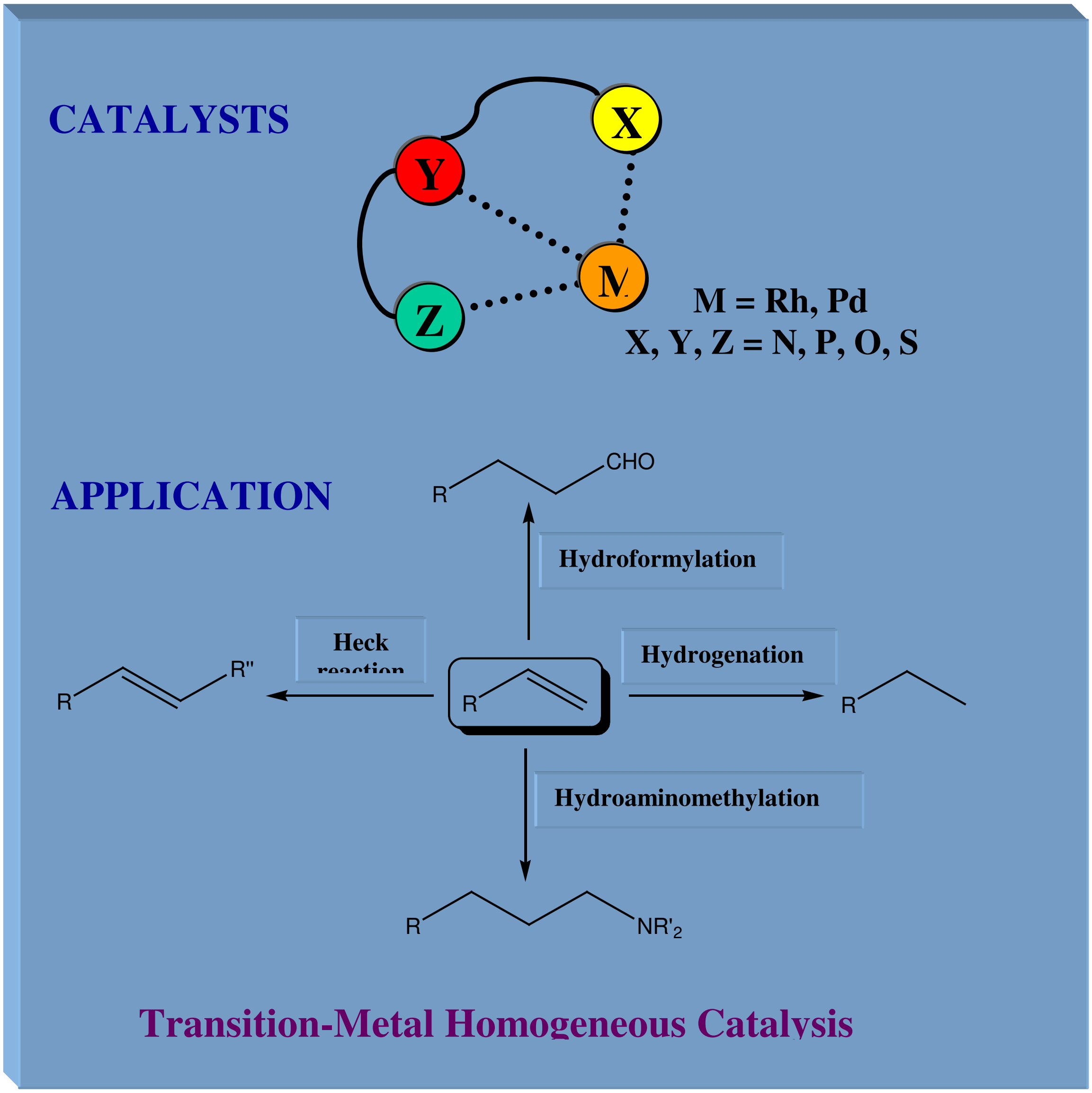
TRANSITION-METAL HOMOGENEOUS CATALYSIS

Transition-metal homogeneous catalysis, which was established from the discovery of hydroformylation (1938, Otto Roelen/Ruhrchemie), today is undoubtedly a highly competitive research field with enormous academic and industrial interest. The development of homogeneous catalysis at the Institute of Organic and Pharmaceutical Chemistry of the National Hellenic Research Foundation started at the end of the 20th century (by I.D. Kostas). Today, our investigations include the development of transition-metal complexes with novel ligands and their evaluation as catalysts in reactions such as hydroformylation, hydrogenation, coupling reactions.



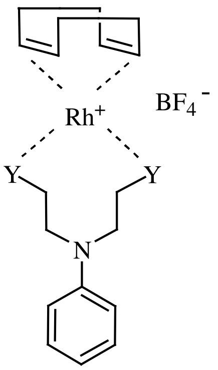
More specifically, our research activities include:

- **Catalysis by hybrid and hemilabile phosphorus ligands**
- **Catalysis in air by phosphane-free ligands**
- **Asymmetric catalysis**
- **Catalysis by high energy techniques**
- **Aqueous catalysis**

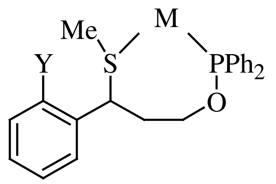
Catalysis by hybrid and hemilabile phosphorus ligands

The project includes the development of transition metal (e.g. Rh, Pd) complexes with functionalized hybrid and hemilabile phosphorus ligands (e.g. phosphines, phosphine oxides, phosphinites, mixed phosphine-phosphinites) possessing additional potent donors such as oxygen, nitrogen, sulfur, and their applications to homogeneous catalysis (hydroformylation, hydroaminomethylation, hydrogenation, Heck reaction).

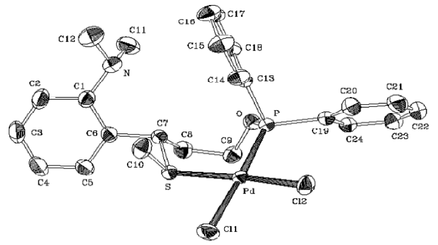
Selected complexes

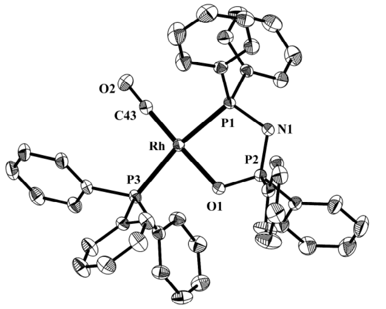


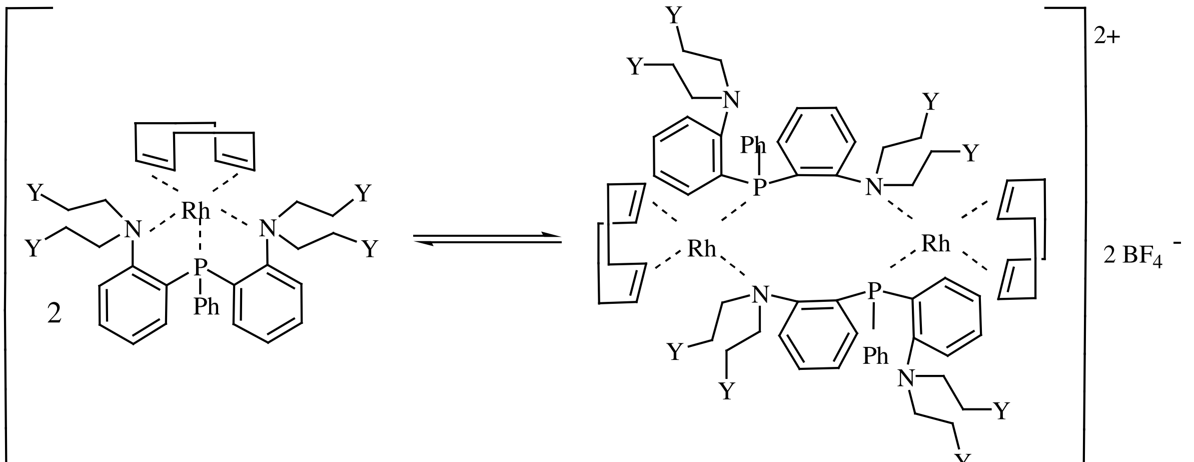
$Y = PPh_2, OPPh_2, P(O)Ph_2$



$M = PdCl_2, Y = NMe_2$
$M = Rh(COD)BF_4, Y = NMe_2$
$M = Rh(COD)BF_4, Y = H$







Y = OMe, OH

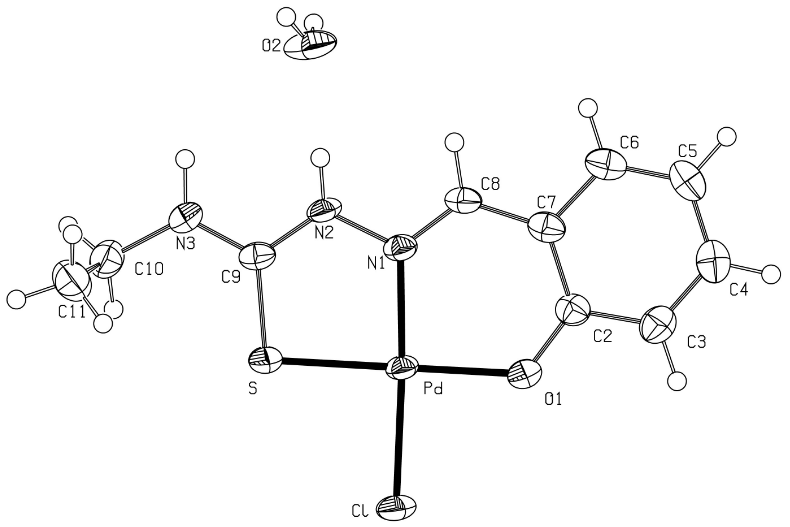
Selected publications

- I.D. Kostas* *J. Organomet. Chem.* **2001**, *626*, 221
- I.D. Kostas* *J. Organomet. Chem.* **2001**, *634*, 90
- I.D. Kostas* *Inorg. Chim. Acta* **2003**, *355*, 424
- I.D. Kostas*, B.R. Steele*, A. Terzis, S. V. Amosova *Tetrahedron* **2003**, *59*, 3467
- I.D. Kostas*, B.R. Steele, F.J. Andreadaki, V.A. Potapov *Inorg. Chim. Acta* **2004**, *357*, 2850
- E.I. Tolis, K.A. Vallianatou, F.J. Andreadaki, I.D. Kostas* *Appl. Organomet. Chem.* **2006**, 20, 335
- K.A. Chatziapostolou, K.A. Vallianatou, A. Grigoropoulos, C.P. Raptopoulou, A. Terzis, I.D. Kostas*, P. Kyritsis*, G. Pneumatikakis *J. Organomet. Chem.* **2007**, *692*, 4129
- A review: I.D. Kostas* *Curr. Org. Synth.* **2008**, *5*(3), 227-249

Catalysis in air by phosphane-free ligands

Palladium-catalysed cross-coupling reactions are amongst the most powerful tools in organic synthesis for carbon-carbon bond formation. The complexes used as catalysts are usually based on phosphorus ligands, which are often water- and air-sensitive. Therefore, catalysis under phosphane-free conditions is a challenge of high importance. In our attempts to evaluate phosphane-free systems in cross-coupling reactions, substituted salicylaldehyde thiosemicarbazones were chosen for this purpose. This project includes the development of novel palladium complexes with thiosemicarbazones and their applications to cross-coupling reactions. Recently, for the **first time**, we used **thiosemicarbazones** as catalyst precursors for palladium-catalyzed coupling reactions (Heck, Suzuki), under aerobic conditions. One of our Pd complexes is currently **commercially available** by **ALDRICH** (Product No.: 674125) and **SANTA CRUZ** (Product No.: sc-253529) as an efficient catalyst for coupling reactions under aerobic conditions.

Selected complex

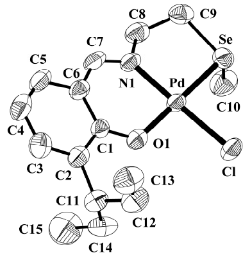


Selected publications

- I.D. Kostas*, F.J. Andreadaki, D. Kovala-Demertzi*, C. Prentjas, M.A. Demertzis *Tetrahedron Lett.* **2005**, *46*, 1967
- D. Kovala-Demertzi*, P.N. Yadav, M.A. Demertzis, J.P. Jasinski**,** F.J. Andreadaki, I.D. Kostas* *Tetrahedron Lett.* **2004**, *45*, 2923.

Additionally, after the development of a synthetic route to S-, Se-, Te-containing Schiff bases, their palladium complexes were successfully applied to the Suzuki coupling, in air.

Selected complex

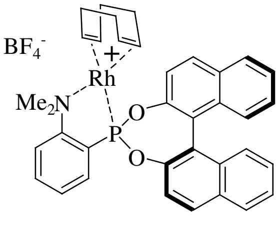


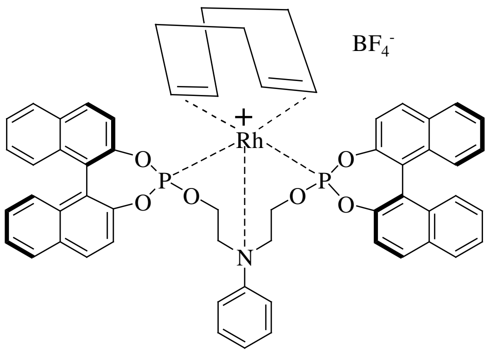
- I.D. Kostas*, B.R. Steele*, A. Terzis, S.V. Amosova, A.V. Martynov, N.A. Makhaeva *Eur. J. Inorg. Chem.* **2006**, 2642

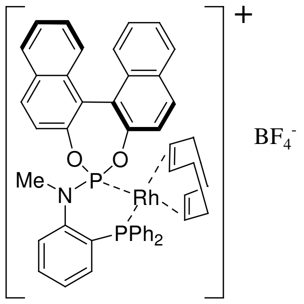
Asymmetric catalysis

This project includes the development of rhodium complexes with new chiral amino diphosphite, phosphonite, phosphine-phosphoramidite and phosphite-phoephoramidite ligands and their applications to enantioselective hydroformylation and hydrogenation. Recently, we developed the chiral ligand **Me-AnilaPhos** as a highly efficient ligand for the rhodium-catalyzed enantioselective olefin hydrogenation.

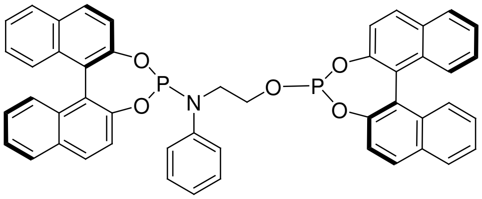
Selected complexes and ligands







Rh/*Me-AnilaPhos*

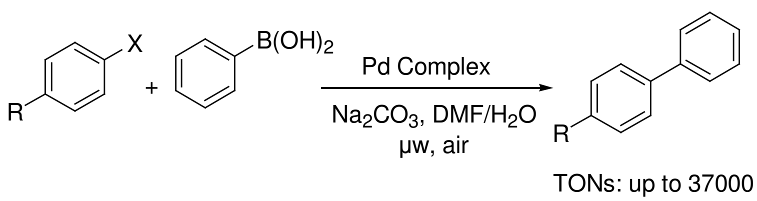


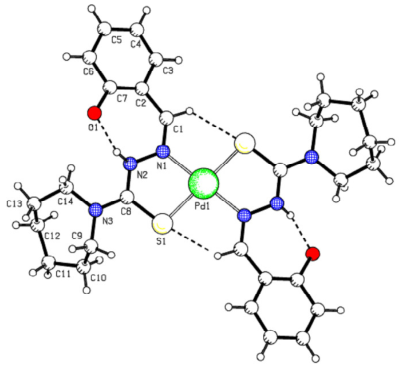
Selected publications

- I.D. Kostas*, K.A. Vallianatou, J. Holz, A. Börner *Appl. Organomet. Chem.* **2005**, *19*, 1090
- K.A. Vallianatou, I.D. Kostas*, J. Holz, A. Börner *Tetrahedron Lett.* **2006**, *47*, 7947. *Selected comments for Me-AnilaPhos:* (a) **“excellent catalyst”** (a critical review: L. Eberhardt, D. Armspach, J. Harrowfield, D. Matt *Chem. Soc. Rev.* **2008**, *37*, 839); (b) **“highly versatile ligand class”** (*ALDRICH:* D. Amoroso et al. *Aldrichimica Acta*, **2008**, *41*, 20).
- I.D. Kostas*, K.A. Vallianatou, J. Holz, A. Börner* *Tetrahedron Lett.* **2008**, *49*, 331.
- Book chapter: I.D. Kostas* “Other P/N-Ligands” (Chiral Bidentate Monophosphorus Ligands: Hybrid Monophosphorus Ligands – Bidentate P/NR2 Ligands – Other P/N-Ligands). In *Phosphorus Ligands in Asymmetric Catalysis – Synthesis and Applications*, A. Börner (Ed.), Wiley-VCH, Weinheim, **2008**, Vol. 2, part IV, chapter 1.2, pp. 596-632.

Catalysis by high energy techniques

The project includes the application of a microwave irradiation to homogeneous catalysis. Recently, we used this technique to the Suzuki coupling in air, catalyzed by a palladium complex with a thiosemicarbazone ligand. Although the complex was inactive as catalyst for the Suzuki coupling under a conventional heating, a microwave irradiation promoted the effective catalytic activity of the complex, under strictly similar conditions with those used under conventional heating. The microwave-promoted cross-coupling reaction by palladium complexes with thiosemicarbazones provides a convenient approach compared to existing methods that require an inert atmosphere due to the air-sensitive nature of other catalysts.



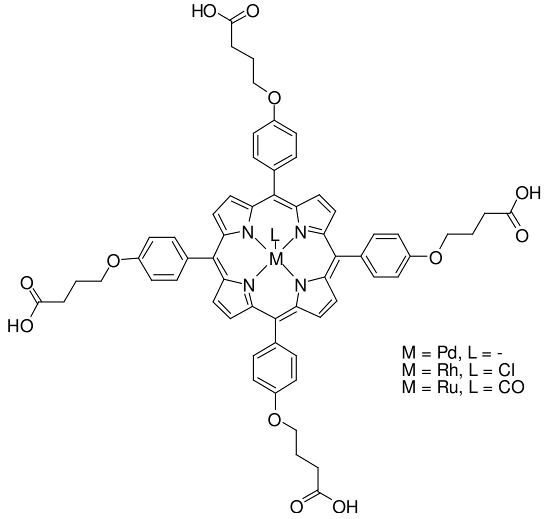


Publication

- I.D. Kostas*, G.A. Heropoulos*, D. Kovala-Demertzi*, P.N. Yadav, J.P. Jasinski, M.A. Demertzis, F.J. Andreadaki, G. Vo-Thanh, A. Petit, A. Loupy *Tetrahedron Lett.* **2006**, *47*, 4403

Aqueous catalysis

The replacement of organic solvents by water in transition metal homogeneous catalysis has received remarkable attention, as water is inexpensive, non-toxic, non-flammable, environmentally sustainable, and allows simple separation and reuse of the catalyst. The present project includes the development of water soluble phosphane-free porphyrins and their use as ligands in metal-catalyzed reactions in aqueous media. Recently, we published **the first study** concerning the evaluation of **porphyrin** ligands in Suzuki reaction in neat water, and also selective hydrogenation of unsaturated aldehydes in aqueous/organic biphasic system. The catalysts could be easily recycled and reused.



Selected publications

- I.D. Kostas*, A.G. Coutsolelos*, G. Charalambidis, A. Skondra *Tetrahedron Lett.* **2007**, *48*, 6688
- C. Stangel, G. Charalambidis, V. Varda, A.G. Coutsolelos,* I.D. Kostas* *Eur. J. Inorg. Chem.* **2011**, DOI: 10.1002/ejic.201100668.