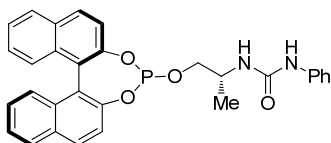
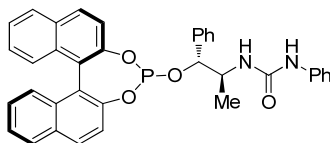


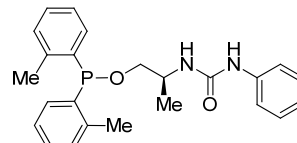
Ligands for Asymmetric Catalysis: UREAPOS



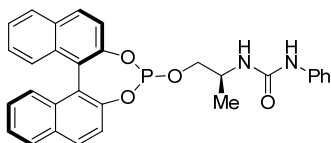
ICT09001A R, 2R-Me-UreaPhos



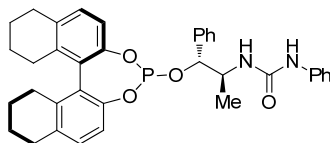
ICT09002A R, 1R,2S-Nor-UreaPhos



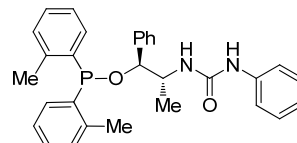
ICT09007A 2S-Me-UreaPhosphinite



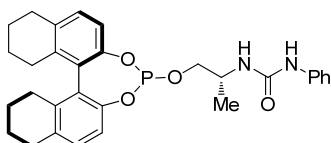
ICT09014A R, 2S-Me-UreaPhos



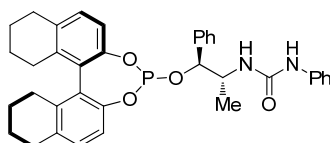
ICT09025A R, 1R,2S-H₈B-Nor-UreaPhos



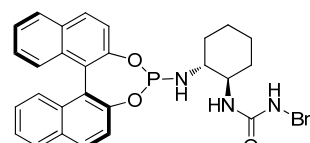
ICT09008B 1R,2S-Nor-UreaPhosphinite



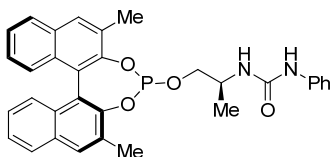
ICT09012A R, 2R-H₈B-Me-UreaPhos



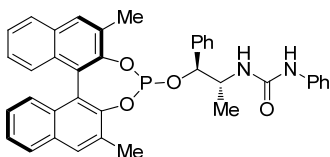
ICT09013A R, 1S,2R-H₈B-Nor-UreaPhos



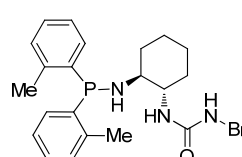
ICT09005B S, 1R,2R-Cyclohexyl-UreaPhos



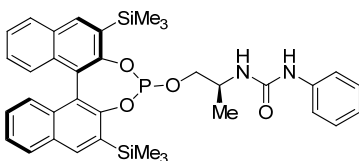
ICT09003B S, 2S-MeB-Me-UreaPhos



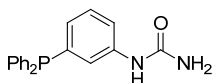
ICT09004A R, 1S,2S-MeB-Nor-UreaPhos



ICT09006A 1S,2S-Cyclohexyl-UreaPhosphinamide



ICT09009A R, 2S-TMSB-Me-UreaPhos



ICT10041A DiPh-UreaPhosphine

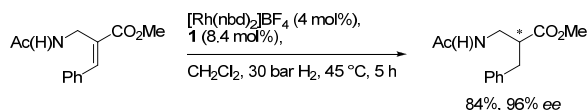
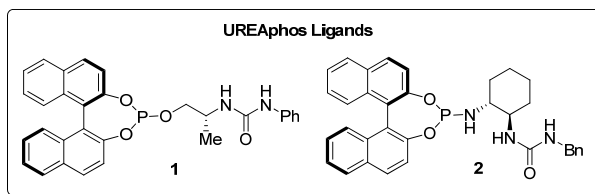
The ligands may be handled and weighed in air but are best stored under inert conditions. Controlled reaction conditions are required, i.e. degassed and dry solvents. It is recommended that the catalysts are studied in a selection of solvents. The monodentate ligands may be mixed in a 1:1 (or other) ratio to obtain heterobidentate supramolecular catalysts instead of homobidentate catalysts, this might enhance catalyst performance. We recommend using of a 2.2:1 ratio of ligand to metal.

APPLICATIONS OF UREAPHOS

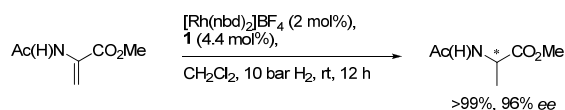
A screening with a set of UREAphos ligands revealed that (*E*)-methyl 2-(acetamidomethyl)-3-phenylacrylate could be converted with very high enantioselectivity using ligand **1**.^[1] After optimization of the reaction conditions the conversion was improved affording the product in 84% yield after five hours (Scheme 1). Also methyl 2-acetamidoacrylate, and dimethyl itaconate were effectively hydrogenated using the same metal-ligand combination (Scheme 2-3). For (*Z*)-methyl 3-acetamidobut-2-enoate the results with ligand **1** were less impressive (45% *ee*), but another member of the UREAphos family, ligand **2**, gave the product with good enantioselectivity (76% *ee*, Scheme 4). A key-advantage of the supramolecular interaction^[2] between the ligands is, in addition to the homobidentate complexes, the possibility to form metal complexes with two different ligands. Especially a strong π -accepting ligand (phosphites, phosphor-amidites) and σ -donating ligand (phosphines, phosphinamides) are an effective combination, because these usually very selectively form a heterobidentate complex. Such type of complex can be highly active and selective in for example the rhodium-catalyzed hydrogenation of methyl 2-(hydroxymethyl)-acrylate (Scheme 5, >99%, 95% *ee*, TOF $1.6 \times 10^3 \text{ h}^{-1}$). This implies that by combining the different ligands a large number of catalysts can be prepared.

[1] J. Meeuwissen, M. Kuil, A. M. van der Burg, A. J. Sandee, J. N. H. Reek, *Chem. Eur. J.* **2009**, *15*, 10272-10279.

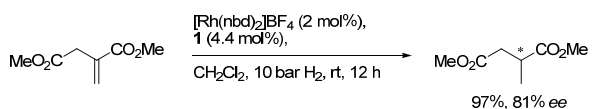
[2] (a) A. J. Sandee, A. M. van der Burg, J. N. H. Reek, *Chem. Comm.* **2007**, 864-866; (b) WO2004103559A2.



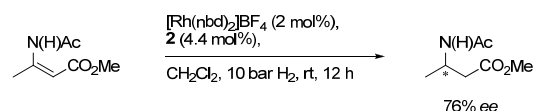
Scheme 1



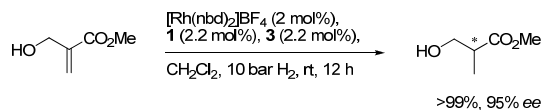
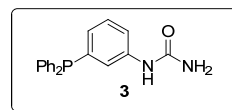
Scheme 2



Scheme 3

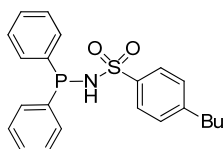


Scheme 4

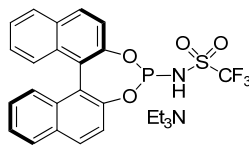


Scheme 5

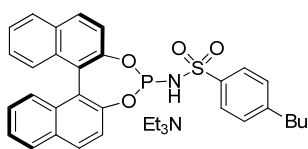
Ligands for Asymmetric Catalysis: METAMORPHOS



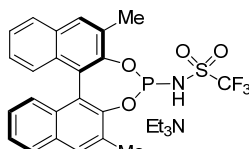
ICT09011A METAMORPhos



ICT09015B S CF₃-METAMORPhos



ICT09010A R (pBu)Ph-METAMORPhos



ICT09011A S MeB-CF₃-METAMORPhos

The ligands may be handled and weighed in air but are best stored under inert conditions. Controlled reaction conditions are required, i.e. degassed and dry solvents. It is recommended that the catalysts are studied in a selection of solvents. Monodentate ligands may be mixed in a 1:1 (or other) ratio to obtain heterobidentate supramolecular catalysts instead of homobidentate catalysts, this might enhance catalyst performance. We recommend using of a 2.2:1 ratio of ligand to metal.

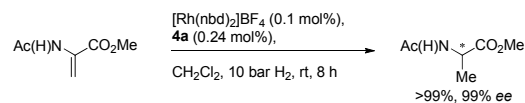
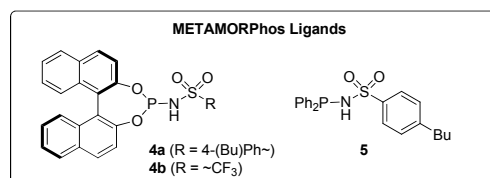
APPLICATIONS OF METAMORPHOS

For the hydrogenation of methyl 2-acetamidoacrylate METAMORPhos-type ligands give excellent results in terms of both conversion and enantioselectivity (Scheme 6).^[4] Interestingly, the activity was doubled when the complex with a combination of ligand **4a** and **5** was used. Although the enantioselectivity slightly decreased (92% ee), these results clearly demonstrate the versatility of the supramolecular approach. Another class of substrates for which METAMORPhos is successful are the cyclic enamides. Both tri- and tetrasubstituted alkenes were converted with high enantioselectivity (Scheme 7 and 8).^[5]

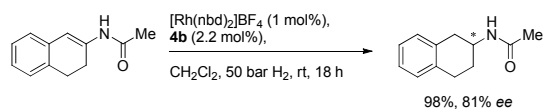
[4] (a) F. W. Patureau, M. Kuil, A. J. Sandee, J. N. H. Reek, *Angew. Chem. Int. Ed.* **2008**, *47*, 3180-3183.
(b) WO2009065856.

[5] F. W. Patureau, S. de Boer, M. Kuil, J. Meeuwissen, P. R. Breuil, M. A. Siegler, A. L. Spek, A. J. Sandee, B.

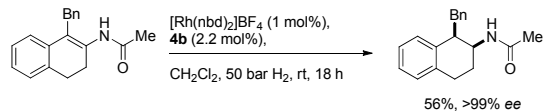
de Bruin, J. N. H. Reek, *J. Am. Chem. Soc.* **2009**, *131*, 6683-6685.



Scheme 6

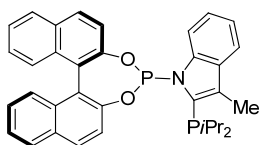


Scheme 7

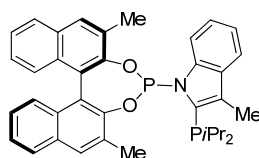


Scheme 8

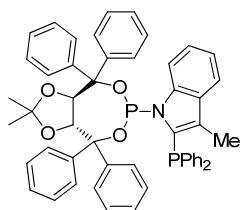
Ligands for Asymmetric Catalysis: IndolPhos



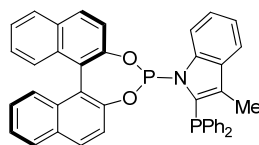
ICT10043A *R* BINOL-Pr-IndolPhos



ICT10044A *R* DiMeBINOL-Pr-IndolPhos



ICT10038A *R,R* TADDOL-Ph-IndolPhos



ICT10042A *R* BINOL-Ph-IndolPhos

The ligands may be handled and weighed in air but are best stored under inert conditions. Controlled reaction conditions are required, i.e. degassed and dry solvents. It is recommended that the catalysts are studied in a selection of solvents. We recommend to use of a 1.1:1 ratio of ligand to metal.

The InCatT Ligand Kit (consisting of 15 ligands of UreaPhos and METAMORPhos) is available for purchase through **Strem Chemicals Inc.**

Other enantiomers are also available. Custom synthesis of other UreaPhos, METAMORPhos, and IndolPhos members is possible on request, also on larger scale.