CATAFLU.or

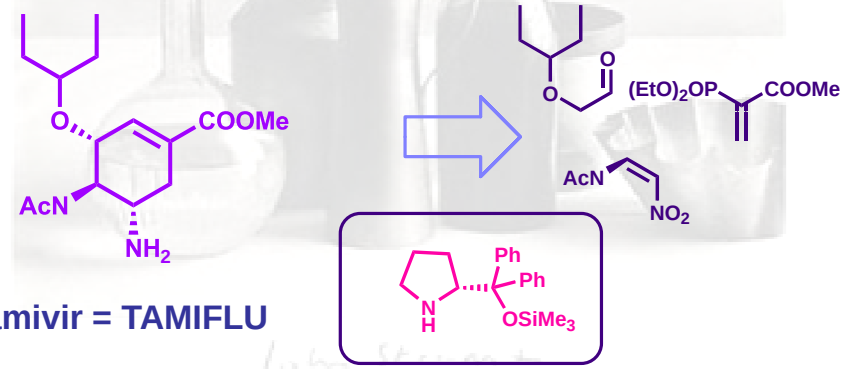
OrganoCATAlytic approaches towards easily synthesized, economical, and high yielding oseltamivir derivatives

COOPERATION

CATAFLU.OR Project

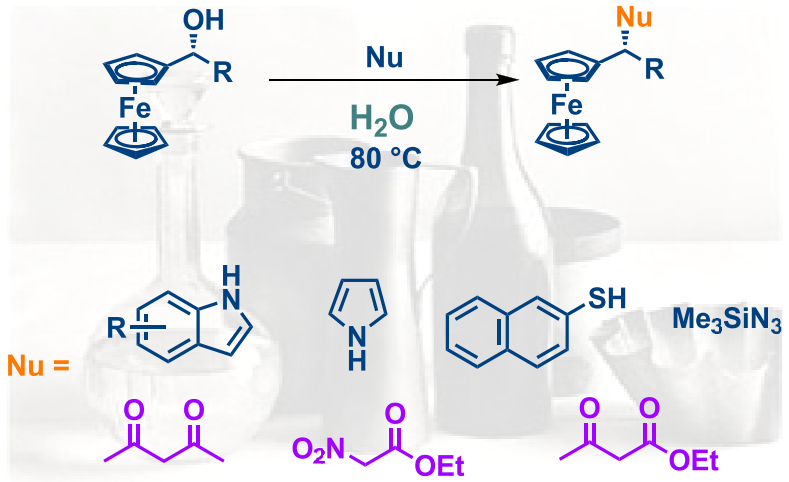
More about the project:
http://www.catafluor.eu/

Organocatalytic approch
To Tamiflu



Oseltamivir = TAMIFLU

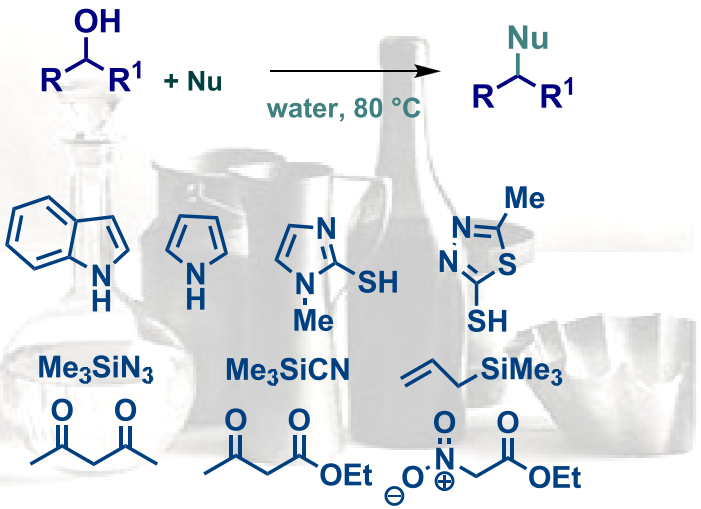
Reaction "on water" of ferrocenyl alcohols



Green Chemistry, 2007, 1292.
ChemSusChem, 2009, 2, 218.

Luca Zoli

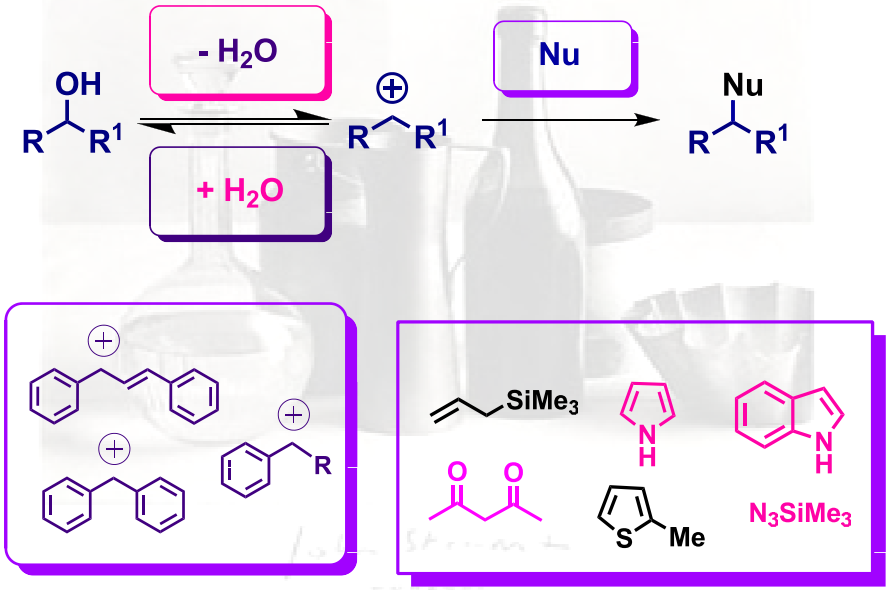
Carbocations can be generated in the presence of water?



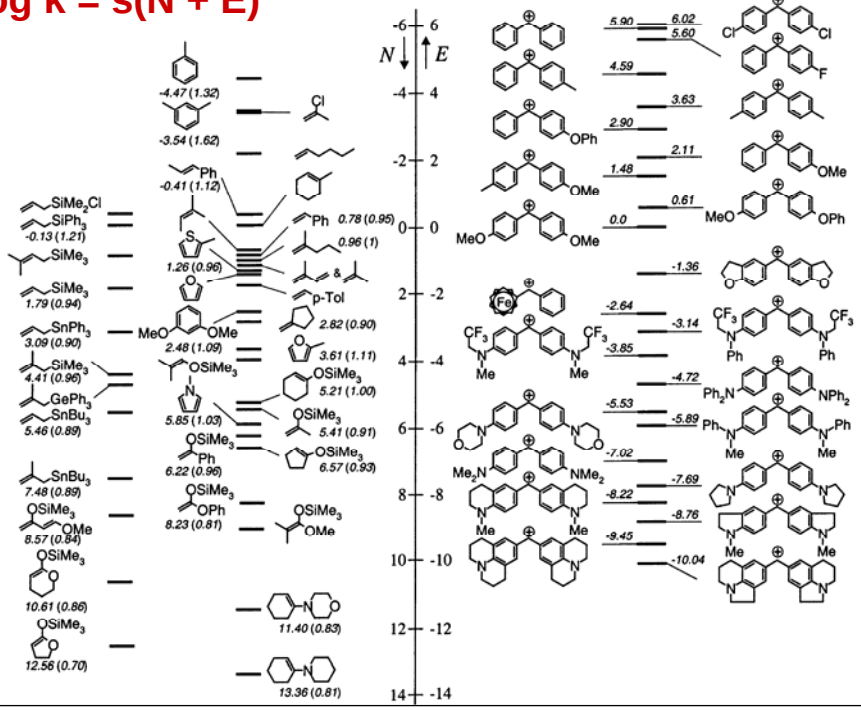
Angew. Chem. Int. Ed. 2008, 47, 4162.

Luca Zoli

Reaction between nucleophile and electrophile ?



Log k = s(N + E)



The Mayr's…LIST.

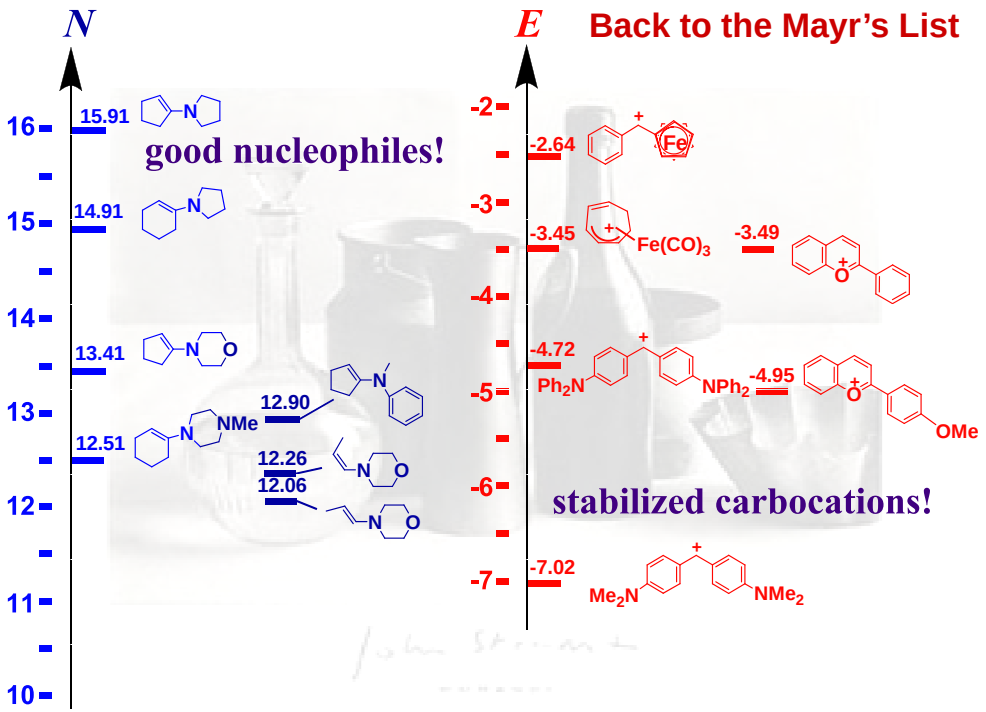
Key references:

a) H. Mayr, T. Bug, M. F. Gotta, N. Hering, B. Irrgang, B. Janker, B. Kempf, R. Loos, A. R. Ofial, G. Remennikov, H. Schimmel, J. Am. Chem. Soc. 2001, 123, 9500 – 9512; b) H. Mayr, M. Patz, Angew. Chem. Int. Ed. Engl. 1994, 33,938 – 957; c) H. Mayr, B. Kempf, A. R. Ofial, Acc.Chem. Res. 2003, 36, 66 – 77; d) H. Mayr, A. R. Ofial, Pure Appl. Chem. 2005, 77, 1807 – 1821; e) H. Mayr, A. R. Ofial, J. Phys. Org. Chem. 2008, 21, 584 – 595.

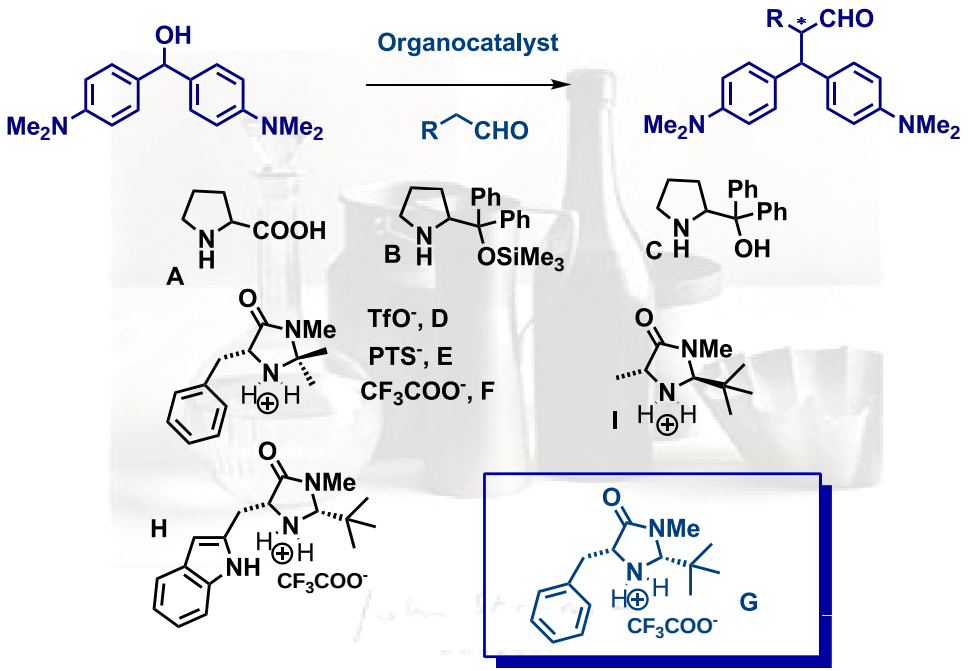
Key studies in organocatalysis:

Org. Lett, 2010, 10, 238; Angew. Chem. Int. Ed. 2009, 48, 5034; Angew. Chem. Int. Ed. 2008, 47, 8723; Angew. Chem. Int. Ed. 2007, 46, 6176.

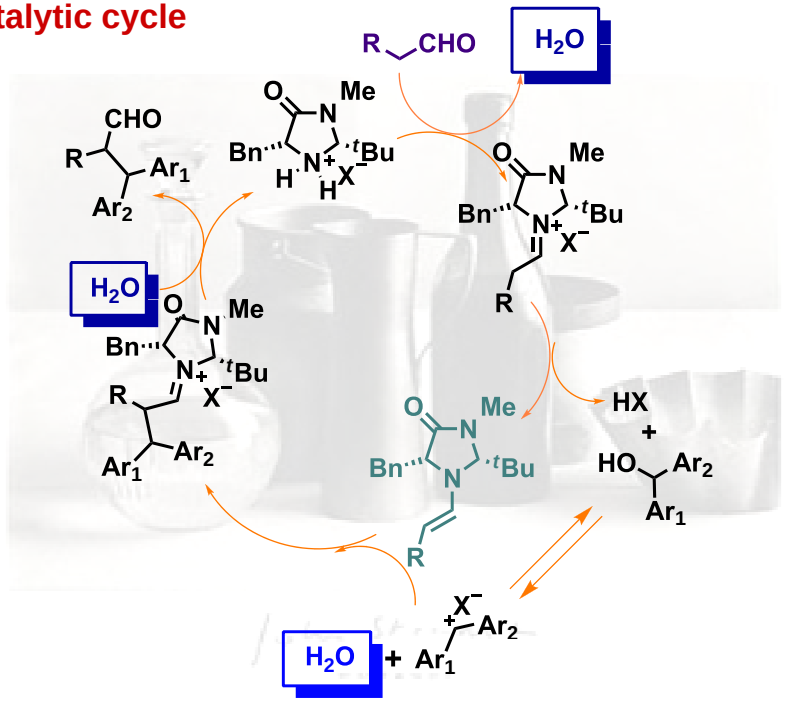
Back to the Mayr's List

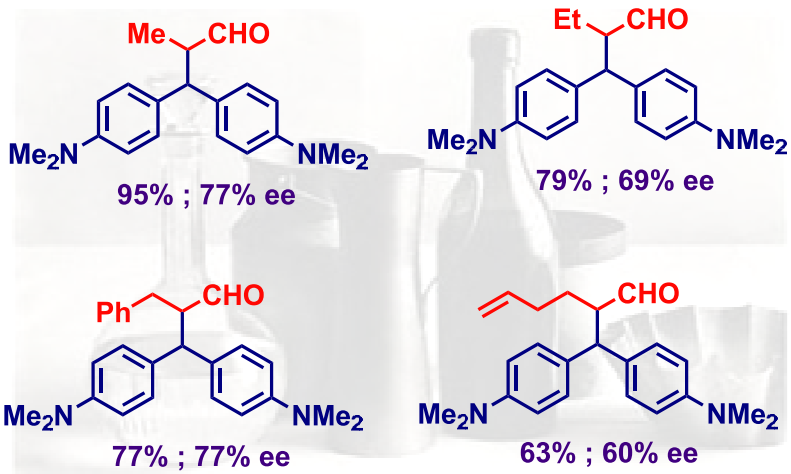


Model reaction

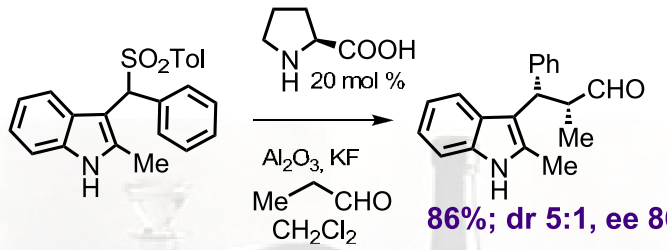


Catalytic cycle



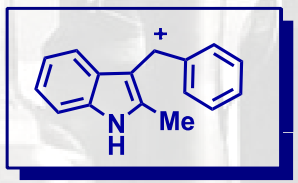


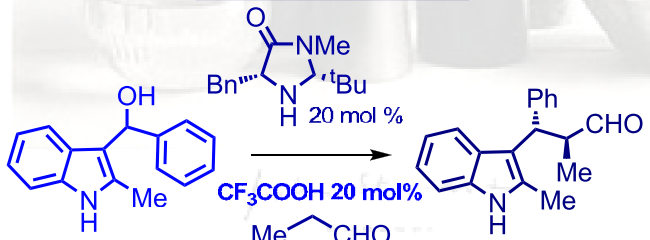
Angew. Chem. Int. Ed. 2009, 48, 1313.



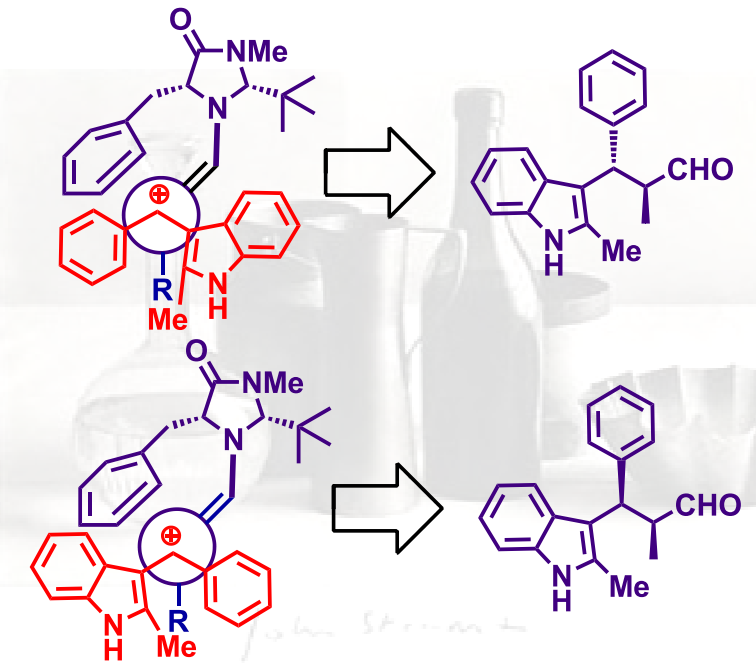
86%; dr 5:1, ee 86%

Melchiorre, Angew. Chem. Int. Ed. 2008, 47, 8707.

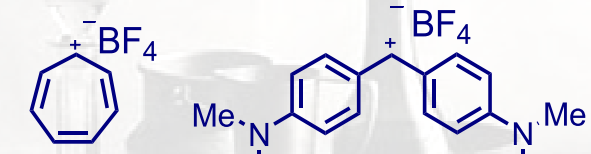


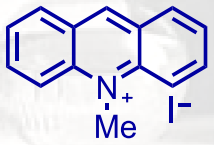


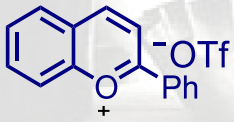
48%; dr 2.6:1, ee 92%



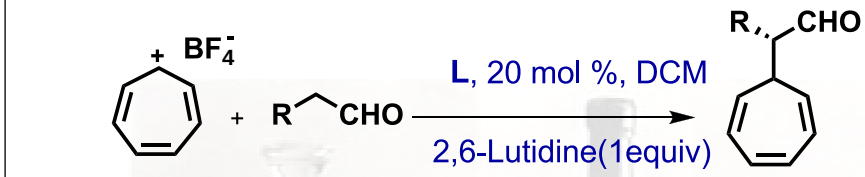
Stereoselective reactions with isolated carbocations

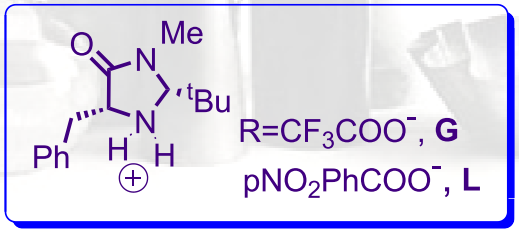






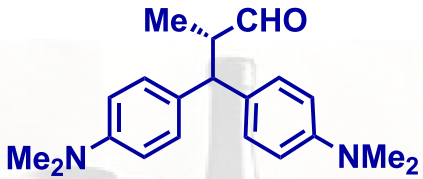
Fides Benfatti,
Elena Benedetto



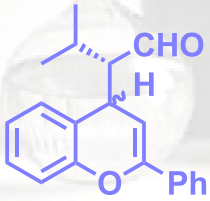


Chem Asian J. 2010, 5, 2047.

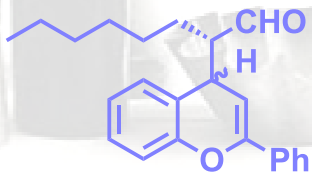
66 %, ee 63%



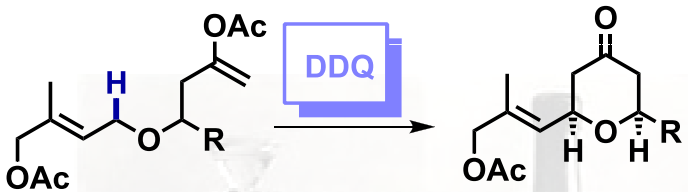
75%, ee 65%



51 %, 4:1 dr, ee 92% maj



68 %, 9:1 dr, ee 80% maj



80%, 1 diasteroisomer

P. E. Floreancig, Synlett 2007, 191;
Angew. Chem. Int. Ed. 2008, 47, 4184.

For other examples of carbon–carbon bond formation through DDQ-mediated ether oxidation, see:

a) T. Mukaiyama, Chem. Lett. 1987, 1811; b) Y.-C. Xu, Org. Lett. 1999, 1, 1599; c) Y.-C. Xu, Org. Lett. 2004, 6, 1523; d) C.-J. Li, Angew. Chem. Int. Ed. 2006, 45, 1949; e) J. Am. Chem. Soc. 2006, 128, 4242.

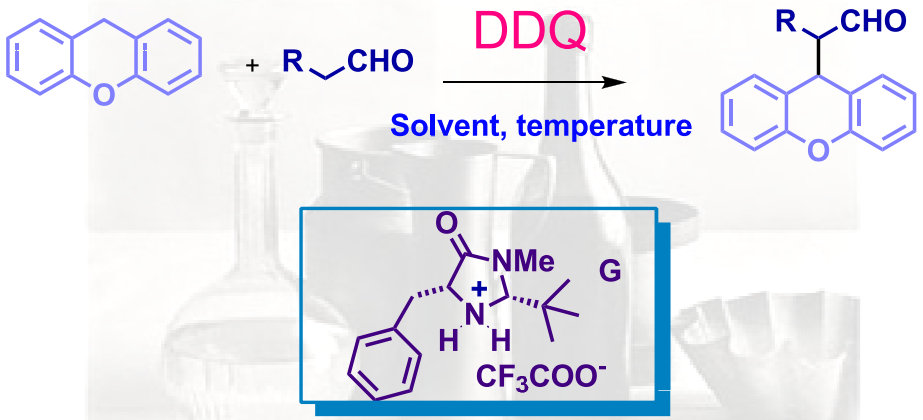
A new strategy

MERGING ORGANOCATALYSIS WITH C-H ACTIVATION

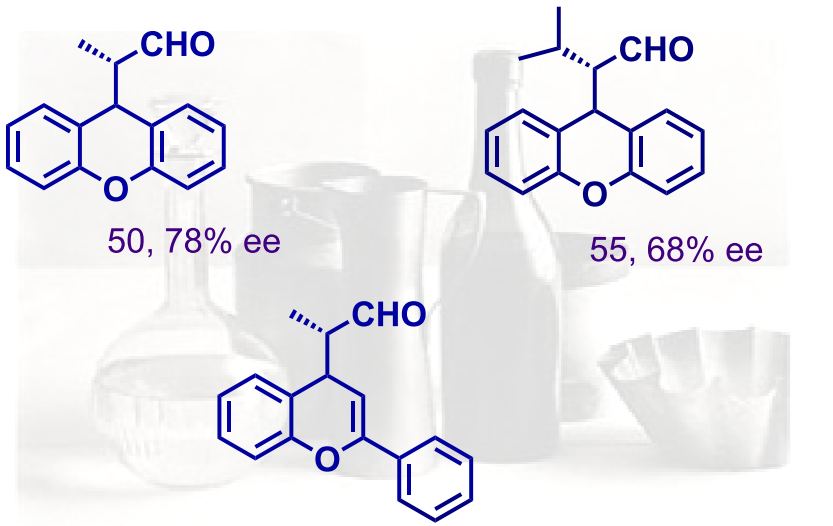
Generation of carbocations
Reaction with MacMillan catalyst

Choice of substrates:

1) Stabilized carbocations
2) Water is generated in the process
3) Strong oxidants are favoring SOMO



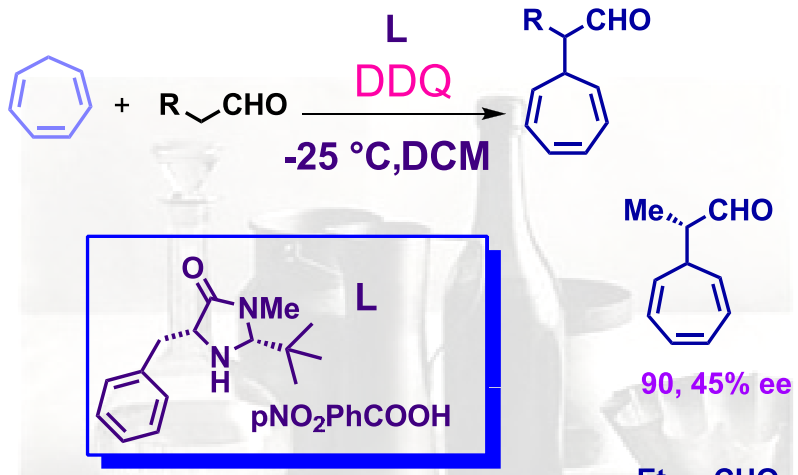
Fides Benfatti, Montse Guiteras Capdevila, Luca Zoli, Elena Benedetto



50, 78% ee

55, 68% ee

30, dr 2:1, 62% ee maj, 10% ee min

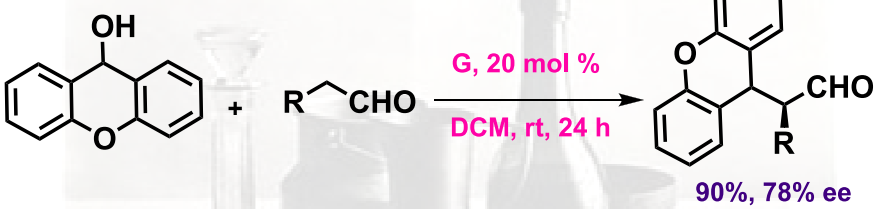


90, 45% ee

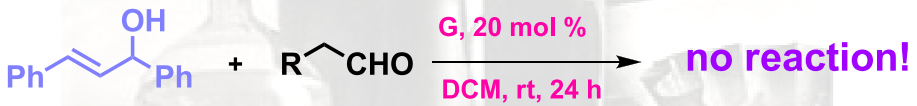
30, 38% ee

Chem. Comm. 2009, 5919.

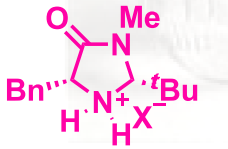
Reaction with allylic alcohols!



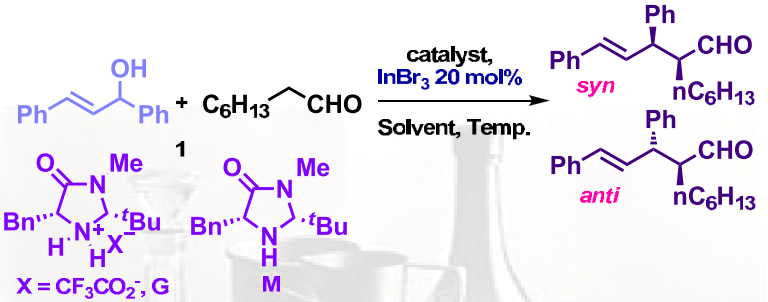
90%, 78% ee



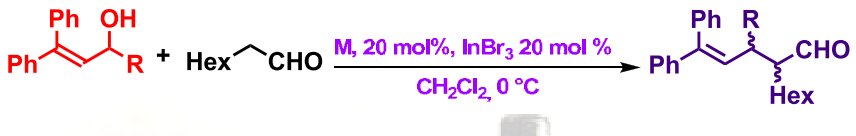
no reaction!

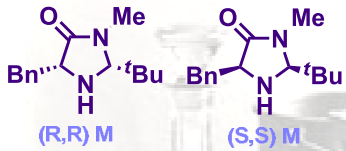


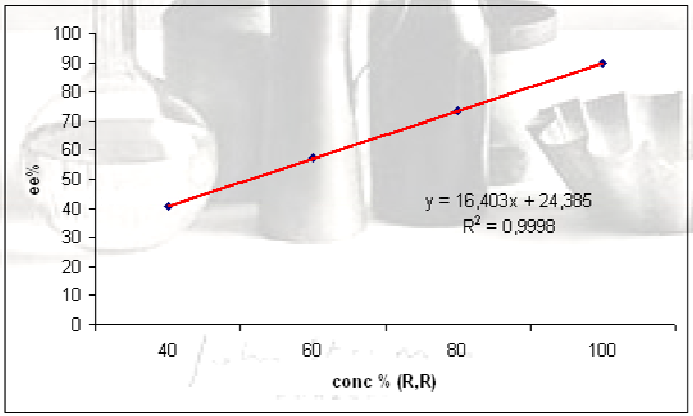
$X = CF_3CO_2^-$, G



Entry	Catalyst	T [° C]	Time [h]	Solvent	*ee* [%]
1	G	rt	60	Toluene	---
2	G	rt	60	^{t}BuOMe	---
3	G	rt	60	CH_3CN	---
4	G	rt	60	CH_3NO_2	---
5	G	0	12	CH_2Cl_2	71
6	M	0	12	CH_2Cl_2	80







New direction in Organocatalysis!

Merging Organocatalysis with Indium(III) (Lewis acids) Mediated Process

Lewis Acids activation of electrophiles

Activation of alkynes and alkene

New substrates

Chiral nucleophiles can be also obtained by the use Of organometallic complexes