Inorganica Chimica Acta 464 (2017) 55–58

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Research paper

Hydrogenation of heteroaromatic nitriles and aromatic dinitriles by heterogeneous or homogeneous ruthenium catalysts derived from $[Ru_3(CO)_{12}]$

Juventino J. García *, Nora Pérez-Lezama, Alma Arévalo

Facultad de Química, Universidad Nacional Autónoma de México, México D. F. 04510, Mexico

ARTICLE INFO

Article history:
Received 22 April 2017
Accepted 25 April 2017
Available online 27 April 2017

Keywords:
Nitriles
Pyridines
Hydrogenation
Ruthenium
Catalysis
Heterocycles

ABSTRACT

The use of the complex $[Ru_3(CO)_{12}]$ (**1**) as a catalyst precursor (0.1 mol%) at 200 °C, 60 psi of H_2, along with triphenylphosphine (TPP) generated ruthenium nanoparticles (Ru-Nps); this occurred in the presence of pyridine-nitriles leading to a variety of hydrogenation (secondary amine, imine, or imidazole) products, depending of the pyridine-nitrile used, under similar reaction conditions. This relates to relatively good to modest yields, determined by the substituents in the corresponding pyridine. In sharp contrast, the use of aromatic dinitriles did not generate Ru-Nps at 140 °C, 150 psi of H_2 and TPP, but allowed the homogeneous catalytic hydrogenation of the 1,4- and 1,3-dicyanobenzenes, to yield the corresponding CN-substituted secondary amine or imine. The main products were characterized by different analytical methods and spectroscopic techniques.

1. Introduction

The use of hydrogen in chemical transformations is generically known as hydrogenation. In the case of nitriles as substrates, hydrogenation yields different products in consecutive and parallel reactions (primary, secondary, and tertiary amines and corresponding imines), which are useful in a variety of important applications in industry and academia [1]. Since many amines are important building blocks of more complex molecules, efficient, selective and versatile hydrogenation for nitriles are important for their preparation, preferentially by catalytic methods [2]. Therefore, using homogeneous or heterogeneous catalysis faces pros and cons; catalytic methods are by far the better option for environmental reasons.

Many homogeneous catalysts based in transition metals have been used for nitrile hydrogenation; in fact, the area has been recently reviewed [3]. However, compared to other functional groups such as C═C, C═O, C═N, the group C≡N has been somewhat less explored. Some relevant examples of the most used metals are ruthenium [4], cobalt [5], and nickel [6]. Many of the above systems cited for ruthenium involve the preparation of multi-dentate ancillary ligands, such as pincers and tridentate ligands, as well as more elaborate ligands to improve selectivity [7]. The production of primary amines usually involves the production of secondary amines and imines for the production of tertiary amines.

The hydrogenation of dinitriles has also been studied, dating back to the 1960s by Freidlin and Sladkova [8], using heterogeneous catalysts of Ni and Co-Raney, with low to moderate yields from diamine derived from the 1,4- and 1,3-dicyanobenzene, but no reactivity found for the 1,2-dicyanobenzene, using high pressure for H_2 (1200–1700 psi) at 100 °C. A later variation of this procedure using Ni-Raney to yield *p*-cyano-benzylamine from 1,4-dicyanobenzene was patented [9], followed by a related patent in the field for the hydrogenation of 1,3-dicyanobenzene to yield o-xylendiamine in high yield, using a Pd-Ru catalyst supported in Al_2O_3 [10]. Other selected examples of heterogeneous hydrogenation of dinitriles include the Rh/Al_2O_3 catalyst by Ishizaka and co-workers [11] and a recent example using a stable cobalt catalyst on inorganic supports [12]. There are very few reports dealing with the homogeneous hydrogenation of dinitriles, except for recent reports including the use of iron-pincer compounds by Beller et al. The scope included aliphatic and aromatic dinitriles [13], plus studies in which Hou and coworkers catalyzed the Rh asymmetric hydrogenation of dicyanoalkenes [14].

Our group has been interested in the hydrogenation of organonitriles and dinitriles, including the use of homogeneous nickel catalysts [6b], and heterogeneous systems based on ruthenium nanoparticles [15]. In this vein, we report our findings using $[Ru_3(CO)_{12}]$ (**1**) as a catalyst precursor with triphenylphosphine (TPP) to

* Corresponding author.
E-mail address: juvent@unam.mx (J.J. García).

http://dx.doi.org/10.1016/j.ica.2017.04.051
0020-1693/

generate ruthenium nanoparticles (Ru-Nps) in the presence of pyridine-nitriles, leading to the production of corresponding hydrogenation products: the expected secondary amine, imine, or imidazole. In contrast, the same catalytic precursors in the presence of 1,4- and 1,3-dicyano-benzenes produced the corresponding CN-substituted secondary amine or imine by a homogeneous pathway.

2. Results and discussion

Optimized reaction conditions used **1** as the catalytic precursor, and 4-cyanopyridine, as in Scheme 1, with a variety of temperatures, H_2 pressures, and reaction time using as reference the ones previously reported by our group in closely related catalytic systems [15], but also considering avoid high reaction temperatures.

The catalytic hydrogenation of 4-cyanopyridine by Ru-Nps generated in situ from $[Ru_3(CO)_{12}]$/TPP gave excellent results (94%) towards the formation of the secondary amine bis(pyridin-4-ylmethyl)amine (**BPA**), with a small amount of corresponding imine (1-(pyridin-4-yl)-*N*-(pyridin-4-ylmethylene)methanamine) (**PPA**). The use of a mercury drop test inhibited the reaction, as expected for nanoparticles being formed; thus, the presence of Ru-Nps (4.64 avg.) was confirmed by transmission electron microscopy (TEM), Fig. 1.

Considering the reactivity that was found, we assessed the same reaction using 3-cyanopyridine, with exactly the same reaction conditions as with 4-cyanopyridine, yet the results creating a different product ratio as depicted in Scheme 2.

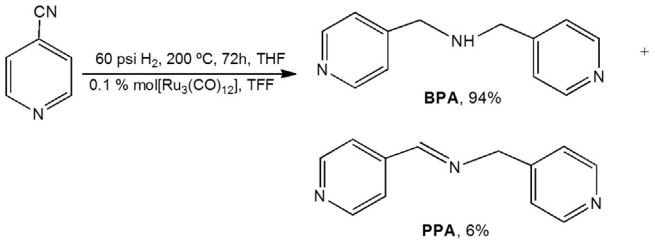
The difference in reactivity found between 4-cyanopyridine and 3-cyanopyridine can be explained in terms of the well-known contrast in reactivity between the 4- and 3-positions in pyridines [16], such that position 4- is prone to a nucleophilic substitution compared with position 3-, consequently achieving a completely reduced product (**BPA**). It is worthy to mention that the reaction was established in both cases under the same reaction conditions, as nanoparticles were being formed in each case and reactivity was being inhibited with a mercury drop test. The corresponding Ru-Nps (4.74 avg.) was isolated and characterized by TEM, with the corresponding micrograph presented in Fig. 2.

Considering these results, we decided to explore the reactivity of the same catalytic system, but using 2-cyanopyridine as a substrate. The reactivity found is illustrated in Scheme 3.

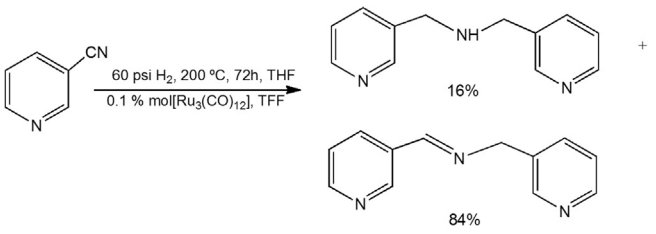
The reaction produced the imidazole 2,2′,2″-(1*H*-imidazole-2,4,5-triyl)tripyridine with a 66% yield, and a total conversion of 78%. This transformation has not yet been reported using a ruthenium catalyst during the nitrile hydrogenation, but has been reported for nickel by our group [17], probably following a closely-related mechanism; this may involve the production of the secondary imine, followed by the insertion of a nitrile and a series of cyclization steps to yield the corresponding imidazole. This reaction was inhibited by a mercury drop test, and Ru-Nps (4.41 avg.) were isolated and characterized (see SI).

Motivated by these results, we assessed the reactivity of 1,4-, 1,3-, and 1,2-aryl-dinitriles with the same catalytic precursor, the dinitriles having lower reaction temperatures, along with shorter possible reaction times as represented in Scheme 4.

The reactivity found for the 1,4- and 1,3-dicyanobenzenes can be explained based on the difference in reactivity between the 4- and 3-positions in benzenes (para and meta, respectively); thus, position 4- is prone to a nucleophilic substitution having an electron-withdrawing substituents compared with position 3-; there-



Scheme 1. Optimized reaction conditions with 4-cyanopyridine.



Scheme 2. Reactivity of RuNps with 3-cyanopyridine.

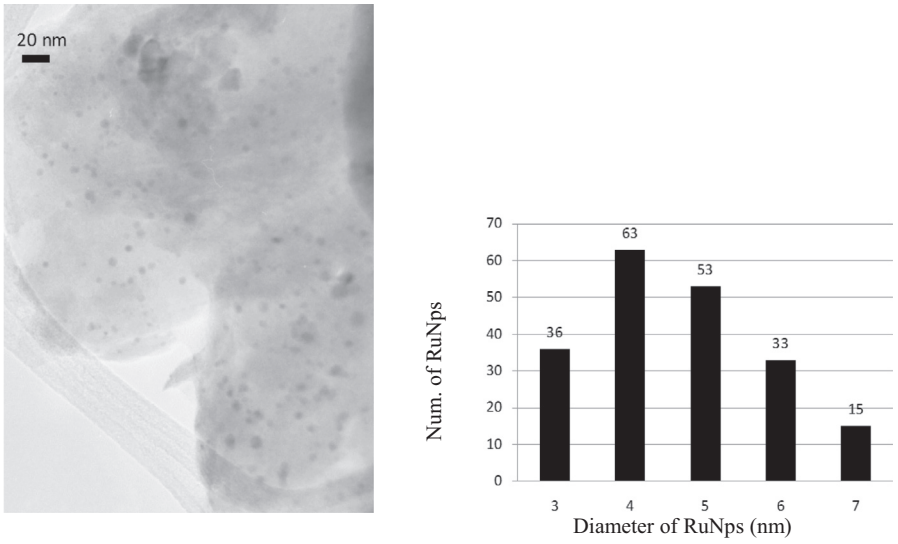


Fig. 1. TEM image of RuNps in the reduction of 4-cyanopyridine.

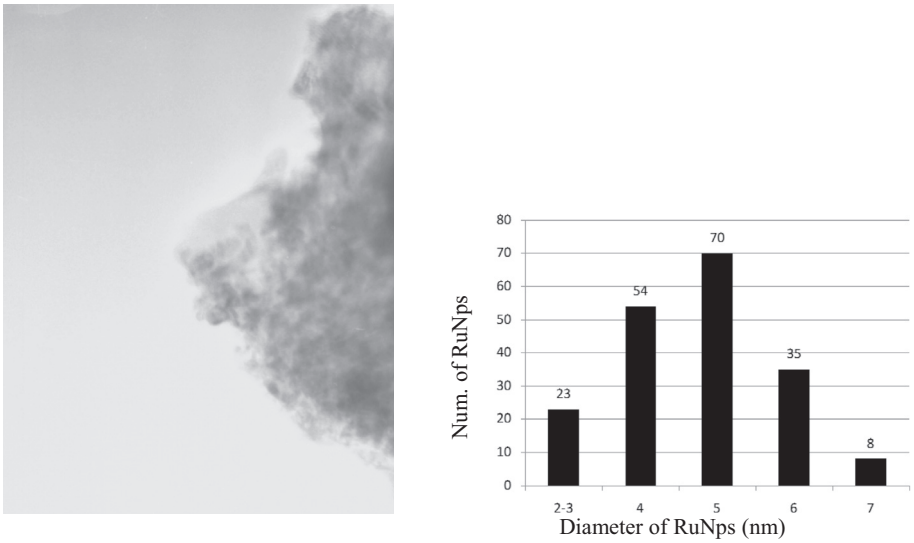
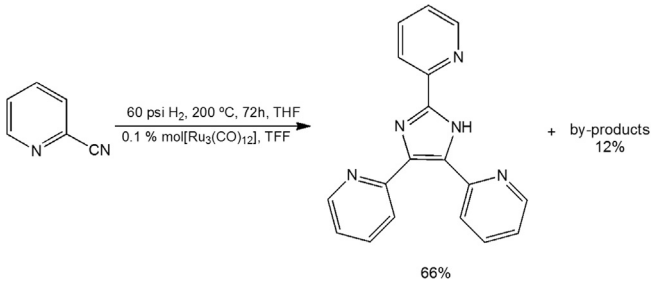
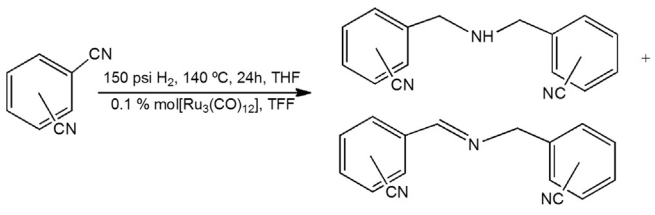


Fig. 2. TEM image of RuNps in the reduction of 3-cyanopyridine.



Scheme 3. Reactivity of RuNps with 3-cyanopyridine.



substrate	% yield amine	imine
1,4-dicyanobenzene	98	2
1,3-dicyanobenzene	71	22
1,2-dicyanobenzene	0	0

Scheme 4. Reactivity of aromatic dinitriles.

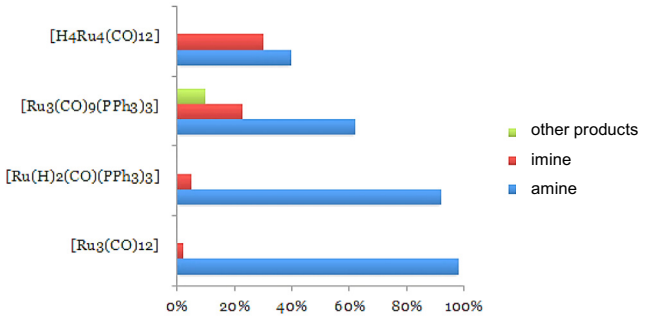


Fig. 3. Use of ruthenium catalytic precursors at 140 °C, 150 psi H_2, and at 24 h.

fore having a better yield towards the hydrogenated product: the secondary amine. In addition, the 1,2-dicyanobenzene did not showed any reactivity at all, as previously observed in our group with nickel catalysts [6b], so we speculate that this substrate may act as a bidentate ligand itself, blocking coordination sites more efficiently than the 1,3- and 1,4-dicyanobenzenes, and consequently inhibiting any further reaction.

Another important aspect of the reactivity in dicyanobenzenes was the assessment for the presence of Ru-Nps; to our surprise, the hydrogenation reaction of 1,4- and 1,3-dicyanobenzenes was not inhibited by a mercury drop test. Despite this, we centrifuged reaction mixtures and studied them with TEM, in which no metallic nanoparticles were found, only crystals from the final Ru-complexes.

Considering this result, and that the hydrogenation of aromatic dinitriles behaves like a homogeneous system, we envisioned several possible catalytic species being formed using **1** as a catalytic precursor, along with TPP and H_2 [18]. Thus, we independently prepared the following compounds by the reported methods and tested them as catalytic precursors: $[Ru_3(CO)_9(PPh_3)_3]$ [19], $[H_4Ru_4(CO)_{12}]$ [20], and $[Ru(H)_2(CO)(PPh_3)_3]$ [21]. The results for the hydrogenation of 1,4-dicyanobenzene are summarized in Fig. 3.

As seen in Fig. 3, the complex $[Ru(H)_2(CO)(PPh_3)_3]$ produced similar reactivity and product distribution, and was likely one of the active catalytic precursors after mixing **1** with TPP and H_2. An experiment using $[Ru(H)_2(CO)(PPh_3)_3]$ and 1,4-dicyano benzene in a 1:1 ratio allowed us to detect two new hydrido-phosphine compounds formed in solution, that may in turn be related to some intermediates during catalysis (see SI, Fig. S8).

3. Conclusions

We demonstrated that catalytic hydrogenation of mono-cyanopyridines can be made with $[Ru_3(CO)_{12}]$ as a precursor of Ru-Nps formed in situ, to produce a particular product that is highly dependent on the substitution in the pyridine ring: a secondary amine was achieved for 4-cyano pyridine, while the secondary imine for 3-cyanopyridine was achieved in both high yields, and a trisubstituted imidazole in the case of 2-cyanopyridine with a good yield. The hydrogenation of 1,4- and 1,3-dicyanobenzenes using **1** was achieved with milder conditions:

temperature and shorter reaction times via a homogeneous catalytic system, leading to the formation of a corresponding secondary amine as a major product.

4. Experimental section

4.1. General considerations

Unless otherwise noted, all manipulations were performed using standard Schlenk techniques in an inert-gas/vacuum double manifold or under an argon atmosphere (Praxair 99.998) in an MBraun UniLab glovebox (<1 ppm H_2O and O_2). All liquid reagents were purchased as reagent grades and degassed before use. All organic nitriles, $[Ru_3(CO)_{12}]$ and TPP were purchased from Sigma-Aldrich and stored in a glovebox before use, while dried with standard techniques. Deuterated solvents were purchased from Cambridge Isotope Laboratories and stored under 4 Å molecular sieves for 24 h before use. NMR spectra were recorded at room temperature on a 300 MHz Varian Unity spectrometer unless otherwise noted. ^1H NMR spectra (δ parts per million) are reported relative to their residual protio-solvent. GC–MS determinations were performed using an Agilent Technologies G3171A equipped with the following column: 5% phenylmethylsilicone, 30 m * 0.25 mm * 0.25 μm. Catalytic experiments were carried out in a 100-mL stainless steel Parr T315SS reactor. Elemental analyses (EAs) were performed by USAII-FQ-UNAM or USAI-UNAM using a PerkinElmer microanalizer 2400. Transmission electron microscopy (TEM) micrographs were determined on a Jeol-2010 microscope equipped with a lanthanum hexaboride filament operating at an accelerating voltage of 200 kV. Samples for TEM observations were prepared by placing a thin film of the heptanes Ru-NPs solution in a holey carbon grid. Metal particle size distribution was estimated at about 200 particles, assuming a spherical shape, and found in an arbitrary chosen area in enlarged micrographs.

4.2. Catalytic experiments

4.2.1. Procedure for the catalytic hydrogenation of cyanopyridines: 4-cyanopyridine

4-cyanopyridine (0.5 g, 4.8 mmol), $[Ru_3(CO)_{12}]$ (**1**) (3 mg, 0.0048 mmol), TPP (4 mg, 0.0144 mmol) and THF (25 mL) were charged in a 100-mL Parr reactor; the reactor was closed and pressurized out of the dry box with H_2 (60 psi). Afterward, the reaction vessel was heated up to 200 °C for 72 h. Following this, the reactor was cooled down to room temperature and vented into a hood; 1 μL of the reaction mixture was directly analyzed by GC–MS. All samples produced at the end of the hydrogenation experiments were centrifuged (10–15 min at 5000 cycles/min) in order to recover the corresponding ruthenium nanoparticles and further analyzed by TEM.

4.2.2. Hydrogenation of 3-cyanopyridine and 2-cyanopyridine

An entirely similar experimental procedure as above was followed, but using substrate 3-cyanopyridine or 2-cyanopyridine.

4.2.3. Mercury drop test

All experiments were performed following the above-described procedure, in addition to use of reagents; that is, two mercury drops were added into the reaction mixture.

4.2.4. Procedure for catalytic hydrogenation of dicyanobenzenes: 1,4-dicyanobenzene

1,4-dicyanopyridine (0.3 g, 2.34 mmol), **1** (1.5 mg, 0.0023 mmol), TPP (1.8 mg, 0.007 mmol) and THF (25 mL) charged in a 100-mL Parr reactor, as it was closed and then pressurized out of the dry box with H_2 (150 psi). Afterward, the reaction vessel was heated to 140 °C for 24 h. Soon after, the reactor was cooled down to room temperature and vented into a hood; 1 μL the reaction mixture was directly analyzed by GC–MS.

4.2.5. Procedure for the catalytic hydrogenation of 1,3- and 1,2-dicyanobenzenes

Following a similar procedure as described for 1,4-dicyanobenzene, both substrates were used in separate experiments, although the 1,2-dicyanobenzene did not react. Mercury drop experiments were done similarly in the presence of two mercury drops.

Acknowledgements

We thank CONACYT (178265) and DGAPA-UNAM (IN-202516) for their financial support. N. P-L also thanks CONACYT for a graduate studies grant.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ica.2017.04.051.

References

[1] S.A. Lawrence, Amines: Synthesis Properties and Applications, Cambridge University Press, Cambridge, UK, 2005.
[2] S. Werkmeister, K. Junge, M. Beller, Org. Process Res. Dev. 18 (2014) 289–302.
[3] D.B. Bagal, B.M. Bhanage, Adv. Synth. Catal. 357 (2015) 883–900.
[4] Selected examples are: (a) T. Li, I. Bergner, F. N. Haque, M. Zimmer-De Iuliis, D. Song, R. H. Morris, Organometallics 26 (2007) 5940–5949.;
(b) R. Reguillo, M. Grellier, N. Vautravers, L. Vendier, S. Sabo-Etienne, J. Am. Chem. Soc. 132 (2010) 7854–7855;
(c) A. Mukherjee, D. Srimani, Y. Ben-David, D. Milstein, ChemCatChem. 9 (2017) 559–563;
(d) R. Adam, E. Alberico, W. Baumann, H.-J. Drexler, R. Jackstell, M. Beller, Chem. Eur. J. 22 (2016) 4991–5002;
(e) R. Adam, C.B. Bheeter, R. Jackstell, M. Beller, ChemCatChem. 8 (2016) 1329–1334.
[5] (a) S.W. Heinzman, B. Ganem, J. Am. Chem. Soc. 104 (1982) 6801–6802;
(b) R. Adam, C.B. Bheeter, J.R. Cabrero-Antonino, K. Junge, R. Jackstell, M. Beller, ChemCatChem. 10 (2017) 1–6.
[6] (a) E. Band, W.R. Pretzer, M.G. Thomas, E.L. Muetterties, J. Am. Chem. Soc. 99 (1977) 7380–7381;
(b) P. Zerecero-Silva, I. Jimenez-Solar, M.G. Crestani, A. Arevalo, R. Barrios-Francisco, J.J. Garcia, App. Cat. A. Gen. 363 (2009) 230–234.
[7] Z. Lu, T.R. Williams, Chem. Comm. 50 (2014) 5391–5393.
[8] L.K. Freidlin, T.A. Sladkova, Russ. Chem. Rev. 33 (1964) 319–329.
[9] K. Miura, S. Suyama, H. Kondo, K. Morikawa, Pat JP09040630, Showa Denko K. K., JP (1995).
[10] A. Okamoto, Pat. JP2007269645A, Mitsubishi Gas Chemical Co., JP (2007).
[11] M. Chatterjee, M. Sato, H. Kawanami, T. Yokoyama, T. Suzuki, T. Ishizaka, Adv. Synth. Catal. 352 (2010) 2394–2398.
[12] F. Chen, C. Topft, J. Radnik, C. Kreyenschulte, H. Lund, M. Schneider, A.-E. Surkus, L. He, K. Junge, M. Beller, J. Am. Chem. Soc. 138 (2016) 8781–8788.
[13] C. Bornschein, S. Werkmeister, B. Wendt, H. Jiao, E. Alberico, W. Baumann, H. Junge, K. Junge, M. Beller, Nat Commun. 5 (2014) 1–11.
[14] M. Li, D. Kong, G. Zi, G. Hou, J. Org. Chem. 82 (2017) 680–687.
[15] C. Ortiz-Cervantes, I. Yañez, J.J. García, J. Phys. Org. Chem. 25 (2012) 902–907.
[16] J.A. Joule, K. Mills, Heterocyclic Chemistry, fifth ed., Wiley, 2010, pp. 115–119.
[17] J.J. Garcia, P. Zerecero-Silva, G. Reyes-Rios, M.G. Crestani, A. Arévalo, R. Barrios-Francisco, Chem. Comm. 47 (2011) 10121–10123.
[18] C.J. Sleigh, S.B. Duckett, R.J. Mawby, J.P. Lowe, Chem. Comm. (1999) 1223–1224.
[19] K. Dallmann, R. Buffon, J. Mol. Catal. A: Chem. 172 (2001) 81–87.
[20] S. Aime, R. Gobetto, A. Orlandi, C.J. Groombridge, G.E. Hawkes, M.D. Mantle, K. D. Sales, Organometallics 13 (1994) 2375–2379.
[21] J.J. Levison, S.D. Robinson, J. Chem. Soc. (A) (1970) 2947–2954.