Cationic Phosphines Hot Paper

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Synthesis, Structure, and Applications of Pyridiniophosphines**

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Dedicated to Professor Walter Thiel on the occasion of his 65th birthday

Abstract: *A new family of cationic ligands, N-alkyl/aryl pyridiniophosphines, has been synthesized through a short, scalable, and highly modular route. Evaluation of their electronic properties evidenced weak σ-donor and quite strong π-acceptor character when used as ancillary ligands. These attributes confer a substantially enhanced π-acidity to the $\mathrm{Pt^{II}}$ and $\mathrm{Au^{I}}$ complexes thereof derived and, as result, they depict an improved ability to activate alkynes towards nucleophilic attack. This superior performance has been demonstrated along several mechanistically diverse $\mathrm{Pt^{II}}$- and $\mathrm{Au^{I}}$-catalyzed transformations.*

For the design of an effective metal-catalyzed process, the choice of the ancillary ligand is crucial; in fact, it can be as critical as the choice of the metal itself. This is due to the extraordinary control that ligands exert over the reactivity of the resulting catalysts and, not less important, over the product selectivity of the catalyzed process. The selection of the most appropriate ligand for each particular transformation must then consider among others, the nature of the rate determining step and the plausible (not desired) reaction pathways.

In this context where ligands that depict different properties are necessary, phosphines play a prominent role because both their donor ability and steric requirements can be easily adjusted at convenience by modification of the substituents attached to the phosphorus atom. Specifically, if strong Lewis acidity is required at the metal, poor electron-releasing phosphites or polyfluorinated phosphines are the ligands of choice. This is often the case in Pt and Au catalysis.[1]

Very recently, we developed an alternative strategy for the synthesis of even weaker electron donor phosphines consisting of the direct attachment of up to three cationic bis(dialkylamino) cyclopropenium substituents to the central P-atom. The positive charges thus introduced account for the poor σ-donor and excellent π-acceptor abilities that these ligands depict. Moreover, taking advantage of these properties, we have been able to develop new $\mathrm{Au^{I}}$ and $\mathrm{Pt^{II}}$ catalysts that exhibit an unmatched ability to activate alkynes toward hydroarylation reactions.[2]

However, the specific use of di(isopropylamino) cyclopropenium substituents compromises to some extend the independent fine tuning of steric and electronic properties in the resulting phosphines owing to the synthetic and geometric restrictions that these cationic groups impose.[3,4] Moreover, the best catalytic performances are often obtained by the employment of di- or tricationic catalysts that, because of their highly charged nature, depict low solubility in typical organic solvents. For these reasons, the use of alternative positively charged substituents, which are more amenable to stereoelectronic modification, seems to be adequate to further expand the still limited repertoire of extreme π-acceptor ligands and their applications in metal catalysis.[5]

Given these considerations, we envisaged that N-(alkyl/arylpyridinium)-substituted phosphines might be a potentially very useful family of strong π-acceptor ligands owing to the simultaneous confluence of tree beneficial factors: a) The low-lying π^* orbitals of the pyridinium moiety should effectively interact with the lone pair at phosphorus making the resulting phosphines very poor donating ligands; b) the fine stereoelectronic tuning of the resulting phosphines can be achieved by an appropriate selection of the other two R groups at phosphorus and additionally, by introduction of substituents on the pyridinium ring (Figure 1); and c) the reaction of 1-alkyl/aryl-2-chloropyridinium salts with different secondary phosphines offers a short, effective and highly modular synthetic route to the target ligands.[6]

To put our design concept into practice, we first prepared pyridinium-substituted phosphines **12–19** in good to excellent yields through a two-step sequence. N-alkylation of readily available 2-chloropyridines **1–4** with trimethyl- or triethyloxonium tetrafluoroborates afforded the corresponding pyr-

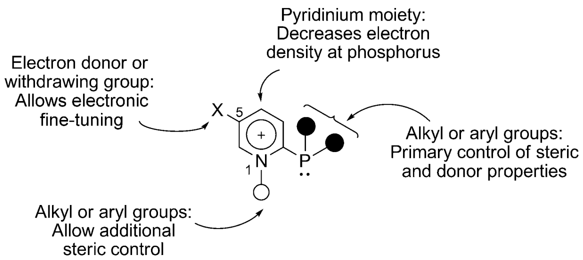

Figure 1. Structural features of pyridinium-substituted phosphines and their impact on the donor properties of the resulting ligand.

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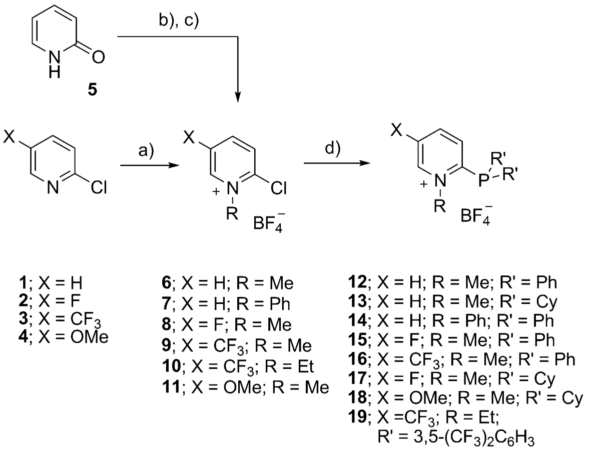
idinium salts **6, 8–11** in excellent yields. 1-Aryl substituted 2-chloropyridinium salts such as **7** could be also obtained through an alternative procedure consisting on an Ullmann coupling between pyridone **5** and iodoarenes[7] followed by treatment with oxalyl chloride.[8] Subsequently, the unprecedented condensation of 2-chloropyridinium salts **6–11** with a range of secondary phosphines efficiently afforded the desired pyridiniophosphines **12–19** in moderate to good yields (see Scheme 1 and the Supporting Information).



Scheme 1. Synthesis of pyridinium-substituted phosphines. Reagents and conditions (yields): a) Me_3OBF_4 or $EtOBF_4$, CH_2Cl_2, RT; **6** (91%); **8** (99%); **9** (99%); **10** (98%); **11** (89%); b) **5** (1.2 equiv), iodobenzene (1 equiv), CuBr (10 mol%), Cs_2CO_3 (2.1 equiv), DMSO, 60°C, (95%); c) oxalyl chloride (3 equiv), $Cl(CH_2)_2Cl$, and then $NaBF_4$ (4 equiv), (71%); d) diaryl/dialkylphosphine (2 equiv), THF, 65°C; 1–3 days; **12** (70%), **13** (80%); **14** (71%); **15** (43%); **16** (60%); **17** (77%); **18** (89%); **19** (30%).

Figure 2 depicts the structure of **12** in the solid state. The P1–C1 distance (1.8551(7) Å) is only slightly longer than the other two C–P bonds (P1–C7, 1.8260(7) Å; P1–C13, 1.8244(7) Å), which is probably due to the increased steric hindrance of the *N*-methylpyridinium group when compared with the two phenyl rings.[9] Furthermore, the degree of pyramidalization at phosphorus (61.3%) is even slightly higher than that observed for PPh_3 (56.7%).[10] These parameters suggest retention of the nonbonding electron pair at the phosphorus atom.

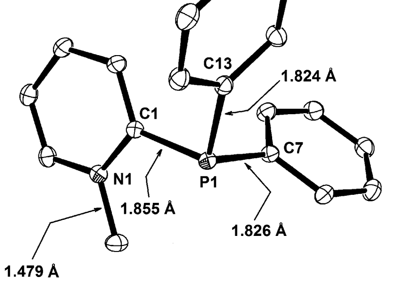
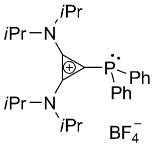


Figure 2. Crystal structure of **12**. Hydrogen atoms and the BF_4 anion were omitted for clarity; ellipsoids are set at 50% probability.[11]

At this point we tried to evaluate the donor endowment of the new cationic phosphines by analysis of the CO stretching frequencies in *trans*-[RhCl(CO)L_2] complexes **20–25** (Table 1 and Scheme 2). However, these data were misleading and certainly should be taken with caution. For example, ligand **19** that bears five CF_3 groups seems to be a stronger electron donor than **16** that shares the same skeleton but carries only one CF_3 substituent (Table 1, entries 3 and 6). This clearly indicates that in Rh complexes **20–25**, the CO stretching frequencies may not only be determined by the electronic properties of the ligands on Rh, but also influenced by small geometric changes around the metal owing to steric factors or

Table 1: Carbonyl stretching frequencies in $[RhCl(CO)L_2](BF_4)_2$ complexes in the solid state and electrochemical redox potential of the ligands. The values of commonly used phosphorus ligands are also included for comparison.

Entry	Ligand	$\tilde{\nu}_{CO}$[a] $[RhCl(CO)L_2](BF_4)_2$	E_p(ox)[b]
1	**12**	1996	1.398
2	**15**	1994	1.355
3	**16**	2004	1.436
4	**17**	1982	1.297
5	**18**	1974	1.269
6	**19**	2001	1.578[c]
7	**26**	1971	1.207
8	**27**	–	1.541
9	Ph_3P	1979	0.687
10	$(MeO)_3P$	2011	1.287



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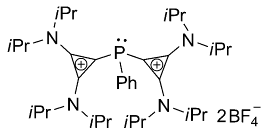

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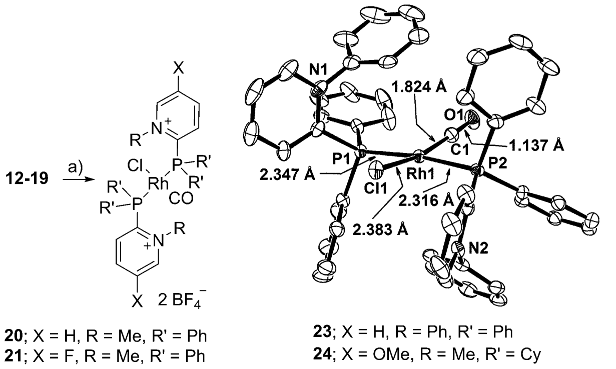
[a] Values in cm^{-1}. [b] Oxidation peak potentials reported in V. Calibrated versus ferrocene/ferrocenium ($E_{1/2}$ = 0.24 V), Bu_4NPF_6 (0.1 M) in CH_2Cl_2. [c] Measured in CH_3CN.



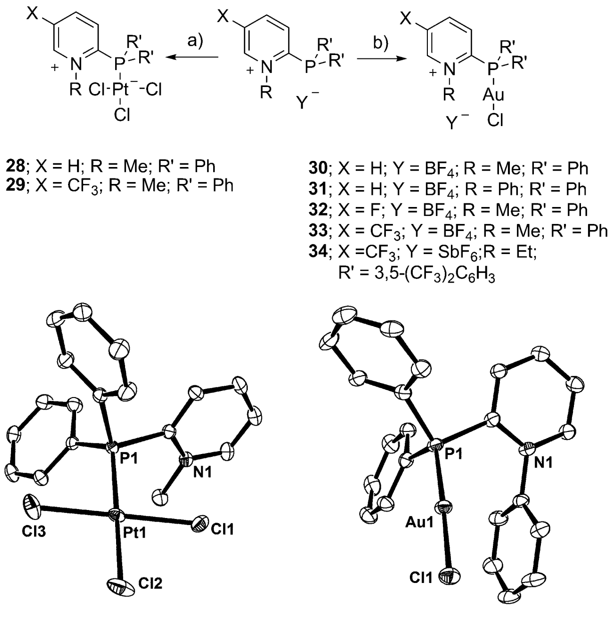
Scheme 2. Synthesis of Rh complexes and crystal structure of **23**. Hydrogen atoms and BF_4 anions were omitted for clarity; ellipsoids are set at 50% probability.[11] Reagent and conditions (yields): a) $[\{RhCl(CO)_2\}_2]$ (0.25 equiv), CH_2Cl_2, RT; **20** (99%); **21** (77%); **22** (57%); **23** (78%); **24** (74%).

through-space interactions between CO and the other ligands.[12,13] For this reason the oxidation potential E_p(ox) determined by cyclic voltammetry was chosen as a more reliable parameter to rank the electronic properties of phosphines **12**–**19**.[14] These data followed the expected tendency and suggest that ligands **17** and **18**, both decorated with two cyclohexyl substituents, depict donor abilities similar to that of $(MeO)_3P$, while **12**, **15**, **16,** and **19** are even weaker donors than this phosphite (Table 1).

The E_p(ox) for cyclopropenium substituted phosphines **26** and **27** are also shown for comparison purposes.[2a,c] These values support the notion that pyridinium substituents are more effective electron withdrawing groups than di(alkylamino)cyclopropenium rings (compare entries 1 and 7), and also indicate that if appropriately substituted, pyridiniophosphines can reach donor abilities characteristic of dicationic ligands (entries 3, 6, and 8).

Encouraged by this analysis, we decided to test the viability of pyridiniophosphines in catalysis and prepared a set of Pt^{II} and Au^{I} complexes in which salts **12**–**19** were used as ligands (Scheme 3). Compounds **28**–**34** were obtained as air-stable solids by addition of K_2PtCl_4 or $(Me_2S)AuCl$ to solutions of the corresponding ligands. Moreover, crystals of **28** and **31** were obtained and their structure determined by X-ray diffraction confirming the expected connectivity.[15]

To compare the catalytic performance of complexes **28** and **29** with standard Pt catalysts, the hydroarylation of propargyl aryl ether **35** to chromene **36** was chosen as first model reaction because the proposed mechanism for this transformation suggests that a platinum catalyst with enhanced cationic character should facilitate the whole process.[16] In fact, increases in rate of reactions were observed when $(C_6F_5)_3P$ was employed as ancillary ligand or if higher oxidized Pt species such as $PtCl_4$ were used as catalysts.[17] Figure 3 also shows the conversion versus time plot for precatalysts **28** and **29** under otherwise identical conditions (2 mol% Pt, 80 °C). Their vastly superior performances, which clearly surpass the other catalytic mixtures, beautifully demonstrate the exquisite ability of pyridiniophosphine ligands to increase the π-acidity of Pt centers. Moreover, a qualitative correlation between the reactivity depicted by catalysts **28** and **29** and the measured oxidation potentials E_p(ox) for their corresponding free ligands could be established. This also supports the use of cyclic voltammetry as an adequate technique to characterize the electronic properties of P-based ligands.



28; X = H; R = Me; R' = Ph
29; X = CF_3; R = Me; R' = Ph

30; X = H; Y = BF_4; R = Me; R' = Ph
31; X = H; Y = BF_4; R = Ph; R' = Ph
32; X = F; Y = BF_4; R = Me; R' = Ph
33; X = CF_3; Y = BF_4; R = Me; R' = Ph
34; X = CF_3; Y = SbF_6; R = Et; R' = 3,5-$(CF_3)_2C_6H_3$

Scheme 3. Synthesis of Pt and Au complexes and crystal structure of **28** and **31**. Hydrogen atoms, solvent molecules and BF_4 anions were omitted for clarity; ellipsoids are set at 50% probability.[11] Reagent and conditions (yields): a) K_2PtCl_4 (1.0 equiv), CH_3CN, RT; **28** (80%); **29** (40%); b) $(Me_2S)AuCl$ (1.0 equiv), CH_2Cl_2, RT; **30** (97%); **31** (69%); **32** (98%); **33** (98%); **34** (51%).

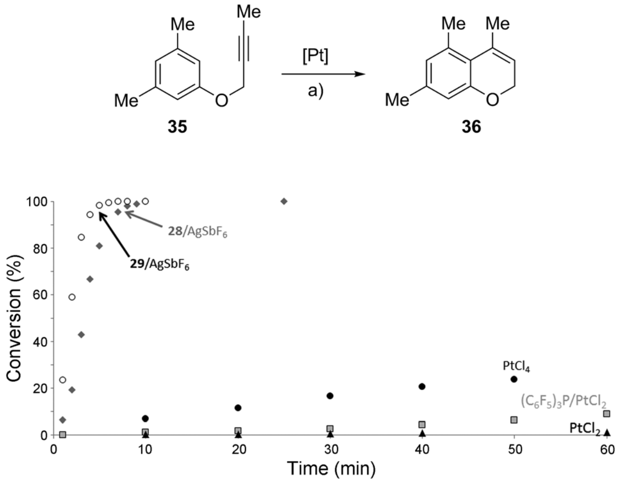


Figure 3. Ligand effect on the Pt-catalyzed hydroarylation of propargyl aryl ether **35** to chromene **36**. Reagents and conditions: a) **35** (0.05 M), Pt precatalysts (2 mol%), $AgSbF_6$ (2 mol%), $(CH_2)_2Cl_2$, 80 °C. Conversions determined by gas chromatography.

Interestingly, other synthetically useful and mechanistically more complex Pt^{II}-promoted transformations also responded to the strong π-acceptor properties of ligands **12**–**19**. Specifically, the cycloisomerization of enyne **37** to cyclobutene **38** was chosen as additional model because this process is known to be accelerated when performed under CO atmosphere (1 atm).[18] Thus, the study of this reaction allows a direct comparison between pyridiniophosphines and the archetypical π-acceptor ligand. Figure 4 shows the kinetic profiles compiled for a set of different catalytic systems under otherwise identical conditions (2 mol% Pt, 80 °C). It can be appreciated that CO performed better in terms of reactivity than any the other π-acceptor ligands tested: $(PhO)_3P$ and $(C_6F_5)_3P$. However, the activity exhibited by catalysts **28** and **29** has no rival, and cyclobutene **38** could be obtained in excellent yields after only few minutes (Figure 4).

Finally, the Au-catalyzed hydroarylation of phenylacetylene (**39**) with mesitylene (**40**) served as preliminary probe to test the utility of pyridiniophosphines beyond Pt chemistry.[19] It has been reported that typical catalytic systems such as $Ph_3PAuCl/AgBF_4$ are ineffective in this particular transfor-

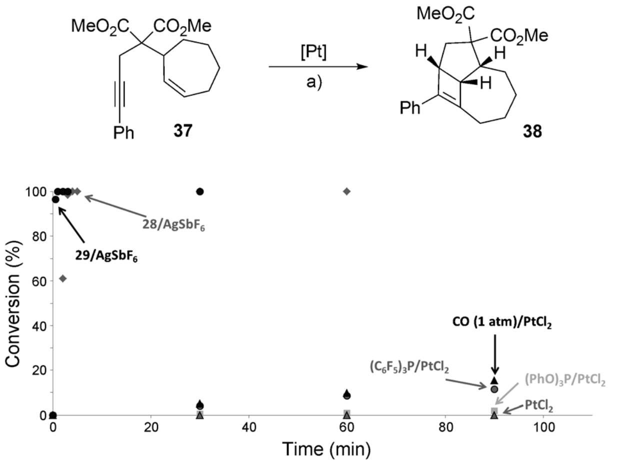


Figure 4. Ligand effect on the Pt-catalyzed cycloisomerization of enyne **37** to cyclobutene **38**. Reagents and conditions: a) **37** (0.05 M), Pt precatalysts (2 mol%), AgSbF$_6$ (2 mol%), (CH$_2$)$_2$Cl$_2$, 80°C Conversions determined by gas chromatography.

mation.[19a] However, the enhanced π-acceptor properties of ligands **12**–**19** render Au particularly electrophilic in complexes **30** and **34**, and as result, their catalytic activities are superior. Note however, that the high activities observed rapidly decay after some minutes and complete conversions of the starting materials into alkene **41** could never be achieved even by using catalyst loads of up to 5 mol% (Figure 5). The design of longer-lived active species for this and other processes is currently under investigation in our laboratories.

In summary, we outlined herein the preparation of a new family of bench stable cationic phosphines, pyridiniophosphines, through a short and highly modular synthesis. When used as ligands, these compounds depict excellent π-acceptor properties, and as a consequence, a remarkable ability to enhance the Lewis acidity of the metals they coordinate. The beneficial effects of this property in the area of homogeneous catalysis are demonstrated along three mechanistically diverse Pt^{II}- and Au^{I}-catalyzed reactions.

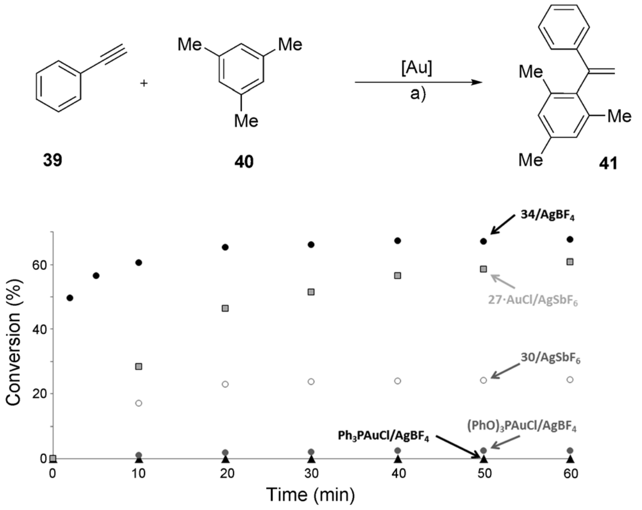


Figure 5. Ligand effect on the Au-catalyzed hydroarylation of alkyne **39** with arene **40**. Reagents and conditions: a) **39** (0.05 M), **40** (4 equiv; 0.2 M) Au^{I} precatalysts (5 mol%), AgBF$_4$ or AgSbF$_6$ (5 mol%), (CH$_2$)$_2$Cl$_2$, 60°C. Conversions determined by gas chromatography.

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