Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Organometallic Chemistry 690 (2005) 430–434
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Efficient synthesis of ferrocenylenones by Friedel–Crafts acylation with $EtAlCl_2$–Me_3Al

Özdemir Dogan [a,*], Volkan Şenol [a], Serhat Zeytinci [a], Hasan Koyuncu [a], Adnan Bulut [b]

[a] Department of Chemistry, Middle East Technical University, ODTU Kimya Bolumu, 06531 Ankara, Turkey
[b] Department of Chemistry, Kırıkkale University, Kırıkkale, Turkey

Received 16 July 2004; accepted 22 September 2004

Abstract

Efficient synthesis of ferrocenylenones using a Friedel–Crafts acylation reaction is described. Acryloyl, methacryloyl, crotonoyl, cinnamoyl, and β-methylcrotonoyl chlorides react with ferrocene in the presence of a Lewis acid ($EtAlCl_2$ or $EtAlCl_2$–Me_3Al) to give the corresponding ferrocenylenones (acryloyl, methacryloyl, crotonoyl, cinnamoyl, and methylcrotonoylferrocenes) in good isolated yields. Besides ferrocenylenones, chloroactylferrocene is also synthesised by this method.

Keywords: Ferrocenylenones; Friedel–Crafts acylation; Ethylaluminum dichloride; Lewis acid

1. Introduction

Ferrocenylenones are important starting materials for the synthesis of substituted ferrocenes [1] and polymers [2]. They found many applications in the literature. They are used as dienophiles in Diels–Alder ractions [3], and as dipolarophiles in 1,3-dipolar cycloaddition reactions [4]. Synthesis of hetero- and carbocyclic-ferrocene derivatives are also based on the use of ferrocenylenones [5]. Syntheses of ferrocenylenones are carried out in diffrent ways. One common method is the Friedel–Crafts acylation reaction. Although this method worked efficiently in the synthesis of crotonoyl-, cinnamoyl-, and β-methylcrotonoylferrocene using $AlCl_3$ as the Lewis acid, the same method failed in the synthesis of acryloyl- and methacryloylferrocene. In the last two cases, Friedel–Craft acylation reaction with $AlCl_3$ resulted in the formation of corresponding ferrocenophan-1-ones [6]. For this reason, alternative methods were used especially in the synthesis of acryloylferrocene. One method is the Mannich reaction of acetylferrocene with formaldehyde and secondary amines [7]. Second method is HCl elimination from 3-chloropropionylferrocene [8]. A third method is elimination of ethyl methyl sulfide from 1-ferrocenyl-3-(ethylsulfanyl)propan-1-one [9]. Another method is the reaction of ferrocenoylsilanes with vinylmagnesium bromide in the presence of $CeCl_3$ [10]. All these methods require two steps and the yields range between 46% and 80% depending on the method.

We developed a one step procedure for the synthesis of acryloyl and methacryloylferrocene. By this method both compounds were obtained in good isolated yields. We also applied this method to the synthesis of crotonoyl-, cinnamoyl-, β-methylcrotonoyl-, and chloroacetylferrocene. These compounds are also synthesised in good yields.

* Corresponding author. Tel.: +903122105134;fax: +90312210-1280.
E-mail address: dogano@metu.edu.tr (Özdemir Dogan).

0022-328X/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2004.09.055

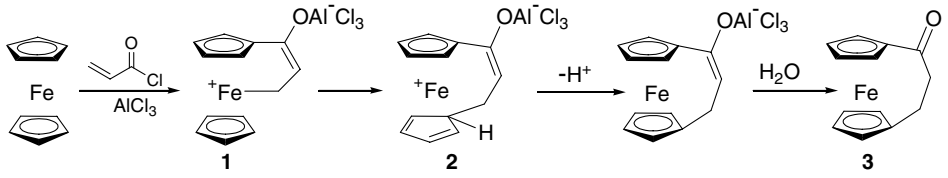
2. Results and discussion

Synthesis of acryloyl and methacryloylferrocene by Friedel–Crafts acylation using $AlCl_3$ as the Lewis acid with ferrocene and acryloyl and methacryloy chloride gave the corresponding ferrocenophan-1-ones (**3**). Watts and Turbitt explained this result by the formation of a metal–alkenyl intermediate (**1**) which was converted to an aluminium enolate (**2**) by methylene group migration from the iron atom to the cyclopentadienyl ring followed by proton loss (Scheme 1) [6a]. They also showed by a control experiment that acryloylferrocene did not undergo cyclization to form ferrocenophan-1-one (**3**) on treatment with $AlCl_3$ or $AlCl_3$–HCl. In the second case, (3-chloropropanoyl)ferrocene (**5**) was obtained as the sole product by HCl addition to carbon–carbon double bond. Ferrocenophan formation did not take place with β-substituted acryloyl chloride derivatives. The β-substituent destabilizes metal–carbon bond of intermediate **1** both electronically and sterically.

We reqiured a larger quantity of acryloyl ferrocene for a different project. For that reason, we wanted to find a direct method for the synthesis of this compound. Considering the enhanced solubility and lower Lewis acidity of alkylaluminum Lewis acids compared to $AlCl_3$, we tried $EtAlCl_2$ first [11]. In the Friedel–Crafts acylation reaction of ferrocene with acryloyl chloride in the presence of $EtAlCl_2$, three products, acryloylferrocene (**4**), ferocenophan-1-one (**3**), and (3-chloropropanoyl)ferrocene (**5**) were isolated in 55%, 15% and 8% yields, respectively (Table 1, entry 1) Scheme 2.

Repeating the same reaction with Me_3Al, acryloylferrocene (**4**) was obtained in 30% yield (Table 1, entry 2). When $EtAlCl_2$ and Me_3Al were used together, the yield of the acryloylferrocene (**4**) was increased to 83%, less than 5% of ferrocenophan-1-one (**3**) was also isolated (Table 1, entry 3). To the best of our knowledge, this is the first example of a one step synthesis of acryloyl ferrocene by a Friedel–Crafts acylation reaction. Obtaining such a good result, we wanted to apply the same procedure to the synthesis of the other ferrocenylenones. When methacryloyl chloride was reacted with ferrocene under the same reaction conditions, methacryloylferrocene (**6**) was isolated in 71% yield (Table 1, entry 4). For this compound **6**, literature has one patent reference for its us in polymers but no information about the synthesis [12]. This work is also the first example of a one step synthesis of methacryloylferrocene (**6**) Scheme 3.

We speculate that in the presence of alkylaluminum Lewis acids ($EtAlCl_2$–Me_3Al), the reaction medium is more basic. Therefore, the formation of metal–alkenyl intermediate (**1**) does not take place. As a result, the reaction does not yield ferrocenophan-1-one (**3**) under these conditions. Also, the α,β-unsaturated acyl chlorides are not strongly activated by these Lewis acids compared to $AlCl_3$. Since the β-position of the acyl unit

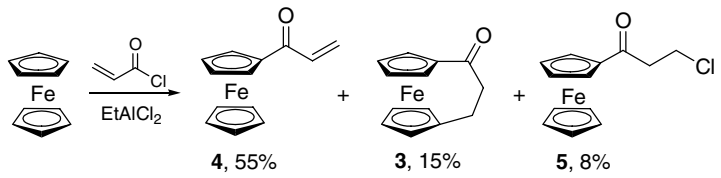


Scheme 1.

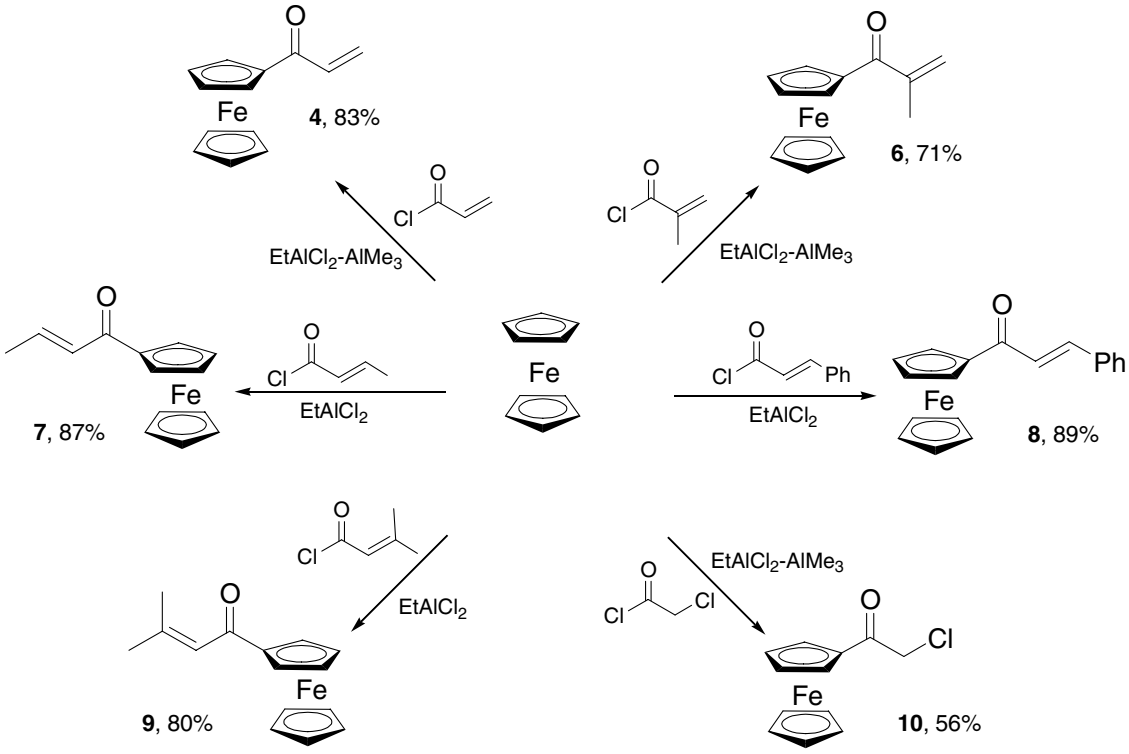
Table 1
Friedel–Crafts reaction of acyl chlorides with ferrocene

Entry	Acyl chloride	Lewis acid	Product	Yield (%)[a]
1	CH_2=CHCOCl	$EtAlCl_2$	**4** + **3** + **5** (6.9/1.9/1.0)	78[b]
2	CH_2=CHCOCl	Me_3 Al	**4**	30[c]
3	CH_2=CHCOCl	$EtAlCl_2$–Me_3Al	**4**	83[c]
4	CH_2=CMeCOCl	$EtAlCl_2$–Me_3Al	**6**	71
5	MeCH=CHCOCl	$EtAlCl_2$	**7**	87
6	PhCH=CHCOCl	$EtAlCl_2$	**8**	89
7	Me_2C=CCOCl	$EtAlCl_2$	**9**	80
8	$ClCH_2COCl$	$EtAlCl_2$–Me_3 Al	**10**	56

[a] Yields are isolated yields. Unreacted ferrocene, 5–10% for the entries 1, 3, 4, 5, 6, and 7 and around 35% for the entries 2 and 8, was recovered.
[b] Extending the time to 6 h did not change the yield and the product ratio significantly, numbers in parenthesis show the approximate ratio of the compounds, respectively.
[c] Minor amounts of **3** and **5** were also seen on the ^1H NMR spectrum of the crude reaction mixture.



Scheme 2.



Scheme 3.

is not active enough, iron in the ferrocenyl group can not attack this position to give intermediate **1**. Another point is the absence of HCl, destroyed by the alkyl group of the Lewis acid, this may also have some effect on preventing ferocenophan-1-one (**3**) formation.

We applied this method to the synthesis of other ferrocenylenones. When crotonoyl chloride was used as the α,β-unsaturated acid chloride, crotonoylferrocene (**7**) was obtained in 87% isolated yield. In the case of cinnamoyl chloride, the same reaction gave the cinnamoylferrocene (**8**) in 89% isolated yield. The commonly used method for the synthesis of this compound is the aldol condensation of acetylferrocene and benzaldehyde [6b,13] In this series, β-methylcrotonoyl chloride was used as the last substrate which resulted in the formation of β-methylcrotonoylferrocene (**9**) in 80% isolated yield. α-Haloacetylferrocenes are also important starting materials especially in the synthesis of ferrocenyl-substituted heterocyclic compounds [14]. In the literature, α-chloroacetylferrocene (**10**) was synthesised by Friedel–Crafts acylation of chloroacetyl chloride and ferrocene with $AlCl_3$ in about 43% yield, together with acetylferrocene [14a]. Lower yield was attributed to an electron transfer from ferrocene to acylium ion to give the oxidised ferrocenium cation in high yield [15]. Our method gave the same compound in a better isolated yield (56%).

In summary, we developed a very efficient method for the synthesis of ferrocenylenones and α-chloroacetylferrocene using alkylaluminum Lewis acids ($EtAlCl_2$–Me_3Al). Although the isolated yield is lower in the case of α-chloroacetylferrocene, the reaction is very clean and a considerable amount of unreacted ferrocene (around 35%) is recovered.

3. Experimental

3.1. Representative experimental procedure

To a stirred solution of ferrocene (186 mg, 1.07 mmol) and α,β-unsaturated acyl chloride/chloroacetyl chloride (1.28 mmol, freshly distilled) in CH_2Cl_2 (3.6 mL, dried over CaH_2) at 0 °C was added Me_3Al (0.27 mL, 0.53 mmol, 2 M in hexanes) and $EtAlCl_2$ (1.07 mL, 1.07 mmol, 1 M in hexanes) drop by drop over 10 min consecutively. The resulting mixture was stirred for another 20 min (in the case of chloroacetyl chloride stirring continued for 80 min) at this temperature. At the end of this time, deep blue colored rection mixture was hydrolized with water (10 mL), and more CH_2Cl_2 (10 mL) was added to the reaction flask. Two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, concentrated, and purified by flash column chromatography on silica gel using (Merck 60 0.040–0.060 nm). ^1H NMR and ^{13}C NMR spectra were obtained in CCl_4–$CDCl_3$ (2:3) solvent system, recorded in a Brucker Spectrospin Avance DPX-400 Ultrashield instrument and reported in ppm on the δ scale relative to residual $CHCl_3$ (δ 7.24 and 77.00). IR spectra were recorded on a Perkin–Elmer 1600 series FT-IR spectrometer and reported in reciprocal centimeters (cm^{-1}). R_f values were determined in a hexanes–EtOAc (5:1) solvent system.

Compound **4** ($R_f = 0.44$). ^1H NMR δ 6.79 (dd, $J = 17.0$ and 10.3 Hz, 1H, CH-α), 6.44 (dd, $J = 17.0$ and 1.6 Hz, 1H, olefinic proton *trans* to CH-α), 5.70 (dd, $J = 10.3$ and 1.6 Hz, 1H, olefinic proton *cis* to CH-α), 4.77 (t, $J = 1.85$ Hz, 2H, ferrocenyl), 4.54 (t, $J = 1.85$ Hz, 2H, ferrocenyl), 4.17 (s, 5H, ferrocenyl); ^{13}C NMR δ 192.9, 133.3, 126.6, 80.1, 73.0 (2 × C), 70.4 (5 × C), 70.1 (2 × C); IR (KBr) 1653.7, 1598.7, 1458.9, 1400.1, 1264.1, 1077.1, 998.9, 820 cm^{-1}.

Compound **6** ($R_f = 0.37$). ^1H NMR δ 5.72 (s, 1H, olefinic proton), 5.52 (s, 1H, olefinic proton), 4.75 (s, 2H, ferrocenyl), 4.42 (s, 2H, ferrocenyl), 4.10 (s, 5H, ferrocenyl), 1.98 (s, 3H, CH_3); ^{13}C NMR 200.6, 145.7, 121.3, 78.5, 72.7 (2 × C), 71.6 (2 × C), 70.5 (5 × C), 20.0; IR (KBr) 1640.1, 1445.5, 1377.9 1224.6, 1066.5, 824.4, 482.1 cm^{-1}; Anal. Calc. for $C_{14}H_{14}FeO$: C, 66.17; H, 5.55. Found: C, 65.95; H, 5.40%.

Compound **7** ($R_f = 0.59$). ^1H NMR δ 7.03 (dq, $J = 15.2$ and 6.94 Hz, 1H, CH-α), 6.52 (dd, $J = 15.2$ and 1.6 Hz, 1H, olefinic proton), 4.79 (t, $J = 1.86$ Hz, 2H, ferrocenyl), 4.50 (t, $J = 1.86$ Hz, 2H, ferrocenyl), 4.17 (s, 5H, ferrocenyl), 1.97 (dd, $J = 6.94$ Hz and 1.6 Hz, 3H, CH_3); ^{13}C NMR δ 192.4, 140.4, 128.1, 80.1, 72.3 (2 × C), 69.9 (5 × C), 69.6 (2 × C), 18.3; IR (KBr) 2359.5, 1661.4, 1609.3, 1458.9, 1294.9, 980.6, 823.5, 668.2 cm^{-1}.

Compound **8** ($R_f = 0.52$). ^1H NMR δ 7.78 (d, $J = 15.6$ Hz, 1H, CH-α), 7.64 (m, 2H, Ph), 7.41 (m, 3H, Ph), 7.11 (d, $J = 15.6$ Hz, 1H, CH-β), 4.90 (t, $J = 1.84$ Hz, 2H, ferrocenyl), 4.57 (t, $J = 1.84$ Hz, 2H, ferrocenyl), 4.20 (s, 5H, ferrocenyl); ^{13}C NMR δ 192.4, 140.9, 135.2, 130.0, 128.9 (2 × C), 128.2 (2 × C), 122.9, 80.7, 72.6 (2 × C), 70.0 (5 × C), 69.7 (2 × C); IR (KBr) 2362.5, 1647.9, 1597.7, 1447.9, 1376.9, 992.2, 757.9, 687.5 cm^{-1}.

Compound **9** ($R_f = 0.40$). ^1H NMR δ 6.34 (s, 1H, olefinic proton), 4.75 (t, $J = 1.86$ Hz, 2H, ferrocenyl), 4.44 (t, $J = 1.86$ Hz, 2H, ferrocenyl), 4.16 (s, 5H, ferrocenyl), 2.21 (s, 3H, CH_3), 1.97 (s, 3H, CH_3); ^{13}C NMR δ 194.6, 153.5, 122.3, 82.0, 72.2 (2 × C), 70.1 (5 × C), 69.8 (2 × C), 28.3, 21.3; IR (KBr) 3085.6, 1647.9, 1602.6, 1456.0, 1375.0, 1263.2, 1109.8, 1053.9, 1000.9, 826.4, 790.7, 506.2 cm^{-1}.

Compound **10** ($R_f = 0.51$). ^1H NMR δ 4.82 (t, $J = 1.84$ Hz, 2H, ferrocenyl), 4.57 (t, $J = 1.84$ Hz, 2H, ferrocenyl), 4.37 (s, 2H, CH_2), 4.23 (s, 5H, ferrocenyl); ^{13}C NMR δ 194.8, 76.0, 72.9 (2 × C), 70.1 (5 × C), 69.7 (2 × C), 45.8; IR (KBr) 2925.5, 1677.8, 1452.1, 1405.9, 1239.1, 1069.3, 822.5, 720.3, 491.8 cm^{-1}.

Acknowledgements

We thank the Middle East Technical University and Kırıkkale University Research Foundations for the financial support.

References

[1] (a) M. Hisatoma, J. Wastanabe, K. Yamakawa, K. Kozawa, T. Uchida, Bull. Chem. Soc. Jpn. 68 (1995) 635;
(b) O. Kocian, R.J. Mortimer, P.D. Beer, J. Chem. Soc. Perkin Trans. 1 (1990) 3203;
(c) S. Kamiyama, A. Kasahara, T. Izumi, I. Shimizu, H. Watabe, Bull. Chem. Soc. Jpn. 54 (1981) 2079.
[2] (a) L. Tataru, I. Mazlu, T. Lxandru, C.R. Smonescu, J. Organomet. Chem. 214 (1981) 107;
(b) D.H. Lewis, B.W. Ponder, J. Polym. 12 (1974) 1313.
[3] (a) M. Prokesova, E. Solcaniova, S. Toma, K.W. Muir, A.A. Torabi, G.R. Konox, J. Org. Chem. 61 (1996) 3392;
(b) S. Toma, P. Elecko, J. Gazova, E. Solcaniova, Coll. Czech. Chem. Commun. 52 (1987) 391.
[4] G.A. Shvekhgeimer, M. Litim, Russ. Chem. Bull. 43 (1994) 136.
[5] T. Klimova, E.I. Klimova, M. Martinez Garcia, J.M. Mendez Stivalet, L. Ruiz Ramirez, J. Organomet. Chem. 633 (2001) 137.
[6] (a) T.D. Türbitt, W.E. Watts, J. Organomet. Chem. 46 (1972) 109;
(b) W. Crawford, T.D. Turbitt, W.E. Watts, J. Organomet. Chem. 105 (1976) 341.
[7] C.R. Hauser, R.L. Pruett, T.A. Mashburn, J. Org. Chem. 26 (1961) 1800.
[8] S. Kaluz, S. Toma, Coll. Czech. Chem. Commun. 51 (1986) 2199.

[9] M.V. Lebedev, V.G. Nenajdedko, E.S. Balenkova, Synthesis (1998) 89.
[10] B.F. Bonini, M. Comes-Franchini, M. Fochi, G. Mazzanti, A. Ricci, A. Alberti, D. Macciantelli, M. Marcaccio, S. Roffia, Eur. J. Org. Chem. (2002) 543.
[11] For the use of $EtAlCl_2$ as the Lewis acid see: B.B. Snider, A.C. Jackson, J. Org. Chem. 47 (1982) 5393.
[12] V.K. Skubin, V.P. Red'ko, D.F. Kutepov, V.V. Korshak, USSR (1974) SU 443876.
[13] (a) S.J. Ji, S.Y. Wang, Z.L. Shen, M.F. Zhou, Chin. Chem. Lett. 14 (2003) 1246;
(b) S.J. Ji, Z.L. Shen, S.Y. Wang, Chin. Chem. Lett. 14 (2003) 663.
[14] (a) J. Fang, Z. Jin, Z.-M. Li, W. Liu, Appl. Organomet. Chem. 17 (2003) 145;
(b) A. Tarraga, P. Molina, D. Curiel, J.L. Lopez, M.D. Velasco, Tetrahedron 55 (1999) 14701;
(c) J. Fang, Z. Jin, Z. Li, W. Liu, J. Organomet. Chem. 674 (2003) 1.
[15] C. Glidewell, S.Z. Ahmed, M. Gottfried, P. Lightfoot, B.J.L. Royles, J.P. Scott, J. Wonnemann, J. Organomet. Chem. 530 (1997) 177.