Chemistry of Tetradentate [*C,N*:*C,N*] Iminophosphorane Palladacycles: Preparation, Reactivity and Theoretical Calculations

Paula Munín-Cruz, Francisco Reigosa, Marcos Rúa-Sueiro, Juan M. Ortigueira, M. Teresa Pereira, and José M. Vila*[a]

Dedicated to the late Professor Bernard L. Shaw, The University of Leeds, UK

A theoretical and experimental study of tetradentate [C,N:C,N] iminophosphorane palladacycles was carried out for the purpose of elucidating their behavior as compared to the parent Schiff base analogues to determine the prospect of encountering new A-frame structures for the iminophosphor-ane derivatives. The DFT calculations were in agreement with the experimental results regarding the performance of these ligands. New insights into the chemistry of the related dinuclear species have been obtained.
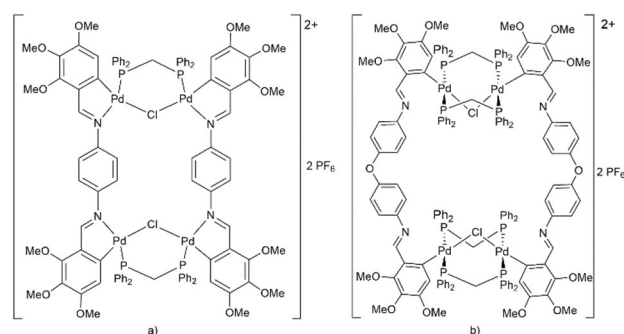
1. Introduction

Palladacycles[1] cover a rather wide range of compounds within the organometallic family; they have been researched for nearly six decades, since the first example was synthesized.[2] One would not be wrong to say that this ever growing interest in such compounds could be mainly due to the variety of the bonds at the metal center, *i.e.*, the palladium atom, which makes their reactivity one of the most extended allowing by far a good deal of applications in numerous fields of chemistry. As well as their use in photochemistry[3] or as liquid crystals[4] two of their most important usages are as pre-catalysts in cross-coupling reactions, such as Suzuki-Miyaura,[5] Mizoroki-Heck[6] or Negishi[7] and as notable powerful anticancer agents[8] Although a majority of palladacycles are prepared from ligands containing C=N double bonds, such as Schiff bases, semicarbazones, thiosemicarbazones and the like, there is growing interest in palladacycles that stem from the iminophosphoranes $R_3P=NR$, where the polarized P=N double bond, shows a strong σ-donor behavior with minor π-acceptor properties which makes them very suitable ligands for the cyclopalladation reaction.[9] Along with our more recent research on palladacycles we have come upon several new behaviors in their chemistry among which we may highlight the following two milestones when employing tetradentate [*C,N:C,N*] ligands, or terdentate [*C,N,O*] iminophos-phorane ligands, namely, the chelate to bridging shift in diphosphane palladacycles[10] and the triphenylphosphine chal-cogenide metallacycles, respectively.[9d] We reasoned that by merging the two concepts we would be able to establish yet another new performance of these species in the hope of further extending the scope of this chemistry, *i.e.*, by treatment of the iminophosphorane tetradentate [*C,N:C,N*] ligand pallada-cycles with tertiary diphosphanes, which should render multi-nuclear complexes with the possibility of A-frame structures[10] as encountered earlier by us, or alternatively display the more classical palladacycle[11] behavior to give complexes with only bridging or chelating diphosphanes, as appropriate (Scheme 1). The polarization of the P=N double bond and hence its greater basicity as compared to its C=N counterpart play an important role in the final result since it produces a stronger metal-donor atom bond. Herein we give an account of our results addressing this issue that has been supported, in part, by DFT calculations.

[a] *Dr. P. Munín-Cruz, F. Reigosa, M. Rúa-Sueiro, Dr. J. M. Ortigueira, Prof. M. T. Pereira, Prof. J. M. Vila*
   Departamento de Química Inorgánica
   Universidad de Santiago de Compostela
   15782 Santiago de Compostela Spain
   E-mail: josemanuel.vila@usc.es

Scheme 1. a) Classical palladacycle with bridging diphosphanes; b) A-frame structure.

ChemistryOpen

Full Papers
doi.org/10.1002/open.202000253

Chemistry Europe
European Chemical
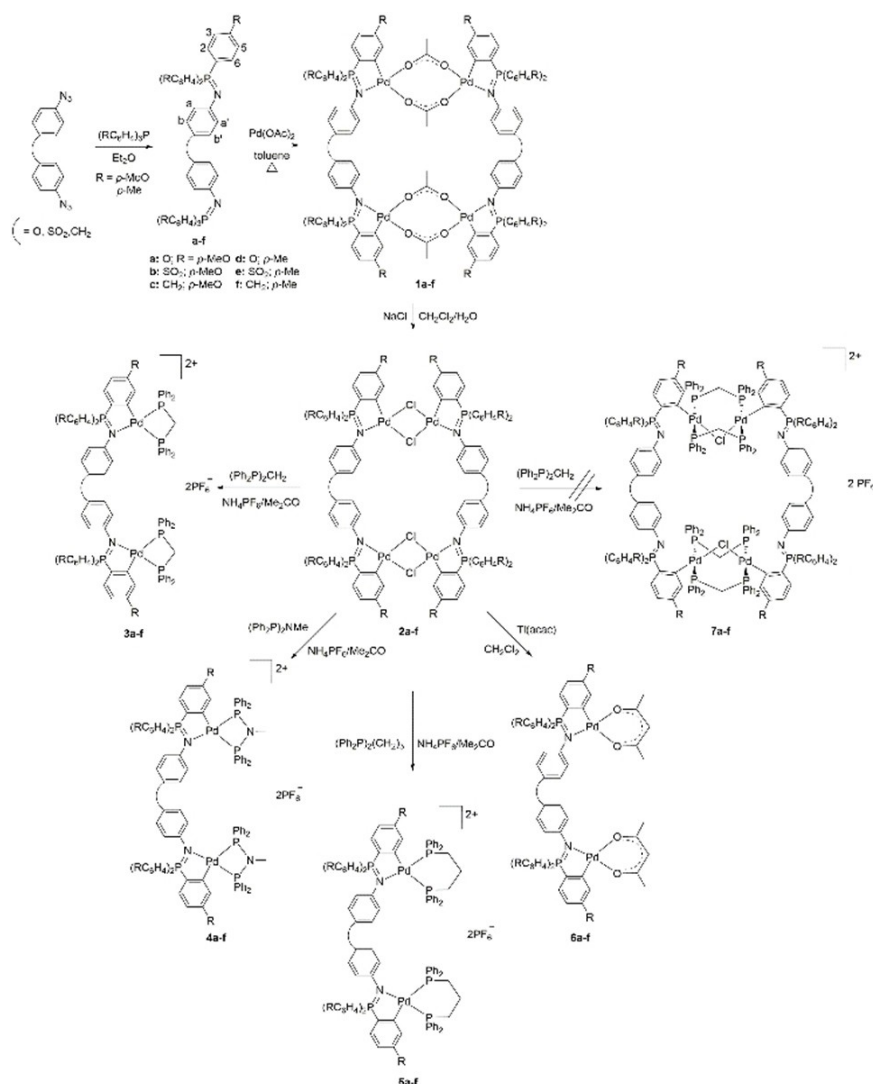Societies Publishing

2. Results and Discussion

For the convenience of the reader the compounds and reactions are shown in Scheme 2. Preparative details, characterising microanalytical data, IR and NMR data are in the Experimental section. Treatment of the diamines $(p\text{-}NH_2C_6H_4)_2X$ $(X=O, SO_2, CH_2)$ with sodium azide followed by $P(RC_6H_5)_3$ $(R=p\text{-}MeO, Me)$ gave the six iminophosphorane ligands **a–f**. The reaction of the latter with palladium(II) acetate in toluene yielded the tetranuclear complexes **1a–f** as air-stable solids which were fully characterized (See Experimental). The IR spectra show the $\upsilon(P{=}N)$ band *ca.* 1220 cm^{-1}, shifted by *ca.* −100 as compared to the starting ligand, and the $\upsilon_{as}(COO)$ and $\upsilon_s(COO)$ acetate stretches *ca.* 1565 and 1410 cm^{-1}, respectively, the separation of which is consistent with bridging acetate ligands.[12]

The acetate-bridged complexes were converted into the halido-bridged analogues by treatment of **1a–f** in dichloromethane with aqueous sodium chloride to give the chloride–bridged **3a–f** complexes as air-stable solids (see Experimental). The IR spectra showed absence of the acetate stretches and two bands assigned to the $\upsilon(Pd–Cl)$ vibration modes for the unsymmetrical Pd_2Cl_2 moiety, *ca.* 310 and 245 cm^{-1} for the $Pd–Cl_{transN}$ and $Pd–Cl_{transC}$ bonds, respectively, along with the differing *trans* influence of the nitrogen and phenyl carbon atoms, also respectively.

In a previous work we described formation of double A-frame complexes which could be accomplished by choosing an appropriate flexible bidentate Schiff base ligand, bis(N-2,3,4-trimethoxybenzylidene)-4,4′-sulfonyldianiline, or -4,4′-oxydianiline,[10] as opposed to the phenylenediimine-*C,N:C,N* analogues, where this was not possible, due to the restricted flexibility of the ligand imposed by the rigidity of the central phenylene ring itself, hindering opening of the metallacycle ring needed to provide the extra vacant coordination site on the metal for coordination of the second phosphine ligand.[11]

These species are closely related to the field of supramolecular coordination complexes (SCCs),[13] and we found

Scheme 2. Reaction sequence leading to the dinuclear and to the expected A-frame compounds.

ChemistryOpen

Full Papers
doi.org/10.1002/open.202000253

**Chemistry
Europe**
European Chemical
Societies Publishing

they may host small molecules such as chloroform or acetone. Then, our purpose was to further investigate those systems showing a similar reactivity in order to delimit the compounds that present these characteristics and expand the family of palladacycle SCCs; where this does not seem to be the case satisfactory explanations would be essential.

We also sought to prepare the dinuclear compounds, which shall be discussed first; they are the derivatives of the halide-bridged complexes with $Ph_2PCH_2PPh_2$ (dppm), $Ph_2PN(Me)PPh_2$ (dppma), as well as $Ph_2P(CH_2)_3PPh_2$ (dppp) included for comparative purposes. Thus, reaction of **2(a–f)** with the corresponding diphosphane in 1:4 molar ratio followed by treatment with ammonium hexafluorophosphate gave the dinuclear palladacycles **3–5(a–f)** as pure air-stable 1:2 electrolytes, which were fully characterized (see Experimental section). In the ^1H NMR spectra a doublet of doublets *ca.* 4.5 and 2.3 ppm was assigned to the PCH_2P **3(a–f)** and PN(*Me*)P **5(a–f)** protons, respectively, whereas the P(CH_2)$_3$P resonances were a multiplet. The H5 resonance showed coupling to both phosphorus nuclei ($^4JP_{trans-N}$H5 *ca.* 10 Hz, $^4JP_{cis-N}$H5 *ca.* 8 Hz). The ^{31}P NMR spectra showed three doublets of doublets for the P=N nucleus and the two inequivalent phosphorus nuclei of the diphosphane in each case. The position of the former resonance remained fairly unchanged in all the complexes *ca.* 45–50 ppm. With respect to this signal those for the dppm and dppp compounds, *ca.* −8.5/−30 ppm, **3(a–f)**, 23/1.5 ppm, **5(a–f)**, appear moderately and very strongly highfield shifted, respectively, in agreement with the influence of ring size on the ^{31}P chemical shifts.[14] On the contrary, the ^{31}P diphosphane resonances of the four-membered ring dppma compounds, **4(a–f)**, 59/51 ppm, underwent highfield shifts with respect to the free diphosphane resonance (+73.7 ppm) associated with shielding caused by the quite strongly strained four-membered ring. In all cases the phosphane resonance at lower frequency was assigned to the phosphorus nucleus *trans* to the phenyl carbon atom, in agreement with the higher *trans* influence of the latter with respect to the nitrogen atom.[15] Furthermore, for some of the compounds close inspection of their spectra revealed two, at times three, sets of resonances for the three ^{31}P nuclei, suggesting existence of conformers. The ratio of the conformers was uneven but reached a 50:50 distribution in some cases. To ascertain this issue a DFT analysis was performed on compound **3f** using the package of programs g16. The reported geometry and frequency calculations were carried out at the B3LYP/LANL2DZ-ECP/6-31G(d) level of theory for compound **3a** and ONIOM B3LYP/LANL2DZ-ECP/6-31G(d): B3LYP/3-21G for compound **3f** and no imaginary frequencies were found, confirming the stationary points. Three conformers were proposed and optimized resulting in structures that vary according to the orientation of the metallated units, the rotation of which is strongly hindered by the presence of the iminophosphorane and phosphane phenyl rings. No restrictions were set for the *para*-disubstituted phenyl rings bonded to the —O— and —CH$_2$— spacers since it was considered that this did not have a significant contribution to the relative energy of the conformers. We considered the two most stable conformers, coined as E and Z, which showed a relative energy difference of

ΔH 5.25, ΔG 1.52 kJ mol⁻¹, **3a**, and ΔH 3.66, ΔG 3.33 kJ mol⁻¹, **3f** (related to the E conformer); these should be responsible for the most intense signals in the ^{31}P NMR spectra, whilst third conformer, ΔH 15.74, ΔG 13.56, **3a**, ΔH 15.49, ΔG 9.46 kJ mol⁻¹, **3f**, would give rise to the weaker signal appearing only occasionally. The angle between the chelated diphosphine rings [Pd,P,C,P] in the ground state conformer E was 84.31°, **3a**, and 80.76°, **3f**, and the palladium coordination planes [C,N,P,P] were at 72.88°, **3a**, 86.58°, **3f**, In conformer Z the analogous values were 58.44° and 54.78°, **3a**, and 49.89° and 46.56, **3f**, respectively. These differences were ascribed to the relative orientations of the [Pd,P,C,P] rings. In conformer E, one ring points out of the spacer angle PhOPh, **3a**, PhCH$_2$Ph, **3f**, and the other one towards the inner side. In Z both rings are orientated outwards from the spacer angle. In both cases these arrangements minimize the repulsions of the phosphine phenyl rings and the Ph$_2$P=N rings. Likewise, as further proof torsion angles were measured referenced to the diamine spacer (Figure 1).

Thus, the [Pd,N,CH$_2$,N] torsion angles were of 166.47° and 79.23° (conformer E); 146.66° and 148.36° (conformer Z), **3a**, and of 174.40° and 92.06° (conformer E); 138.96° and 157.00° (conformer Z), **3f**; data which are in agreement with the proposed layouts. The third conformer, which has the highest energy, displays the phenyl rings from the diphosphine close to the N=PPh$_2$ units with steric hindrance that lead to the most unstable arrangement; the corresponding NMR resonance was observed only once, in **3f**. Low and high temperature ^{31}P NMR were run for compound **3f**. At 193 K the spectrum showed both conformers E and Z were still present, albeit the E/Z ratio was modified from an initial 50:50% to 65:35%, and no signal attributable to the third conformer was observed. At 313 K the signals appeared as only one set of resonances for the P=N, and diphosphane nuclei, with all the possible arrangements merging into one sole conformer.

The tests carried out in order to prepare tetranuclear A-frame species **7a–f** similar to those reported earlier by us,[10] from the dinuclear complexes **3a–f** (*e.g.* **3f**→**7f**, see Scheme 3), where unsuccessful. Thus, upon the negative outcome obtained in attempts to synthesize the tetranuclear compounds depicted in Scheme 2, we performed DFT calculations in order to provide theoretical confirmation of these results. The structure that would result from the formation of a double A-frame com-
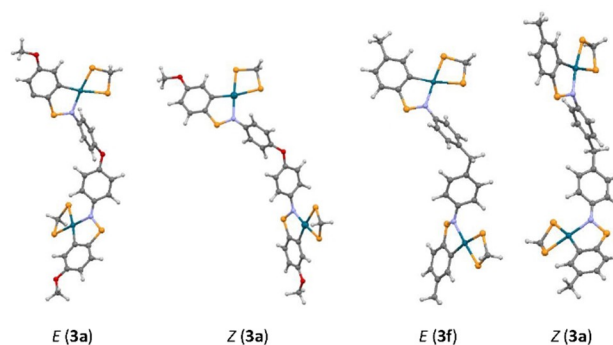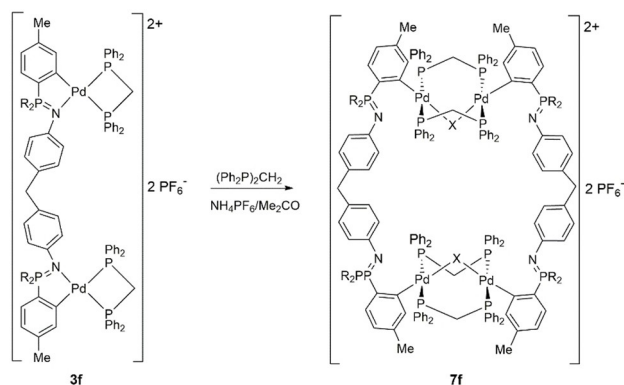

Figure 1. Conformers E and Z for **3a** and **3f**. Phenyl rings on the phosphorus atoms have been omitted for clarity.

ChemistryOpen

Full Papers
doi.org/10.1002/open.202000253

Chemistry
Europe
European Chemical
Societies Publishing

Scheme 3. Proposed formation of tetranuclear A-frame complex **7f** from compound **3f**.

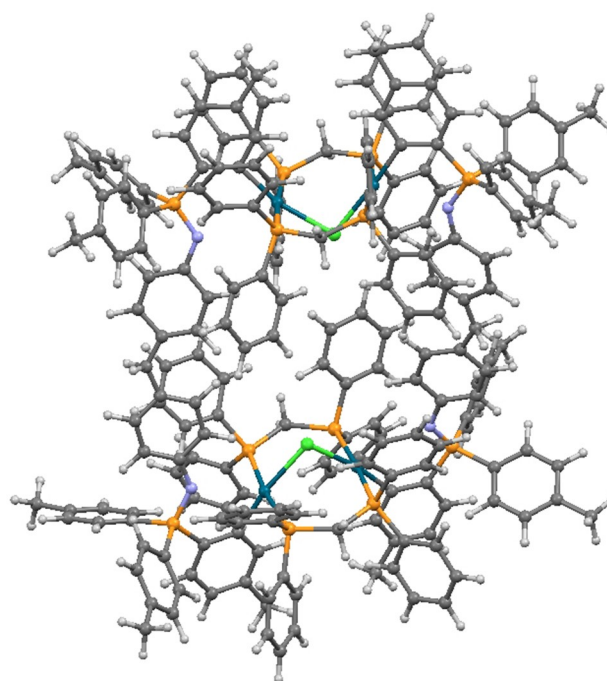**Figure 2.** Calculated tetranuclear A-frame palladacycle **7f**.

pound from compounds type **7a–f**, namely **7f** with the CH$_2$ spacer as depicted in Scheme 3, was studied.

The crystal structure of a previous work[10] was used as a base optimized using a B3LYP/3-21G level of theory. The frequency study was carried out with the same basis as for the chelated **f** type compounds (*vide supra*), using an ONIOM model studying the close environment of the cyclometalated moiety at a B3LYP/L2DZ2-ECP/6-31G(d) level and the rest of the molecule at 3-21G.

The resulting structure shows imaginary frequencies, but they are coincident with the rotation of the methyl groups attached to the phenyl rings and are not considered to significantly affect the energy values used to calculate the energy of the formation reaction of this compound. To further investigate the thermochemistry involved in the transformation of the chelated species into the less common double A-frame structures, as we observed in previous work,[10] the energy of the reaction was calculated with the data obtained for the chelate structures, the resulting A-frame structure and the chloride ion optimized using a B3LYP/6-31G(d) level of theory (Figure 2).

The enthalpy and Gibbs free energy values for this reaction were −18.14 kcal/mol and 87.37 kcal/mol respectively, making this reaction exothermic, albeit endergonic. This explains why the spontaneous formation of the A-frame structure that occurred in the case of double Schiff bases was not observed, where the study by DFT yielded negative values for enthalpy and negative reaction free energy of *ca.* 200 kcal/mol.[10]

After gas phase geometries were optimized, solvation effects were taken into account in order to further investigate the thermochemistry of the reaction. The structures were optimized and frequency calculations were performed at the same level of theory but using the polarizable continuum model, acetone as solvent and the ONIOMPCM=x setting, where the reaction field is computed separately for each level using the cavity of the real system. The enthalpy and Gibbs free energy values for this reaction were 189.98 kcal/mol and 291.96 kcal/mol respectively. Thus, both positive values show that the reaction should be endothermic, as opposed to the gas

phase situation, and endergonic in solution, confirming that this reaction is not spontaneuous.

For comparative reasons with the phosphine derivatives, we prepared the acac [*O,O*] complexes **6(a–f)** containing two stable six–membered rings at the metal centers, which were characterized accordingly. The IR spectra showed υ(C–C) and υ(C–O) stretches in the expected ranges, and in the ^{1}H NMR spectra two singlet resonances were assigned to the two inequivalent methyl groups *ca.* 1.9 and 1.6 ppm. The ^{1}H NMR spectrum for **6a** and **6f** did not show additional resonances to those expected and the low and high temperature NMR spectra did not provide any variations with respect to the room temperature spectra. This leads us to conclude that it is the presence of phenyl rings on the chelating ligand at palladium, that hinders the structural rearrangement/rotation/interconversion leading to the aforementioned conformers.

3. Conclusions

Phosphorus NMR spectra of the dinuclear chelated phosphine compounds showed the presence of several diverse spatial arrangements assignable to the existence of the conformers found in the DFT calculations, in terms of the most energetically stable and of their spatial disposition. High and low temperature NMR were also performed with the chelated phosphine and the acac derivatives, showing that in the case of the acac the presence of conformers was not detected. Also, DFT calculations confirmed the experimental fact that complexes with the chelated diphosphines are more stable than the tetranuclear framework; this has to do presumably with the relative strengths of the C=P→Pd and C=N→Pd bonds in either

ChemistryOpen

Full Papers
doi.org/10.1002/open.202000253

Chemistry Europe
European Chemical
Societies Publishing

case. Thus, in principle the hoped-for tetranuclear A-frame palladacycles with iminophosphorane ligands could not be obtained, as occurred with their Schiff base analogues.

Experimental Section

General Comments

Solvents were purified by standard methods.[16] Palladium(II) acetate, Thallium(I) acetylacetonate, $(p\text{-}NH_2C_6H_4)_2SO_2$, $(p\text{-}NH_2C_6H_4)_2O$, $(p\text{-}NH_2C_6H_4)_2CH_2$, and the phosphines $P(p\text{MeOPh})_3$, $P(p\text{MePh})_3$, $Ph_2PCH_2PPh_2$ (dppm) and $Ph_2P(CH_2)_3PPh_2$ (dppp) were purchased from commercial sources; $Ph_2PN(Me)PPh_2$ (dppma), personal loan to Professor JM Vila. Elemental analyses were performed with a Fisons elemental analyzer, Model 1108. IR spectra were recorded on BRUKER FT-MIR model VERTEX 70 V, and Jasco model FT/IR-4600 spectrophotometers. ^1H NMR spectra in solution were recorded in $CDCl_3$, DMSO-d_6, CD_2Cl_2, or $(CD_3)_2CO$ at room temperature on Bruker DPX 250 and Varian Inova 400 spectrometers operating at 250.13 MHz and 400.14 MHz respectively and using 5 mm o.d. tubes; chemical shifts, in ppm, are reported downfield relative to TMS using the solvent signal ($CDCl_3$, $\delta^1H = 7.26$ ppm; DMSO-d_6, $\delta^1H = 2.50$ ppm; CD_2Cl_2 d_6 $\delta^1H = 5.32$ ppm, MeCOMe-d_6 $\delta^1H = 2.05$ ppm) as reference. ^{31}P NMR spectra were recorded at 161.91 MHz and on a Varian Inova 400 spectrometer using 5 mm o.d. tubes and are reported in ppm relative to external H_3PO_4 (85%). Coupling constants are reported in Hz.

Conflict of Interest

The authors declare no conflict of interest.

[1] a) Y. Huang, L. Wang, J. Li, H. Qiu, P.-H. Leung, *ACS Omega* **2020**, *5*, 15936–15941; b) R. A. Arthurs, D. L. Hughes, C. J. Richards, *Org. Biomol. Chem.* **2020**; c) B. Su, A. Bunescu, Y. Qiu, S. J. Zuend, M. Ernst, J. F. Hartwig, *J. Am. Chem. Soc.* **2020**, *142*, 7912–7919.

[2] J. P. Kleiman, M. Dubeck, *J. Am. Chem. Soc.* **1963**, *85*, 1544–1545.

[3] a) B. Ma, P. I. Djurovich, M. E. Thompson, *Coord. Chem. Rev.* **2005**, *249*, 1501–1510; b) M. Ghedini, I. Aiello, A. Crispini, A. Golemme, M. La Deda, D. Pucci, *Coord. Chem. Rev.* **2006**, *250*, 1373–1390; c) M. S. Lowry, S. Bernhard, *Chem. Eur. J.* **2006**, *12*, 7970–7977; d) L.-L. Wu, C.-H. Yang, I. W. Sun, S.-Y. Chu, P.-C. Kao, H.-H. Huang, *Organometallics* **2007**, *26*, 2017–2023; e) S. C. F. Kui, I. H. T. Sham, C. C. C. Cheung, C.-W. Ma, B. Yan, N. Zhu, C.-M. Che, W.-F. Fu, *Chem. Eur. J.* **2007**, *13*, 417–435.

[4] a) M. Marcos, *Metallomesogens*, VCH, Weinheim, **1996**; b) D. Pucci, G. Barberio, A. Bellusci, A. Crispini, M. Ghedini, *J. Organomet. Chem.* **2006**, *691*, 1138–1142.

[5] a) M.-T. Chen, C.-A. Huang, C.-T. Chen, *Eur. J. Inorg. Chem.* **2006**, 4642–4648; b) J. F. Civicos, D. A. Alonso, C. Najera, *Eur. J. Org. Chem.* **2012**, *2012*, 3670–3676, S3670/3671-S3670/3665; c) F. Lucio-Martínez, L. A. Adrio, P. Polo-Ces, J. M. Ortigueira, J. J. Fernández, H. Adams, M. T. Pereira, J. M. Vila, *Dalton Trans.* **2016**, *45*, 17598–17601.

[6] a) D. A. Alonso, C. Najera, M. C. Pacheco, *Adv. Synth. Catal.* **2002**, *344*, 172–183; b) D. E. Bergbreiter, P. L. Osburn, J. D. Frels, *Adv. Synth. Catal.* **2005**, *347*, 172–184.

[7] Y. Yang, N. J. Oldenhius, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2013**, *52*, 615–619.

[8] a) A. Garoufis, S. K. Hadjikakou, N. Hadjiliadis, *Coord. Chem. Rev.* **2009**, *253*, 1384–1397; b) N. Cutillas, G. S. Yellol, C. de Haro, C. Vicente, V. Rodriguez, J. Ruiz, *Coord. Chem. Rev.* **2013**, *257*, 2784–2797.

[9] a) D. Aguilar, R. Navarro, T. Soler, E. P. Urriolabeitia, *Dalton Trans.* **2010**, *39*, 10422–10431; b) D. Aguilar, G. Gonzalez, P. Villuendas, E. P. Urriolabeitia, *J. Organomet. Chem.* **2014**, *767*, 27–34; c) J. Vicente, J.-A. Abad, R. Clemente, J. Lopez-Serrano, M. C. Ramirez de Arellano, P. G. Jones, D. Bautista, *Organometallics* **2003**, *22*, 4248–4259; d) A. Fernández-Figueiras, F. Lucio-Martínez, P. Munín-Cruz, P. Polo-Ces, F. Reigosa, H. Adams, M. T. Pereira, J. M. Vila, *Dalton Trans.* **2018**, *47*, 15801–15807.

[10] P. Frieiro-Gomis, F. Lucio-Martínez, P. Munín-Cruz, J. M. Ortigueira, M. T. Pereira, P. Polo-Ces, D. Vázquez-García, J. M. Vila, *Chem. Commun.* **2018**, *54*, 2662–2665.

[11] L. Adrio, J. M. Antelo, J. M. Ortigueira, J. J. Fernandez, A. Fernandez, M. Teresa Pereira, J. M. Vila, *J. Organomet. Chem.* **2009**, *694*, 1273–1282.

[12] K. Nakamoto, *IR and Raman Spectra of Inorg. and Coord. Comp.*, WILEY, Hoboken, New Jersey, 5th ed. **1997**.

[13] a) D. Preston, A. Fox-Charles, W. K. C. Lo, J. D. Crowley, *Chem. Commun. (Camb.)* **2015**, *51*, 9042–9045; b) S. Wang, T. Sawada, K. Ohara, K. Yamaguchi, M. Fujita, *Angew. Chem. Int. Ed.* **2016**, *55*, 2063–2066; c) S. Bandi, D. K. Chand, *Chem. Eur. J.* **2016**, *22*, 10330–10335.

[14] P. E. Garrou, *Chem. Rev.* **1981**, *81*, 229–266.

[15] P. S. Pregosin, R. W. Kunz, *31P and 13C NMR of Trans. Met. Phosphine Comp.*, Springer-Verlag Berlin Heidelberg, Berlin, **1979**.

[16] D. D. Perrin, W. L. F. Armarego, *Purification of Laboratory Chemicals*, Butterworth-Heinemann, London, 4th ed. **1996**.