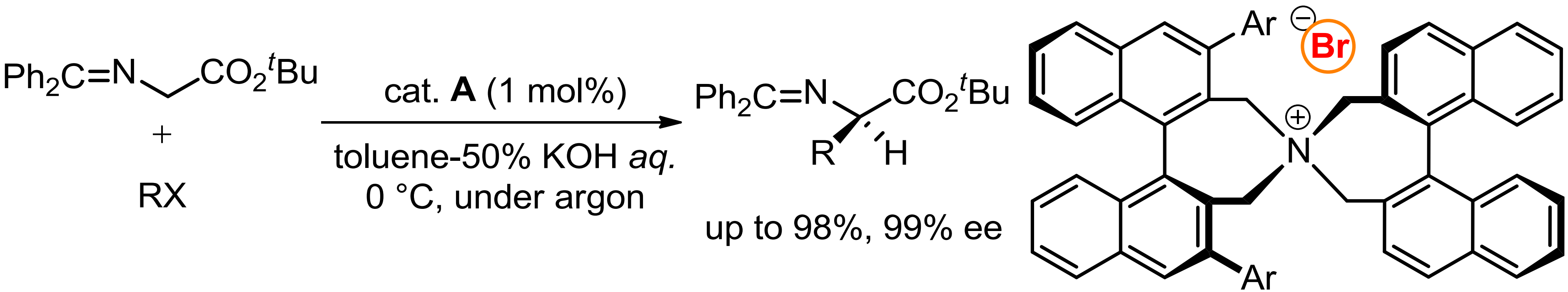
Development of Ion-Pair Cooperative Asymmetric Catalyses of Chiral Tetraaminophosphonium Salts Possessing Functional Organic Anions

Yusuke Ueki

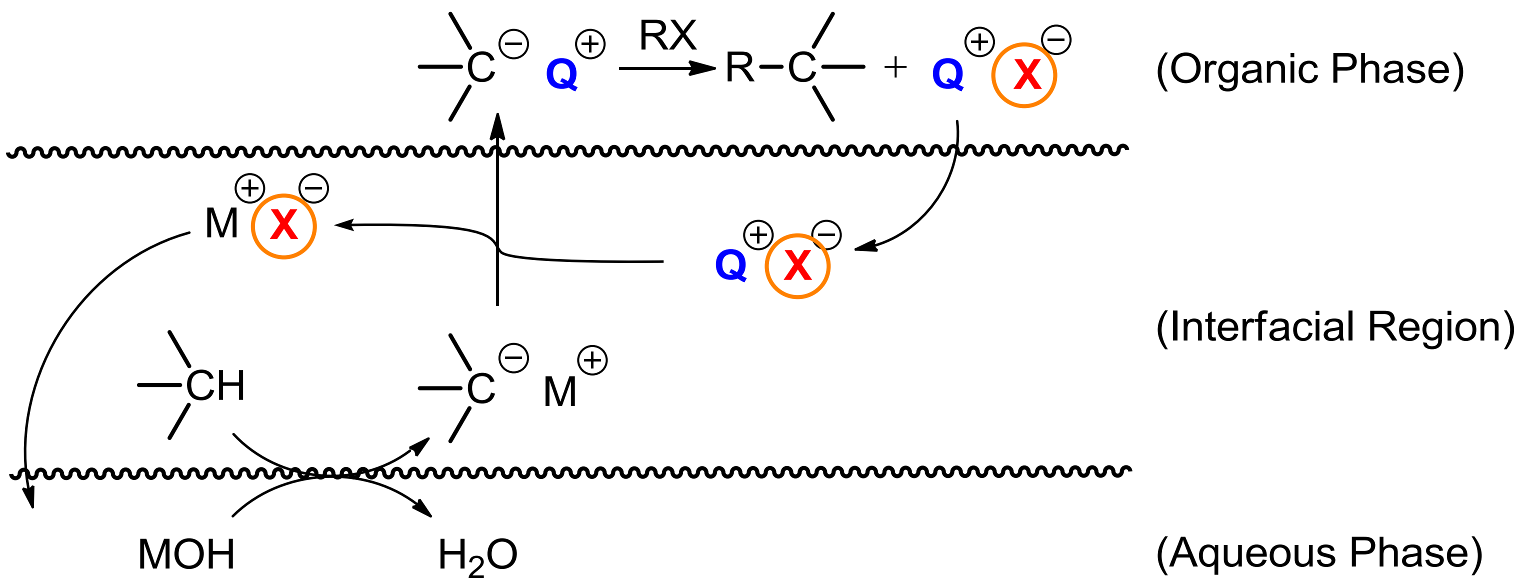
Onium Salts for Phase-Transfer Catalyst



Ooi, T.; Kameda, M.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 5139.

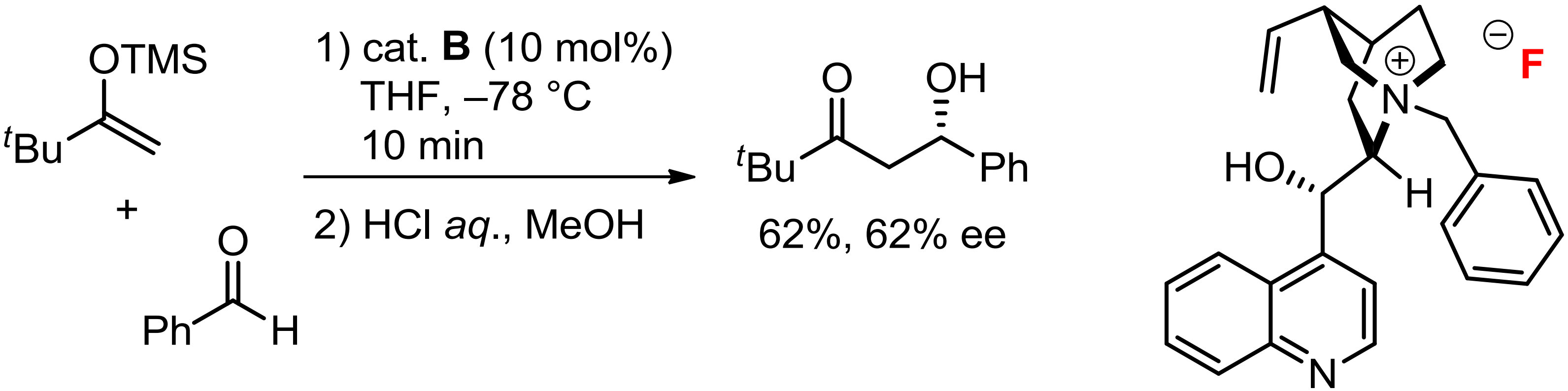
cat. **A**
(Ar = 3,4,5-F_3–C_6H_2)

Plausible Mechanism



$Q^{\oplus}$: quaternary ammonium cation $M^{\oplus}$: alkaline metal ion

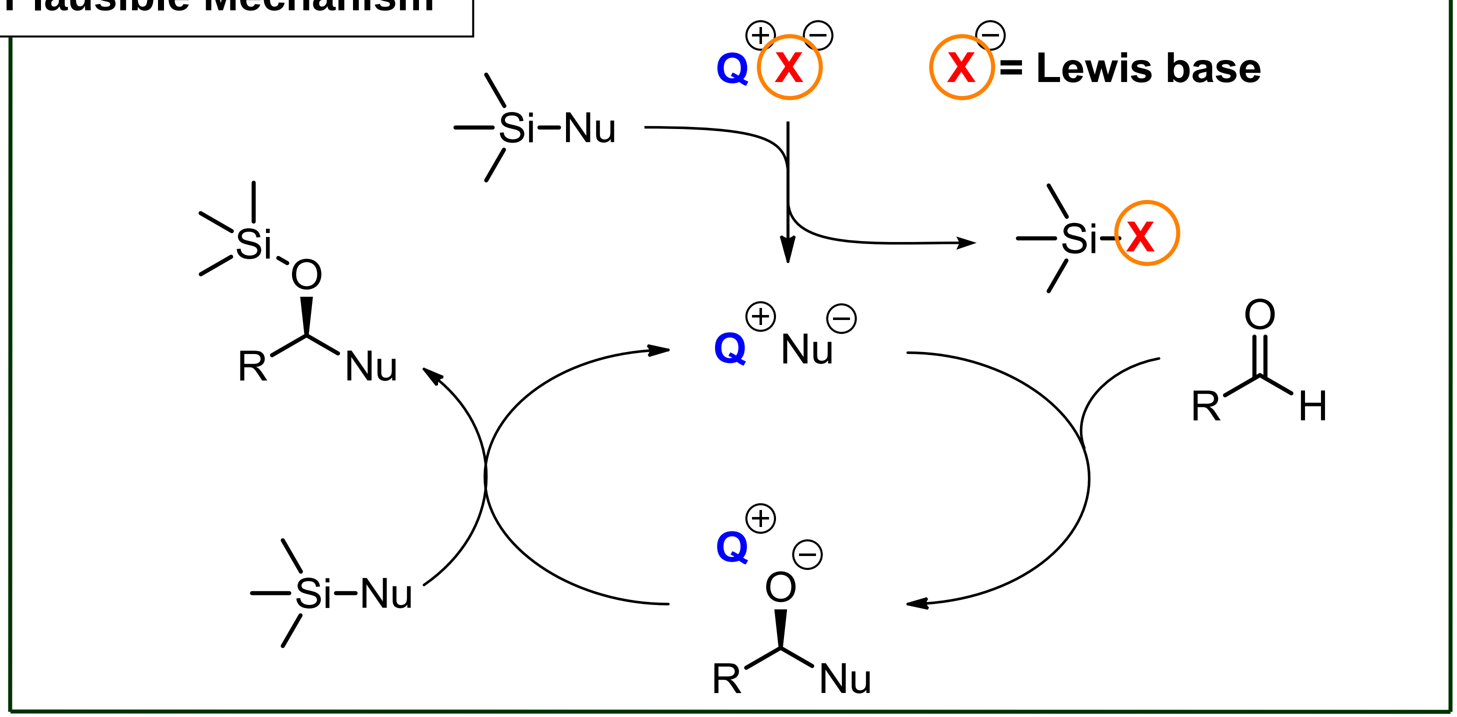
Example of Homogeneous Onium Salt Catalysis



cat. **B**

Ando, A.; Miura, T.; Tatematsu, T.; Shioiri, T. *Tetrahedron Lett*. **1993**, *34*, 1507.

Plausible Mechanism



Example of Homogeneous Onium Salt Catalysis

$Q^{\oplus}$

controlling the reactivity
and selectivity

$X^{\ominus}$

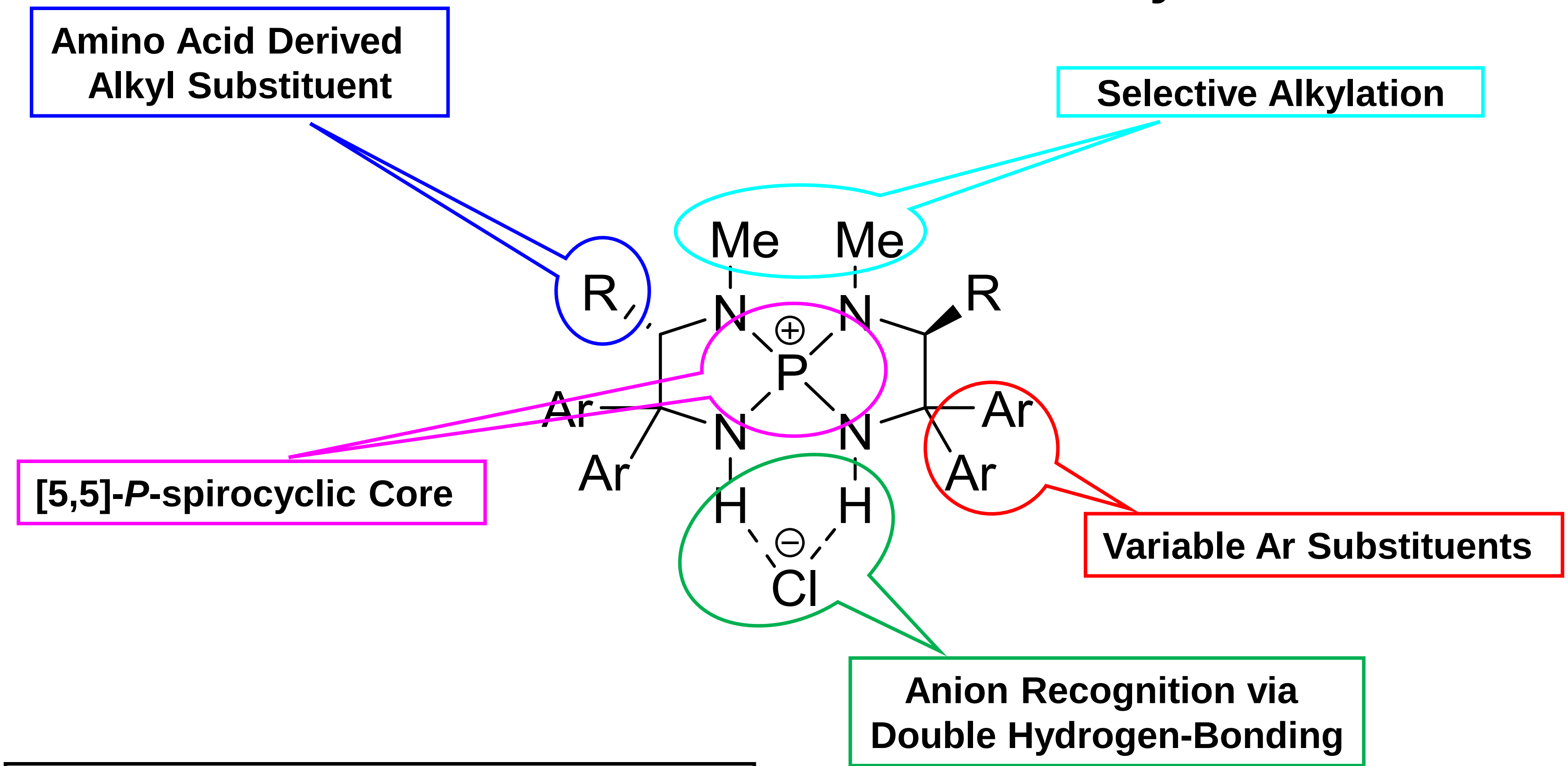
neutralizing the charge
initiation of the reaction

⇓ ***continuous participation in the catalytic cycle***

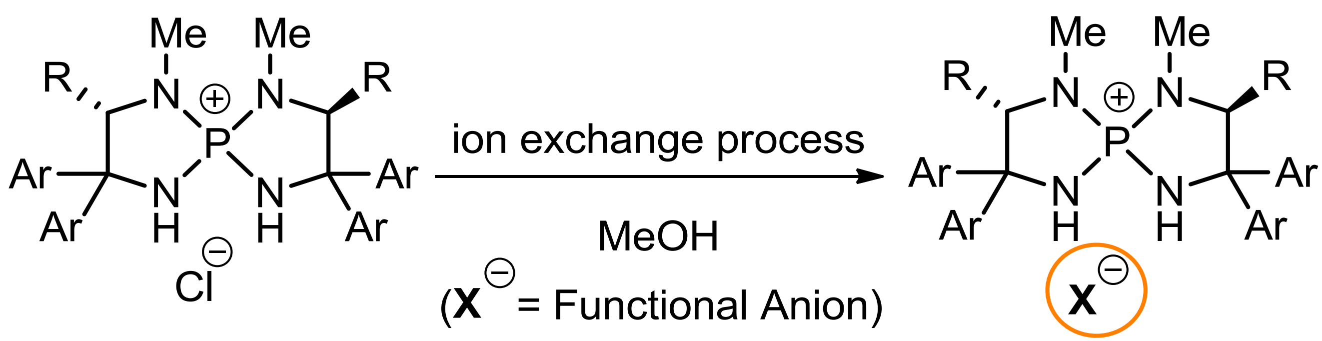
controlling the reactivity
and selectivity

a new cooperative catalysis of chiral onium salts possessing an appropriate organic anion

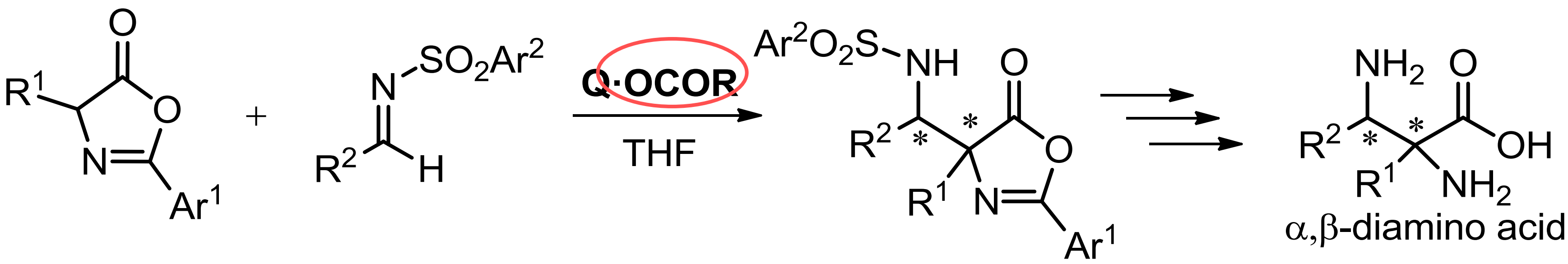
Characteristic Features of Catalyst

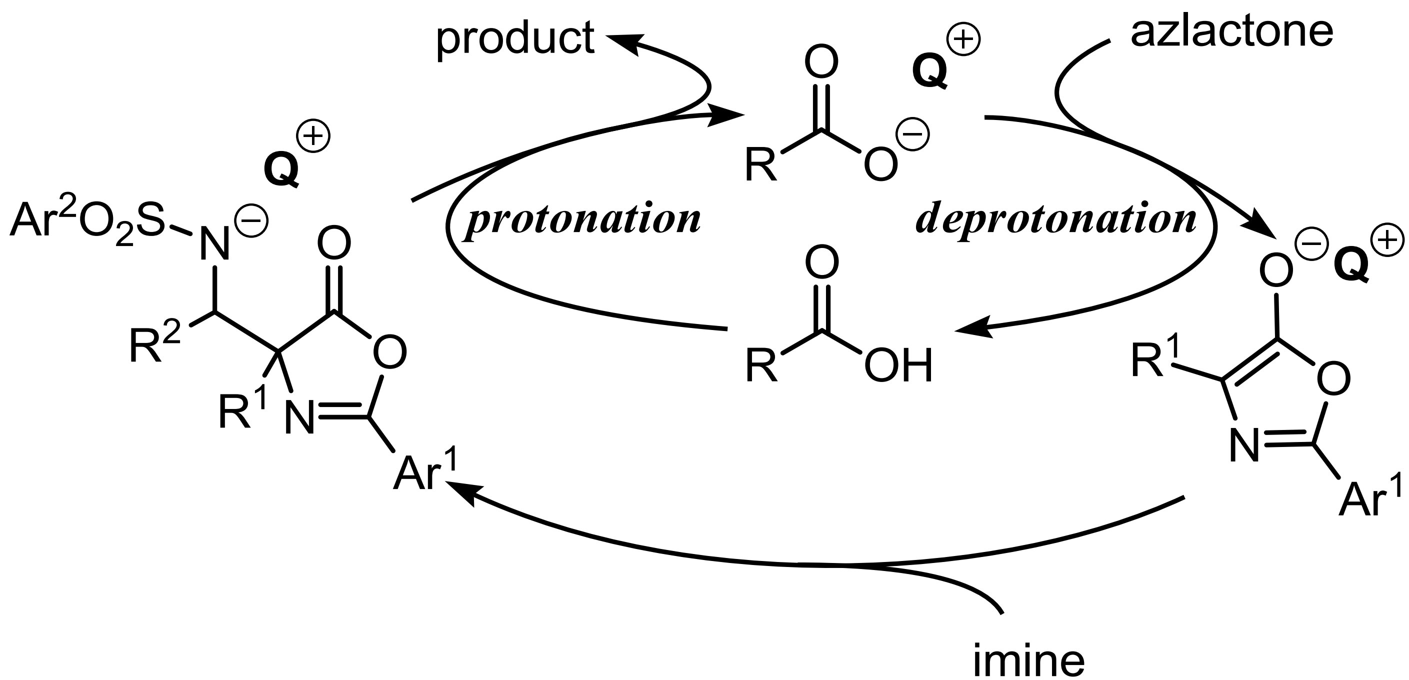


Catalyst Preparation: Ion Exchange

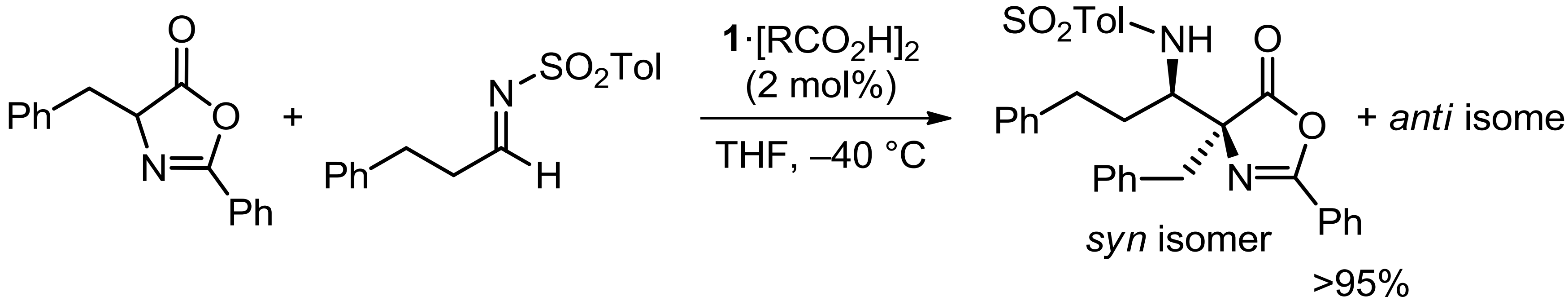


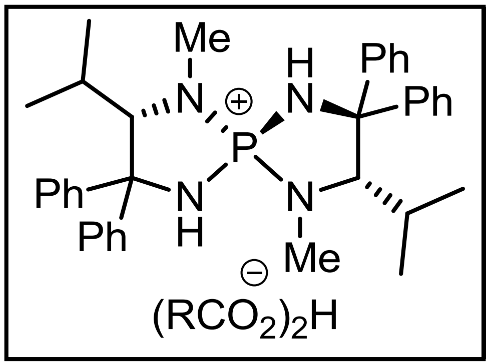
Working Hypothesis



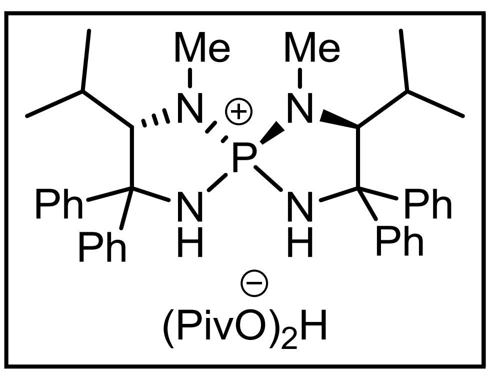


Effect of Catalyst on Reactivity and Selectivity





$\mathbf{1a}_{\boldsymbol{M}}$·[RCO$_2$H]$_2$



$\mathbf{1a}_{\boldsymbol{P}}$·[PivOH]$_2$

$\mathbf{1a}_{\boldsymbol{M}}$ = (*M*,*S*), $\mathbf{1a}_{\boldsymbol{P}}$ = (*P*,*S*)

$\mathbf{1a}_{\boldsymbol{M}}$·[HCO$_2$H]$_2$: 3.5 h, *syn*/*anti* = 1.3:1
6% ee, (*syn* isomer)

$\mathbf{1a}_{\boldsymbol{M}}$·[AcOH]$_2$: 2 h, 1.2:1, 5% ee

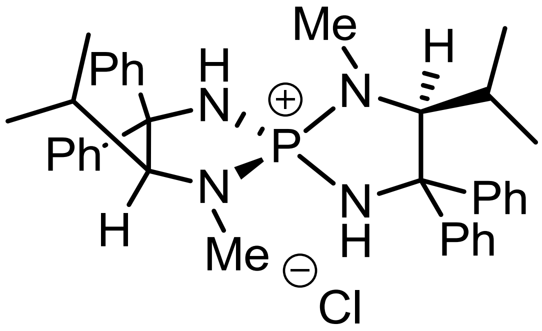
$\mathbf{1a}_{\boldsymbol{M}}$·[PivOH]$_2$: 0.5 h, 1.3:1, 6% ee

$\mathbf{1a}_{\boldsymbol{P}}$·[PivOH]$_2$: 1 h, 1.6:1, 60% ee

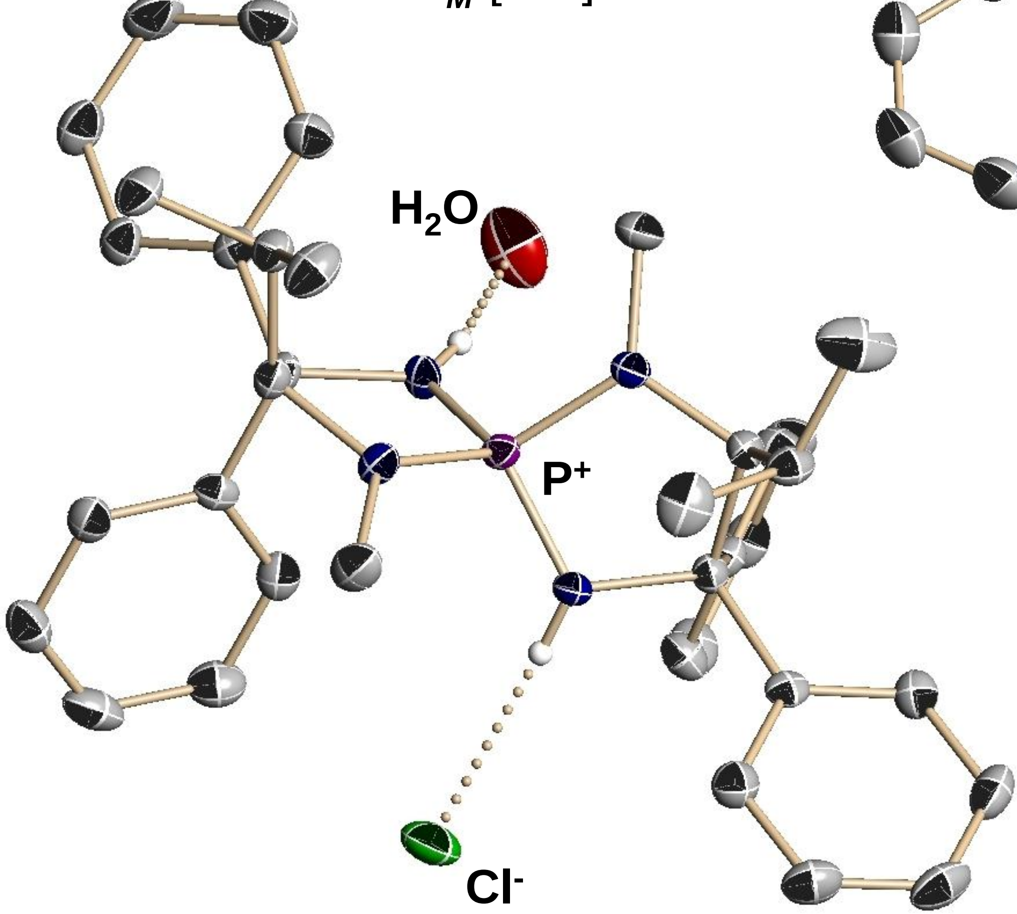
pK_a of carboxylic acid in H_2O

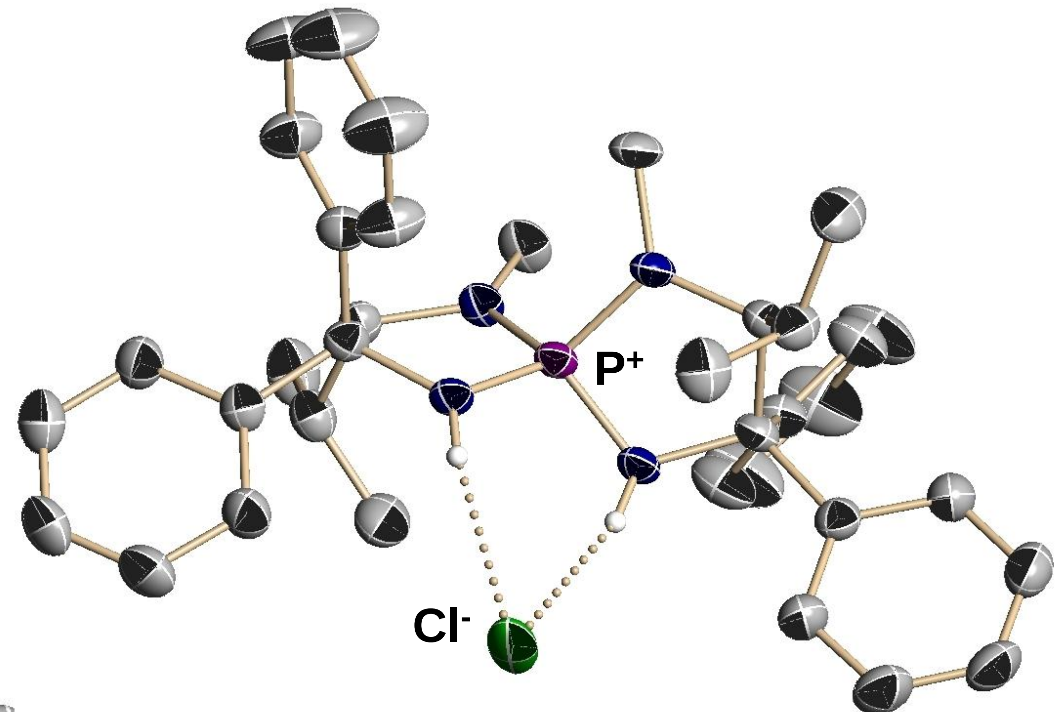
HCO_2H	3.77
AcOH	4.76 (12.6 in DMSO)
PivOH	5.03

Hydrogen-Bonding Mode of Phosphonium Salts

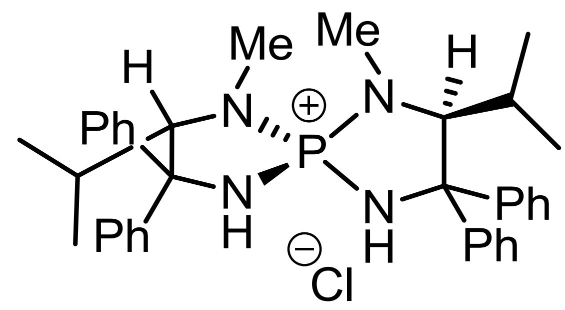


$1a_M$·[HCl]

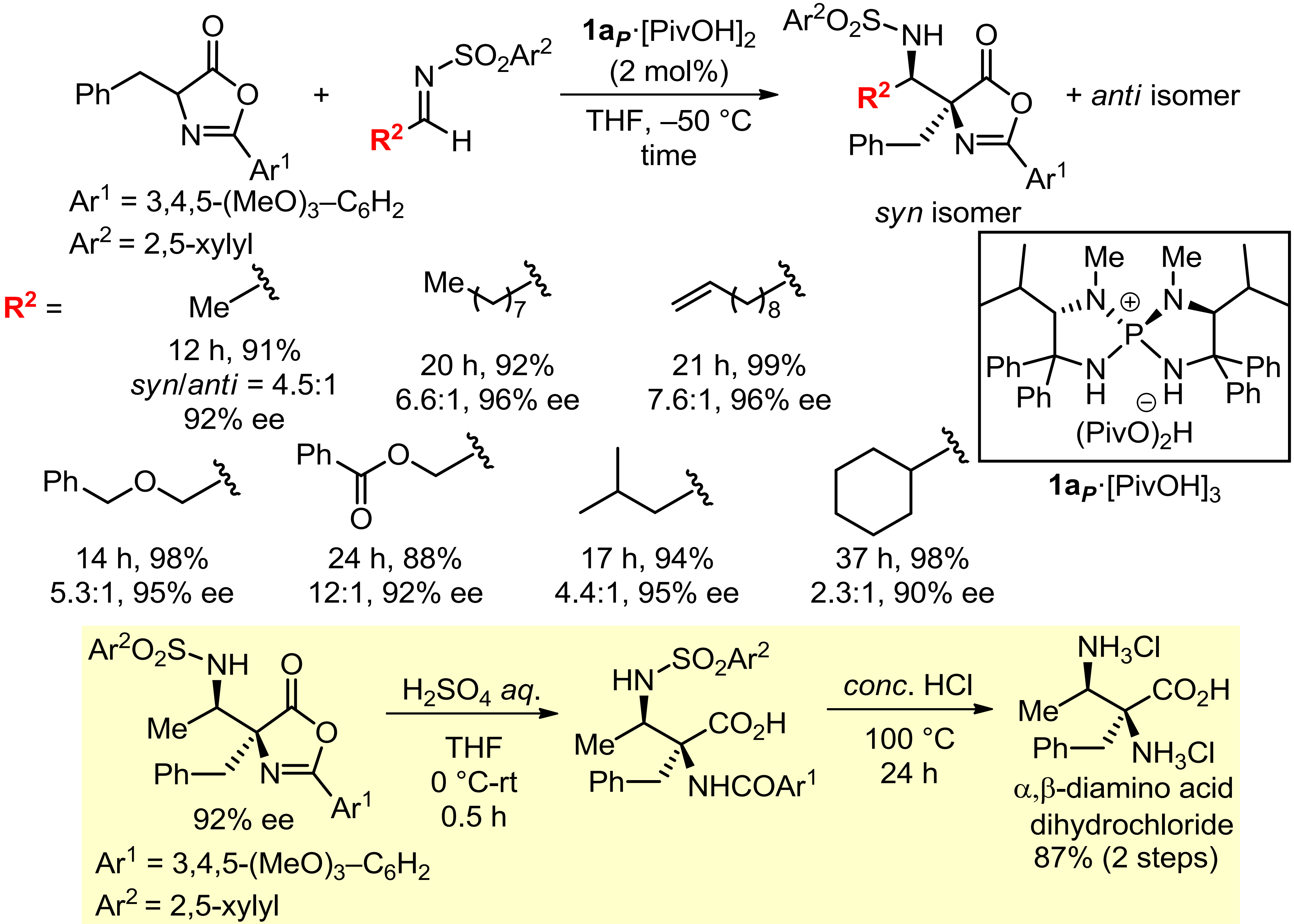




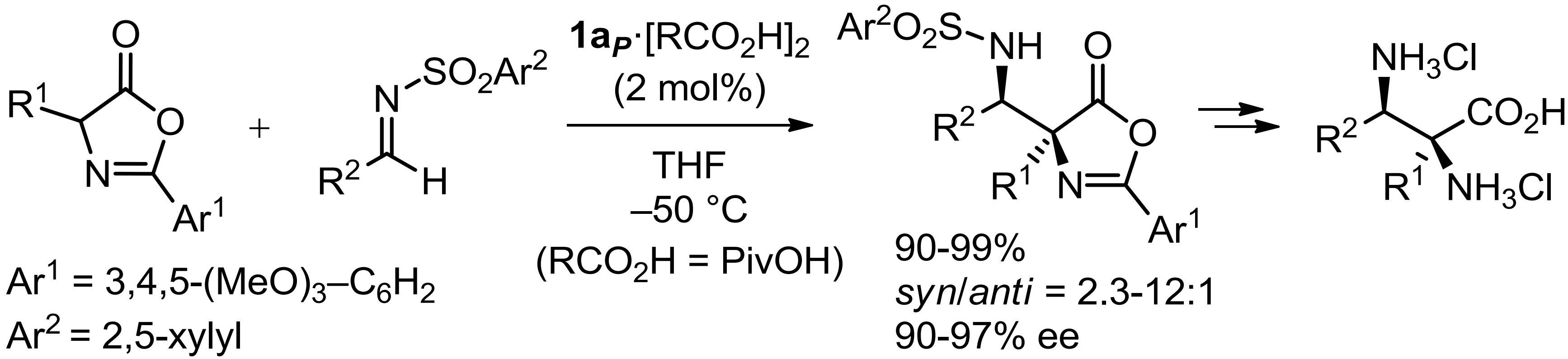
$1a_P$·[HCl]



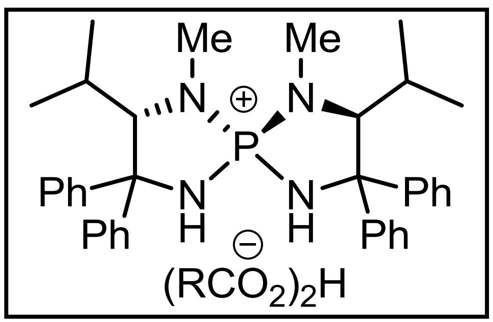
Scope of Imines



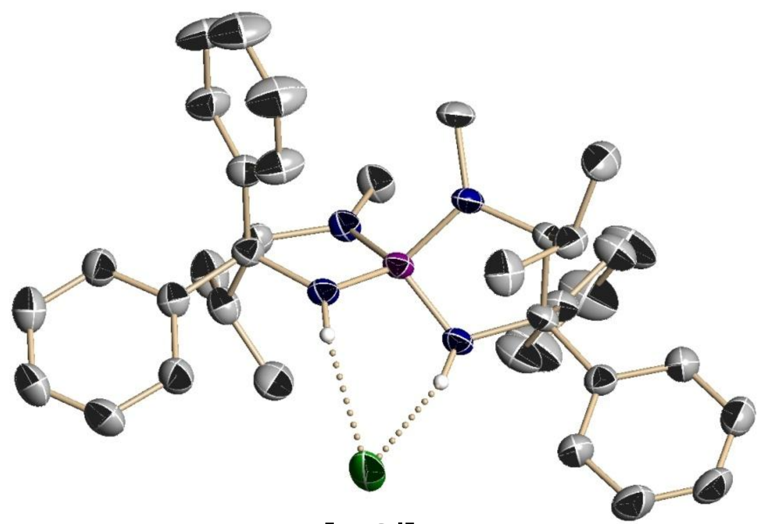
Summary 1



Uraguchi, D.; Ueki, Y.; Ooi, T. *J. Am. Chem. Soc.* **2008**, *130*, 14088.

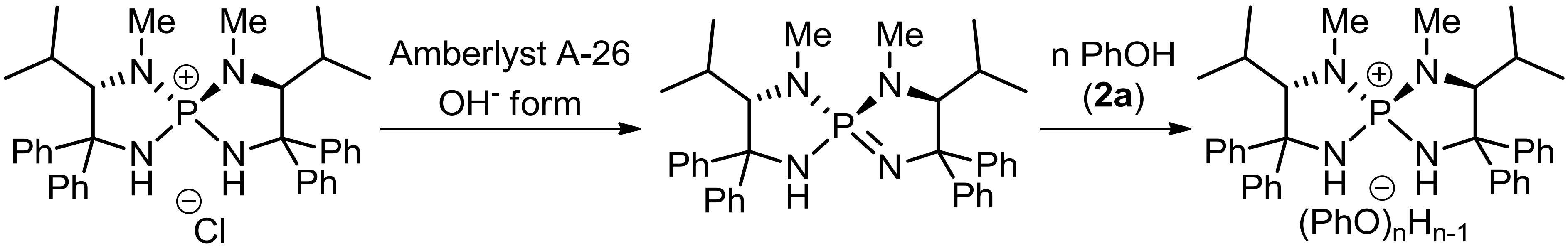


1a$_{P}$·[RCO_2H]$_2$



1a$_{P}$·[HCl]

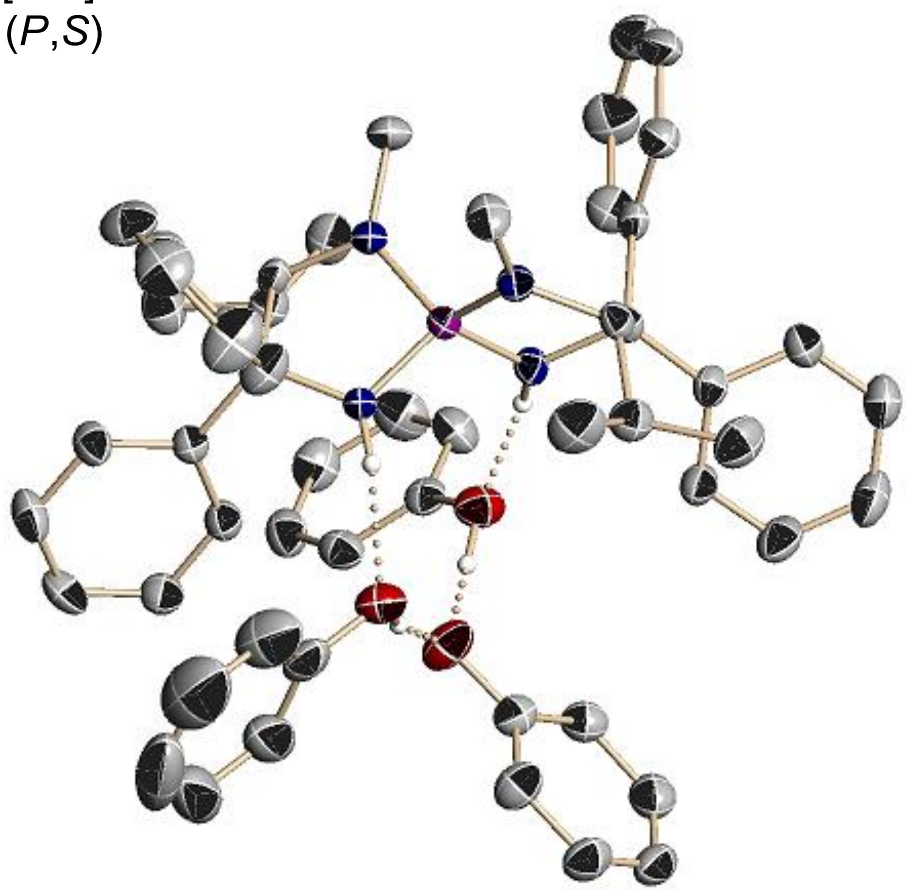
Preparation and Structure of Phosphonium Phenoxide

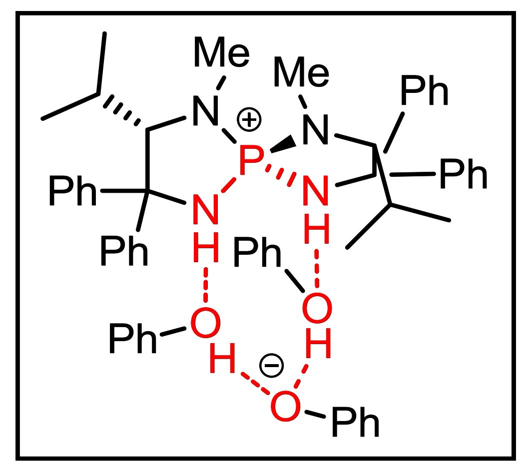


1a·[HCl]
1 = (*P*,*S*)

1a

1a·[**2a**]$_n$

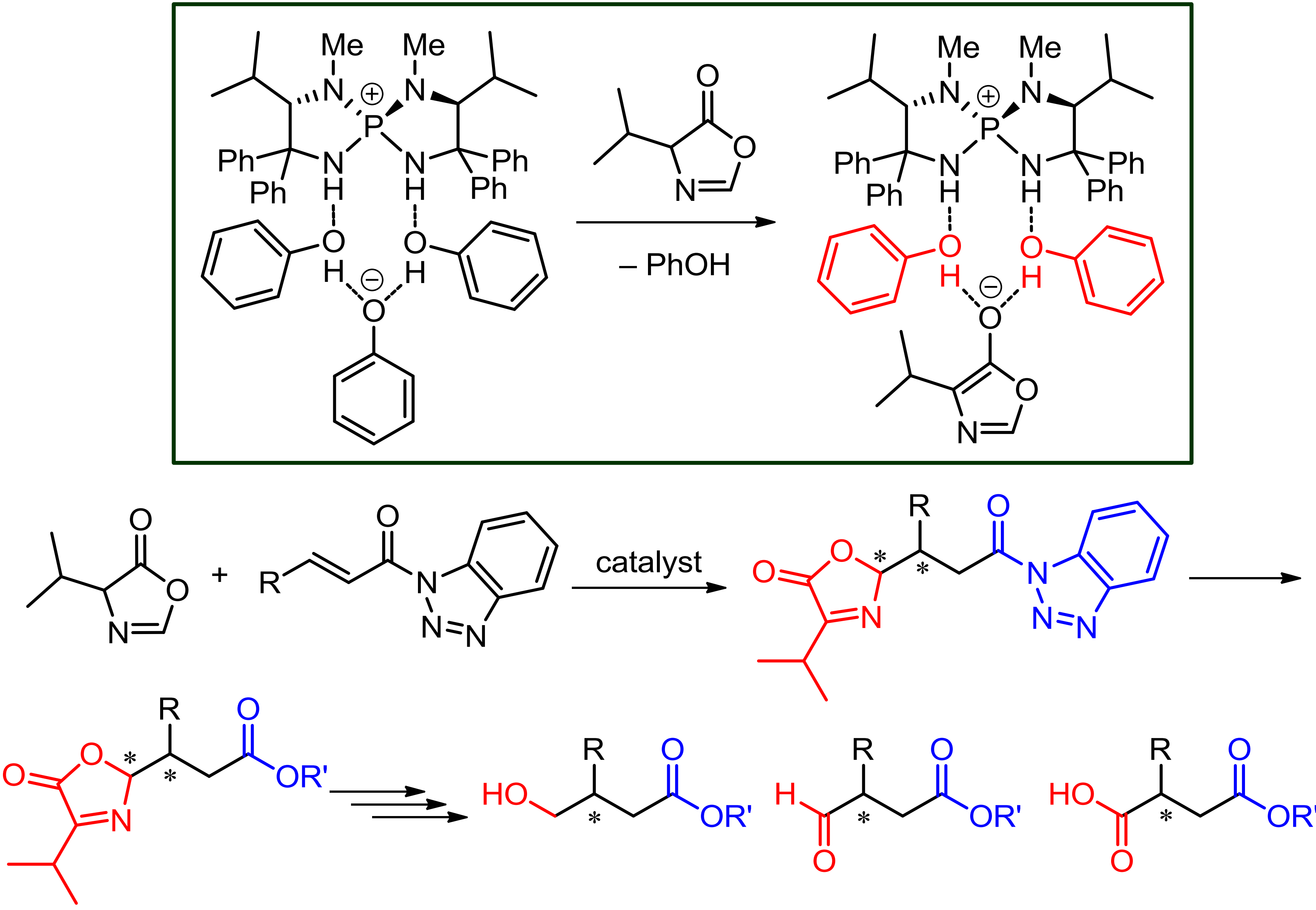




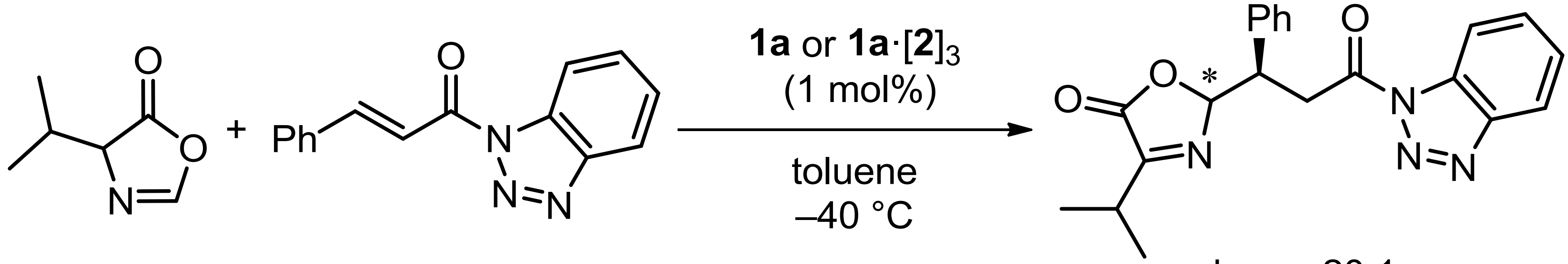
1a·[**2a**]$_3$

Tozawa, T.; Nagao, H.; Yamane, Y.; Mukaiyama, T. *Chem. Asian. J.* **2007**, *2*, 123.

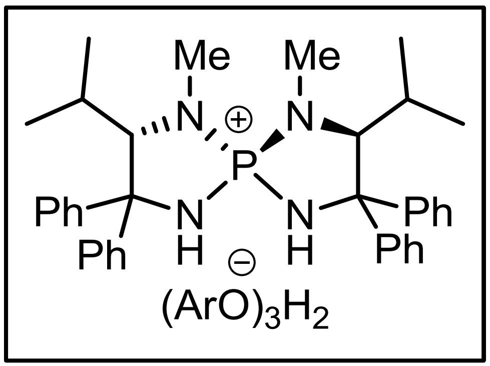
Conjugate Addition of Acyl Anion Equivalent



Effect of Counter Anion Structure on the Selectivity

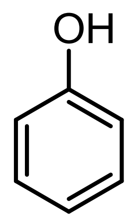


d.r. = >20:1

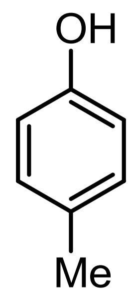


1a·[**2**]3

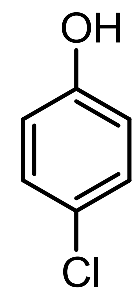
2 =



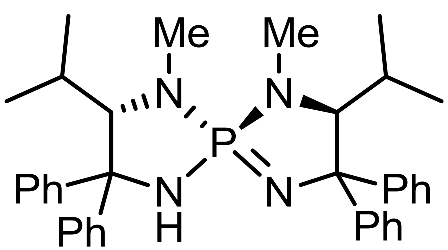
6 h, 99%
60% ee



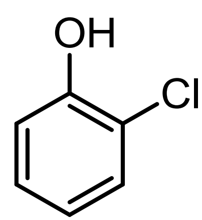
4 h, 96%
58% ee



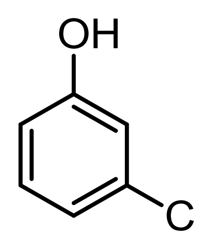
10 h, 97%
75% ee



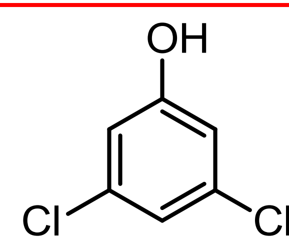
1a
2 h, 99%
34% ee



12 h, 94%
63% ee

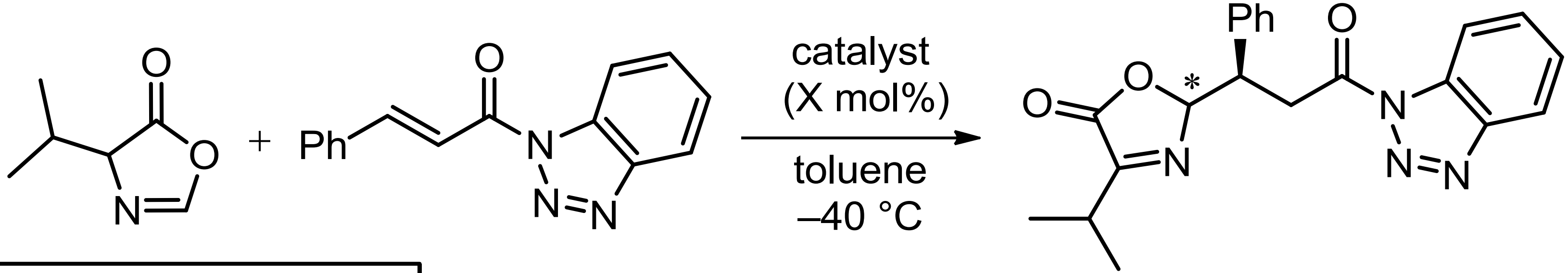


6 h, 93%
70% ee

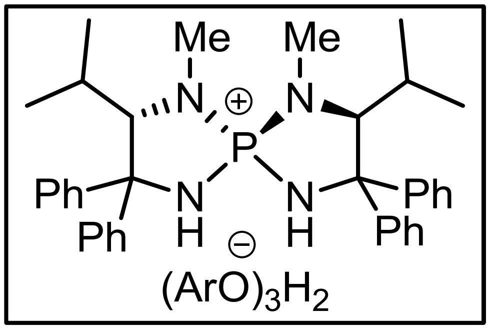


16 h, 92%
80% ee

Effect of Catalyst Concentration and Cation Structure

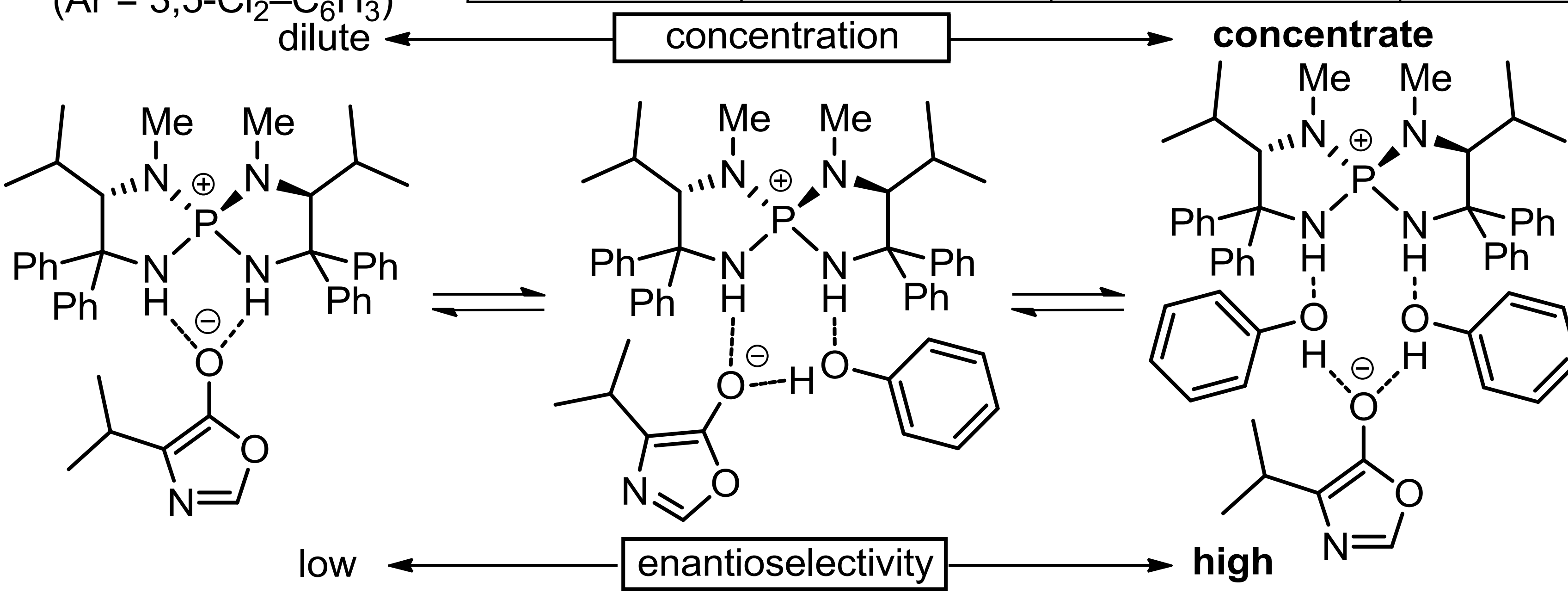


>90%, d.r. = >20:1

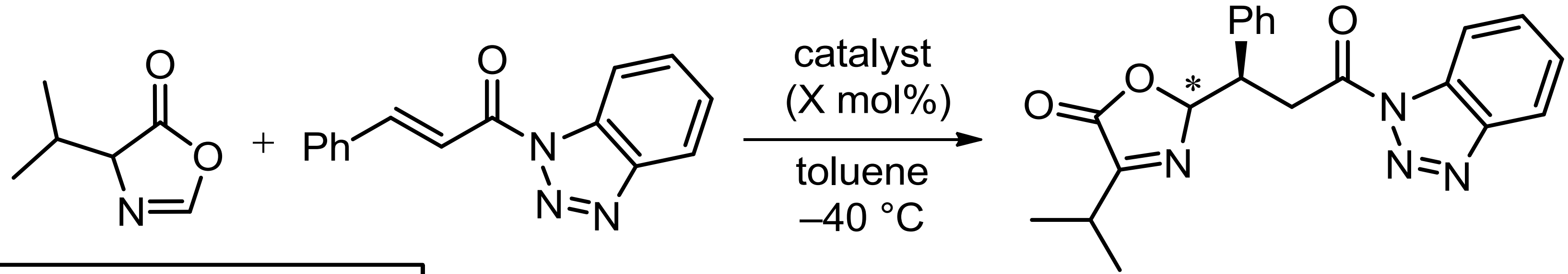


1a·[**2b**]$_3$
(Ar = 3,5-Cl_2–C_6H_3)

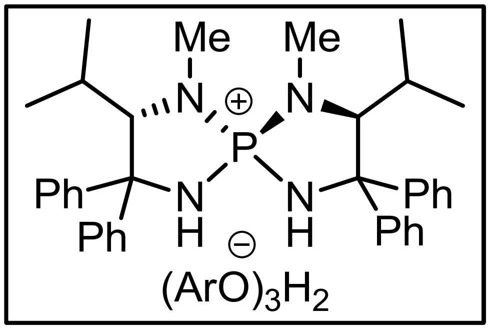
X	Conc. (Catalyst)	Conc. (Substrate)	ee (%)
1 mol%	1 mM	0.1 M	80% ee
1 mol%	10 mM	1.0 M	87% ee
10 mol%	10 mM	0.1 M	89% ee



Effect of Catalyst Concentration and Cation Structure

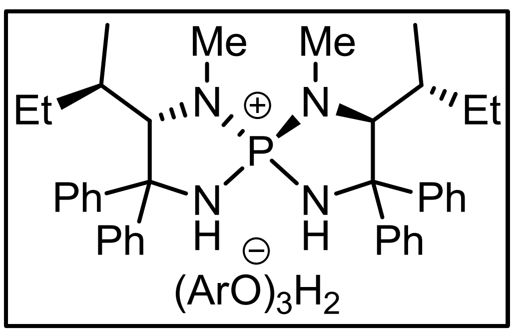


>90%, d.r. = >20:1



1a·[**2b**]$_3$
(Ar = 3,5-Cl_2–C_6H_3)

X	Conc. (Catalyst)	Conc. (Substrate)	ee (%)
1 mol%	1 mM	0.1 M	80% ee
1 mol%	10 mM	1.0 M	87% ee
10 mol%	10 mM	0.1 M	89% ee

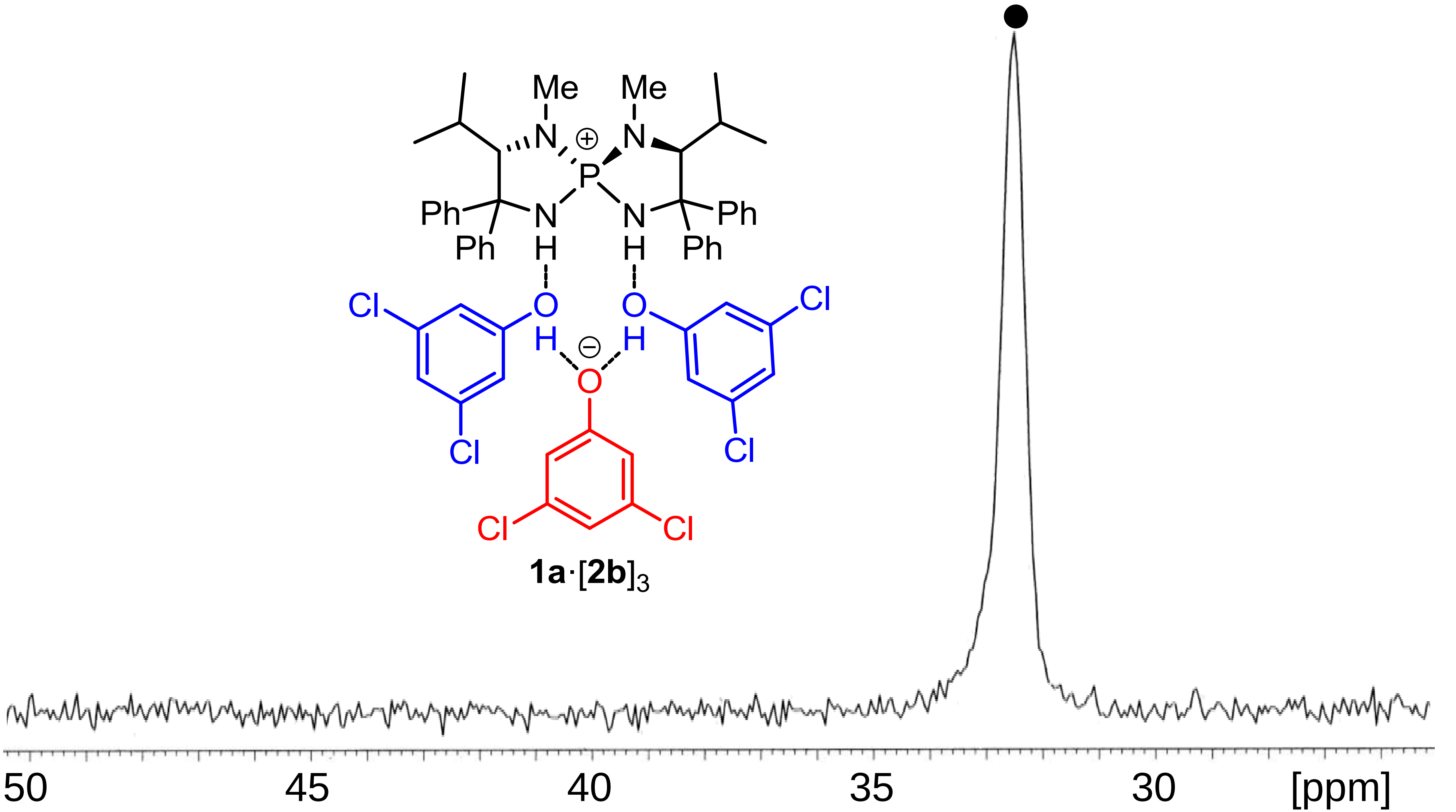


1b·[**2b**]$_3$
(Ar = 3,5-Cl_2–C_6H_3)

1 mol%, 10 mM*
4 h, 95%
95% ee

* Concentration was calculated based on the amount of catalyst.

^{31}P NMR Study 1: toluene, –98 °C



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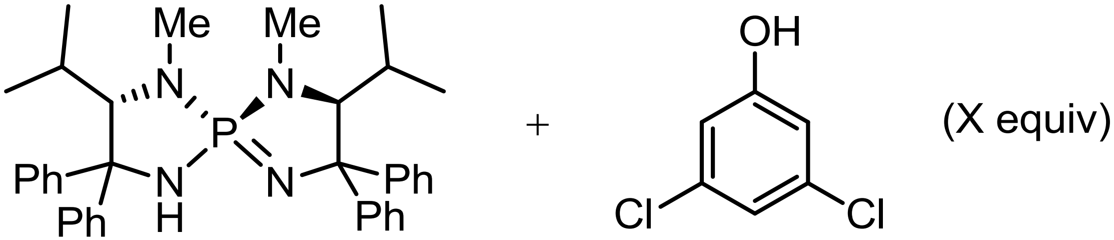
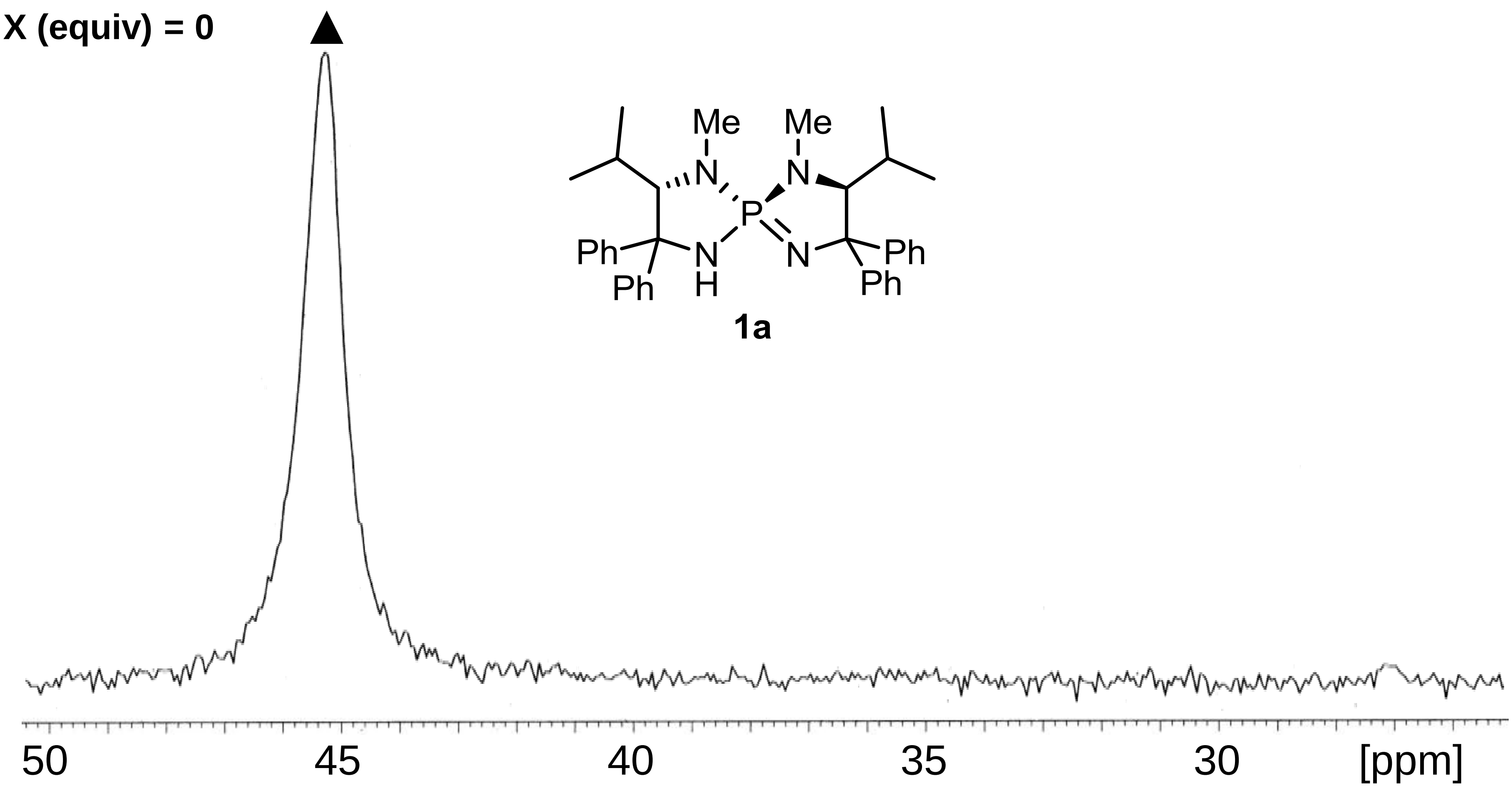


1a **2b**



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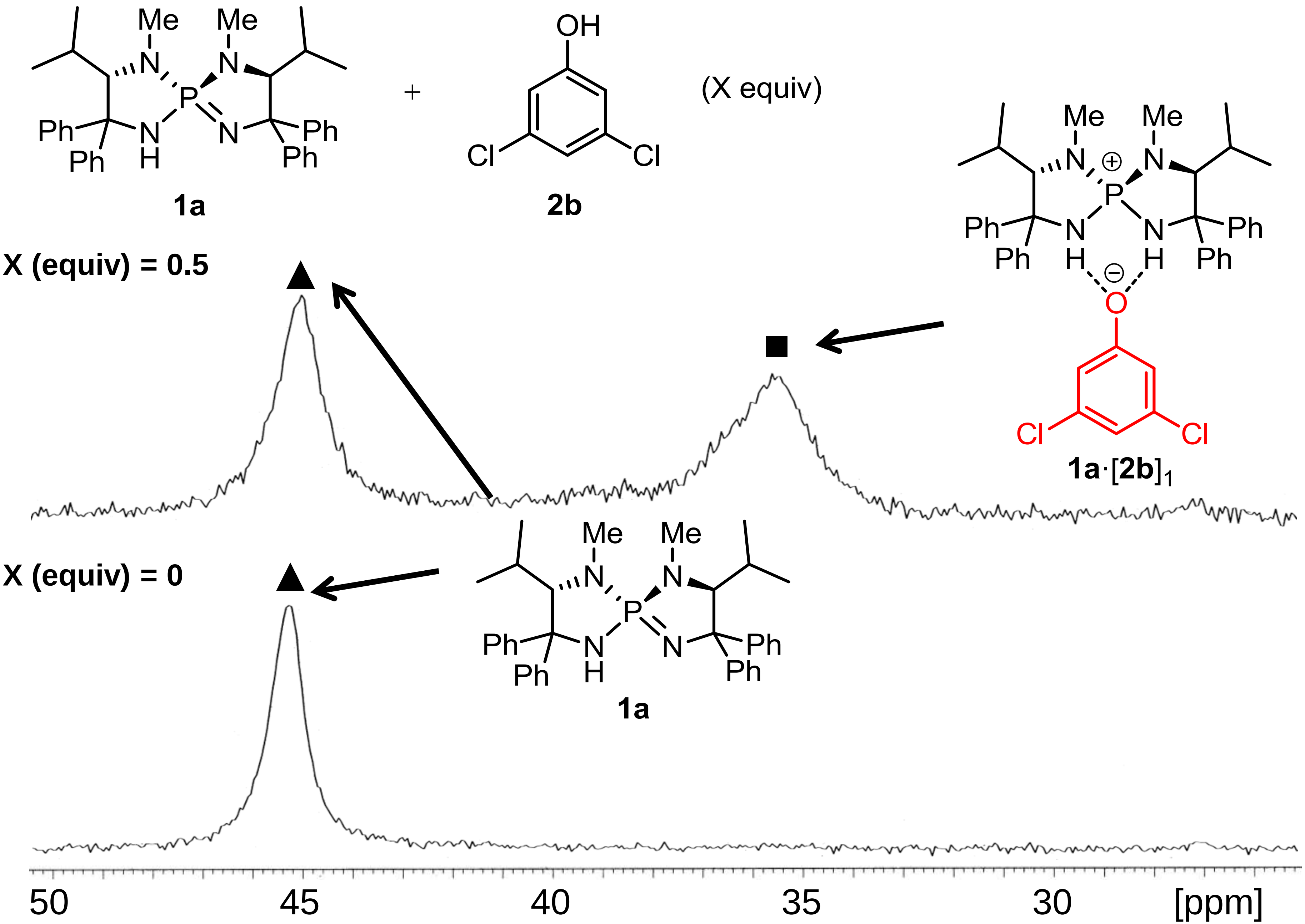

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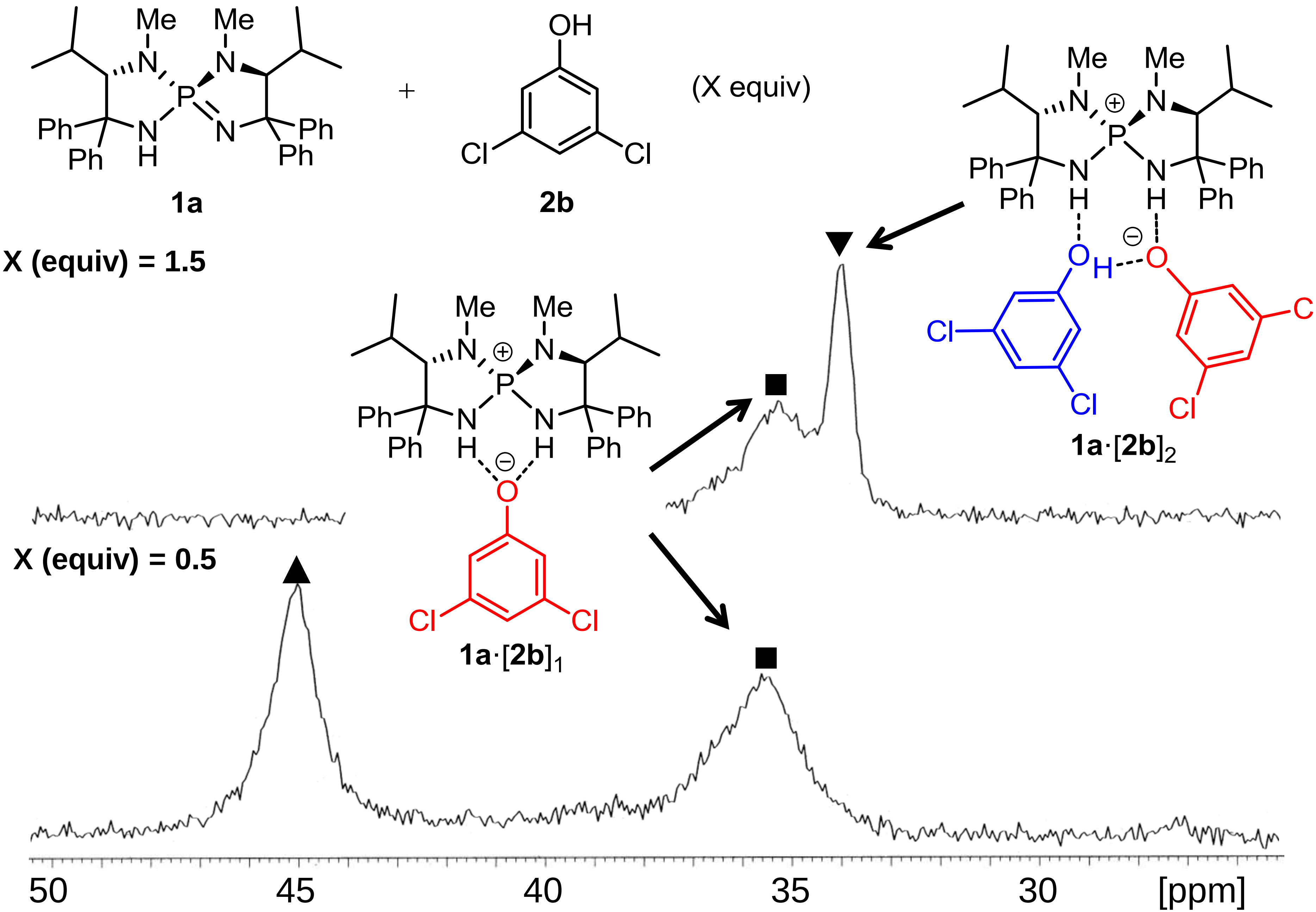
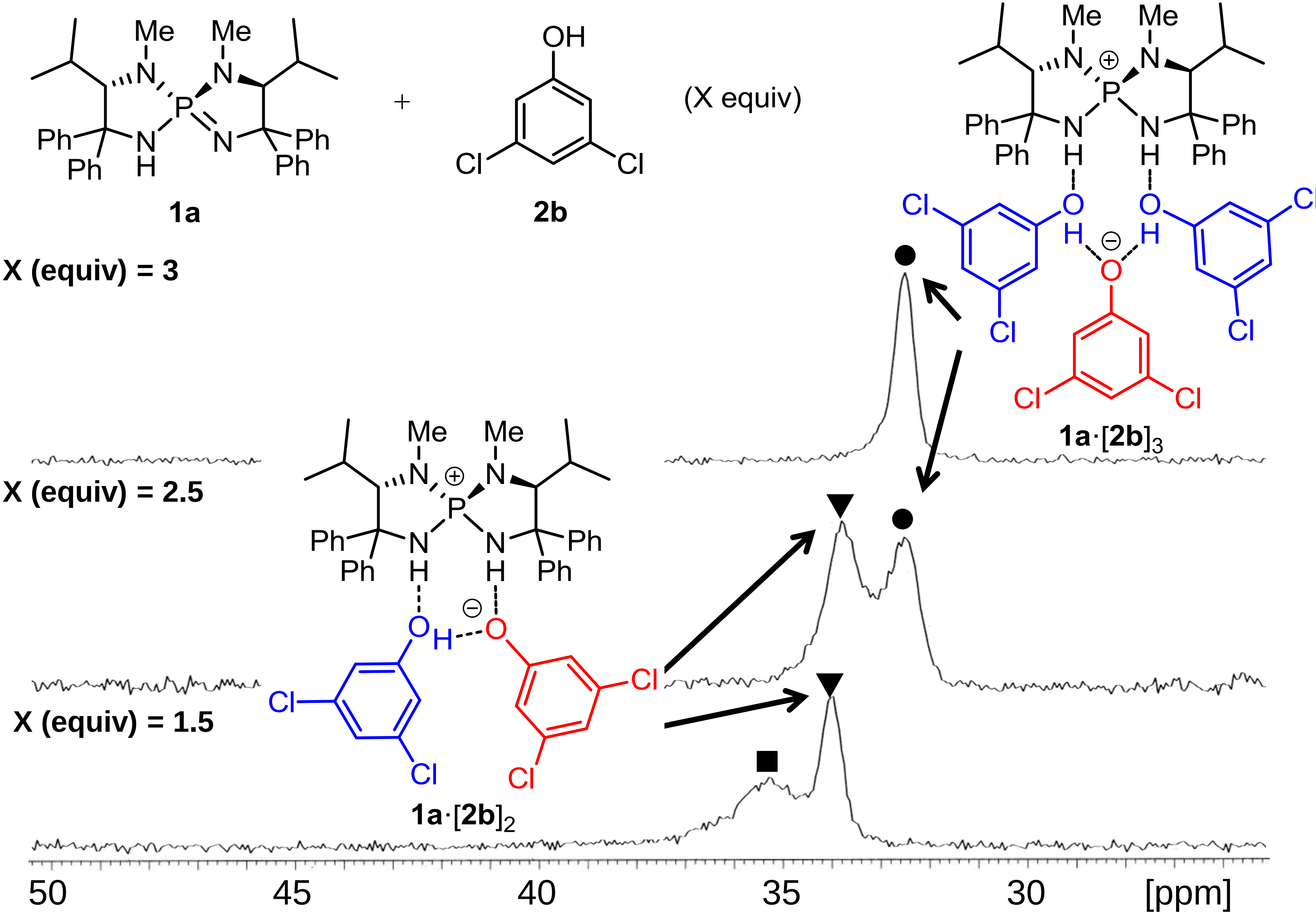
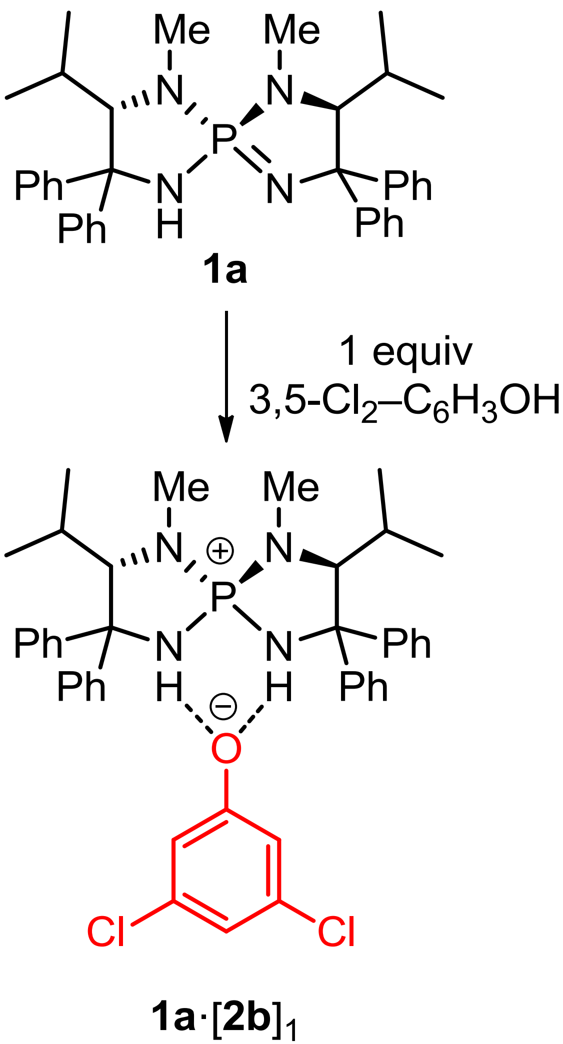
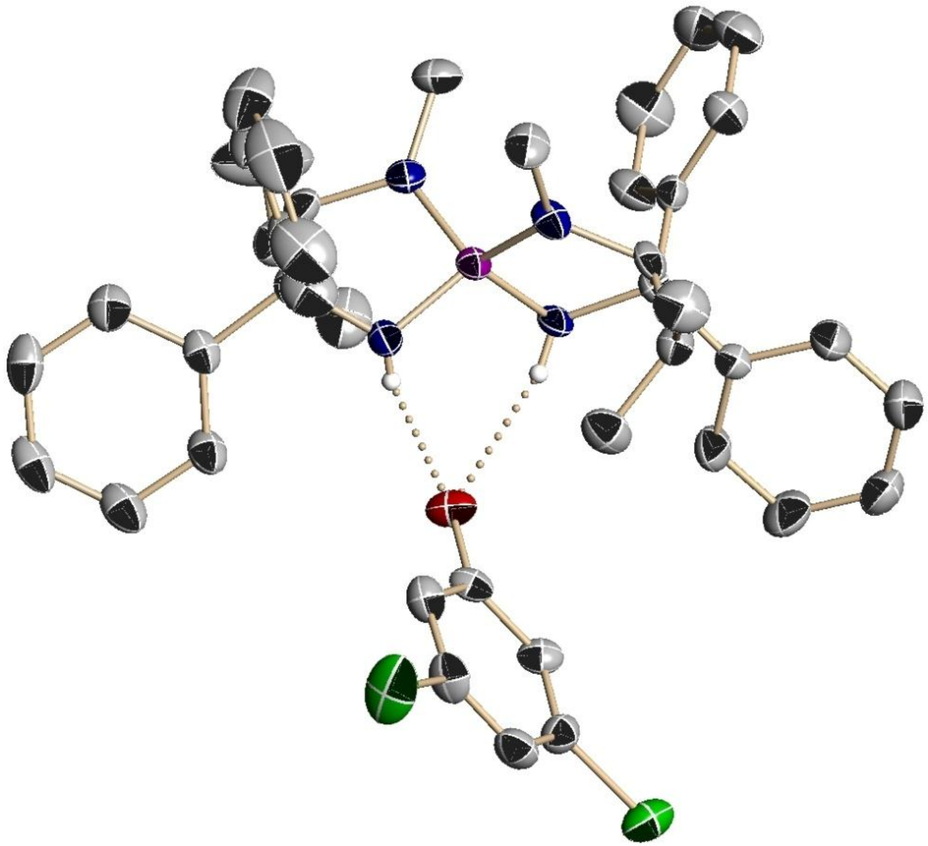


^{31}P NMR Study 1: toluene, –98 °C

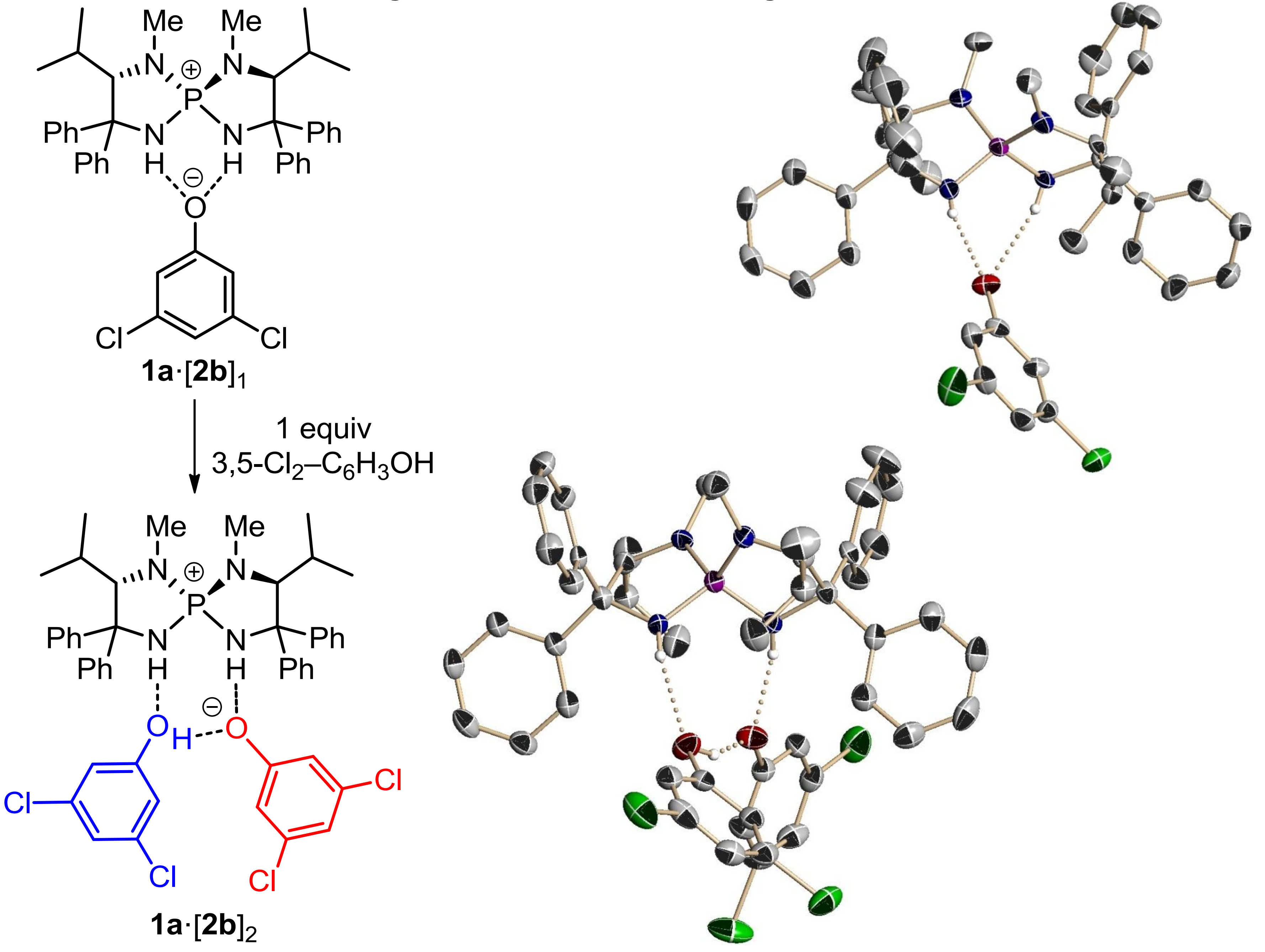


X-ray Diffraction Analysis

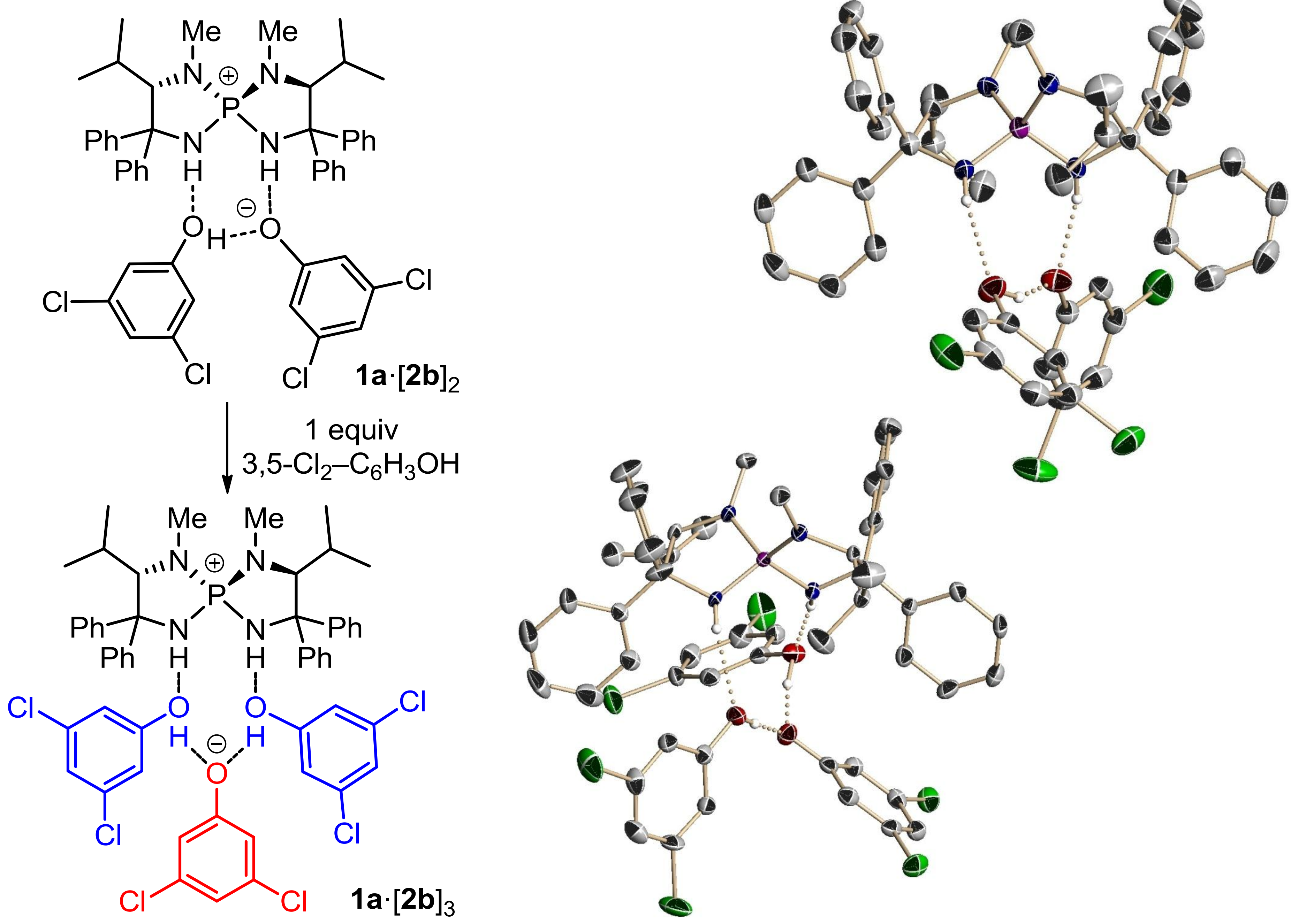




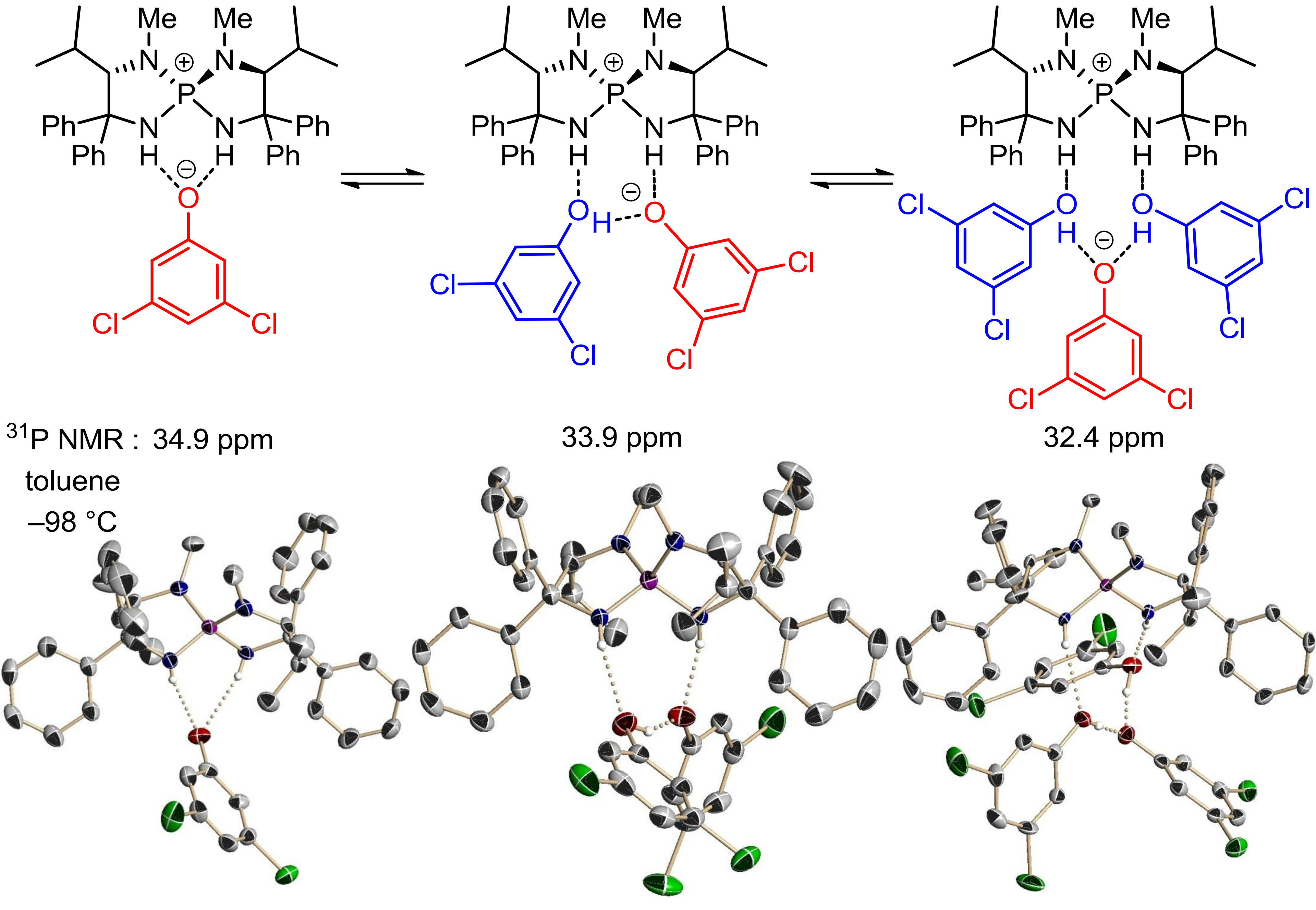
X-ray Diffraction Analysis



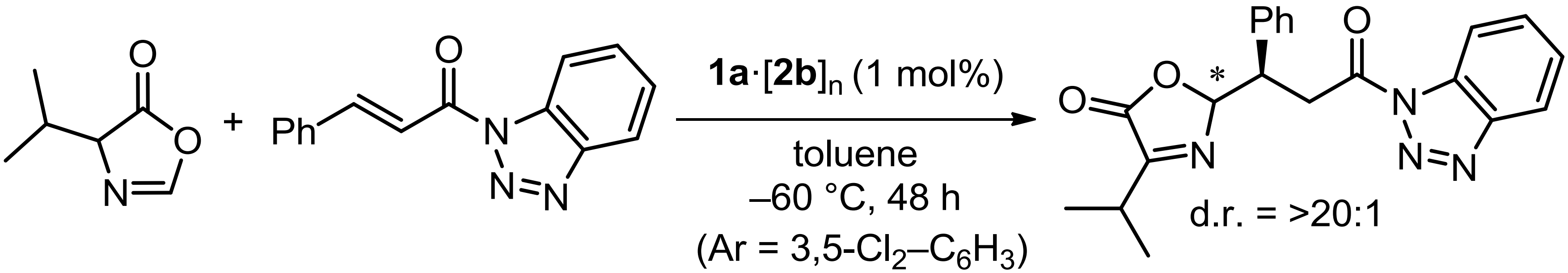
X-ray Diffraction Analysis

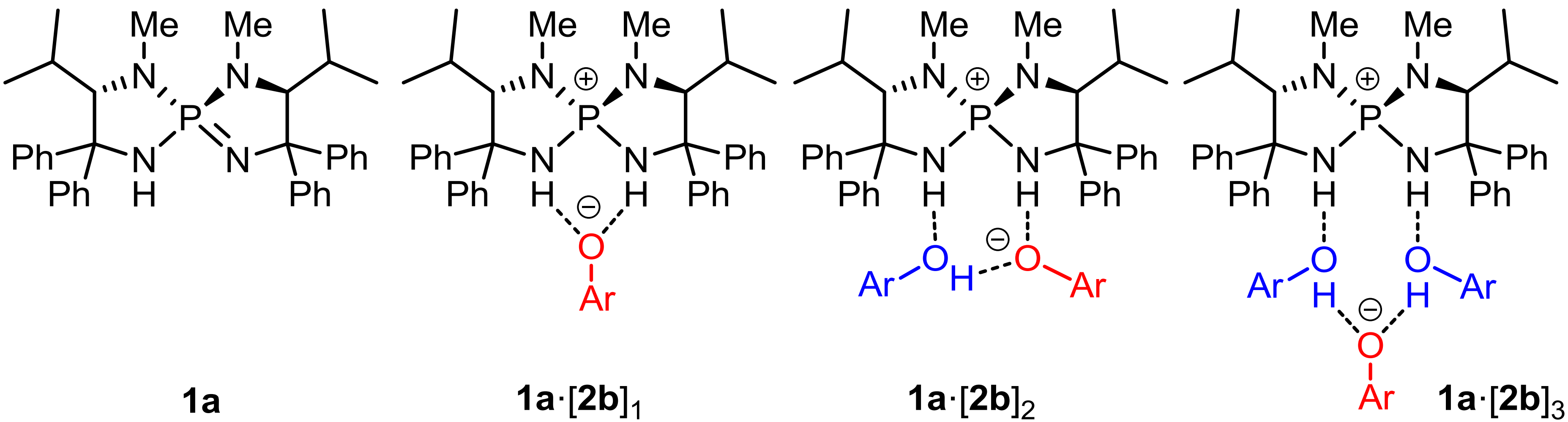


X-ray Diffraction Analysis



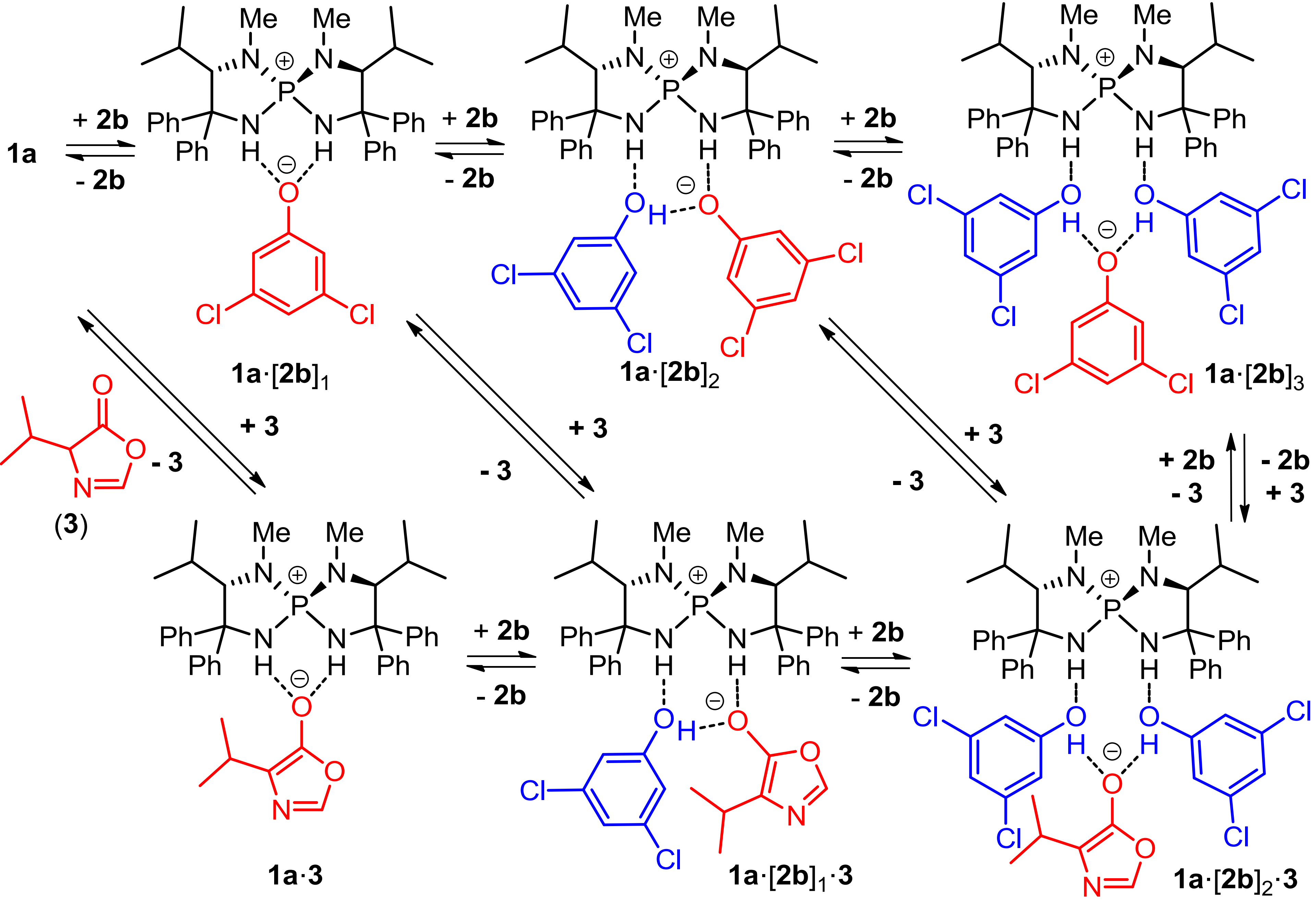
Effect of the Mode of Self-Assembly



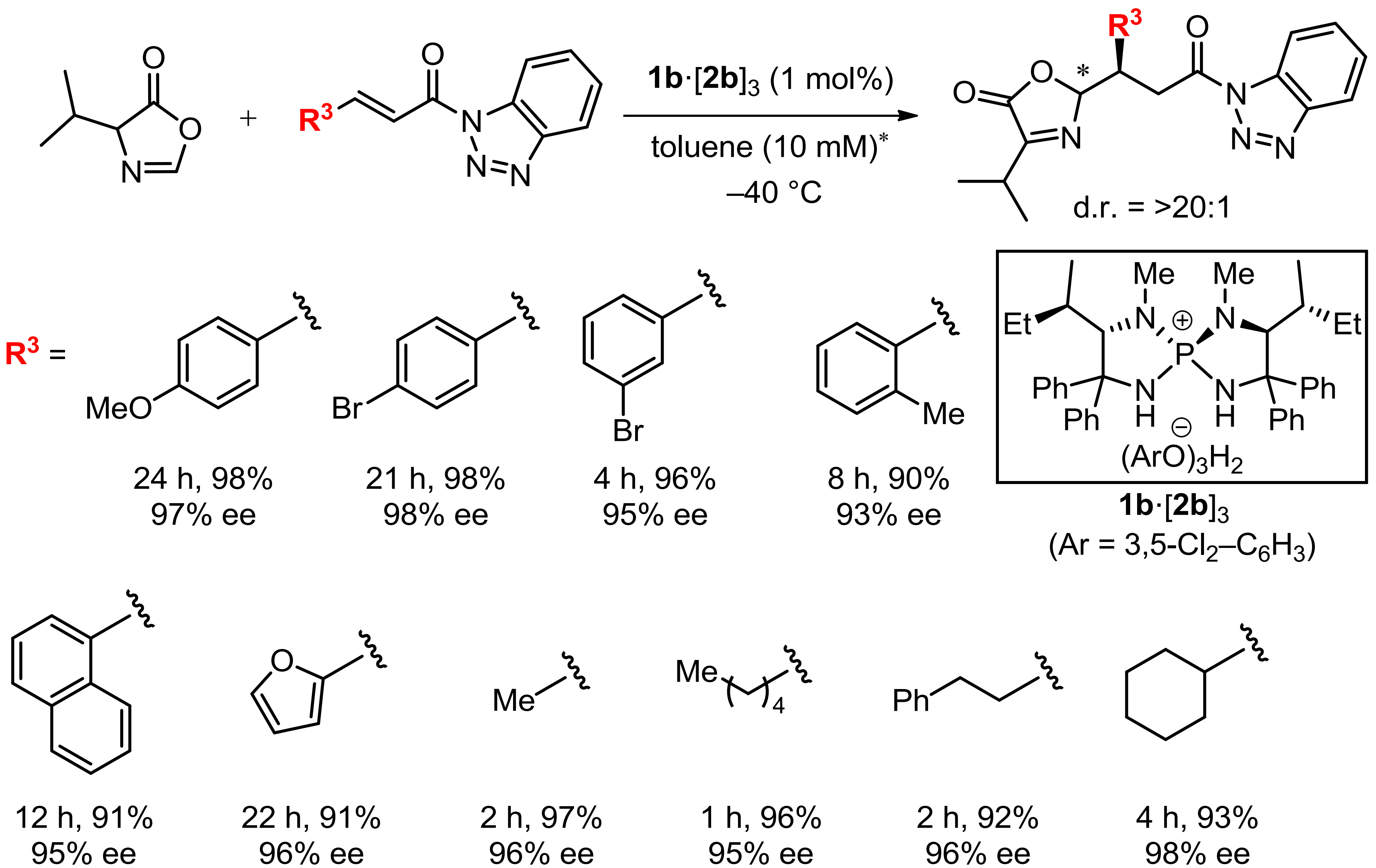


1a	1a·[2b]1	1a·[2b]2	1a·[2b]3
85%, 51% ee	81%, 67% ee	82%, 89% ee	89%, 90% ee

Plausible Molecular Assemblies

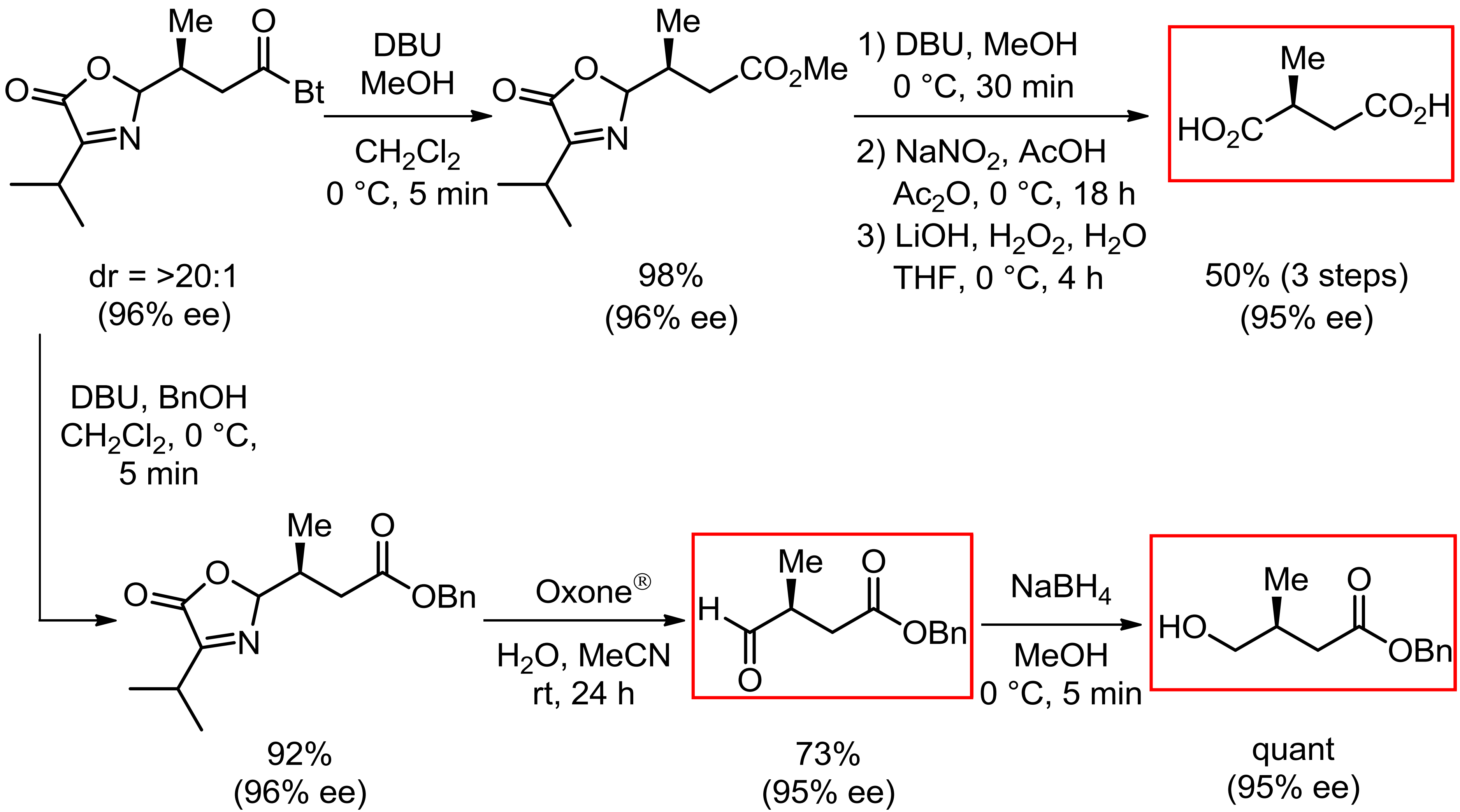


Substrate Scope of α,β-unsaturated Acylbenzotriazole

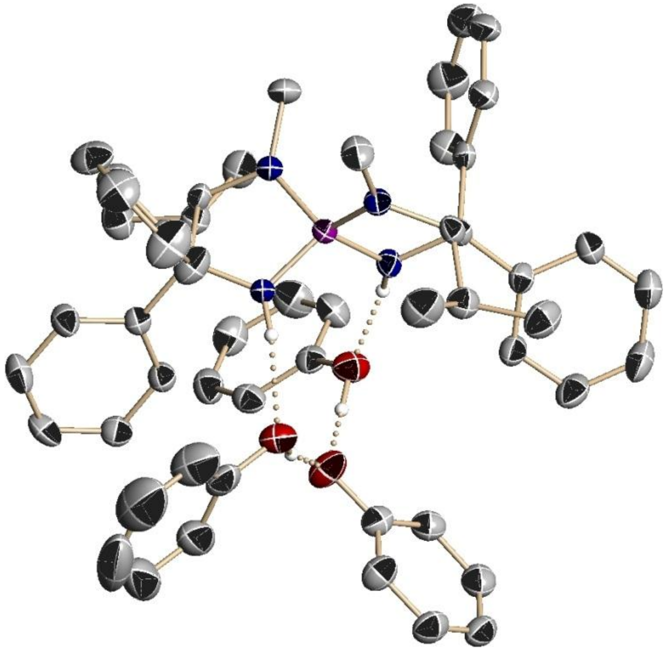


* Concentration was calculated based on the amount of catalyst.

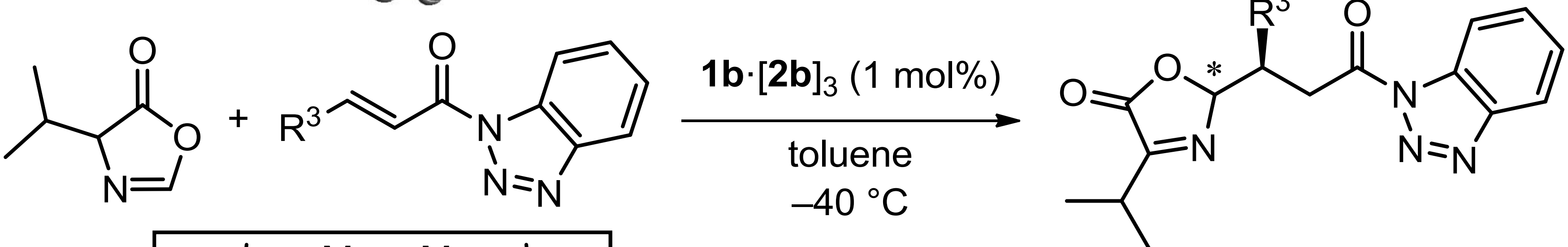
Derivatization of the Product



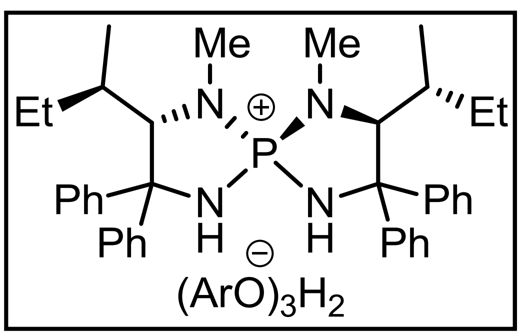
Summary 2



- *All the structural components of catalyst cooperatively participate in the stereocontrolling event.*
- *Increase catalyst loading and decreased solvent volume further improved the enantioselectivity.*



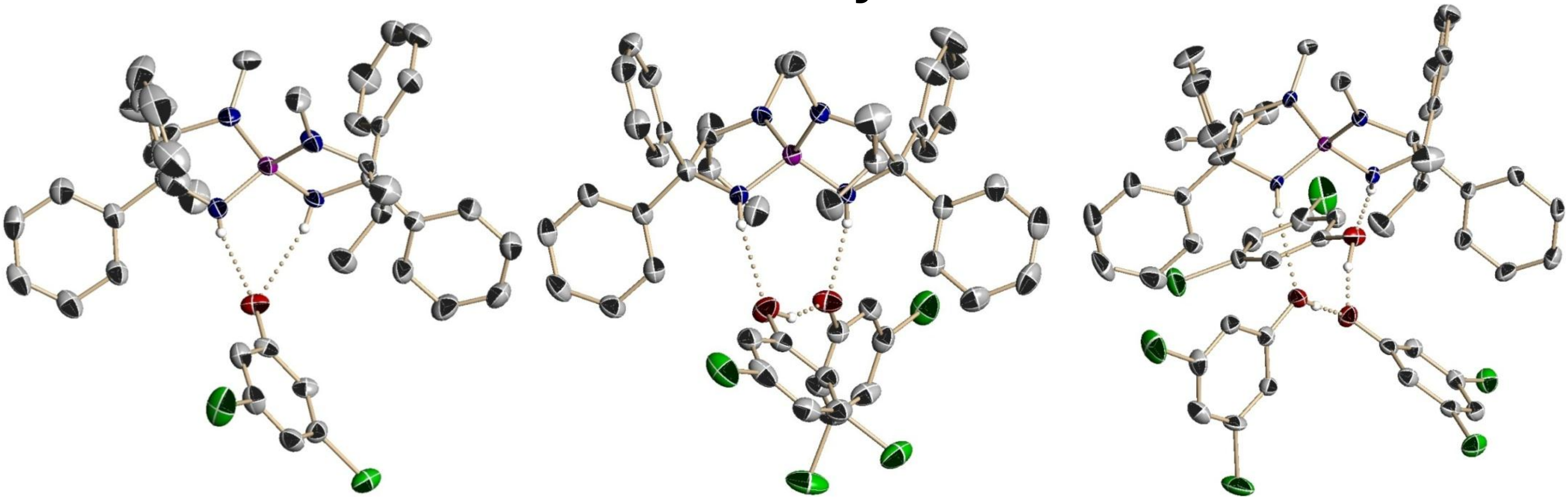
90-98%, d.r. = >20:1
93-98% ee for major isomer

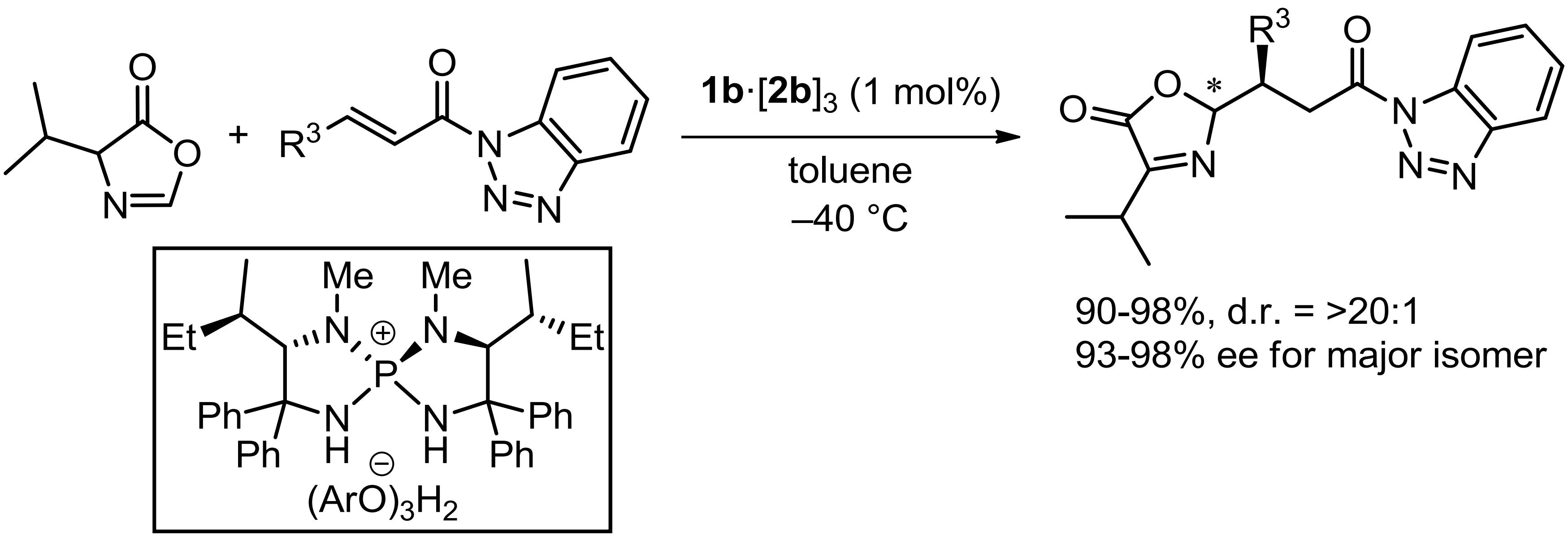


1b·[**2b**]$_3$
(Ar = 3,5-Cl_2–C_6H_3)

Uraguchi, D.; Ueki, Y.; Ooi, T. *Science* **2009**, *326*, 120.
Uraguchi, D.; Ueki, Y.; Ooi, T. *Angew. Chem. Int. Ed*. **2011**, *50*, 3681.

Summary 2





$1b \cdot [2b]_3$
(Ar = 3,5-Cl_2–C_6H_3)

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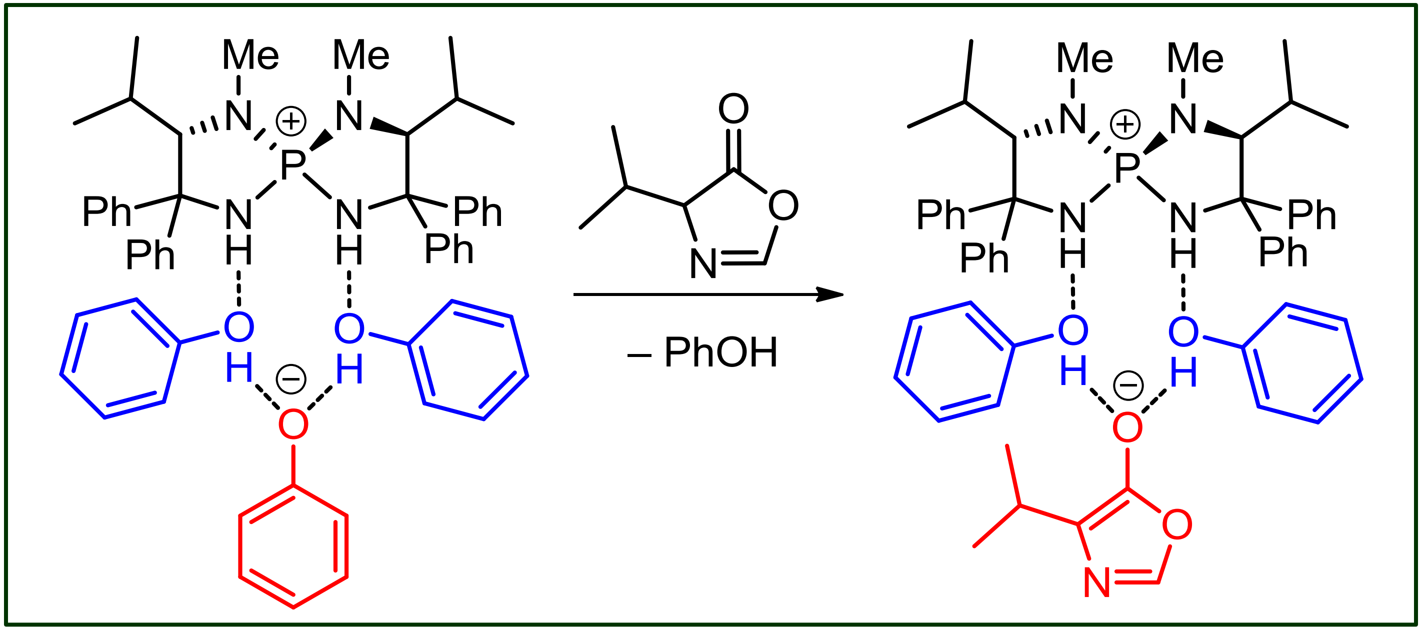
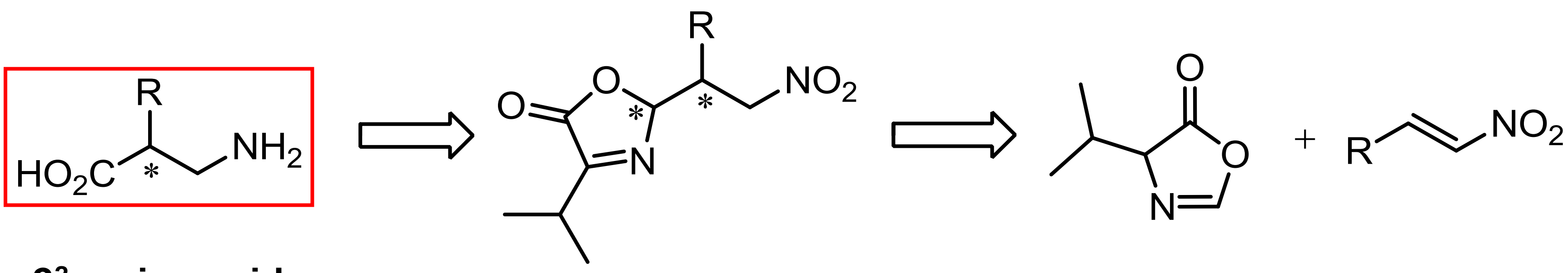
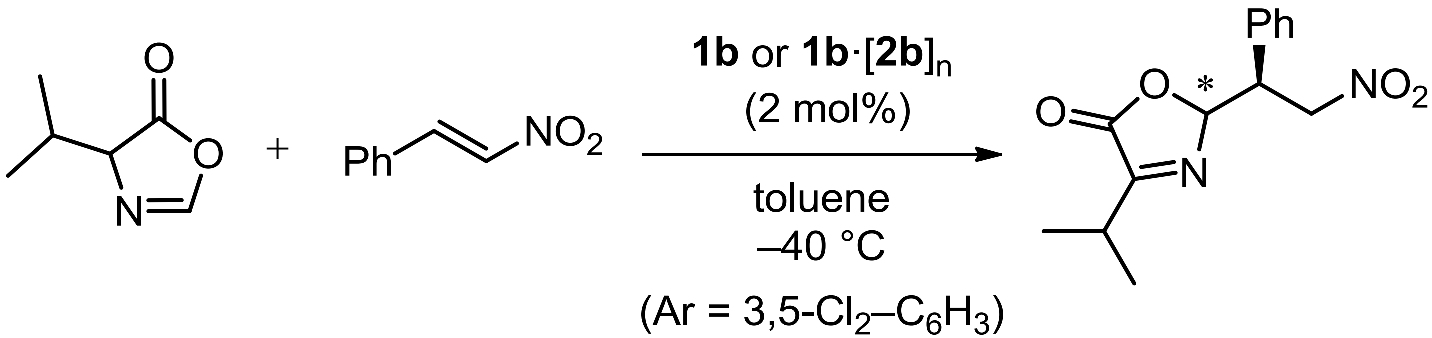
Conjugate Addition to Nitroolefin

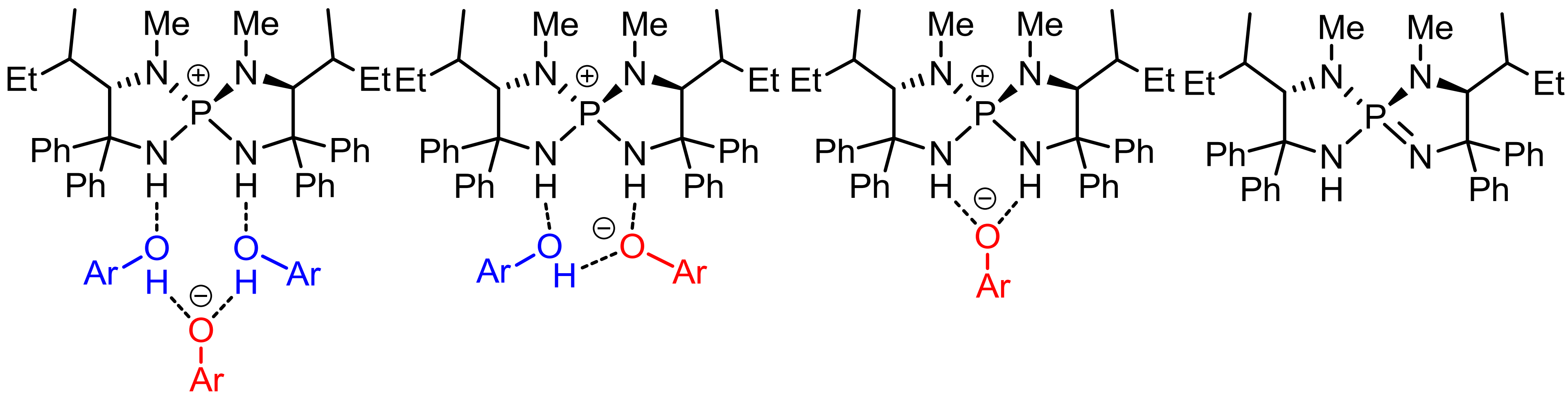




β²-amino acid

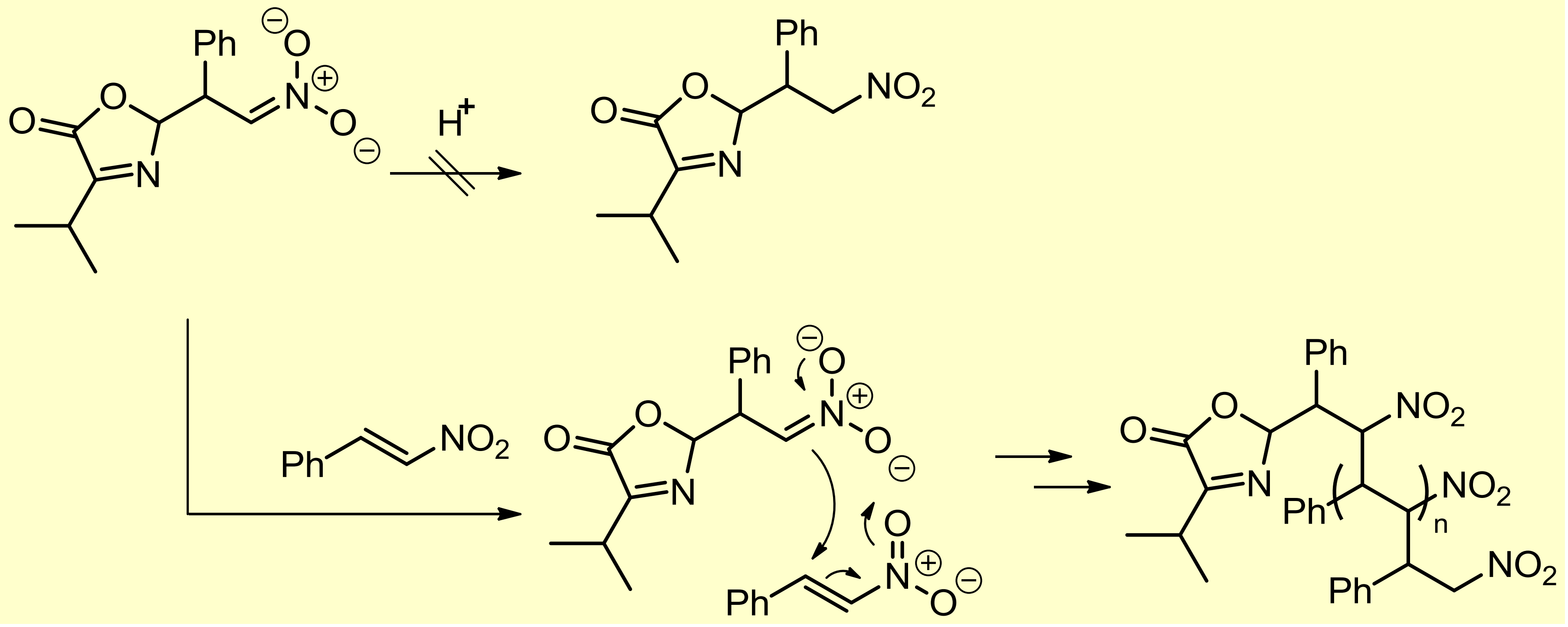
Effect of the Mode of Self-Assembly



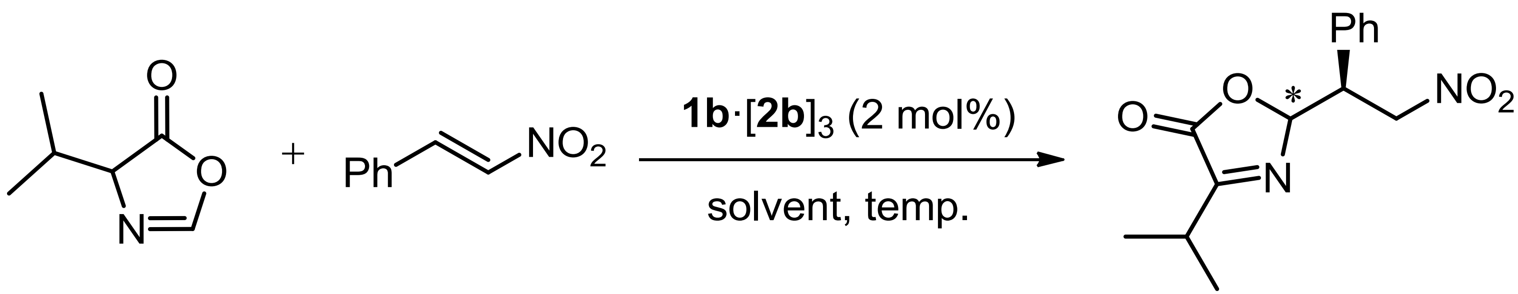


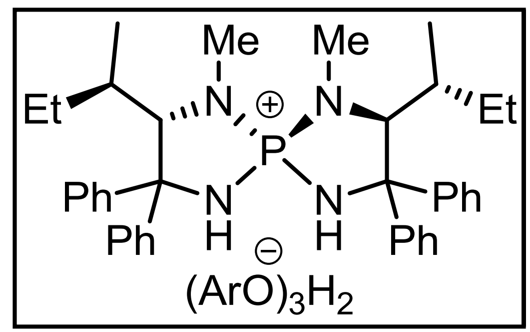
1b·[2b]$_3$	**1b·[2b]**$_2$	**1b·[2b]**$_1$	**1b**
8 h, 90%	4 h, <77%	4 h, <61%	16 h, <10%
d.r. = 1:1.3	d.r. = 1:1.3	d.r. = 1:1	d.r. = 1:2.4
82, 13% ee	89, 10% ee	90, <5% ee	72, 69% ee

Effect of the Mode of Self-Assembly



Modification of Reaction Conditions

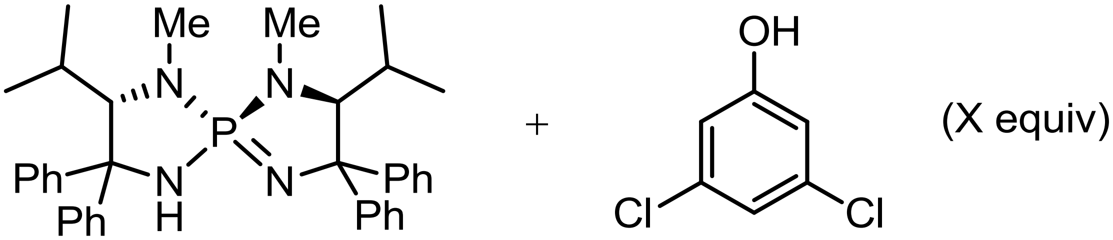




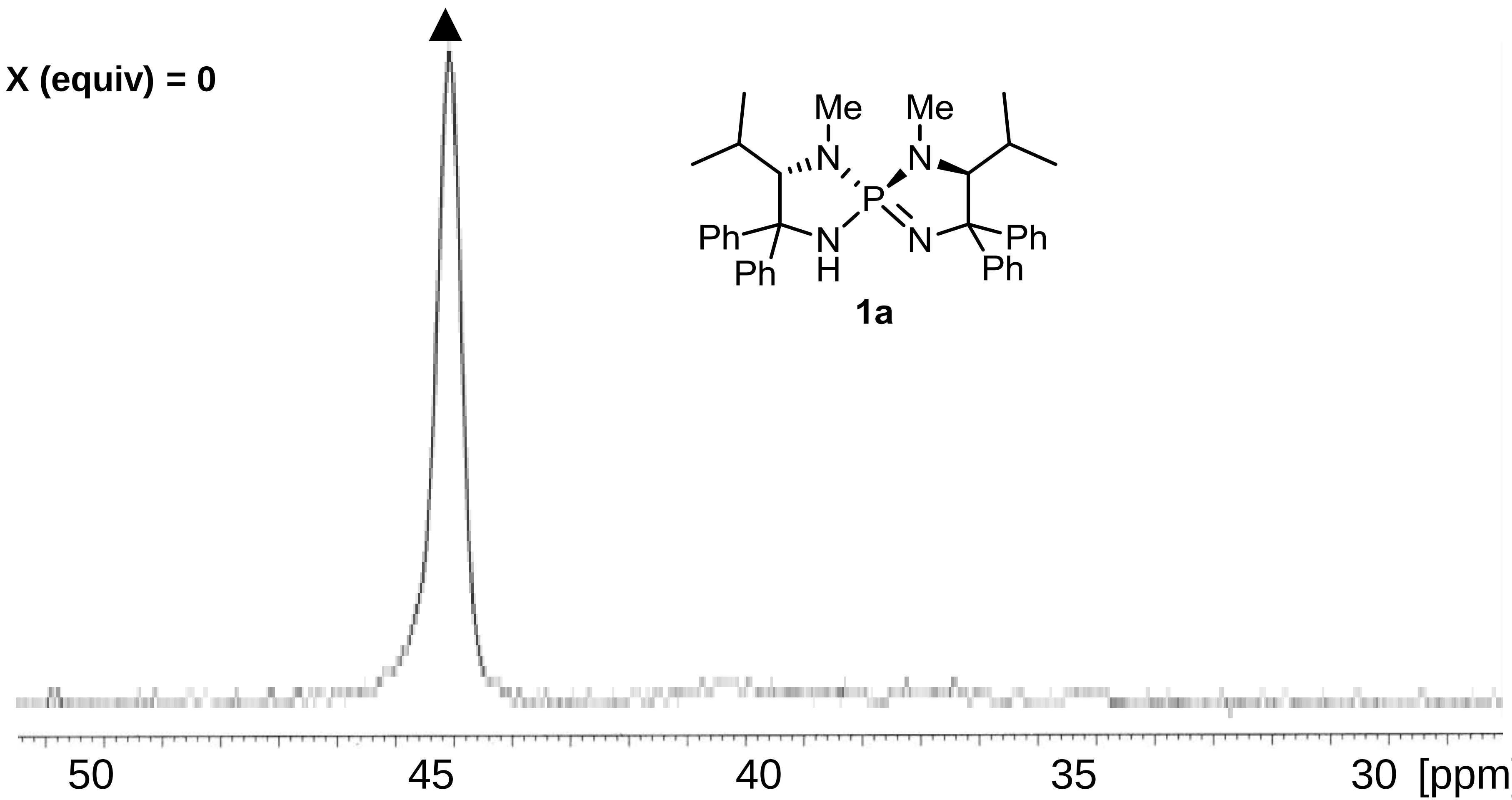
1b·[**2b**]$_3$
(Ar = 3,5-Cl_2–C_6H_3)

toluene, –40 °C	8 h, 90% d.r. = 1:1.3 82, 13% ee
THF, –40 °C	3 h, 99% d.r. = 5.9:1 90, <5% ee
THF, –60 °C	12 h, 96% d.r. = 13:1 94, <5% ee
THF/DMF (5%), –60 °C	12 h, 90% d.r. = >20:1 97, 11% ee

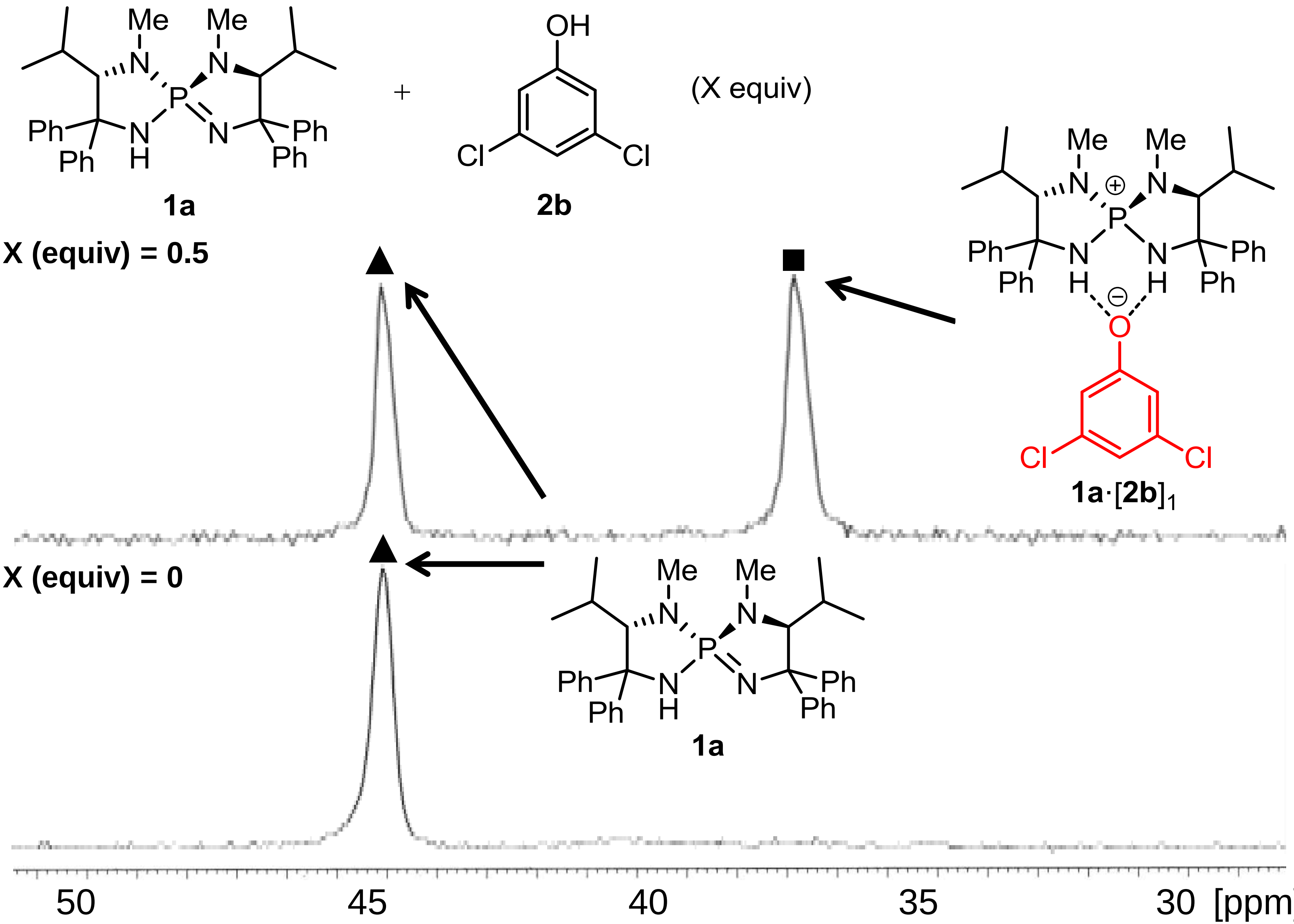
^{31}P NMR Study 2: THF, –98 °C



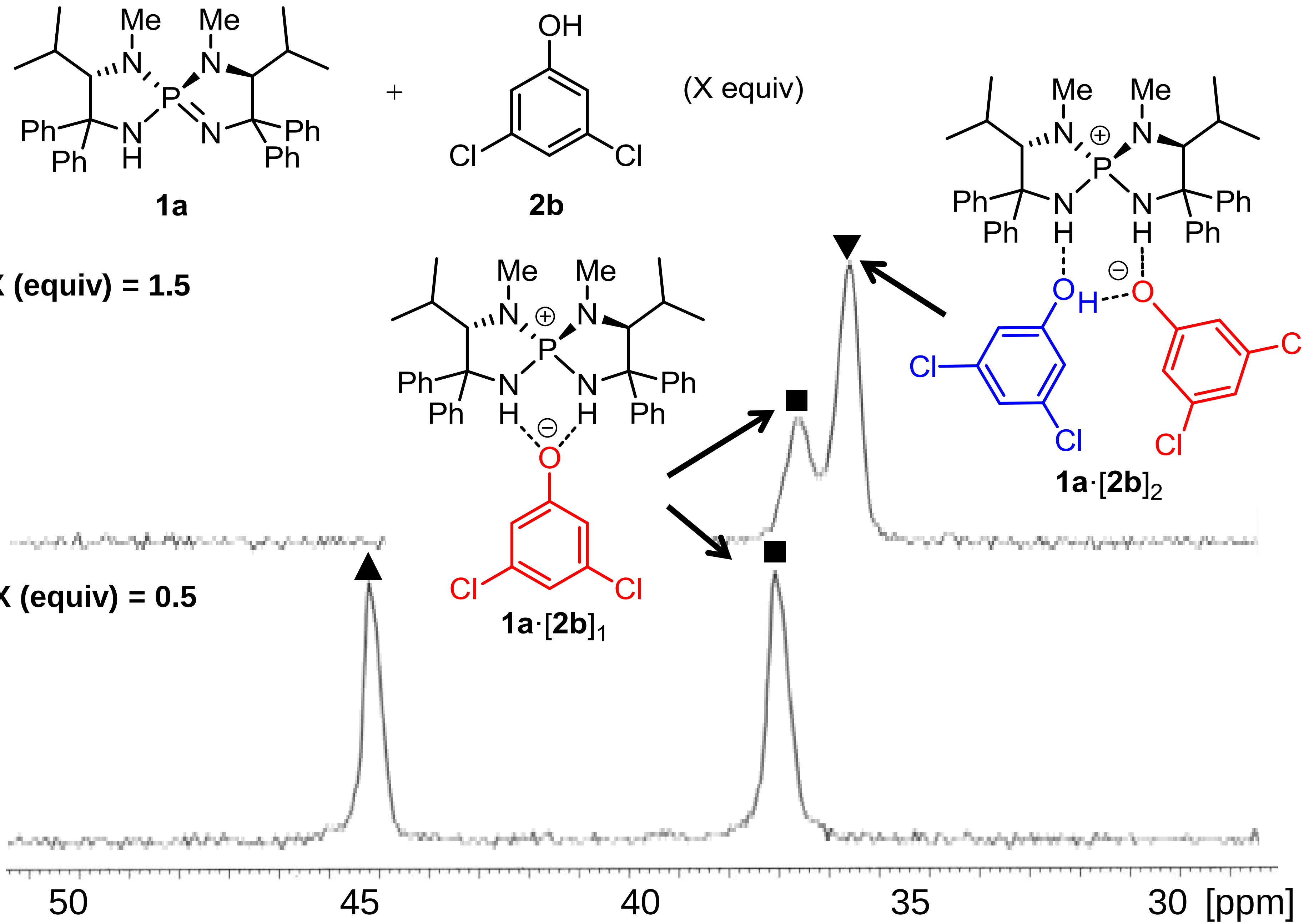
1a **2b**



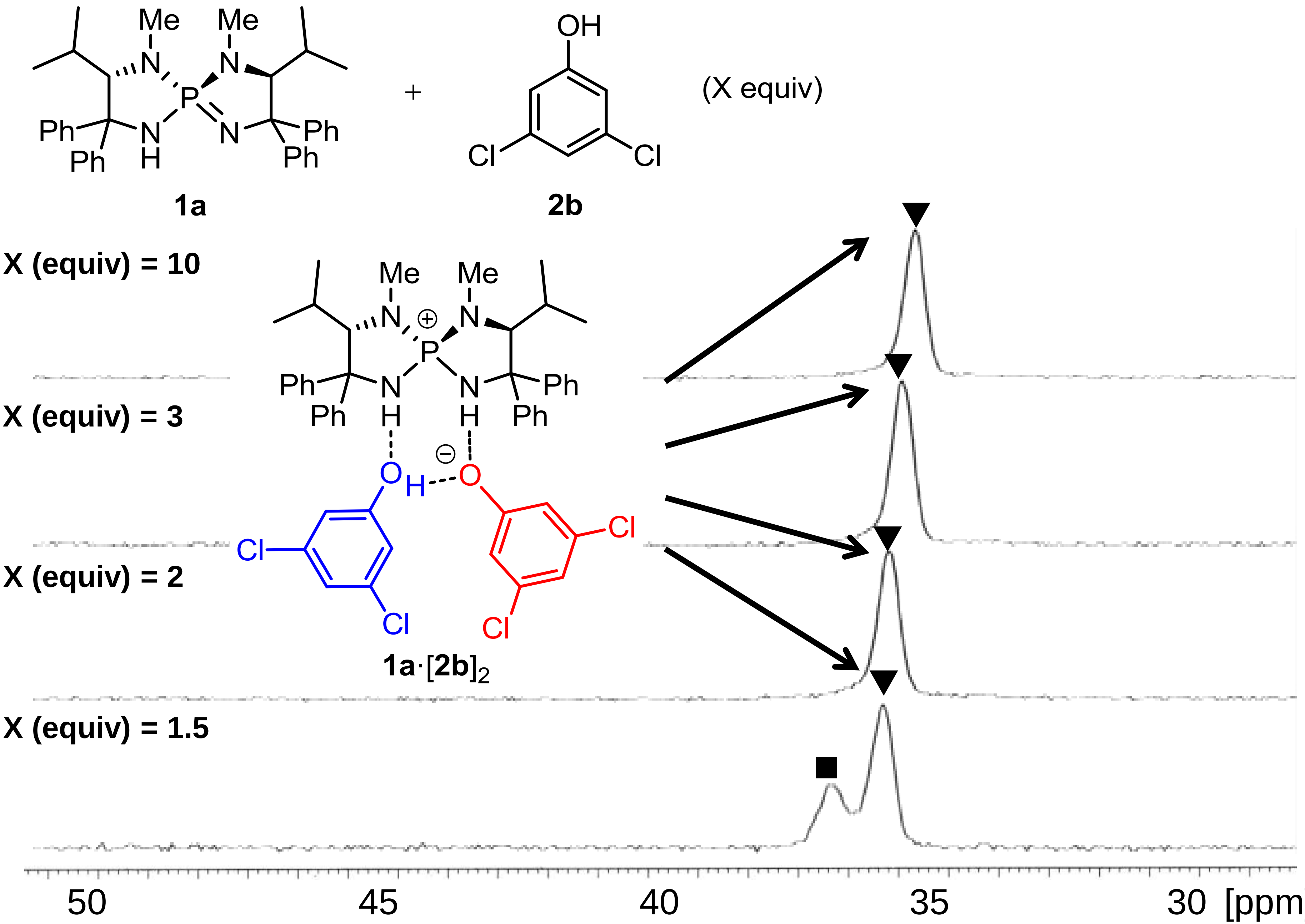
^{31}P NMR Study 2: THF, –98 °C



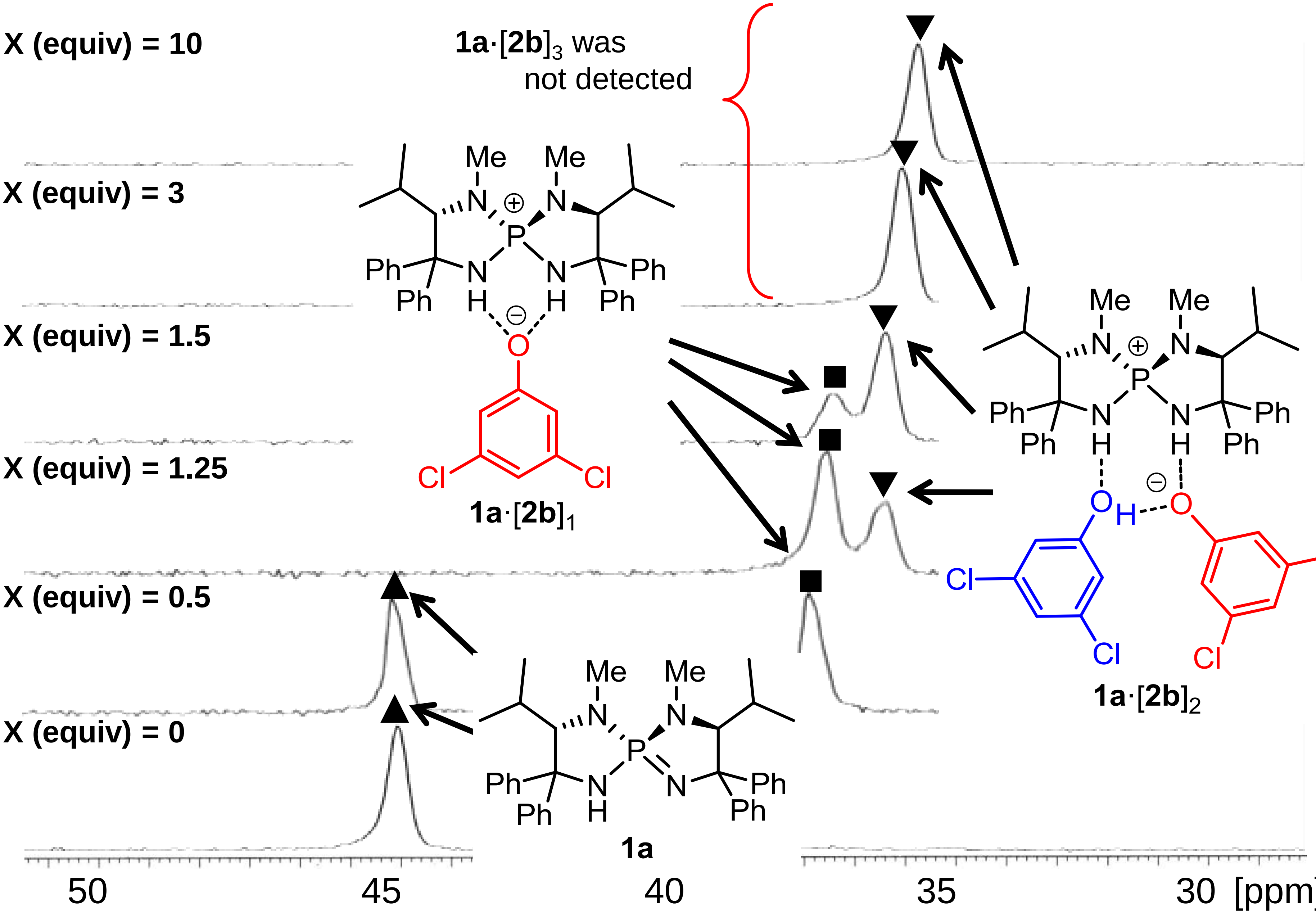
^{31}P NMR Study 2: THF, –98 °C



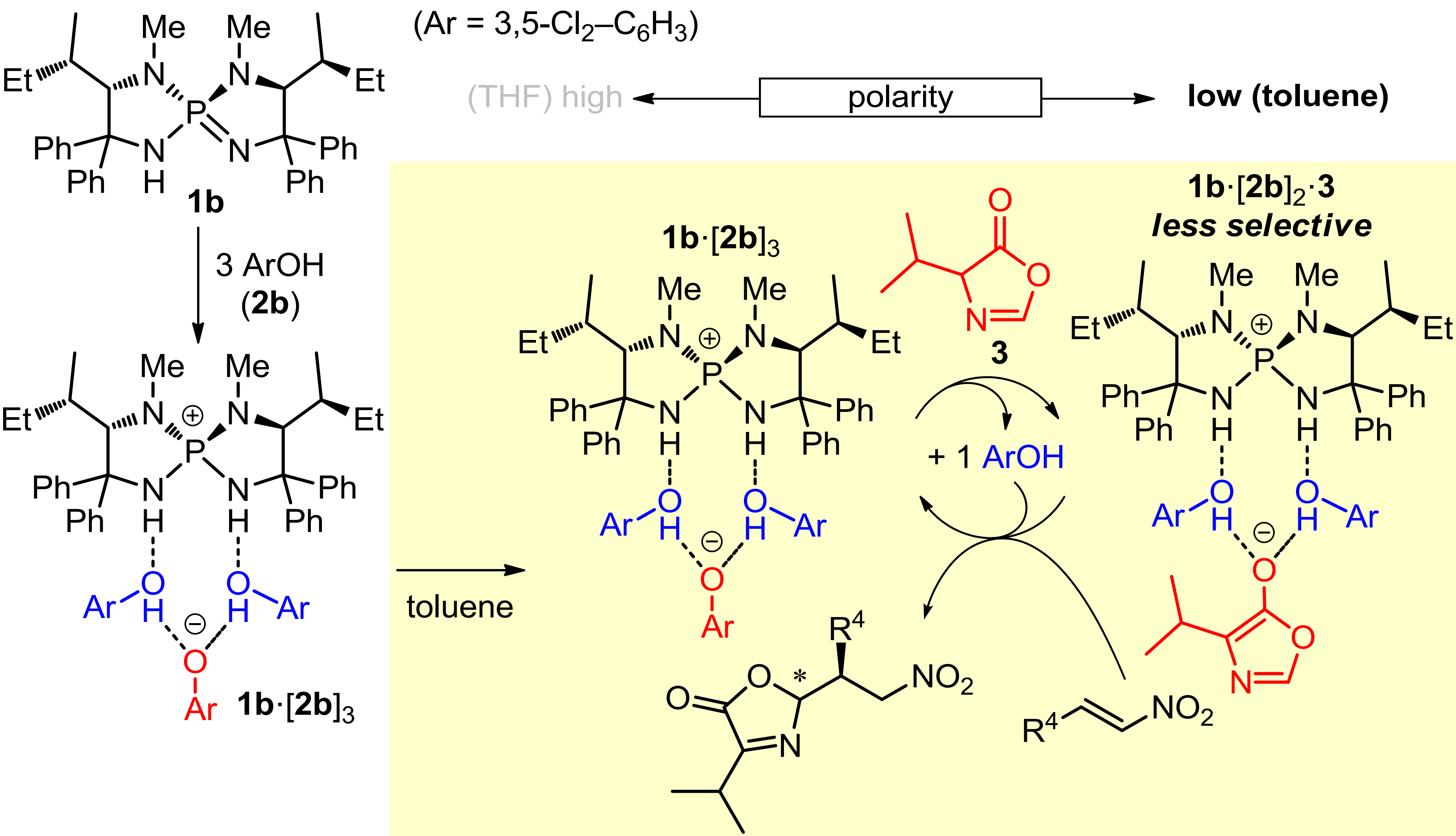
^{31}P NMR Study 2: THF, –98 °C



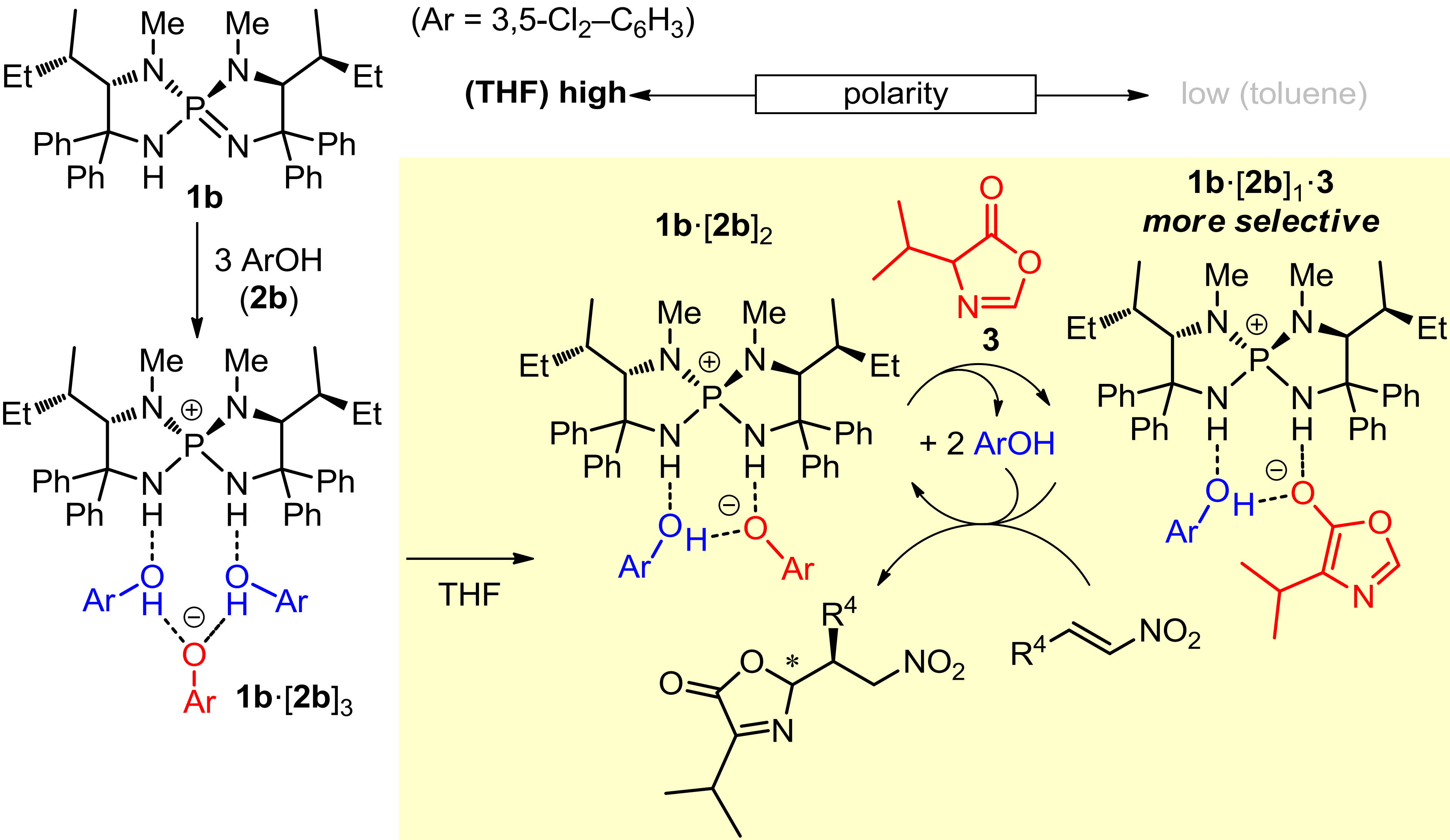
^{31}P NMR Study 2: THF, –98 °C



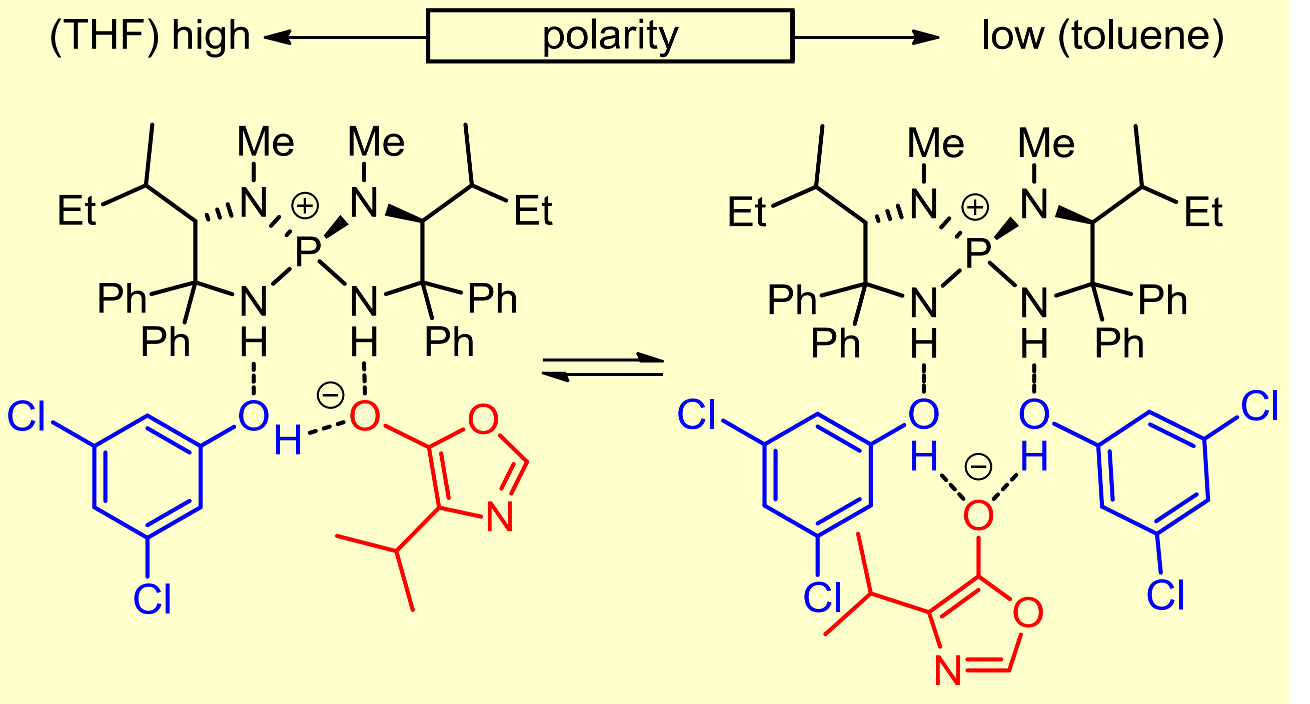
Consideration of the Self-Assembled Catalyst Structure



Consideration of the Self-Assembled Catalyst Structure



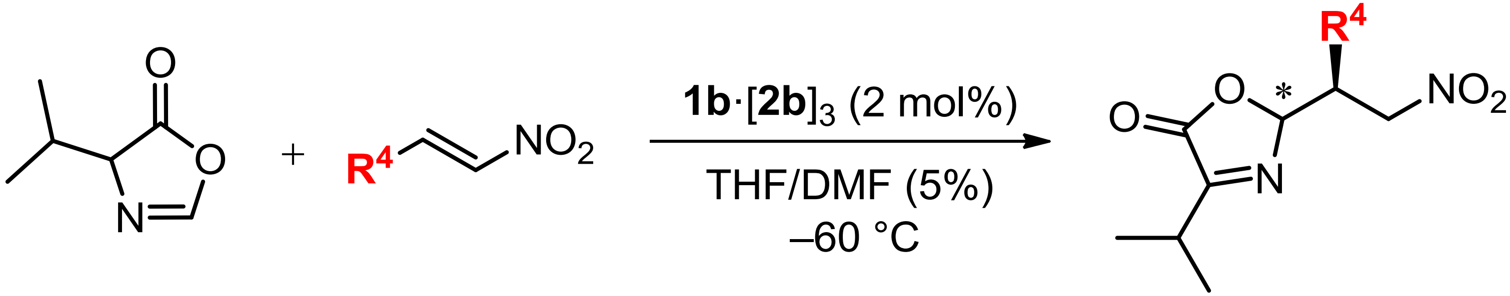
Consideration of the Self-Assembled Catalyst Structure

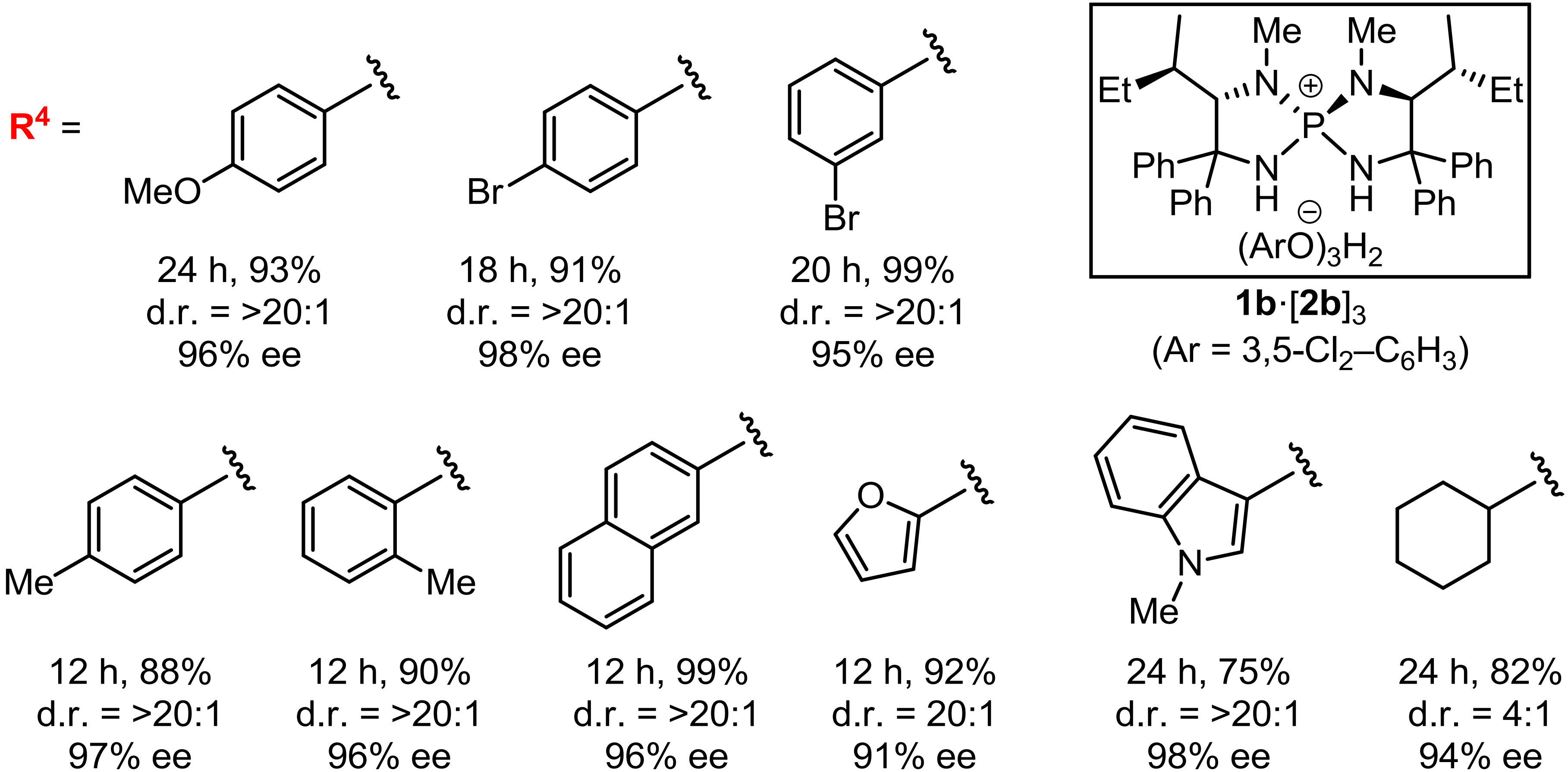


1b·[**2b**]$_1$·**3**
more selective

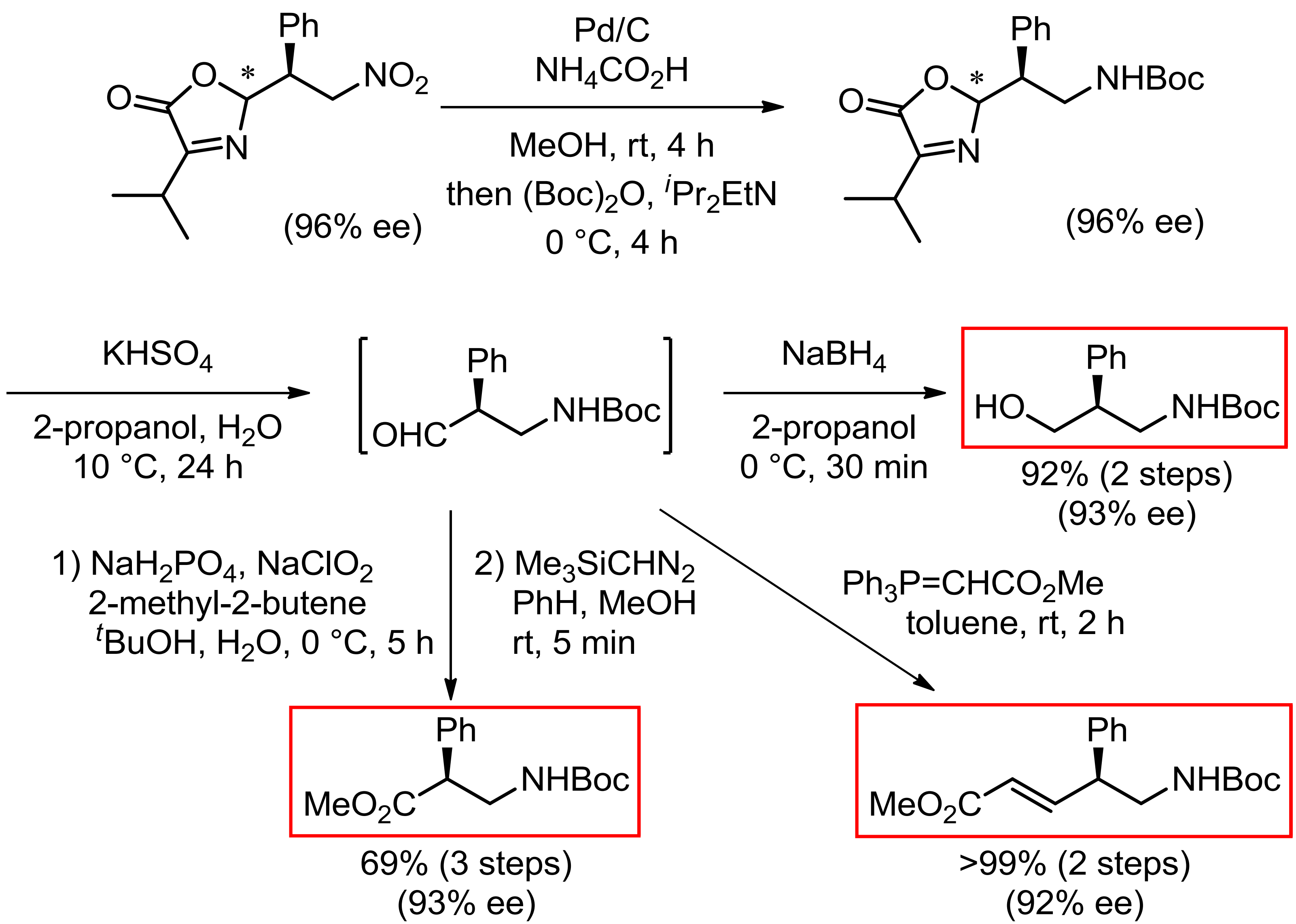
1b·[**2b**]$_2$·**3**
less selective

Substrate Scope of Nitroolefin

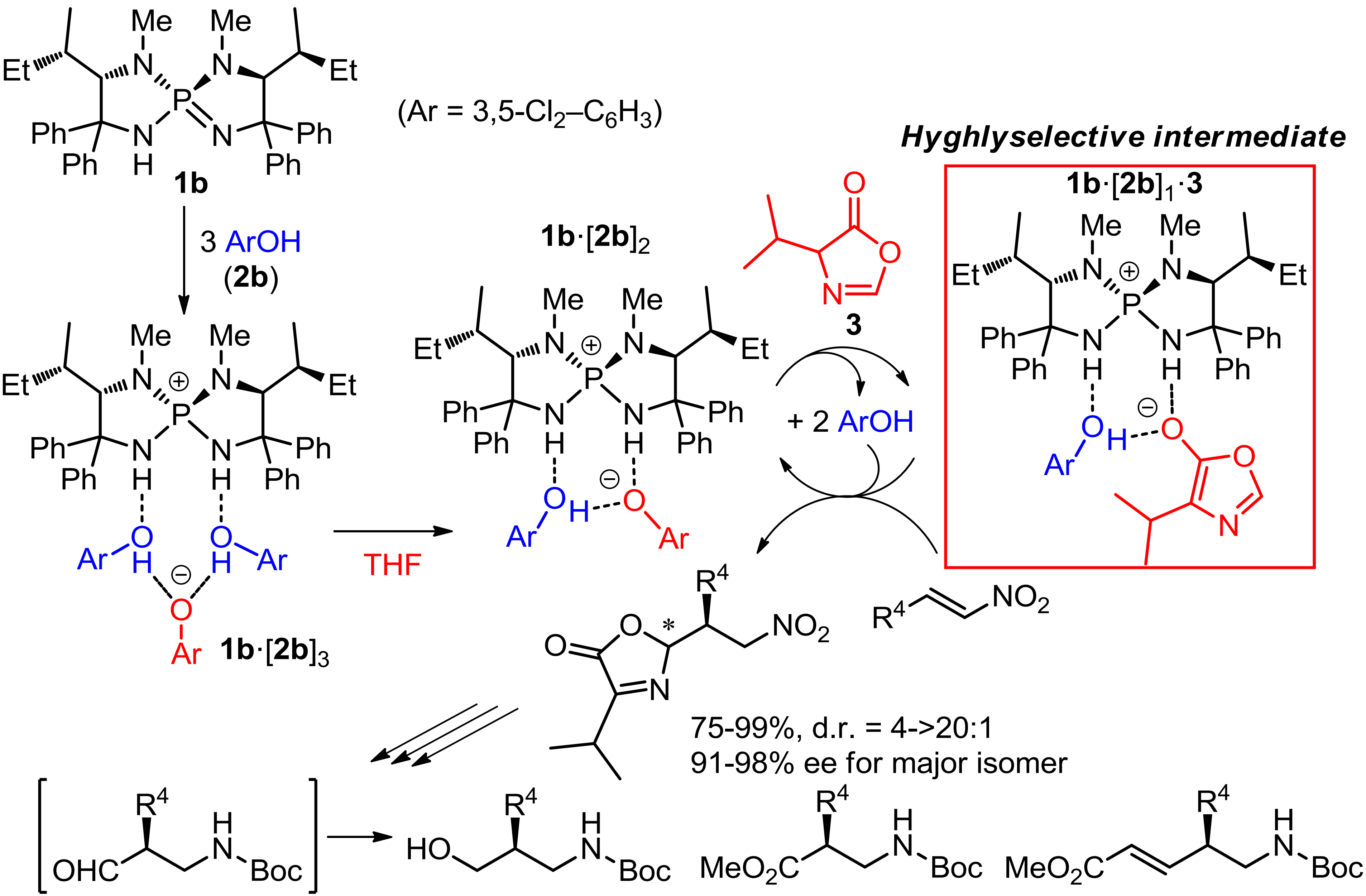




Derivatization of the Product



Summary 3



Uraguchi, D.; Ueki, Y.; Ooi, T. *Chem*. *Sci*. **2012**, *3*, 842.