Available online at www.sciencedirect.com

SCIENCE DIRECT®

Journal of Organometallic Chemistry 679 (2003) 10–13

Journal of Organometallic Chemistry

www.elsevier.com/locate/jorganchem

Solvent-free aldol condensations: synthesis of ferrocenyldienones

Daniel I. Méndez[a], Elena Klimova[b,*], Tatiana Klimova[a], León Fernando[b], Simón O. Hernández[a], Marcos G. Martínez[a]

[a] Universidad Nacional Autónoma de México, Instituto de Química, Cd. Universitaria, Coyoacán, C.P. 04510 Mexico D.F., Mexico
[b] Universidad Nacional Autónoma de México, Facultad de Química, Cd. Universitaria, Coyoacán, C.P. 04510 Mexico D.F., Mexico

Received 17 February 2003; received in revised form 8 May 2003; accepted 8 May 2003

Abstract

The aldol condensation of ferrocenecarbaldehyde and acetylferrocene with aldehydes and ketones proceeded more efficiently and stereoselectively in the absence of a solvent than in solution. In all the cases, *E*-configured enones were obtained, which was confirmed by X-ray crystallographic studies of one of the products.

Keywords: Aldol condensation; Solvent-free conditions; Ferrocenylenones

1. Introduction

The aldol reactions are usually carried out under classical homogeneous conditions in ethanol [1–4]. In most cases, the condensation of ferrocenyl derivatives has been focused on the Claisen–Schmidt reaction of ferrocenecarbaldehyde with aromatic aldehydes or ketones in homogeneous solutions [5]. However, the methods have serious disadvantages, such as low product yields [4–7], and the use of large amounts of solvents [8,9]. In the last years, some aldol reactions were described which made use of microwave radiation, 18-crown-6 as a catalyst, or pulverized KOH or NaOH in the absence of a solvent [10,11].

In the present work, we report the results of a comparison of the condensation of ferrocenecarbaldehyde and acetylferrocene with aromatic aldehydes and ketones (Scheme 1) in EtOH or benzene as solvents and KOH, NaOH, or ^{t}BuOK as the base with the solvent-free condensation using powdered solid KOH as the base and Aliquat 336.

2. Discussion

The reactions of ferrocenecarbaldehyde (**1**) with ketones **2a–e** under homogeneous conditions were carried out at room temperature in ethanol. The aldehyde **1** also reacts rapidly with acetophenone (**2a**) or acetylferrocene (**2d**) in aqueous NaOH at room temperature, the condensation products being obtained in yields 95 and 98%, respectively. With other ketones, the reactions were more slow than with **2a**, **d** and after 24 h the reaction was still incomplete. When the substituent R_2 differed from the CH_3 group, the yield decreased in parallel with an increase in its size.

1-Ferrocenylpropan-1-one (**2e**) and ferrocenecarbaldehyde (**1**) react more slowly than other ketones and after 72 h the reaction was still incomplete (Table 1).

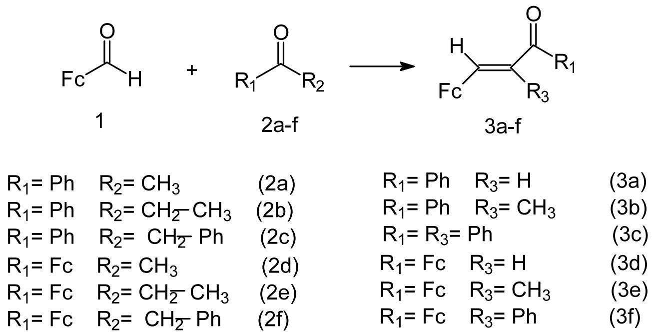
With potassium hydroxide as the base, better yields were obtained, the same effect was observed when potassium *tert*-butoxide in refluxing benzene was used.

Using the method reported by Villemin et al. [9] (with potassium hydroxide, under solvent-free conditions), we obtained good results (60% yields) in all cases. The reaction time was reduced to maximum 1 h, and for the ketone **2c**, the reaction time was only 30 min.

---

* Corresponding author. Tel./fax: +52-55-5622-3722.
E-mail address: klimova@servidor.unam.mx (E. Klimova).

0022-328X/03/$ - see front matter © 2003 Elsevier Science B.V. All rights reserved.
doi:10.1016/S0022-328X(03)00459-5



Scheme 1.

All the ferrocenylenones obtained by this way have the *E*-configuration. This was confirmed by data from ^{1}H- and ^{13}C-NMR and IR spectroscopy and, for compound **3b**, by X-ray diffraction analysis (Fig. 1).

In the condensation of acetylferrocene (**2d**) with acetophenone (**2a**) under homogeneous conditions with potassium or sodium hydroxide in a refluxing solvent benzene, no expected 3-ferrocenyl-3-methyl-1-phenylprop-2-en-1-one (**5**) was obtained. With potassium *tert*-butoxide in refluxing benzene (24 h), we obtained a mixture of enones **4** (22%) and **5** (18%). This same reaction being carried out under solvent-free conditions gives only **4** in 16% (Scheme 2).

In the NMR ^{1}H spectrum of compound **4**, were observed a singlet at δ 2.16 for the CH_3 group, two singlets at δ 4.16 and 4.20 for the the protons of the $2C_5H_5$ groups of the ferrocenyl moiety, four multiplets at δ 4.43, 4.49, 4.61, and 4.82 for the protons of the $2C_5H_4$ group, and a doublet at δ 6.74 ($J = 1.2$ Hz) due to the vinylic proton.

In the NMR ^{1}H spectrum of compound **5**, were observed a doublet at δ 2.57 ($J = 1.5$ Hz) for the CH_3 group, a singlet at δ 4.17 for the C_5H_5 protons of the ferrocenyl moiety, two multiplets at δ 4.44 and 4.63 for the protons of the C_5H_4 group, a doublet at δ 7.11 ($J = 0.9$ Hz) due to the vinylic proton, and a multiplet at δ 7.43–7.96 due to the aromatic ring.

3. Experimental

Table 1
Reaction conditions of aldol condensations of ferrocenecarbaldehyde with ketones

Ketone (**2**)	Reaction conditions	Solvent	% Yield
2b	24 h, r.t.	EtOH–NaOH 40%	30
	24 h, r.t.	EtOH–KOH 40%	32
	24 h, reflux	C_6H_6, *t*-BuOK	25
	1 h, 85–90 °C	Without solvent	63
2c	24 h, r.t.	EtOH–NaOH 40%	10
	24 h, r.t.	EtOH–KOH 40%	13
	24 h, reflux	C_6H_6, *t*-BuOK	42
	1/2 h, 70–75 °C	Without solvent	60
2e	72 h, r.t.	EtOH–NaOH 40%	15
	72 h, r.t.	EtOH–KOH 40%	20
	24 h, reflux	C_6H_6, *t*-BuOK	50
	3/4 h, 75–80 °C	Without solvent	66
2f	24 h, r.t.	EtOH–NaOH 40%	46
	24 h, r.t.	EtOH–KOH 40%	50
	24 h, reflux	C_6H_6, *t*-BuOK	55
	3/4 h, 75–80 °C	Without solvent	61

Infrared spectra were recorded on a Nicolet FT-IR Magna 700 spectrometer. ^{1}H- and ^{13}C-NMR spectra were collected on a Varian Unity 500 instrument operating at 500 and 125 MHz, respectively. For both ^{1}H and ^{13}C, the chemical shifts are expressed in ppm relative to tetramethylsilane (Me_4Si, δ 0.00) used as the internal standard. Elemental analyses were performed at Galbraith Laboratories, Inc., Knoxville. FAB$^+$ mass spectra were taken with a JEOL JMS AX505 HA mass spectrometer. X-ray crystallographic data for compound **2b** were collected at room temperature on a Siemens P/4 diffractometer, the program used for elucidation was SHELXTL version 6.10 Bruker. Axs (2000) and are listed in Table 2.

3.1. Synthesis of enones (general procedures)

A, (homogeneous conditions). Ferrocenecarbaldehyde (**1**, 1 mmol) and a ketone (**2**, 1 mmol) were dissolved in ethanol or benzene, an alkali was added, and the reaction was conducted under conditions specified in the particular experiments (see Table 1).

B, (solvent-free conditions). To a mixture of the aldehyde (**1**, 1 mmol) and a ketone (**2**, 1 mmol), 5 mmol of powdered NaOH is added with stirring and the mixture was stirred for a period of time at a temperature specified in the particular experiments (see Table 1). In all the cases one drop of Aliquat 336 was added and chromatographed on alumina (Brockmann activity III) using hexane as eluent.

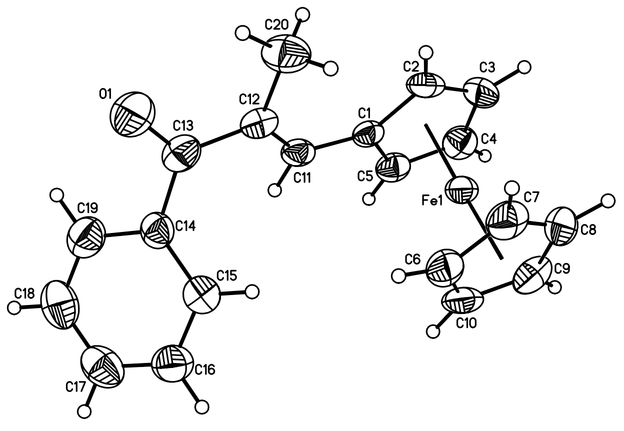
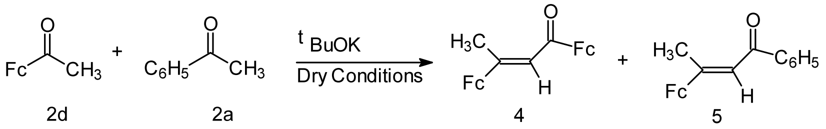


Fig. 1. Crystal structure of compound **3b**. Selected bond lengths: C(1)–C(11) = 1.452(4); C(11)–C(12) = 1.340(3); C(12)–C(13) = 1.475(4); C(13)–C(14) = 1.505(4); C(12)–C(20) = 1.499(3); O(1)–C(13) = 1.230(3).



Scheme 2.

3.2. 3-Ferrocenyl-1-phenylprop-2-enone (*3a*)

Procedure *A*, 2.14 g (10 mmol) of **1** and 1.16 ml (10 mmol) of **2a** in 10 ml of ethanol and 5 ml of 40% NaOH. Yield 96% of **3a**. M.p. 142–144 °C. Red solid, (lit: 55%, m.p. 139–140 °C) [1,3], IR (KBr) cm^{-1}: 1658 (C=O), 1595 (C=C), ^{1}H-NMR ($CDCl_3$), δ: 4.18 (s, 5H, C_5H_5); 4.49 (t, 2H, $J = 1.6$ Hz, C_5H_4); 4.60 (t, 2H, $J = 1.6$ Hz, C_5H_4); 7.09 (d, 1H, $J = 15$ Hz, =CH); 7.72 (d, 1H, $J = 15$ Hz, =CH); 7.49–7.57 (m, 3H, C_6H_5); 7.95–8.00 (m, 2H, C_6H_5); ^{13}C-NMR ($CDCl_3$), δ: 69.93 (C_5H_5); 69.11, 71.51 (C_5H_4); 79.32 (Fc_{ipso}); 119.16 (HC=CH); 146.84 (HC=CH); 128.45, 128.51, 132.35 (C_6H_5); 136.98 ($C_{ipso}C_6H_5$); 190.11 (C=O). MS, *m/z* (I_{rel}. %): 316 (100) $[M]^+$. Anal. Calc. for $C_{19}H_{16}FeO$: C, 72.17; H, 5.10. Found: C, 72.14; H, 5.09%.

Table 2
Crystallographic data and structure refinement parameters for compound **3b**

Data	**3b**
Empirical formula	$C_{20}H_{18}FeO$
Formula weight	330.19
Temperature (K)	291(2)
Wavelength (Å)	0.71073
Crystal system	Orthorhombic
Space group	*Pbca*
Unit cell dimensions	
a (Å)	14.7869(8)
b (Å)	10.5514(6)
c (Å)	20.2294(11)
α (°)	90
β (°)	90
γ (°)	90
V (Å^3)	3156.2(3)
Z	8
D_{calc} (g/cm^3)	1.390
Absorption coefficient (mm^{-1})	0.954
F(000)	1376
Crystal size (mm)	0.35 × 0.20 × 0.04
θ Range for data collection (°)	2.01–25.00
Index ranges	$-17 \leq h \leq 17$, $-12 \leq k \leq 12$, $-24 \leq l \leq 24$
Reflections collected	24 274
Independent reflections	2783 [$R_{int} = 0.0801$]
Completeness to $\theta = 25.00°$	100.0%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2783/0/199
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0396$, $wR_2 = 0.0583$
R indices (all data)	$R_1 = 0.0724$, $wR_2 = 0.0630$
Goodness-of-fit on F^2	0.901
Largest difference peak and hole (e Å^{-3})	0.657 and −0.204

3.3. 3-Ferrocenyl-2-methyl-1-phenylprop-2-enone (*3b*)

Procedure *B*, 2.14 g (10 mmol) of **1**, 1.32 ml (10 mmol) of **2b**, and 2.00 g (50 mmol, 5 equiv.) of powdered NaOH. Yield 63% of **3b**. Red solid, m.p. 84–86 °C. IR (KBr) cm^{-1}: 1606 (C=O), ^{1}H-NMR ($CDCl_3$) δ: 2.15 (s, 3H, CH_3); 4.15 (s, 5H, C_5H_5); 4.42 (t, 2H, $J = 1.8$ Hz, C_5H_4); 4.51 (t, 2H, $J = 1.8$ Hz, C_5H_4); 7.00 (s, 1H, =CH); 7.45–7.64 (m, 5H, C_6H_5); ^{13}C-NMR ($CDCl_3$) δ: 18.01 (CH_3); 69.43 (C_5H_5); 70.75, 70.86 (C_5H_4); 79.08 (Fc_{ipso}); 128.07, 128.07, 131.04 (C_6H_5); 132.89 (=C–CH_3); 139.37 ($C_{ipso}C_6H_5$); 144.22 (=CH); 198.2 (C=O). MS *m/z* (I_{rel}.%): 330 (100) $[M]^+$. Anal. Calc. for $C_{20}H_{18}FeO$: C, 72.74; H, 5.49. Found: C, 72.70; H, 5.39%.

3.4. 3-Ferrocenyl-1,2-diphenylprop-2-enone (*3c*)

2.14 g (10 mmol) of **1**, 1.96 g (10 mmol) of **2c** and 2.00 g (50 mmol, 5 equiv.) of powdered NaOH. Yield 60% of **3c**. Red solid, m.p. 125–127 °C. IR (KBr) cm^{-1}: 1637(C=O), 1593(C=C), ^{1}H-NMR ($CDCl_3$) δ: 3.88 (t, 2H, $J = 1.8$ Hz, C_5H_4); 4.12 (s, 5H, C_5H_5); 4.25 (t, 2H, $J = 1.8$ Hz, C_5H_4) 7.20 (s, 1H, =CH); 7.45–7.79 (m, 10H, C_6H_5); ^{13}C-NMR ($CDCl_3$) δ: 69.62 (C_5H_5); 70.94, 71.06 (C_5H_4); 78.05 (Fc_{ipso}); 127.6, 128.12, 128.52 (C_6H_5); 129.36, 129.79, 131.33 (C_6H_5); 137.12, 137.47 ($2C_{ipso}C_6H_5$); 139.31 (=C–Ph); 143.72 (=CH); 196.5 (C=O). MS *m/z* (I_{rel}.%): 392 (100) $[M]^+$. Anal. Calc. for $C_{25}H_{20}FeO$: C, 76.53; H, 5.10. Found: C, 76.50; H, 5.13%.

3.5. 1,3-Diferrocenylprop-2-enone (*3d*)

2.14 g (10 mmol) of **1**, 2.28 g (10 mmol) of **2d** and 2.00 g (50 mmol, 5 equiv.) of powdered NaOH. Yield 98% of **3d**. Red solid, m.p. 200–202 °C. IR (KBr) cm^{-1}: 1643 (C=O), 1578(C=C), ^{1}H-NMR ($CDCl_3$) δ: 4.17 (s, 5H, C_5H_5); 4.19 (s, 5H, C_5H_5); 4.46 (s, 2H, C_5H_4); 4.55 (s, 2H, C_5H_4); 4.59 (s, 2H, C_5H_4); 4.87 (s, 2H, C_5H_4); 6.71 (d, 1H, $J = 15.3$ Hz, =CH); 7.67 (d, 1H, $J = 15.3$ Hz, =CH); ^{13}C-NMR ($CDCl_3$) δ: 69.71, 70.03 ($2C_5H_5$); 70.15, 70.94, 71.25, 71.66 ($2C_5H_4$); 79.50, 80.75 ($2Fc_{ipso}$); 120.28 (=CH); 142.03 (=C–Fc); 192.00 (C=O). MS *m/z* (I_{rel}.%): 424 (100) $[M]^+$. Anal. Calc. for $C_{23}H_{20}Fe_2$: C, 65.11; H, 4.75. Found: C, 65.10; H, 4.73%.

3.6. 1,3-Diferrocenyl-2-methylprop-2-enone (**3e**)

2.14 g (10 mmol) of **1**, 2.42 g (10 mmol) of **2e** and 2.00 g (50 mmol, 5 equiv.) of powdered NaOH. Yield 66% of **3e**. Red solid, m.p. 114–116 °C. IR (KBr) cm^{-1}: 1616 (C=O), ^{1}H-NMR ($CDCl_3$) δ: 2.12 (d, 3H, $J=1.2$ Hz, CH_3); 4.17 (s, 5H, C_5H_5); 4.21 (s, 5H, C_5H_5); 4.40 (t, 2H, $J=1.8$ Hz, C_5H_4); 4.53 (m, 4H, C_5H_4); 4.85 (t, 2H, $J=1.9$ Hz, C_5H_4); 7.34 (d, 1H, $J=1.7$ Hz, =CH); ^{13}C-NMR ($CDCl_3$) δ: 14.89 (CH_3); 69.34, 70.02 ($2C_5H_5$); 70.17, 70.46, 71.29, 71.60 ($2C_5H_4$); 79.19, 79.81 ($2Fc_{ipso}$); 136.00 (=CH); 134.24 (=C–CH_3); 170.00 (C=O). MS *m*/*z* (I_{rel}.%): 438 (100) $[M]^+$. Anal. Calc. for $C_{24}H_{22}Fe_2O$: C, 76.19; H, 5.82. Found: C, 76.14; H, 5.79%.

3.7. 1,3-Diferrocenyl-2-phenylprop-2-enone (**3f**)

2.14 g (10 mmol) of **1**, 3.04 g (10 mmol) of **2f** and 2.00 g (50 mmol, 5 equiv.) of powdered NaOH. Yield 61% **3f**. Red solid, m.p. 114–116 °C. IR (KBr) cm^{-1}: 1633 (C=O), 1596 (C=C), ^{1}H-NMR ($CDCl_3$) δ: 3.90 (t, 2H, $J=1.8$ Hz, C_5H_4); 4.131 (s, 5H, C_5H_5); 4.138 (s, 5H, C_5H_5); 4.23 (t, 2H, $J=1.8$ Hz, C_5H_4); 4.42 (t, 2H, $J=1.9$ Hz, C_5H_4); 4.56 (t, 2H, $J=1.9$ Hz, C_5H_4); 7.33 (s, 1H, =CH); 7.35–7.49 (m, 5H, C_6H_5); ^{13}C-NMR ($CDCl_3$) δ: 69.55, 70.00 ($2C_5H_5$); 70.49, 70.84, 71.39, 71.93 ($2C_5H_4$); 78.54, 79.44 ($2Fc_{ipso}$); 127.71, 128.55, 129.91 (C_6H_5); 137.68 ($C_{ipso}C_6H_5$); 137.14 (=CH); 138.14 (=C–ph); 196.27(C=O). MS *m*/*z* (I_{rel}.%): 500 (100) $[M]^+$. Anal. Calc. for $C_{29}H_{24}Fe_2O$: C, 69.94; H, 4.78. Found: C, 69.90; H, 4.80%.

3.8. 1,3-Diferrocenyl-3-methylprop-2-enone (**4**)

2.28 g (10 mmol) of **2d**, 1.16 ml (10 mmol) of **2a** and 2.00 g (50 mmol, 5 equiv.) of powdered NaOH. Yield 16% of **6**. Red solid, m.p. 119–121 °C. (Lit: 9%. M.p. 120–122 °C) [9]. IR (KBr) cm^{-1}: 1638 (C=O), 1581 (C=C), ^{1}H-NMR ($CDCl_3$) δ: 2.57 (s, 3H, CH_3); 4.16 (s, 5H, C_5H_5); 4.20 (s, 5H, C_5H_5); 4.43 (t, 2H, $J=1.8$, 2.1 Hz, C_5H_4); 4.49 (t, 2H, $J=1.8$, 2.1 Hz, C_5H_4); 4.61 (t, 2H, $J=1.8$ Hz, C_5H_4); 4.82 (t, 2H, $J=1.8$ Hz, C_5H_4); 6.74(d, 1H, $J=1.2$ Hz, =CH); ^{13}C-NMR ($CDCl_3$) δ: 18.01 (CH_3); 66.97, 69.36, 69.81, 69.72 ($2C_5H_4$); 70.44, 71.96 ($2C_5H_5$); 82.51, 86.18 ($2Fc_{ipso}$); 117.72 (=CH); 153.35 (=C–CH_3); 193.74 (C=O). MS *m*/*z* (I_{rel}.%): 438 (23); 228 (100) $[M]^+$. Anal. Calc. for $C_{24}H_{22}Fe_2O$: C, 65.75; H, 5.02. Found: C, 65.70; H, 5.00%.

3.9. 3-Ferrocenyl-3-methyl-1-phenylprop-2-enone (**5**)

2.28 g (10 mmol) of **2d**, 1.16 ml (10 mmol) of **2a** and 5.61 g (50 mmol, 5 equiv.) of powdered Bu^tOK in anhydrous benzene. Yield 18%. Red solid, m.p. 84–86 °C. IR (KBr) cm^{-1}: 1646 (C=O), 1570 (C=C), ^{1}H-NMR ($CDCl_3$) δ: 2.57 (d, 3H, $J=1.5$ Hz, CH_3); 4.17 (s, 5H, C_5H_5); 4.44 (t, 2H, $J=2.1$ Hz, C_5H_4); 4.63 (t, 2H, $J=2.1$ Hz, C_5H_4); 7.11 (d, 1H, $J=0.9$ Hz, =C–H); 7.43–7.96 (m, 5H, C_6H_5); ^{13}C-NMR ($CDCl_3$) δ: 18.43 (CH_3); 67.24 (C_5H_4); 69.83 (C_5H_5); 70.79 (C_5H_4); 85.79 (Fc_{ipso}); 116.66 (=CH); 127.28, 128.42, 132.00 (C_6H_5); 140.15 ($C_{ipso}C_6H_5$); 157.38 (=C–CH_3); 190.59 (C=O). MS *m*/*z* (I_{rel}.%): 330 (90); 265 (100) $[M]^+$. Anal. Calc. for $C_{20}H_{18}FeO$: C, 72.74; H, 5.49. Found: C, 72.77; H, 5.52%.

4. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 202755 for compound **3b**. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgements

This work was supported by a grant from CONACyT No 34862-E. We want to thank L. Velasco, J. Perez, E.R. Patiño, H. Rios and A. Peña for their technical assistance.

References

[1] K. Schlögl, Monatsh. Chem. 88 (1957) 601.
[2] P. Furdick, P. Elecko, S. Toma, J Suchy, Chem. Zvesti. 15 (1960) 501.
[3] J. Boichard, J.P. Morin, J. Tirouflet, Bull. Soc. Chim. Fr. (1963) 851.
[4] M. Salisova, M. Puciova, V.N. Postnov, S. Toma, Chem. Pap. 44 (1990) 201.
[5] M. Drößmar-Wolf, Gmelin handbook, in: Fe-Org. Comp. Part A, Ferrocene 8, 8th ed., Springer-Verlag, Berlin, Heidelberg, New York, Tokyo, 1986, p. 38.
[6] P. Elecko, Chem. Zvesti. 23 (1969) 198.
[7] F.D. Popp, E.B. Moynahan, J. Heterocycl. Chem. 7 (1970) 351.
[8] J.A. Winstead, J. Org. Chem. 37 (1972) 1271.
[9] D. Villemin, B. Martin, M. Puciova, S. Toma, J. Organomet. Chem. 484 (1994) 27.
[10] W. Liu, Q. Xu, B. Chen, Y. Liang, Y. Ma, W. Liu, J. Organomet. Chem. 484 (2001) 27.
[11] F. Toda, K. Tanaka, K. Hamai, J. Chem. Soc., Perkin Trans. 1 (1990) 3207.