RCC
18-11-10

Kishor Mohanan

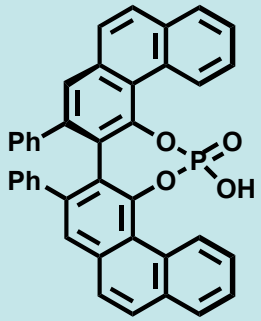
Chiral Brønsted acid Catalysis

N-Phosphinyl Phosphoramide—A Chiral Brønsted Acid Motif for the Direct Asymmetric N,O-Acetalization of Aldehydes

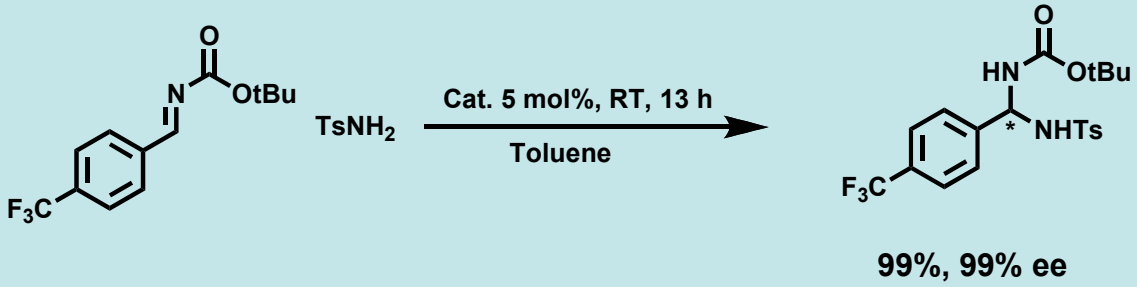
Benjamin List and co-workers,
Angew. Chem. Int. Ed. 2010, 2009, Early View

Max-Planck-Institut

Brønsted acid catalyzed imine amidation

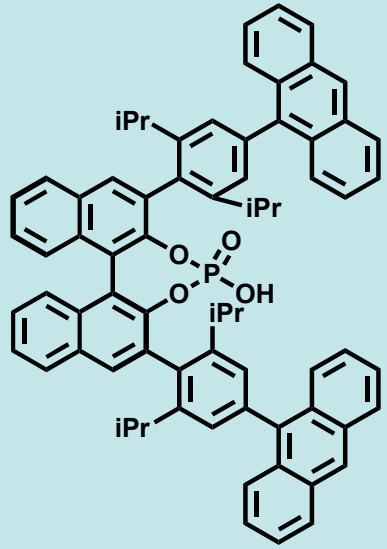


S-Vapol derived phosphoric acid

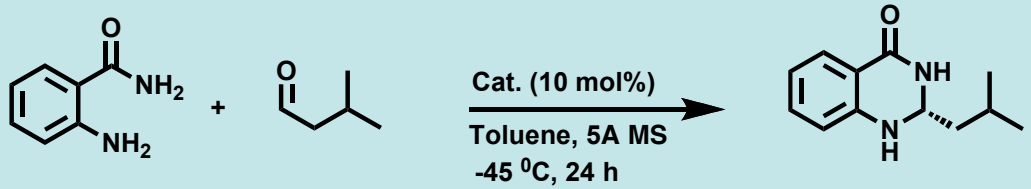


99%, 99% ee

Antilla et al. *J. Am. Chem. Soc.* 2005, *127*, 15697.



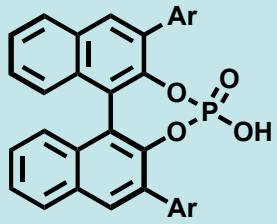
(S)-An-TRIP

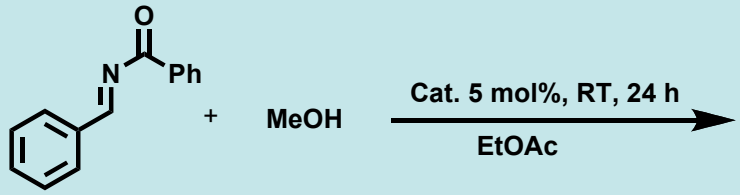


86%, 98% ee

List et al. *J. Am. Chem. Soc.* 2008, *130*, 15786

Asymmetric Addition of Alcohols to Imines



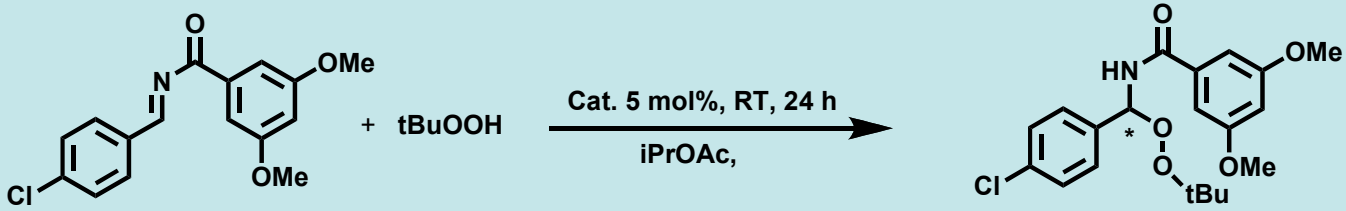


93%, 94% ee

Ar = 9-anthracenyl

Antilla et al. *J. Am. Chem. Soc.* 2008, *130*, 12216.

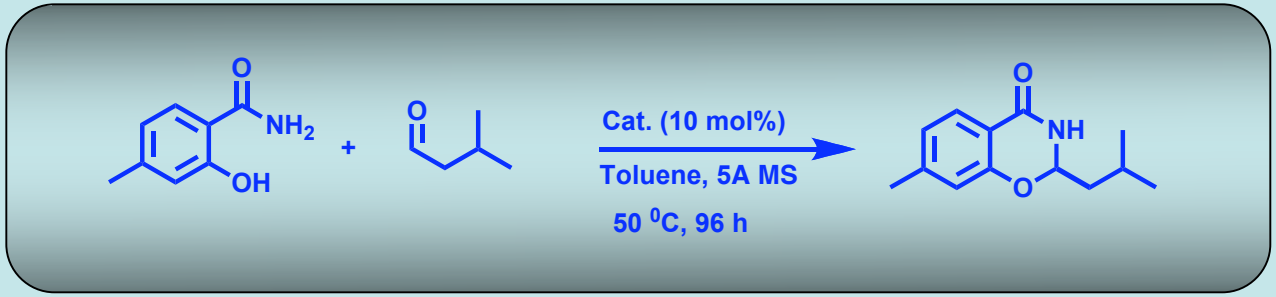
Peroxidation of Imines

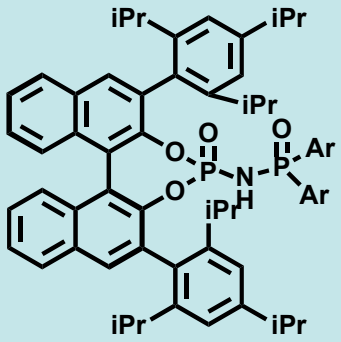


87%, 98% ee

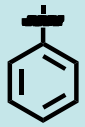
Antilla et al. *Angew. Chem. Int. Ed*. 2010, *49*, 6589

The present work..



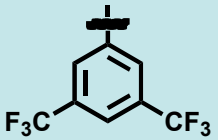


Ar =



52% (93.5:6.5)

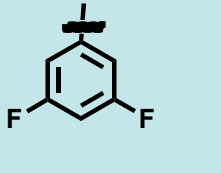
50% (94:6)



75%(60:40)

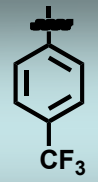
73% (95:5)

64% (94.5:5.5)



73% (87.5:12.5)

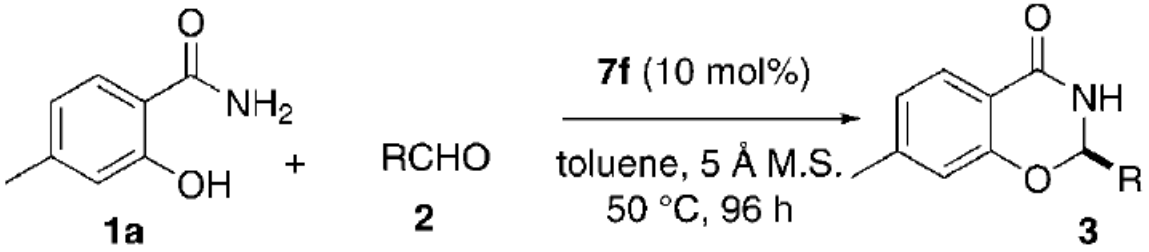
With 8 equivalents of aldehyde

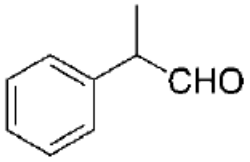
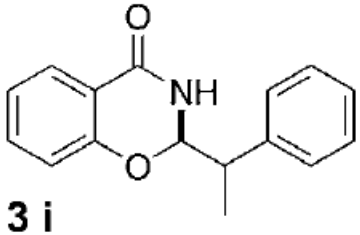


90% (95:5)

Synthesis of benzoxazinone..substrate scope..

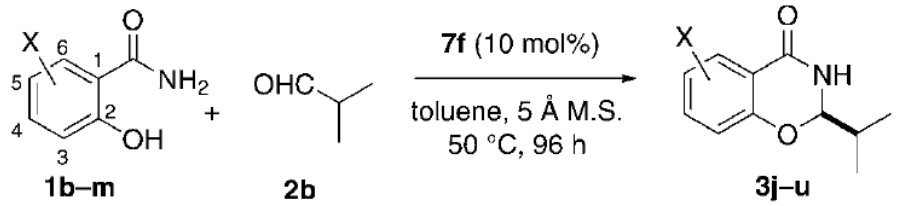
Table 2: Aldehyde scope.



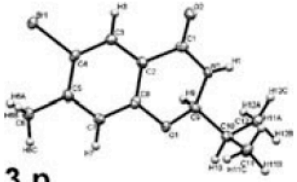
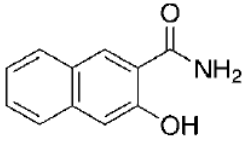
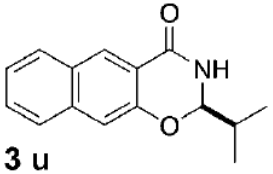
Entry[a]	RCHO	Product	Yield [%][b]	e.r.[c]
1	*i*BuCHO (**2a**)	**3a**	90	95.0:5.0
2	*t*BuCH$_2$CHO (**2b**)	**3b**	94	94.5:5.5
3	*i*PrCHO (**2c**)	**3c**	90	96.0:4.0
4	(Et)$_2$CHCHO (**2d**)	**3d**	81	98.0:2.0
5	CyCHO (**2e**)	**3e**	95	96.0:4.0
6	PhCH$_2$CHO (**2f**)	**3f**	83	91.5:8.5
7	*n*PrCHO (**2g**)	**3g**	97	92.0:8.0
8	PhCHO (**2h**)	**3h**	50	75.5:24.5
9[d]	 **2i**	 **3i**	69	*syn*: 98.5:1.5 *anti*: 86.5:13.5

Synthesis of benzoxazinone..substrate scope..

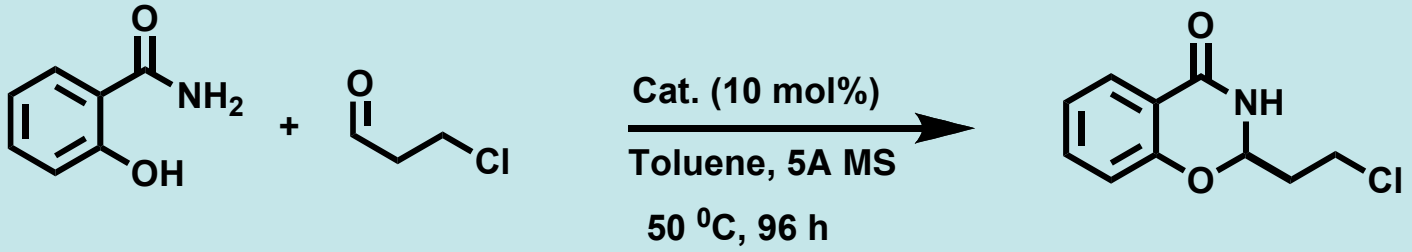
Table 3: 2-Hydroxybenzamide scope.



1b–m **2b** **3j–u**

Entry[a]	X	Product	Yield [%][c]	e.r.[d]
1	H (**1b**)	**3j**	89	95.0:5.0
2[b]	3-Me (**1c**)	**3k**	96	96.0:4.0
3	5-Me (**1d**)	**3l**	97	96.0:4.0
4	6-Me (**1e**)	**3m**	97	94.0:6.0
5	4-OMe (**1f**)	**3n**	98	95.5:4.5
6	5-OMe (**1g**)	**3o**	95	94.5:5.5
7	4-Me, 5-Br (**1h**)	 **3p**	91	96.0:4.0
8[b]	5-Me, 3-Br(**1i**)	**3q**	84	95.0:5.0
9	4-Me, 3,5-Cl (**1j**)	**3r**	78	95.5:4.5
10	5-Cl (**1k**)	**3s**	88	95.0:5.0
11	5-F (**1l**)	**3t**	89	95.0:5.0
12	 **1m**	 **3u**	95	93.5:6.5

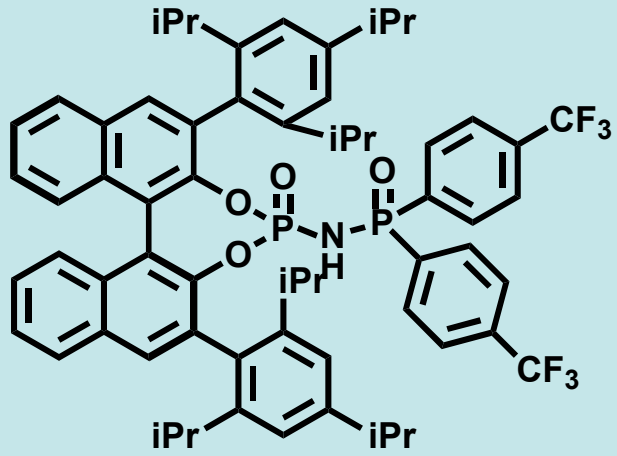
Application towards the synthesis of Chlorothenoxazine



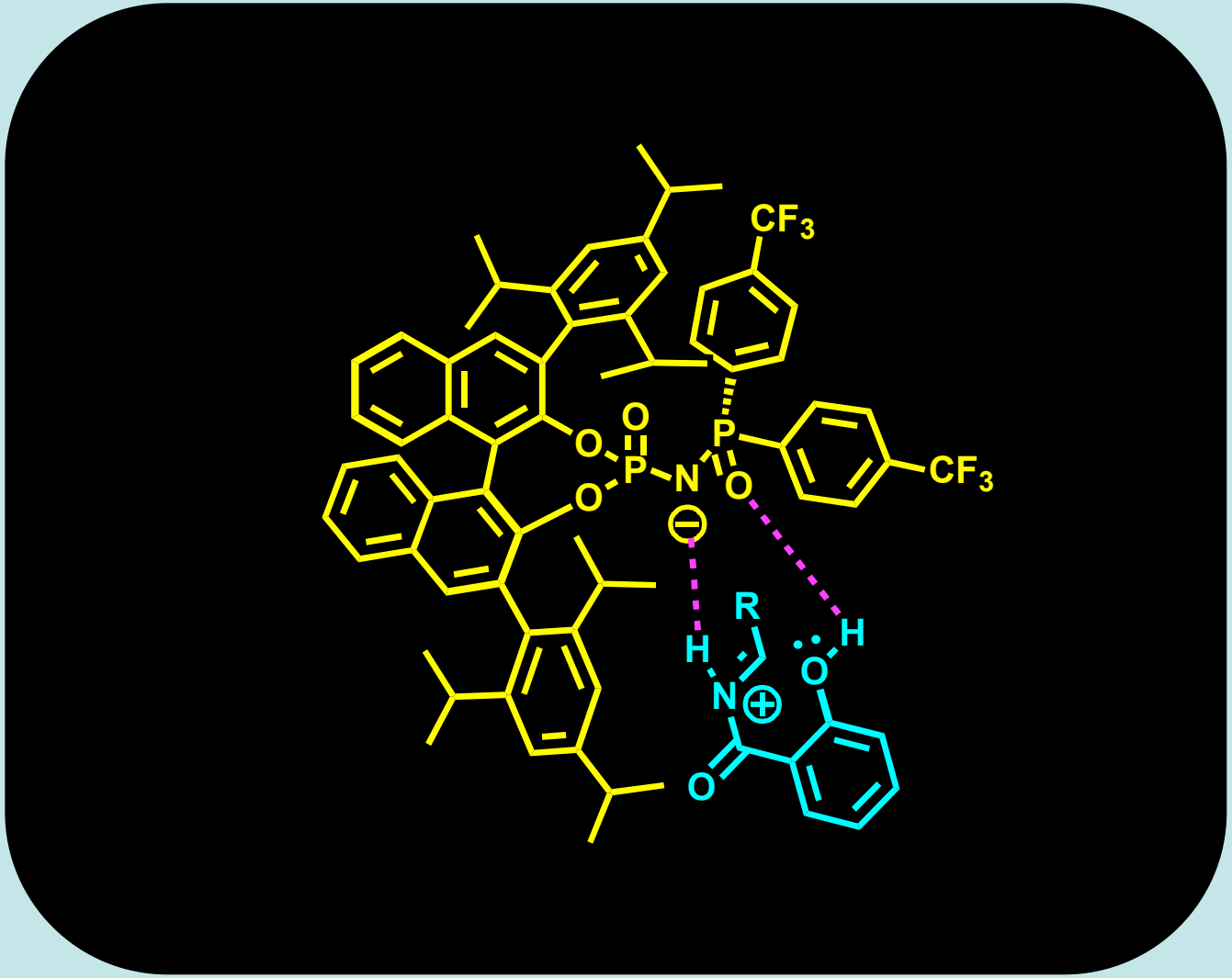
e.r. 86:14 (96.5:3.5)

Chlorothenoxazine

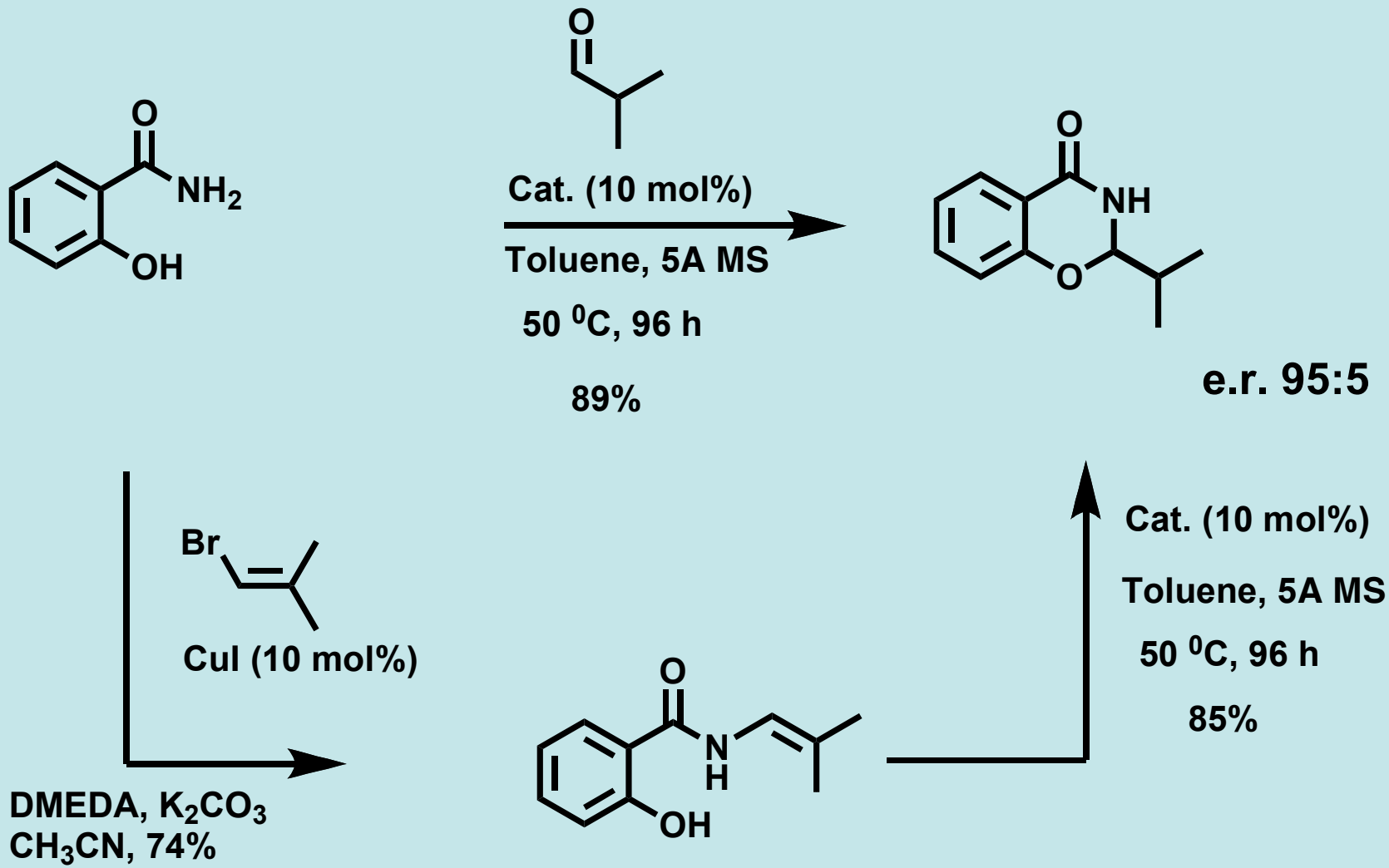
Analgesic pharmaceutical



Stereochemical model for chiral induction



Evidence for intermediacy of benzoyl imine..



To Conclude….

- *N-Phosphinyl Phosphoramide—A New Chiral Brønsted Acid catalyst*
- *Enantioselective direct synthesis of N,O-acetals*
- *Synthesis of Chlorothenoxazine*

Thank YOU