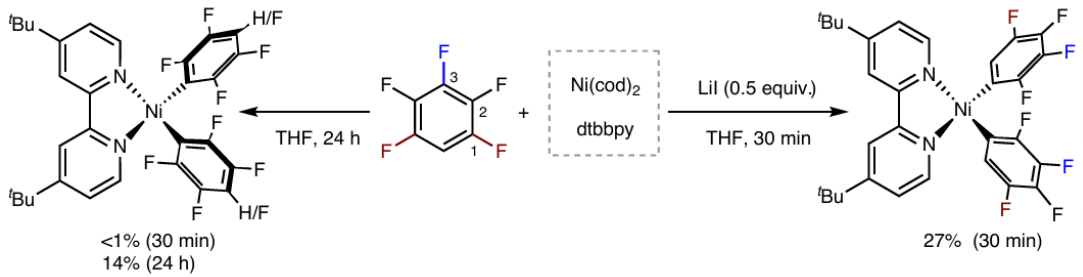
2.1、过渡金属参与的脱氟反应

Xie, 2025：





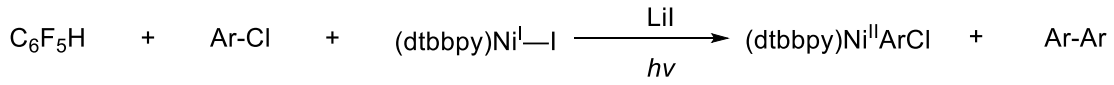


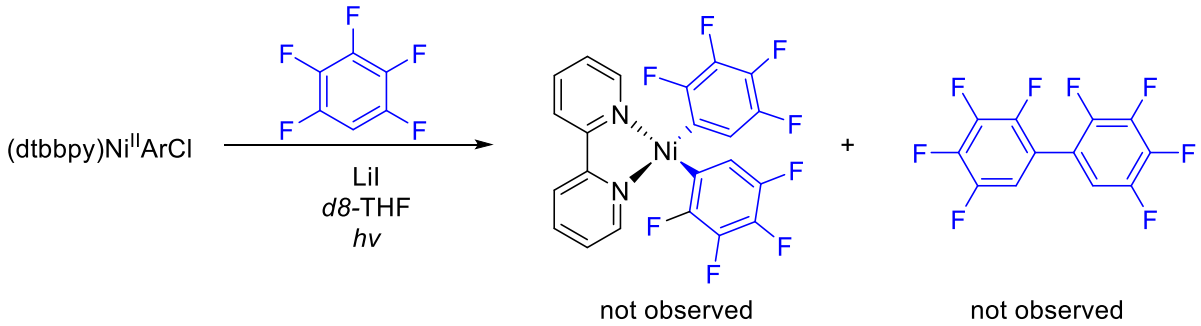


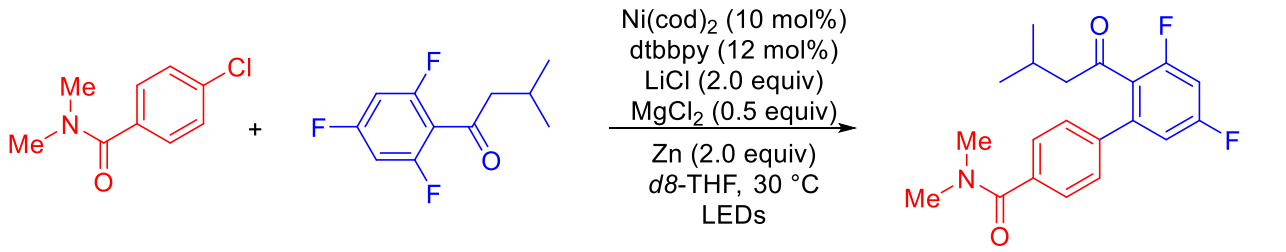
Xie, J. *et. al*. *Nat Chem* **2025**. s41557-025-01962-1.

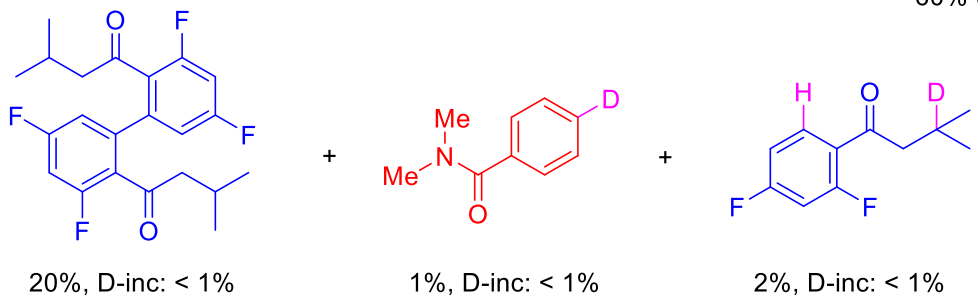
2. 1、过渡金属参与的脱氟反应

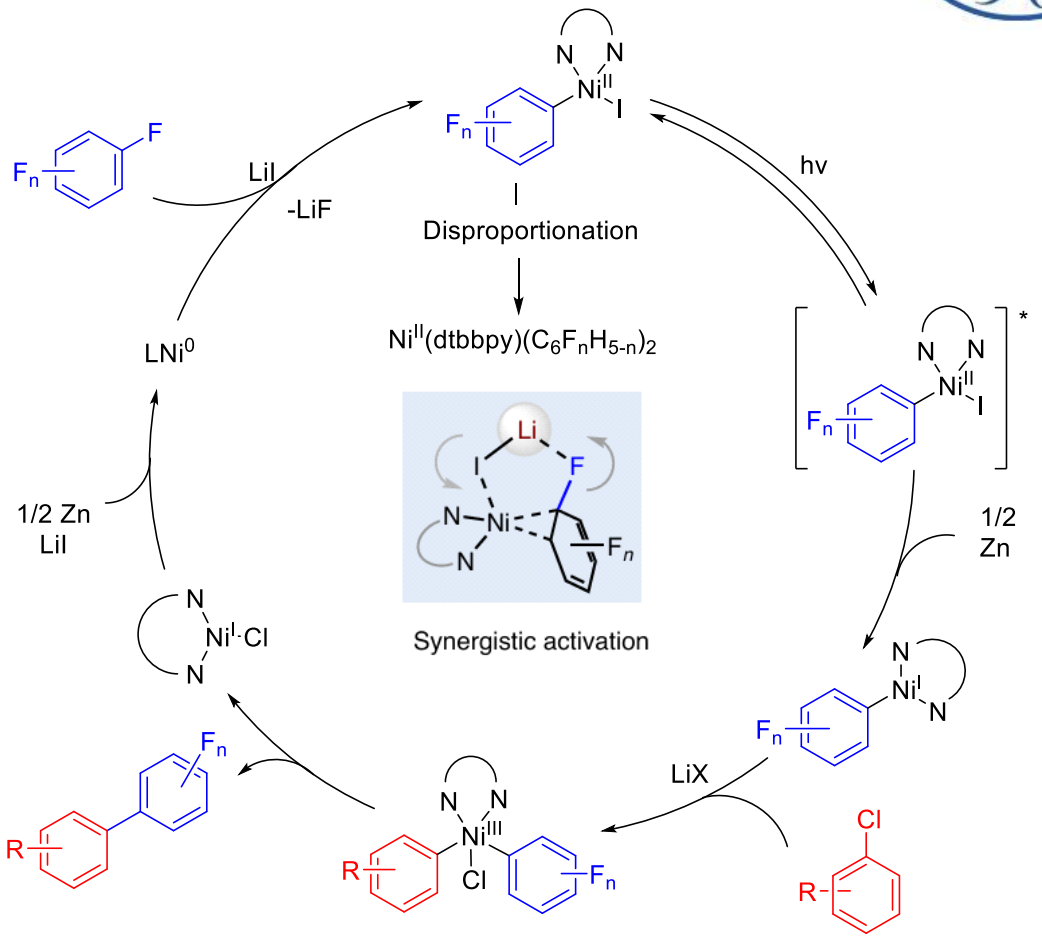
Xie, 2025 :







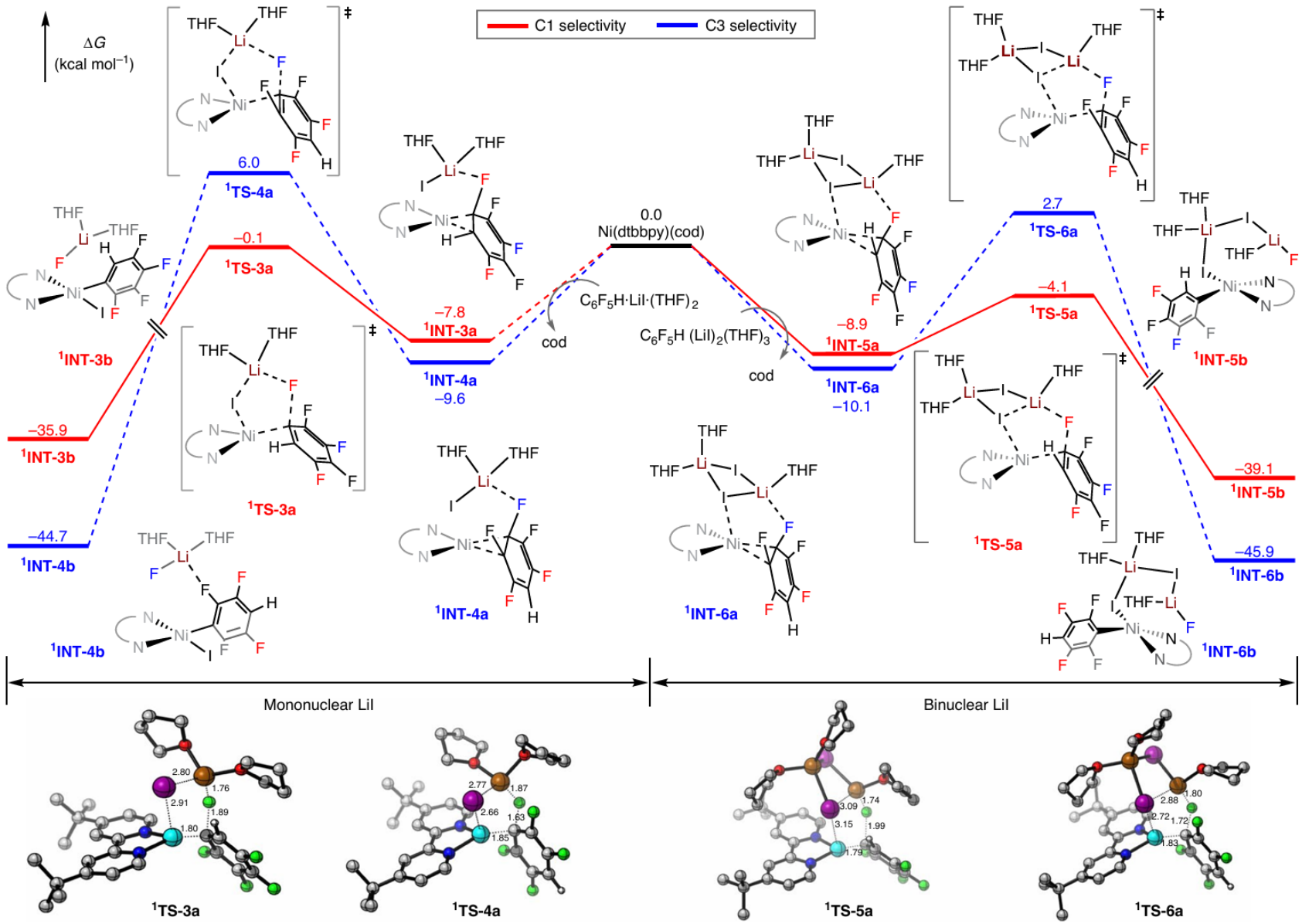




Xie, J. *et. al*. *Nat Chem* **2025**. s41557-025-01962-1.

2.1、过渡金属参与的脱氟反应

Xie, 2025：

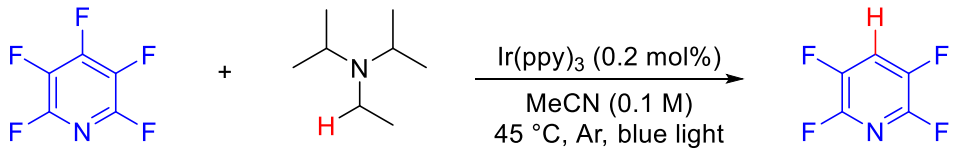


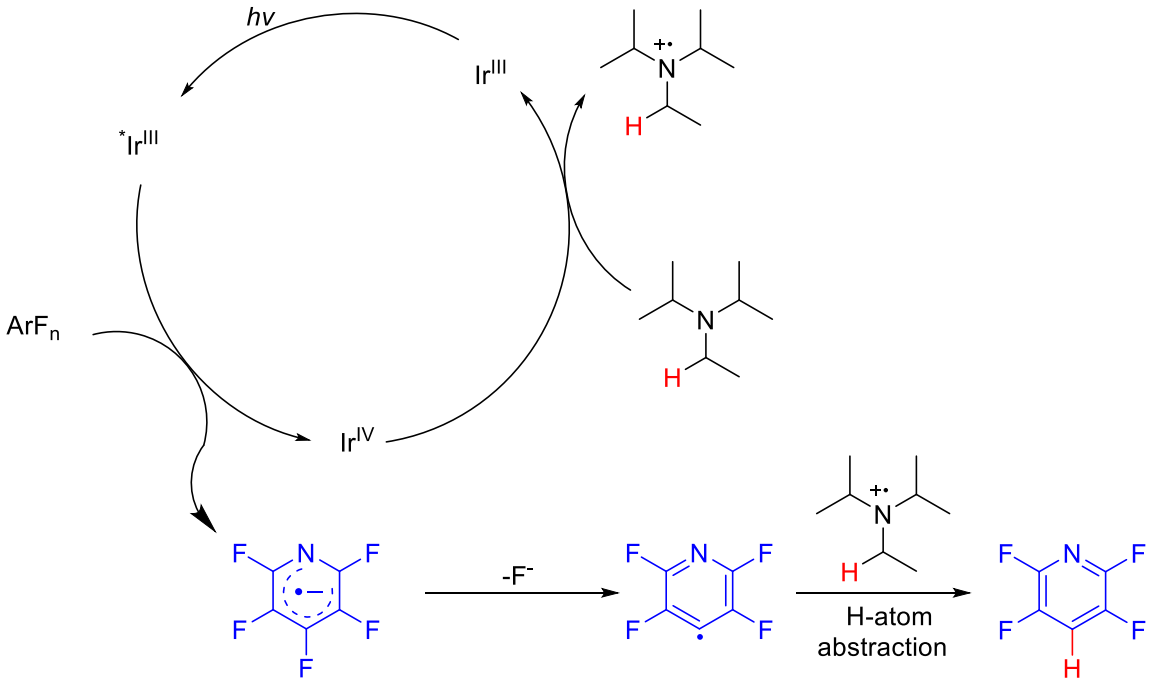
Xie, J. *et. al*. *Nat Chem* **2025**. s41557-025-01962-1.

目录

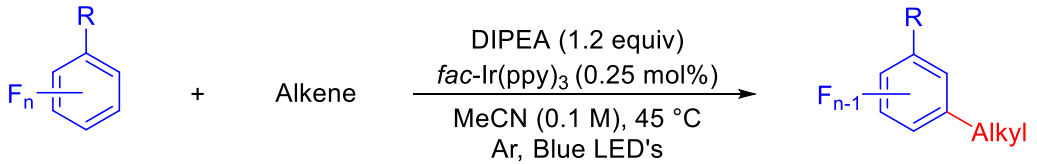
2.2、光催化的脱氟反应

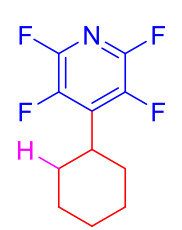
Weaver, 2014：





Weaver, 2015：





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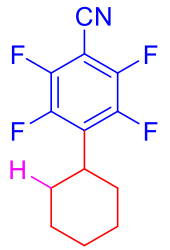
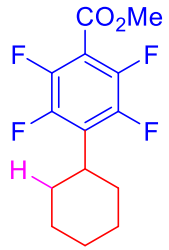


64%



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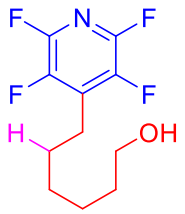
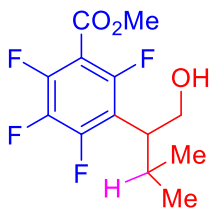


53%
rr>20:1



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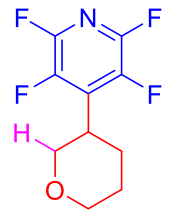
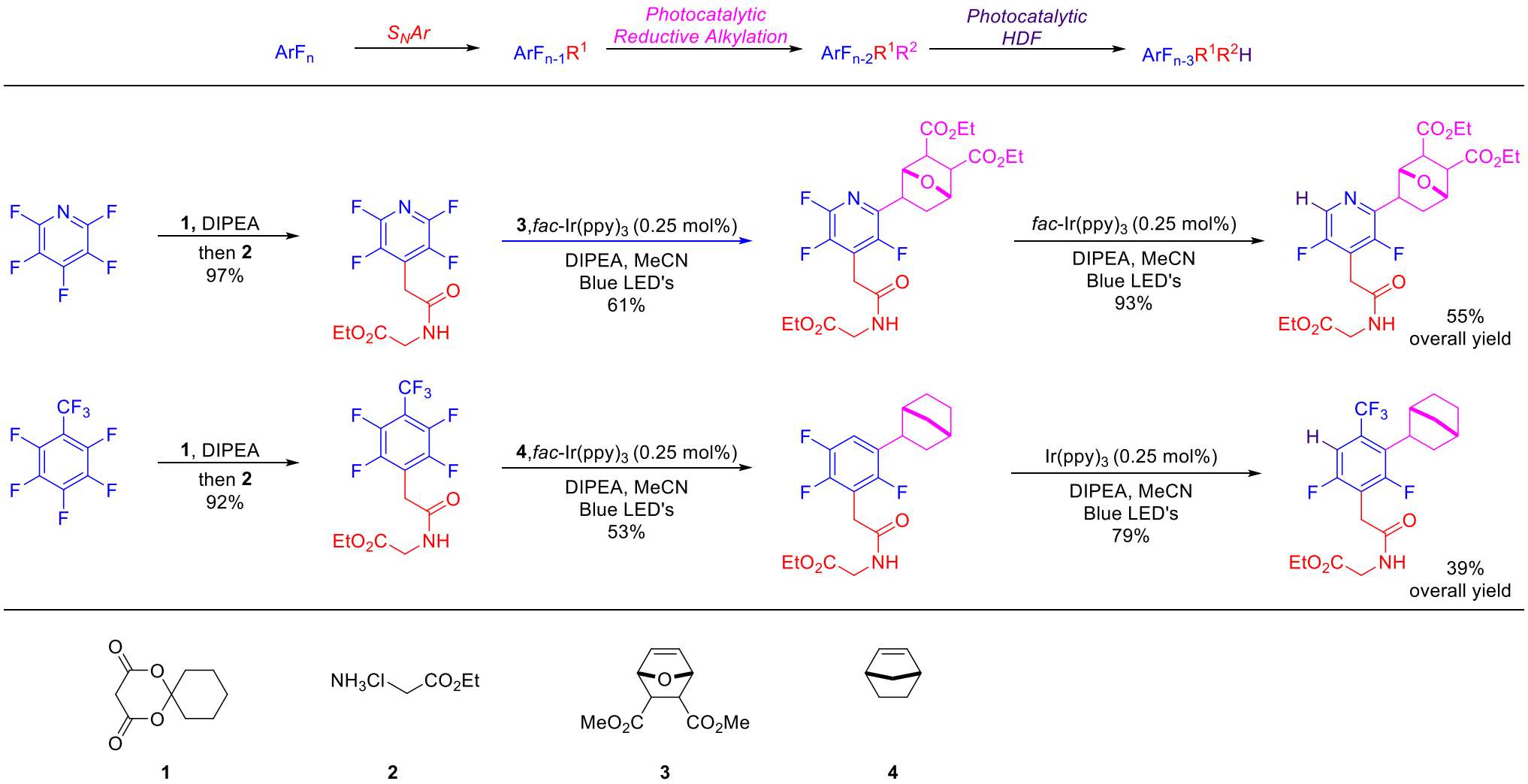


72%
rr~1:1

Weaver, J. D. *et. al. J. Am. Chem. Soc*. **2014,** *136*, 3002–3005.
Weaver, J. D. *et. al. Chem. Sci.* **2015**, *6*, 7206−7212.

2.2、光催化的脱氟反应

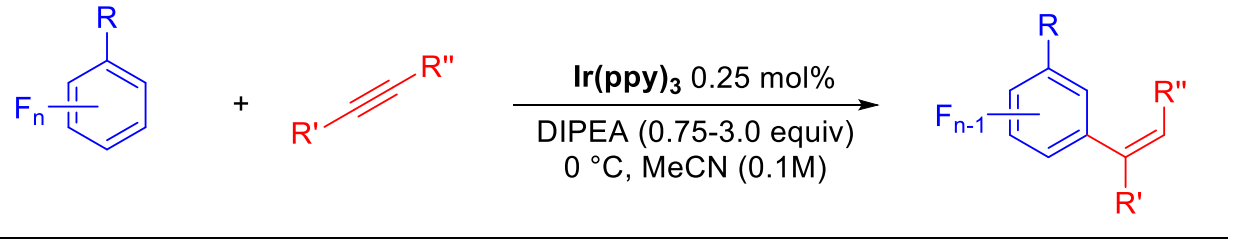
Weaver, 2015：

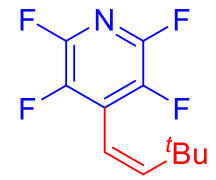


Weaver, J. D. *et. al. Chem. Sci.* **2015**, *6*, 7206−7212.

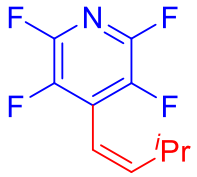
2.2、光催化的脱氟反应

Weaver, 2016：

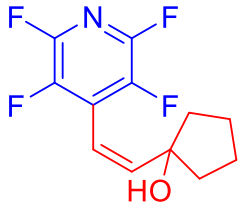




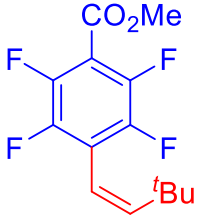
85%, Z:E = 24:1



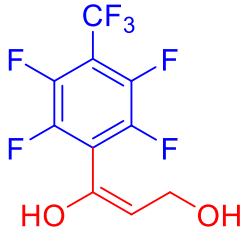
74%, Z:E > 25:1



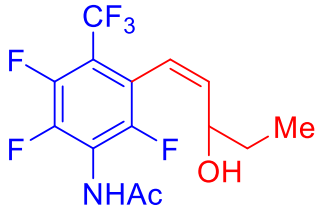
61%, Z:E = 25:1



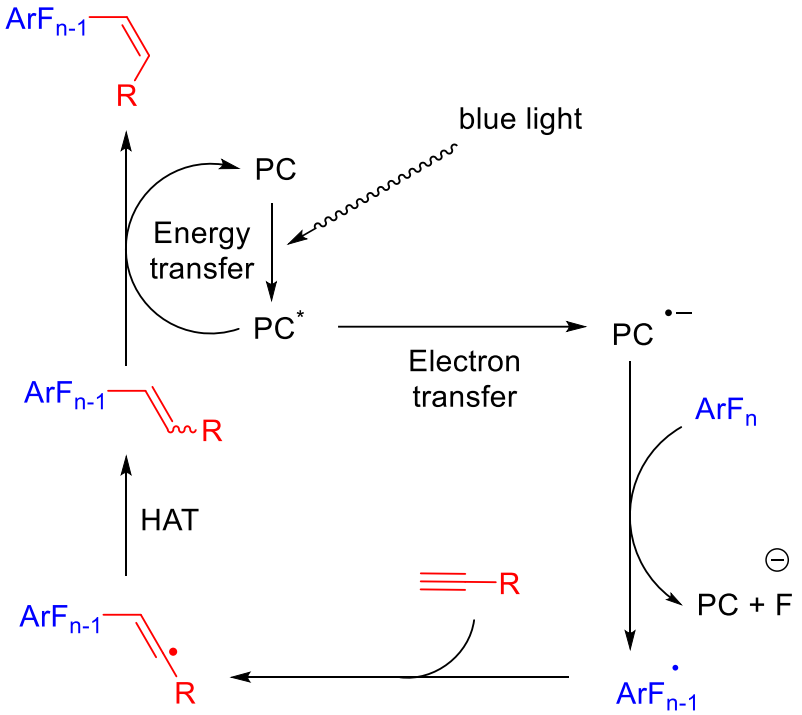
86%, Z:E = 24:1



63%, Z:E > 25:1



51%, Z:E > 25:1



Weaver, J. D. *et. al. Chem. Sci.* **2016,** *7*, 6796–6802

2.2、光催化的脱氟反应

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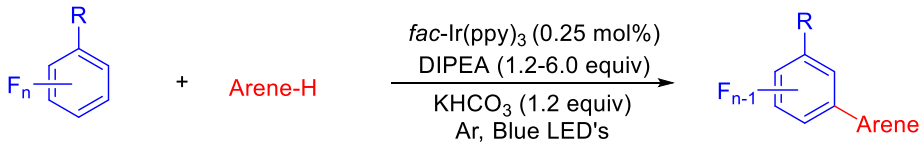
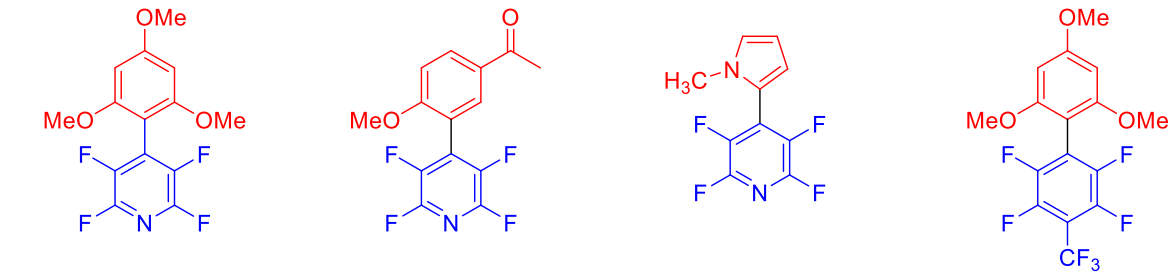
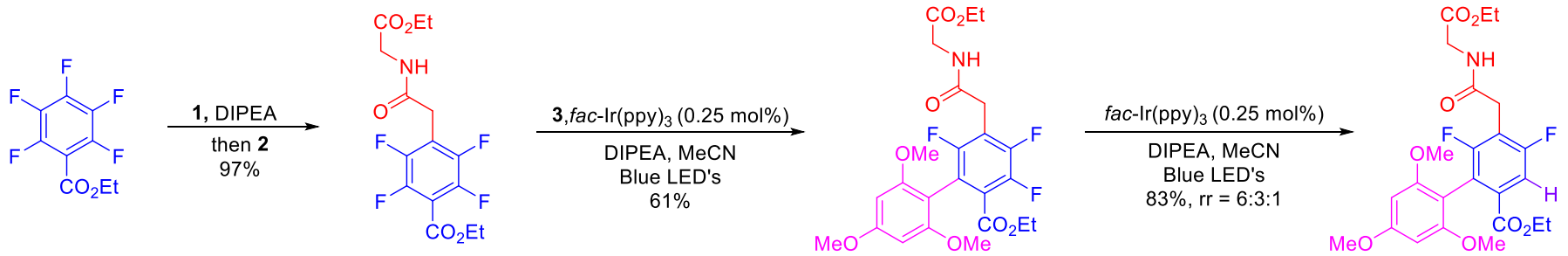
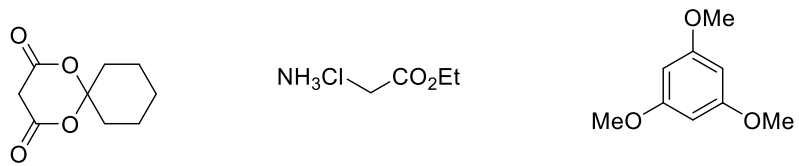




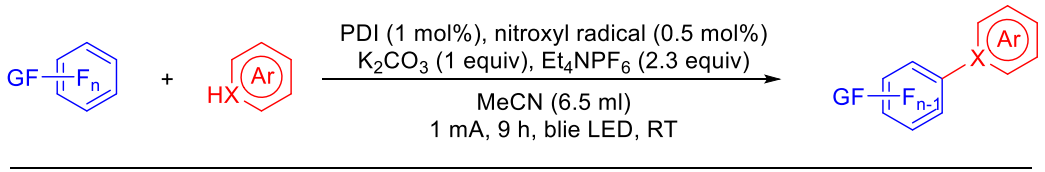


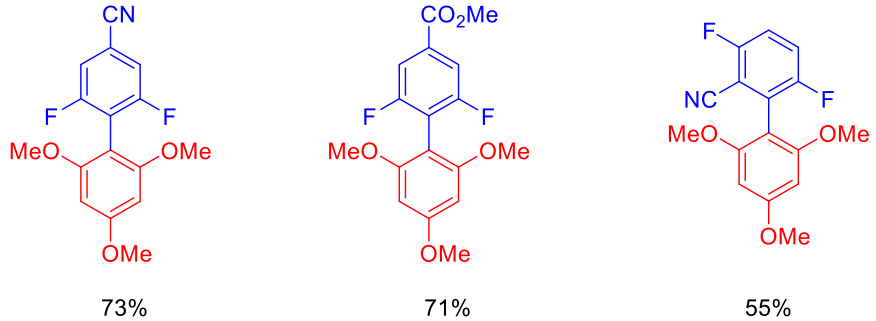


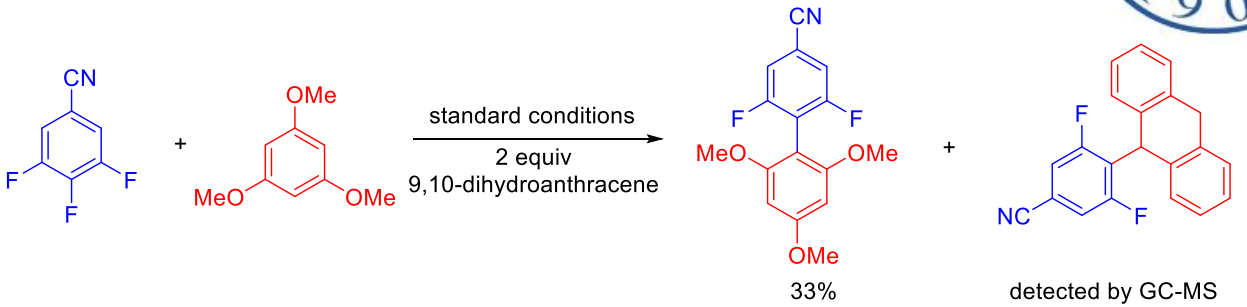
Weaver, J. D. *et. al. J. Am. Chem. Soc*. **2016**, *138*, 2520-2523.

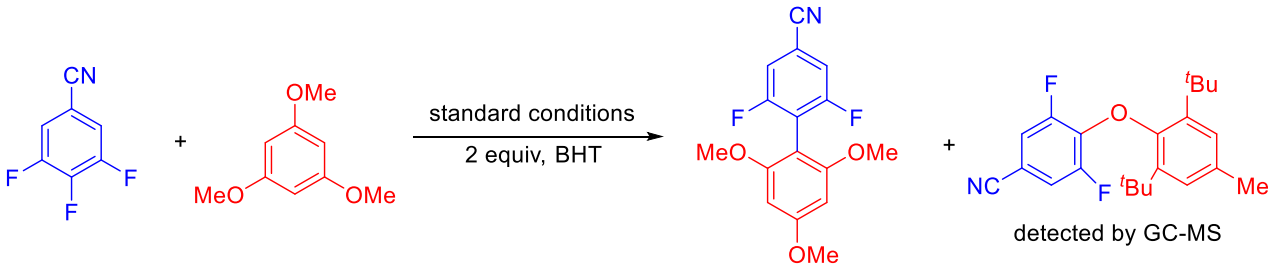
2.2、光催化的脱氟反应

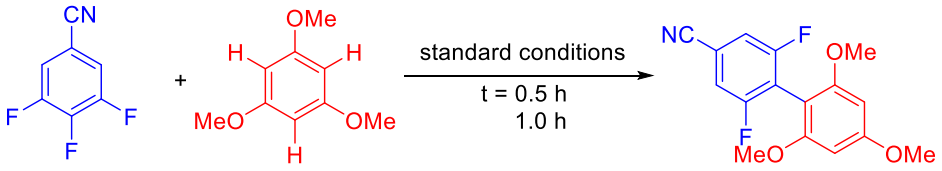
Wu, 2022：

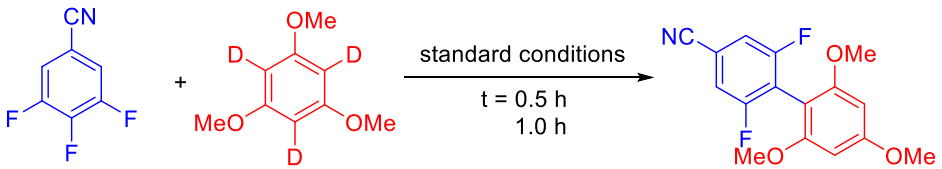












t = 0.5 h k_H/k_D = 1.33

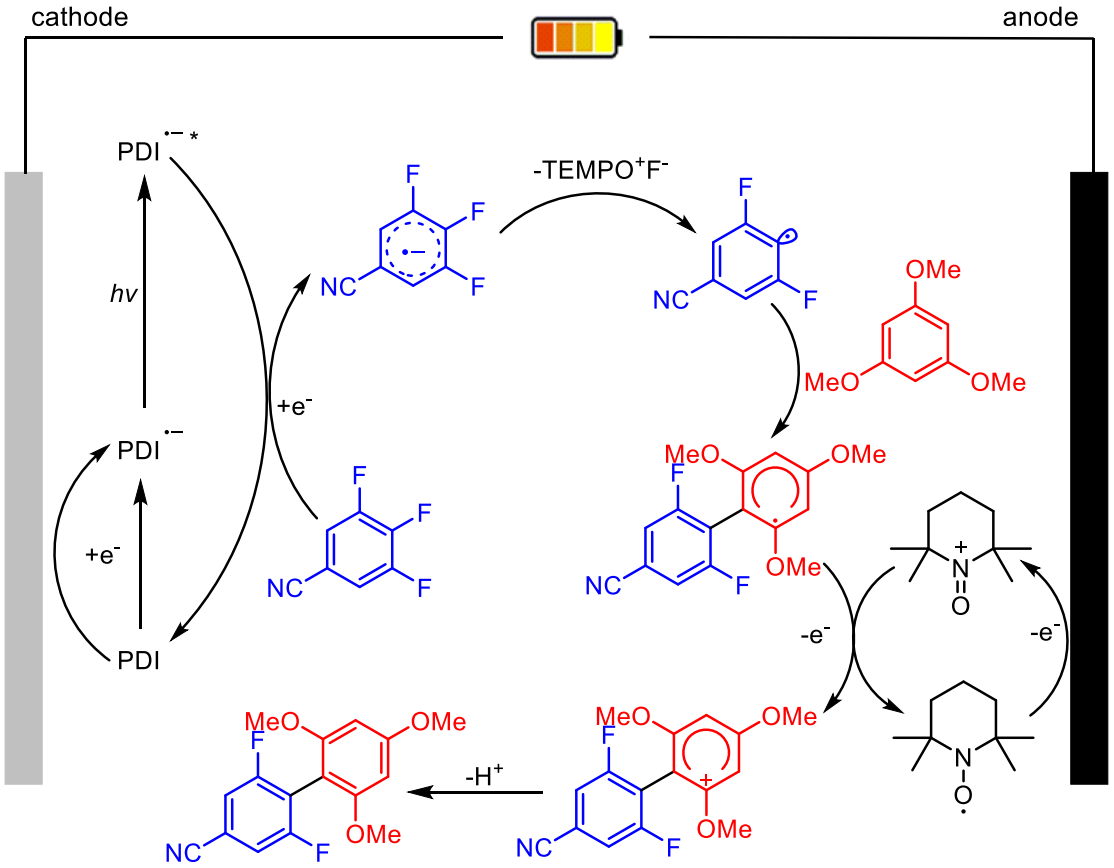
t = 1.0 h k_H/k_D = 1.33

Wu, L. Z. *et. al. J. Am. Chem. Soc.* **2022**, *144*, 17261-17268.

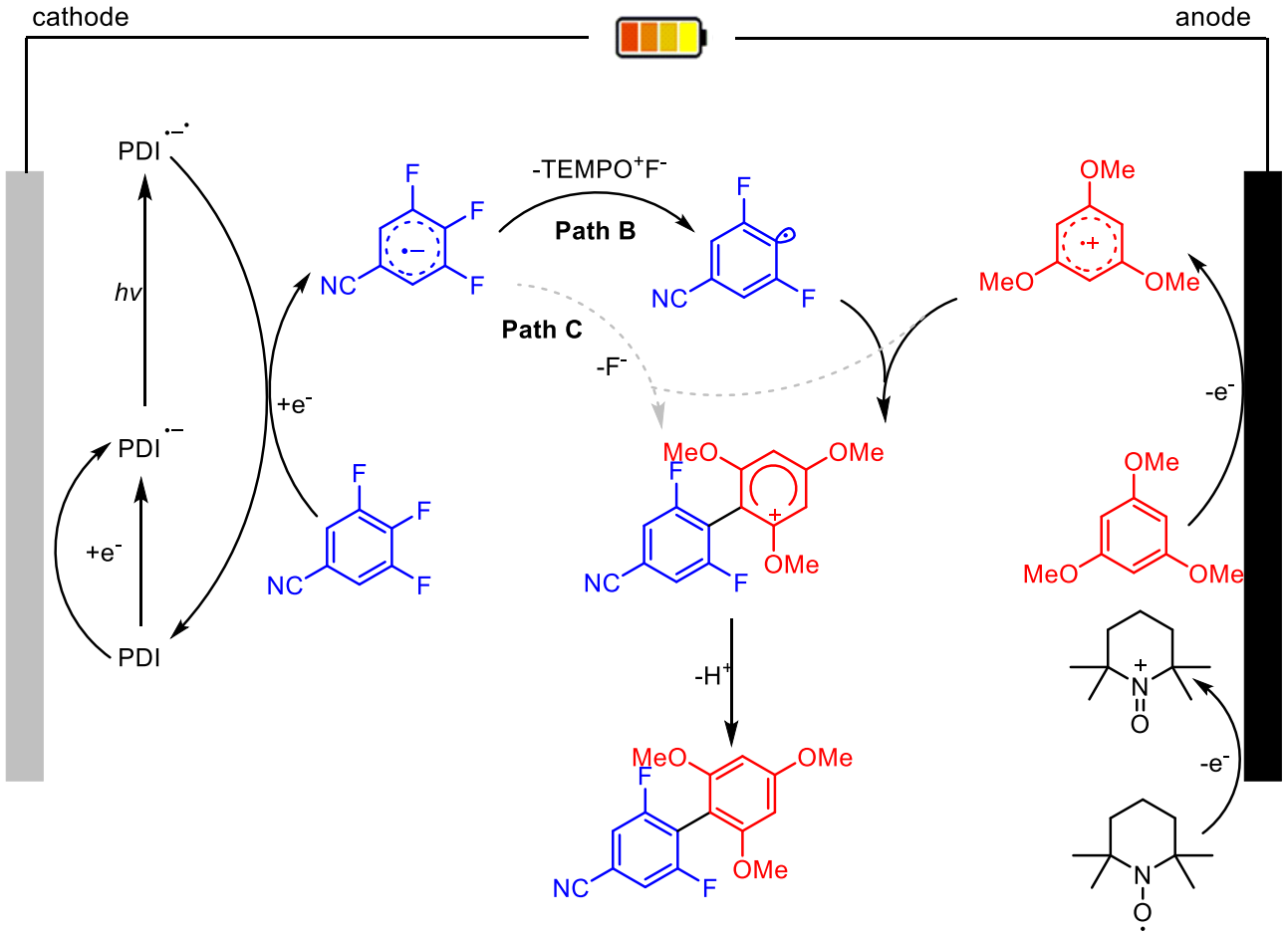
2.2、光催化的脱氟反应

Wu, 2022：

Path A：



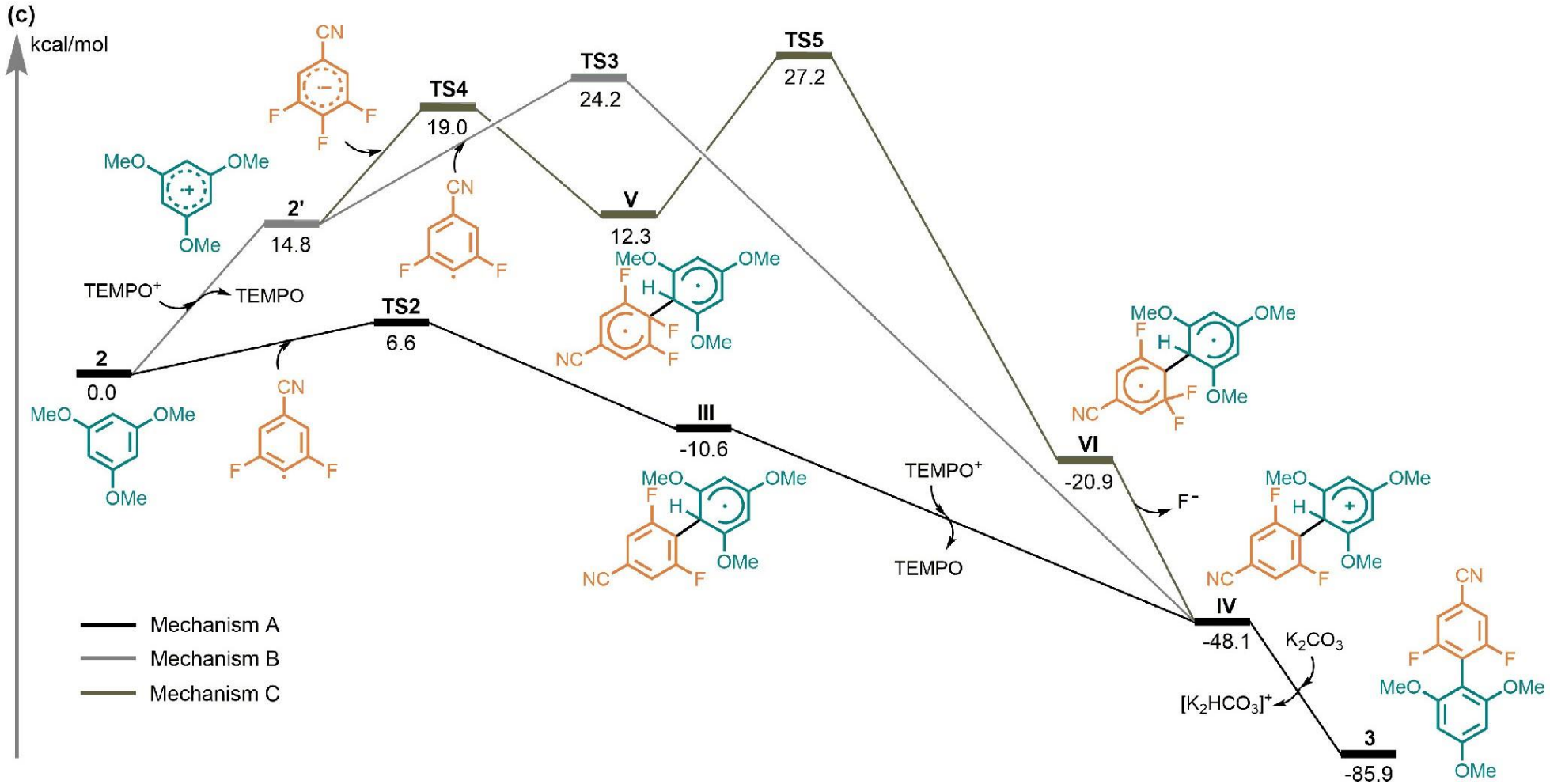
Path B and C：



Wu, L. Z. *et. al. J. Am. Chem. Soc.* **2022**, *144*, 17261-17268.

2.2、光催化的脱氟反应

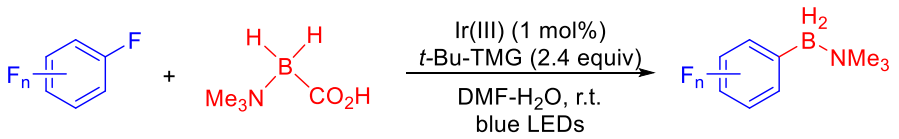
Wu, 2022：

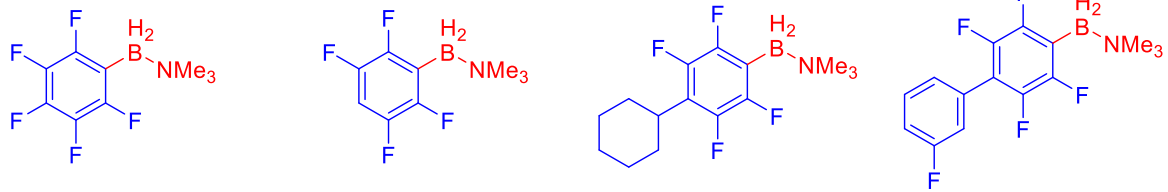


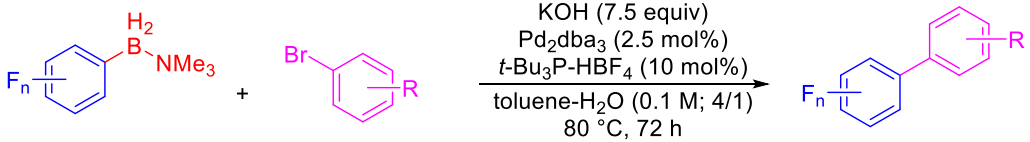
Wu, L. Z. *et. al. J. Am. Chem. Soc.* **2022**, *144*, 17261-17268.

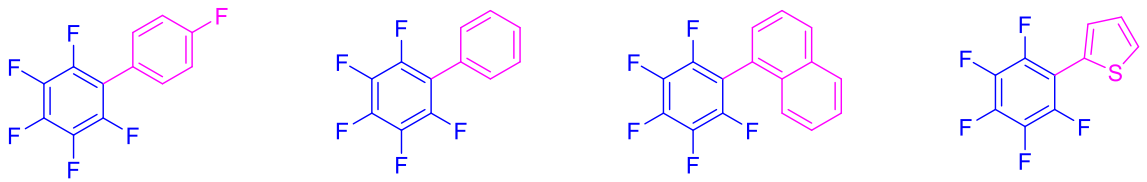
2.2、光催化的脱氟反应

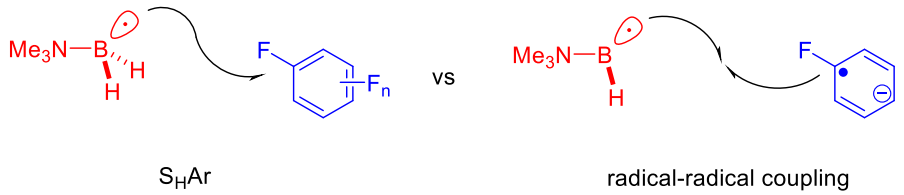
Nakamura, 2025:

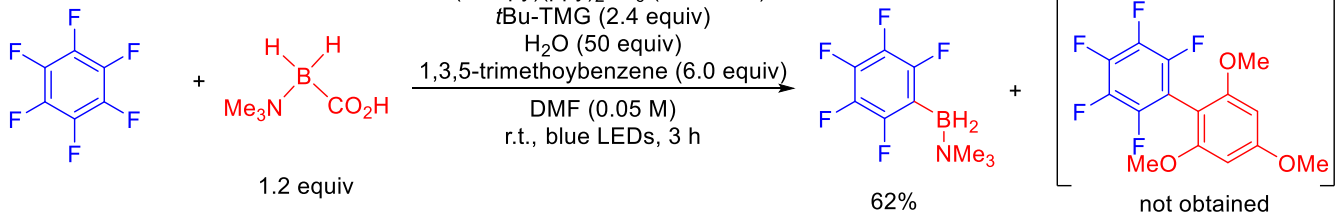


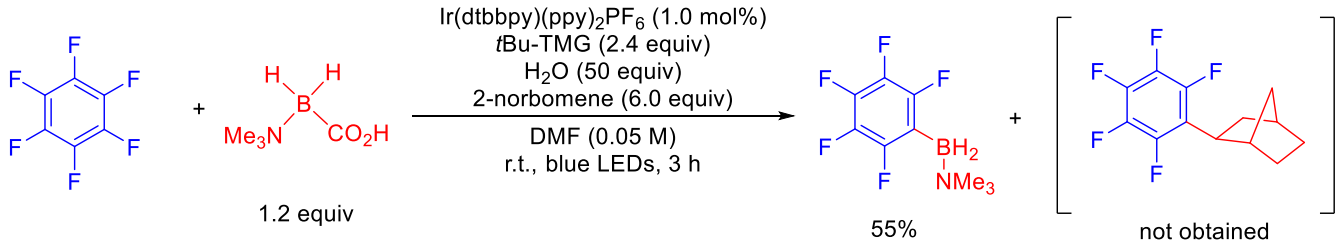


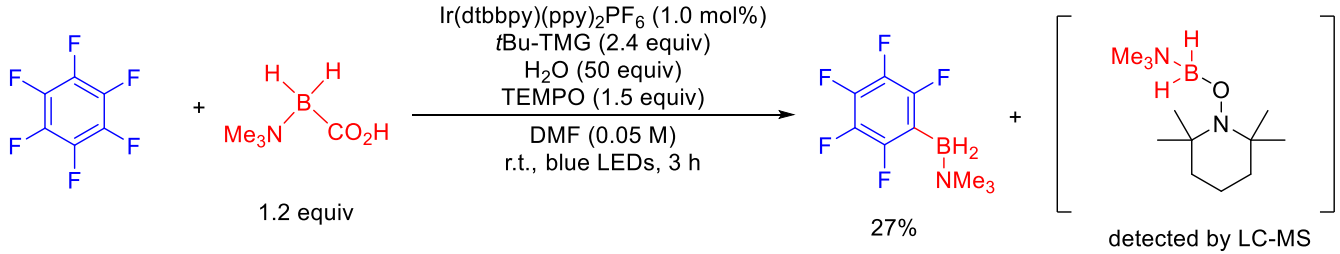








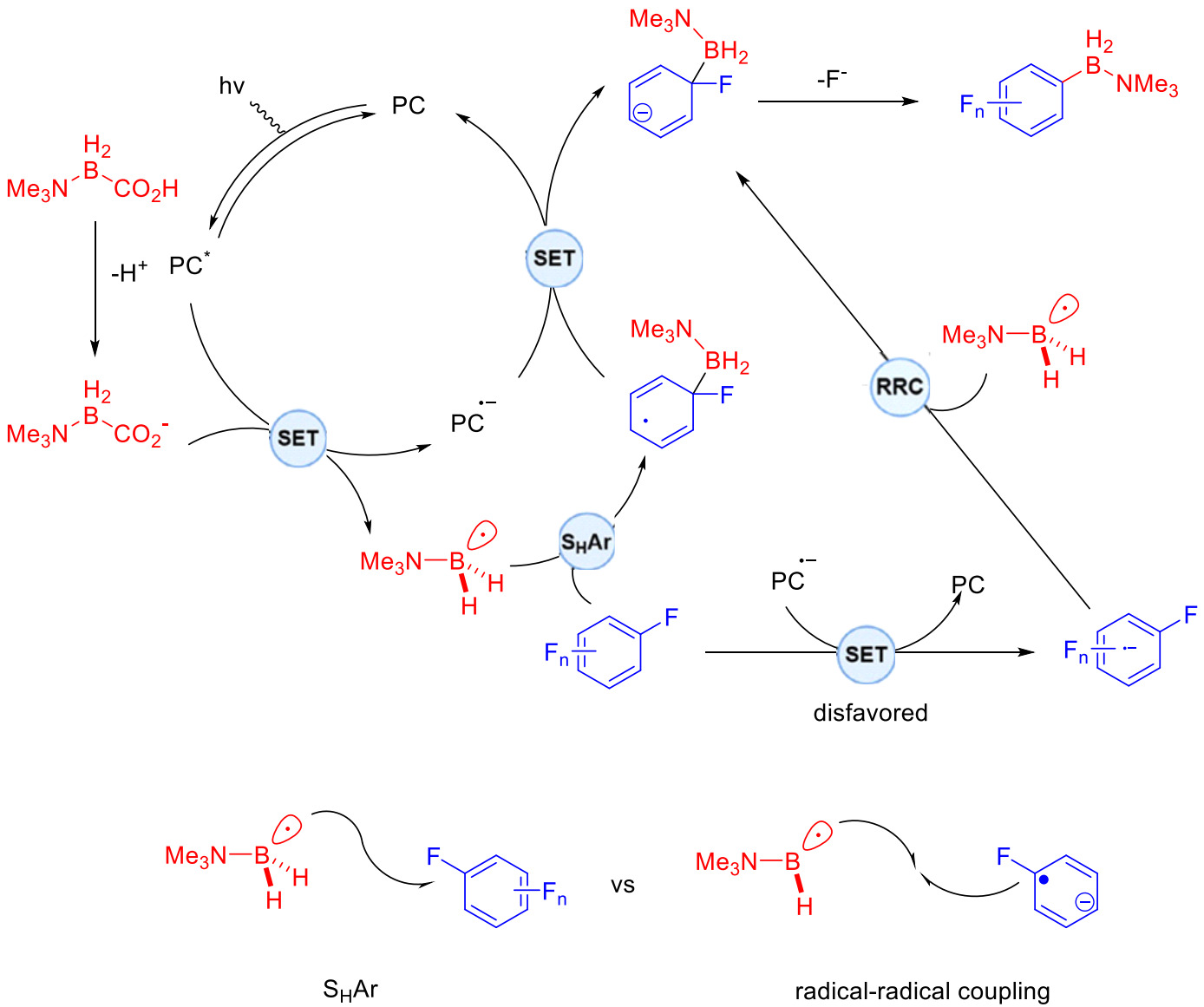




S. Nakamura, *et. al. Angew. Chem. Int. Ed.*. 2025, e202514741.

2.2、光催化的脱氟反应

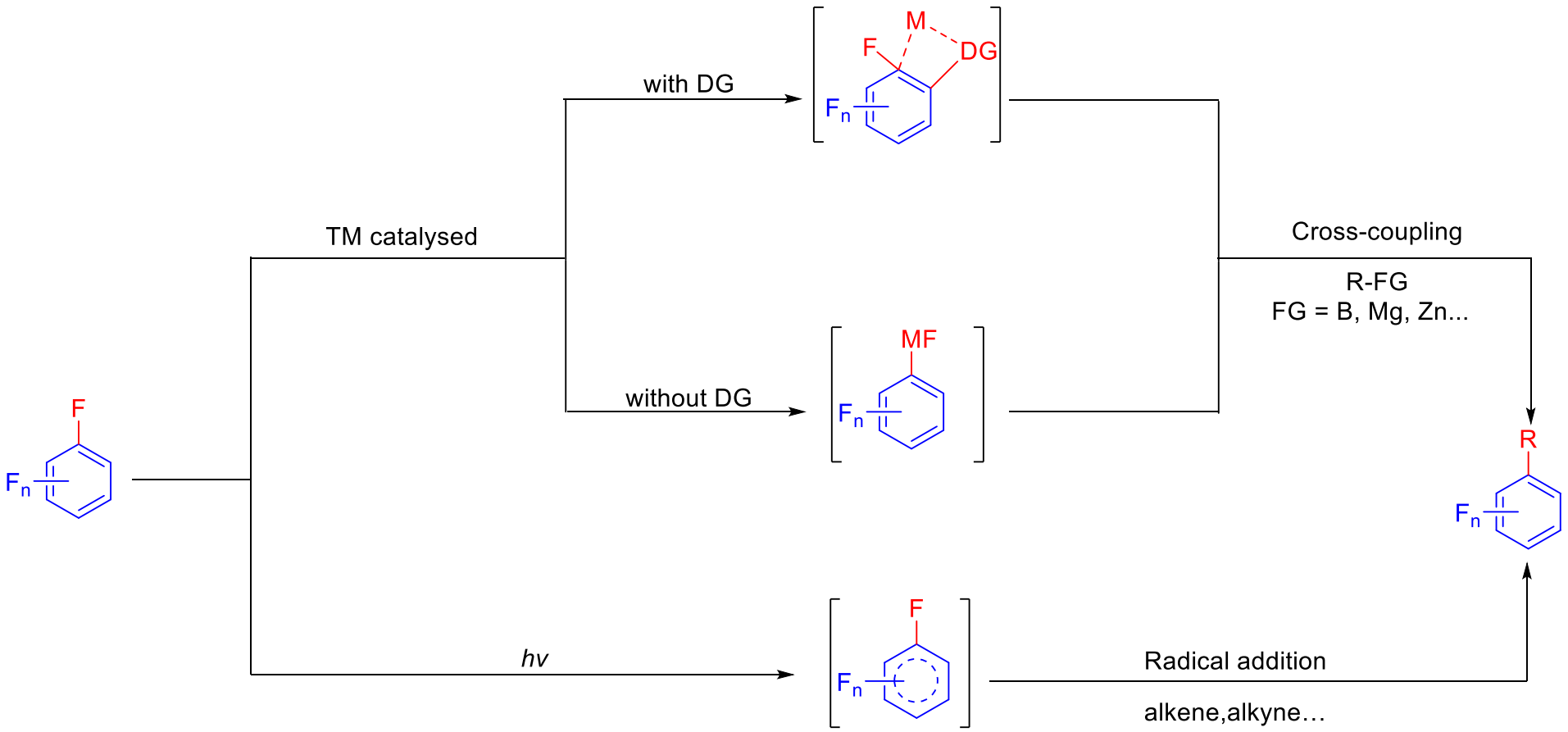
Nakamura, 2025:



S. Nakamura, *et. al. Angew. Chem. Int. Ed.*. 2025, e202514741.

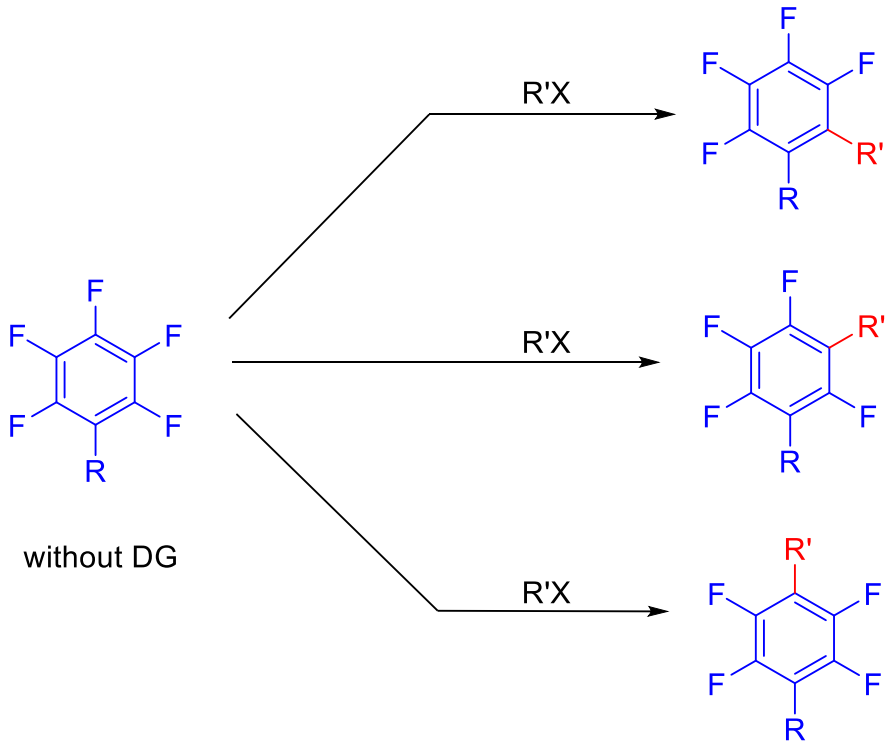
目录

3、总结与展望

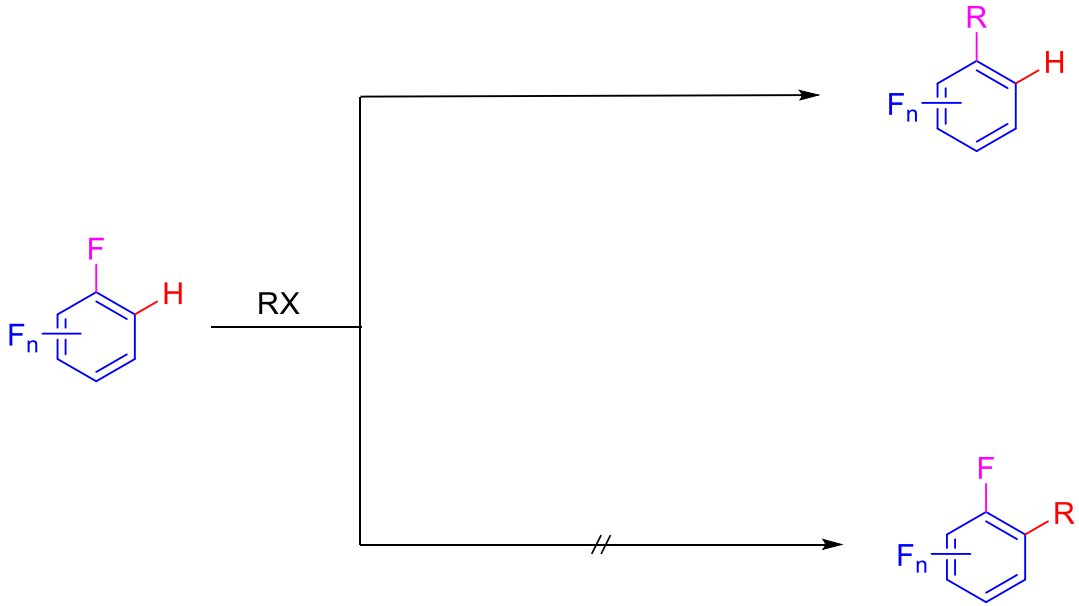

with DG
TM catalysed
without DG
hv
Cross-coupling
R-FG
FG = B, Mg, Zn...
Radical addition
alkene,alkyne…

3、总结与展望

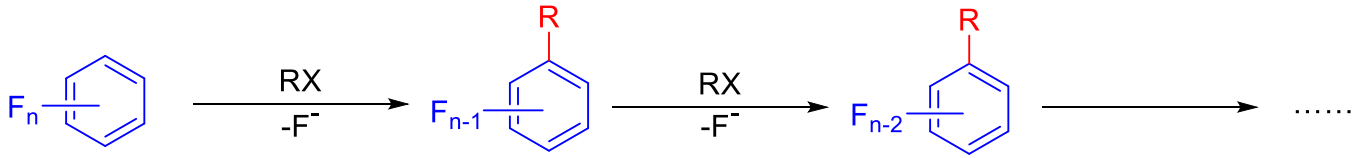
实现无导向基时的精准脱氟：



调控碳氟键与碳氢键之间的竞争：

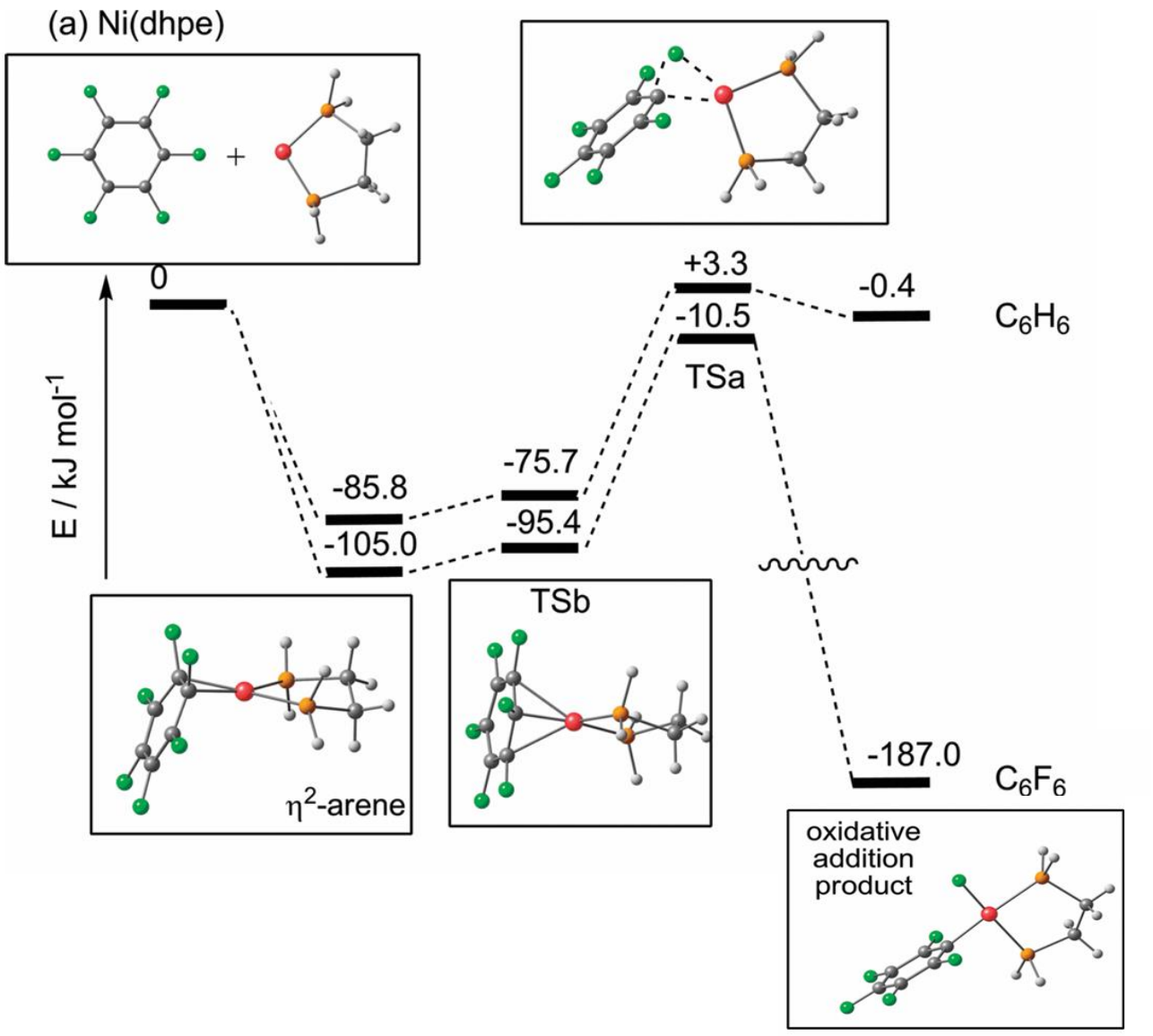


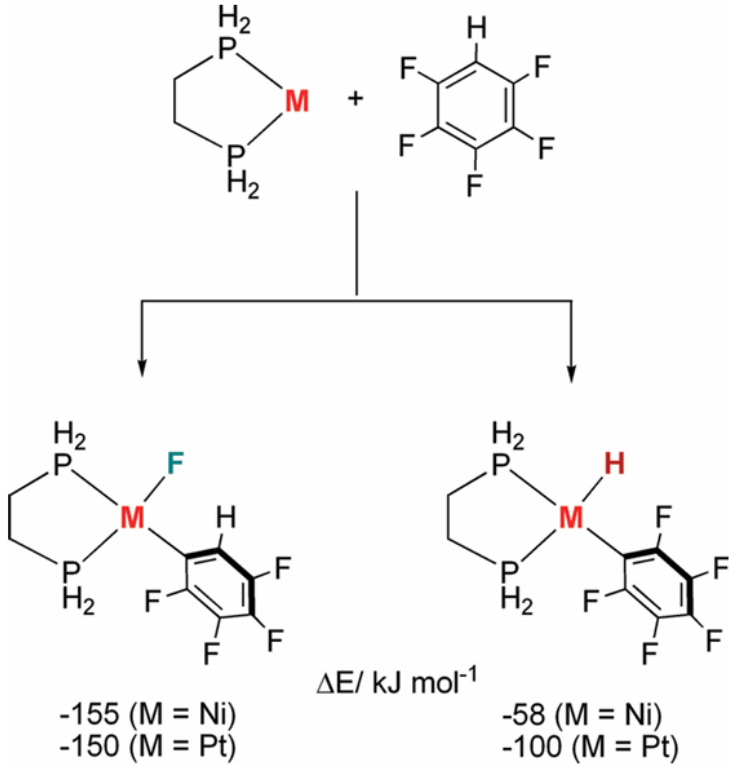
通过连续可控脱氟官能团化构建复杂分子：



Thanks for your listening

4、Supporting Information





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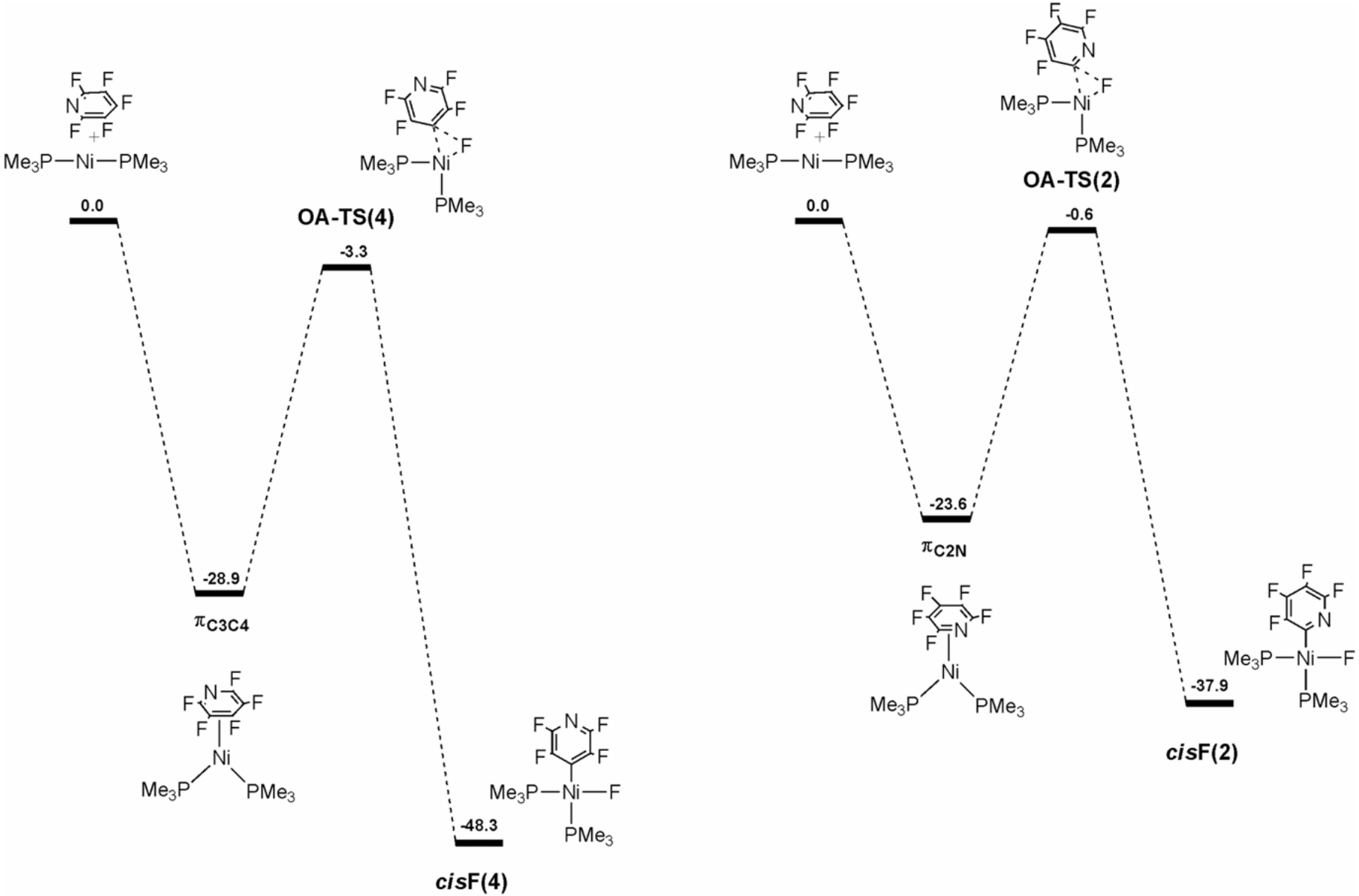

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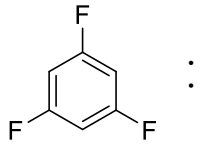

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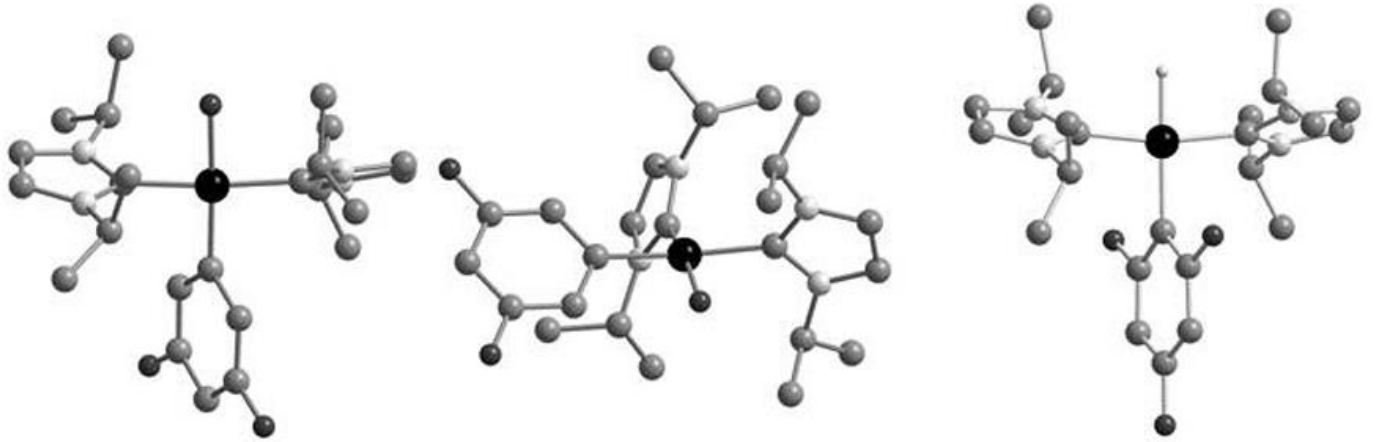
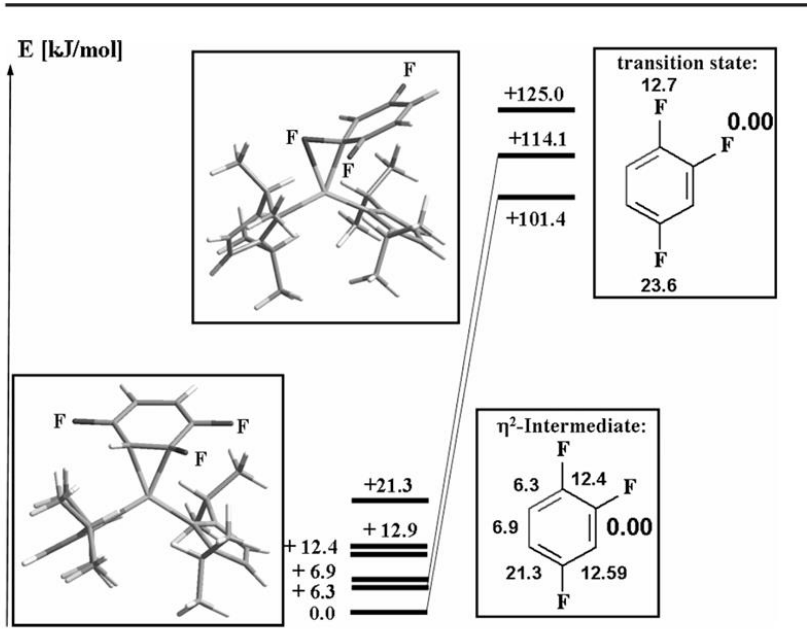


trans-[Ni(ᵗPr₂Im)₂(F)(3,5-C₆F₂H₃)] **ΔE = 0.0 kJ/mol**

cis-[Ni(ᵗPr₂Im)₂(F)(3,5-C₆F₂H₃)] **ΔE = 28.8 kJ/mol**

trans-[Ni(ᵗPr₂Im)₂(H)(2,4,6-C₆F₃H₂)] **ΔE = 86.4 kJ/mol**



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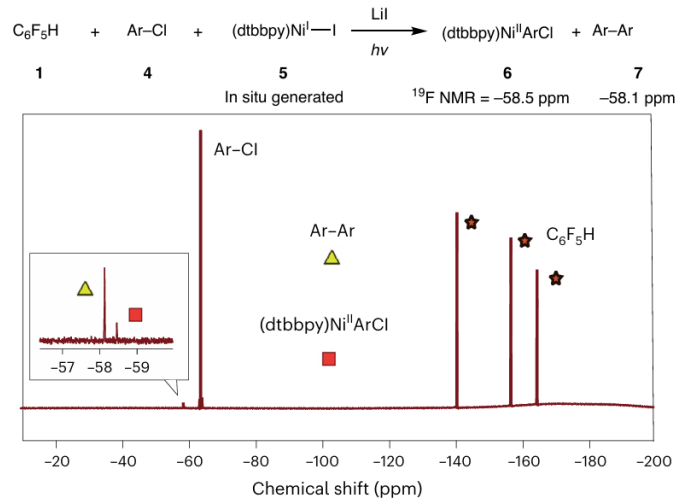

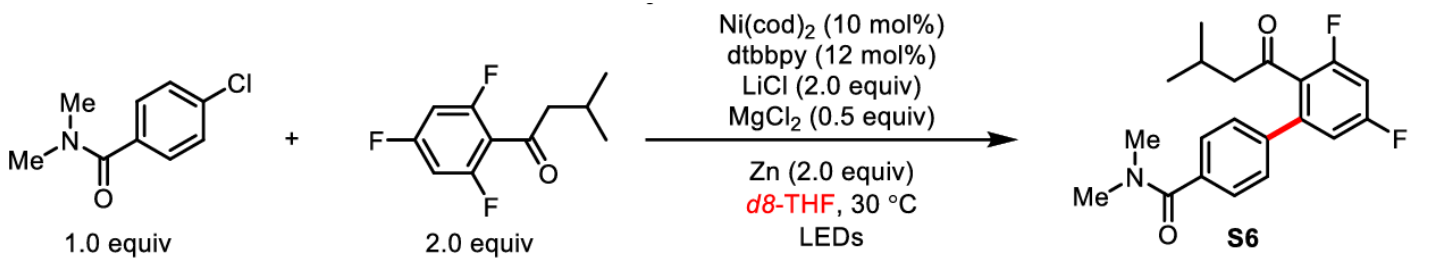

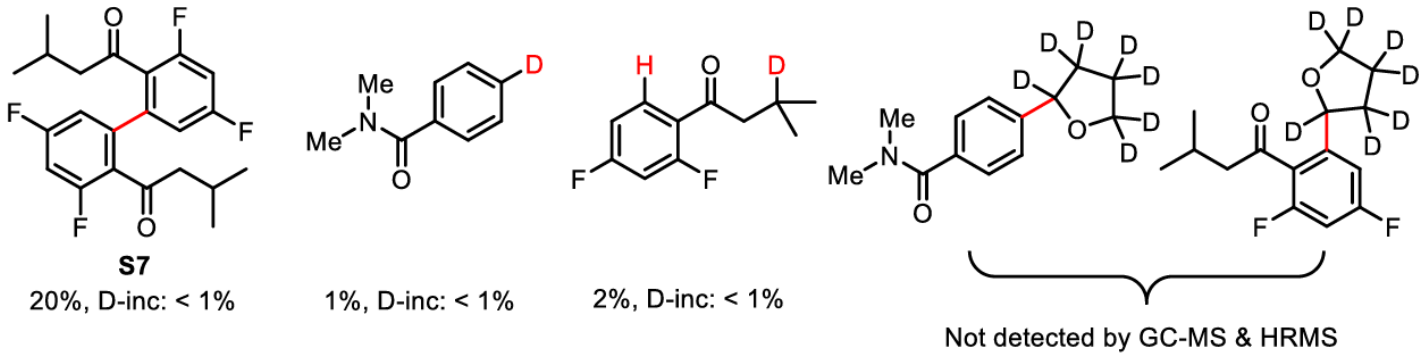

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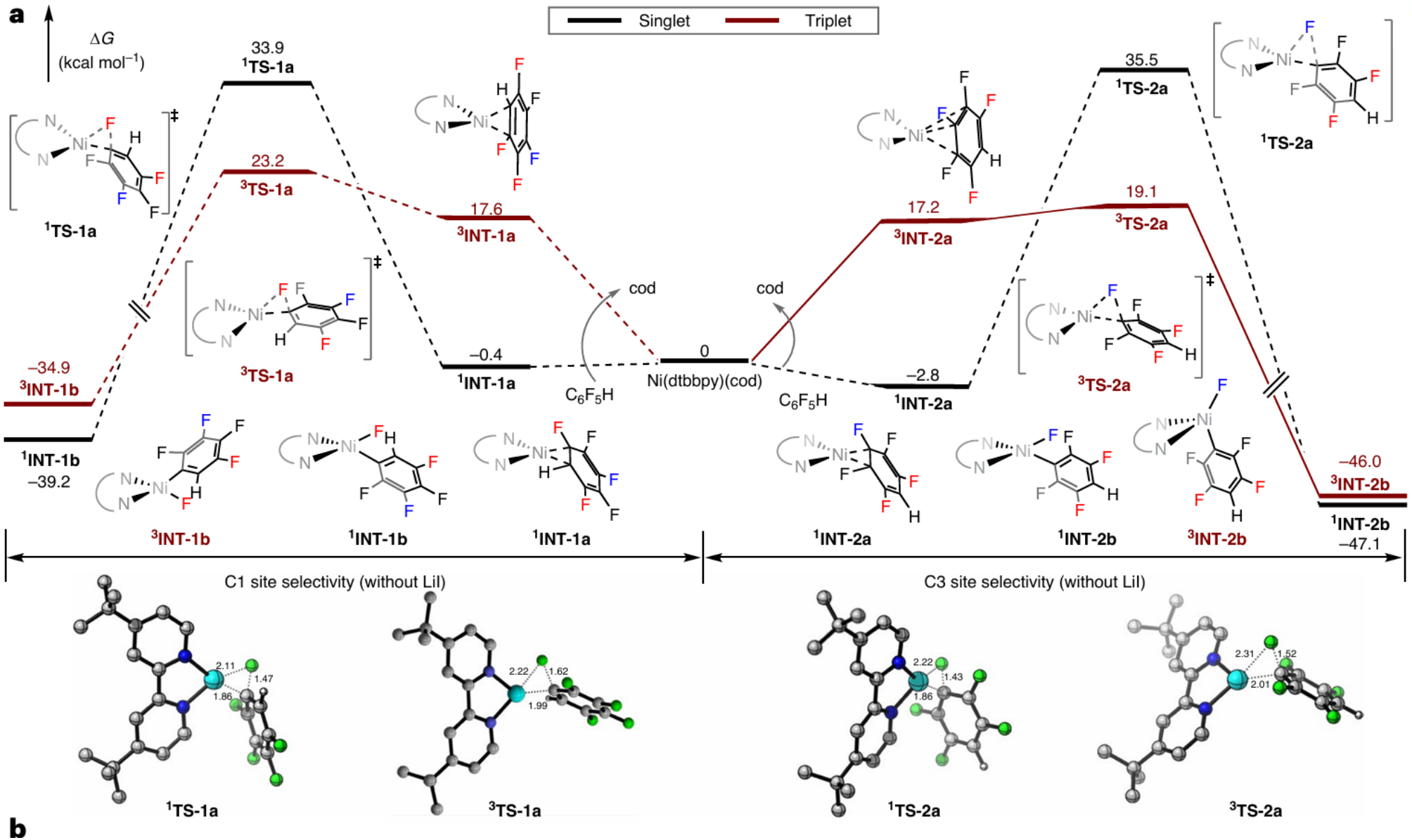

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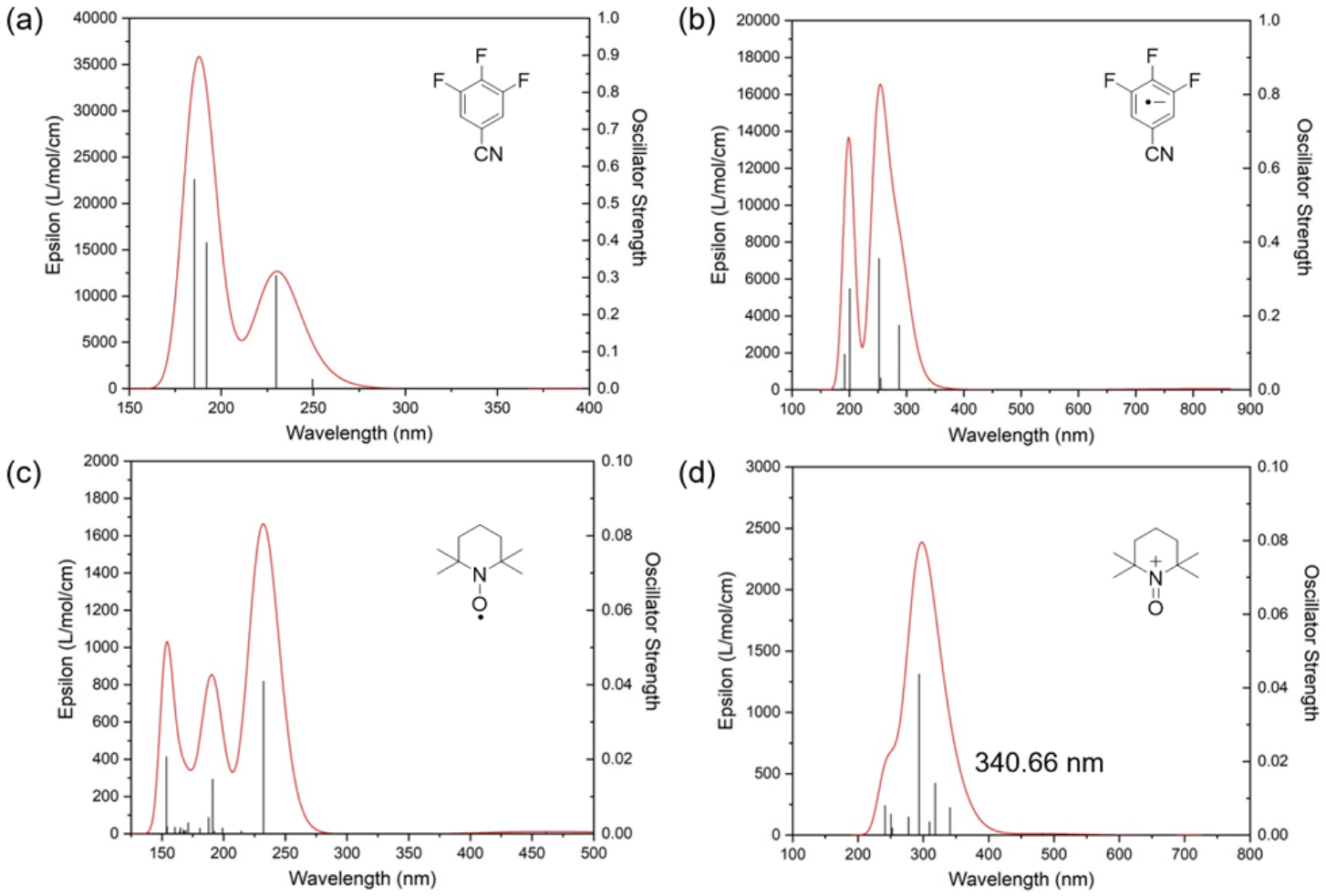

S25

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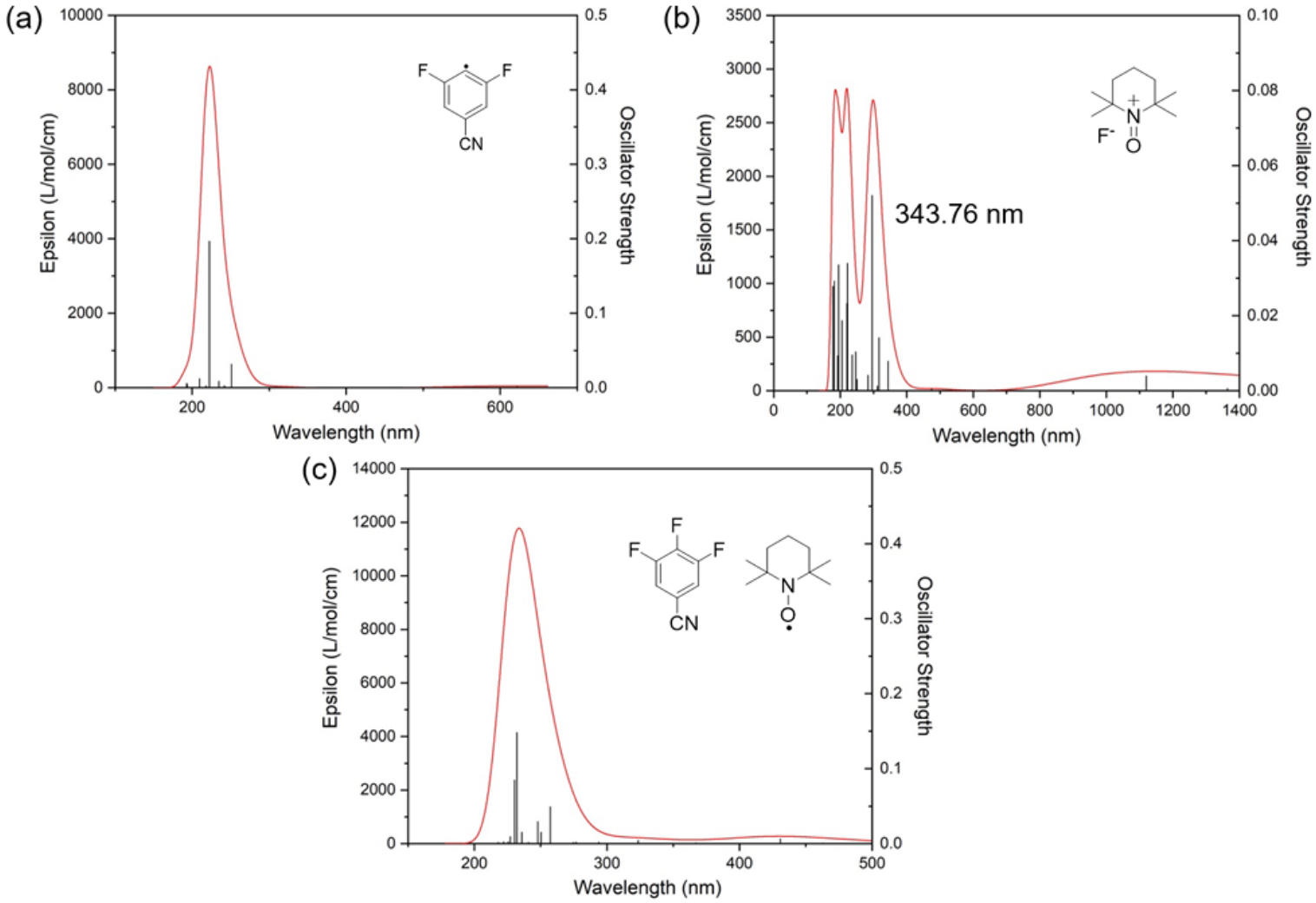

4、Supporting Information