



钆试剂的偶联反应

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导师： 陆 平 青年研究员



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1.1 锆的应用



第五周期 第IVB族

原子序数40

外层电子排布：4d²5s²

过渡金属

族	I A	II A											III A	IV A	V A	VI A	VII A	0	电子层	电子数
1	1 H 氢 1s ¹ 1.008																	2 He 氦 1s ² 4.003	K	2
2	3 Li 锂 2s ¹ 6.941	4 Be 铍 2s ² 9.012											5 B 硼 2s ² 2p ¹ 10.81	6 C 碳 2s ² 2p ² 12.01	7 N 氮 2s ² 2p ³ 14.01	8 O 氧 2s ² 2p ⁴ 16.00	9 F 氟 2s ² 2p ⁵ 19.00	10 Ne 氖 2s ² 2p ⁶ 20.18	L	8
3	11 K 钾 3s ¹ 22.99	12 Mg 镁 3s ² 24.31											13 Al 铝 3s ² 3p ¹ 26.98	14 Si 硅 3s ² 3p ² 28.09	15 P 磷 3s ² 3p ³ 30.97	16 S 硫 3s ² 3p ⁴ 32.07	17 Cl 氯 3s ² 3p ⁵ 35.45	18 Ar 氩 3s ² 3p ⁶ 39.95	M	8
4	19 K 钾 4s ¹ 39.10	20 Ca 钙 4s ² 40.08	21 Sc 钪 3d ¹ 4s ² 44.96	22 Ti 钛 3d ² 4s ² 47.87	23 V 钒 3d ³ 4s ² 50.94	24 Cr 铬 3d ⁵ 4s ¹ 52.00	25 Mn 锰 3d ⁵ 4s ² 54.94	26 Fe 铁 3d ⁶ 4s ² 55.85	27 Co 钴 3d ⁷ 4s ² 58.93	28 Ni 镍 3d ⁸ 4s ² 58.69	29 Cu 铜 3d ¹⁰ 4s ¹ 63.55	30 Zn 锌 3d ¹⁰ 4s ² 65.39	31 Ga 镓 4s ² 4p ¹ 69.72	32 Ge 锗 4s ² 4p ² 72.61	33 As 砷 4s ² 4p ³ 74.92	34 Se 硒 4s ² 4p ⁴ 78.96	35 Br 溴 4s ² 4p ⁵ 79.90	36 Kr 氪 4s ² 4p ⁶ 83.80	N	8
5	37 Rb 铷 5s ¹ 85.47	38 Sr 锶 5s ² 87.62	39 Y 钇 4d ¹ 5s ² 88.91	40 Zr 锆 4d ² 5s ² 91.22	41 Nb 铌 4d ⁴ 5s ¹ 92.91	42 Mo 钼 4d ⁵ 5s ¹ 95.94	43 Tc 锝 4d ⁵ 5s ² [99]	44 Ru 钌 4d ⁷ 5s ¹ 101.1	45 Rh 铑 4d ⁸ 5s ¹ 102.9	46 Pd 钯 4d ¹⁰ 106.4	47 Ag 银 4d ¹⁰ 5s ¹ 107.9	48 Cd 镉 4d ¹⁰ 5s ² 112.4	49 In 铟 5s ² 5p ¹ 114.8	50 Sn 锡 5s ² 5p ² 118.7	51 Sb 锑 5s ² 5p ³ 121.8	52 Te 碲 5s ² 5p ⁴ 127.6	53 I 碘 5s ² 5p ⁵ 126.9	54 Xe 氙 5s ² 5p ⁶ 131.3	O	8
6	55 Cs 铯 6s ¹ 132.9	56 Ba 钡 6s ² 137.3	57-71 La-lu 镧系 镧系	72 Hf 铪 5d ² 6s ² 178.5	73 Ta 钽 5d ³ 6s ² 180.9	74 W 钨 5d ⁴ 6s ² 183.8	75 Re 铼 5d ⁵ 6s ² 186.2	76 Os 锇 5d ⁶ 6s ² 190.2	77 Ir 铱 5d ⁷ 6s ² 192.2	78 Pt 铂 5d ⁹ 6s ¹ 195.1	79 Au 金 5d ¹⁰ 6s ¹ 197.0	80 Hg 汞 5d ¹⁰ 6s ² 200.6	81 Tl 铊 6s ² 6p ¹ 204.4	82 Pb 铅 6s ² 6p ² 207.2	83 Bi 铋 6s ² 6p ³ 209.0	84 Po 钋 6s ² 6p ⁴ [209]	85 At 砹 6s ² 6p ⁵ [210]	86 Rn 氡 6s ² 6p ⁶ [222]	P	8
7	87 Fr 钫 7s ¹ [223]	88 Ra 镭 7s ² 226.0	89-103 Ac-Lr 锕系 锕系	104 Rf 𬬻 6d ² 7s ² [261]	105 Db 𬬺 6d ³ 7s ² [262]	106 Sg 𬬻 6d ⁴ 7s ² [263]	107 Bh 𬬾 6d ⁵ 7s ² [262]	108 Hs 𬬽 6d ⁶ 7s ² [265]	109 Mt 𬬼 6d ⁷ 7s ² [266]	110 Ds 𬬻 6d ⁸ 7s ² [269]	111 Rg 𬬾 6d ⁹ 7s ² [272]	112 Cn 𬬽 6d ¹⁰ 7s ² [285]	113 Uut * [284]	114 Fl 𫓪 6d ¹⁰ 7s ² [289]	115 Uup * [288]	116 Lv 𫓯 6d ¹⁰ 7s ² [293]	117 Uus * [294]	118 Uuo * [294]	N	8

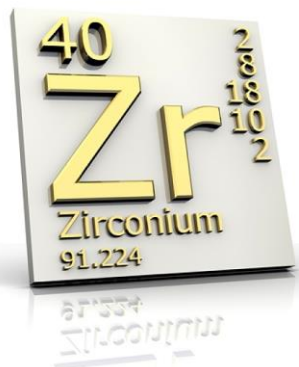
注：
1.相对原子量录自1995年国际原子量表，全部取4位有效数字。
2.相对原子量加括号的，为放射性元素半衰期最长的同位素原子量。

镧系	57-La 镧 5d ¹ 6s ² 138.9	58-Ce 铈 4s ¹ 5d ¹ 6s ² 140.1	59-Pr 镨 4f ³ 6s ² 140.9	60-Nd 钕 4f ⁴ 6s ² 144.2	61-Pm 钷 4f ⁵ 6s ² [147]	62-Sm 钐 4f ⁶ 6s ² 150.4	63-Eu 铕 4f ⁷ 6s ² 152.0	64-Ga 镱 4f ⁷ 5d ¹ 6s ² 157.3	65-La 铽 4f ⁹ 6s ² 158.9	66-Dy 镝 4f ¹⁰ 6s ² 162.5	67-Ho 铥 4f ¹¹ 6s ² 164.9	68-Er 铒 4f ¹² 6s ² 167.3	69-Tm 铥 4f ¹³ 6s ² 168.9	70-Yb 镱 4f ¹⁴ 6s ² 173.0	71-Lu 镥 4f ¹⁵ 6s ² 175.0
锕系	89 Ac 锕 6d ¹ 7s ² 227.0	90 Th 钍 6d ² 7s ² 232.0	91 Pa 镤 5f ² 6d ¹ 7s ² 231.0	92 U 铀 5f ³ 6d ¹ 7s ² 238.0	93 Np 镎 5f ⁴ 6d ¹ 7s ² 237.0	94 Pu 钚 5f ⁶ 7s ² [244]	95 Am 镅 5f ⁷ 7s ² [243]	96 Cm 锔 5f ⁶ 6s ¹ 7s ² [247]	97 Bk 锫 5f ⁹ 7s ² [247]	98 Cf 锿 5f ¹⁰ 7s ² [251]	99 Es 镅 5f ¹¹ 7s ² [252]	100 Fm 镆 5f ¹² 7s ² [257]	101 Md 钆 (5f ¹³ 7s ²) [258]	102 No 锎 (5f ¹⁴ 7s ²) [259]	103 Lr 铹 (5f ¹⁴ 6d ¹ 7s ²) [260]

1.1 锆的应用

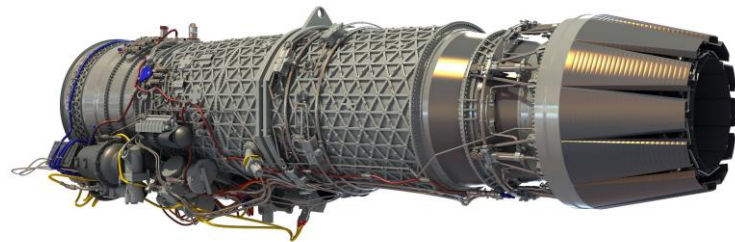


冶金工业



脱氧、除氮、去硫的作用

喷气发动机



锆-锌镁合金:轻且耐高温, 强度高

核反应堆中: 铀燃料元件的包壳



抗腐蚀性能、极高的熔点

人工关节



耐腐蚀性和生物相容性

航空航天及军工领域

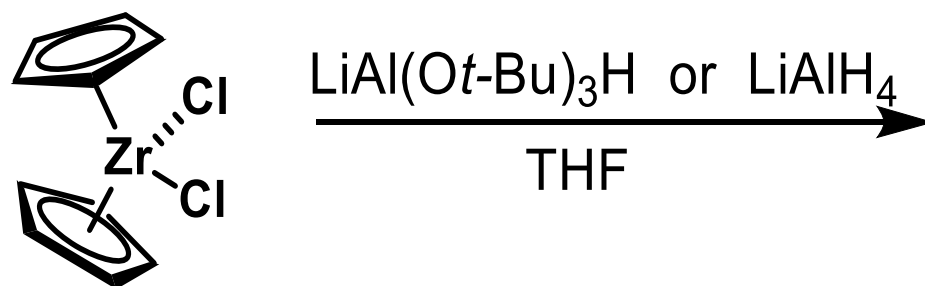


高的熔点、超高的硬度和强度

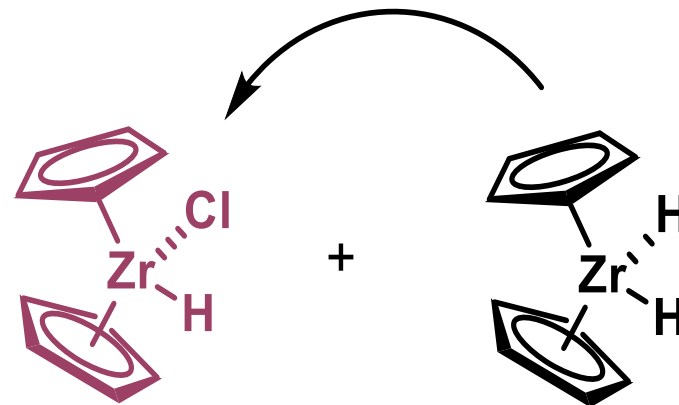
1.2 锆试剂的制备与特点



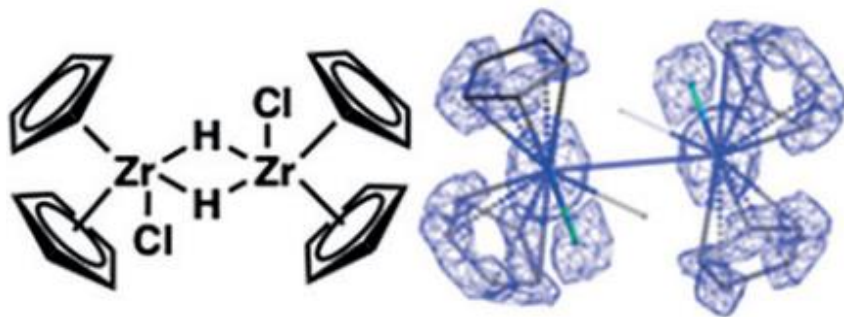
Schwartz试剂



CH₂Cl₂ wash



Schwartz reagent



Schwartz试剂的存在形式

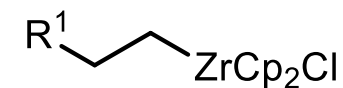
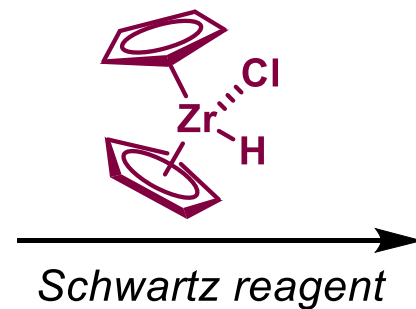
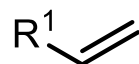
- 对空气，水敏感
- 少量的溶于常见的有机溶剂
- 光照下变成橙色或粉红色

1.2 锆试剂的制备与特点

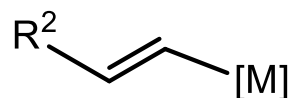


烷基锆试剂的制备

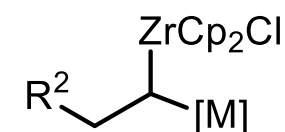
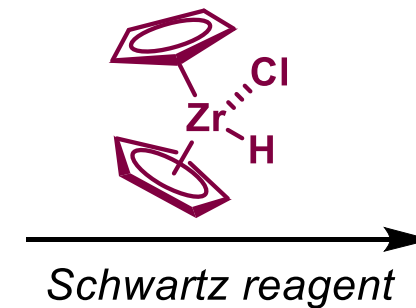
Primary alkylzirconocenes



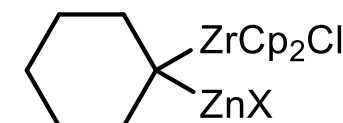
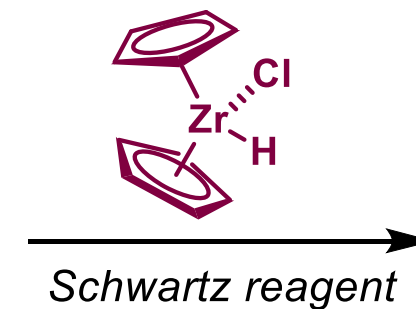
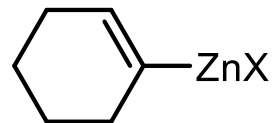
Secondary alkylzirconocenes



M = B, Zn, Al



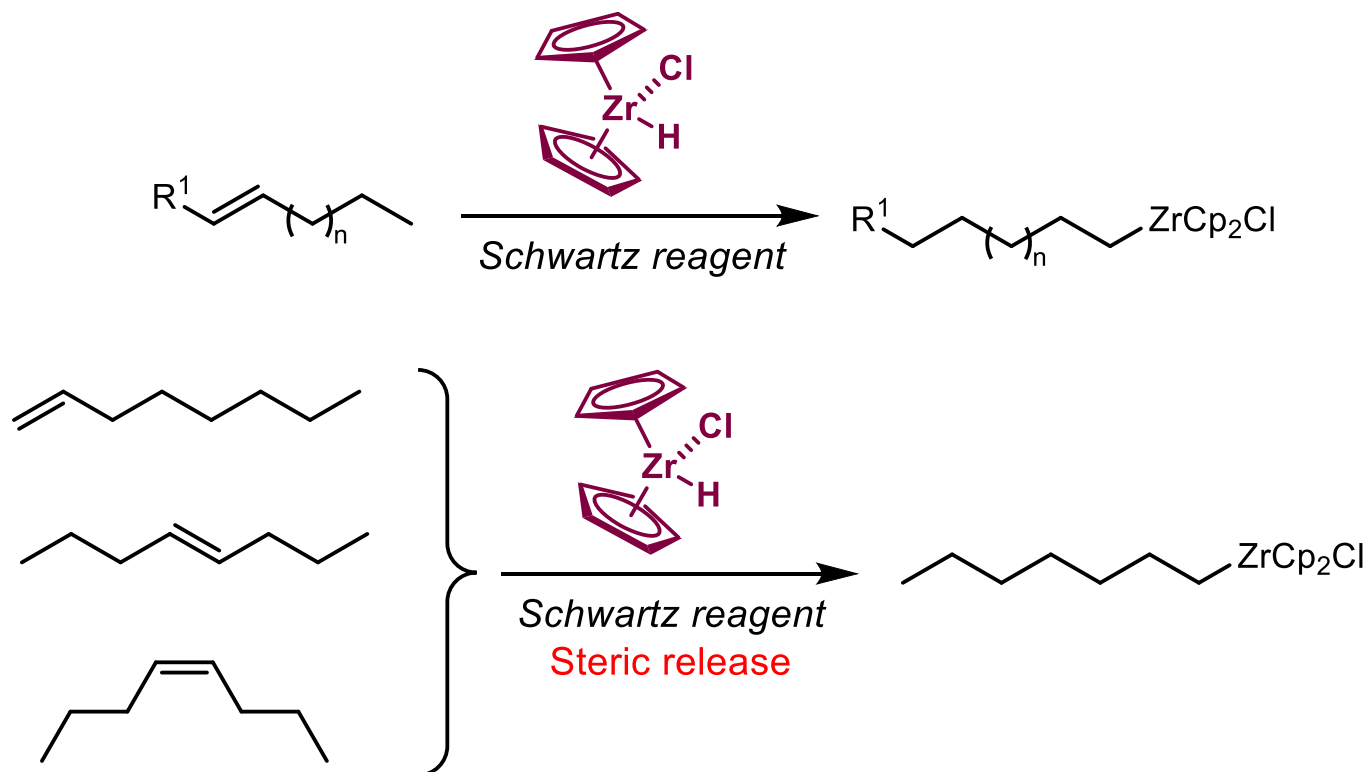
Tertiary alkylzirconocenes



1.2 锆试剂的制备与特点



锆试剂的特点



chain walking

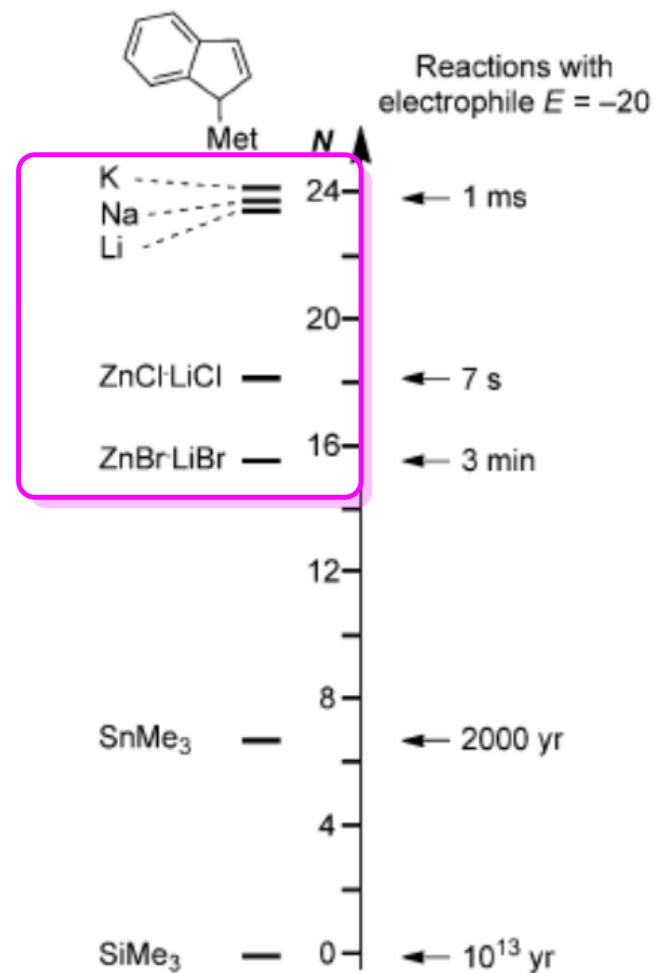
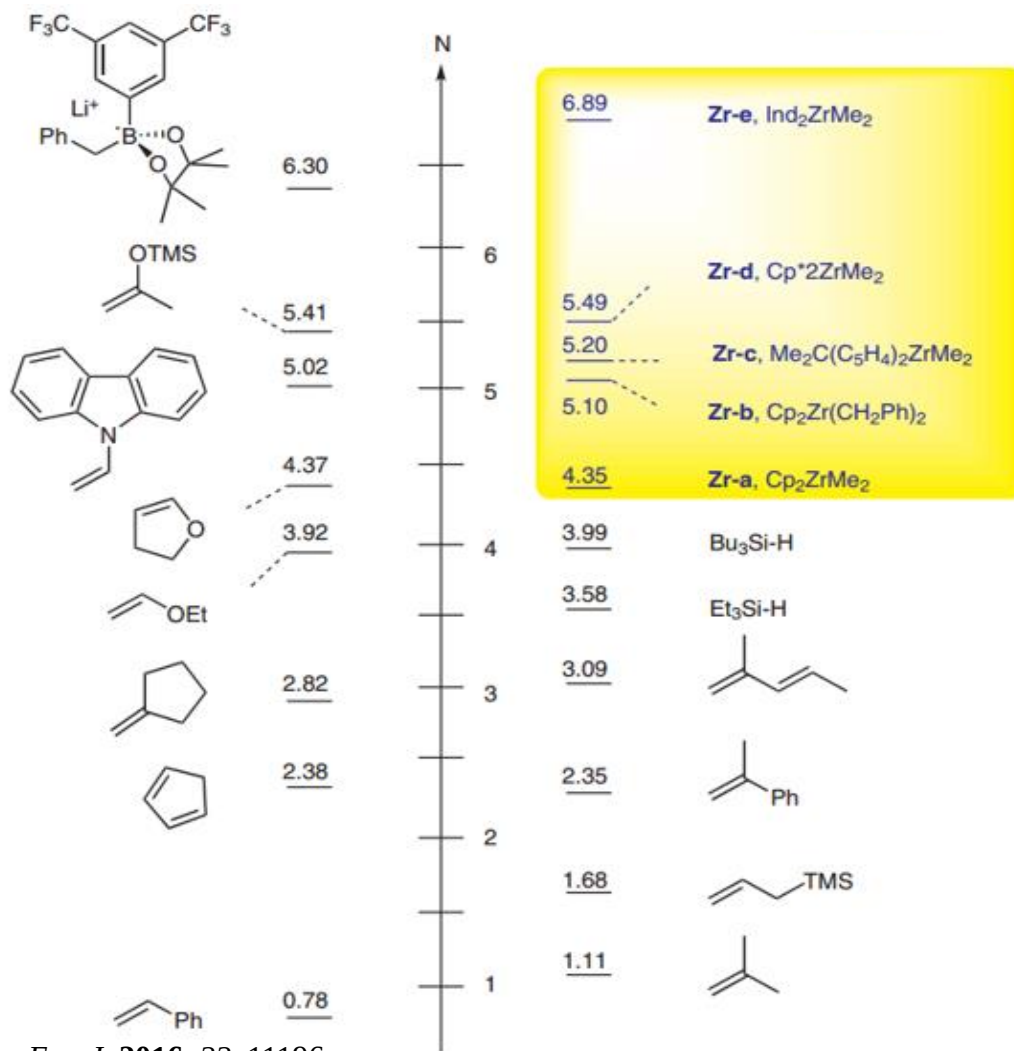
- 水，空气和光敏感
- 亲核性较低

Hydrozirconation of alkenes and **chain-walking** in internal alkenes

1.2 锆试剂的制备与特点



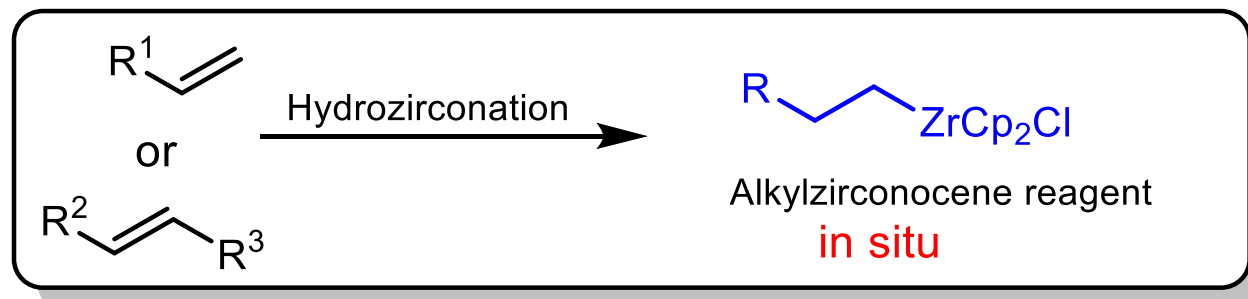
有机金属试剂亲核性的相关研究



1.2 锆试剂的制备与特点



锆试剂的优点

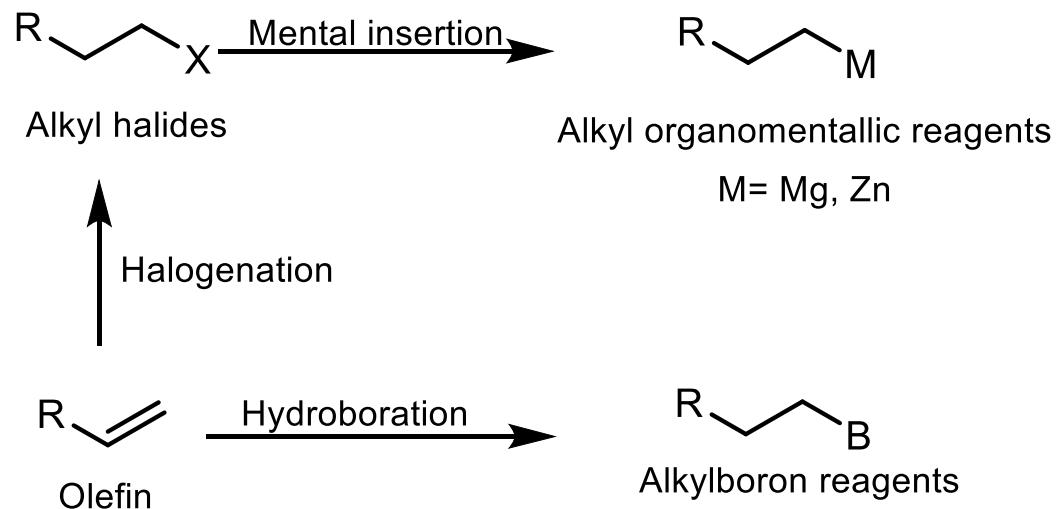


1. 通过锆氢化制备几乎当量转化。
2. 活性相对较低，适用于复杂化合物的合成。
3. 合成条件温和，适用范围更广。
4. 锆氢化过程中存在chain walking，可以利用该特点实现远程官能团化。
5. 可以由烯烃出发，通过一锅法实现锆氢化和后续偶联反应。

1.2 钯试剂的制备与特点



与钯试剂相比其他金属试剂的不足之处：

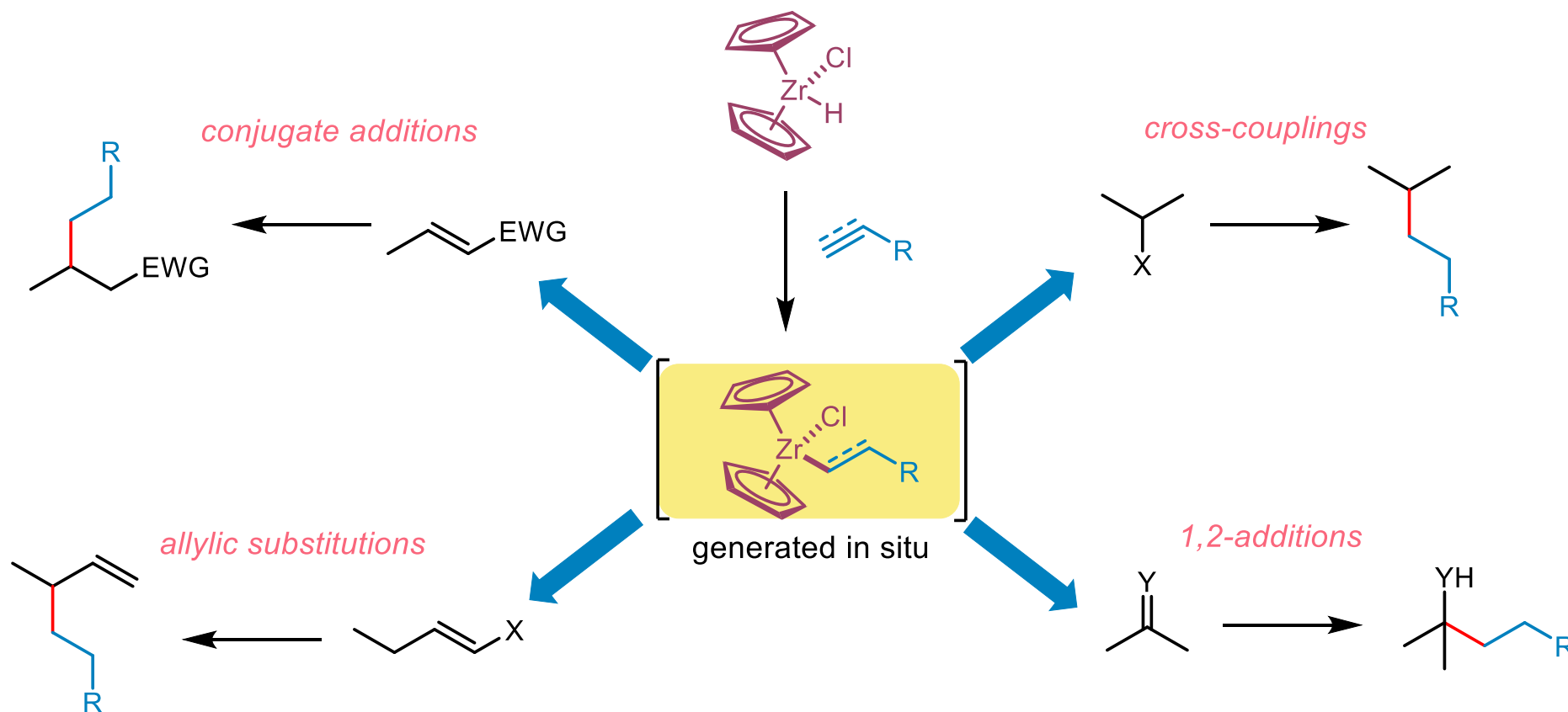


1. 制备时大部分不能完成当量转化，产率较低。
2. 锌试剂和镁试剂等，反应活性相对较高，不适用于复杂化合物的制备。
3. 锌试剂和镁试剂的制备，常通过脱质子，金属卤素交换，转金属化过程，条件苛刻，适用范围有限。
4. 硼试剂通过烯烃的硼氢化制备，条件较为温和，但不存在chain walking。
5. 硼试剂可以由烯烃一锅法实现钯氢化和后续偶联反应，但仅限于9BBN类硼试剂，故存在局限性。

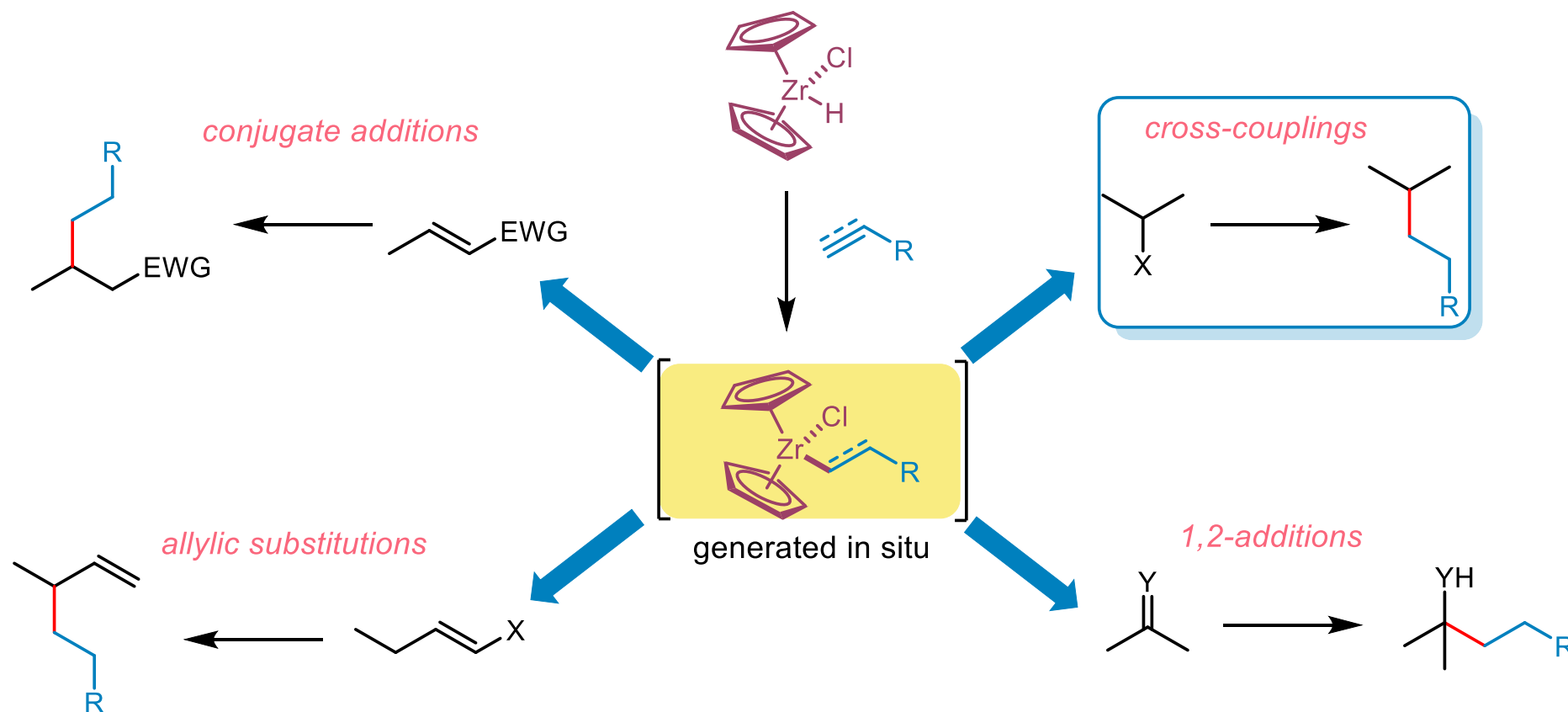
[illegible]

- (6) Negishi, E. *Tetrahedron Lett.* **1988**, 29, 1631.

1.3 锆试剂在有机合成中的应用



1.3 锆试剂在有机合成中的应用



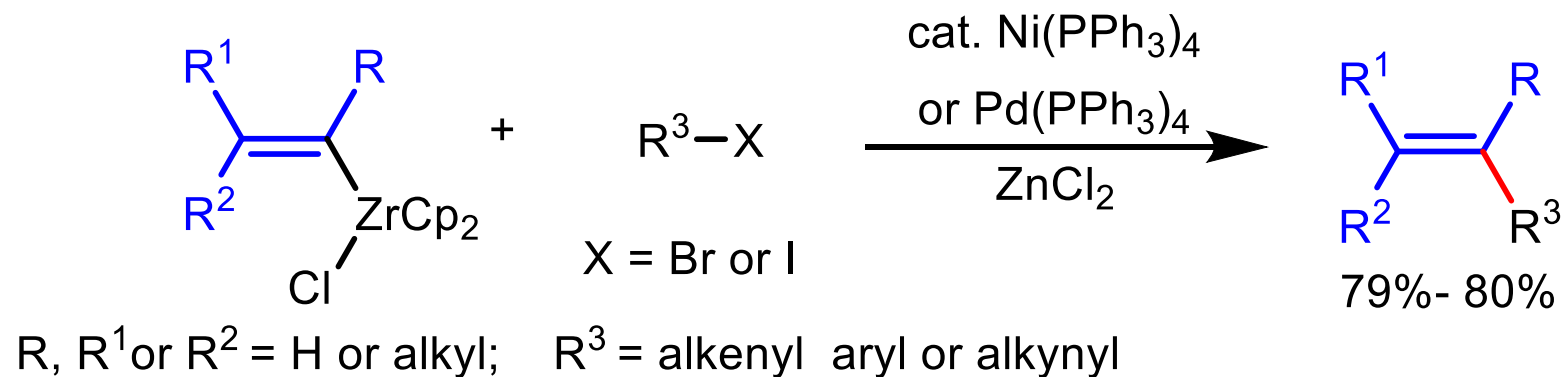
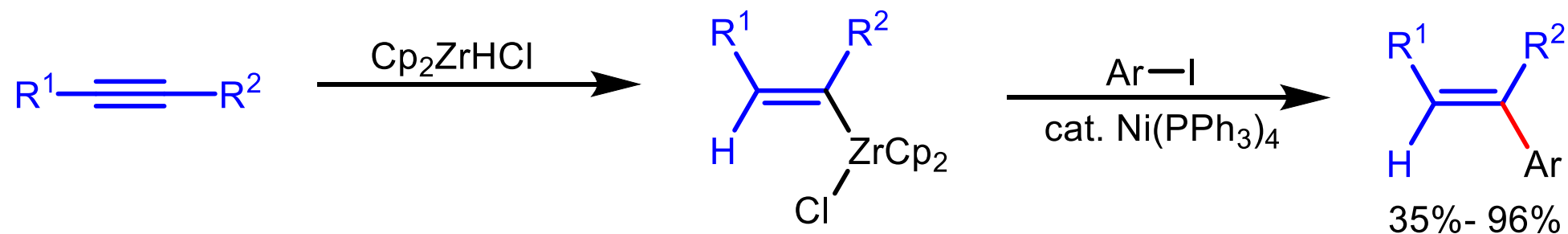


钨试剂的偶联反应

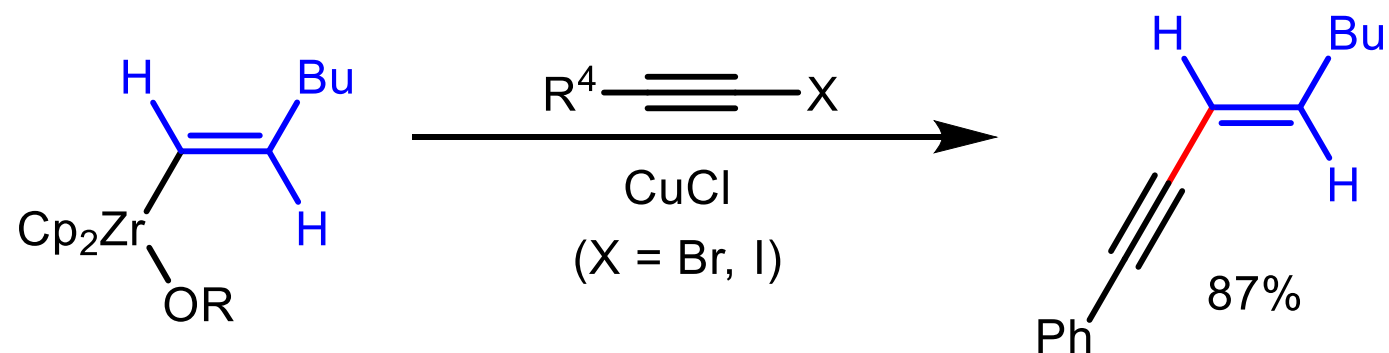
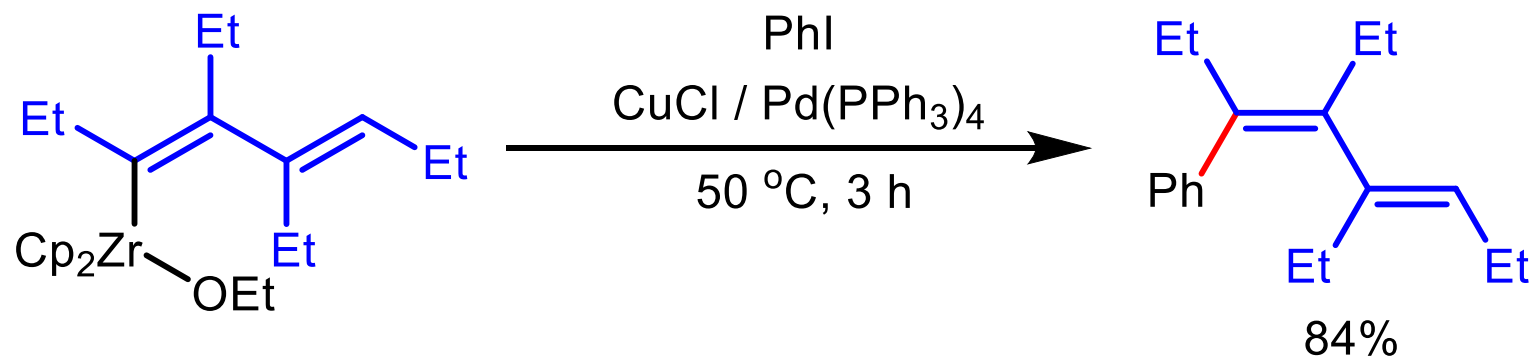
01 烯基钨试剂的偶联反应

02 烷基钨试剂的偶联反应

2.1 烯基锆试剂的偶联反应



2.1 烯基锆试剂的偶联反应



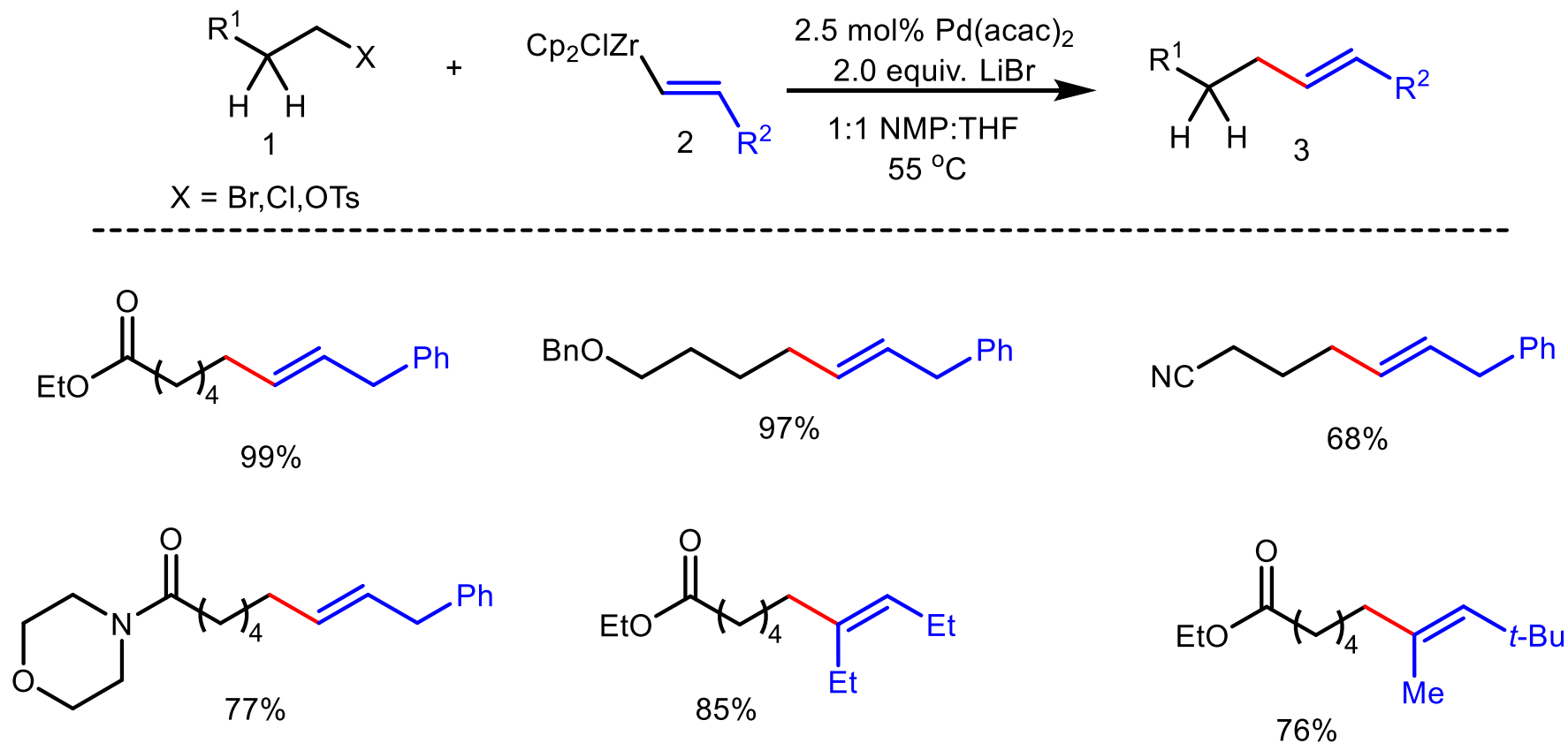
Takahashi, T. *Tetrahedron Lett.* **1997**, 38, 447.

Takahashi, T. *Tetrahedron Lett.* **1997**, 38, 4103.

2.1 烯基锆试剂的偶联反应



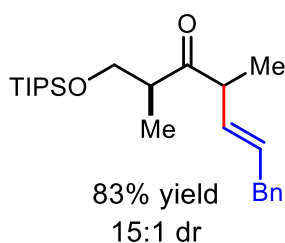
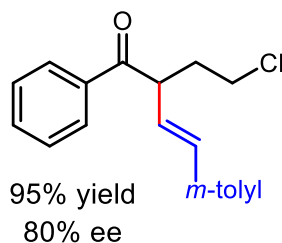
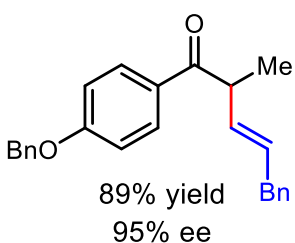
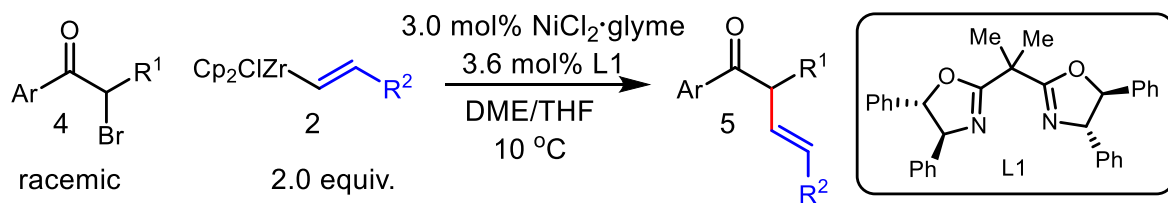
烷基卤化物/烷基对甲苯磺酸酯



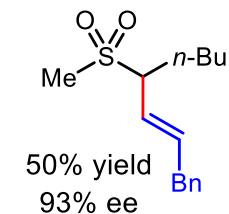
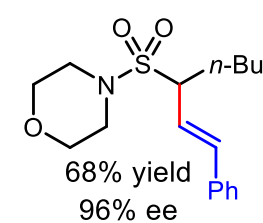
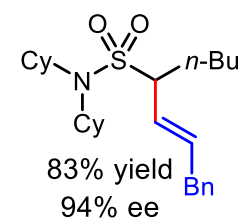
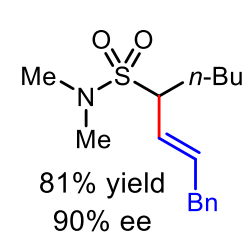
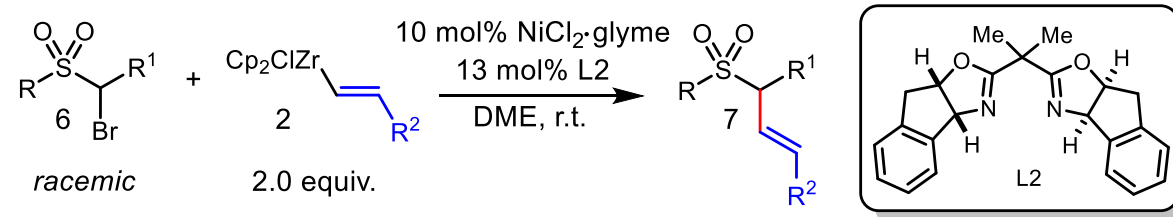
2.1 烯基锆试剂的偶联反应



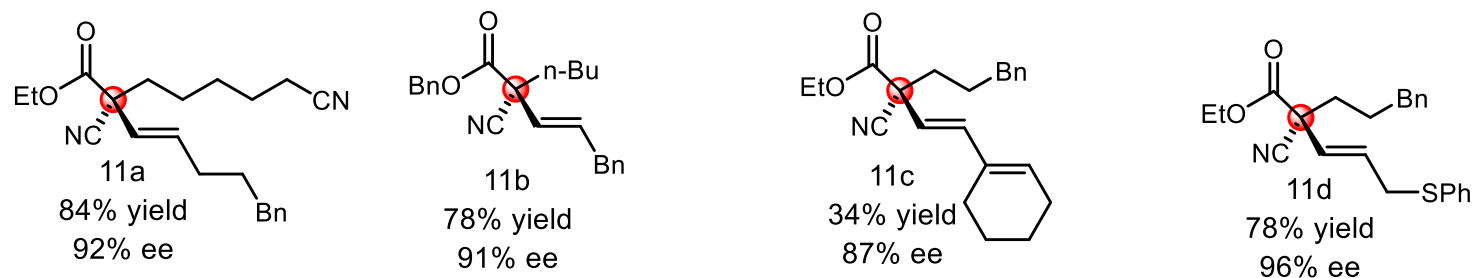
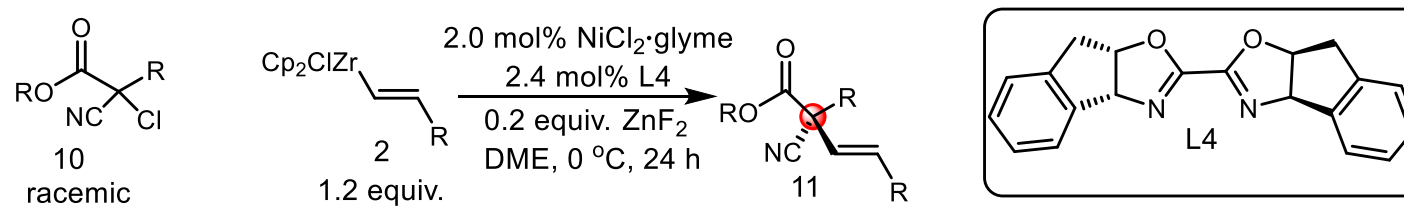
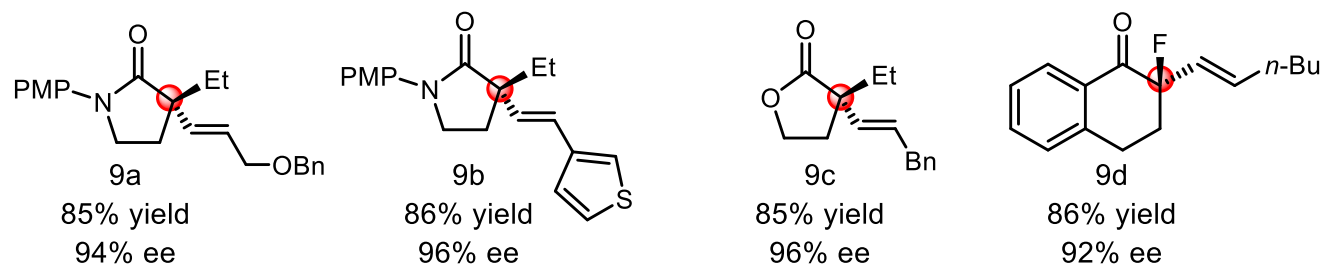
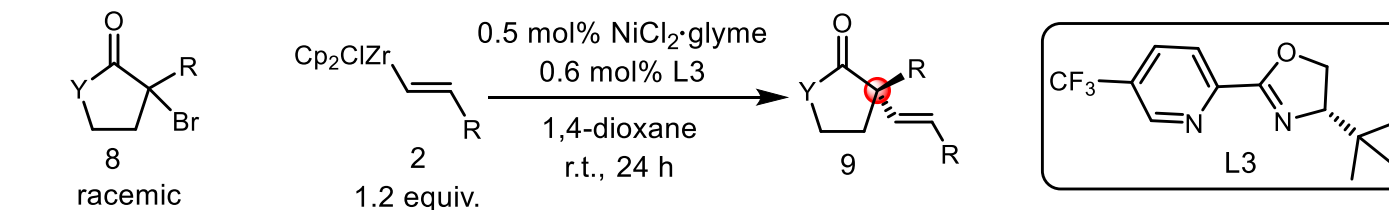
α -溴代酮



α -溴磺酰胺/甲基亚砜



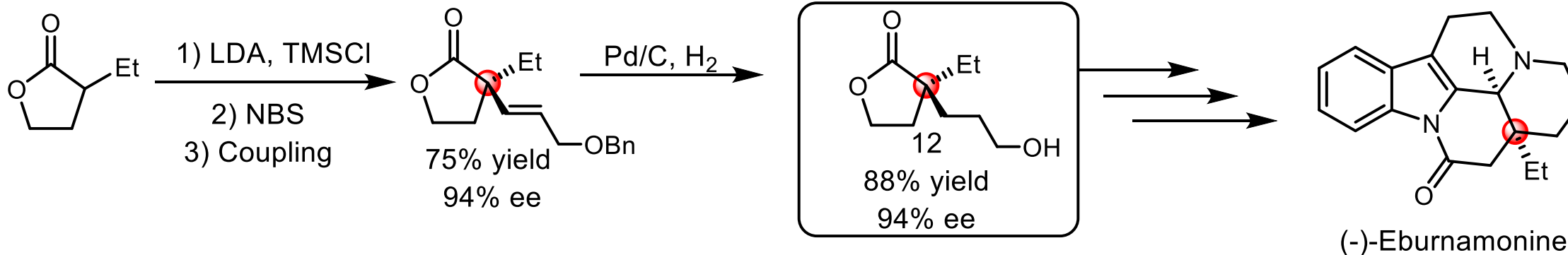
2.1 烯基锆试剂的偶联反应



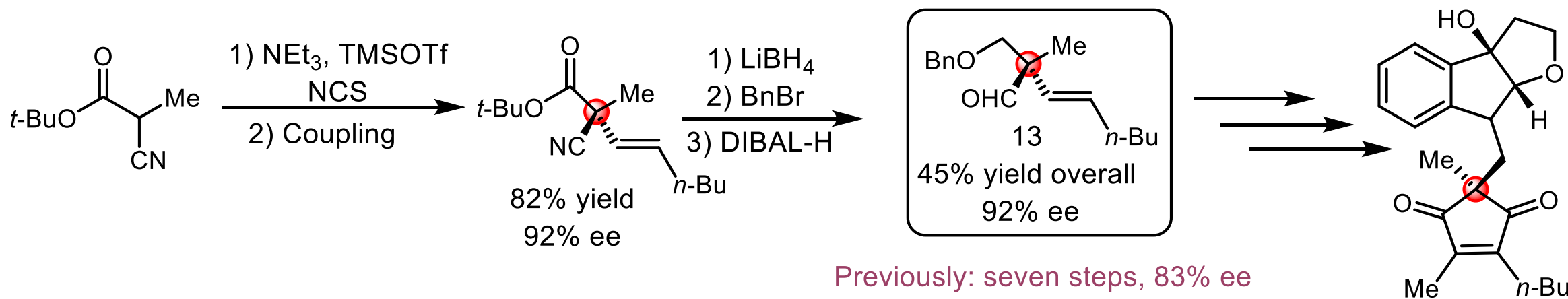
2.1 烯基锆试剂的偶联反应



在天然产物全合成中应用



Previously: five steps, 85% ee

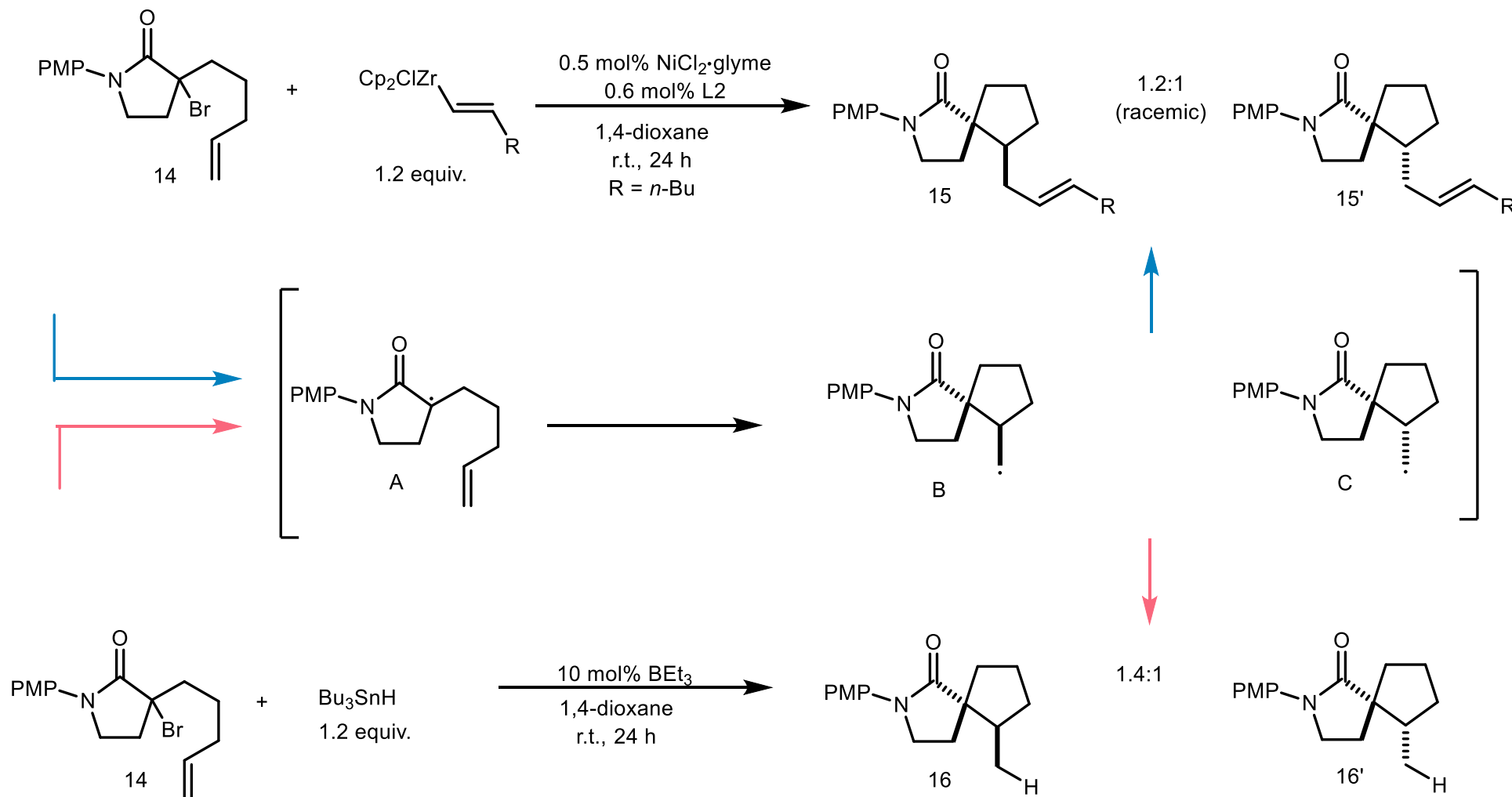


Previously: seven steps, 83% ee

2.1 烯基锆试剂的偶联反应



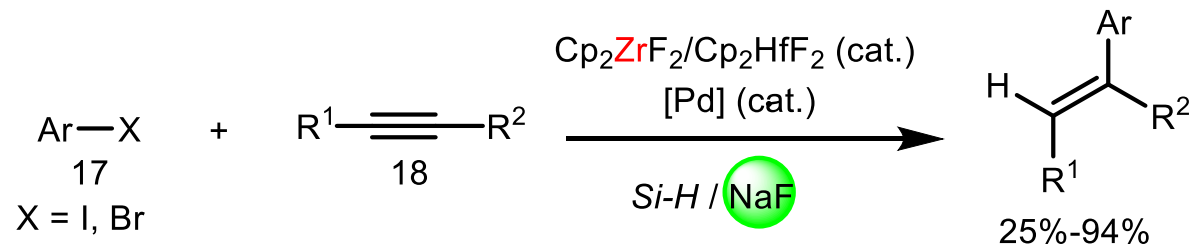
控制实验证明 叔烷基卤化物会转化成自由基



2.1 烯基钼试剂的偶联反应

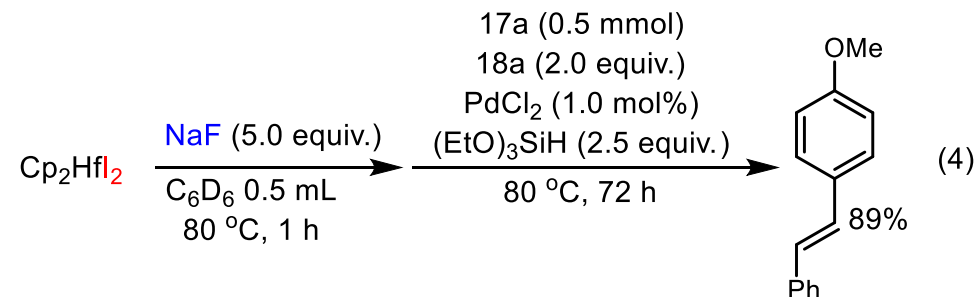
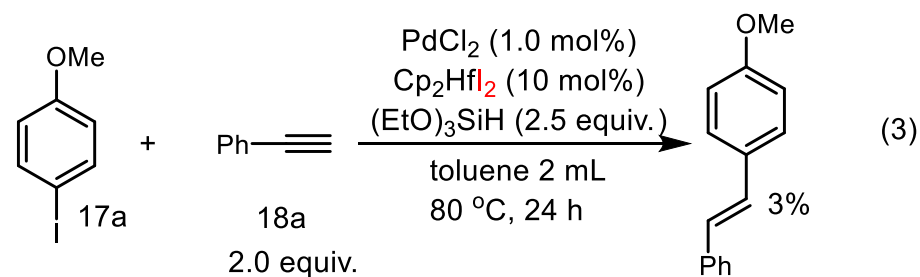
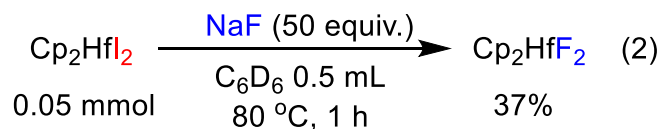
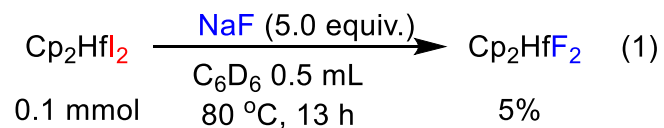


催化量的金属二茂化合物



NaF promotes the regeneration of a $\text{Cp}_2\text{ZrF}_2/\text{Cp}_2\text{HfF}_2$

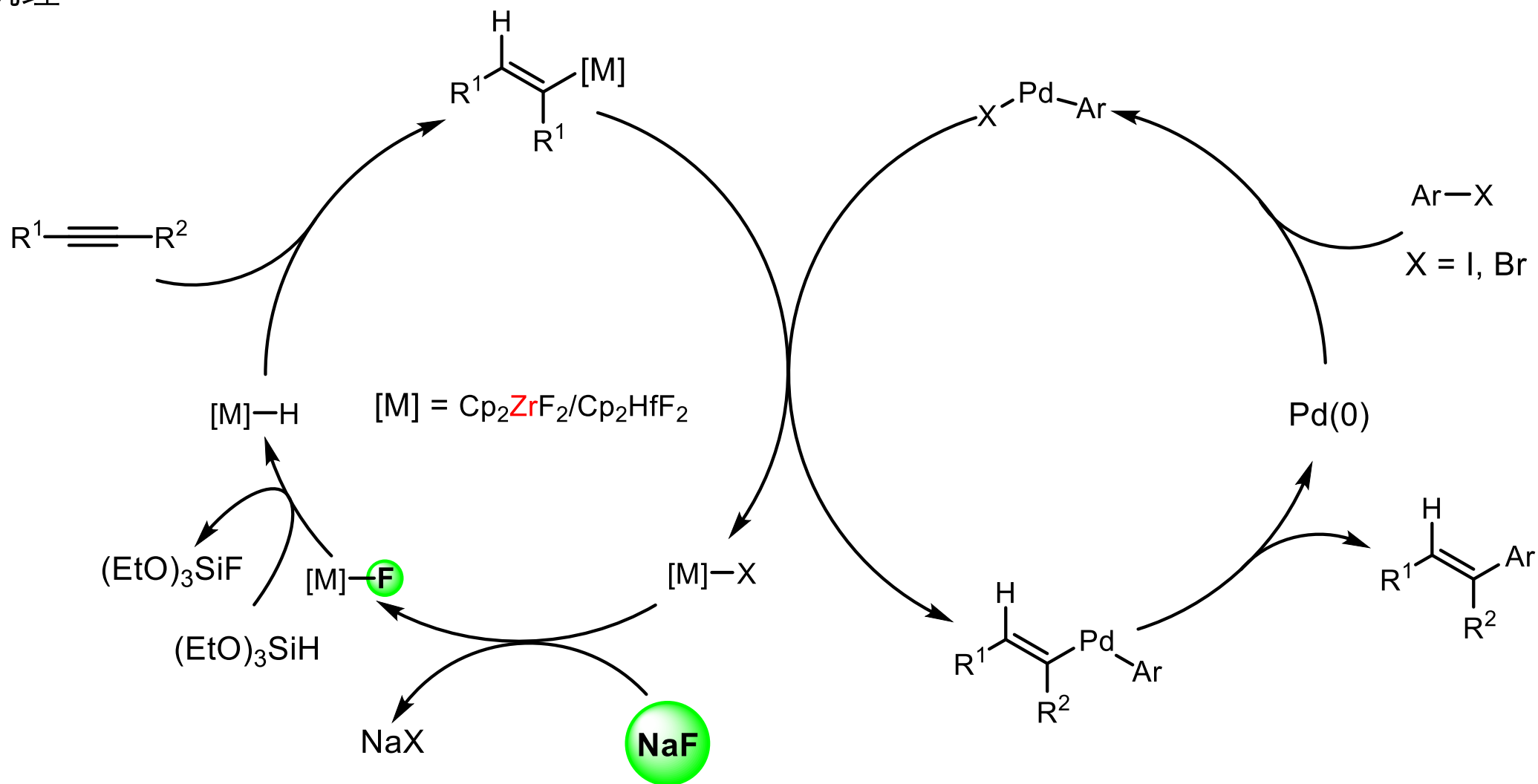
Mechanistic Aspects for Conversion of Cp_2HfI_2 to Cp_2HfF_2 in the Presence of NaF



2.1 烯基钼试剂的偶联反应



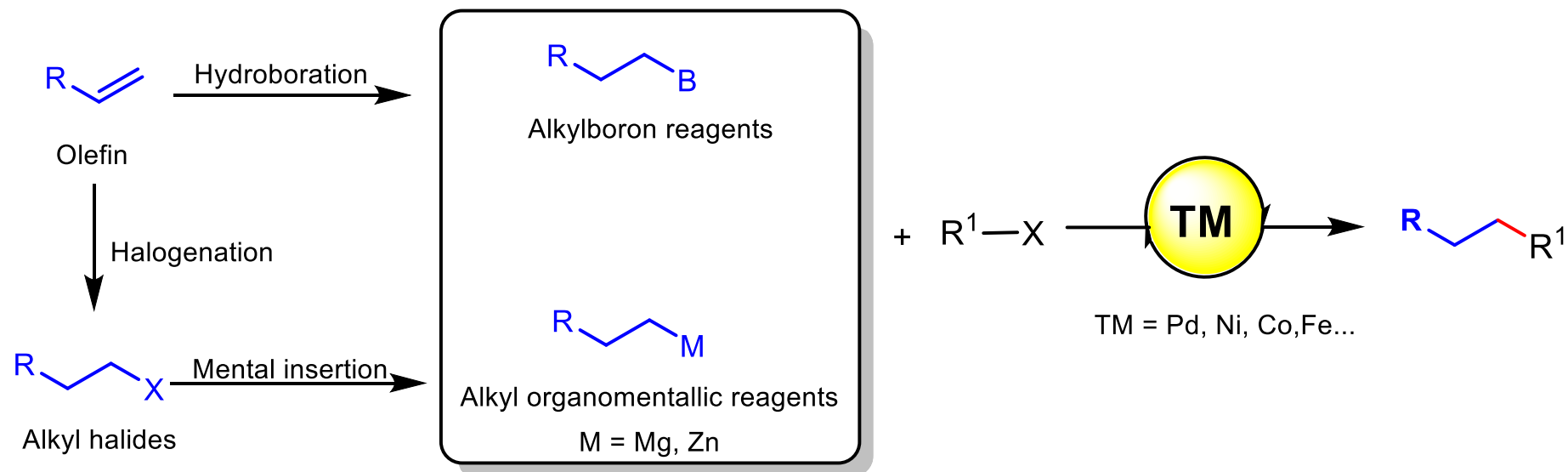
反应机理



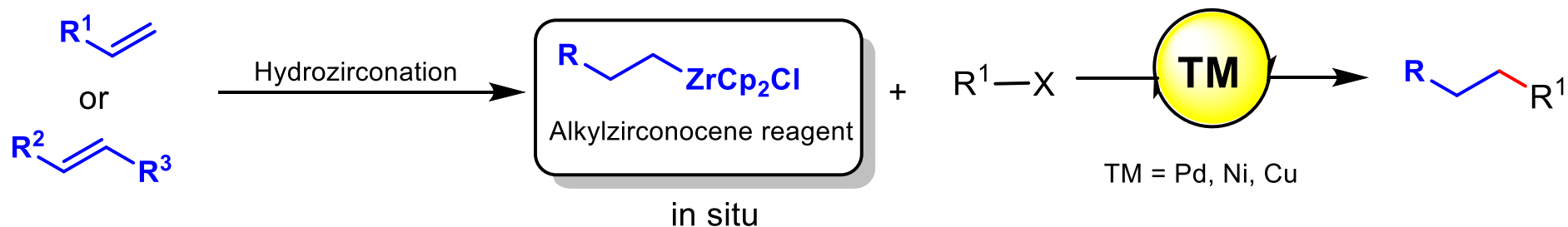
2.2 烷基锆试剂的偶联反应



Cross-coupling with sp^3 -hybridized organometallic reagents



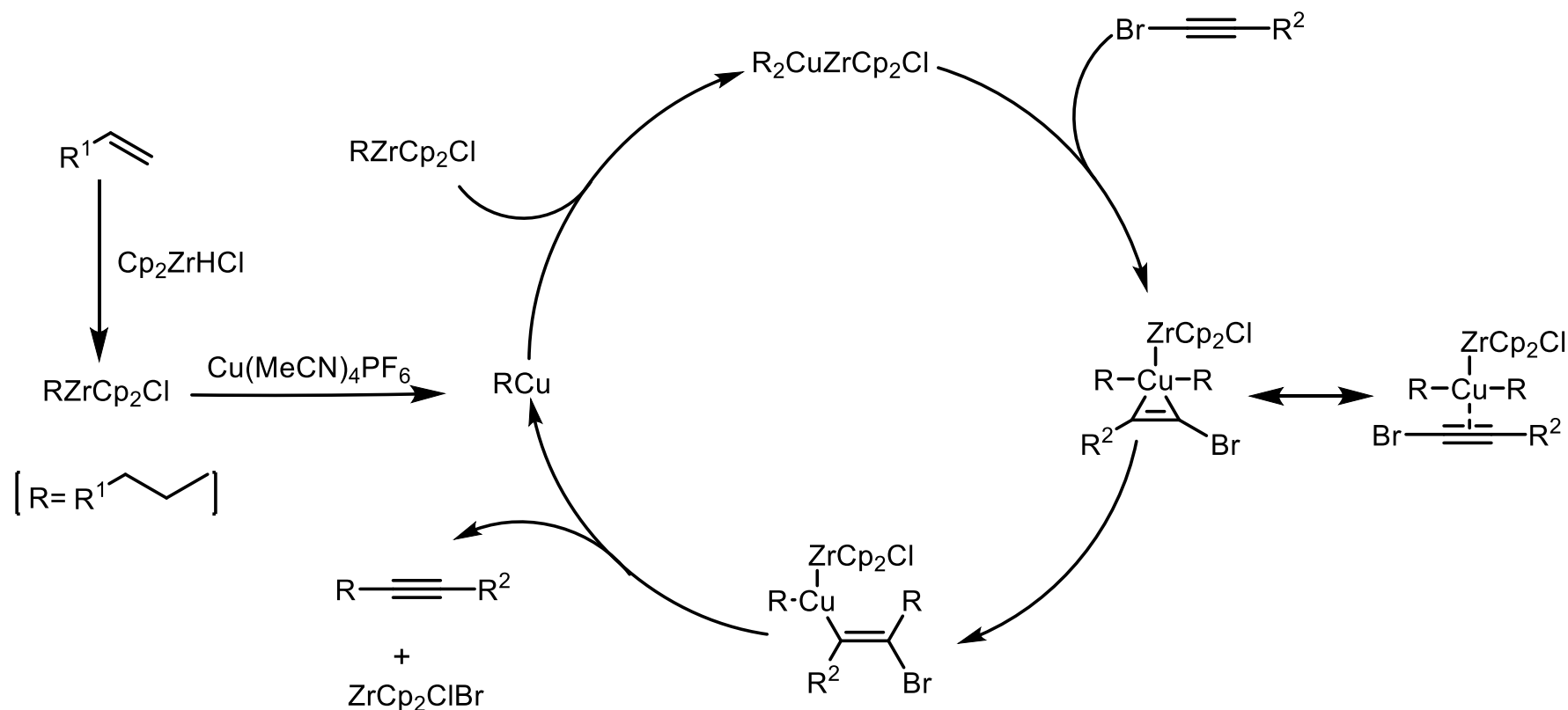
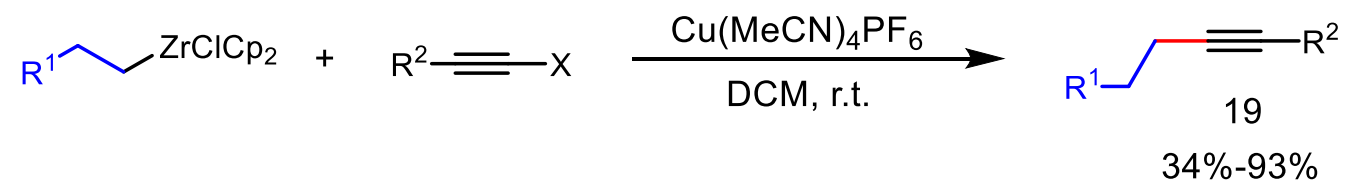
Cross-coupling with alkylzirconocenes



2.2 烷基锆试剂的偶联反应



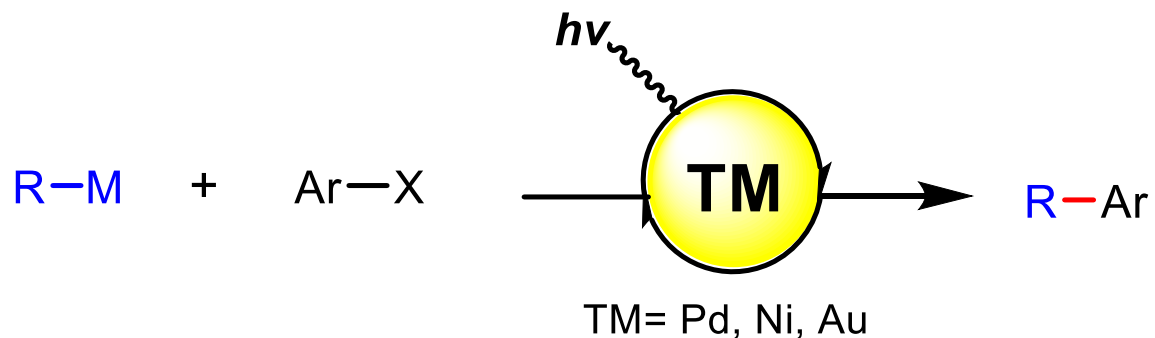
铜催化烷基-炔基偶联



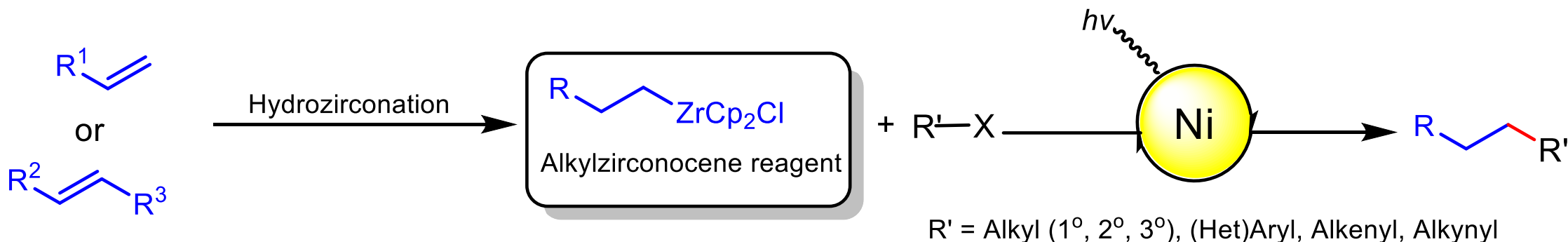
2.2 烷基锆试剂的偶联反应



1) Visible-light-induced coupling with single metal



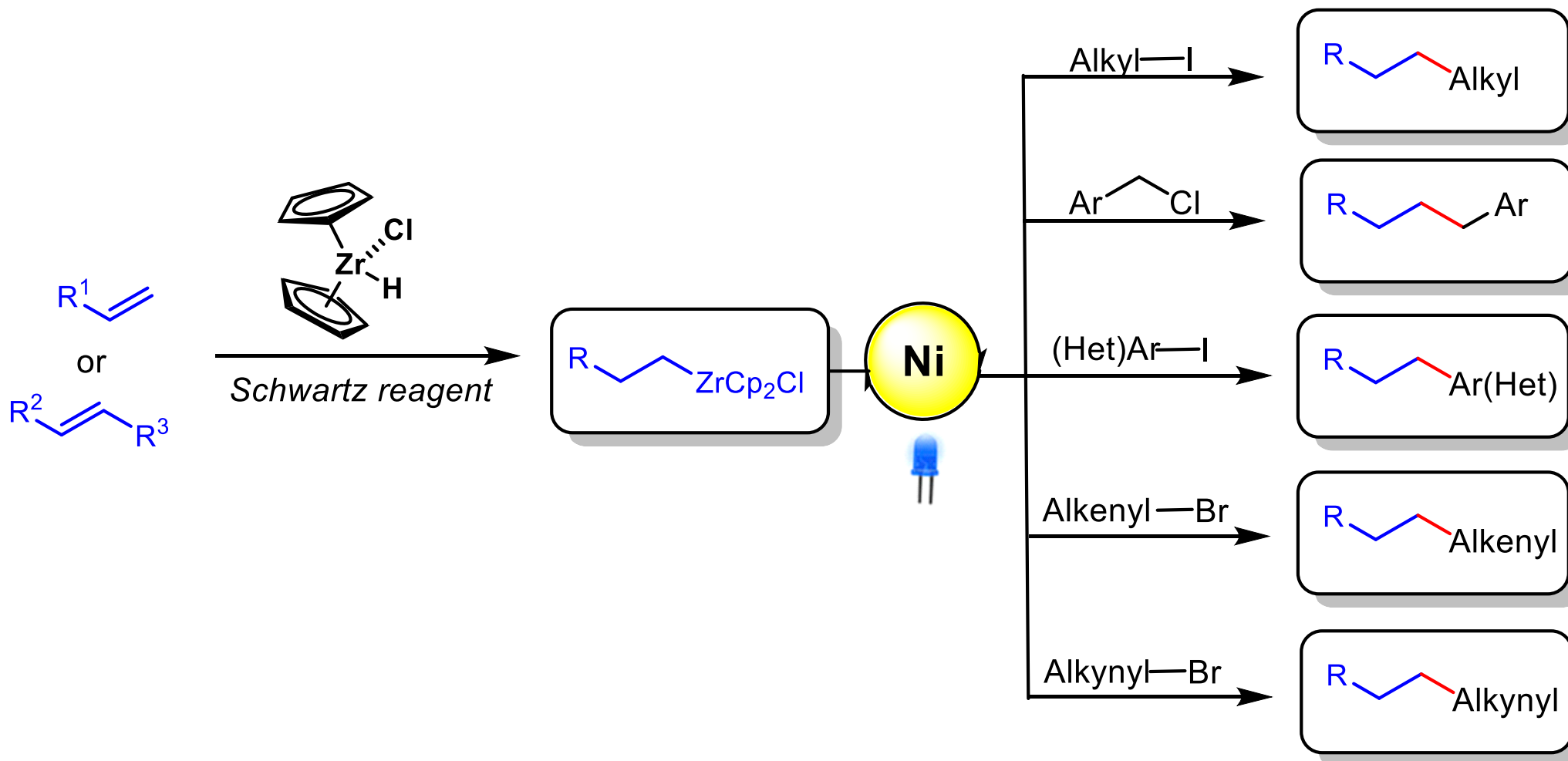
2) Visible-light-induced nickel-catalyzed cross-coupling with alkylzirconocenes



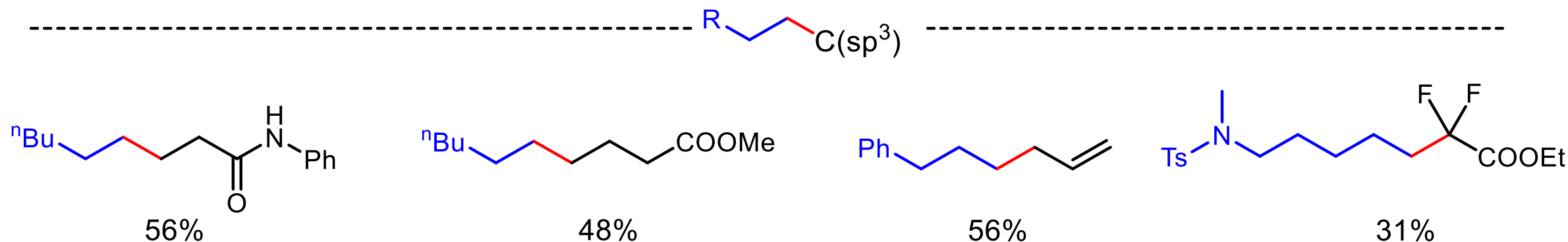
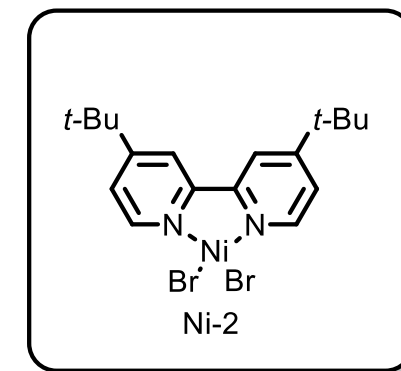
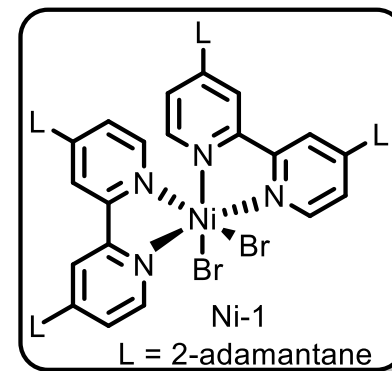
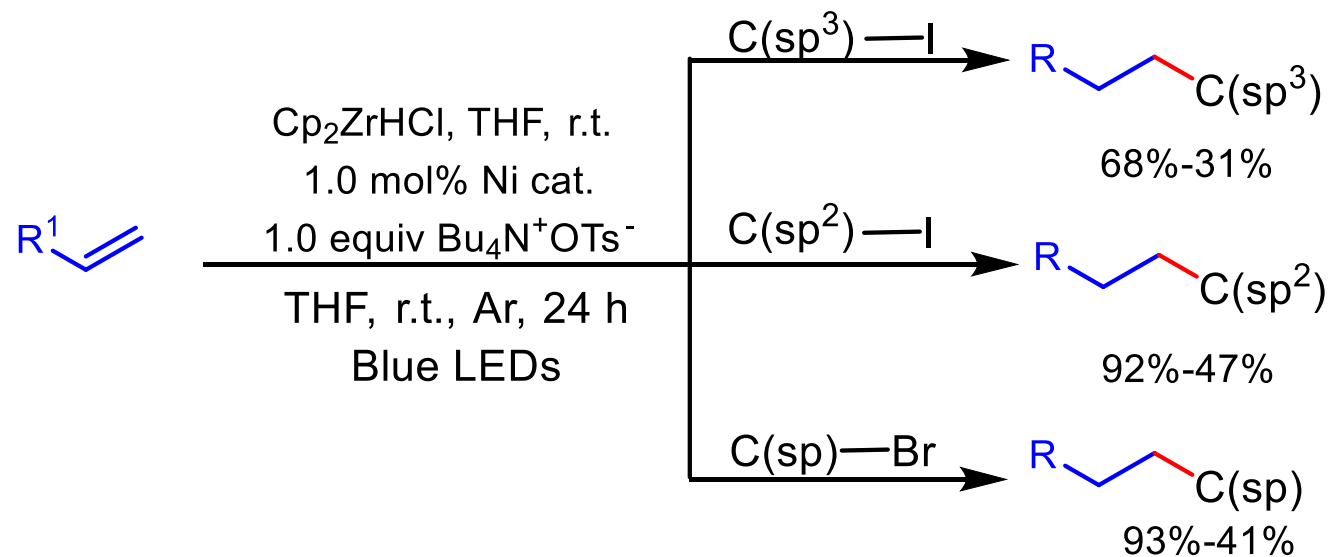
2.2 烷基锆试剂的偶联反应



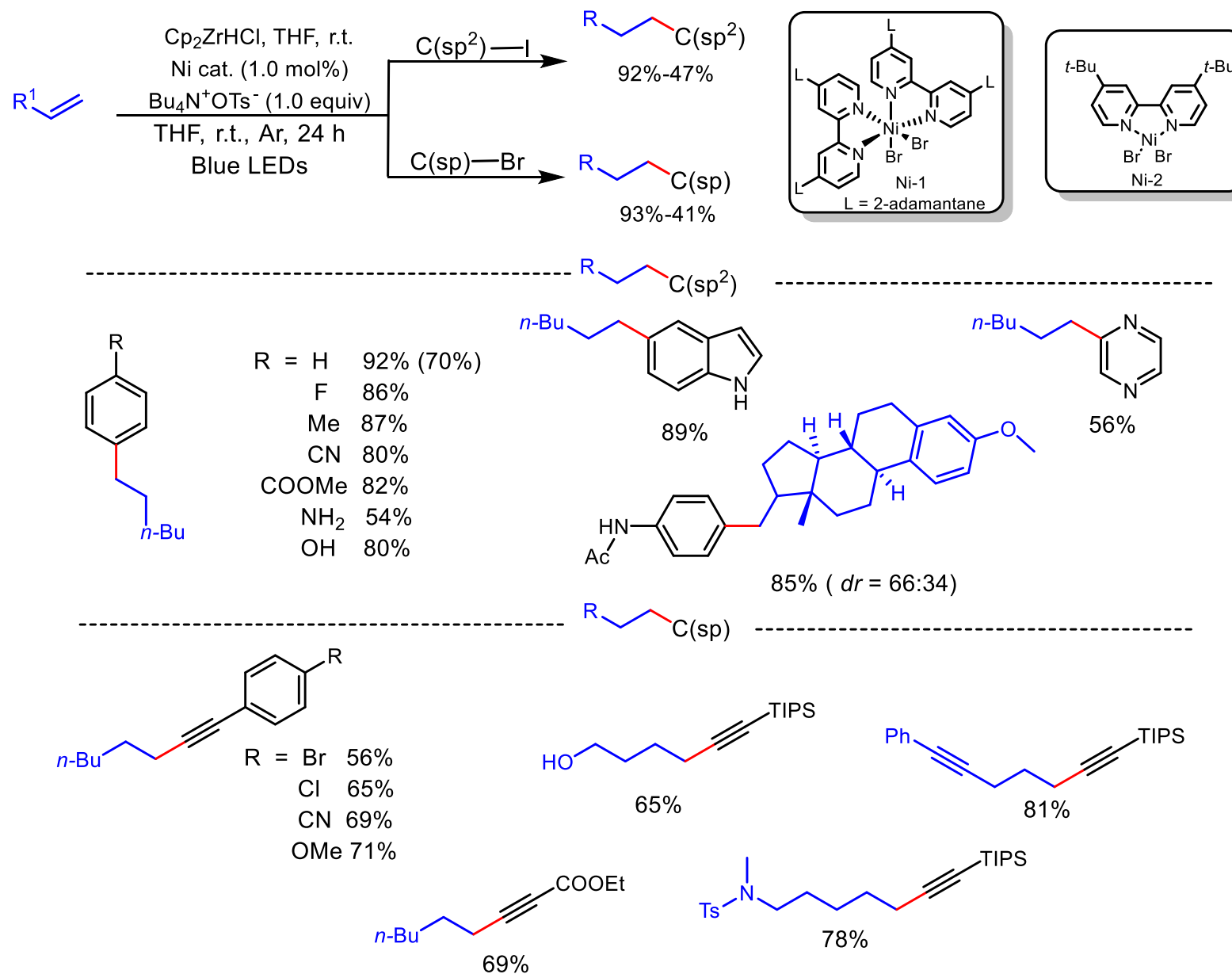
蓝光诱导镍催化的偶联反应



2.2 烷基锆试剂的偶联反应



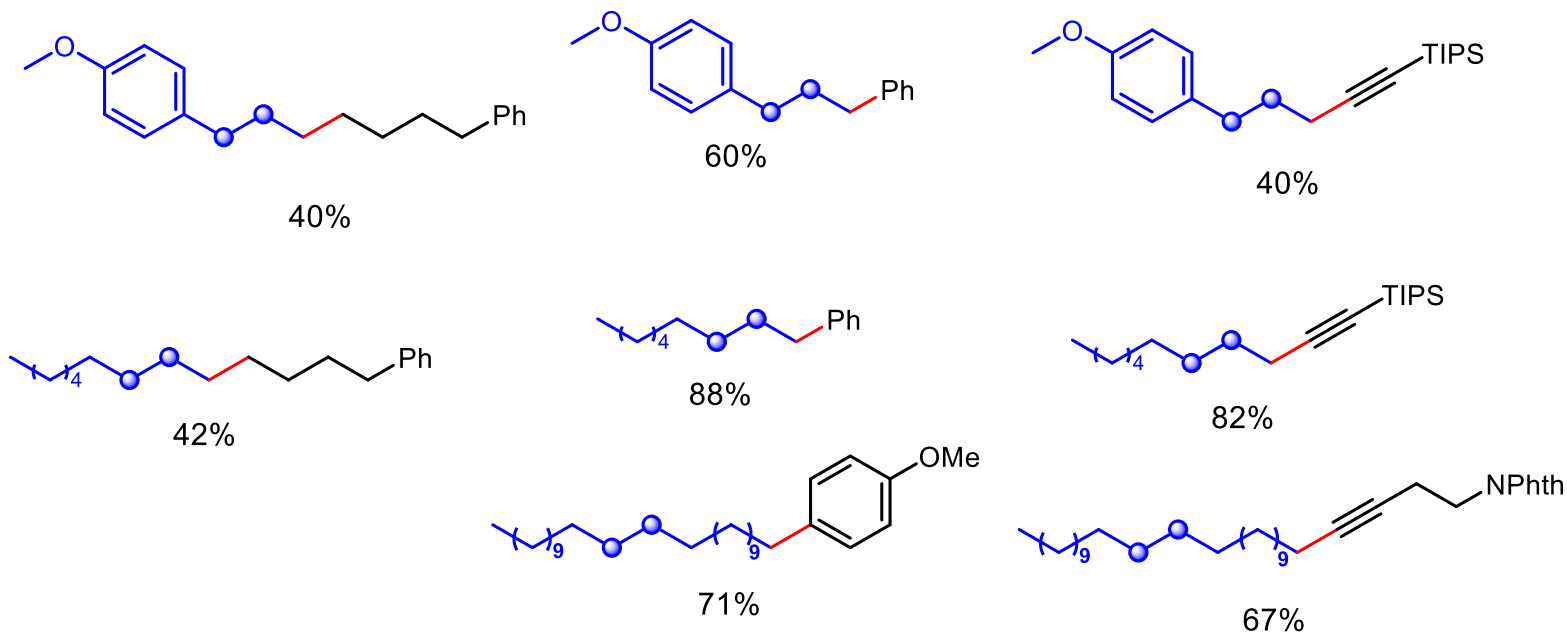
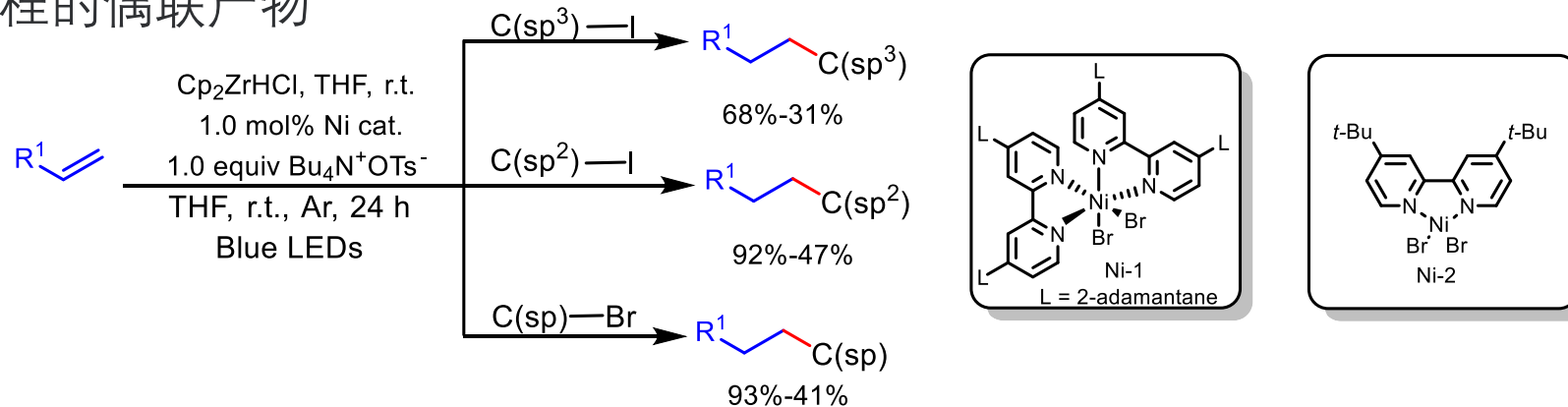
2.2 烷基锆试剂的偶联反应



2.2 烷基锆试剂的偶联反应



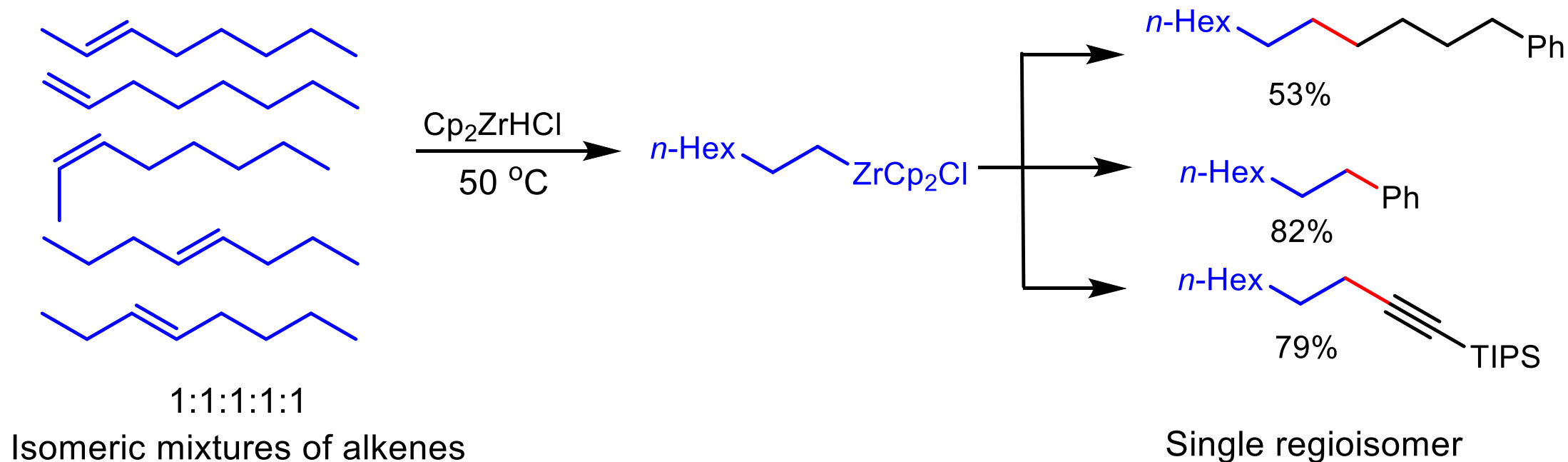
经chain walking过程的偶联产物

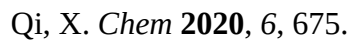


2.2 烷基锆试剂的偶联反应



双键异构的辛烯混合物偶联得单一偶联产物



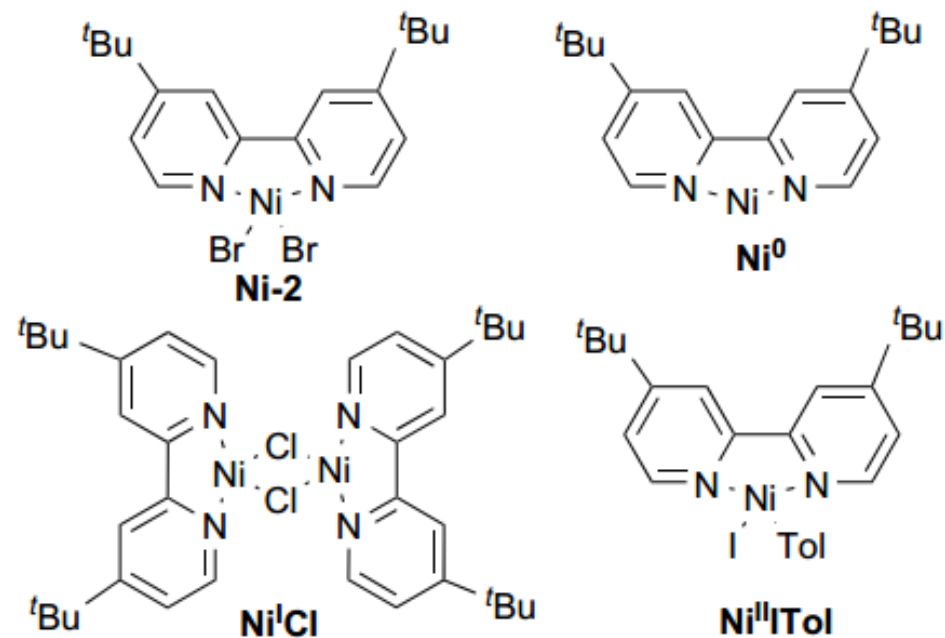


2.2 烷基锆试剂的偶联反应

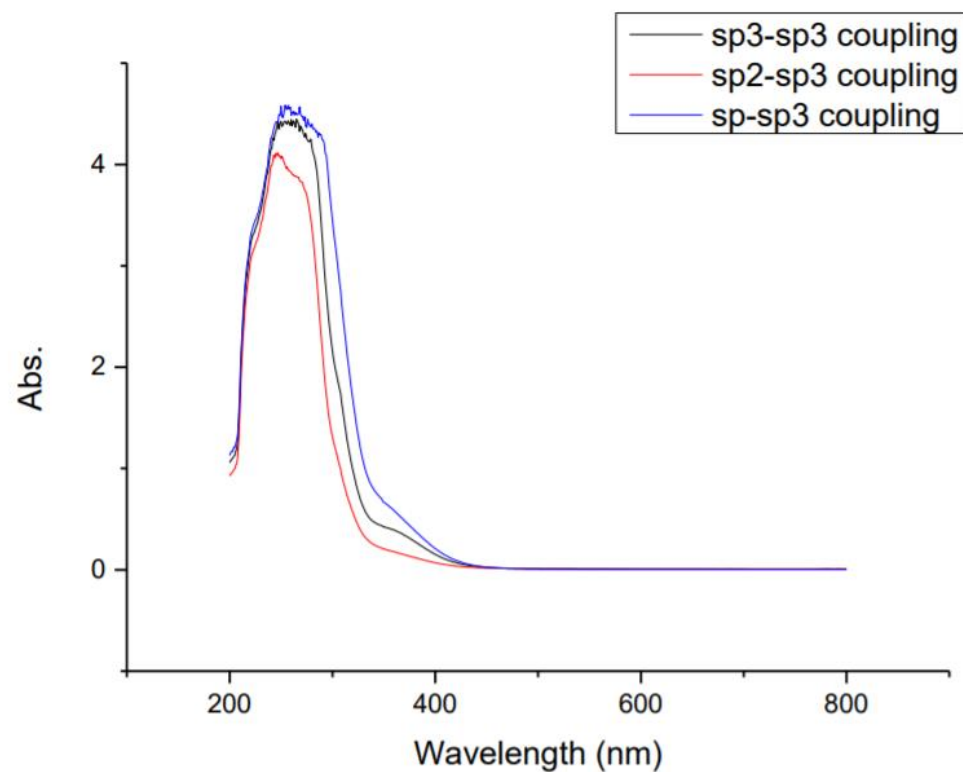


Ni⁰, Ni^I和Ni^{II},催化的交叉偶联

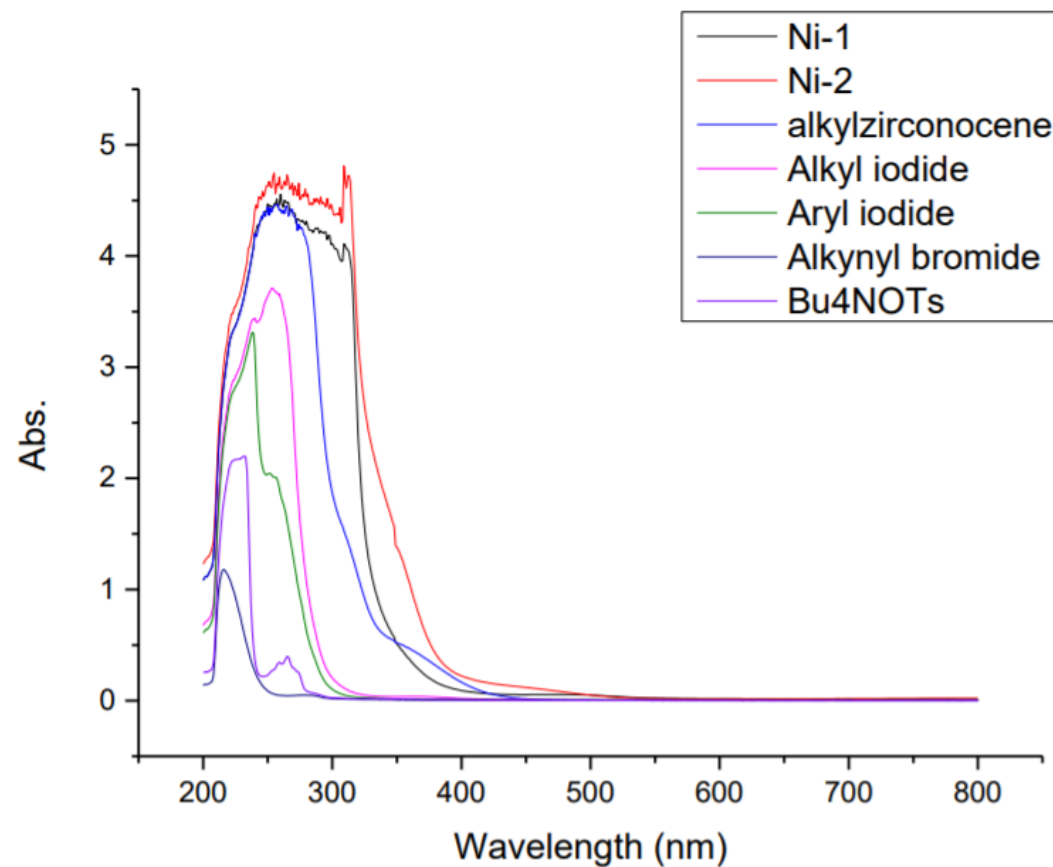
$R-X + {}^n\text{Bu}-\text{CH}_2\text{CH}_2-\text{ZrCp}_2\text{Cl}$	$\xrightarrow[\text{Standard conditions}]{\text{Ni cat.}}$				$R-\text{CH}_2\text{CH}_2-{}^n\text{Bu}$
	Ni-2	Ni ⁰	Ni ^I Cl	Ni ^{II} ITol	
$\text{Ph}-\text{CH}_2\text{CH}_2-\text{I}$	69%	32%	38%	28%	
$\text{Ph}-\text{I}$	99%	77%	68%	74%	
$\text{TIPS}-\text{C}\equiv\text{C}-\text{Br}$	99%	37%	49%	53%	



2.2 烷基锆试剂的偶联反应

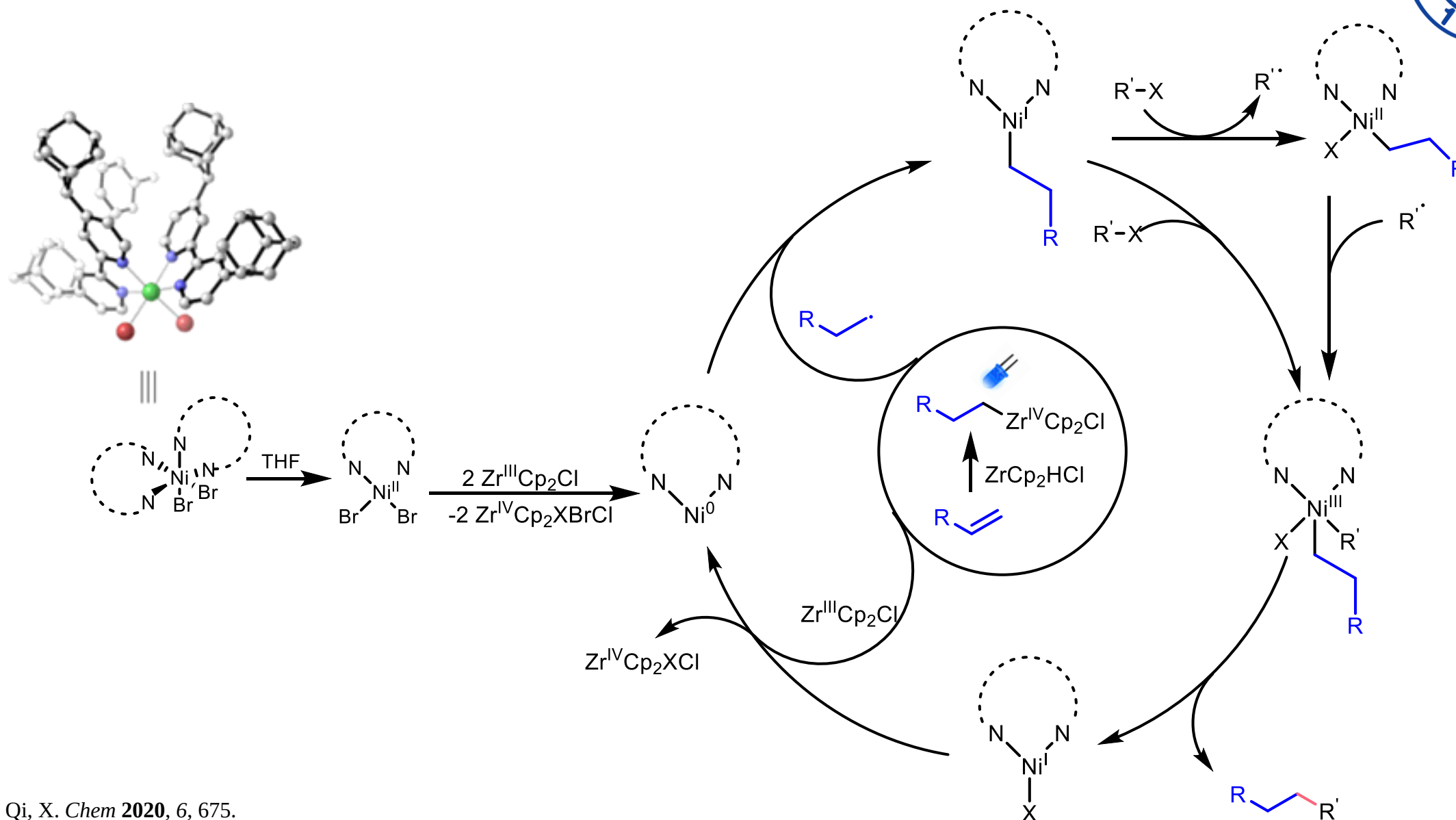


UV-visible absorbance spectra of cross-coupling reaction mixtures

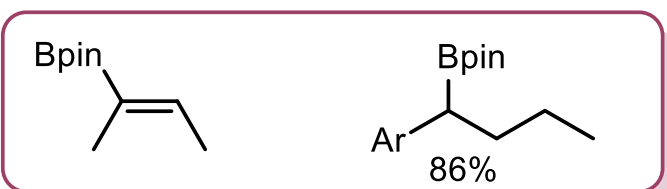
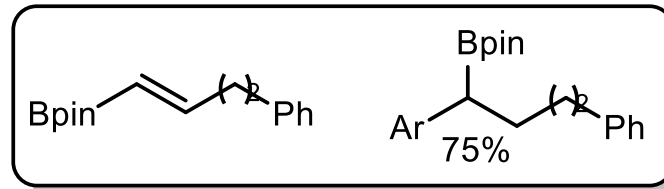
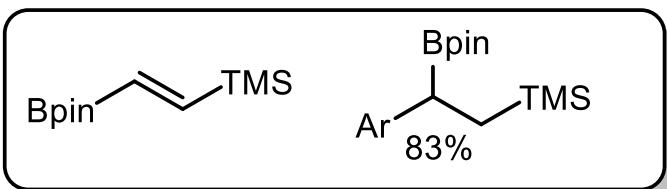
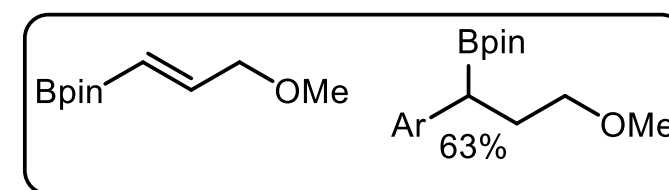
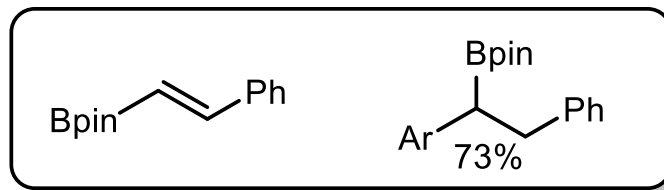
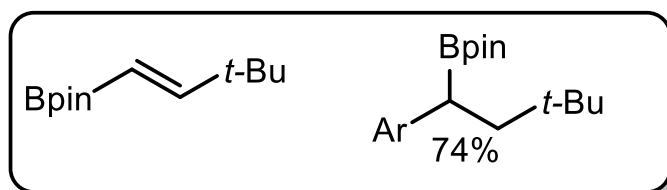
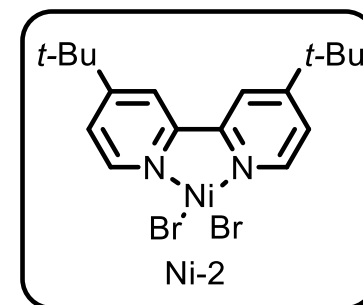
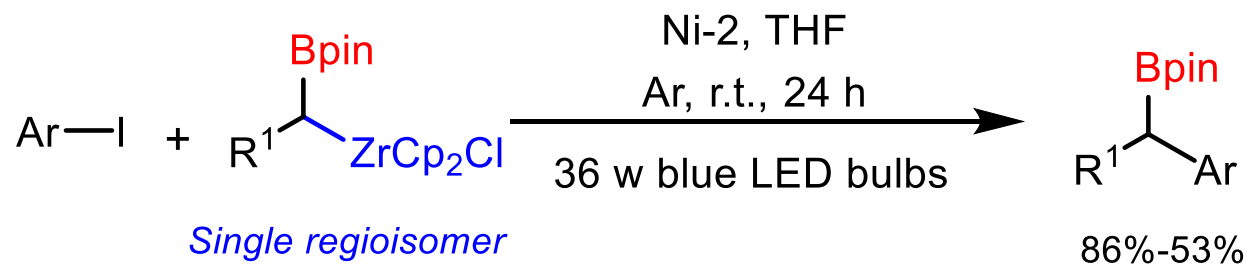


UV-visible absorbance spectra of each component

2.2 烷基锆试剂的偶联反应



2.2 烷基锆试剂的偶联反应



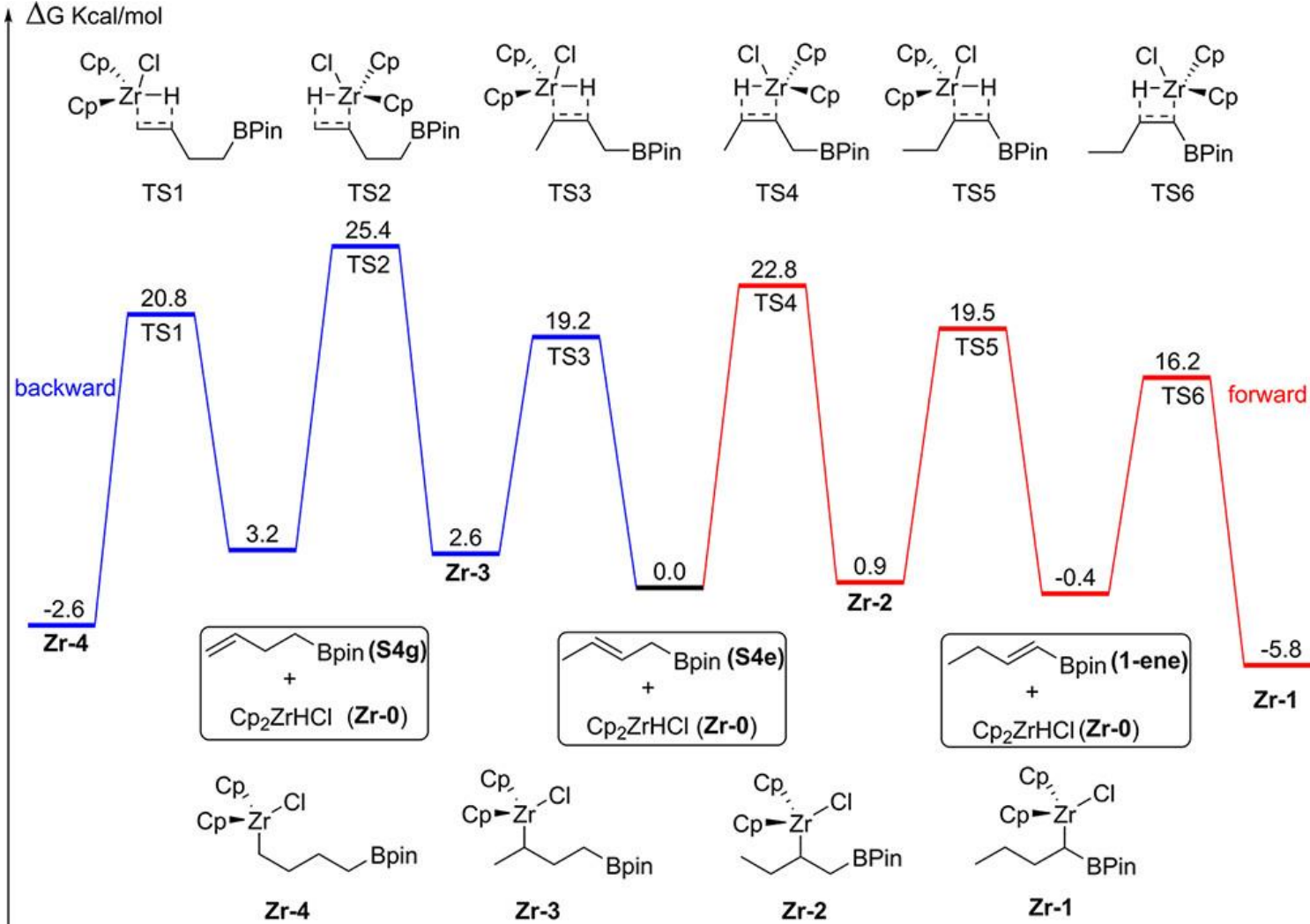
2.2 烷基锆试剂的偶联反应

chain walking的走向控制

2.2 烷基锆试剂的偶联反应



锆氢化过程的DFT计算结果

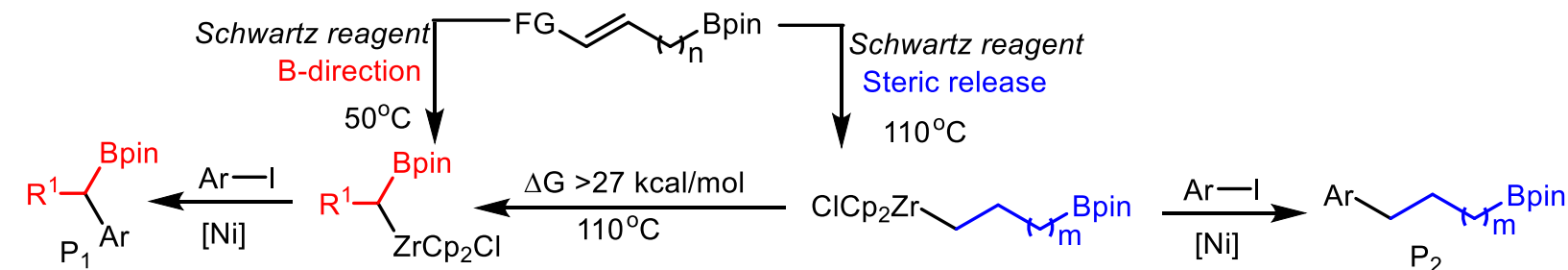


Qi, X. *J. Am. Chem. Soc.* **2020**, *142*, 11506.

2.2 烷基锆试剂的偶联反应



升温后，硼导向的chain walking



	50 °C	$P_1:P_2 = 2:1$	75%
	110 °C	only P_1	42%
	50 °C	only P_2	74%
	110 °C	only P_1	78%
	50 °C	only P_2	72%
	110 °C	only P_1	35%



总结

总结与展望

1. 亲核性较低的有机锆试剂适用于合成结构复杂的分子，例如在天然产物全合成研究中，有广阔的应用。
2. 烯烃的锆氢化存在chain walking 过程，可以用于远程官能团化，并且相关的导向基研究也有初步进展。
3. 烯炔锆氢化可以原位生成有机锆试剂，过程简单，条件温和在有机合成中有一定的开发价值。

请老师同学批评指正
谢谢

