ELSEVIER

Journal of Molecular Catalysis A: Chemical 168 (2001) 75–80

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

www.elsevier.com/locate/molcata

(2-Furyl)phenyl(2-pyridyl)phosphine as a new ligand in the alkoxycarbonylation of terminal alkynes

Alberto Scrivanti, Valentina Beghetto, Eleonora Campagna, Ugo Matteoli*

Dipartimento di Chimica, Università di Venezia, Calle Larga S. Marta 2137, 30123 Venezia, Italy

Received 20 July 2000; accepted 23 October 2000

Abstract

(2-Furyl)phenyl(2-pyridyl)phosphine has been synthesised by reaction of 2-furyllithium with chlorophenyl(2-pyridyl)phosphine. The new ligand in combination with $Pd(OAc)_2$ and methanesulphonic acid provides a catalytic system highly active in the alkoxycarbonylation of terminal alkynes. The catalytic activity of the system depends on both the metal to ligand and metal to acid ratios. The new ligand seems to be more efficient than the widely used (2-pyridyl)diphenylphosphine.

Keywords: Carbonylation; Alkynes; (2-Furyl)phenyl(2-pyridyl)phosphine; Palladium

1. Introduction

The carbonylation of 1-alkynes (Scheme 1) is a very useful reaction which allows to obtain in one step α,β-unsaturated carboxylic acids and their derivatives [1–3] starting from readily available substrates.

At the present time, the most efficient catalytic system is the one generated by mixing together palladium acetate, a tertiary phosphine bearing a 2-pyridyl substituent, typically (2-pyridyl)diphenylphosphine, and a strong organic acid whose conjugate base is weakly co-ordinating (e.g. sulphonic acids) [4].

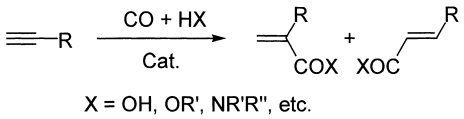
The high activity and selectivity of this system warrants its use not only in the commercial synthesis of important large-scale chemical intermediates such as methacrylates [5] but also in the preparation of fine chemicals [6,7].

Nevertheless, improvements in the original formulation of the catalyst are advisable; as a matter of fact, the use of relatively large amounts of acid cocatalyst can cause side reactions with certain substrates.

Owing to our interest in the use of the carbonylation of terminal alkynes for the synthesis of fine chemicals, we have recently studied the catalytic activity of systems obtained replacing (2-pyridyl)diphenylphosphine with phosphines bearing 2-furyl substituents such as (2-furyl)diphenylphosphine and tri(2-furyl)phosphine (Fig. 1) [8]. Although we found that none of these ligands can compete in activity with (2-pyridyl)diphenylphosphine, we observed that the catalytic efficiency increases in the order triphenylphosphine < (2-furyl)-diphenylphosphine < tri(2-furyl)phosphine. In particular, tri(2-furyl)phosphine furnishes a system at least an order of magnitude more active than the one based on triphenylphosphine. This finding prompted us to

* Corresponding author. Tel.: +39-041-2578572; fax: +39-041-2578517.
E-mail address: matteol@unive.it (U. Matteoli).

1381-1169/01/$ – see front matter
PII: S1381-1169(00)00539-2



Scheme 1.

investigate if a ligand bearing at the same time both a 2-pyridyl and a 2-furyl substituent (**1**, in Fig. 1) could be particularly active.

2. Results and discussion

2.1. Synthesis of the ligand

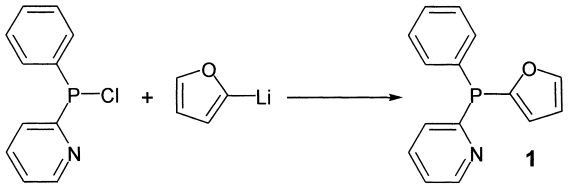
The new ligand (2-furyl)phenyl(2-pyridyl)phosphine (**1**) was obtained in moderately good yield by reacting chlorophenyl(2-pyridyl)phosphine [9] with 2-furyllithium [10] in diethylether as outlined in Scheme 2.

The complete characterisation of **1**, a slightly air sensitive oil, is reported in Section 4.

2.2. Catalytic studies

To investigate the catalytic efficiency of **1**, we choose as model reaction the methoxycarbonylation of phenylacetylene (Scheme 3). The reactions were carried out in a magnetically stirred stainless steel autoclave (see Section 4 for more details).

Some preliminary experiments were carried out using a **1**:Pd ratio of 40 and variable amounts of methanesulphonic acid. The relevant data together with the reaction conditions are reported in Table 1.



Scheme 2.

Table 1
Carbonylation of phenylacetylene (**1**:Pd = 40): influence of the H^+:Pd ratio[a]

CH_3SO_3H:Pd (mol/mol)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
20	25.6	13.0	Traces	100
40	45.8	38.8	0.3	99.2
60	91.5	81.6	0.6	99.2
80	95.7	82.9	0.7	99.1
100	98.0	83.2	0.6	99.2

[a] Reaction conditions — *P*(CO): 40 atm; *T*: 50°C; *t*: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; **1**: 0.26 mmol; $Pd(OAc)_2$: 0.0065 mmol; substrate:Pd = 4000 (mol/mol).

[b] $R = [\mathbf{3}/(\mathbf{3} + \mathbf{4})] \times 100$.

The data reported in Table 1 reveal that the catalytic activity is strongly dependent on the relative amount of acid cocatalyst employed. In particular, very good reaction rates can be achieved working with very high H^+:Pd ratios. Moreover, the regioselectivity towards the branched 2-phenyl substituted acrylic ester is always higher than 99% and seems to be independent on the H^+:Pd ratio.

The chemoselectivity of the reaction is not complete, since analyses of the reaction crudes using an internal standard demonstrate that variable amounts of GC non-detected by-products are formed together with the sought esters. The nature of these species,

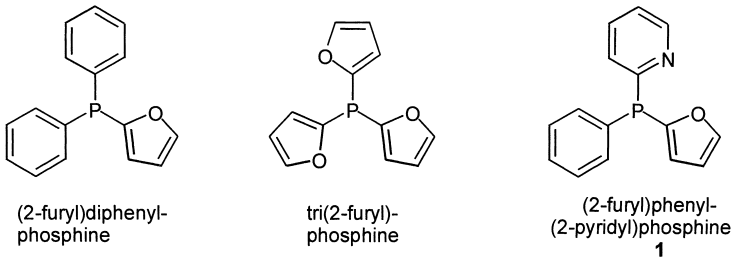
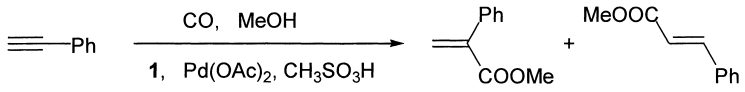


Fig. 1. Schematic structure of the ligands used.



Scheme 3.

Table 2
Carbonylation of phenylacetylene (**1**:Pd = 80)[a]

CH_3SO_3H:Pd (mol/mol)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
80	5.9	4.2	–	100

[a] Reaction conditions — *P*(CO): 40 atm; *T*: 50°C; *t*: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; **1**: 0.52 mmol; $Pd(OAc)_2$: 0.0065 mmol; substrate:Pd = 4000 (mol/mol).
[b] $R = [\mathbf{3}/(\mathbf{3}+\mathbf{4})] \times 100$.

probably oligomers deriving either from the substrate or the acrylic ester, has not been deeper investigated.

These excellent results prompted us to systematically investigate the effects of the reaction parameters and catalyst's composition in order to optimise the catalytic activity.

In an experiment carried out using a very large **1**:Pd ratio (Table 2), we observed a strong decrease in the reaction rate, therefore, we decided to use lower amounts of ligand in further investigations.

Accordingly, the data in Tables 3–5 were obtained using a phosphine to palladium ratio of 20, 10 and 5, respectively.

The experiments allowed to recognise an intricate dependence of the catalytic activity upon both the phosphine to palladium and acid to palladium ratios. A graphical representation of the data (Fig. 2) helps to visualise such intricate behaviour.

Table 3
Carbonylation of phenylacetylene (**1**:Pd = 20): influence of the H^+:Pd ratio[a]

CH_3SO_3H:Pd (mol/mol)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
20	86.2	75.9	0.6	99.2
40	96.5	87.7	0.7	99.2
60	99.6	90.3	0.7	99.2

[a] Reaction conditions — *P*(CO): 40 atm; *T*: 50°C; *t*: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; **1**: 0.13 mmol; $Pd(OAc)_2$: 0.0065 mmol; substrate:Pd = 4000 (mol/mol).
[b] $R = [\mathbf{3}/(\mathbf{3}+\mathbf{4})] \times 100$.

Table 4
Carbonylation of phenylacetylene (**1**:Pd = 10): influence of the H^+:Pd ratio[a]

CH_3SO_3H:Pd (mol/mol)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
0	0	–	–	–
5	81.3	76.6	0.6	99.2
10	99.3	96.9	0.7	99.3
20	100	99.2	0.8	99.2

[a] Reaction conditions — *P*(CO): 40 atm; *T*: 50°C; *t*: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; **1**: 0.065 mmol; $Pd(OAc)_2$: 0.0065 mmol; substrate:Pd = 4000 (mol/mol).
[b] $R = [\mathbf{3}/(\mathbf{3}+\mathbf{4})] \times 100$.

Table 5
Carbonylation of phenylacetylene (**1**:Pd = 5): influence of the H^+:Pd ratio[a]

CH_3SO_3H:Pd (mol/mol)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
5	44.8	35.2	0.3	99.1
10	49.6	43.3	0.3	99.3
15	62.2	50.3	0.4	99.2
20	67.0	63.5	0.5	99.2
30	70.0	65.3	0.5	99.2

[a] Reaction conditions — *P*(CO): 40 atm; *T*: 50°C; *t*: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; **1**: 0.032 mmol; $Pd(OAc)_2$: 0.0065 mmol; substrate:Pd = 4000 (mol/mol).
[b] $R = [\mathbf{3}/(\mathbf{3}+\mathbf{4})] \times 100$.

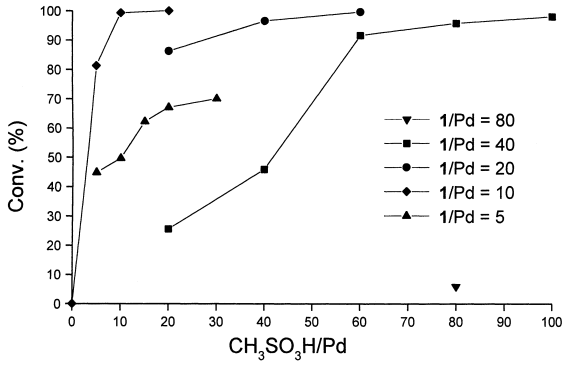


Fig. 2. Influence of the **1**:Pd and H^+:Pd ratios on the catalytic activity.

Table 6
Carbonylation of phenylacetylene: comparison of ligand's efficiency[a]

Run	Ligand	H^+:Pd (mol/mol)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
1	$P(C_6H_5)_2(2\text{-}C_5H_4N)$	20:1	100	98.8	1.2	98.8
2	$P(C_6H_5)(2\text{-}C_5H_4N)(2\text{-}C_4H_3O)$	20:1	100	99.2	0.8	99.2
3	$P(C_6H_5)_2(2\text{-}C_5H_4N)$	5:1	53.5	52.8	0.7	98.7
4	$P(C_6H_5)(2\text{-}C_5H_4N)(2\text{-}C_4H_3O)$	5:1	75.3	74.7	0.6	99.2

[a] Reaction conditions — *P*(CO): 40 atm; *T*: 50°C; *t*: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; ligand: 0.065 mmol; $Pd(OAc)_2$: 0.0065 mmol; substrate:Pd = 4000 (mol/mol).
[b] $R = [\mathbf{3}/(\mathbf{3} + \mathbf{4})] \times 100$.

In particular, it appears that if the **1**:Pd ratio is too high (i.e. **1**:Pd = 80) or too low (i.e. **1**:Pd = 5), whatever the amount of acid used, no acceptable reaction rates can be achieved. On the other hand, if the **1**:Pd ratio is in the 10–40 range, an increase of the **1**:Pd ratio must be accompanied with an increase of the H^+:Pd ratio in order to obtain high catalytic activities. A possible explanation of this behaviour is that the presence of large amounts of non-protonated ligand makes the co-ordination of the substrate to the metal centre more difficult. It is worth noting that the regioselectivity of the reaction is always very high (ca. 99.2%) and does not depend on the **1**:H^+:Pd ratio.

Summing up, it appears that the best results are obtained with a **1**:Pd ratio of 10 and a H^+:Pd ratio in the range 10–20; under these conditions also the polymer formation is minimised.

In order to compare the catalytic activity of the new ligand with that of the usually employed (2-pyridyl)diphenylphosphine, we have carried out two sets of experiments at different H^+:Pd ratios keeping constant the **1**:Pd ratio. The relevant results are reported in Table 6.

The experiments carried out using the higher acid to palladium ratio (runs 1 and 2) do not enable to perceive differences in reactivity, since both ligands allow total conversion of the substrate in ca. 1 h.

On lowering the amount of the acid, the catalytic activity of both systems decreases disclosing an higher efficiency of **1**. In our opinion, this finding is very interesting in particular as far as the carbonylation of substrates bearing acid sensitive moieties is concerned.

Another feature which deserves some comments is the regioselectivity of the reaction which in the presence of **1** is higher than using (2-pyridyl)diphenylphosphine. Since the new ligand is less sterically demanding than (2-pyridyl)diphenylphosphine, the enhancement of regioselectivity should be attributed to electronic rather than steric effects. To study the influence of the *P*(CO), we have carried out a set of experiments using a **1**:H^+:Pd ratio = 10:5:1. The relevant data are presented in Table 7.

Table 7
Carbonylation of phenylacetylene: influence of the *P*(CO)[a]

P(CO) (atm)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
10	91.6	90.3	0.7	99.2
20	99.2	97.9	0.7	99.3
30	98.3	96.3	0.6	99.4
40	81.3	76.6	0.6	99.2

[a] Reaction conditions — *T*: 50°C; *t*: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; **1**: 0.065 mmol; $Pd(OAc)_2$: 0.0065 mmol; CH_3SO_3H: 0.032 mmol; substrate:Pd = 4000 (mol/mol).
[b] $R = [\mathbf{3}/(\mathbf{3} + \mathbf{4})] \times 100$.

The results indicate that the reaction rate increases on increasing the CO pressure until a maximum rate is attained at 20 atm; a further increase of the CO pressure leads to a decrease of the catalytic activity. A similar trend is observed using a **1**:H^+:Pd ratio of 10:20:1. In fact, also in this case, best conversions are obtained operating at 20 atm of CO. This behaviour has previously been observed [8,11] and may be accounted for by admitting that at low CO pressure, the CO insertion is probably the slowest step in the reaction, while at CO pressures over 20 atm, there is competition with the substrate for the co-ordination to the metal centre.

Catalytic data obtained at different reaction temperatures are reported in Table 8. As the temperature is increased from 30 to 80°C, a strong enhancement in the reaction rate is observed, however, the chemoselectivity and, to a minor extent, the regioselectivity decrease.

Finally, we have evaluated the influence of the nature of the reaction medium (Table 9) using some

Table 8
Carbonylation of phenylacetylene: influence of the temperature[a]

T (°C)	Conversion (%)	**3** (%)	**4** (%)	R^b (%)
30	24.8	21.9	0.2	99.1
50	81.3	76.6	0.6	99.2
80	100	90.1	1.2	98.7

[a] Reaction conditions — P(CO): 40 atm; t: 1 h; CH_3OH: 15 ml; phenylacetylene: 26.0 mmol; **1**: 0.065 mmol; $Pd(OAc)_2$: 0.0065 mmol; CH_3SO_3H: 0.032 mmol; substrate:Pd = 4000 (mol/mol).

[b] $R = [\mathbf{3}/(\mathbf{3}+\mathbf{4})] \times 100$.

solvents commonly employed in these reactions. The best reaction rates are obtained using dichloromethane, a non-co-ordinating solvent of medium polarity. Much less effective is a solvent of low polarity such as toluene. On the other hand, also polar solvents such as THF and *N*-methylpyrrolidinone afford low reaction rates; in particular, in the latter solvent, the catalysis is almost completely depressed. This result is probably to be attributed to its behaviour as a Lewis base [12] which outweighs the action of the acid cocatalyst.

Anyway, it is to point out that the nature of the solvent does not seem to influence the regioselectivity of the reaction which is always over 99%.

3. Experimental

3.1. Materials and instruments

All the operations were carried out under argon in Schlenk-type glassware. Commercial solvents (C. Erba) were purified following methods described in [13]. Chlorophenyl(2-pyridyl)phosphine was synthesised according to literature method [9]. Furan (Aldrich) was distilled from sodium. Phenylacetylene (Aldrich) was distilled prior to use; methanesulphonic acid (Aldrich) and $Pd(OAc)_2$ (Engelhard) were used as received. High purity CO was purchased by SIAD. The carbonylation experiments were carried out in a magnetically stirred stainless steel autoclave (total volume ca. 150 ml). Conversion and yield of the carbonylation reactions were determined by GLC on a Hewlett-Packard 5830 II series gas chromatograph, using cumene as internal standard. GLC–MS analyses were carried out on an HP 5830 II series gas chromatograph interfaced to a Hewlett-Packard 5971 mass detector.

^{1}H-, ^{13}C- and ^{31}P-NMR spectra were recorded in $CDCl_3$ on a Bruker AC 200 NMR spectrometer operating at 200, 50 and 81 MHz, respectively.

Table 9
Carbonylation of phenylacetylene: influence of the solvent[a]

Solvent	Conversion (%)	**3** (%)	**4** (%)	Polymeric species (%)	R^b (%)
CH_3OH	81.3	76.6	0.6	4.1	99.2
CH_2Cl_2	87.3	84.7	0.8	1.8	99.1
Toluene	18.5	12.5	0.1	5.9	99.2
NMP	5.3	3.4	–	1.9	100
THF	33.9	28.7	0.2	5.0	99.3

[a] Reaction conditions — P(CO): 40 atm; T: 50°C; t: 1 h; solvent: 15 ml; phenylacetylene: 26.0 mmol; CH_3OH: 52 mmol; **1**: 0.065 mmol; $Pd(OAc)_2$: 0.0065 mmol; CH_3SO_3H: 0.032 mmol; substrate:Pd = 4000 (mol/mol).

[b] $R = [\mathbf{3}/(\mathbf{3}+\mathbf{4})] \times 100$.

3.2. Synthesis of (2-furyl)phenyl(2-pyridyl)phosphine

A 2.0 M solution of *n*-butyllithium in pentane (67.5 ml, 0.135 mol) is added dropwise to a solution of furan (9.18 g, 0.135 mol) in diethylether (100 ml). The resulting yellow solution is stirred at RT for further 2 h. Then a solution of chlorophenyl(2-pyridyl)phosphine (10 g, 0.045 mol) in diethylether (100 ml) is added dropwise. The mixture is heated to reflux for 4 h. The resulting cream suspension is cooled at RT and treated with 100 ml of 10% aqueous NH_4Cl. The organic layer is separated, dried over $MgSO_4$ and concentrated at reduced pressure. Distillation of the oily residue at 135°C (0.01 Torr) affords 3.9 g (33% yield) of (2-furyl)phenyl(2-pyridyl)phosphine as a pale yellow oil.

Analytical data; calculated C: 71.14%, H: 4.78%; found: C: 71.40%, H: 4.96%.

^{1}H-NMR ($CDCl_3$, δ, ppm): 6.44 (m, 1H, H_4-furyl); 6.83 (m, 1H, H_3-furyl); 7.10–7.22 (m, 2H); 7.28–7.40 (m, 3H); 7.45–7.62 (m, 3H); 7.68 (m, 1H, H_5-furyl); 8.67 (m, 1H, Py).

^{31}P-NMR ($CDCl_3$, ppm): −26.8 (s).

^{13}C-NMR ($CDCl_3$, ppm): 111.4 (1C, d, J_{C-P} = 6 Hz); 122.7 (1C, s); 123.5 (1C, d, J_{C-P} = 27 Hz); 127.9 (1C, d, J_{C-P} = 15 Hz); 129.1 (2C, d, J_{C-P} = 7 Hz); 129.8 (1C, s); 134.6 (2C, d, J_{C-P} = 20 Hz); 135.4 (1C, d, J_{C-P} = 5 Hz); 136.2 (1C, s); 148.3 (1C,

s); 150.7 (1C, d, $J_{C-P} = 13$ Hz); 151.6 (1C, d, $J_{C-P} = 19$ Hz); 163.5 (1C, d, $J_{C-P} = 11$ Hz).

3.3. Carbonylation experiments

To illustrate the carbonylation procedure, the experimental details for run 2 of Table 1 are reported. Under inert atmosphere, a Schlenk flask containing a small magnetic bar is charged with 66 mg (0.26 mmol) of (2-furyl)phenyl(2-pyridyl)phosphine, 1.5 mg (0.0065 mmol) of $Pd(OAc)_2$, 15 ml of CH_3OH, 2.65 g (26.0 mmol) of phenylacetylene, 29 mg (0.26 mmol) of CH_3SO_3H and 240 mg (2.0 mmol) of cumene (GC internal standard). The resulting solution is transferred via cannula into the autoclave, which is then pressurised with CO. The reactor is maintained at the desired temperature ($\pm 1^{\circ}$C) by circulating a thermostatic fluid. At the end of the reaction, the residual gas is vented off and the composition of the raw reaction mixture determined by GLC.

4. Conclusions

The new ligand here reported is able to catalyse the alkoxycarbonylation of alkynes with high efficiency. Owing to the strict structural similarity with (2-pyridyl)diphenylphosphine, this result is not unexpected and brings additional evidence confirming the key role played by the 2-pyridyl moiety [4]. However, it is interesting to observe that the data obtained indicate that in this reaction the formal substitution of a phenyl group with a 2-furyl one causes an enhancement of the catalytic activity as we observed previously [8]. This effect could be attributed to the electron withdrawing character of the 2-furyl group, even if further studies are necessary to confirm this hypothesis.

Finally, we deem particularly interesting that the new phosphine exhibits its maximum efficiency at low **1**:Pd and H^+:Pd ratios since it could allow to employ acid-sensitive substrates.

Acknowledgements

This work was supported by the Italian C.N.R. Progetto Finalizzato “Beni Culturali” and MURST Ministero Università Ricerca Scientifica e Tecnologica.

References

[1] A. Mullen, in: J. Falbe (Ed.), New Syntheses with Carbon Monoxide, Springer, Berlin, 1980, p. 243.
[2] B. El Ali, H. Alper, in: M. Beller, C. Bolm (Eds.), Transition Metals for Organic Synthesis, Vol. 1, Wiley-VCH, Weinheim, 1998, p. 57.
[3] E. Drent, W.W. Jager, J.J. Keijsper, F.G.M. Niele, in: B. Cornils, W.A. Herrmann (Eds.), Applied Homogeneous Catalysis with Organometallic Compounds, Vol. 2, VCH, Weinheim, 1996, p. 1119.
[4] E. Drent, P. Arnoldy, P.H.M. Budzelaar, J. Organomet. Chem. 455 (1993) 247.
[5] M.J. Doyle, J. van Gogh, J. van Ravenswaay Claase, Eur. Patent Appl. EP-A-392,601 (1990), Chem. Abstr. 114 (1991) p. 102997.
[6] A. Scrivanti, U. Matteoli, Tetrahedron Lett. 36 (1995) 9015.
[7] U. Mattedi, C. Botteghi, F. Sbrogiò, V. Beghetto, S. Paganelli, A. Scrivanti, J. Mol. Catal. A 143 (1999) 287.
[8] A. Scrivanti, V. Beghetto, M. Zanato, U. Matteoli, J. Mol. Catal. A 160 (2000) 331.
[9] P.H.M. Budzelaar, J.H.G. Frijns, Organometallics 9 (1990) 1222.
[10] D.W. Allen, B.G. Hutley, T.C. Rich, J. Chem. Soc., Perkin Trans. II (1973) 820.
[11] A. Scrivanti, V. Beghetto, E. Campagna, M. Zanato, U. Matteoli, Organometallics 17 (1998) 630.
[12] R.L. Adelman, J. Org. Chem. 29 (1964) 1837.
[13] W.L.F. Armarego, D.D. Perrin, Purification of Laboratory Chemicals, 4th Edition, Butterworth-Heinemann, Oxford, 1996.