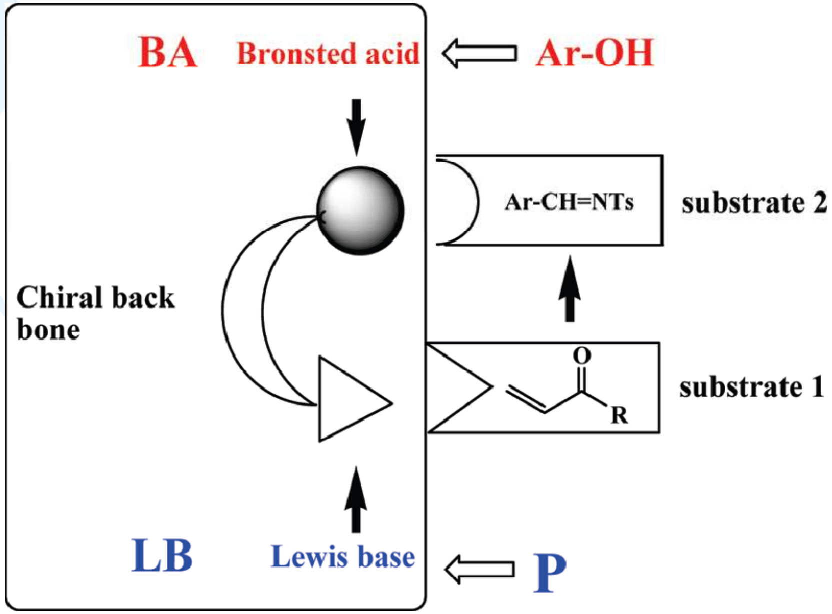
Faisal NAWAZ
Biblio-1, 19-05-2010
ISM2, Marseille

Multifunctional Chiral Phosphine Organocatalysts in Catalytic Asymmetric Morita-Baylis-Hillman and Related Reaction



Introduction

•**C**atalytic asymmetric synthesis has received considerable attention over the past few decades.

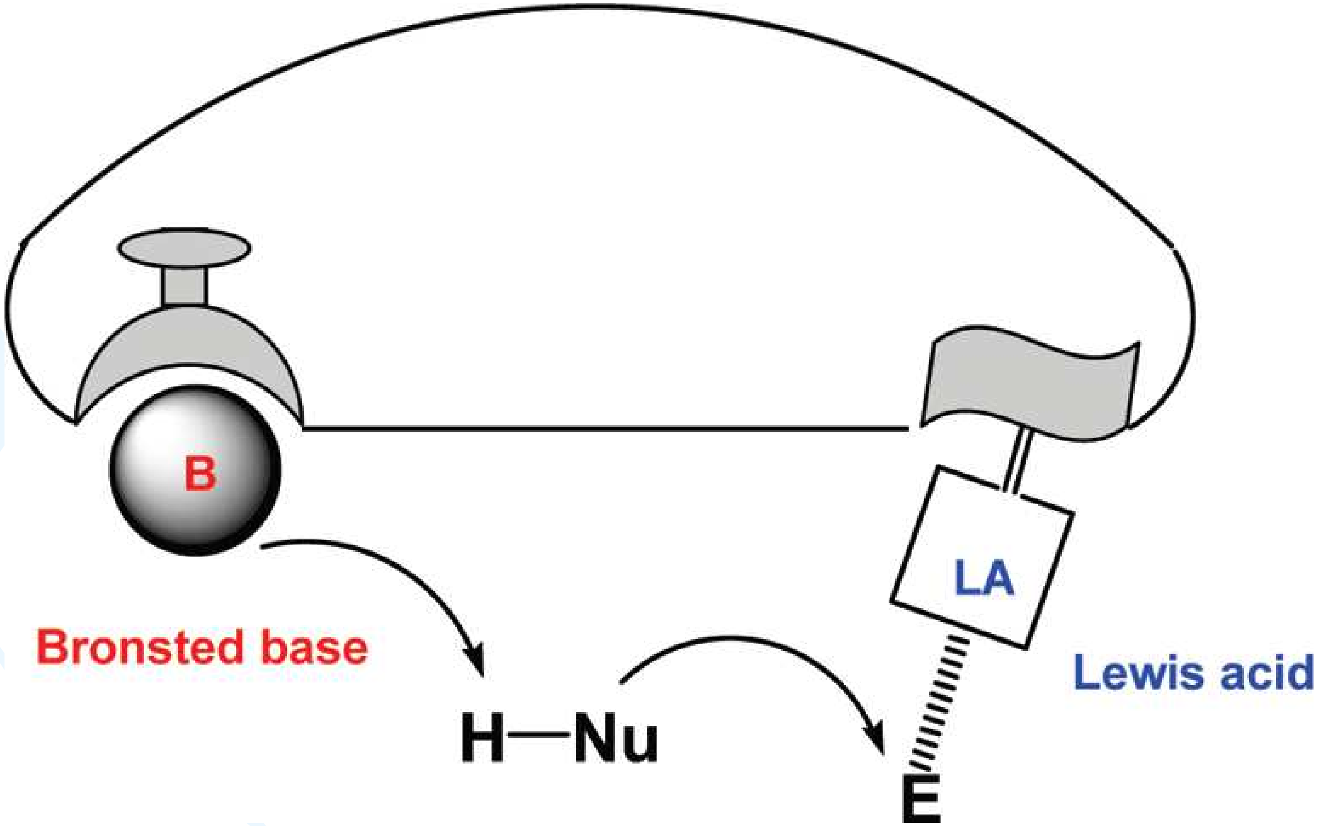
•Becoming a highly dynamic area of chemical research with significant contributions to the field of organic synthesis.

•Artificial catalysts now provide highly economic access to many desirable compounds, but the general adaptability and reactivity of these platforms remain problematic, particularly in comparison to nature's catalysts, enzymes.

•The multifunctional organocatalysts described in this Account represent another positive step in the synthetic chemist's efforts to profitably mimic nature's catalytic platform, helping develop small-molecule catalysts with enzyme-like reactivities and selectivities

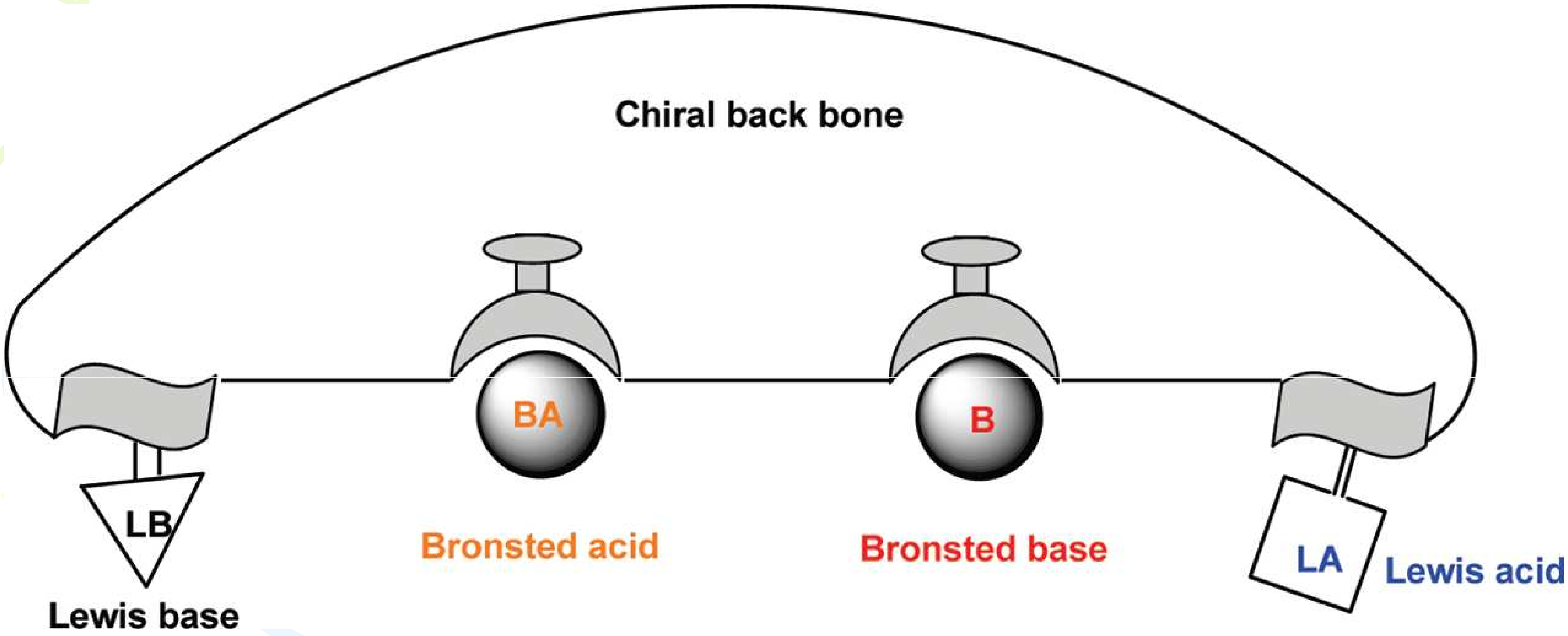
These multifunctional chiral phosphines, which contain Lewis basic and Brønsted acidic sites within one molecule, provide good-to-excellent reactivities and stereoselectivities in the asymmetric aza-MBH reaction, the MBH reaction, and other related reactions

Introduction



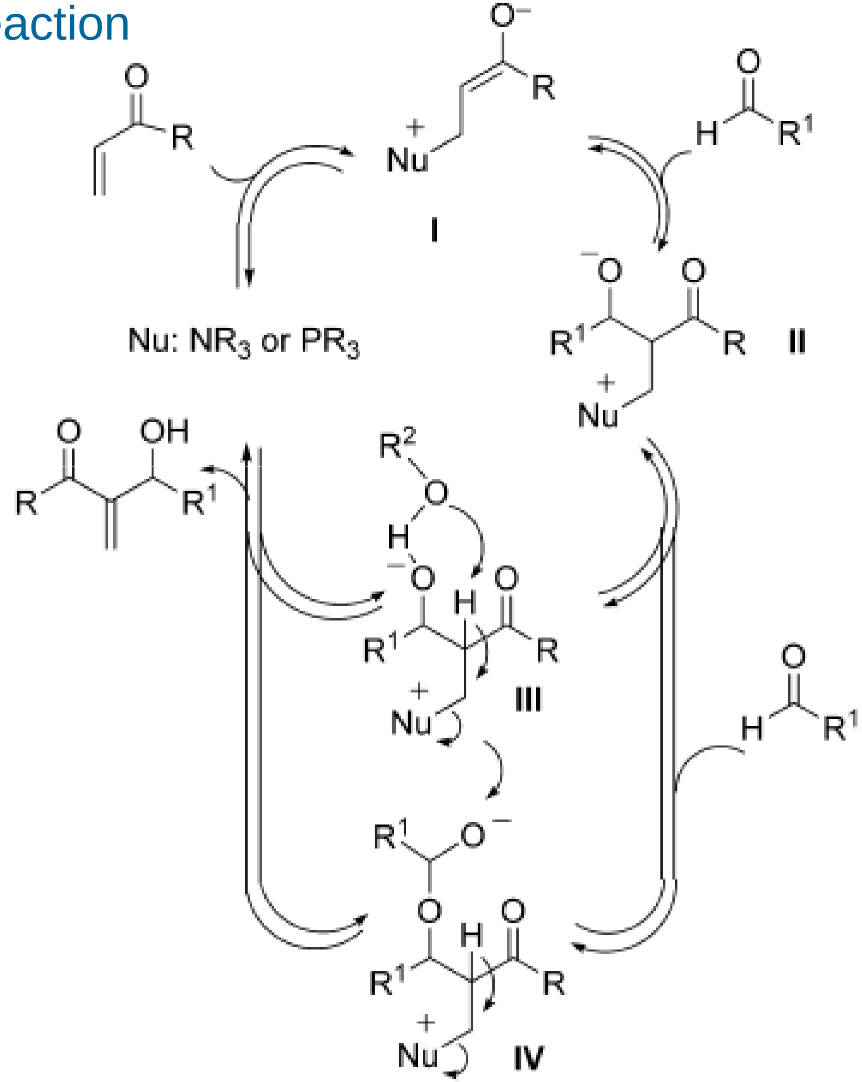
Multifunctional catalysts employing the synergistic function of a Lewis acid and a Brønsted base: LA, Lewis acid; B, Brønsted base; E, electrophile; Nu-H, nucleophile.

Introduction



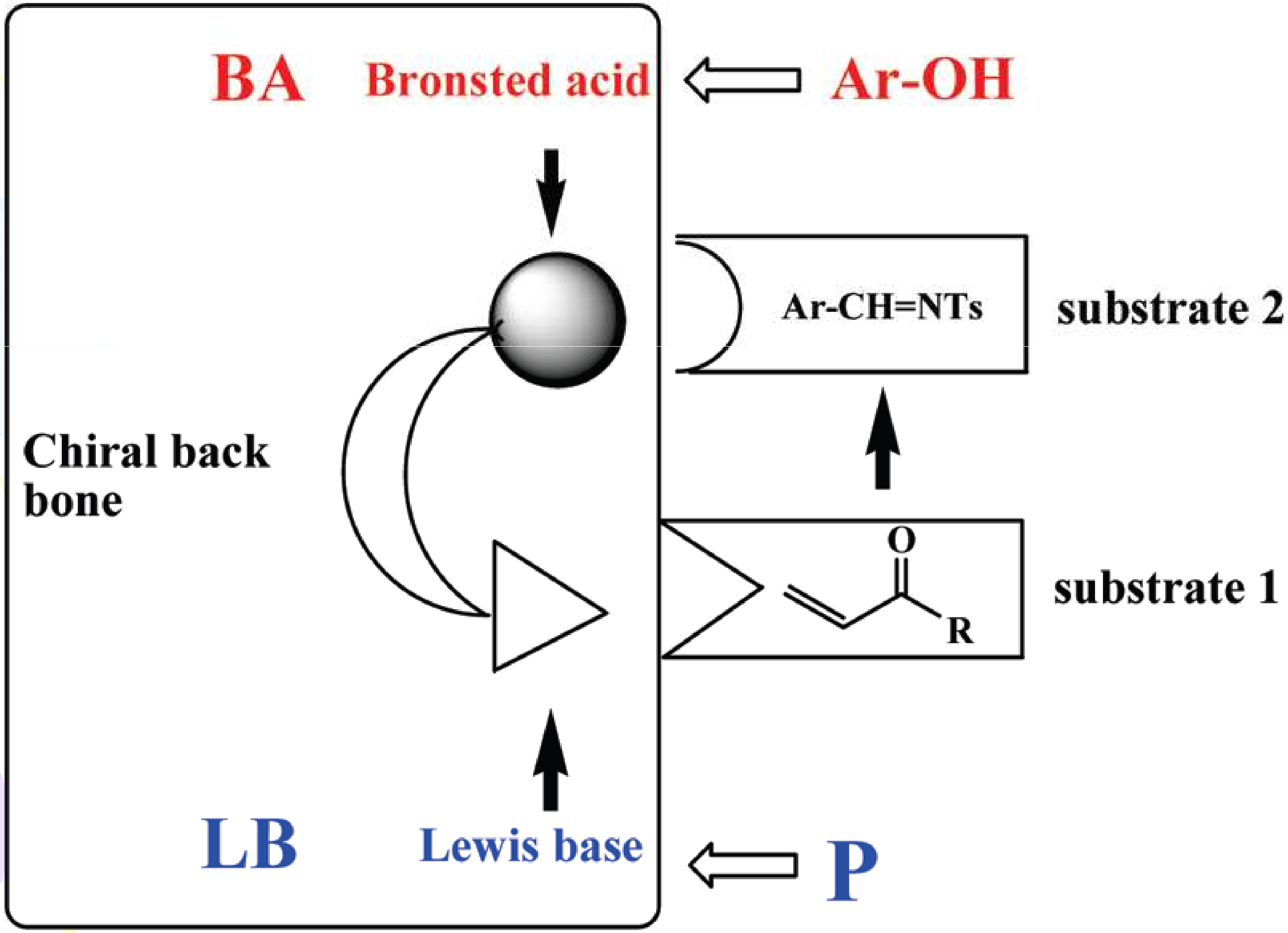
Ideal multifunctional chiral catalysts containing Lewis acid, Brønsted base, Brønsted acid, and Lewis base as active catalytic sites: LA, Lewis acid; B, Brønsted base; BA, Brønsted acid; LB, Lewis base.

The Proposed Mechanism of MBH Reaction



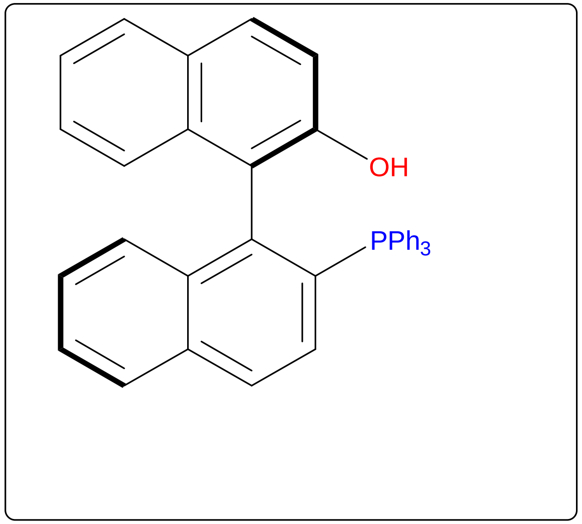
Introduction

Multifunctional chiral phosphine Lewis base catalyst, LBBA bifunctional catalytic system: LB, Lewis base; BA, Brønsted acid.



Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

In 1993, Hayashi first synthesized the chiral phosphorus compound **CP1** as a chiral monodentate phosphine ligand:

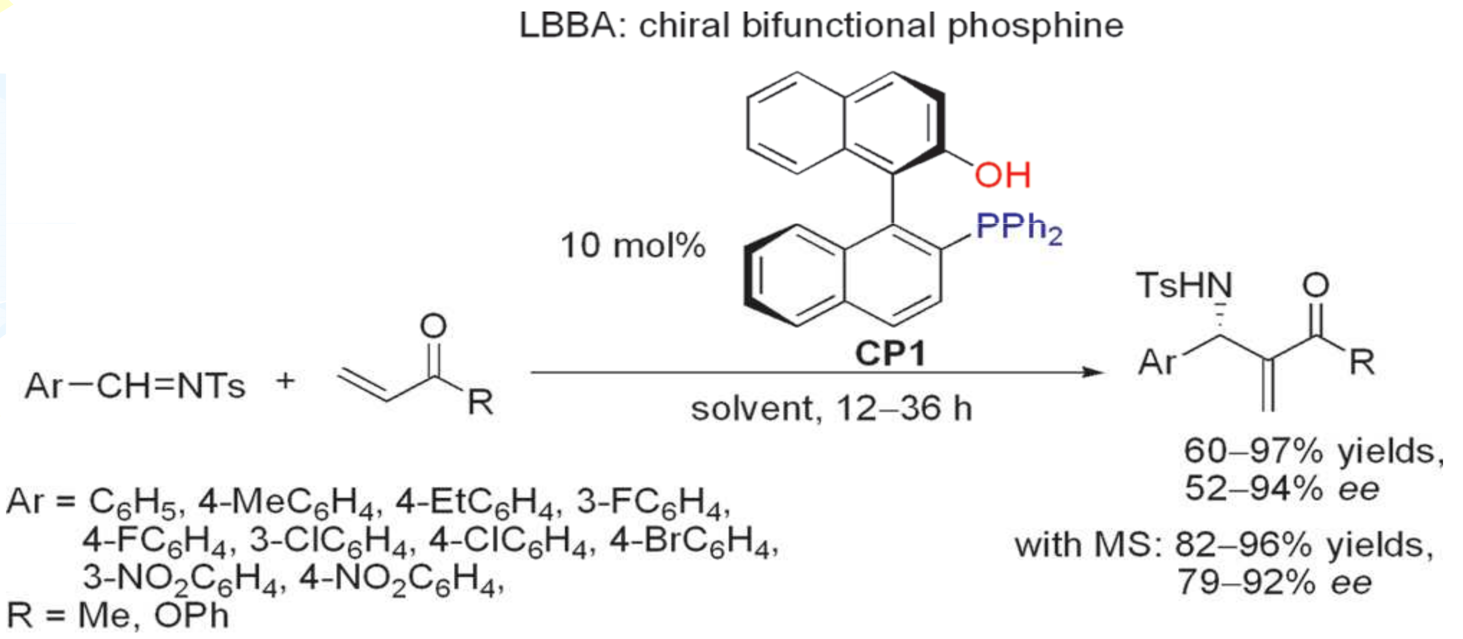


CP1

Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem. 1993, 58, 1945–1948.*

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

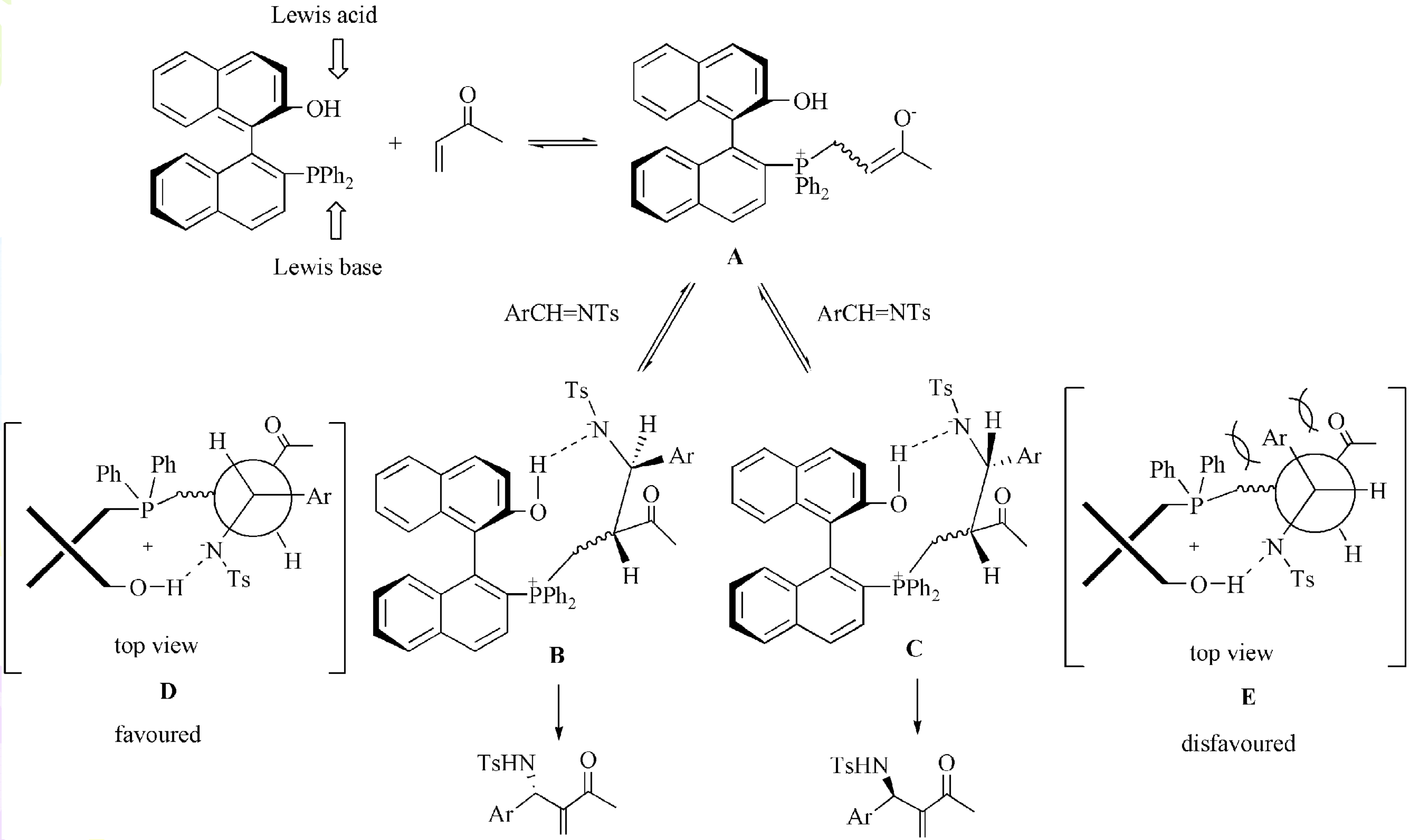
In2002, Min Shi first demonstrated that this 1,1′-bi-2,2′-naphthol(BINOL)-derived chiral LBBA bifunctional phosphine **CP1**(LB) PPh3, BA) Ph-OH)



Min Shi* and Lian-Hui Chen *CHEM. COMMUN.*, 2003, 1310–1311

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

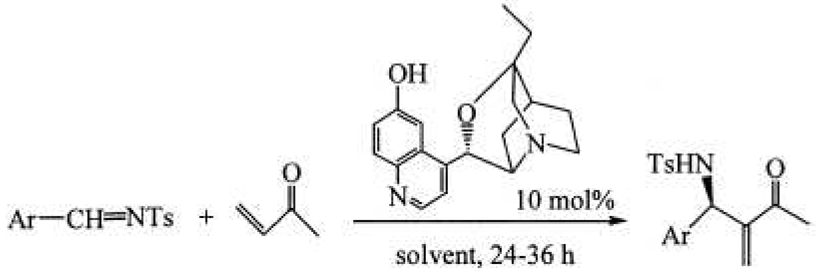
Mechanistic speculation on the chiral Lewis base **CP1**



Min Shi* and Lian-Hui Chen *CHEM. COMMUN.*, 2003, 1310–1311

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

The asymmetric induction of CP1 catalyst is comparable to that of the quinidine derivatives



1

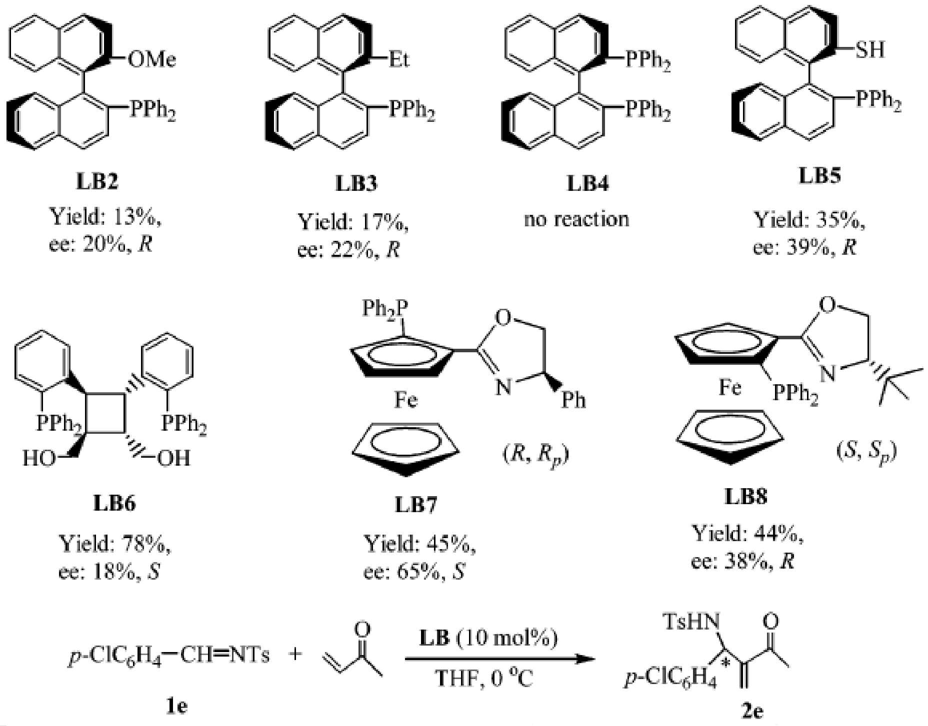
Entry	Ar	1	Solvent	t [h]	T [°C]	Yield of 1 [%][a]	ee value [%]
1	p-EtC_6H_4	c	THF	36	20	30	62
2	p-EtC_6H_4	c	THF	24	−25	33	76
3	p-EtC_6H_4	c	MeCN	24	0	50	78
4	p-EtC_6H_4	c	MeCN	24	−20	64	86
5	p-EtC_6H_4	c	DMF	24	−20	55	93
6	p-EtC_6H_4	c	DMF	24	−40	50	96
7	p-ClC_6H_4	e	THF	24	0	71	42
8	p-ClC_6H_4	e	THF	24	−20	65	63
9	p-ClC_6H_4	e	MeCN	24	−30	80	81
10	p-ClC_6H_4	e	DMF	24	−30	51	95

[a] Yields of isolated products.

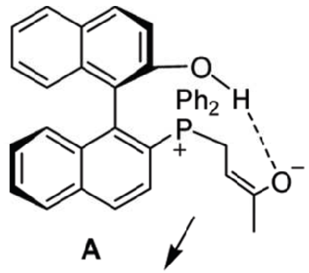
Shi, M.; Xu, Y.-M. Catalytic,. *Angew. Chem., Int. Ed. 2002, 41, 4507*–4510.

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

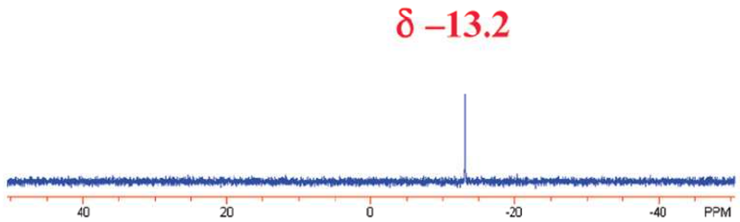
The presence of a phenolic hydroxyl group in catalyst **CP1** seems crucial for good yield and high ee.



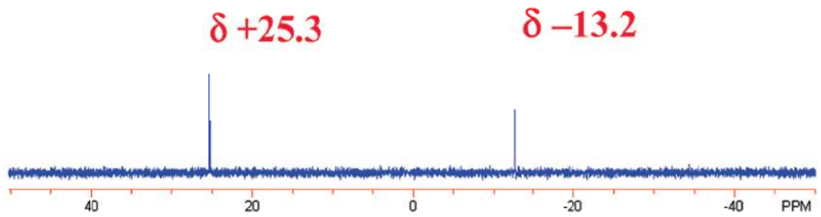
Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:



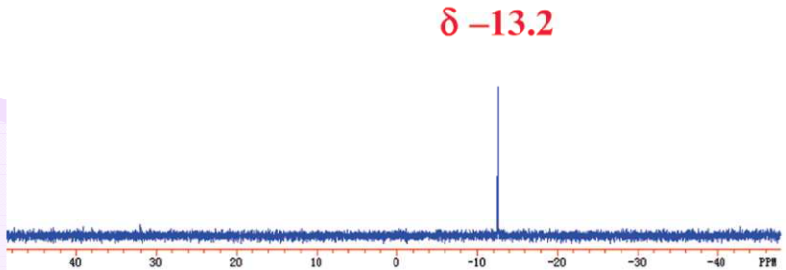
A



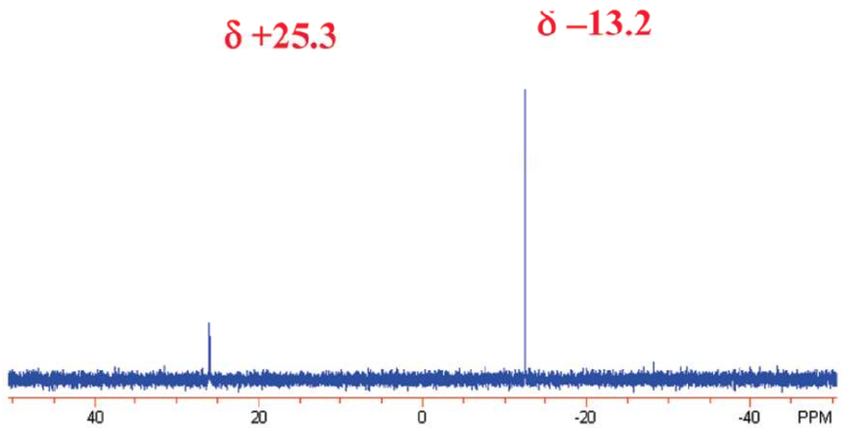
^{31}P NMR of **CP1**



^{31}P NMR of the mixture of **CP1** and methyl vinyl ketone



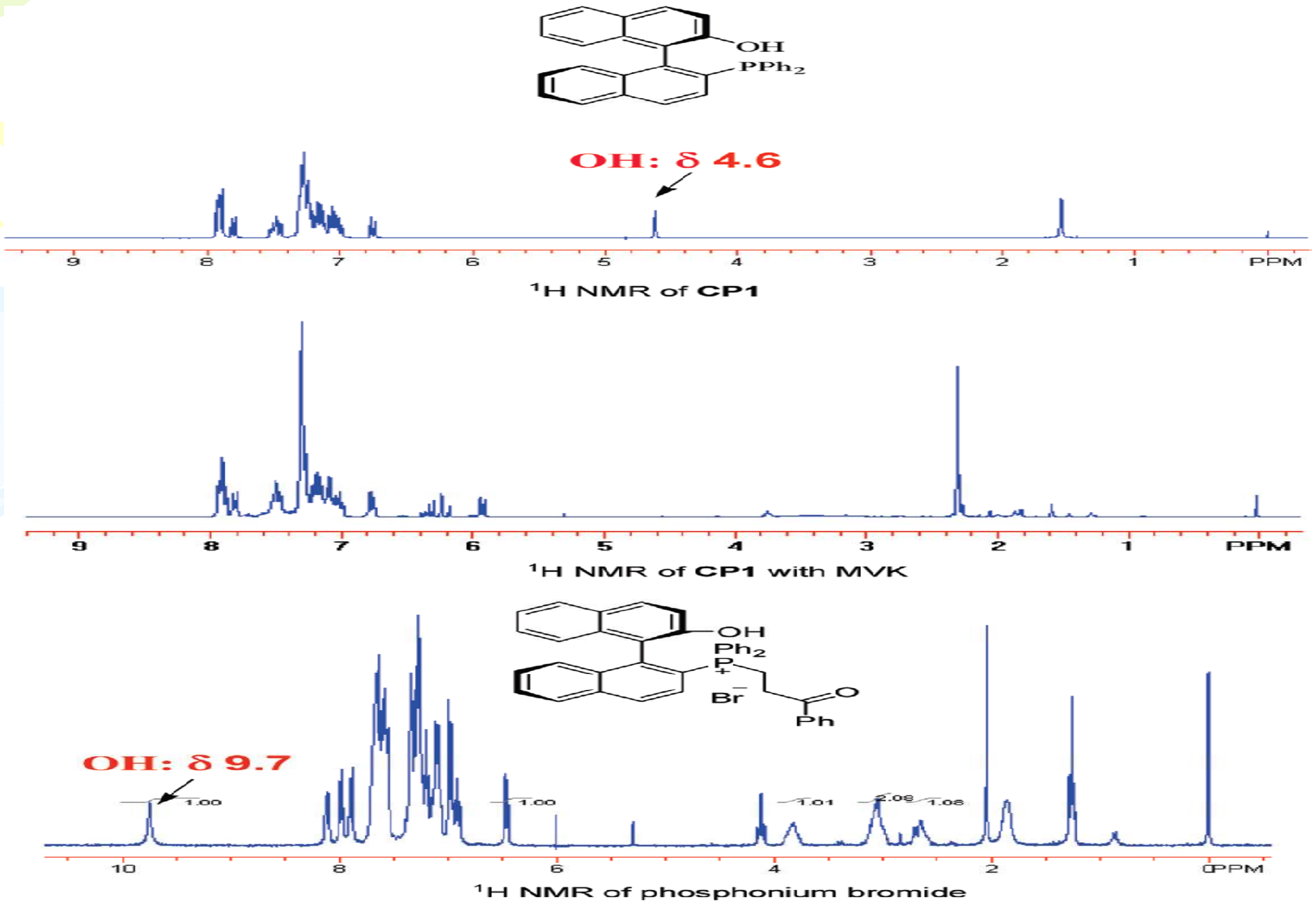
^{31}P NMR of the mixture of **CP1** and imine



^{31}P NMR of the mixture of **CP1**, methyl vinyl ketone and imine

Pascal Buskens, Ju¨rgen Klankermayer, and Walter Leitner***J. AM. CHEM. SOC.** 9 VOL. 127, NO. 48, 2005

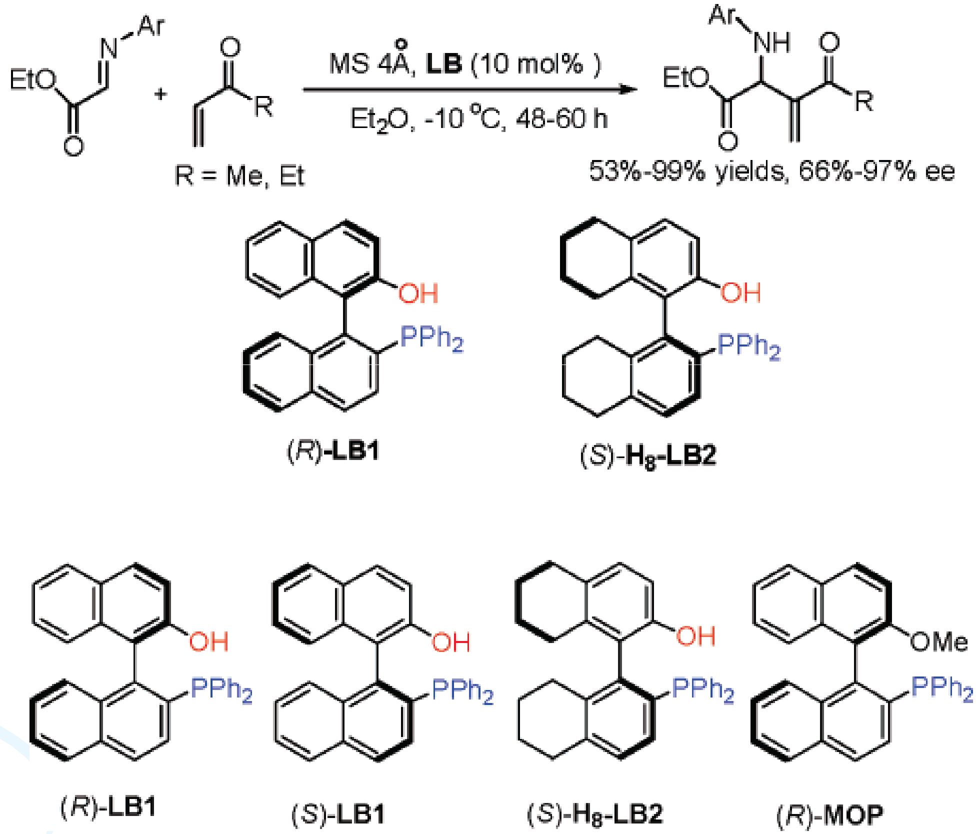
Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:



Pascal Buskens, Ju¨rgen Klankermayer, and Walter Leitner* **J. AM. CHEM. SOC.** 9 VOL. 127, NO. 48, 2005

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

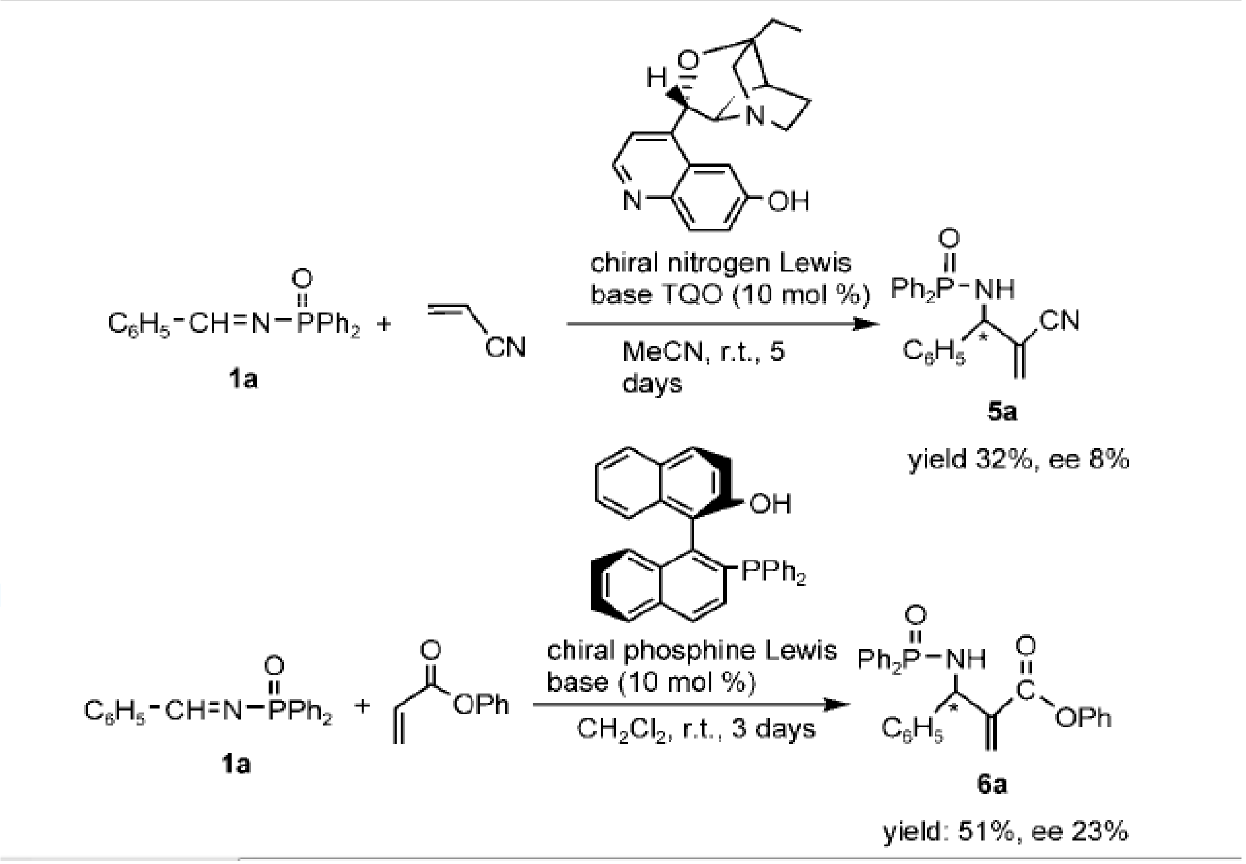
The chiral catalyst **CP1** did not induce any racemization on a similar time scale.



Min Shi,* *J. Org. Chem.* **2007**, *72*, 9779-9781

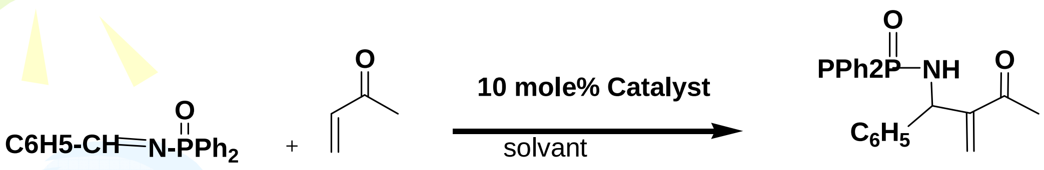
Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

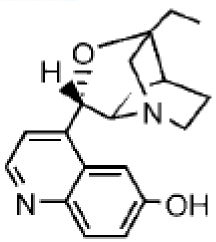
However,catalyst **CP1** could not give good enantiomeric excess in the reaction of *N*-arylmethylidenediphenylphosphinamides with activated alkenes such as MVK, acrylonitrile, or phenyl acrylate



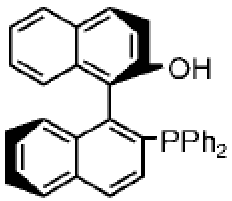
Min Shi,* Gui-Ling Zhao Adv. Synth. Catal. 2004, 346, 1205 –1219

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:



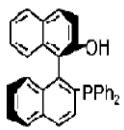


chiral nitrogen Lewis base TQO



chiral phosphine Lewis base

Table 18. Catalytic, asymmetric *aza*-Baylis–Hillman reactions of *N*-benzylidenediphenylphosphinamide (**1a**; 1.0 equiv.) with MVK (1.2 equiv.) in the presence of chiral phosphine and nitrogen catalysts (10 mol %).

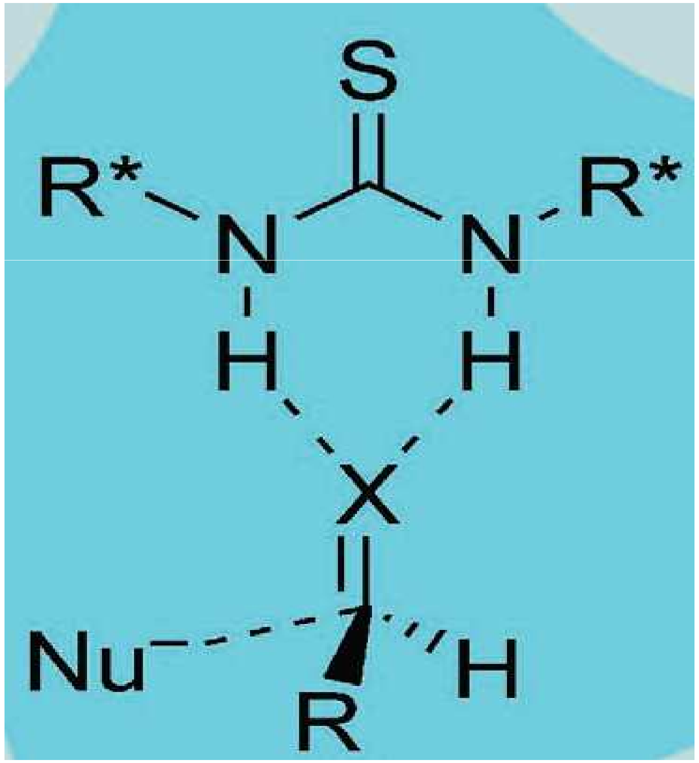
Entry	Catalyst	Solvent	Temp. [°C]	Time [h]	Yield [%][a] 2a	ee [%][b]	$[\alpha]_D$[c]
1	TQO	DMF	r.t.	48	43	23	+7.7
2		CH_2Cl_2	r.t.	48	73	28	+8.0
3		MeCN	r.t.	48	13	12[d]	+3.0
4		DMF	–20	72	32	23	+8.4
5		CH_2Cl_2	–20	120	<10	ND[e]	ND
6		DMF	r.t.	48	27	38	+9.7
7		CH_2Cl_2	r.t.	48	82	47	+14.6
8		CH_2Cl_2	–20	120	<10	ND	ND
9		DMF	–20	72	15	43[d]	+13.2
10		THF	r.t.	72	26	31[d]	+8.9

[a] Yields of isolated products.
[b] Determined by chiral HPLC.
[c] Measured in chloroform at 20 °C.
[d] Calculated by comparing the optical rotation.
[e] Not determined.

Min Shi,* Gui-Ling Zhao Adv. Synth. Catal. 2004, 346, 1205 –1219

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

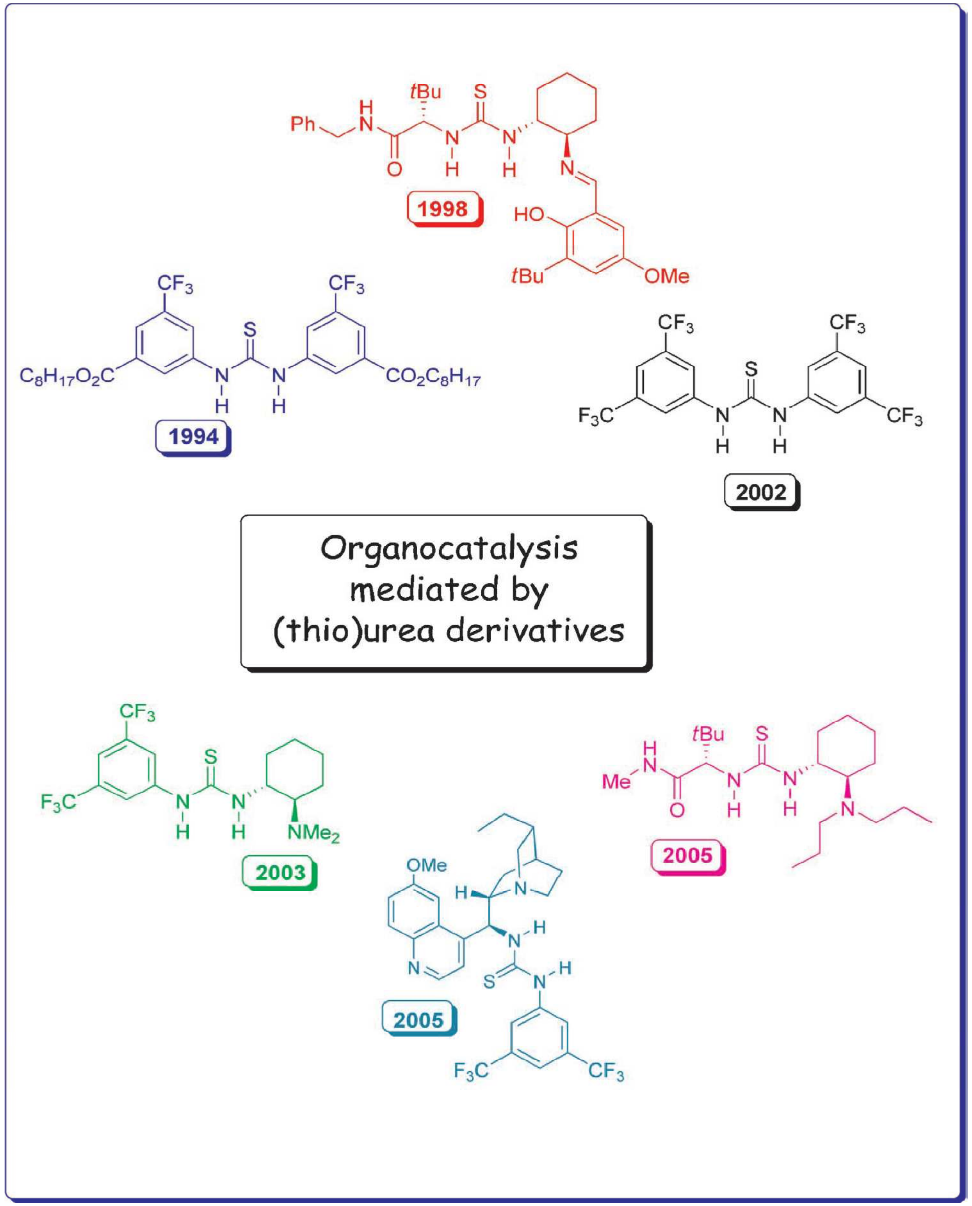
(thio-)urea group might also give high catalytic activity and good asymmetric induction, because the acidic NH protons provide good opportunity to form a hydrogen bond, which may stabilize certain intermediates



Angew. Chem. Int. Ed. 2006, 45, 1520 – 1543

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

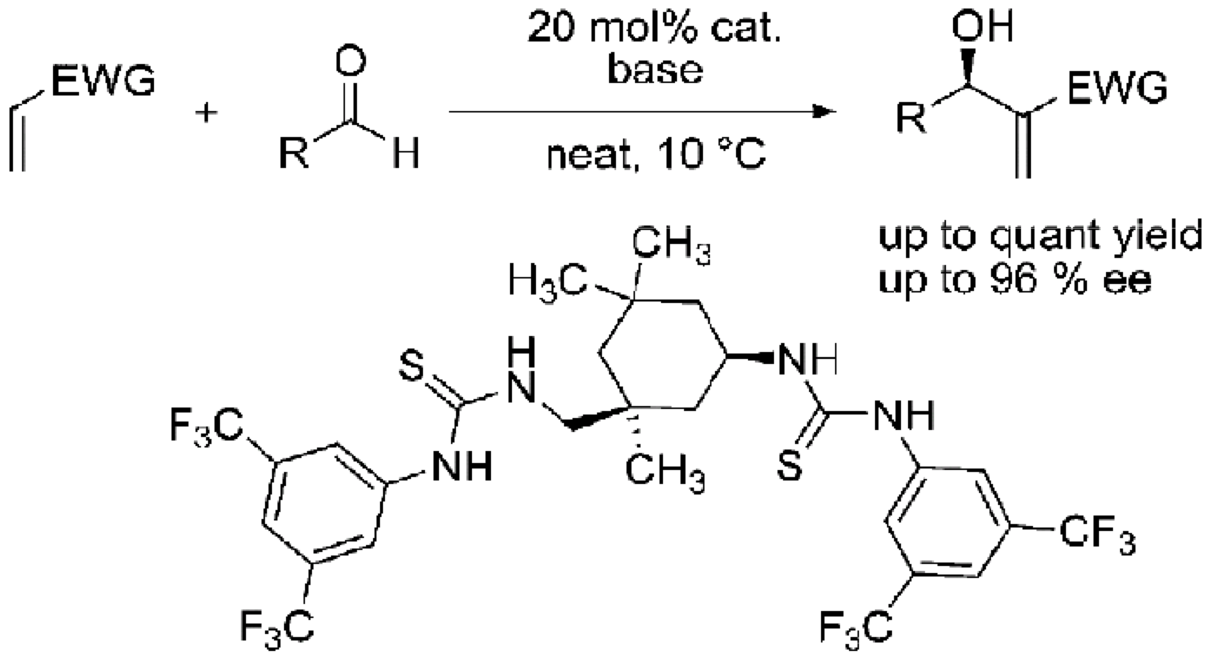
Organocatalysis mediated by (thio) urea derivatives



Stephen J. Connon Chem. Eur. J. 2006, 12, 5418 –5427

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

In Baylis Hilman reaction previously used organocatalyst which has thio urea functional group and give quantitative yield and high ee.

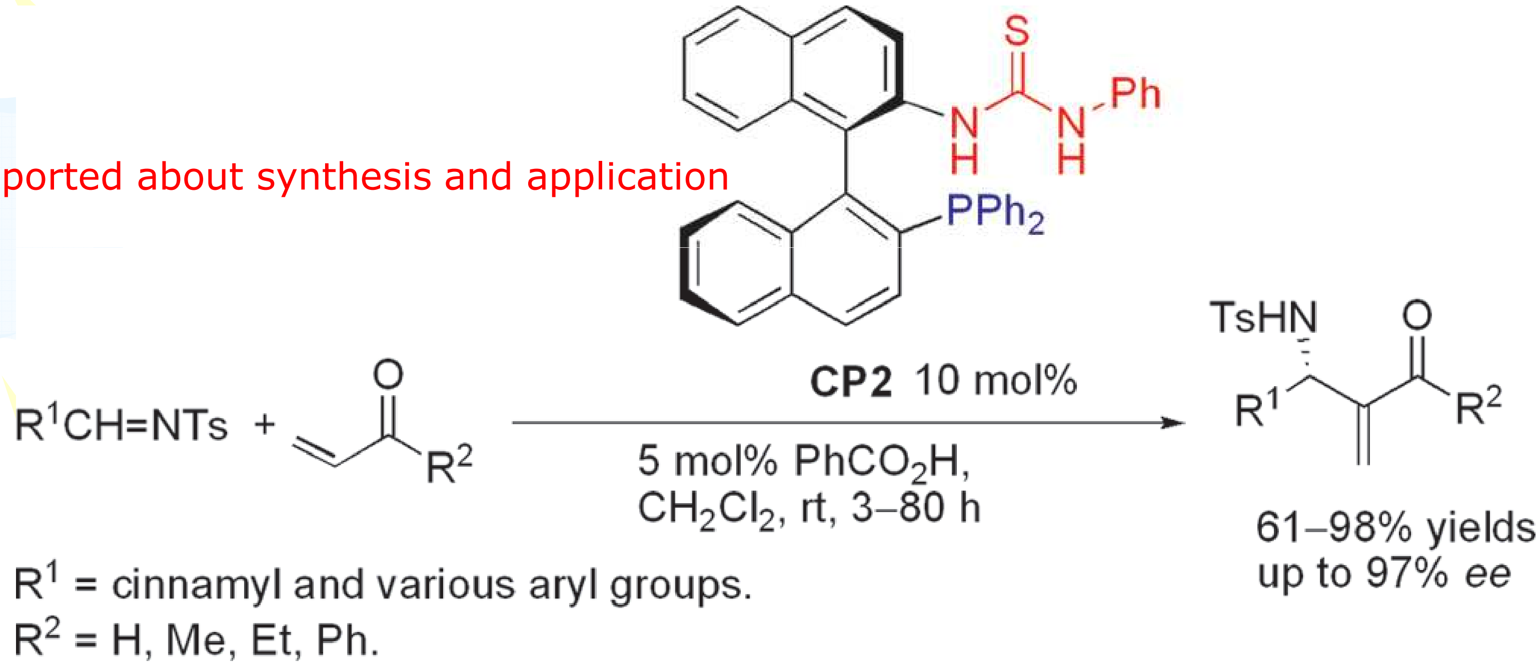


Albrecht Berkessel,* Katrin Roland, Org. Lett., Vol. 8, No. 19, 2006

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

The chiral thiourea-phosphine **CP2** in combination with benzoic acid was a very successful catalytic system for the aza-MBH reaction of *N*-tosyl imines with MVK, PVK, EVK.

First reported about synthesis and application

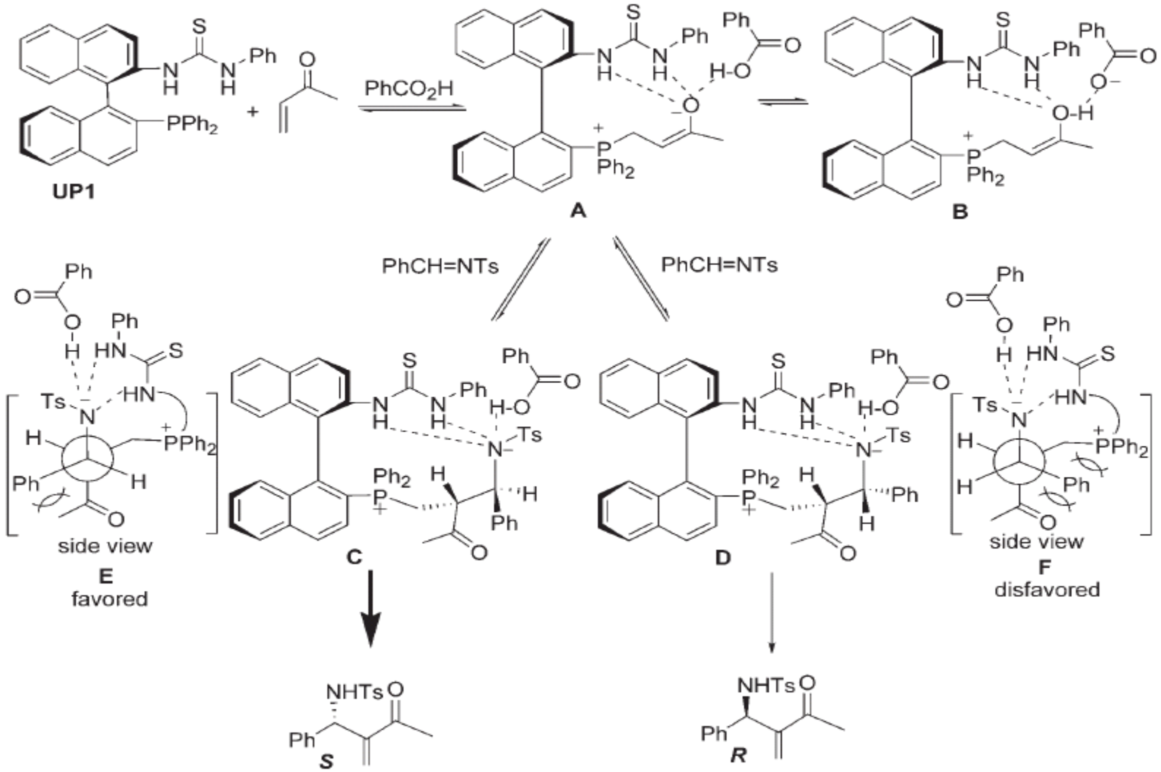


Yong-Ling Shi and Min Shi Adv. Synth. Catal. 2007, 349, 2129 –2135

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

A new kind of bifunctional (thio)ureaphosphine catalyst.

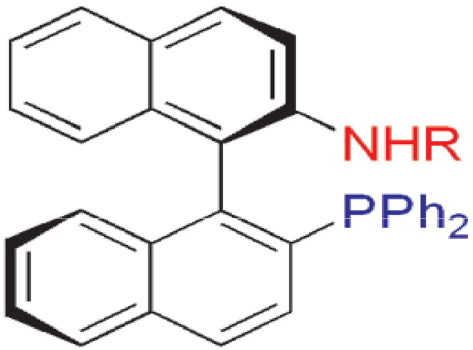
A plausible reaction mechanism.



Yong-Ling Shi and Min Shi Adv. Synth. Catal. 2007, 349, 2129 –2135

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

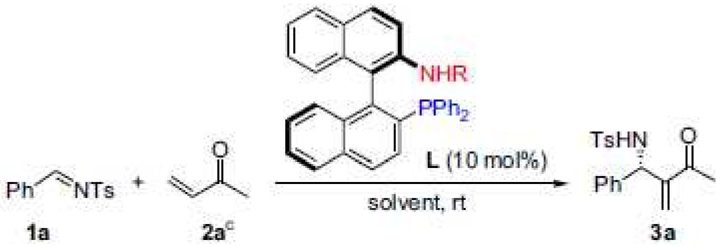
In order to further improve the catalytic activity and enantioselectivity, designed and synthesized a series of bifunctional chiral phosphine amides



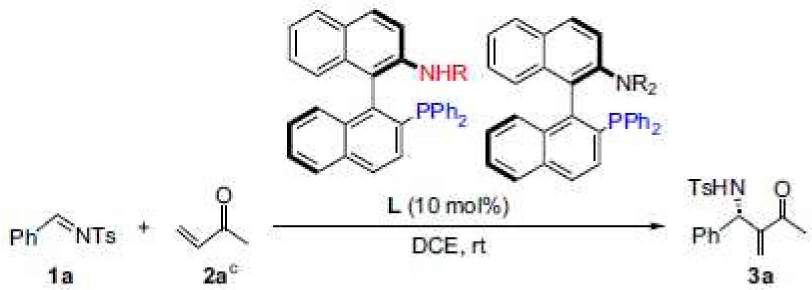
CP3: R = SO_2CH_3; **CP4**: R = SO_2CF_3,
CP5: R = $SO_2C_6H_4CH_3$-*p*; **CP6**: R = COC_6H_5;
CP7: R = $COCH_3$; **CP8**: R = CO_2CH_3; **CP9**: R = $PO(C_6H_5)_2$

M.-J. Qi et al. / Tetrahedron 64 (2008) 1181e1186

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

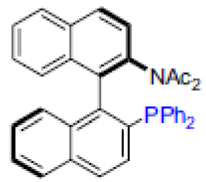


Entry	Catalyst	Solvent	Time (h)	Yield[a] (%)	ee[b] (%)
1	L1	DCM	72	99	75
2	L1	PhMe	72	99	51
3	L1	THF	120	49	45
4	L1	CH_3CN	74	99	75
5	L1	$CHCl_3$	72	99	82
6[d]	L1	DCM	48	99	61
7[e]	L1	DCM	90	96	90
8	L5	DCM	24	99	88
9[e]	L5	DCM	24	99	95
10	L5	PhMe	160	90	27
11	L5	THF	160	91	39
12	L5	DMSO	36	89	52
13	L5	CH_3CN	48	94	79
14[d]	L5	DCM	36	99	86
15[e]	L5	DCM	20	95	91
16[f]	L5	DCM	23	89	96



Entry	Catalyst	Time (h)	Yield[a] (%)	ee[b] (%)
1	L1	48	95	89
2	L2	48	0	—
3	L3	96	94	86
4	L4	48	89	78
5	L5	48	99	93
6	L6	60	91	59
7	L7	96	85	72
8	L8	96	0	—

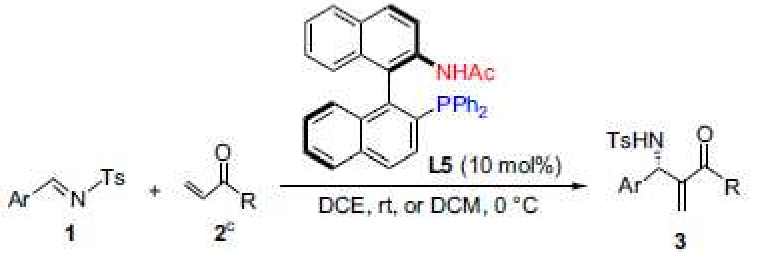
L1: R = SO_2CH_3
L2: R = SO_2CF_3
L3: R = $SO_2C_6H_4CH_3$-*p*
L4: R = COC_6H_5
L5: R = $COCH_3$
L6: R = CO_2CH_3
L7: R = $PO(C_6H_5)_2$



L8

M.-J. Qi et al. / Tetrahedron 64 (2008) 1181e1186

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

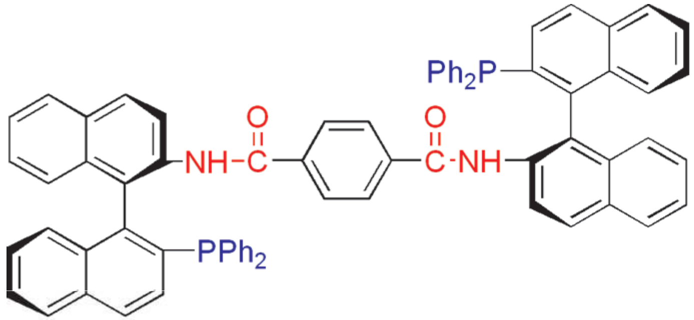


Entry	Ar	R	DCE at rt			DCM at 0 °C		
			Time (h)	Yield[a] (%)	ee[b] (%)	Time (h)	Yield[a] (%)	ee[b] (%)
1	*p*-BrC_6H_4 **1b**	Me	48	**3b**, 98	82	24	**3b**, 86	90
2	*p*-$NO_2C_6H_4$ **1c**	Me	24	**3c**, 75	80	7	**3c**, 99	90
3	*o*-$NO_2C_6H_4$ **1d**	Me	12	**3d**, 78	46	28	**3d**, 85	61
4	*m*-$NO_2C_6H_4$ **1e**	Me	12	**3e**, 99	80	8	**3e**, 99	82
5	*o*-ClC_6H_4 **1f**	Me	12	**3f**, 76	65	48	**3f**, 80	65
6	*p*-ClC_6H_4 **1g**	Me	36	**3g**, 99	82	24	**3g**, 99	90
7	*m*-ClC_6H_4 **1h**	Me	12	**3h**, 89	84	24	**3h**, 90	89
8	*p*-FC_6H_4 **1i**	Me	36	**3i**, 99	85	24	**3i**, 90	91
9	*m*-FC_6H_4 **1j**	Me	20	**3j**, 77	75	24	**3j**, 91	80
10	*p*-$MeOC_6H_4$ **1k**	Me	48	**3k**, 99	46	48	**3k**, 98	82
11	*p*-MeC_6H_4 **1l**	Me	60	**3l**, 99	84	48	**3l**, 99	90
12	C_6H_5 **1a**	Et				60	**3m**, 95	74
13	*p*-BrC_6H_4 **1b**	Et				60	**3n**, 80	65
14	*p*-ClC_6H_4 **1g**	Et				60	**3o**, 86	51

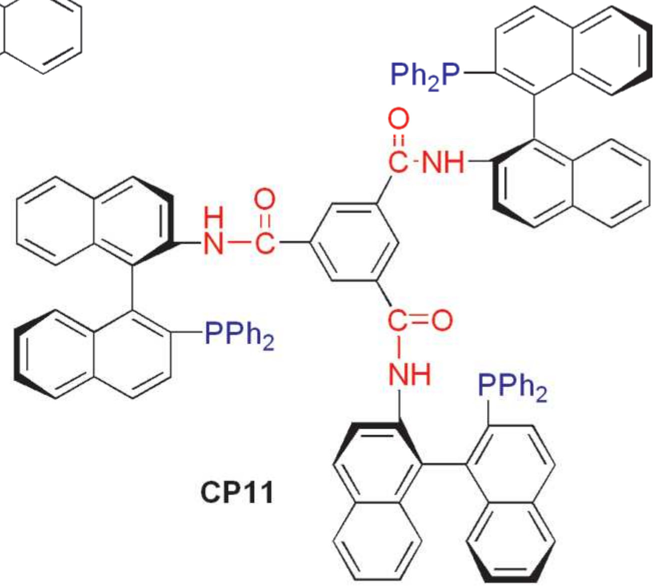
M.-J. Qi et al. / Tetrahedron 64 (2008) 1181e1186

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

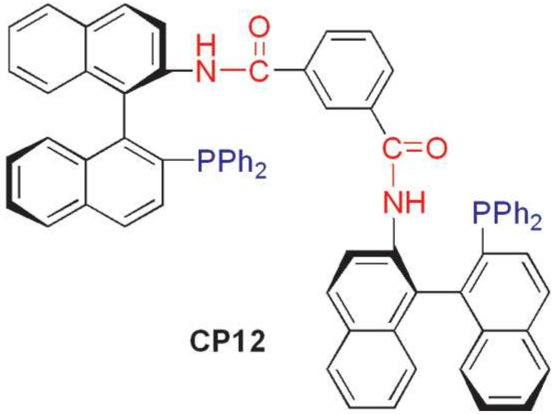
Three sterically congested bifunctional chiral phosphane-amides, **synthesized** in order to evaluate the steric effect for asymmetric induction.



CP10



CP11

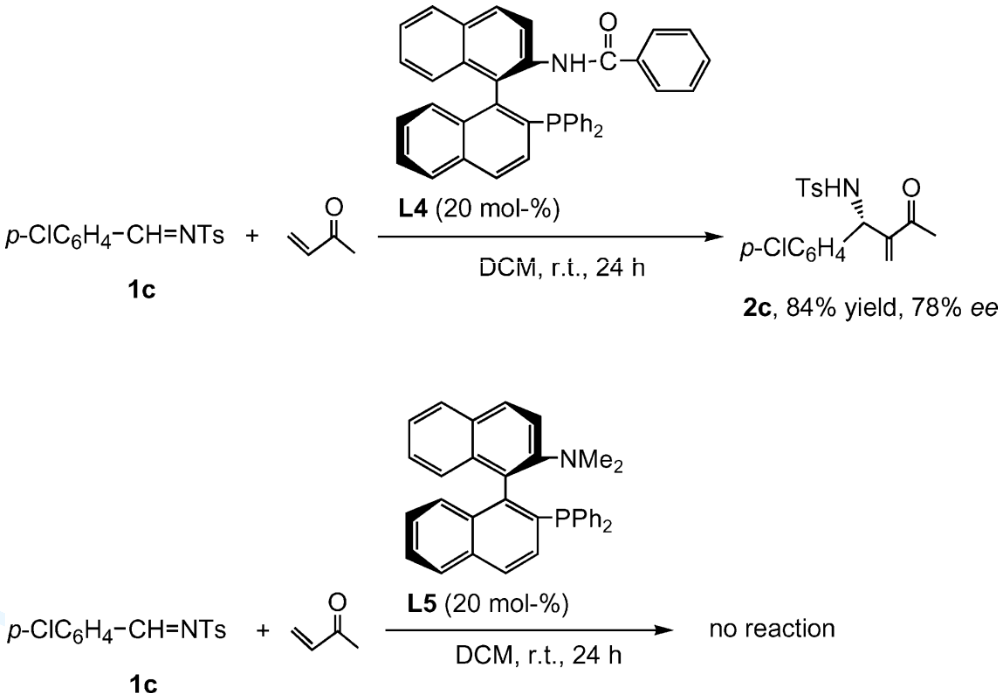


CP12

X.-Y. Guan, Y.-Q. Jiang, M. Shi *Eur. J. Org. Chem.* ***2008, 2150–2155***

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

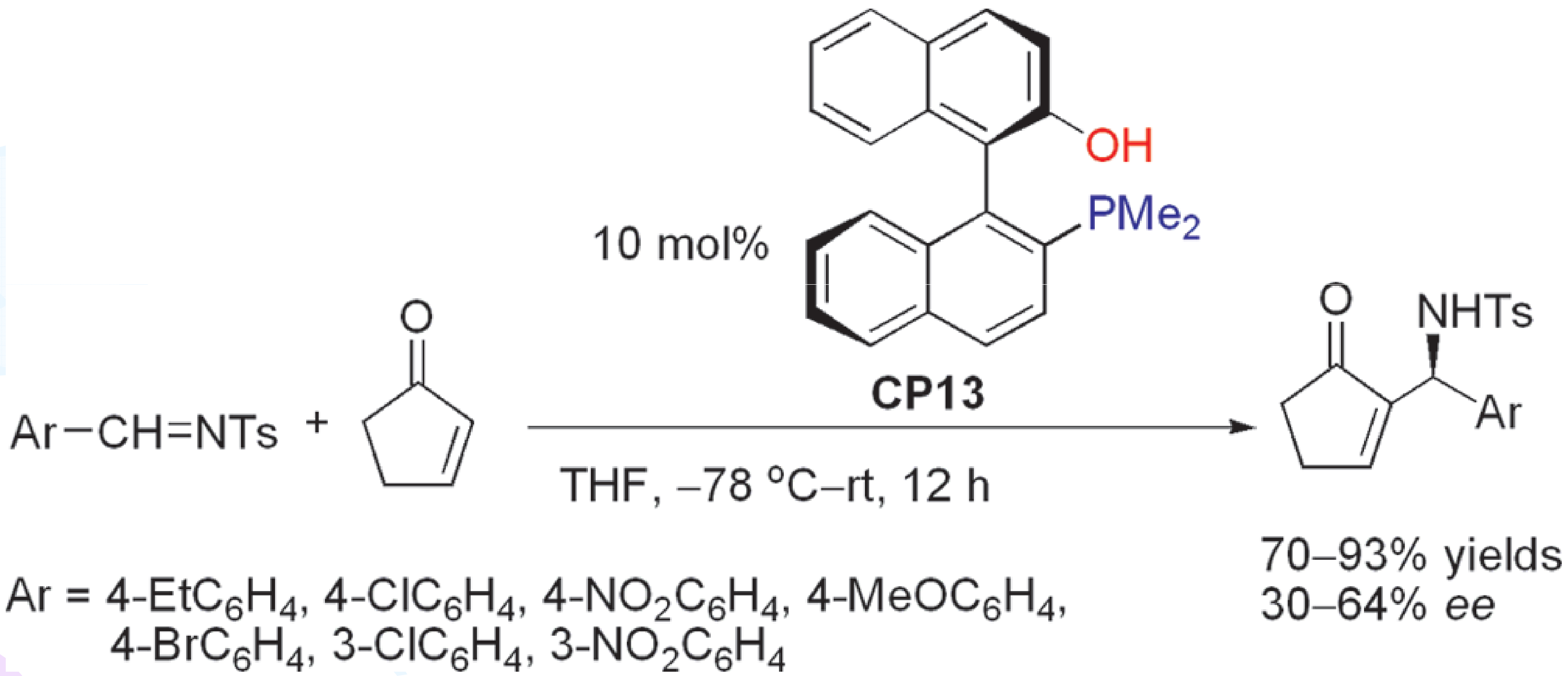
The chiral sterically congested phosphane-amide bifunctional phosphanes



X.-Y. Guan, Y.-Q. Jiang, M. Shi *Eur. J. Org. Chem.* ***2008, 2150–2155***

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

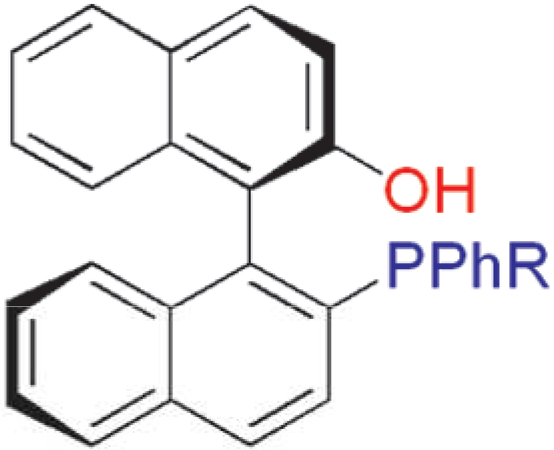
The nucleophilicity of the phosphorus center in the catalyst may affect catalytic activity.



Shi, M.; Li, C.-Q. *Tetrahedron: Asymmetry 2005, 16, 1385–1391.*

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

The nucleophilicity of the phosphorus center in the catalyst may affect catalytic activity.



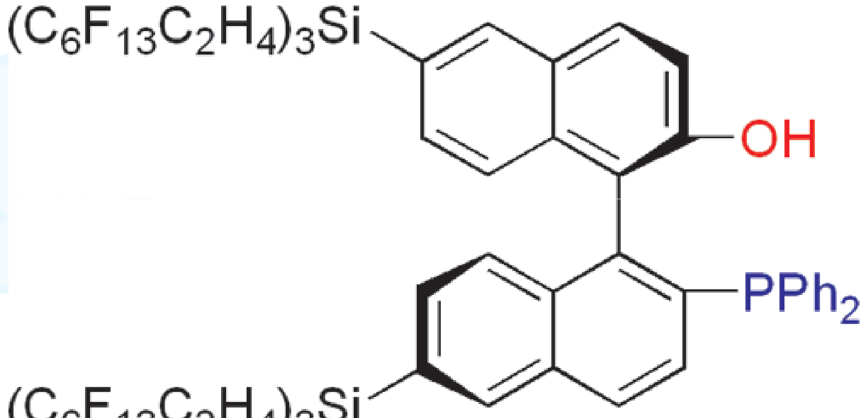
CP14: R = Et
CP15: R = *i*Pr
CP16: R = *n*Bu
CP17: R = Cy

Structures of more nucleophilic phosphane-phenol type bifunctional chiral phosphines.

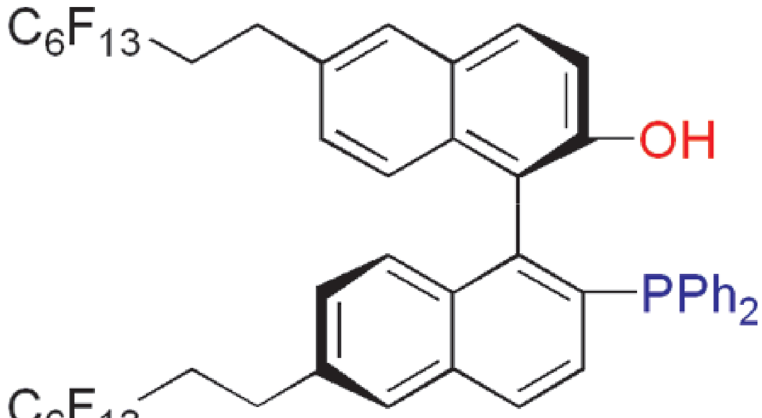
Lei, Z.-Y.; Ma, G.-N.; Shi, M. *Eur. J. Org. Chem. 2008, 3817–3820.*

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

A few reports have demonstrated that introducing a longchainalkyl group in a variety of chiral ligands could improve the catalytic activity and enantioselectivity in homogeneous asymmetric.



CP18



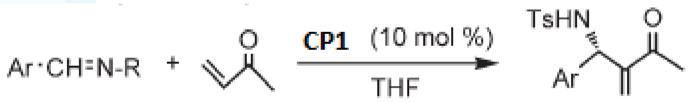
CP19 More effective

Phosphane-phenol-type bifunctional chiral phosphines bearing perfluoroalkane chains.

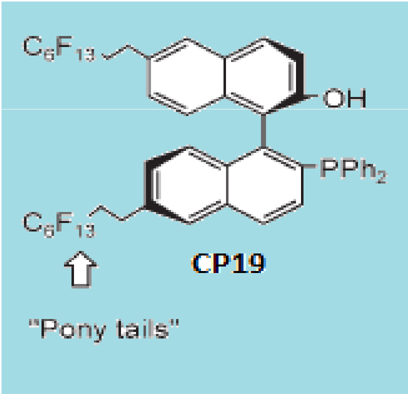
Min Shi et al. Adv. Synth. Catal. 2005, 347, 1781 – 1789

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

catalyst **CP19** was more effective in the aza-MBH reaction of *N-tosyl imines*with MVK than the previously reported original chiral phosphine **CP1.**



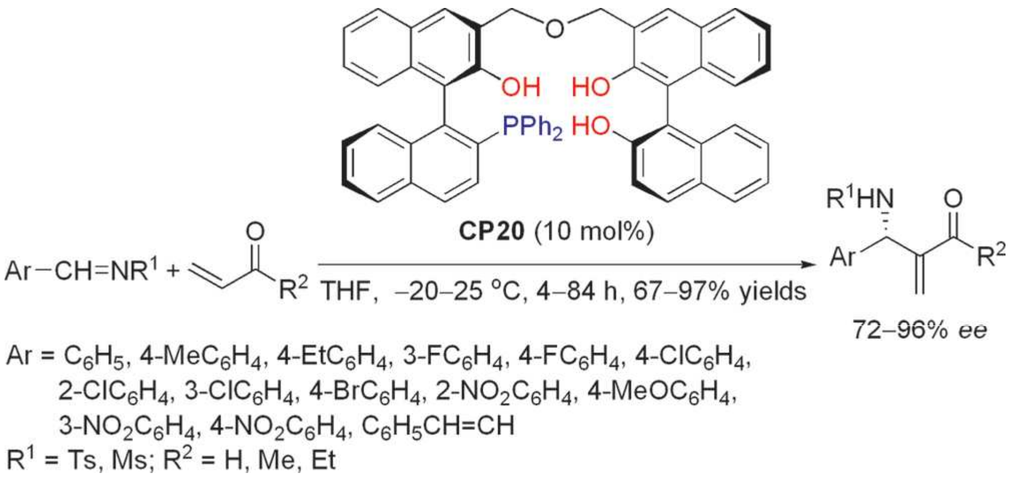
Up to 88% yield, and 82% ee.

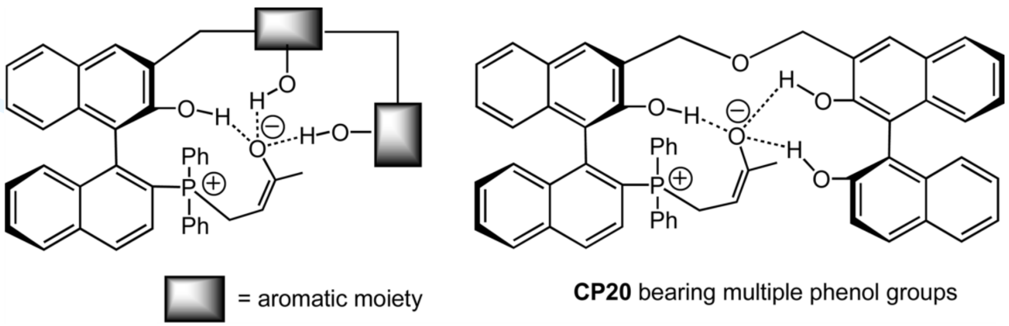


Shi M. Adv. Synth. Catal. 2005, 347, 1781 – 1789

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

Another approach to improve the catalytic activity and enantioselectivity is to increase the number of hydrogen bond donors in the bifunctional chiral phosphines.

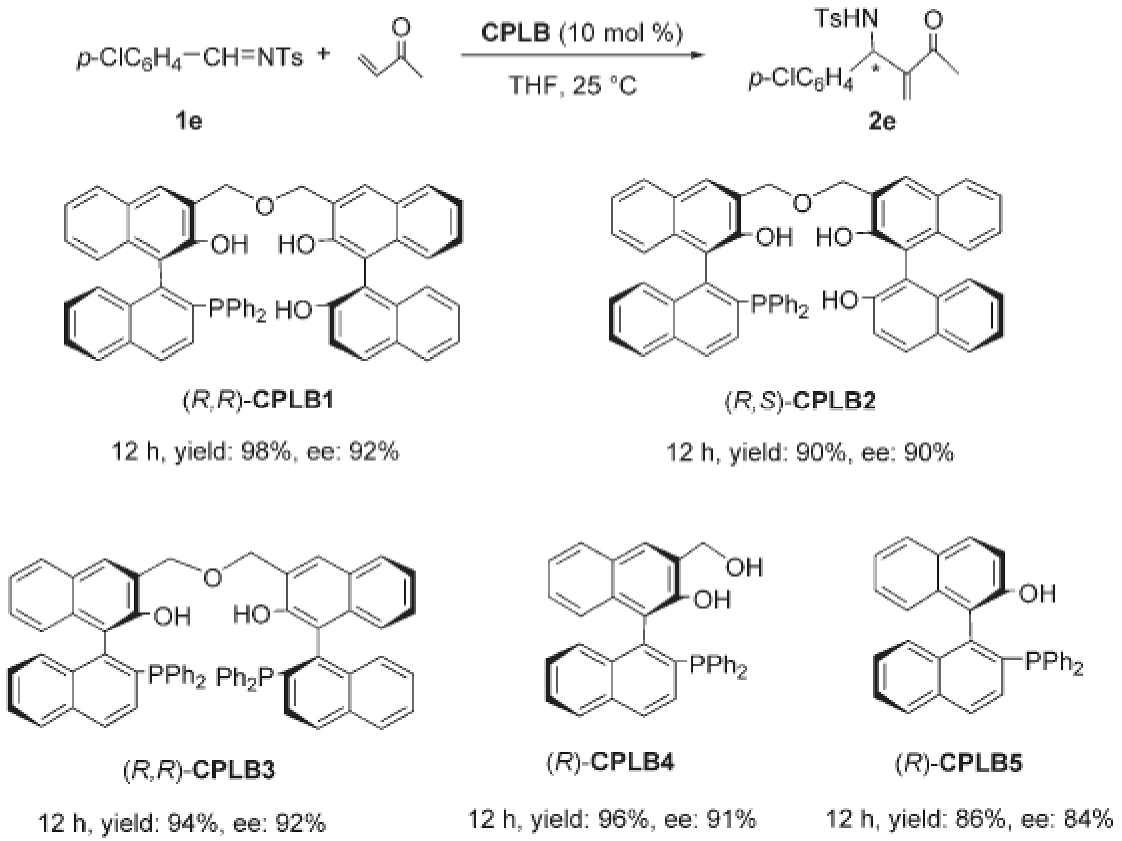




CP20 bearing multiple phenol groups

Min Shi* et al. Adv. Synth. Catal. 2006, 348, 973– 979

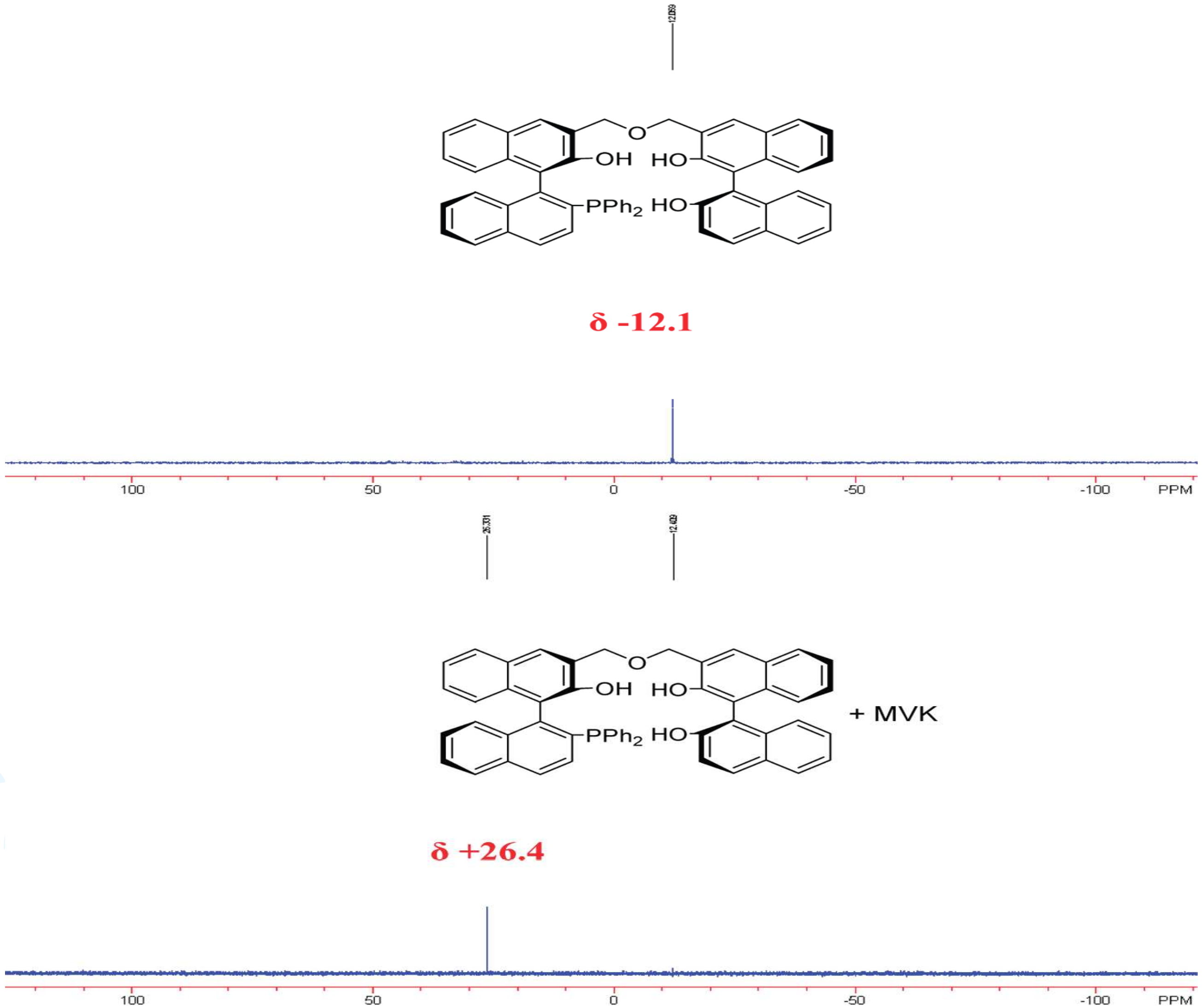
Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:



Min Shi* et al. Adv. Synth. Catal. 2006, 348, 973– 979

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

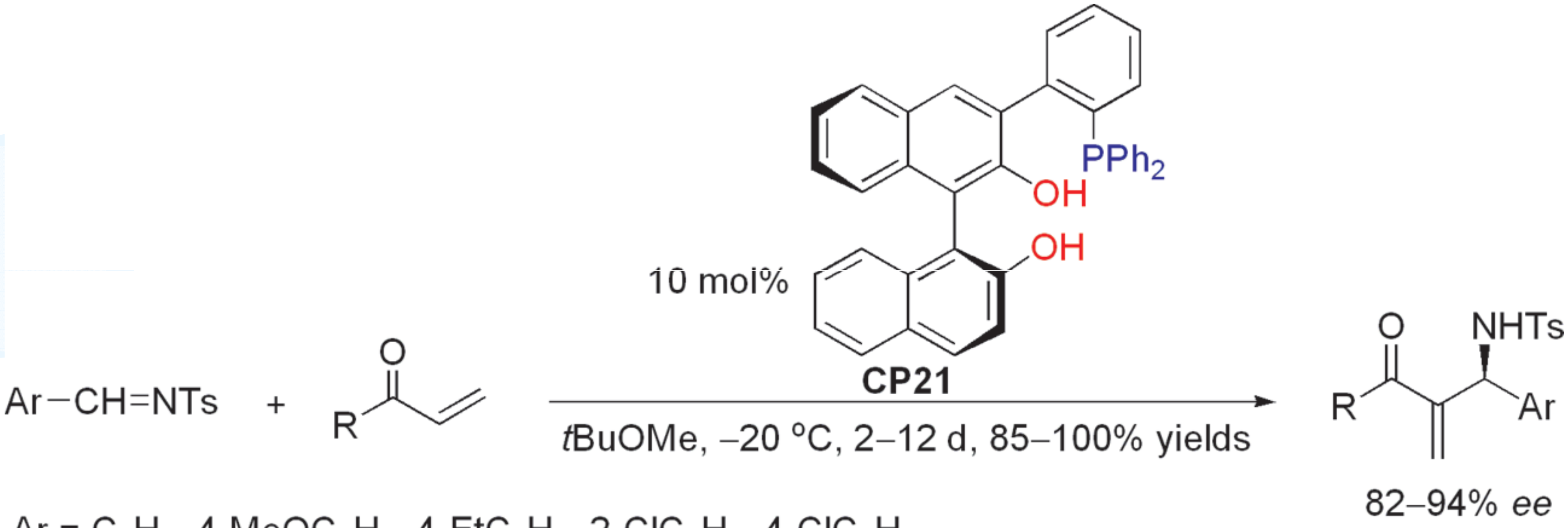
The 31P NMR measurements for **CP20 and the mixture of CP20 and MVK**



Min Shi* et al. Adv. Synth. Catal. 2006, 348, 973– 979

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

Catalyst **CP21 could effectively** catalyze asymmetric aza-MBH reaction of *N-tosyl imines with* vinyl ketones



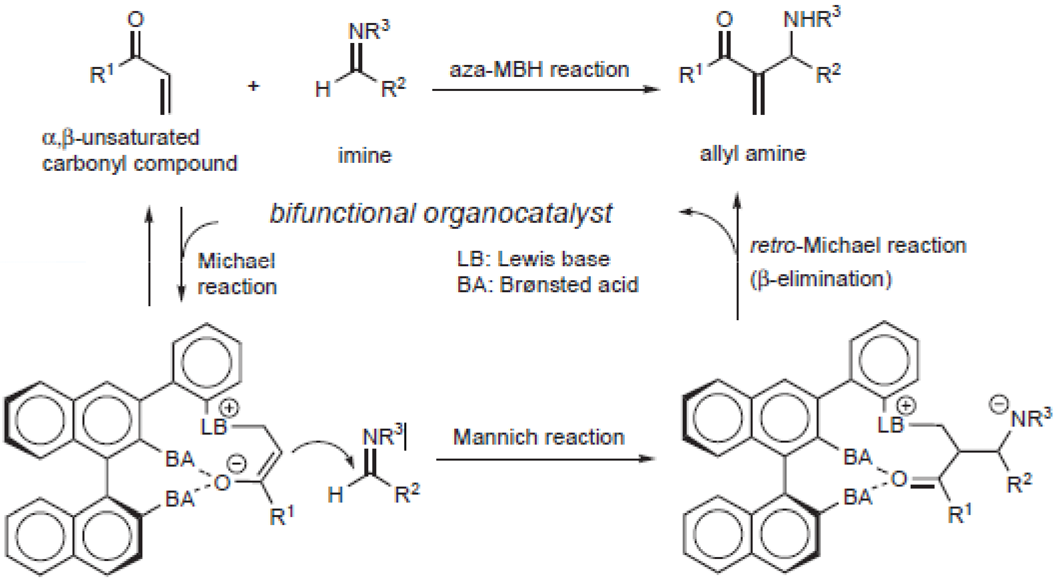
Ar = C_6H_5, 4-MeOC_6H_4, 4-EtC_6H_4, 2-ClC_6H_4, 4-ClC_6H_4, 4-$NO_2C_6H_4$, 4-BrC_6H_4, 2-furyl, 1-naphthyl, 2-naphthyl

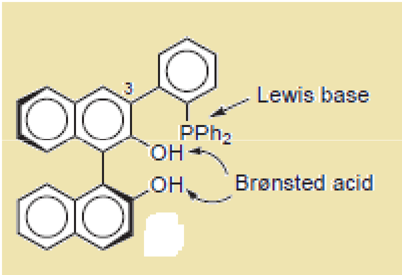
R = Me, Et, Ph

Matsui, K.; Takizawa, S.; Sasai, H. *Synlett* 2006, 761–765

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

The aza-MBH reaction promoted by asymmetric bifunctional catalysts

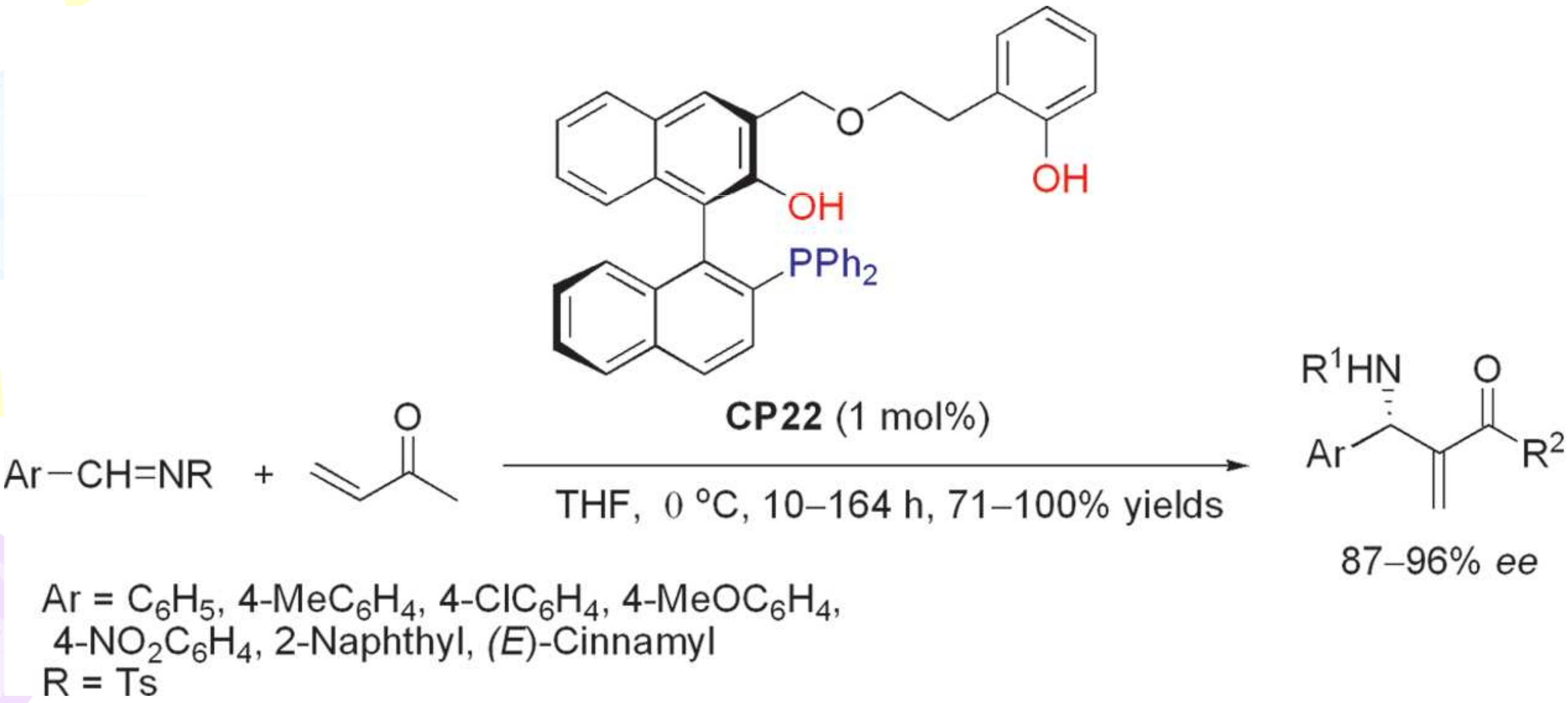




Matsui, Shinobu Takizawa, Hiroaki Sasai* Synlett 2006, No. 5, 761–765

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

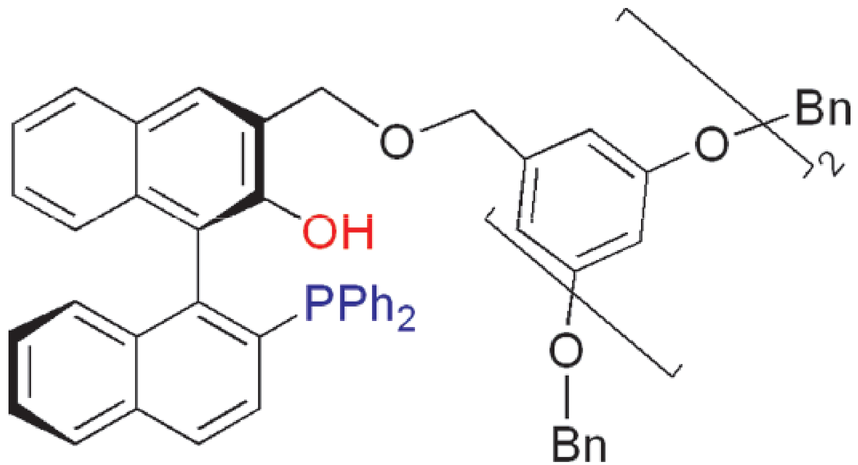
biphenol-based bifunctional catalyst **CP22 for aza-** MBH reaction of *N-tosyl imines with MVK High e*nantioselectivity up to 96% ee was achieved by **CP22 with** catalyst loading of 1 mol %.



Ito, K.; Nishida, K.; Gotauda, T.. *Tetrahedron Lett.* 2007, *48*, 6147–6149.

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

In order to recycle the catalyst, immobilized **CP1 on** a series of dendrimers. It was found that the dendrimerimmobilized catalyst **CP23 was more effective** than catalyst **CP1 for the aza-MBH reaction of *N-sulfonyl***imines with MVK, EVK, or acrolein.



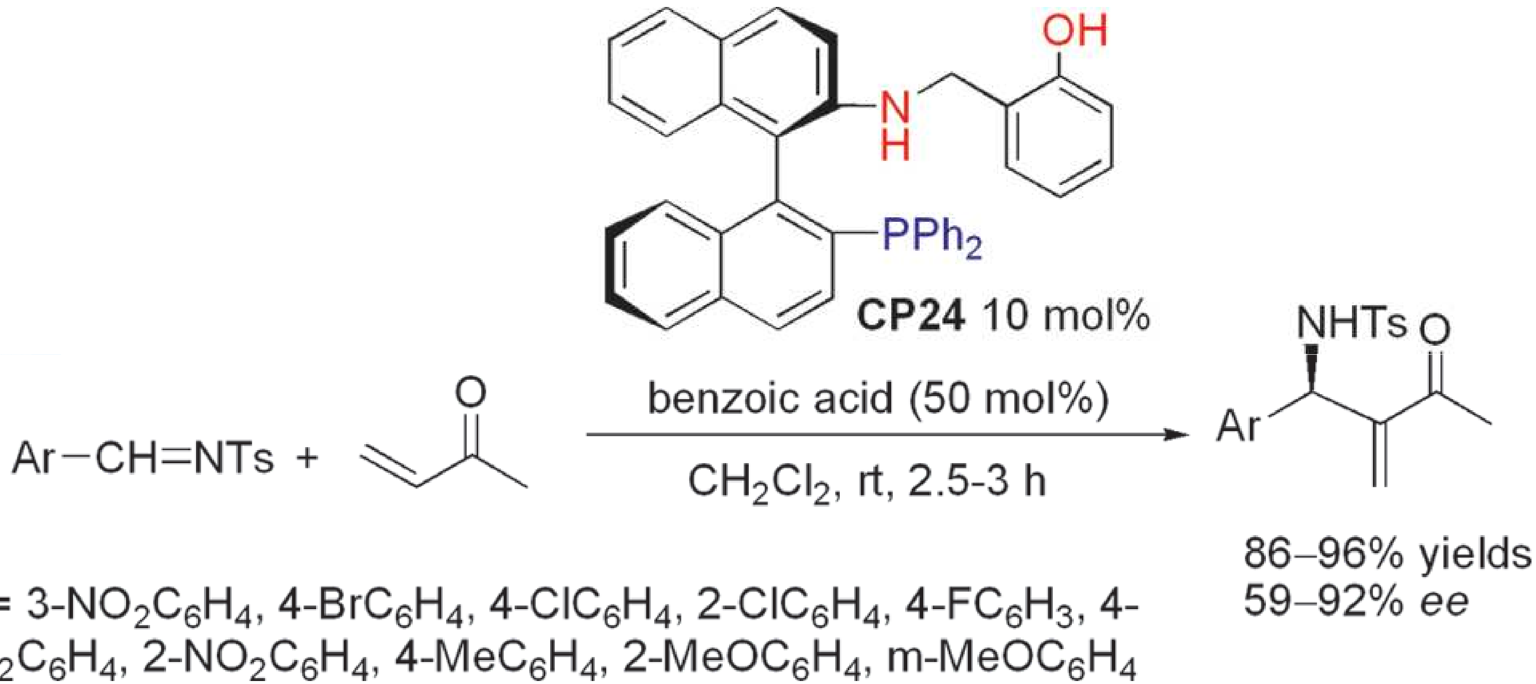
CP23

Dendrimer immobilized phosphine-phenol type of multifunctional chiral phosphines

A.-M.; Servin,P.; Laurent, R.; Majoral, J.-P. *Chem. Soc. Rev.* 2008, *37*, 56–67.

Multifuntional Chiral Phosphine Catalysts in Aza-Morita-Baylis-Hillman Reaction:

Trifunctional Phosphine Organocatalyst-Promoted Aza- MBH Reaction

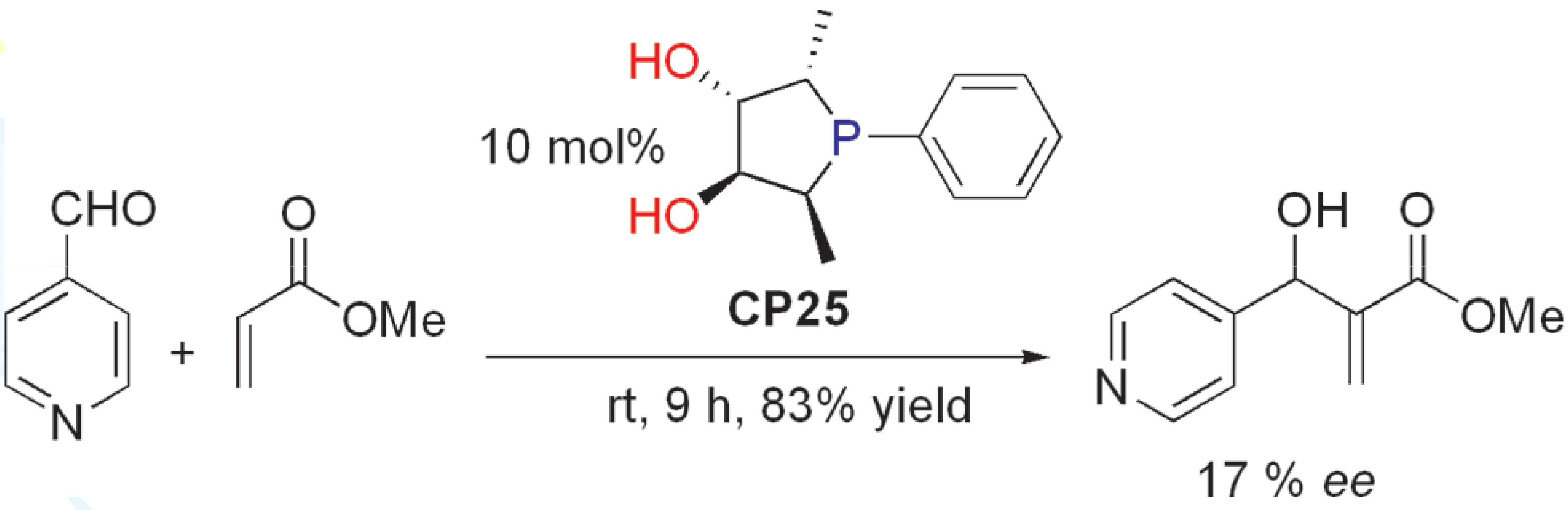


It was used for the first time to catalyze aza-Morita- Baylis–Hillman reactions between N-tosylimines and methyl vinyl ketone with fast reaction rates and good enantioselectivity at room temperature

Jean-Marc Garnier,a Christopher Anstiss,a and Fei Liua,*Adv. Synth. Catal. 2009, 351, 331 – 338

Multifunctional Chiral Phosphine Catalysts in Morita-Baylis-Hillman Reaction

CP25 catalyzed MBH reaction between 4-pyridinecarboaldehyde and methyl acrylate

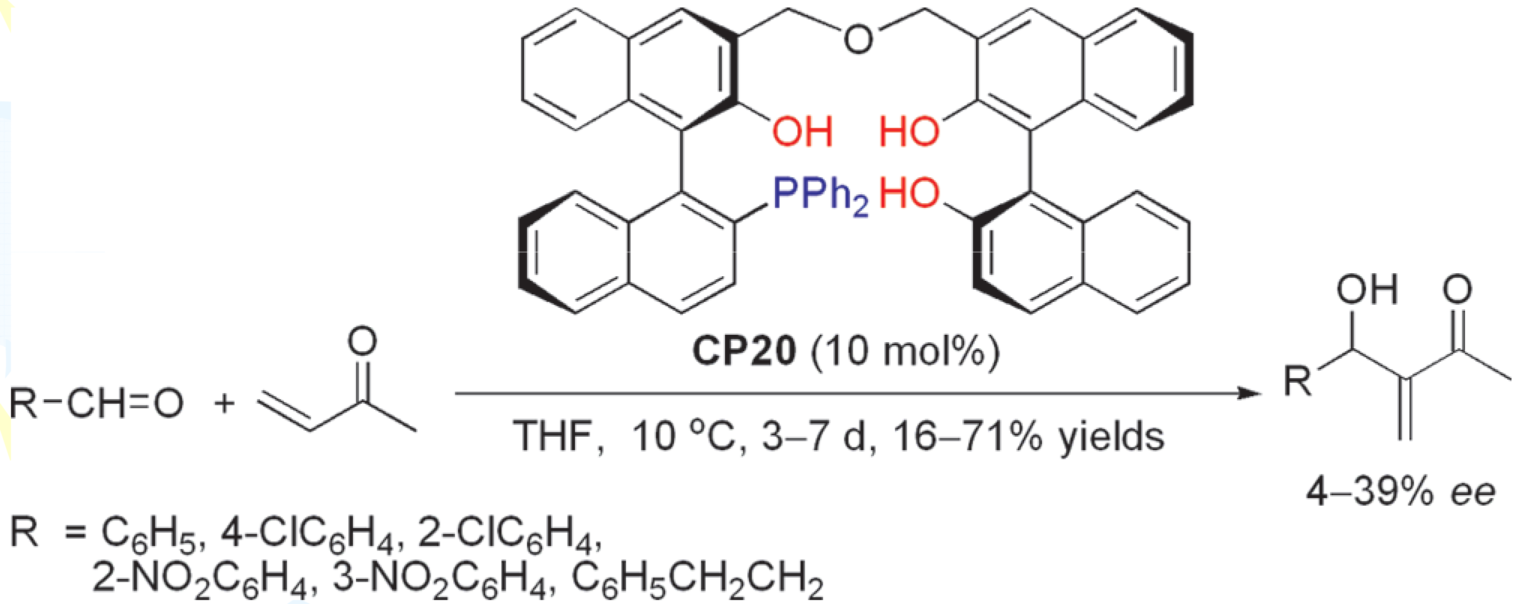


Phosphane-Hydroxy-Type Multifunctional Chiral Phosphine-Catalyzed Asymmetric MBH Reaction

Wenge Li, Zhaoguo Zhang, Dengming Xiao, and Xumu Zhang* *J. Org. Chem.* ***2000, 65, 3489-3496***

Multifunctional Chiral Phosphine Catalysts in Morita-Baylis-Hillman Reaction

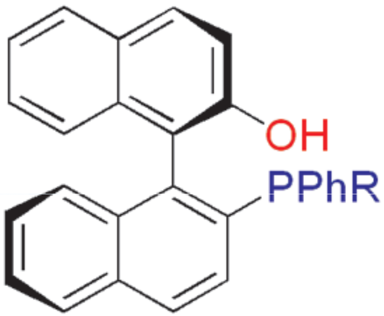
Phosphane-Multiphenol Groups of Chiral Phosphines in Asymmetric MBH Reaction of Aldehydes with MVK



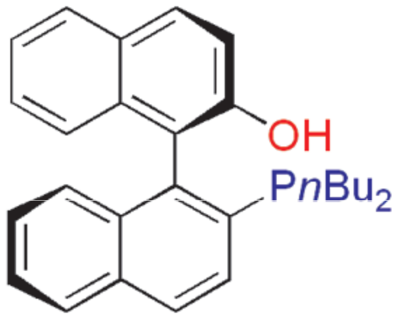
Shi, M.; Liu, Y.-H.; Chen, L. *Chirality 2007, 19, 124–128.*

Multifunctional Chiral Phosphine Catalysts in Morita-Baylis-Hillman Reaction

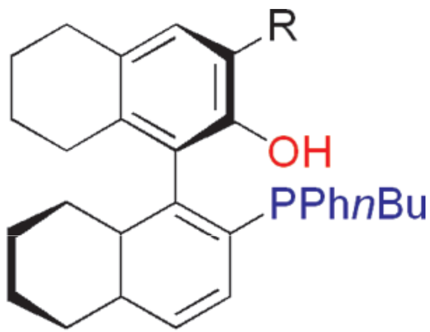
Unfortunately, the effective catalyst **CP1 for aza-MBH reaction did** not show catalytic activity for the reaction of 3-phenylpropanal and MVK. **CP16 was still the most effective catalyst with** respect to a wide range of substrates, affording the corresponding products in good yields with moderate ee's.



CP14: R = Et
CP15: R = *i*Pr
CP16: R = *n*Bu
CP17: R = Cy
CP26: R = *i*Bu



CP27



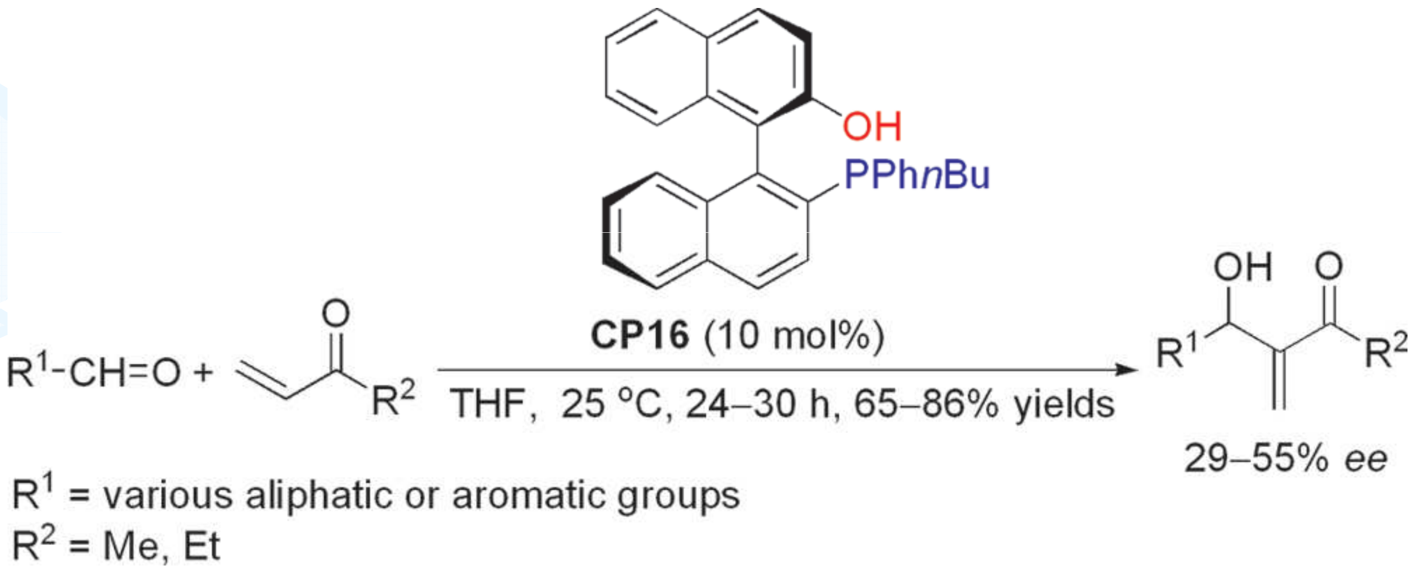
CP28: R = H
CP29: R = Ph
CP30: R = Br

Structures of more nucleophilic phosphine-phenol-type bifunctional chiral phosphines.

Lei, Z.-Y.; Liu, X.-G.; Shi, M.; Zhao, M. *Tetrahedron: Asymmetry 2008, 19, 2058–2062.*

Multifunctional Chiral Phosphine Catalysts in Morita-Baylis-Hillman Reaction

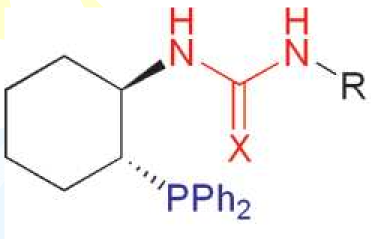
Phosphane-Phenol-Type Multifunctional Chiral Phosphine-Catalyzed Asymmetric MBH Reaction of Aldehydes with R,-Unsaturated Ketones



Lei, Z.-Y.; Liu, X.-G.; Shi, M.; Zhao, M. *Tetrahedron: Asymmetry 2008, 19, 2058–2062.*

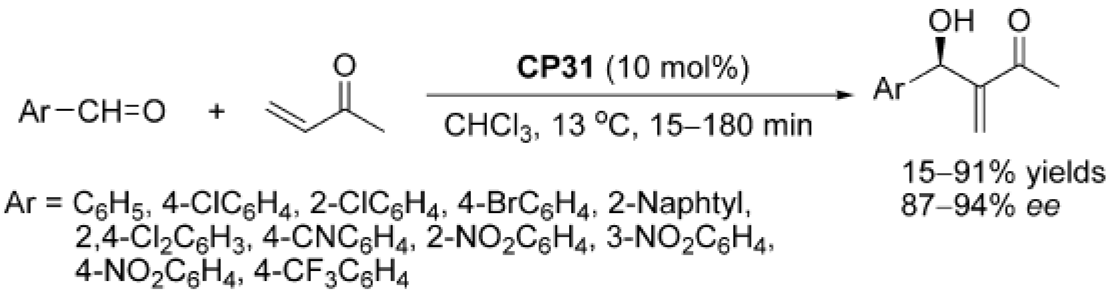
Multifunctional Chiral Phosphine Catalysts in Morita-Baylis-Hillman Reaction

Recently, Wu's group reported a series of chiral phosphino(thio)ureas **CP31-CP36 derived from *trans-2-*** amino-1-(diphenylphosphino)cyclohexane. **CP31 was the best** catalyst for the MBH reaction of various aromatic aldehydes with MVK giving the products with excellent enantiomeric excesses under mild conditions in relative short reaction time.



CP31: X = S, R = C_6H_5
CP32: X = O, R = C_6H_5
CP33: X = S, R = 3,5-$(CF_3)_2C_6H_3$
CP34: X = S, R = 4-ClC_6H_4
CP35: X = S, R = 4-$MeOC_6H_4$
CP36: X = S, R = c-Hexyl

Structures of phosphine-(thio)urea multifunctional chiral phosphines.

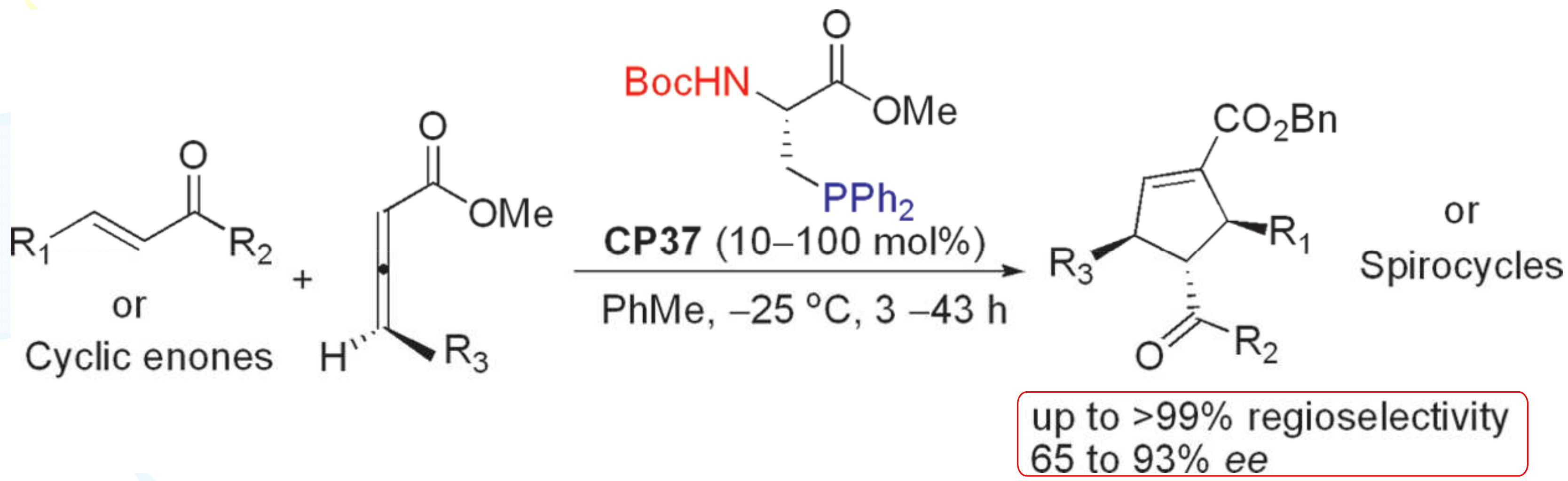


CP31 is the best catalyst for the MBH reaction.
Products with excellent enantiomeric excesses

Yuan, K.; Zhang, L.; Song, H.-L.; Hu, Y.; Wu, X.-Y.. *Tetrahedron Lett.* 2008, *49*, 6262–6264.

Multifunctional Chiral Phosphine Catalysts in Other Reactions

Since 2007, bifunctional chiral phosphines can be applied in reactions beyond MBH/aza-MBH reaction, such as enantioselective [3 + 2] cycloaddition reactions.

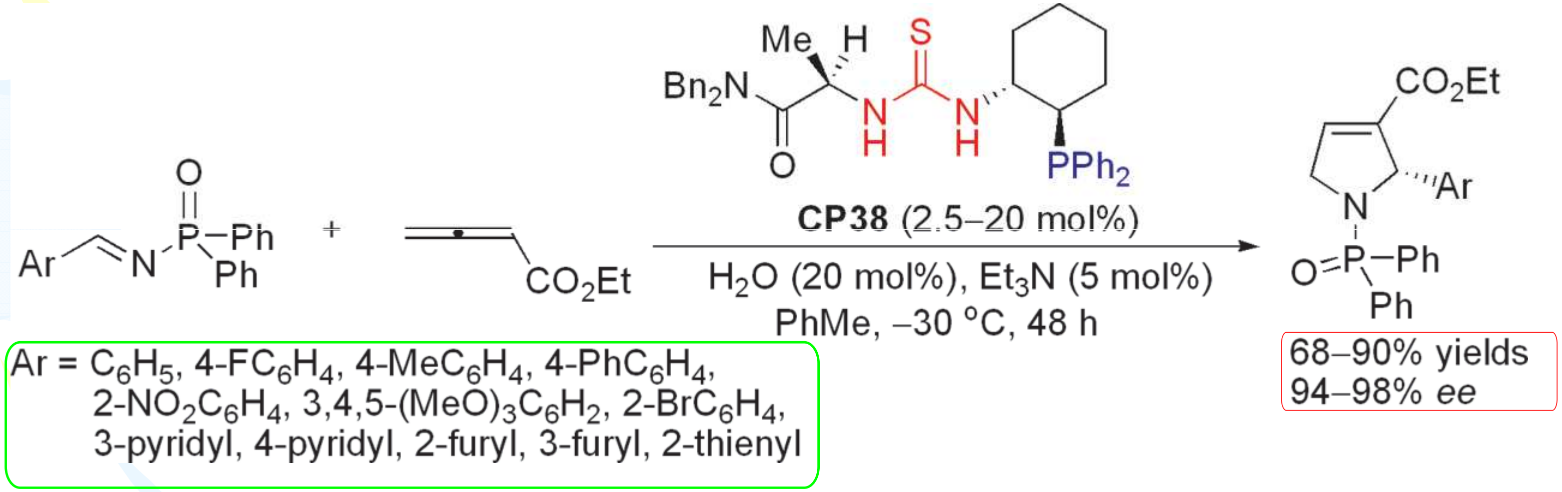


Phosphine-amide-Type Multifunctional Chiral Phosphine Catalyzed Asymmetric [3 + 2]Cycloaddition Reaction

Cowen, B. J.; Miller, S. J. *J. Am. Chem. Soc.* 2007, *129, 10988–10989.*

Multifunctional Chiral Phosphine Catalysts in Other Reactions

More recently, ***Jacobsen*** developed a series of bifunctional phosphorus thiourea derivatives for highly enantioselective synthesis of chiral dihydropyrroles via imine-allene [3 + 2] cycloaddition.

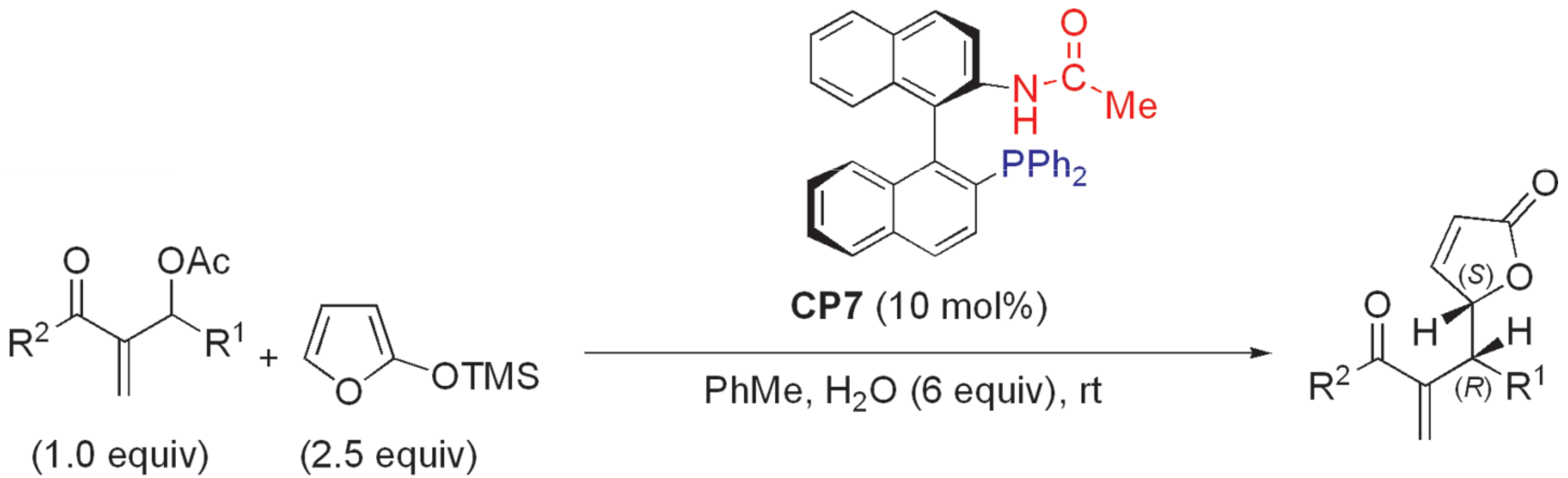


CP38 as the best catalyst

Fang, Y.-Q.; **Jacobsen**, E. N. Cooperative,. *J. Am. Chem. Soc. 2008,* 5660–5661.

Multifunctional Chiral Phosphine Catalysts in Other Reactions

Interestingly, previously developed catalyst **CP7 for** aza-MBH reaction has a new application. Catalyst **CP7** achieved high yield and excellent ee for the reaction of MBH acetates with 2-trimethylsilyloxy furan, which is an effective approach for the asymmetric synthesis of *γ-butenolides.*



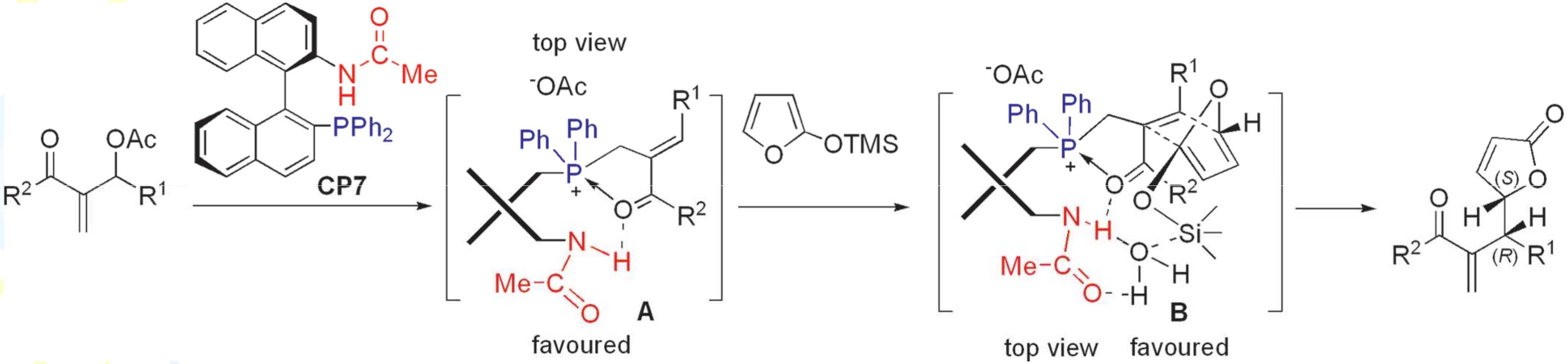
R^1 = aromatic group or C_3H_7, R^2 = Me, Et, OMe

45-98% yields
71-96% *ee*

Jiang, Y.-Q.; Shi, Y.-L.; Shi, M. *J. Am. Chem. Soc. 2008,* 7202

Multifunctional Chiral Phosphine Catalysts in Other Reactions

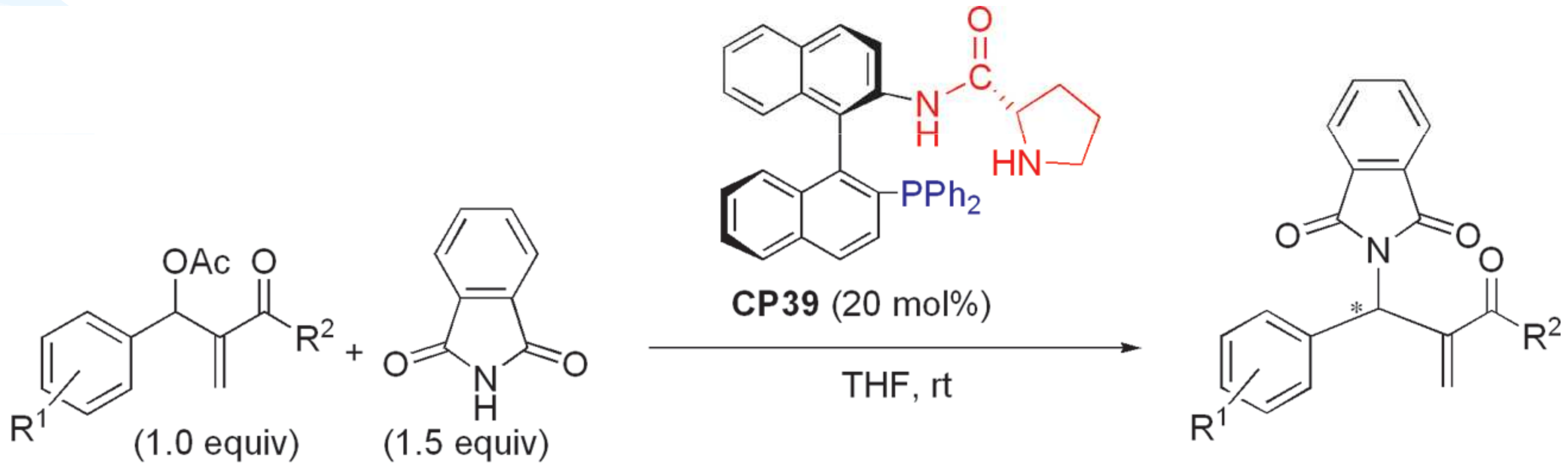
The proposed Mechanism



Jiang, Y.-Q.; Shi, Y.-L.; Shi, M. *J. Am. Chem. Soc. 2008,* 7202

Multifunctional Chiral Phosphine Catalysts in Other Reactions

Chiral Phosphine-Catalyzed Regio- andEnantioselective Allylic Amination of Morita-Baylis-Hillman Acetates



R^1 = H, *m*-NO_2, *p*-Cl, *m*-Cl, *o*-Cl, *p*-Br, *p*-F, *p*-CF_3, *p*-CN, *p*-Me, *m*-Me, *p*-NO_2 , R^2 = Me, Et

70-91% yields
34-58% *ee*

the product in good yields
with moderate ee

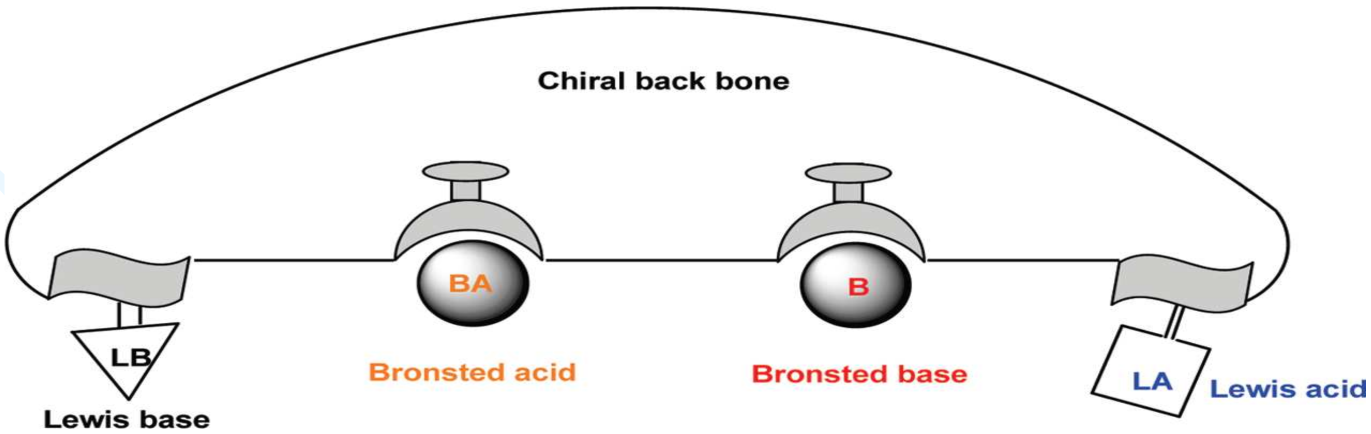
Ma, G.-N.; Cao, S.-H.; Shi, M.. *Tetrahedron Asymmetry* 2009, *20*, 1086–1092.

Conclusion

Multifunctional/bifunctional chiral phosphine organocatalysts have established themselves as efficient enantioselective catalysts in catalytic asymmetric MBH and related reactions due to the combination of a hydrogen-bonding motif with a highly nucleophilic phosphorus center within one molecule.

The reactivities and enantioselectivies of these multifunctional/bifunctional chiral phosphine organocatalysts can be finely tuned through enhancing the reactive center's nucleophilicity and varying and increasing hydrogen bond donors.

Multifunctional catalysis will remain as a powerful strategy to inspire the design of new efficient and selective catalysts.



Mahodand Lake: Pakistan