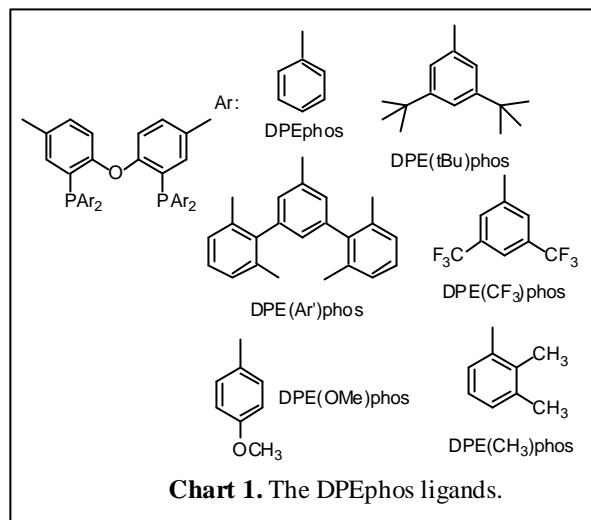


## Scientific Highlights of the Overall Research Activity of PALLADIUM

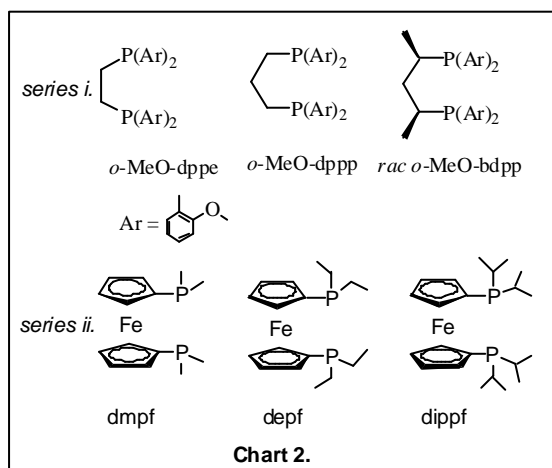
With respect to the contract, now at the end of the PALLADIUM Network lifetime, the overall research activity, carried out by the PALLADIUM Teams during the four years of joint work, can be grouped into three Work Packages (WP): **WP1 P-P ligands**; **WP2 N-N ligands**; **WP3 P-X ligands**. For each WP the topics, which are considered the most relevant in terms of Network research objectives, Network joint work and advance of the international state-of-the-art, have been chosen and are schematically reported below.

**WP1 P-P ligands.-** Both bidentate and monodentate phosphorus-donor ligands have been studied. The first remarkable improvement of the state-of-the-art was achieved with the synthesis of new flexible bidentate diphosphines with variable steric bulk containing a diphenyl ether (DPE) backbone (Chart 1). The corresponding dicationic palladium complexes  $[\text{Pd}(\text{DPEphos})(\text{CH}_3\text{CN})_2][\text{OTf}]_2$  were tested as precatalysts in the co-oligomerization of ethene with carbon monoxide. The catalytic results clearly show the effect of the steric bulk of the DPEphos ligand on the selectivity of the reaction, being methyl propionate (MP) the favored product when the bulkiest ligand is used (Table 1a). The electronic effect is also evident: no reaction proceeds when ligands with electron withdrawing substituents are used, while a higher selectivity in the oligomers with respect to methyl propionate is observed when ligands with electron donating groups are present (Table 1b).



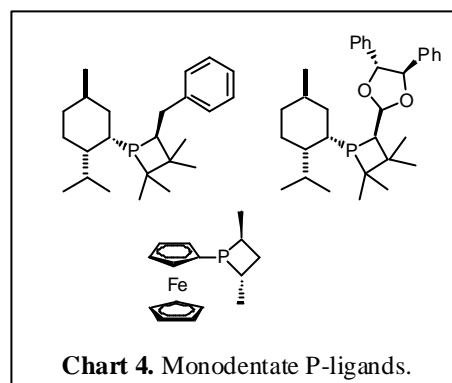
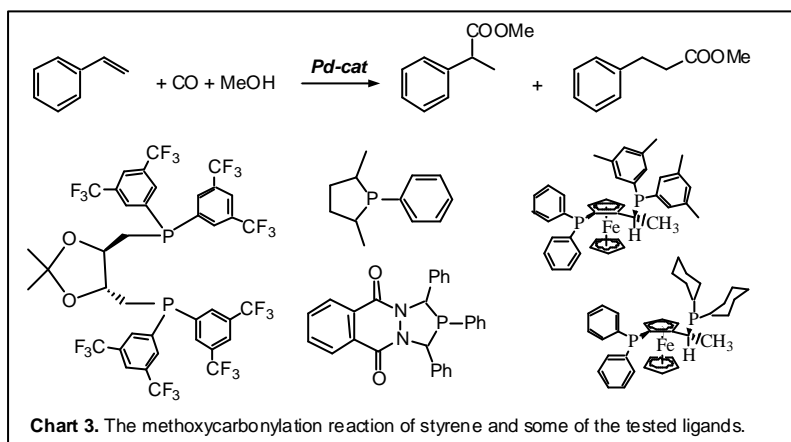
**Table 1.** CO/ethylene oligomerization: effect of the DPEphos ligand.

| a: steric effect |                 |                        | b: electronic effect      |                 |                        |
|------------------|-----------------|------------------------|---------------------------|-----------------|------------------------|
| Ligand           | MP<br>(g/gPd·h) | oligomers<br>(g/gPd·h) | Ligand                    | MP<br>(g/gPd·h) | oligomers<br>(g/gPd·h) |
| DPEphos          | 267             | 28                     | DPEphos                   | 267             | 28                     |
| DPE(tBu)phos     | 92              | 150                    | DPE(CF <sub>3</sub> )phos | 0               | 0                      |
| DPE(Ar')phos     | 120             | 9                      | DPE(OMe)phos              | 113             | 188                    |



The carbonylation of ethene was also chosen as model reaction for testing the catalytic behavior of Pd complexes bearing P-P ligands of other two families: *i. ortho-anisyl diphosphine ligands*; *ii. 1,1'-bis(dialkylphosphino)ferrocene* (Chart 2). A new synthetic protocol was applied for the synthesis of ligands of series *i.* Afterwards, neutral Pd(II) complexes, of general formula  $[\text{Pd}(\text{P-P})(\text{X})_2]$  ( $\text{X} = \text{Cl}^-$ ,  $\text{AcO}^-$ ) were prepared and used in the mentioned reaction. The direct comparison with the activity of the complexes with the corresponding ligands with no methoxy substituent in *ortho*-position showed that *o*-MeO-dppe and *o*-MeO-dppp are better performing than the non-substituted analogues. In all cases, the molecular weight values of the synthesized polyketones are higher than those obtained with the non-substituted analogues, suggesting that the higher steric congestion at the Pd center due to the *ortho*-anisyl diphosphine may decrease the rate of the  $\beta$ -hydrogen elimination. The effect

of the steric hindrance around palladium on the selectivity of the ethene carbonylation reaction was clearly evidenced when complexes containing ligands of series *ii.* were applied. While Pd complexes with either dmpf or depf led to the formation of CO/ethene polyketones, those having the dippf ligand produced MP and 3-pentanone with a selectivity higher than 89%.



The synthesis of esters was also studied by using styrene as comonomer and applying both monodentate and bidentate phosphines with the aim to address the regioselectivity of the reaction toward the formation of the chiral branched product (Chart 3). Both isolated and *in situ* catalytic systems were used. The main results were that the introduction of electron withdrawing groups enhanced the regioselectivity toward the desired product and that the chiral ferrocenyl diphosphines require more drastic reaction conditions than the monodentate ligands affording the target product with high enantioselectivity but low regioselectivity. On the other hand, palladium complexes with the monodentate phosphorus ligands of Chart 4 promote the methoxy carbonylation of styrene with high regioselectivity (up to 99%) in the branched product.

**This work relates to Tasks: 1, 2, 3, 5, 9**

**Teams involved: CNR.ICCOM, URV, TU/e**

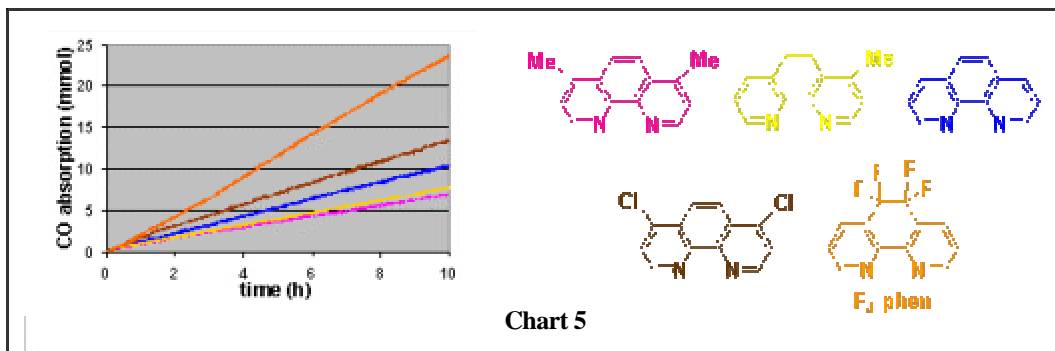
**Collaborations: CNR.ICCOM/URV, URV/TU/e**

**Related publications: references 1-8**

**WP2 N-N ligands.-** Nitrogen-donor ligands (N-N) are the ligands of choice for the co- and terpolymerization reaction of carbon monoxide with vinyl arenes. The ligands to be used have been chosen with the aim to obtain palladium catalysts enabling the control of both the catalyst stability and the stereochemistry of the synthesized polyketones.

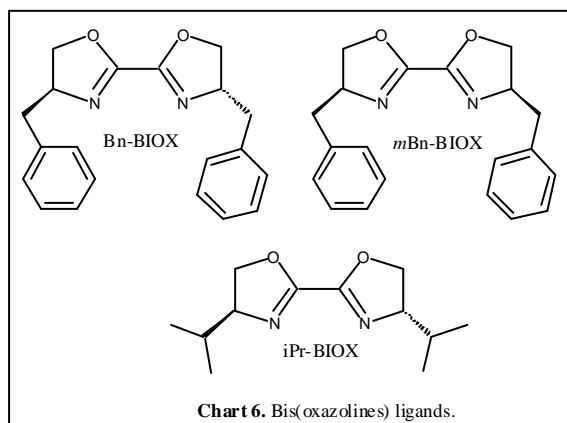
The problem of the control of catalyst stability was mainly addressed by using ligands with a phenanthroline skeleton. The detailed kinetic analysis carried out by taking advantage of the multivessel reactor present in the labs of TU/e Team

showed a linear CO uptake for all the catalysts tested and a clear effect of the substituents present on the phen-skeleton on the rate of CO uptake (Chart 5). The Pd complex containing the F<sub>4</sub>-phen proved to be thus far the most active among those tested both in the CO/styrene and CO/4-Me-styrene copolymerizations, without showing any evident

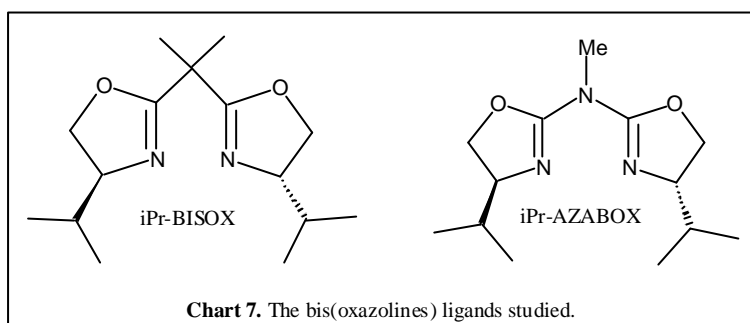


decomposition to inactive palladium metal for at least 96 h of reaction. Moreover, the synthesized polyketone has a syndiotactic microstructure with the highest degree of stereoregularity reported so far (96%).

The study of the control of the stereochemistry of the copolymers was focused on the development of ligands able to produce in high yield the copolymer with an isotactic microstructure. The ligands preferentially tested are characterized by a bis(oxazoline) backbone and a benzyl or an isopropyl group on the stereogenic centers. Ligands in both the enantiomerically pure (N\*-N\*) and *meso* (N-N<sup>m</sup>) form were used (Chart 6). With these ligands, both mono- and dicationic palladium (II) complexes were synthesized. The first breakthrough concerns the unprecedented effect of the



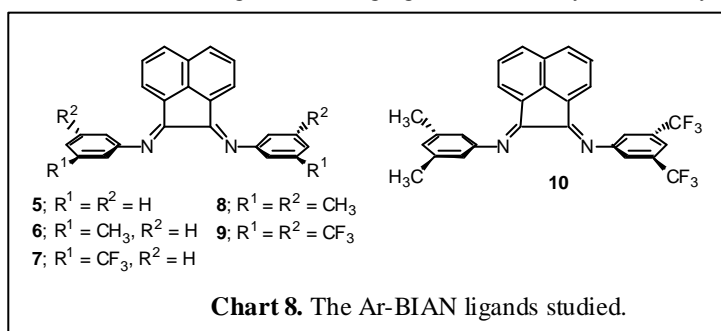
anion on the stereochemistry of the CO/styrene copolymer synthesized with the complexes  $[\text{Pd}(\text{mBn-BIOX})(\text{H}_2\text{O})_2][\text{X}]_2$  ( $\text{X} = \text{OTf}, \text{PF}_6^-, \text{BF}_4^-$ ). When the catalyst with the triflate (OTf) anion was used, the isotactic copolymer was formed, whereas the other two precatalysts ( $\text{X} = \text{PF}_6^-, \text{BF}_4^-$ ) led to polyketones with a syndiotactic microstructure. A surprising effect of the nature of the precatalyst on the tacticity of the polymer was also shown: while the  $[\text{Pd}(\text{mBn-BIOX})(\text{H}_2\text{O})_2][\text{OTf}]_2$  led to the isotactic polymer, the corresponding monocationic derivative  $[\text{Pd}(\text{CH}_3)(\text{CH}_3\text{CN})(\text{mBn-BIOX})][\text{OTf}]$  yielded the syndiotactic polymer. The effect of the anion on the control of the stereochemistry was also observed when the enantiomerically pure *i*Pr-BIOX was used. The monocationic Pd-complexes  $[\text{Pd}(\text{CH}_3)(\text{CH}_3\text{CN})(\text{iPr-BIOX})][\text{X}]$  ( $\text{X} = \text{BArF}, \text{PF}_6^-, \text{OTf}$ ) always catalyzed the synthesis of the CO/styrene copolymer with an isotactic microstructure, but with a different degree of stereoregularity depending on the nature of the anion and of the reaction medium. When the copolymerization was carried out in dichloromethane, the obtained polymer was fully isotactic but the yield of the reaction was very poor (only traces of polyketones were isolated); on the other hand the productivity of the system was remarkably enhanced when the reaction medium was trifluoroethanol. In this case the control of the stereochemistry was partially lost and it was affected by the nature of the anion; it decreased on going from BArF to  $\text{PF}_6^-$  to OTf.



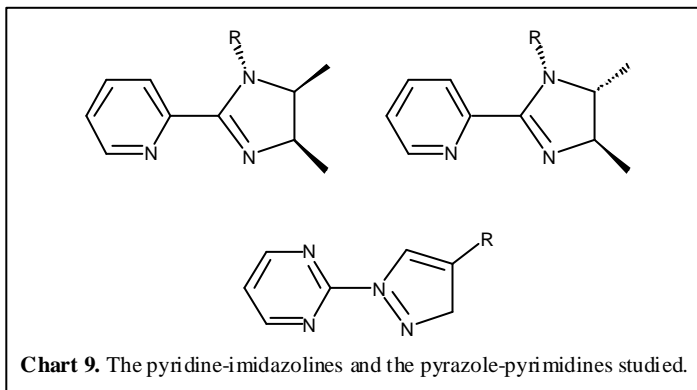
Complete isotactic CO/styrene and CO/4-Me-styrene polyketones were obtained in trifluoroethanol by using the monocationic complexes with both the chiral bisoxazoline *i*Pr-BISOX and the chiral azabis(oxazoline) *i*Pr-AZABOX (Chart 7). A remarkable effect of the nature of the bridge between the two oxazoline rings was observed: the productivity of the catalyst with the *i*Pr-AZABOX ligand was more than double of that with the *i*Pr-BISOX and the polyketone has a molecular

weight value 5 times higher compared to that obtained with the *i*Pr-BISOX. In conclusion, for the synthesis of fully isotactic CO/vinyl arene polyketones in alcoholic medium at ambient pressure *i*Pr-AZABOX exceeds previously known ligands in terms of productivity and molecular weight.

Finally, in a collaboration between UNITS and UAMSK Teams, ligands belonging to the family of bis(aryl)-acenaphthene-a-diimines (Ar-BIAN) (Chart 8) were synthesized and the corresponding monocationic palladium complexes tested as precatalysts in the CO/vinyl arene copolymerization. The ligands studied differs from those reported in the literature by the presence of substituents of different nature on the *meta* positions of the aryl rings. A remarkable effect of both the nature of the substituents and the number of *meta* positions substituted was found on the productivity of the system and on the molecular weight of the synthesized polyketones. Moreover, all the synthesized polymer are regioregular, atactic, polyketones regardless of the symmetry of the ligand present in the catalyst.



Monocationic palladium complexes containing bidentate nitrogen-donor ligands belonging to the family of pyridine-imidazolines and pyrazole-pyrimidines (Chart 9) were tested as precatalysts for the CO/4-*tert*-butylstyrene/ethylene terpolymerization reaction. The results evidence that the alkene preferentially inserted into the terpolymer chain is strictly related to the nature of the nitrogen ligand present in the catalyst, mainly to its steric constraints. Terpolymers with a different relative amount of the aromatic and the aliphatic alkene can be synthesized by choosing the catalyst with the proper nitrogen-donor ligand.



The CO/styrene/ethene terpolymerization reaction was also studied by using dicationic, bischelated palladium complexes of general formula  $[\text{Pd}(\text{N-N})_2][\text{PF}_6]_2$  ( $\text{N-N} = 1,10$ -phenanthroline or its symmetrically or unsymmetrically substituted derivatives) as precatalysts. The comparison of the results obtained for the terpolymerization reaction with those already available for the two corresponding copolymerizations, CO/styrene and CO/ethylene, allows to point out some important features of the catalytic system: *i.* the stability of the catalyst is remarkably affected by the nature of the alkene; in particular the

aliphatic olefin has such a negative effect on the catalyst stability that neither the presence of the aromatic alkene nor the use of trifluoroethanol as reaction medium were able to prevent catalyst decomposition; *ii.* as a consequence, addition of 1,4-benzoquinone was required to achieve high productivities, and the catalyst lifetime was dictated by the benzoquinone-to-palladium ratio; *iii.* MALDI-TOF-MS analysis of the terpolymers suggests that the insertion of ethylene into the Pd-H bond is unlikely, and, when the amount of styrene in the reaction mixture is low, the preferential initiation step involves the oxidant.

Finally, the CO/styrene/4-methylstyrene terpolymer was synthesized for the first time by using the dicationic bischelated palladium complex containing the 1,10-phenanthroline. The polyketone was obtained in high yield and with molecular weight values around 100 000.

For the second time with respect to the data reported in the literature, MALDI-TOF spectrometry was applied to study terpolymers. In particular, in the case of CO/ethylene/styrene and CO/styrene/4-methylstyrene terpolymers it allowed the unambiguous determination of the chemical composition of the macromolecules, and, for the first time, the effect of the different amounts of the two alkene monomers present in the polymeric chain was clearly evidenced in the MALDI-TOF mass spectra.

**This work relates to Tasks: 1, 2, 4, 6, 11**

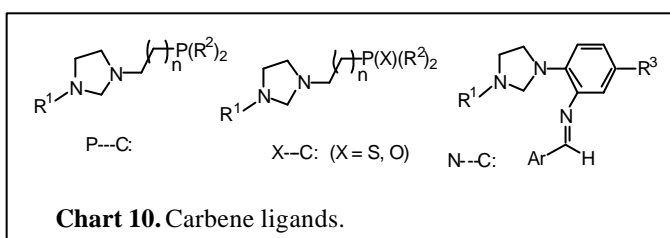
**Teams involved: UNITS, URV, ETHZ, UAMSK, TU/e**

**Collaborations: UNITS/URV, UNITS/ETHZ, UNITS/UAMSK, UNITS/TU/e**

**Related publications: references 9-18**

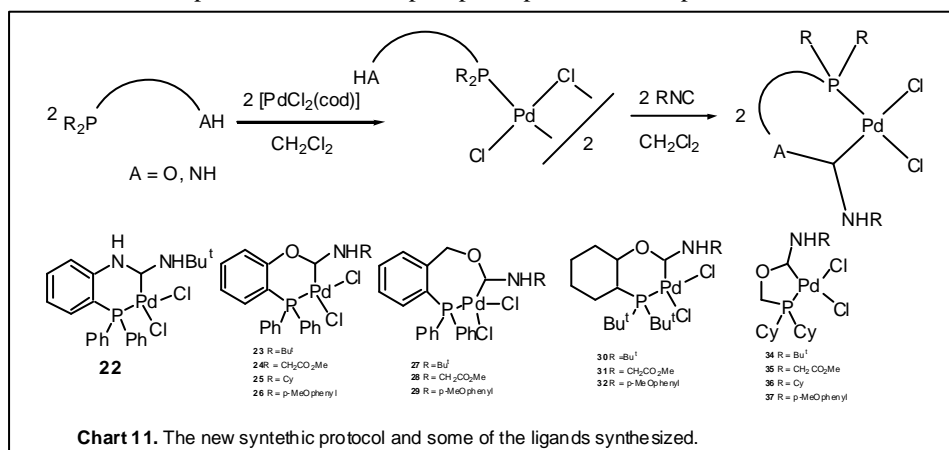
**WP3 P-X ligands.-** The potential hemilability properties of the hybrid P-X ligands makes them an interesting class of molecules in coordination chemistry. Thus, some of the Teams of PALLADIUM have been involved in the synthesis of new hybrid P-X ligands and in the study of their coordinating behavior to palladium. Depending on the nature of X, the P-X ligands studied belong to the families of carbenes (X = C), phosphino-pyridines, phosphino-oxazolines or phosphino-quinolines (X = N).

As far as the carbene ligands are concerned (Chart 10), a novel methodology for the synthesis of palladium complexes with new bidentate C-N and C-P ligands featuring an N-heterocyclic carbene as the carbon moiety has been developed. Another approach relies on the capability to obtain directly the final complex by starting from a precursor of the ligand by coordinating it to the palladium species and reacting it with isonitrile to yield the bidentate carbene-phosphine ligand bound to the metal center (Chart 11).

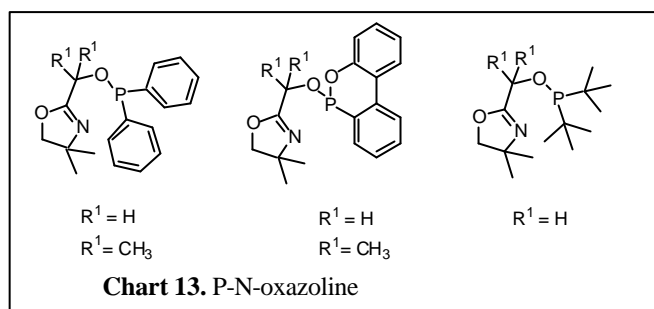
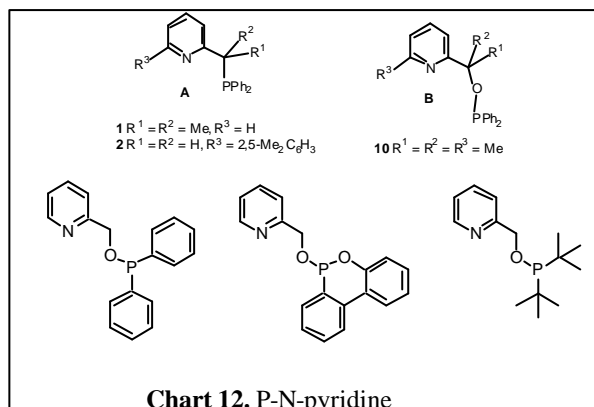


**Chart 10.** Carbene ligands.

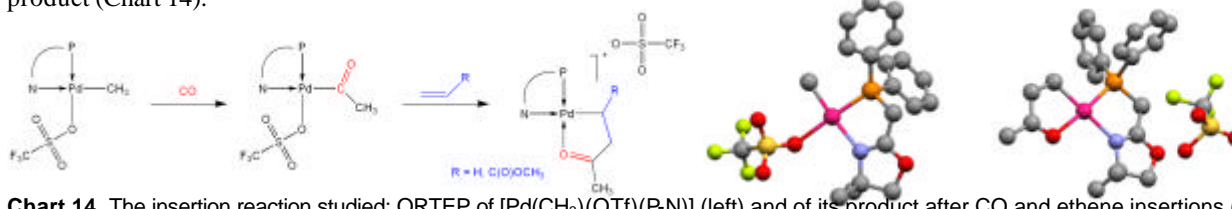
This novel route has been demonstrated to be simple, straightforward and general, thus allowing the synthesis of a number of new “open-chain” carbene-phosphine palladium complexes.



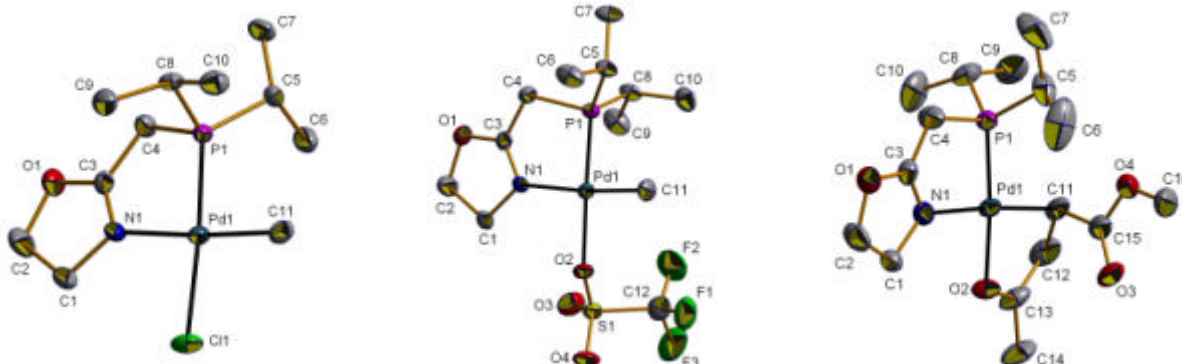
During the first two years several new PN-pyridines (Chart 12) and PN-oxazolines (Chart 13) ligands have been synthesized and characterized. With these ligands, the corresponding neutral palladium complexes [Pd(CH<sub>3</sub>)(X)(P-N)] (X = Cl, OTf) were synthesized and characterized both in solid state and in solution.



The neutral complexes were properly tailored for mechanistic investigations. They were used to study the stepwise insertion of CO and ethylene into the Pd-CH<sub>3</sub> bond (Chart 14). Single crystals, suitable for X ray analysis, of the intermediates resulting from the insertion of both monomers into the Pd-CH<sub>3</sub> bond were obtained, evidencing that the ligand is bound to the metal center with the Pd-N bond *trans* to the Pd-C bond, both in the precursor and in the inserted product (Chart 14).

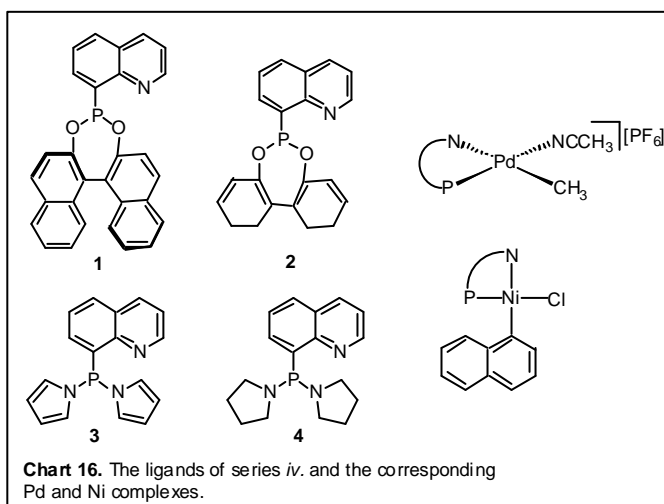


During the 4<sup>th</sup> year the series of phosphino-oxazoline derivatives has been extended to the ligand with isopropyl groups on the phosphorus donor. The corresponding neutral Pd(II) complexes [Pd(CH<sub>3</sub>)(X)(P-N)] (X = Cl, CF<sub>3</sub>SO<sub>3</sub>) have been fully characterized, including by X-ray diffraction (Chart 15).



The CO/ethylene and CO/methyl acrylate insertion steps were studied on the triflate derivative and the resulting alkyl complex was isolated and characterized. The solid state structure of the intermediate obtained after the insertion of methyl acrylate is a rare example of a structurally characterized CO/methyl acrylate insertion product. The comparison of these results with those obtained on the palladium complexes, where the P-N-ligand has two phenyl rings on phosphorus, indicates that the higher basicity of the P(*i*-Pr)<sub>2</sub> group compared to PPh<sub>2</sub> did not translate into significant reactivity differences.

The last series of P-N-ligands studied comprises molecules differing by the nature of the P moiety but with the same nitrogen part, that is derived from quinoline (Chart 16). The monocationic palladium complexes, [Pd(CH<sub>3</sub>)(CH<sub>3</sub>CN)(P,N)][PF<sub>6</sub>], containing these ligands were tested in CO/styrene and CO/ethylene copolymerization as well as in the



ethylene oligomerization. Complex with ligand **2** was the only one found active. The corresponding nickel derivatives were synthesized and tested in ethylene oligomerization in the presence of MAO. All the nickel complexes were found to be catalytically active. The selectivity in the oligomeric products was related to the nature of the ligand bound to Ni: ligands **1** and **2** led to the selective synthesis of C<sub>4</sub> and C<sub>6</sub> oligomers, while, when ligands **3** and **4**, were used C<sub>8</sub> – C<sub>12</sub> oligomers were obtained in a range of 10-15%.

**This work relates to Tasks: 1, 2, 3, 4, 6, 9**

**Teams involved: UAMSK, ULP, ETHZ**

**Collaborations: ULP/UAMSK**

**Related publications: references 19-25**