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Trip Report: 37th Middle Atlantic Regional Meeting Rutgers University Piscataway, New Jersey May 22 – 25, 2005

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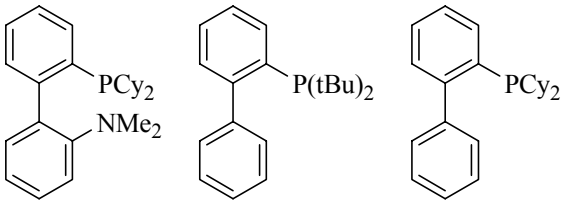
Abstract. *The 37th Middle Atlantic Regional Meeting was held at Rutgers University May 22-25, 2005. This report highlights selected presentations from the seminars and poster sessions.*

"A Synergy between Synthetic Organic and Organometalic Chemistry,"
John F. Hartwig, (Yale University), New Haven, CT.

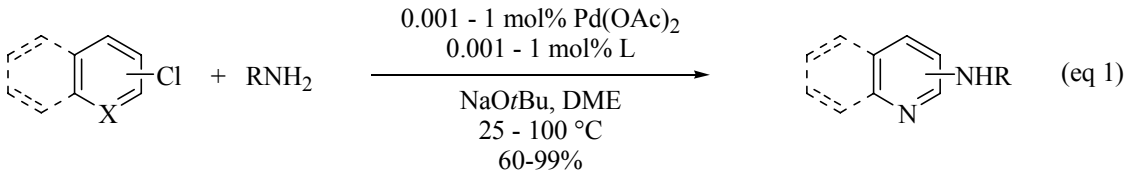
Professor Hartwig discussed a number of aspects of transition metal catalysis and organometallic chemistry. Example topics included the development of highly reactive, general catalysts for coupling aryl chlorides with primary nitrogen nucleophiles, including the use of zinc trimethylsilylamide as a mild ammonia equivalent and base for the amination of aryl halides and triflates.

Catalysts are available that will couple a wide range of amines with aryl halides; however, there are several limitations such as short lifetimes in reactions of primary amines and aryl chlorides, limited scope and the need for large amounts of catalyst. These limitations are present even when using the most recently developed hindered alkylmonophosphines (Figure 1).

Figure 1: Examples of hindered alkylmonophosphines.

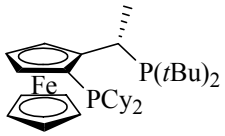


Selecting ligands (Josiphos) that combine steric hindrance, strong electron donation and tight chelation led to a catalyst that possesses a long lifetime as well as high activity for reactions of chloropyridines and aryl chlorides with primary nitrogen nucleophiles (eq 1).



(eq 1)

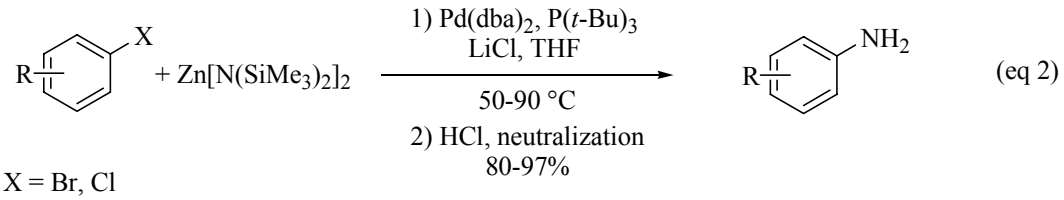
X = C, N
R = 1°, 2°, 3° amines; aniline, aryl imines, aryl hydrazines, 1° aryl amides

L = 

Josiphos

Shen, Q.; Shekhar, S.; Stambuli, J. P.; Hartwig, J. F. **2005** *Angew. Chem. Int. Ed*, 44, 1371-1375.

Zinc trimethylsilylamide ($Zn[N(SiMe_3)_2]_2$) was shown to be a mild ammonia surrogate and base for the amination of aryl halides or triflates. Both electron poor and electron rich meta- and para-substituted aryl halides or triflates perform well in the reaction (eq 2). However, the bulkiness of the reagent does not allow reaction to occur with ortho-substituted aryl substrates.



(eq 2)

X = Br, Cl
R = H, *p*-CN
NO_2, CO_2Et
CF_3, Me
OMe, C(O)Ph
C(O)Et, 3,5-$(CF_3)_2$

Lee, D.; Hartwig, J. F.; **2005** *Org. Lett.* 7, 6, 1169-1172

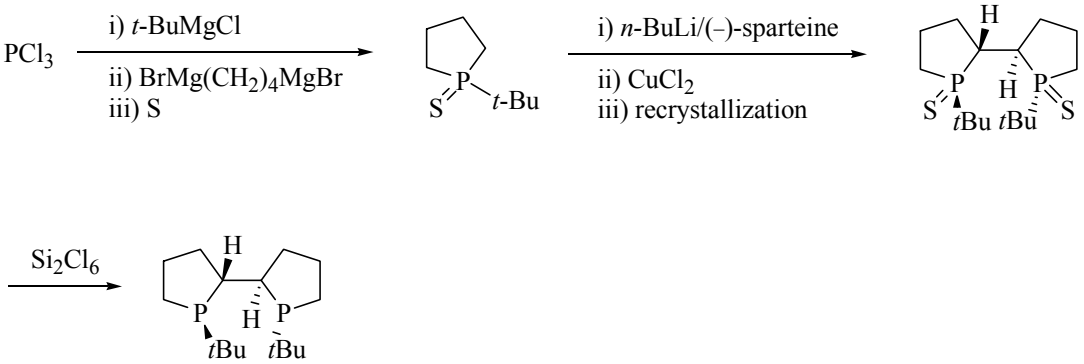
Reactions performed with $Zn[N(SiMe_3)_2]_2$ in the presence of (*S*)-naproxen methyl ester gave high yields of recovered ester (88-98% recovery, ≥97% ee) illustrating the mild reaction conditions.

"Development of A New Generation of Asymmetric Hydrogenation Catalysts,"
Xumu Zhang, (Penn State University), University Park, PA.

A number of chiral ligands have been developed that give excellent enantioselectivities in asymmetric hydrogenations. However development of more practical and efficient ligands in terms of synthetic accessibility, high enantioselectivity, and high turnover number remains an important goal.

The conformational properties of Rh-ligand complexes are important in determining enantioselectivity. Generally a rigid backbone in the ligand leads to high product enantioselectivies. Building on that principle Dr. Zhang's group developed a conformationally rigid ligand with a new structural motif differing from previous chiral ligands. The ligand, (1*S*, 1*S*', 2*R*, 2*R*')-TangPhos, is prepared from phosphorous trichloride in three steps (Scheme 1).

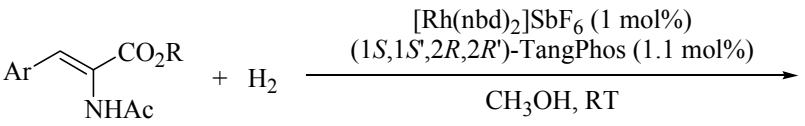
Scheme 1



(1*S*,1*S*',2R,2*R*')-TangPhos

Tang, W.; Zhang, X. **2002** *Angew. Chem. Int. Ed.*, 41, 9, 1612-1614

Examples of asymmetric hydrogenation of α-(acrylamino)acrylic esters and α-arylenamides are given below (eq 3 and eq 4 respectively).

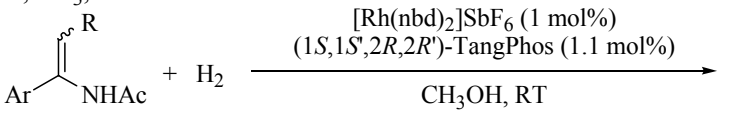


(eq 3)

≥ 99% ee for all example substrates

Ar = Ph, *p*-FPh
p-MeOPh, *m*-BrPh
o-ClPh, 2-thienyl
2-napthyl

R = H, CH_3, *N*-Bz

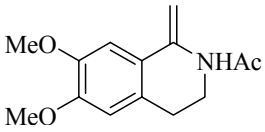


(eq 4)

≥ 97% ee for all example substrates

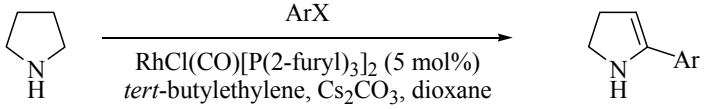
Ar = Ph, *m*-MePh
p-CF_3Ph, *p*-CyPh
p-PhPh, 2-napthyl
p-MeOPh

R = H, CH_3, *i*-Pr, Bn



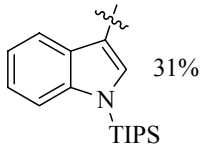
"C-H Bond Functionalization in Complex Organic Synthesis,"
Dalibor Sames, (Columbia University), New York, NY.

Functional group introduction or C-C bond formation via C-H bond functionalization has intrigued synthetic chemists for years. Multi-step procedures for introducing new functionality could be considerably shortened by C-H functionalization. Although transition metals are well documented to activate C-H bonds, key challenges remain such as linking C-H activation with C-C bond formation in a one-pot process, while still achieving high functional group tolerances. Dr. Sames presented work on a number of C-H functionalizations including arylation (in the presence of a free N-H) of sp^3 C-H bonds (eq 5 and eq 6), and the synthesis of the Telocidin B4 core (Scheme 2).



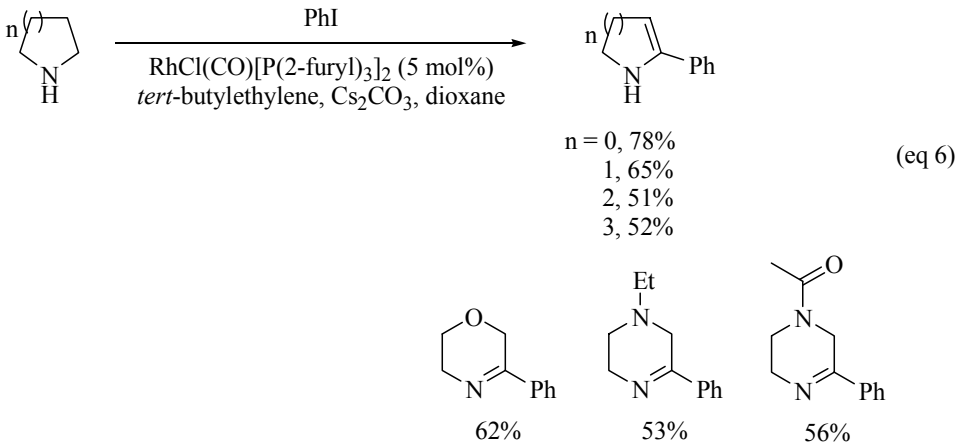
(eq 5)

Ar = *p*-OMePh, 62%
p-CO_2MePh, 56%
3-pyridyl, 39%
2-thienyl, 44%



31%

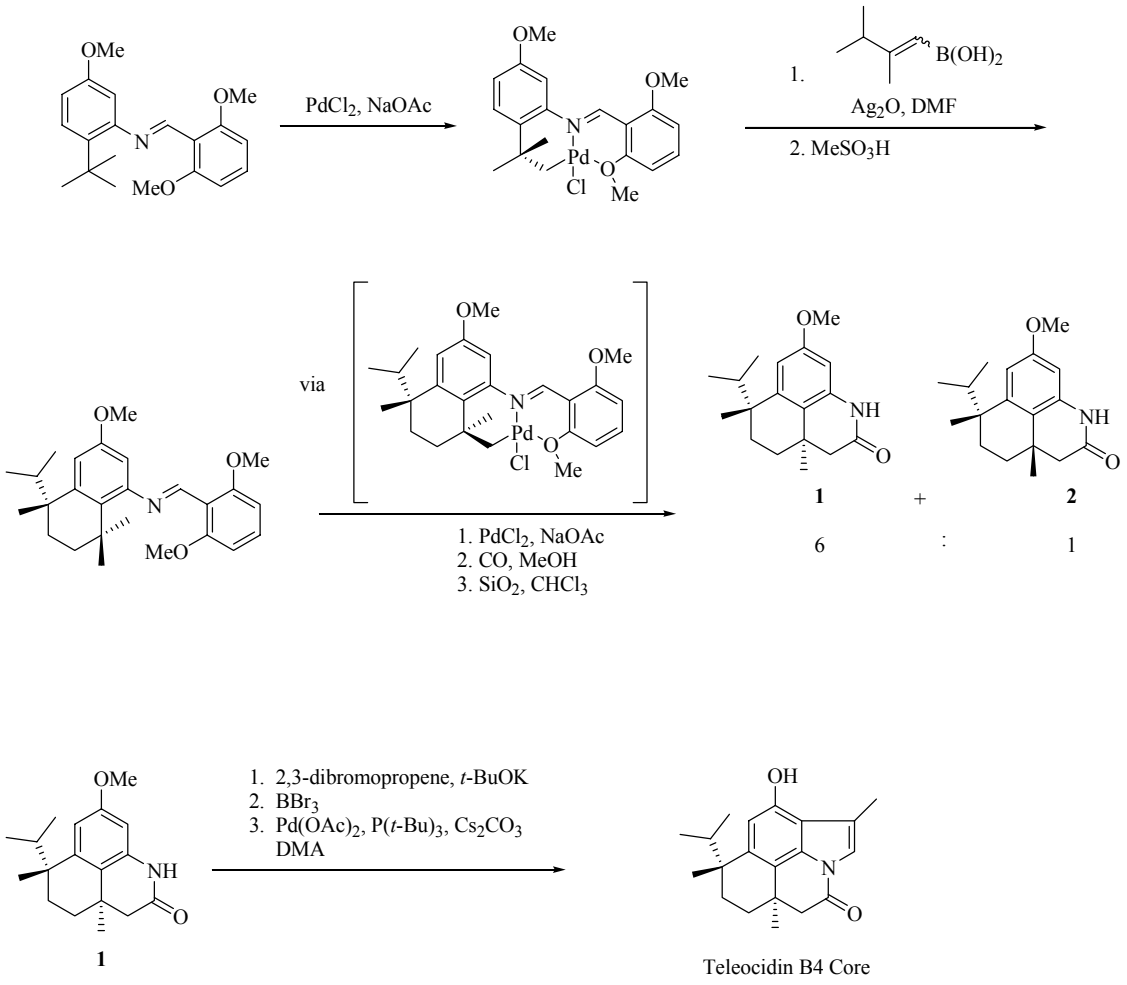
Sezen, B.; Sames, D. **2004** *J. Am. Chem. Soc.*, 126, 13244-13246



(eq 6)

The synthesis of the Teleocidin B4 core using C-H bond activation, of an unactivated methyl group, in two of the four key C-C bond forming steps is depicted below (Scheme 2).

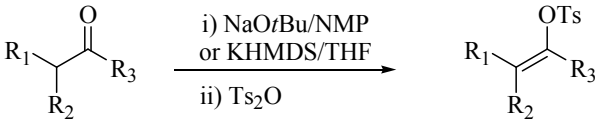
Scheme 2



Dangel, B.; Godula, K.; Youn, S.; Sezen, B.; Sames, D. **2002** *J. Am. Chem. Soc.* 124, 11856-11857

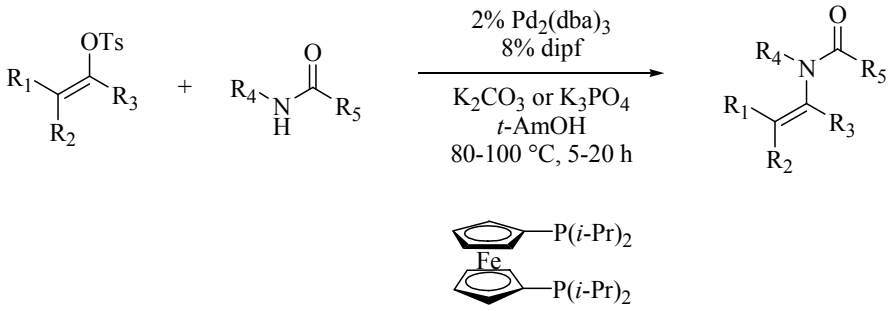
"Preparation of Enamides via Palladium-Catalyzed Amidation of Enol Tosylates,"
Artis Klapars,(Merck & Co, Inc.), Rahway, NJ.

When combined with asymmetric hydrogenation enamides provide an efficient route to chiral amines; however, there are relatively few methods for their preparation. In this presentation Artis Klapars discussed the extension of previous work on the amidation of enol triflates to the amidation of enol tosylates. Enol tosylates have two important advantages over enol triflates: 1) Tosylating agents are less expensive and more readily available than N-phenyltriflimide and 2) the crystallinity of enol tosylates simplifies product isolation and purification. The preparation of the requisite enol tosylates is shown in eq 7.



(eq 7)

The general coupling conditions are given in eq 8.



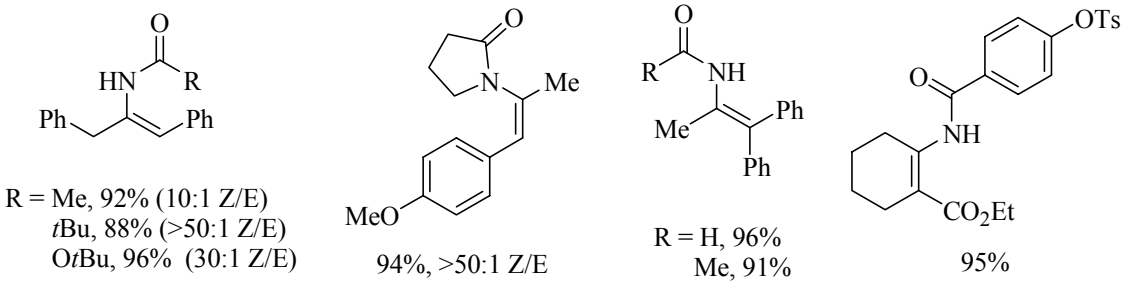
(eq 8)

dipf

Klapars, A.; Campos, K.; Chen, C.; Volante, R. **2005** *Org. Lett.* 7, 6, 1185-1188

The reaction scope is currently limited to enol tosylates substituted with an aryl ring or electron withdrawing group in the β-position of the enol tosylate. The reaction is quite tolerant of steric hindrance in the enol tosylate leading to a convenient synthesis of tri- and tetrasubstituted enamides. Selected examples enol tosylate/amide couplings are listed below (Figure 2).

Figure 2: Examples of Enol Tosylate/Amide Couplings



Illustrative examples of enol tosylates that do not perform well in the coupling reaction are given in Figure 3.

Figure 3: Enol Tosylates That Are Poor Substrates