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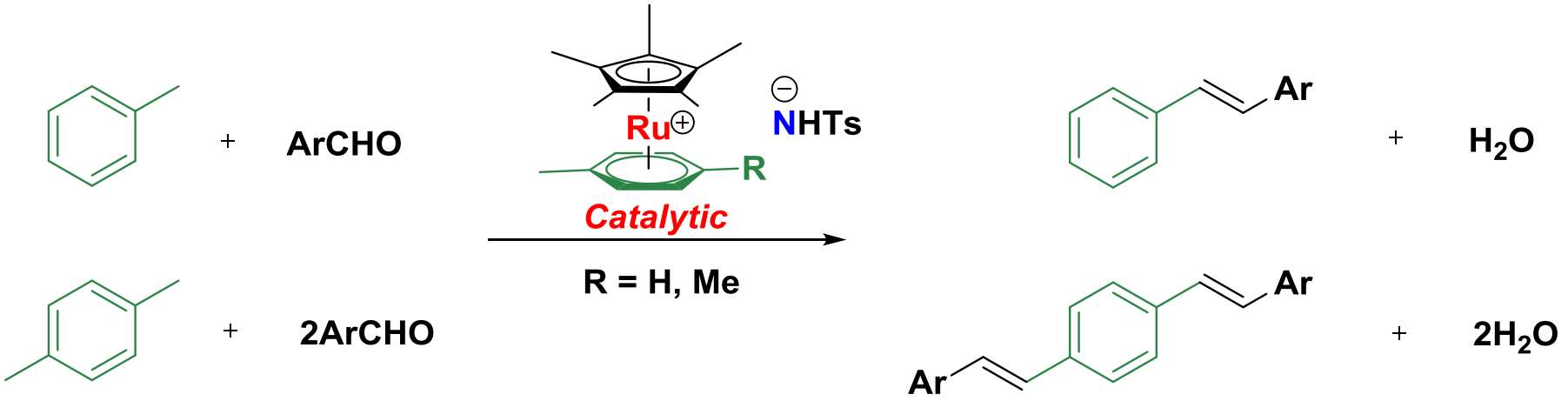
Ruthenium Sulfonamide-Catalyzed Direct Dehydrative Condensation Of Benzylic C-H Bonds With Aromatic Aldehydes

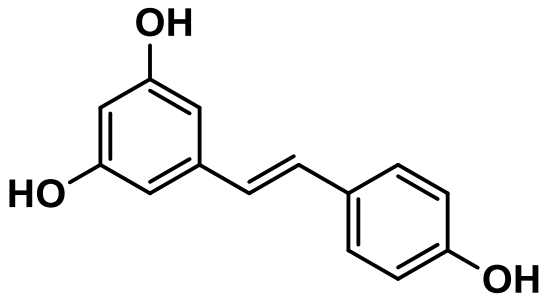


S. Takemoto,* E. Shibata, M. Nakajima, Y. Yumoto, M. Shimamoto, and H. Matsuzaka*, *J. Am. Chem. Soc.*, **2016**, **DOI: 10.1021/jacs.6b08863**

Properties and Utilization of Stilbenes and Distyrylbenzene Derivatives

➢ *Bioactive Stilbenes Derivatives*

Red grapes, cranberry



trans-resveratrol

Isolated by **Takaoka** from the roots of white hellebore in **1940**

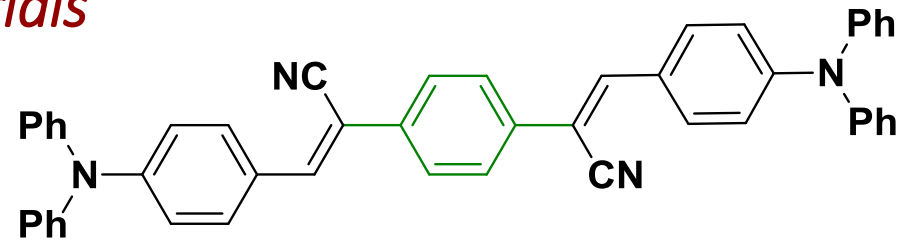
Constituant of red wine : 1.56 to 1042 nmol/g

Anti-oxidant, anti-inflammatory, anti-tumorals effects

Likhtenshtein, G. *Stilbenes : Applications in Chemistry, Life Science and Materials Science*; Wiley-VCH: Weinheim, **2010**.

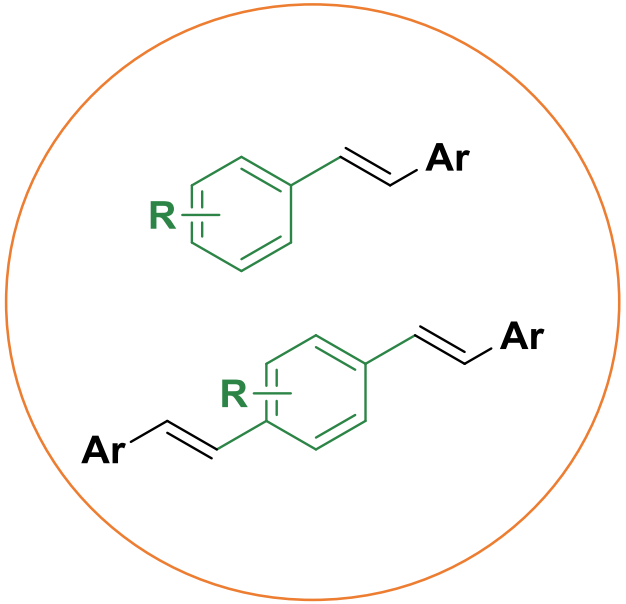
➢ *Distyrylbenzene-Based Luminescent Materials*

OLED: Organic Light-Emitting Diodes



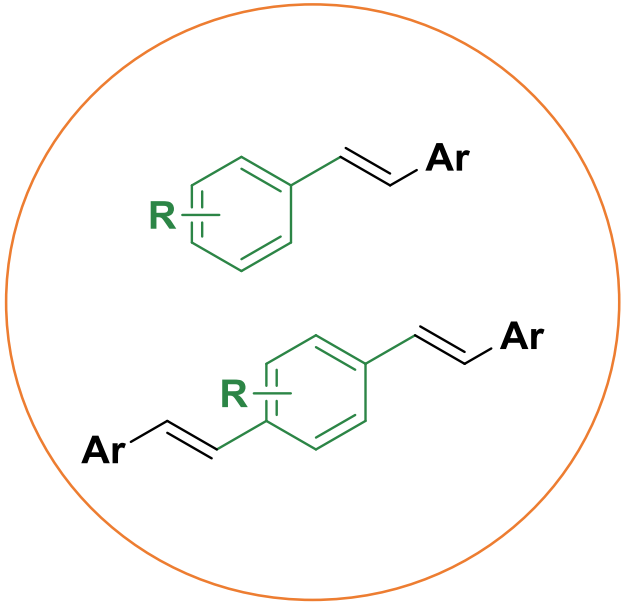
C. Li, M. Hanif, X. Li, S. Zhang, Z. Xie, L. Liu, B. Yang, S. Sua and Y. Ma *J. Mater. Chem. C*, **2016**, *4*, 7478-7484.

Background

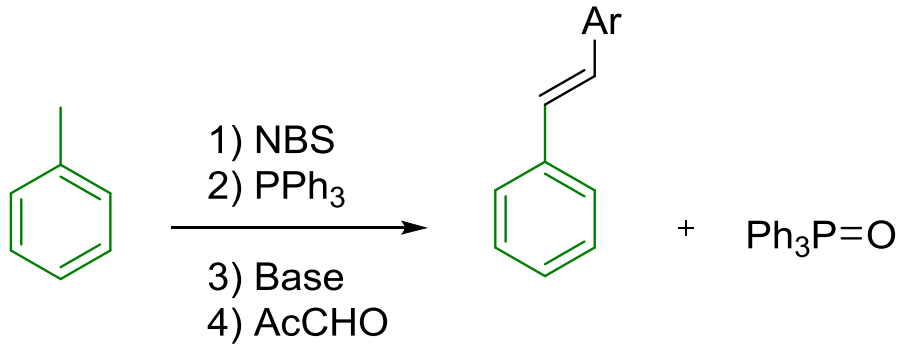


Background

Wittig reaction



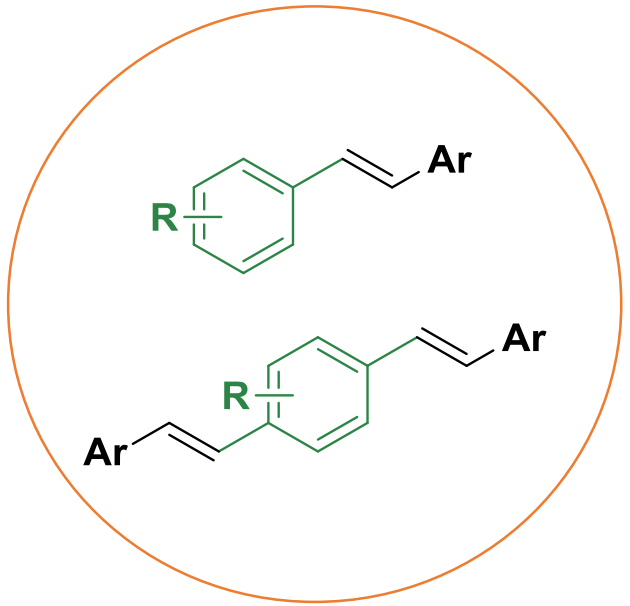
- **Multiple steps**
- **Hazardous reagents** to generate phosphorus ylide intermediates
- Production **of stoichiometric quantities** of halogen- and phosphorus- containing byproducts.



A. J. Hudson, S. Tamura, M. B. Grieve, T. Richardson, J. E. Wong, D. W. Bruce, *J. Mater. Chem*. **1995**, *5*, 1867.

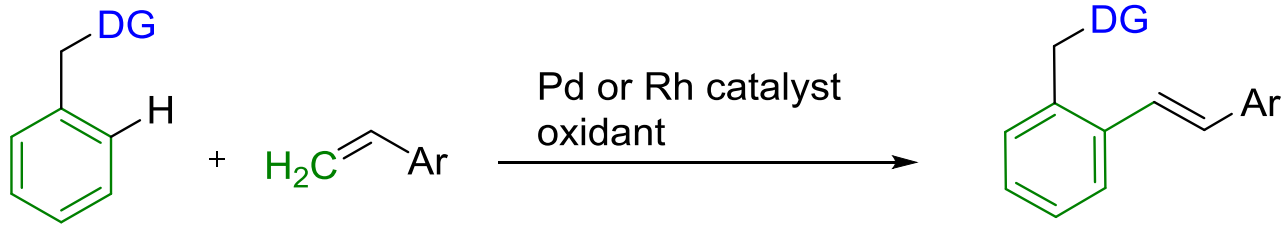
Background

Wittig reaction



Aromatic C-H olefination

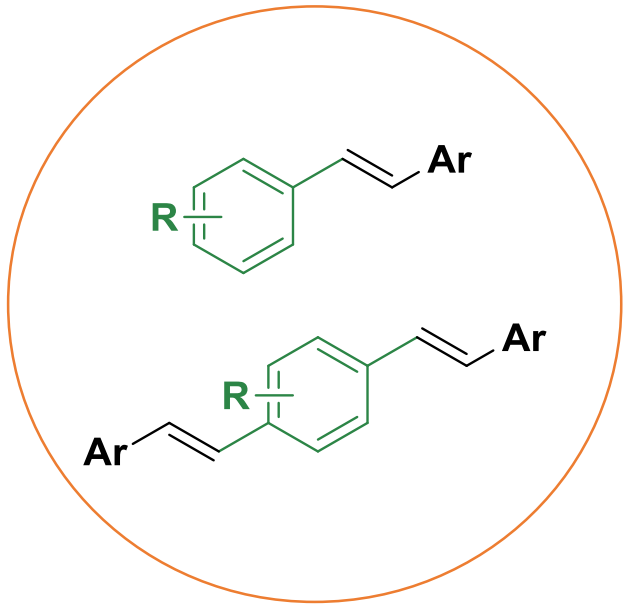
- Use of **directing groups** (DGs) to ensure high regioselectivity
- **Cost-effective** and **highly atom-economical** if the terminal oxidant come from the molecular oxygen or air
- **Expensive oxidants** such as Ag(I) or Cu(II) salts in **stoichiometric amounts**



A. Bechtoldt, C. Tirer, K. Raghuvanski, S. Warratz, C. Kornhaaß, L. Lutz Ackermann, *Angew. Chem. Int. Ed.* **2016**, *55*, 264 –267.

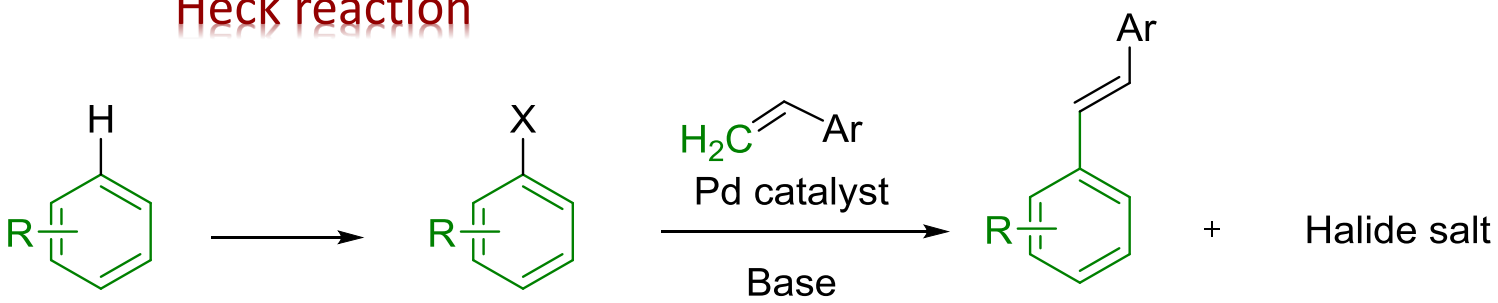
Background

Wittig reaction



Aromatic C-H olefination

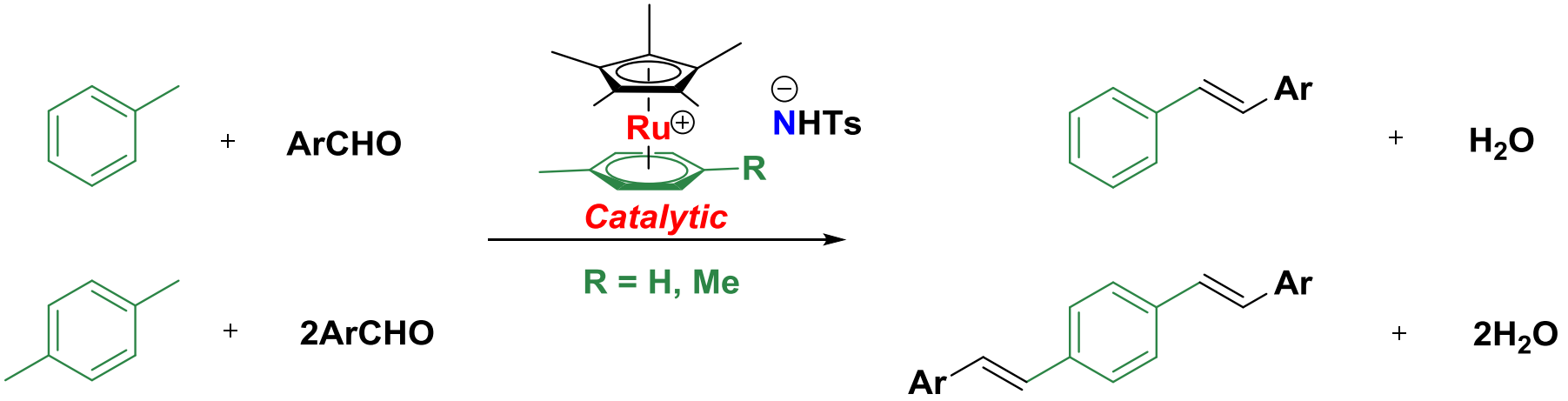
Heck reaction



- **Less waste**
- Problem of **regioselectivity**

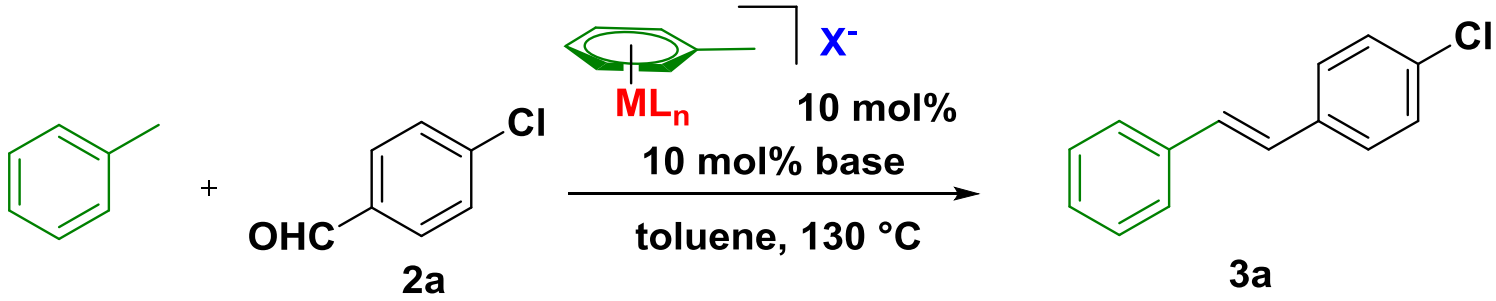
Werner E. W., Sigman M. S. *J. Am. Chem. Soc.* **2011**, *133*, 9692.

This work



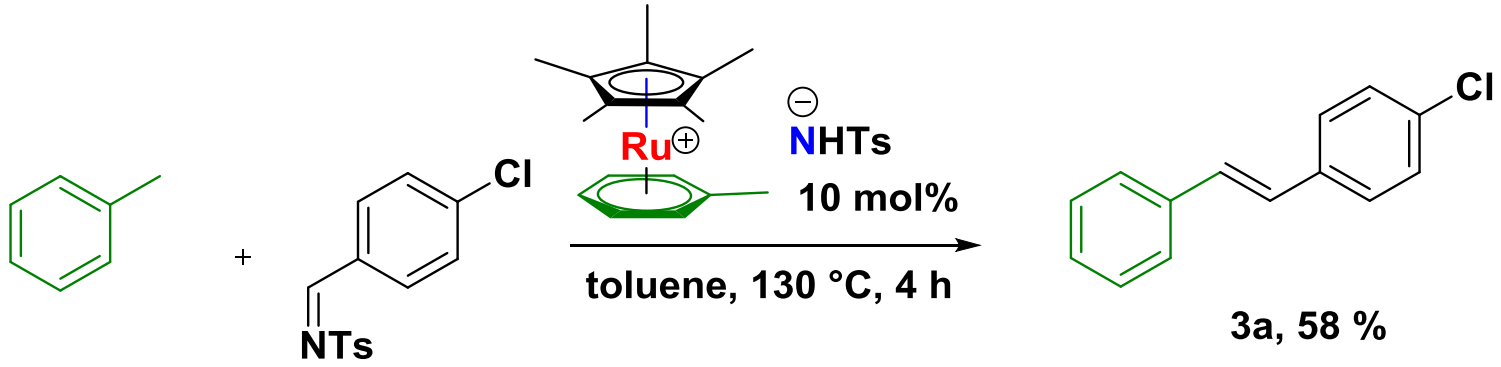
- **Direct dehydrative condensation** of the benzylic C-H bonds of toluene and *p*-xylene with aromatic aldehydes
- **First catalytic version**
- Novel **cooperative catalysis** of a cationic Cp*Ru(ŋ^6-arene) complex and a sulfonamide anion $NHTs^-$

Active Catalyst Components



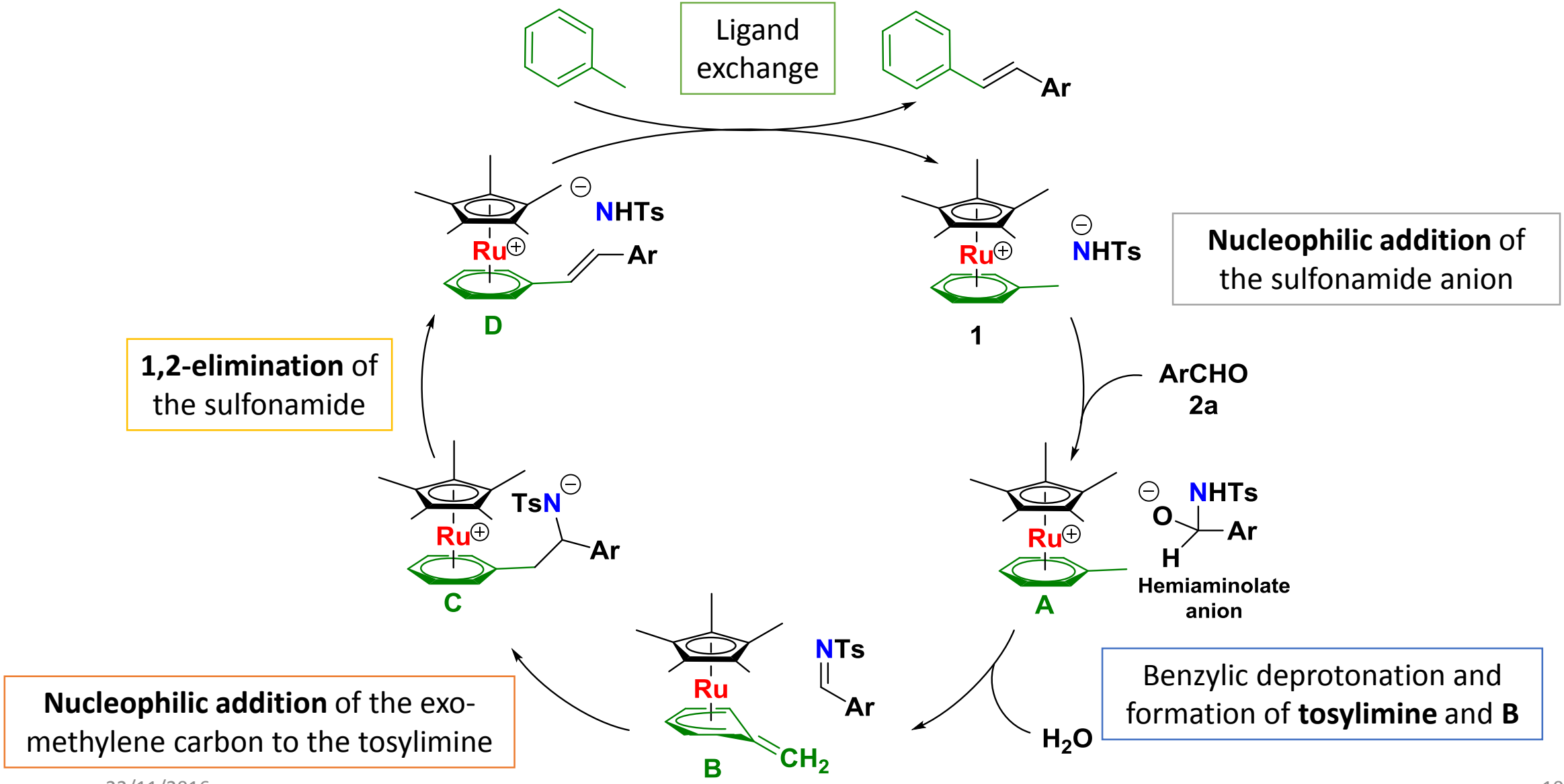
Entry	ML$_n$	X$^-$	Base	Reaction time	Yield (%)	Entry	ML$_n$	X$^-$	Base	Reaction time	Yield (%)
1	Cp*Ru$^+$	NHTs$^-$	None	4 h	50	11	CpRu$^+$	PF_6^-	KNHTs	19 h	8
2		OTf$^-$			0	12	Cp*Fe$^+$				5
3		Cl$^-$				13	CpFe$^+$				9
4			KNHTs		40	14	(PCP)Ru$^+$	OTf$^-$			0
5			KNHMs		24	15	$Mn(CO)_3^+$	PF_6^-			
6			KNMeTs		2	16	$Cr(CO)_3$	None			
7			KN^{t}BuTs								

Active Catalyst Components

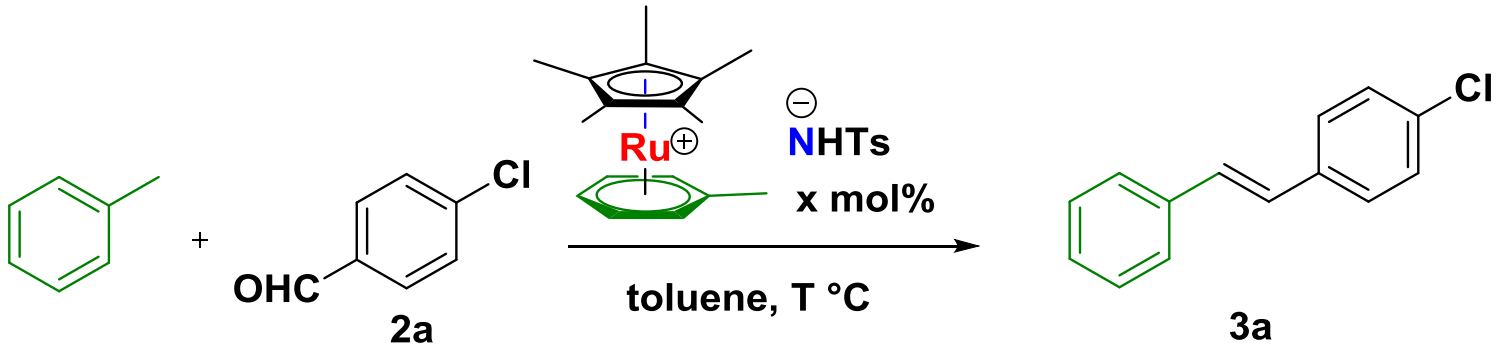


- **Primary sulfonamide anions** play an essential role: Base and facilate the C-C bond formation by a tosylimine intermediate

Proposed Catalytic Cycle

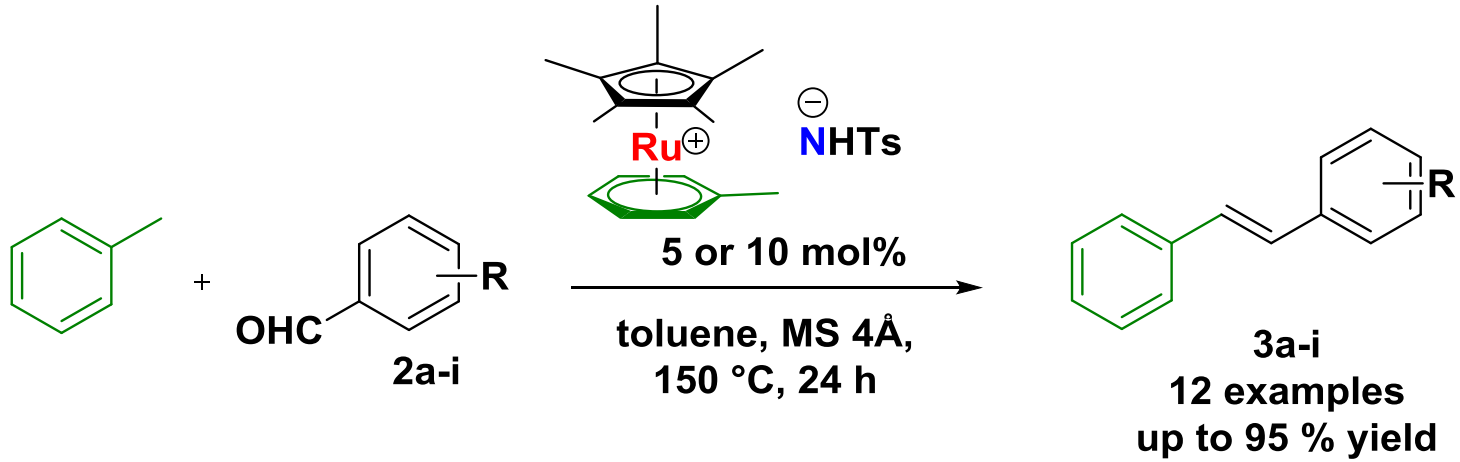


Optimization of Reaction Conditions

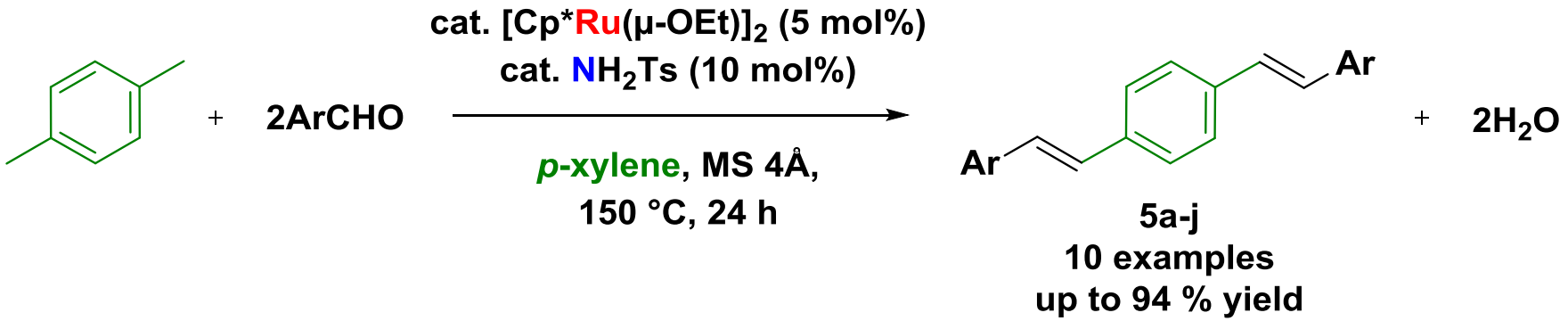


Entry	x	T °C	Time (h)	Additive	Conv. (%)	Yield (%)
1	10	130	4	None	88	50
2		150			100	72
3					71	58
4	5			MS 4Å	70	70
5			24		100	98
6	2,5				57	51

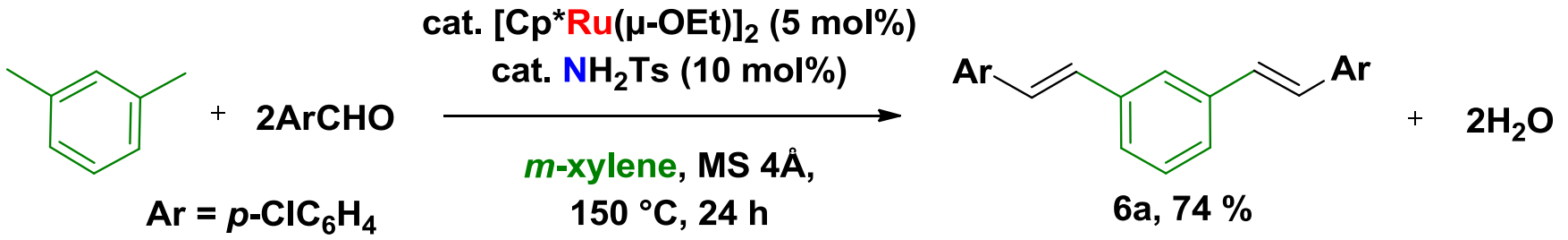
Scope of Aromatic Aldehydes



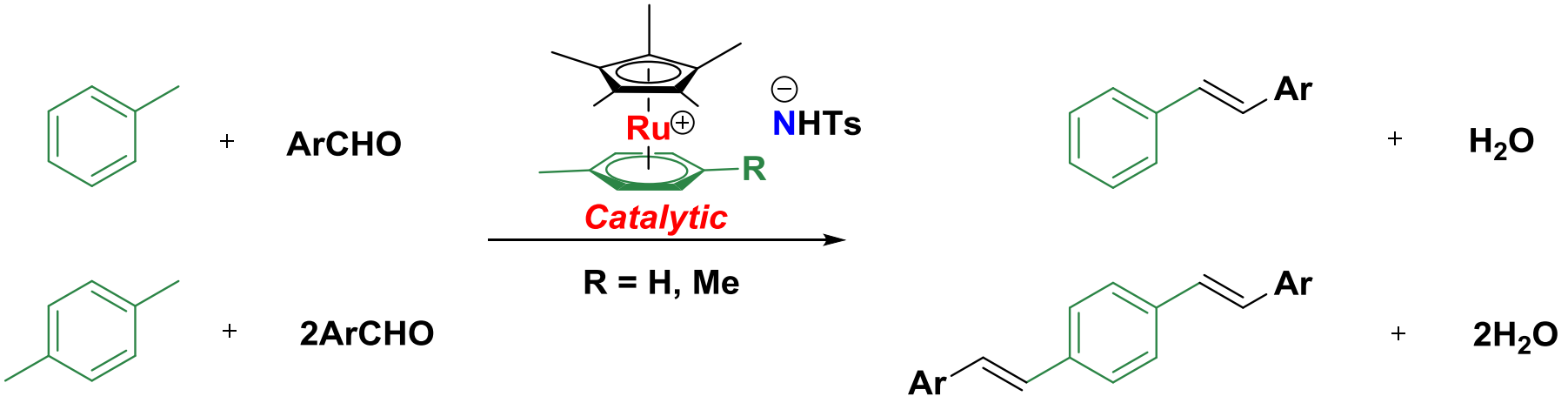
Dehydrative Condensation of *p*-xylene with Aromatic Aldehydes



Dehydrative Condensation of *m*-xylene with p-chlorobenzaldehyde



Conclusion



- **Direct dehydrative condensation** of the benzylic C-H bonds of toluene and *p*-xylene with aromatic aldehydes
- **First catalytic version** by a **new cooperative catalyst** cationic Cp*Ru(η^6-arene) complex and a sulfonamide anion $NHTs^-$
- **Highly atom-economical access** to relatively simple stilbene and *p*-distyrilbenzene derivatives
- Only **water** byproduct
- **Two roles** of sulfonamide anion