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Journal of Molecular Catalysis A: Chemical 118 (1997) 173–179

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

# Study on the regioselectivity in the rhodium-catalyzed hydroformylation of vinyl-pyridine derivatives

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Received 27 June 1996; revised 24 September 1996; accepted 25 September 1996

**Abstract**

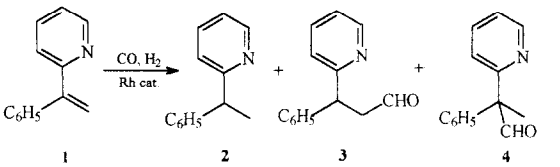
1-alkyl- and 1-arylpyridylethenes were hydroformylated using rhodium catalysts in good yield, the regioselectivity of the CO-insertion being strongly affected by the position of the nitrogen atom of the pyridine moiety. In the case of 1'-alkyl- or 1'-aryl-2-vinylpyridine hydroformylation occurs with the exclusive formation of the more branched aldehyde, whereas in the case of aryl substituted 1'-aryl-4-vinylpyridine only the more linear aldehyde was detected. Attempts to rationalize the results have been made.

*Keywords:* Hydroformylation; Pyridine complexes; Pyridylethenes; Rhodium catalysts

## 1. Introduction

The hydroformylation of vinylpyridines and their 1'-alkyl- or 1'-aryl-substituted derivatives (Fig. 1) is a reaction of great interest because the pyridine aldehydes obtained represent useful precursor compounds for a variety of fine chemicals [1,2].

In a previous paper [3] we reported some results obtained in the rhodium catalyzed *oxo*-reaction of 1-phenyl-1-(2-pyridyl)ethene and its *p*-chloro- and *p*-bromoderivatives: only using rather high substrate-to-catalyst ratio chemoselectivity $> 80\%$ was achieved in the presence of $HRh(CO)(PPh_3)_3$ under standard conditions, in several cases the hydrogenation of the substrate being the most important reaction. Very high regioselectivity towards the formation of the more branched isomer was found:




This rather unusual outcome was associated to the presence of the nitrogen atom in a strategic position with respect to the olefinic double bond. Both kinetic and thermodynamic effects were invoked to clarify the role played by the heteroatom in determining the strong predominance of the aldehyde **4** among the reaction products [3].

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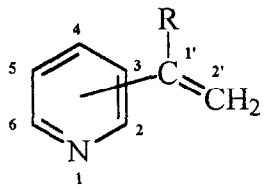
*PII* S1381-1169(96)00398-6




R = alkyl- or aryl-group

Fig. 1. General structure of the vinylpyridine used.

This result was confirmed by other authors [4], which reported that the hydroformylation of 2-vinylpyridine in the presence of $[Rh(CO)_2Cl]_2/PPhMe_2$ afforded 2-(2-pyridyl)propanal in very high yield at 60°C and 120 atm ($CO/H_2 = 1:1$).

The fact that the pyridine nitrogen in 2-vinylpyridine-like substrates is strongly involved in the catalytic cycle of the reaction was unequivocally documented by the results obtained in the hydroformylation of 1,1-diphenylethene and structurally related compounds, in which no heteroatoms are present: in these cases the more linear aldehyde, 3,3-diarylpropanal, was formed with a regioselectivity as high as 99% [5,6].

Now, we wish to present further findings coming from the hydroformylation of: (i) 1-aryl- or 1-alkyl-1-(2-pyridyl)ethenes in the aim to improve the yield of the more useful linear pyridine aldehydes significantly; (ii) 1-phenyl-1-(3-pyridyl)- and 1-phenyl-1-(4-pyridyl)ethene to gain more information on the effect of the pyridine nitrogen atom in promoting the formation of the branched aldehyde.

## 2. Experimental

### 2.1. General methods and chemicals

$HRh(CO)(PPh_3)_3$ was prepared according to a well known procedure [7]. $[RhCl(CO)_2]_2$ and $Rh(PPh_3)_3Cl$ were Strem products.

2-vinylpyridine was purchased by Aldrich Chemical. 1-phenyl-1-(2-pyridyl)ethene (**1**) was prepared (80% overall yield) by Mannich reaction on 2-benzylpyridine with dimethylamine hydrochloride and paraformaldehyde followed by deamination using acetic anhydride and sodium acetate (reflux) [8].

1-methyl-1-(2-pyridyl)ethene (**5b**), 1-phenyl-1-(3-pyridyl)ethene (**9a**) and 1-phenyl-1-(4-pyridyl)ethene (**9b**) were prepared from the corresponding acetylpyridines by addition of the appropriate Grignard reagent followed by dehydration with 85% sulfuric acid [9]. 1-*t*-butyl-1-(2-pyridyl)ethene (**5c**) was obtained from 2-acetylpyridine by reaction of *t*-butyllithium and successive dehydration with excess of thionylchloride [10]. Finally, 1,1-di(2-pyridyl)ethene (**5d**) was prepared by dehydration with $H_2SO_4$ 85% from the corresponding carbinol deriving from the reaction of 2-lithiumpyridine with 2-acetylpyridine [9]. Elemental analyses and $^1H$ NMR spectral data of the afore mentioned olefinic substrates were consistent with the expected structures.

Elemental analyses were performed using an elemental analyzer Perkin Elmer model 240C. $^1H$ NMR (300 MHz) spectra of $CDCl_3$ solutions were recorded using a Varian VXR 300s spectrometer.

### 2.2. General procedure for the hydroformylation experiments

In a typical run a mixture of the olefin (5.5 mmol) and rhodium complex (0.015 mmol) in benzene (20 mL) was introduced in a 0.15 L stainless steel reaction vessel and pressurized to the desired atmosphere with synthesis gas ($CO/H_2 = 1:1$). After 24 h at 80°C the reaction was completed. From the reaction mixture the aldehydes were obtained as yellow oils by distillation under reduced pressure followed by purification using flash chromatography (eluant 9:1 hexane/diethyl ether) and identified by $^1H$ NMR spectra.

**4**: $^1H$ NMR ($CDCl_3$) $\delta$ 10.12 (s, 1H), 8.60–8.54 (complex multiplets, 1H), 7.75–7.59 (td,

1H), 7.50–7.02 (complex multiplets, 7H), 1.82 (s, 3H).

**8a**: This *oxo*-aldehyde consists in an about 70:30 equilibrium mixture of the enol- and aldehydo-form; $^1$H NMR ($CDCl_3$) $\delta$ 9.82 (d, 1H), 8.65–8.55 (complex multiplets, 1H), 8.32–8.25 (complex multiplets, 1H), 7.75–7.59 (complex multiplets, 2H), 7.30–7.20 (complex multiplets, 1H) 7.05–6.96 (complex multiplets, 4H), 3.75–3.85 (q, 1H), 1.81 (s, 3H), 1.43 (d, 3H).

**8b**: $^1$H NMR ($CDCl_3$) $\delta$ 9.75 (s, 1H), 8.43–8.38 (complex multiplets, 1H), 7.45–7.40 (td, 1H), 7.36–7.05 (complex multiplets, 4H), 1.48 (s, 6H).

**11a**: $^1$H NMR ($CDCl_3$) $\delta$ 9.76 (t, 1H), 8.84–8.78 (dd, 1H), 8.72–8.68 (complex multiplet, 1H) 7.80–7.20 (complex multiplets, 7H), 4.65 (t, 1H), 3.27–3.19 (complex multiplets, 2H).

**12a**: $^1$H NMR ($CDCl_3$) $\delta$ 9.88 (s, 1H), 8.84–8.78 (dd, 1H), 8.72–8.68 (complex multiplet, 1H) 7.80–7.20 (complex multiplets, 7H), 1.82 (s, 3H).

**11b**: $^1$H NMR ($CDCl_3$) $\delta$ 9.76 (t, 1H), 8.62–8.43 (complex multiplets, 2H), 7.38–7.15 (complex multiplets, 7H), 4.62 (t, 1H), 3.22 (dd, 2H).

### *2.3. Preparation of the acyl complex* ***13***

The aldehyde **4** (0.12 mmol) was added, under inert atmosphere to a saturated solution of $RhCl(PPh_3)_3$ (0.12 mmol) in $CH_2Cl_2$ [11]. The mixture was stirred for about 10 minutes at room temperature, than the solid product formed was washed with diethyl ether and dried in vacuo to give the pale-yellow complex **13** in almost quantitative yield.

Elemental analysis for $C_{50}H_{43}ClNOP_2Rh$: C, 68.41; H, 5.06; N, 1.51 (calcd.: C, 68.70; H, 4.96; N, 1.60). IR (KBr) $\nu_{max}$ ($cm^{-1}$): 2014 (w), 1659 (s), 232 (w); $^1$H NMR ($CDCl_3$): $\delta$: 9.0 (d, 1H pyridinic proton), 8.0–6.7 (complex multiplet, pyridinic and aromatics protons), 1.0 (s, 3H, $CH_3$), −12.6 (m, 1H, Rh–H); $^{31}$P NMR ($CDCl_3$): $\delta$ $P_A$ 37.09, $\delta$ $P_B$ 33.53; $J(P_A–P_B)$ 359 Hz, $J(Rh–P_A)$ 127 Hz, $J(Rh–P_B)$ 125 Hz [11].

### *2.4. Reaction between $[Rh(CO)_2Cl]_2$ and olefin* ***5d***

To a solution of $[Rh(CO)_2Cl]_2$ (38.8 mg, 0.1 mmol) in *n*-hexane (8 mL), a solution of **5d** (18.2 mg, 0.1 mmol) in *n*-hexane (1 mL) was added dropwise under argon. After the addition was complete, the solution was stirred at room temperature for 1 h. The yellow solid formed was separated by filtration and dried in vacuo. The IR spectrum (KBr) shows two groups of bands in the range 2087–2065 and 2027–1985 $cm^{-1}$ associated to stretching vibrations of a carbon monoxide ligand coordinated to the rhodium atom; this data strongly suggest the presence of different complexes. The NMR analysis gave more circumstantiated information: the presence in the $^{13}$C NMR ($CDCl_3$) spectrum of a doublet centered at $\delta$ 153.21 ppm ($J = 3.5$ Hz) and a double doublet at $\delta$ 151.52 ppm ($J_1 = 3.8$ Hz; $J_2 = 4.5$ Hz) can be explained by a mixture of two complexes, in which the olefin **5d** behaves as monodentate and chelating ligand, respectively. The slight difference observed for the chemical shift in the $^1$H NMR spectra of the vinylic protons of the olefinic double bond in the pure ligand ($\delta = 6.03$ (s, 2H)) and in the coordinated ligand ($\delta = 6.23$ (s, 2H)) indicates no coordination of the olefinic double bond to the metal center.

## 3. Results and discussion

Hydroformylation experiments on 1-phenyl-1-(2-pyridyl)ethene were carried out using various catalytic systems with substrate-to-rhodium catalyst molar ratio ranging from 80/1 to 500/1 and benzene as the solvent at 80°C and 90–100 atm of $CO/H_2$ (1:1 mixture). In Table 1 new results are collected and compared with others previously reported.

The data collected in Table 1 lead to the following considerations: (i) the marked tendence of the substrate **1** to undergo hydrogenation reaction of the olefinic double bond is in

Table 1
Hydroformylation of 1-phenyl-1-(2-pyridyl)ethenes catalyzed by rhodium complexes

| Entry | Catalytic precursor | Molar ratio S/C | Reaction time (h) | Solvent | Conv. (%) | Hydrogenation yield (%) | Aldehydes yield (%) | *b/n* | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | $HRh(CO)(PPh_3)_3$ | 500/1 | 24 | benzene | 61.7 | 10.8 | 50.9 | 100/0 | [3] |
| 2 | $HRh(CO)(PPh_3)_3$ | 80/1 | 24 | benzene | 95.4 | 10.6 | 84.8 | 95/5 | [3] |
| 3 | $HRh(CO)(PPh_3)_3/PPh_3$ (1:50) | 500/1 | 24 | benzene | 37.3 | 6.7 | 30.6 | 90/10 | [3] |
| 4 | $[Rh(CO)_2Cl]_2$/P–N (1:2) | 500/1 | 24 | benzene | 51.4 | 48.5 | 3.0 | 100/0 | [3] |
| 5 [a] | $HRh(CO)(PPh_3)_3$ | 360/1 | 48 | pyridine | 82.4 | 7.7 | 74.7 | 99/1 | — |
| 6 | $Rh(CO)_2$(acac)/pydiphos oxide (1:2.5) | 360/1 | 69 | benzene | 100 | 39.0 | 60.0 | 100/0 | [6] |
| 7 | $Rh(CO)_2$(acac)/pydiphos (1:2.5) | 360/1 | 21 | benzene | 47.0 | 34.0 | 13.0 | 99/1 | [6] |
| 8 | $[Rh(CO)_2Cl]_2/PPhMe_2$ (1:8) | 280/1 | 24 | benzene | 43.1 | 19.9 | 23.2 | 76/24 | [4] |

[a] Substrate = 5.5 mmol; solvent (benzene) = 20 mL; temperature = 80°C; $P(CO) = P(H_2) = 50$ atm. P–N = 1-(2-pyridyl)-1-diphenylphosphinoethane.

most cases confirmed; (ii) the use of excess $PPh_3$ or of a coordinating solvent such as pyridine reduces significantly the amount of the reduction product **2**; (iii) the aldehyde **4** is always the predominant reaction product, in most cases being regiospecifically formed.

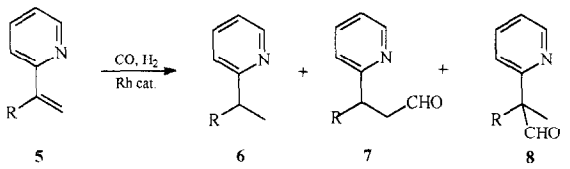
Other substrates structurally related to 1-phenyl-1-(2-pyridyl)ethene such as 2-vinylpyridine, 1-methyl- and 1-*t*-butyl-1-(2-pyridyl)ethene and 1,1-di(2-pyridyl)ethene gave more disappointing results when subjected to *oxo*-reaction under comparable conditions (Table 2). Unsubstituted 2-vinylpyridine gave high yields of *oxo*-products especially using PY-DIPHOS in contrast to the result obtained in the case of olefin **1** under the same conditions (Table 1). Generally the presence of an alkyl- or an arylsubstituent in 1'-position drastically reduces the chemoselectivity because of the concomitant olefinic double bond hydrogenation.

Table 2
Hydroformylation of 1'-substituted-2-vinylpyridine catalyzed by rhodium complexes

| Entry | Substrate | Catalytic Precursor | Molar ratio S/C | Reaction time, h | T, °C | Conv., % | Hydrog. yield, % | Aldehyd. yield, % | b/n | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | $Rh(CO)_2$(acac)/Pydiphos (1:2.5) | 360/1 | 3 | 80 | 97.0 | 1.0 | 96.0 | 100/0 | [6] |
| 2 |  | $[Rh(CO)_2Cl]_2/PPhMc_2$ (1:4) | 180/1 | 7 | 60 | 100 | 6.0 | 90.0 | 99/1 | [4] |
| 3[a] |  | $HRh(CO)(PPh_3)_3$ | 360/1 | 96 | 80 | 100 | 89.3 | 10.7 | 100/0 | --- |
| 4[a] |  | $HRh(CO)(PPh_3)_3$ | 360/1 | 48 | 80 | 81 | 60.0 | 21.0 | 100/0 | --- |
| 5[a] |  | $HRh(CO)(PPh_3)_3$ | 360/1 | 140 | 120 | --- | --- | --- | --- | --- |
| 6[a] |  | $HRh(CO)(PPh_3)_3$ | 360/1 | 48 | 80 | 20[b] | 3.1 | --- | --- | --- |

[a] Substrate = 5.5 mmol; solvent (benzene) 20 mL; $P(CO) = P(H_2) = 50$ atm.
[b] 3% of a dimerization product of **5d** was detected in the reaction solution together with about 13–14% of unidentified high-boiling by-products.

As expected, substrate **5c** bearing the bulky *t*-butyl group in 1'-position undergo neither hydrogenation nor hydroformylation of the olefinic double bond. Moreover, the strongly coordinating olefin **5d** repressed remarkably the catalyst activity, giving only 20% conversion after 48 h reaction but no hydroformylation products (Table 2).




5 6 7 8

**5a, 6a, 7a, 8a**: R = H-; **5b, 6b, 7b, 8b**: R = $CH_3$-; **5c, 6c, 7c, 8c**: R = $(CH_3)_3C$-; **5d, 6d, 7d, 8d**: R = 2-Py-

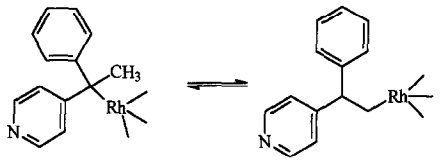
Interesting results from a mechanistic point of view came from the hydroformylation of 1-phenyl-1-(3-pyridyl)ethene (**9a**) and 1-phenyl-1-(4-pyridyl)ethene (**9b**) (Table 3). Both the olefins showed a lower reactivity towards hydroformylation: also for these substrates the reduction of olefinic double bond is an important side reaction. The most striking outcome arising from the *oxo*-reaction on substrates **9a** and **9b** consisted in the fact that in both cases the more linear aldehyde is predominantly produced (Table 3). Furthermore, olefin **9b** afforded regiospecifically 3-phenyl-3-(4-pyridyl)propanal, showing a behaviour quite opposite with respect to that of olefin **1**.

The data coming from the hydroformylation of vinylpyridine derivatives catalyzed by rhodium carbonyl complexes confirmed that the pyridine nitrogen atom plays a crucial role in determining the regioselectivity of the reaction. As a matter of fact, the more branched aldehyde is the strongly predominant *oxo*-product in the hydroformylation of 2-vinylpyridine derivatives independently from the nature of the substituent present in 1'-position. 1-aryl-1-(4-pyridyl)ethene, in which the heteroatom is far from the olefinic double bond, exhibits the same behaviour as

Table 3
Hydroformylation of 1-phenyl-1-(3-pyridyl)ethene and 1-phenyl-1-(4-pyridyl)ethene catalyzed by rhodium complexes [a]

| Entry | Substrate | Catalytic Precursor | Reaction time, h | T, °C | Conv., % | Hydrog. yield, % | Aldehyde yield, % | b/n |
|---|---|---|---|---|---|---|---|---|
| 1 |  | $HRh(CO)(PPh_3)_3$ | 24 | 80 | 11.0 | 3.0 | 8.0 | 33/67 |
| 2 |  | $HRh(CO)(PPh_3)_3$ | 96 | 80 | 41.0 | 5.0 | 36.0 | 32/68 |
| 3 |  | $Rh(CO)_2(acac)$ | 144 | 80 | 92.0 | 51.0 | 38.0 | 25/75 |
| 4 |  | $HRh(CO)(PPh_3)_3$ | 24 | 80 | 50.0 | 42.7 | 7.3 | 0/100 |
| 5 |  | $HRh(CO)(PPh_3)_3$ | 48 | 100 | 100 | 79.6 | 20.4 | 0/100 |
| 6 |  | $[Rh(CO)_2Cl]_2$ | 90 | 100 | 62.3 | 62.0 | -- | -- |
| 7 |  | $[Rh(CO)_2Cl]_2/PPhMe_2$ (1:4) | 90 | 100 | 95.0 | 80.2 | 14.8 | 0/100 |

[a] Substrate = 5.5 mmol; molar ratio substrate/catalyst = 360:1; solvent (benzene) = 20 mL; $P(CO) = P(H_2) = 50$ atm.

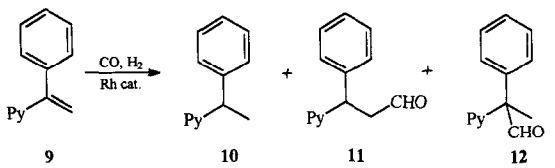


14 15

Fig. 2. Equilibrium between σ-alkylrhodium intermediate complexes.

1,1-diphenylethene as far as the regioselectivity towards the formation of the more linear aldehyde is concerned. This fact is in contrast with the results obtained by Lazzaroni et al. [4] in the hydroformylation of 4-vinylpyridine: in this case the behaviour of this substrate is very close to that of 2-vinylpyridine and the branched isomer is almost regiospecifically formed.

Assuming that the regioselectivity of the reaction reflects the regioselectivity of the formation of the σ-alkylrhodium species, we should expect in the case of 1-phenyl-1-(4-pyridyl)ethene that the intermediate complex **14** is preferentially formed, as in the case of 4-vinylpyridine. The lack of the corresponding branched aldehyde among the *oxo*-products can be explained: (i) the bulky phenyl group forced an anti-Markovnikov addition of the active rhodium hydride complex to the double bond (**14** formation); (ii) species **14** and **15** are in equilibrium and, whereas **14** without the nitrogen atom cooperation does not practically undergo migratory CO insertion (or undergo it only very slowly), complex **15** evolves more easily to aldehyde, giving substantial amount of linear isomer, even if its actual equilibrium concentration is very low (Fig. 2).

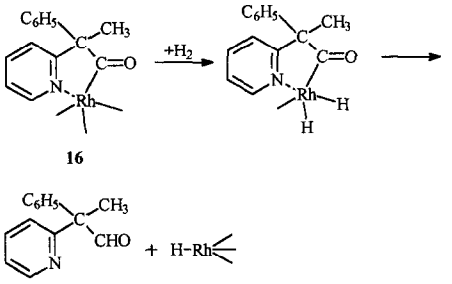


9 10 11 12

**9a, 10a, 11a, 12a**: Py = 3-pyridyl-; **9b, 10b, 11b, 12b**: Py = 4-pyridyl-

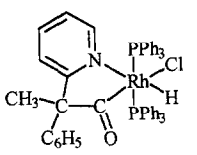
The fact that we found a higher amount of the more branched aldehyde among the reaction products of olefin **9a** with respect to the olefin **9b** (Table 3) may imply a weak coordination of the heteroatom to the metal center of the catalytically active species.

The crucial role played by the pyridine nitrogen atom in shifting the regioselectivity of the *oxo*-process towards the formation of the more branched aldehyde could be also envisaged in terms of relative stability of intermediate complexes involved in the catalytic cycle. For example, the formation of the more branched aldehydes **4** and **8** can be promoted by an increased stability of the σ-acyl complex **16** due to the intramolecular coordination of pyridine nitrogen atom to the metal through a five-membered ring. This stabilization may remarkably affect the energy activation of the aldehyde formation process by hydrogenolysis of **16**:



16

Species strictly related to **16** are described in the literature as exceptionally stable easily isolable complexes [11]. Thus, the addition of the branched aldehyde **4** to a saturated methylene chloride solution of $Rh(PPh_3)_3Cl$ brought about the rapid and nearly quantitative formation of a pale-yellow complex **13** (Fig. 3), which was isolated and purified. Elemental, IR, $^1H$ and $^{31}P$ NMR analysis data are in keeping with the following octaedrical structure (see Section 2).



13

Fig. 3. Five-membered cyclic σ-alylrhodium complex.

The fact that the rhodium atom exhibits a marked tendency to coordinate the pyridine nitrogen atom was previously documented by us [3]. This is further confirmed by the result obtained in the hydroformylation of olefin **5d**, which presents three coordination sites: the two heteroatoms and the olefinic linkage. The absence of hydroformylation products is very probably to impute to a double coordination of the pyridine nitrogen atoms to the rhodium, competing with the double bond activation pathway. This hypothesis is supported by the easy formation of stable complexes from $[Rh(CO)_2Cl]_2$ and olefin **5d**, for which the analytical data $^{1}H-^{13}C$ NMR and IR indicate that the nitrogen atoms rather than the olefinic double bond are coordinated to the metal center [12]. When the attack to the heteroatom, which is the favoured coordination site, is sterically hindered by a bulky substituent in 2-position as in the case of substrate **5c**, no reaction will take place even at 120°C.

## References

[1] C. Botteghi, S. Paganelli, A. Schionato and M. Marchetti, Chirality 3 (1991) 355.
[2] A. Von Kleemann, Chem. Ztg. 101 (1977) 389.
[3] C. Botteghi, S. Paganelli, L. Bigini and M. Marchetti, J. Mol. Catal. 93 (1994) 279.
[4] R. Settambolo, S. Pucci and R. Lazzaroni, J. Organomet. Chem. 489 (1995) C50.
[5] C. Botteghi, L. Cazzolato, M. Marchetti and S. Paganelli, J. Org. Chem. 60 (1995) 6612.
[6] C. Basoli, C. Botteghi, M.A. Cabras, G. Chelucci and M. Marchetti, J. Organomet. Chem. 488 (1995) C20.
[7] N. Ahmad, S.D. Robinson and M.F. Uttley, J. Chem. Soc. Dalton Trans. (1972) 843.
[8] M. Tramontini, Synthesis (1973) 703.
[9] D.W. Adamson and J.W. Billinghurst, J. Chem. Soc. (1950) 1039.
[10] A. Schwartz and P. Madan, J. Org. Chem. 51 (1986) 5463.
[11] J.W. Suggs, J. Am. Chem. Soc. 100 (1976) 640.
[12] A.S. Dias, A.W. Downs and W.R. McWhinnie, J. Chem. Soc. Dalton Trans. (1974) 162.