

SYNTHESIS OF IMINOPHOSPHORANES AS LIGANDS FOR ORGANOMETALLIC COMPOUNDS

Adolfo Fernández-Figueiras *, Fátima Lucio-Martínez, Paula Munín, Francisco Reigosa , José M. Vila , M. Teresa Pereira , Paula Polo-Ces

Departamento de Química Inorgánica, Facultad de Química, Campus Vida, Universidade de Santiago de Compostela, adolfo.fernandez@rai.usc.es

Abstract

Iminophosphoranes are organic compounds of general composition $R_3P=NR$ and can be considered as nitrogen analogues to phosphorus ylides. They can be obtained by the Staudinger [1] and Kirsanov [2] reactions. These compounds have multiple applications: they can be used as intermediates in reactions such as the Aza-Wittig [3], as a protecting group for amines or as ligands for coordinated or cyclometallated compounds [4].

The P=N bond is highly polarized, so that the nitrogen bears a partial negative charge. This feature makes them act as σ -donors with only minor π -acceptor properties, so when forming coordination compounds they can be displaced by other ligands [5].

Keywords

Iminophosphorane, cyclometallated, organometallic

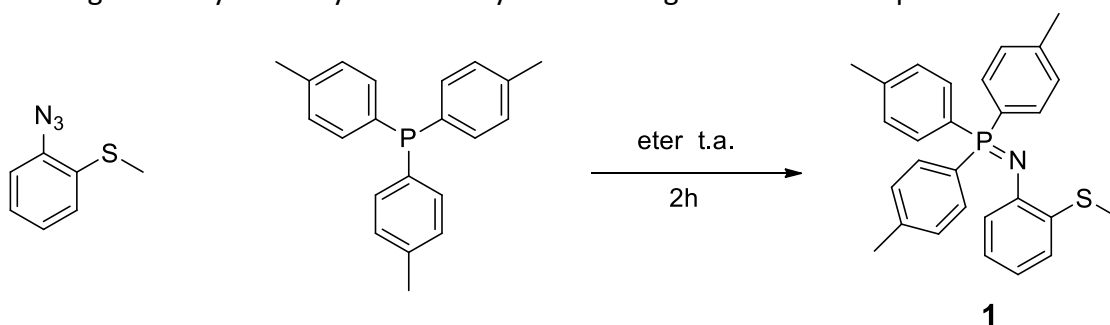
Introduction

The chemistry of iminophosphoranes has had a steady growth and it has been the focus of considerable interest in the last decade. The biological applications and anticancer properties of coordinated and cyclometallated iminophosphoranes of Pd(II), Pt(II) and Au(III) have been studied due to the non-toxic character of iminophosphoranes can be synthesized [6]. An extra advantage is that the P atom in the PR_3 fragment can be used as a "spectroscopic marker" to study the *in vitro* stability (and oxidation state) by $^{31}P\{^1H\}$ NMR [7]. Moreover, the luminescent properties of some of these compounds make them in molecular probes in teragnosis potentially useful [8]. On the other hand, iminophosphorane cyclometallated compounds are active in many types of catalysis such as Suzuki or Heck cross-coupling reactions [9].

Consequently, our research group has considered important to study the synthesis of new palladium (II) cyclometallated iminophosphorane compounds and their reactivity with phosphine ligands.

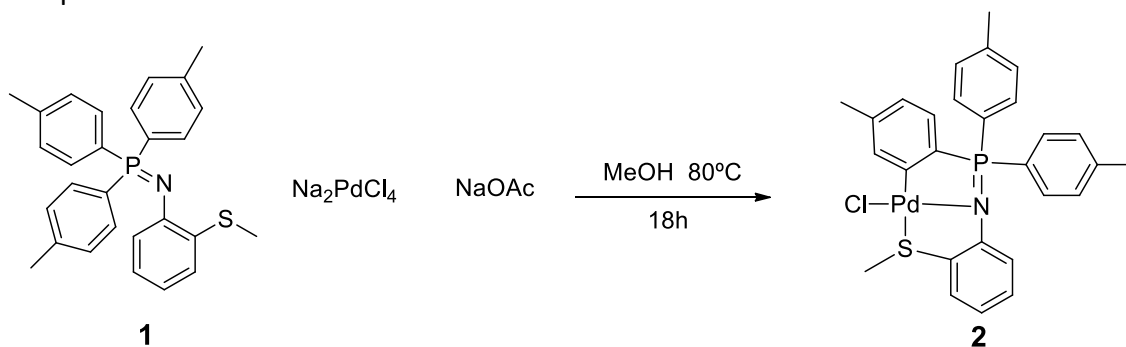
Results and discussion

2-(methylthio)aniline iminophosphoranes derivatives can act as tridentate ligands. Such ligands may be easily obtained by the Staudinger reaction as depicted in *Scheme 1*



Scheme 1

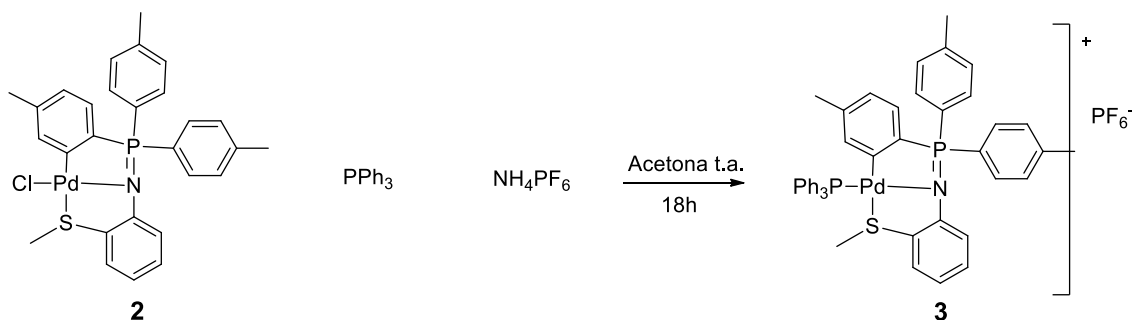
Compound **2** may be obtained by the reaction of a palladium salt with the iminophosphorane ligand. The presence of a base is not necessary but facilitates the cyclometallation reaction and prevents de formation of the [N,S] coordination compound.



Scheme 2

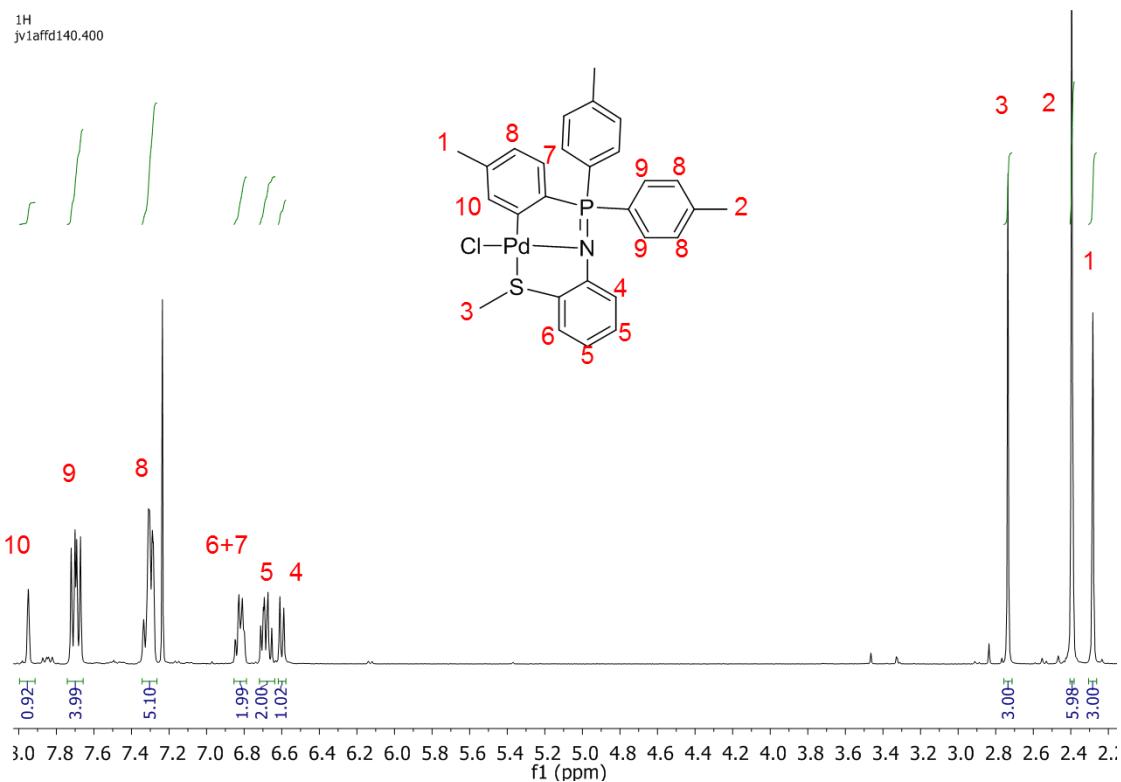
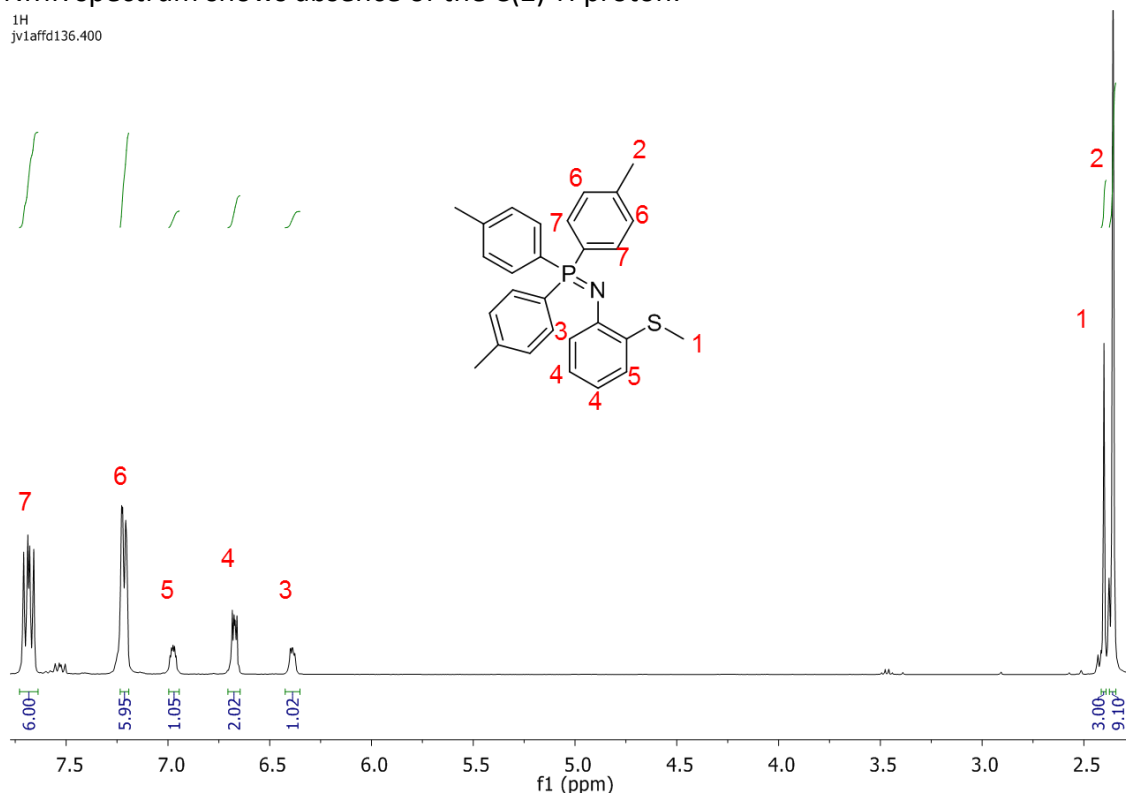
Compound **2** obtained in this reaction is an air-stable bright yellow solid. The metal atom shows a square-planar geometry and has two covalent coordinate bonds with the nitrogen and the sulfur atoms and one σ bond with de carbon atom.

Compound **3** bearing a triphenylphosphine ligand can be made by the direct reaction of **2** with the phosphine and ammonium hexafluorophosphate.



Scheme 3

The ^1H NMR analysis for **2** confirms the formation of the compound (*Figure 2*). The ^1H NMR spectrum shows absence of the C(2)-H proton.



¹H
jv1affd142.400

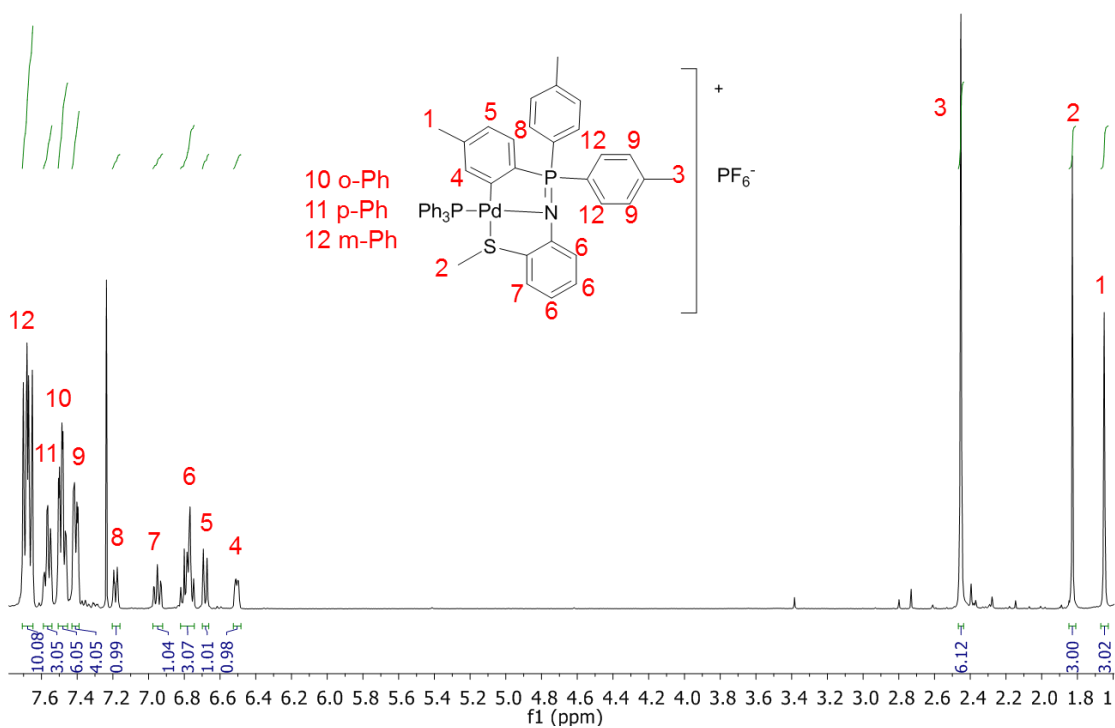


Figure 3: ¹H NMR spectrum for **3**

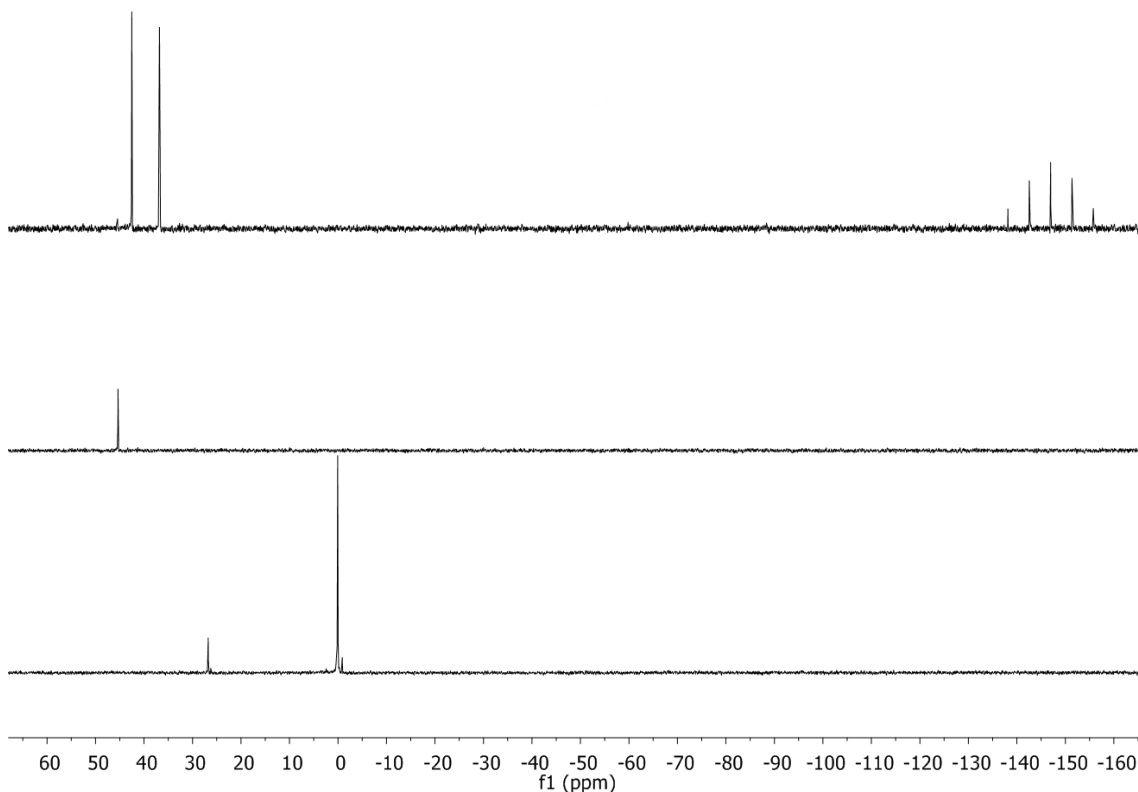
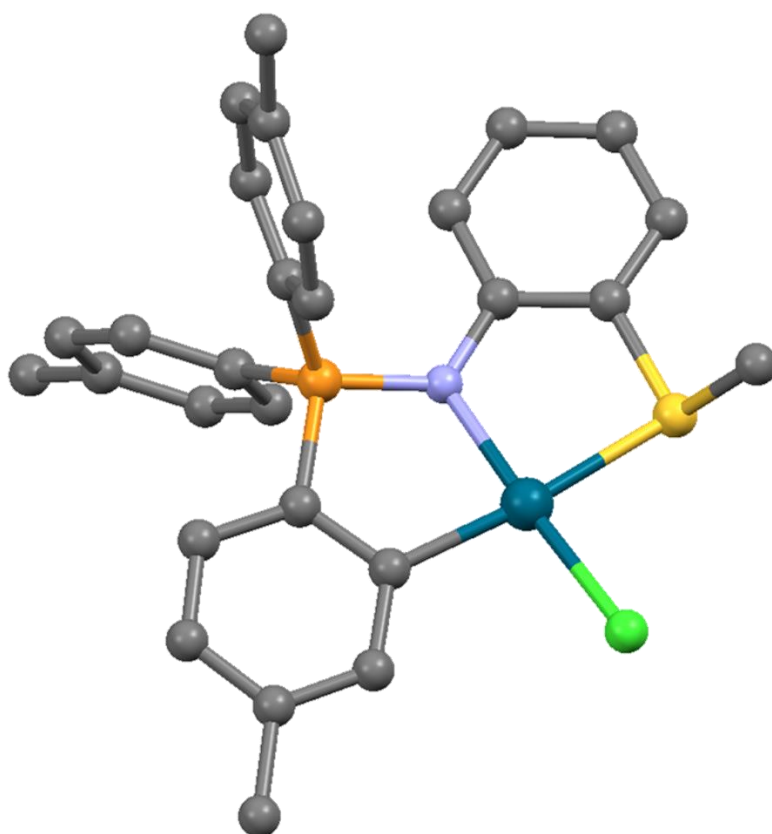


Figure 4. ³¹P{¹H} NMR spectrum for **3** (top), **2** (middle), **1** (bottom)

Crystals of compound **2** were obtained by slow evaporation from a chloroform solution. The X-ray diffraction study of the crystal confirms the formation of the cyclometallated compound.



Empirical Formula	C ₂₈ H ₂₇ ClNPPdS
Formula Weight	528.39
Temperature	100.0 (1)K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 10.862(5) Å α = 90.000(5)° b = 12.097(5) Å β = 90.000(5)° c = 19.282(5) Å γ = 90.000(5)°
Volume	2533.6(17) Å ³
Z	4
Density (calculated)	1.527 Mg/m ³
Absorption Coefficient	1.001 mm ⁻¹
Crystal size	0.44 x 0.17 x 0.06 mm
θ Range for data collection	1.99 - 28.28°
Index ranges	-14 ≤ h ≤ 14, -15 ≤ k ≤ 15, -25 ≤ l ≤ 25
Reflections collected	23880
Independent reflections	6273 [R _{int} = 0.0485]
Data/restriction/parameters	6273 / 0 / 298
Goodness-of-fit on F ²	0.879
Final R Indices [I > 2σ(I)]	R ₁ = 0.0380, wR ₂ = 0.0876
R indices (all data)	R ₁ = 0.0435, wR ₂ = 0.0913

Experimental

[Na₂PdCl₄], PPh₃ and 2-(methylthio)aniline were obtained from Aldrich and were used without further purification.

Synthesis of 2-(methylthio)phenylazide

To a mixture of 2-(methylthio)aniline (1000 mg, 7.183 mmol), in water (1.5 cm³), ethyl acetate (7 cm³) and HCl 37% (1.5 cm³) was added dropwise sodium nitrite (843 mg, 12.211 mmol) in water under vigorous stirring at 0-5 °C. After 30 min aqueous NaN₃ (793 mg, 12.211 mmol) was added dropwise to the reaction mixture at 0-5 °C for 30 minutes. The mixture was extracted with ethyl acetate and washed with water. The organic layer was evaporated and a pale yellow powder was obtained. Yield 1021 mg (86%).

Synthesis of the compound 1

To a solution of 2-(methylthio)phenylazide (163 mg, 0,986 mmol) in diethyl ether (20 cm³) was added tri(*p*-tolyl)phosphine (300 mg, 0,986 mmol) and stirred at room temperature for two hours. The solvent of the resulting solution was evaporated to dryness giving a yellow powder. Yield 398 mg (91.5%). Anal. Calc. for C₂₈H₂₈NPS: C, 76.16; H, 6.39; N, 3.17. Found: C, 76.18; H, 6.42; N, 3.17. ¹H NMR (CDCl₃): σ = 2.36 (s, 9H), 2.40 (s, 3H), 6.39 (m, 1H), 6.67 (m, 2H), 6.97 (m, 1H) 7.21 (m, 6H), 7.68 (m, 6H) ³¹P{¹H} NMR (CDCl₃): σ = 0.06 s.

Synthesis of the compound 2

To a mixture of [Na₂PdCl₄] (75 mg, 0,255 mmol), NaOAc (19 mg, 0,255 mmol,) and compound **1** (110 mg, 0,255 mmol) was added methanol (10cm³) and heated to 80 °C for 18 hours. The resulting solution was evaporated, the solid obtained was dissolved in dichloromethane and filtered through silica, after which the solvent was removed under vacuum and a yellow bright powder was obtained. Yield 117 mg (78,9%). Anal. Calc. for C₂₈H₂₇ClNPPdS: C, 57.74; H, 4.67; N, 2.40. Found: C, 57.70; H, 4.71; N, 2.36. ¹H NMR (CDCl₃): σ = 2.28 (s, 3H), 2.39 (s, 6H), 2.74 (s, 3H), 6.60 (d, 1H), 6.69 (m, 2H), 6.82 (m, 2H), 7.29 (m, 5H), 7.70 (m, 4H), 7.95 (m, 1H), ³¹P{¹H} NMR (CDCl₃): σ = 45.37 s.

Synthesis of the compound 3

To a mixture of triphenylphosphine (22,5 mg, 0,086 mmol), compound **2** (50 mg, 0,086 mmol) and ammonium hexafluorophosphate (14 mg, 0,086 mmol) were added acetone (10 cm³) and stirred for 18. The resulting white solid (NH₄Cl) was separated by centrifugation and the solution was evaporated to give a yellow powder. Yield 61mg (71%). Anal. Calc. for C₄₆H₄₂F₆NP₃PdS: C, 68.27; H, 5.23; N, 1.73. Found: C, 68.28; H, 5.27; N, 1.71. ¹H NMR (CDCl₃): σ = 1.65 (s, 3H), 1.83 (s, 3H), 2.45 (s, 6H), 6.51 (m, 1H), 6.68 (d, 1H), 6.78 (m, 3H), 6.69 (m, 1H), 7.18 (t, 1H), 7.40 (m, 4H), 7.49 (m, 6H), 7.56 (m, 3H), 7.67 (m, 10H), ³¹P{¹H} NMR (CDCl₃): σ = 36.82 (s), 42.51 (s)

Acknowledgments

We wish to thank the financial support received from the Xunta de Galicia (Galicia, Spain) under the Grupos de Referencia Competitiva Programme Projects GRC2015/009. F. Lucio-Martínez and F. Reigosa thank the Spanish Ministry of Education (grant FPU13/05014 and FPU15/07145)

References

- [1] H Staudinger, J Meyer, *Helv. Chim. Acta* **2** (1): 635
- [2] A.V. Kirsanov, *Izv. Akad. Nauk. SSSR, Ser. Khim.* (1950) 426-437
- [3] F. Palacios, C. Alonso, D. Aparicio, G. Rubiales, J.M. de los Santos, *Tetrahedron* **63** (2006) 523-575;
- [4] Pingrong Wei, Katie T. K. Chan and Douglas W. Stephan *Dalton Trans.* 2003, 3804–3810
- [5] M. Fukui, K. Itoh, Y. Ishii, *Bull. Chem. Soc. Jpn.* **48** (1975) 2044- 2046
- [6] N. Lease, V. Vasilevski, M. Carreira, A. de Almeida, M. Sanaú, P. Hirva, A. Casini and M. Contel, *J. Med. Chem.*, 2013, **56**, 5806
- [7] N. Shaik, A. Martinez, I. Augustin, H. Giovinazzo, A. Varela, R. Aguilera, M. Sanaú, M. Contel, *Inorg. Chem.* **48** (2009) 1577–1587
- [8] D. L. Ma, H. Z. He, K. H. Leung, D. S. H. Chan and C.H. Leung, *Angew. Chem., Int. Ed.*, 2013, **52**, 2.
- [9] S. Ramírez-Rave, F. Estudiante-Negrete, R. A. Toscano, S. Hernández-Ortega, D. Morales-Morales, J.-M. Grévy, *J. Organomet. Chem.* 2014, **749**, 287-295.