Rh₂(OAc)₄/CeCl₃-Catalyzed Olefination of Carbonylferrocenes with α-Diazocarbonyl Compounds: A Convenient Synthesis of Alkenylferrocenes

Shufeng Chen, Lele Zhang, Yan Du, Baoguo Li*

College of Chemistry and Chemical Engineering, Inner Mongolia University, Hohhot 010021, P. R. of China Fax +86(471)4992982; E-mail: bauoguol@sohu.com

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Abstract: A concise and efficient protocol for the synthesis of alkenylferrocene derivatives based on the olefination of carbonylferrocenes with α -diazocarbonyl compounds using Rh₂(OAc)₄/CeCl₃ as efficient catalysts was developed. The present method was applicable to many kinds of substituted carbonylferrocenes and α -diazocarbonyl compounds providing good to excellent yields of desired products.

Key words: carbonylferrocenes, diazo compounds, olefination, alkenylferrocene

Ferrocene and its derivatives are a class of important building blocks¹ and widely used in many areas such as asymmetric catalysis,² nonlinear optics,³ material science,⁴ and bioorganometallic chemistry.⁵ Among which, synthesis of alkenylferrocenes has attracted considerable attention due to their increasing applications in the asymmetric catalysis² and diversities of the double bonds in organic transformations.

Over the past decades, there have been some investigations on the development of synthetic methodologies of alkenylferrocene derivatives.6 The most commonly applied synthesis of such compounds is the Wittig reaction of ferrocenecarboxaldehyde with various phosphorous ylides.⁷ However, the Wittig protocol often produces a mixture of E/Z stereoisomers; the separation of which is not always easy. It is noted that unlike the conventional Wittig reaction, the Horner-Wadsworth-Emmons (HWE) reaction unambiguously affords the E-isomers with moderate to good yields.⁸ A different but interesting approach is developed by Blakemore's group, using ethyl (benzothiazol-2-ylsulfonyl)acetate as olefination reagent, which reacts with ferrocenecarboxaldehyde under mild reaction conditions (DBU, CH₂Cl₂, r.t.) to give alkenylferrocene in good yield.9 Another successful method for the synthesis of alkenylferrocenes is the dehydration of the corresponding alcohols with suitable dehydration reagents.¹⁰ The major drawbacks of this method are that they require preliminary preparation of ferrocenyl alcohols using moisture-sensitive lithium aluminum hydride as reduction reagent as well as involving multistep manipulations. Alternatively, transition-metal-catalyzed crosscoupling reactions of iodoferrocene or iodovinylferrocene with electron-deficient alkenes and the organometallic ad-

SYNLETT 2012, 23, 943–947 Advanced online publication: 15.03.2012 DOI: 10.1055/s-0031-1290612; Art ID: W80711ST © Georg Thieme Verlag Stuttgart · New York dition reactions were successfully applied in the synthesis of ferrocenyl-based conjugated compounds.¹¹ However, all these approaches were encountered with high reaction temperatures and the restricted availability of substrates. Considering the limited methods available for their preparation, further development of synthetically useful methodologies for alkenylferrocene derivatives is highly desirable. In this paper, we wish to report an efficient method for the preparation of alkenylferrocene derivatives based on the olefination of carbonylferrocenes with α -diazocarbonyl compounds using Rh₂(OAc)₄/CeCl₃ as efficient catalysts (Scheme 1).¹²



Scheme 1 Synthesis of alkenylferrocene derivative

On the outset of this study, we employed ferrocenecarboxaldehyde (1a) and ethyl diazoacetate (EDA, 2a) as the substrates (Table 1). After the initial experiment using $Rh_2(OAc)_4$ as the catalyst in the presence of Ph_3P in 1,2dichloroethane at room temperature, we obtained the olefination product 3a in 50% yield with an excellent E stereoselectivity (Table 1, entry 1). Furthermore, we were delighted to find that the isolated yield of **3a** enhanced to 64% when the reaction was carried out at 80 °C (Table 1, entry 2). Encouraged by these results, we next carefully examined the effect of various transition-metal catalysts on this olefination reaction. For comparison, we first examined CuI, $Cu(OAc)_2 \cdot H_2O$ and $FeCl_3$ as the catalysts. These transition-metal complexes have been proven to be the efficient catalysts for diazo decomposition reactions. However, in the reaction of ferrocenecarboxaldehyde (1a) with EDA (2a), the expected product 3a was obtained only with trace to moderate yields using these catalysts under the similar conditions (Table 1, entries 3-5). Interestingly, when Rh₂(OAc)₄ and CeCl₃ were used as combination catalysts in this reaction, the olefination product 3a was isolated with higher yield (Table 1, entry 6). Next we also screened the commercial available SmCl₃ as cocatalyst in this reaction; the result showed that only moderate yield of 3a was obtained (Table 1, entry 7). Finally, when we changed the cocatalyst loading of CeCl₃ from 5 mol% to 50 mol% (Table 1, entries 8-10), it was found that us-

Fe	CHO N ₂ catalyst + H CO ₂ Et Ph ₃ P, DCE		e Se	-CO ₂ Et
-	1a 2a		3a	
Entry	Catalyst (mol%)	Temp (°C)	Time (h) ^a	Yield (%) ^b
1	$Rh_2(OAc)_4 (0.5)$	25	48	50
2	Rh ₂ (OAc) ₄ (0.5)	80	24	64
3	CuI (20)	80	24	60
4	$Cu(OAc)_2 \cdot H_2O$ (20)	80	48	trace
5	FeCl ₃ (20)	80	48	38
6	Rh ₂ (OAc) ₄ (0.5), CeCl ₃ (20)	80	24	83
7	Rh ₂ (OAc) ₄ (0.5), SmCl ₃ (20)	80	24	62
8	Rh ₂ (OAc) ₄ (0.5), CeCl ₃ (5)	80	24	74
9	Rh ₂ (OAc) ₄ (0.5), CeCl ₃ (10)	80	24	76
10	Rh ₂ (OAc) ₄ (0.5), CeCl ₃ (50)	80	24	87

Table 1Transition-Metal-Catalyzed Olefination Reaction of Fer-rocenecarboxaldehyde (1a) with Ethyl Diazoacetate $(2a)^a$

^a Reactions were carried out with 0.3 mmol of 1a, 0.45 mmol of 2a, and 0.33 mmol of Ph_3P .

^b Yield of isolated product after chromatography, calculated based on the reacted **1a**.

ing 50 mol% of $CeCl_3$ could give the best result under the same conditions (Table 1, entry 10).

With the optimized reaction conditions in hand, the scope of this transformation was investigated by using a variety of carbonylferrocenes as the substrates (Table 2).¹³ Various substitutions on the cyclopentadiene ring could be tolerated, and the reaction gave moderate to good yields of the products 3a-f with excellent E stereoselectivities. It was found that the yield was decreased along with the influence of steric effect on cyclopentadiene rings of the substrates (Table 2, entries 2-4). Moreover, when 3-ferrocenylpropenal was used as the substrate in this reaction, only 42% yield product 3e was obtained after workup (Table 2, entry 5). However, when 3-chloro-3-ferrocenylpropenal (1f) was employed as the substrate in this reaction, we were delighted to find that the reaction proceeded smoothly under the present conditions providing a higher yield and stereoselectivity of the desired product (Table 2, entry 6).

Next, we examined the scope of diazo compounds, as shown in Table 3. The reaction tolerates a relatively small range of substituents and functional groups on the aryldiazoacetates (Table 3, entries 2–7). It was found that substrates with phenyl ring bearing halogen and nitro group generally gave moderate yields (Table 3, entries 2–5), while substrates with electron-donating substituent on the phenyl ring, such as 3,4-(MeO)₂, only trace of olefination product was detected (Table 3, entry 6). Moreover, it was noted that the ester moiety of the diazo compounds did not affect the reaction (Table 3, entry 7).

R ¹ Fe	$\begin{array}{c} \text{CHO} & \text{N}_2 \\ \text{+} & \text{CO}_2\text{Et} \end{array} \xrightarrow{\begin{array}{c} \text{Rh}_2(\text{OAc})_4, \\ \text{CeCl}_3 \\ \text{Ph}_3\text{P}, \text{DCE} \\ 80 \ ^\circ\text{C} \end{array}} \xrightarrow{\begin{array}{c} \text{R1} \\ \text{Fe} \\ \text{S0} \ ^\circ\text{C} \end{array}}$	CO ₂ Et R ² 3a-f		
Entry	Carbonylferrocene 1	Product 3	Yield (%) ^b	E/Z^{c}
1	СНО Fe Ia	Fe Ja	87	>20:1
2	Fe Et 1b	$ \begin{array}{c} $	48	>20:1
3	Et CHO Fe Et Ic	$Et \xrightarrow{Fe} Et$	33	15:1

Table 2 Rh₂(OAc)₄/CeCl₃-Catalyzed Reaction of Various Carbonylferrocenes with Ethyl Diazoacetate (2a)^a

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 Table 2
 Rh₂(OAc)₄/CeCl₃-Catalyzed Reaction of Various Carbonylferrocenes with Ethyl Diazoacetate (2a)^a (continued)



^a Reactions were carried out with 0.3 mmol of carbonylferrocenes, 0.45 mmol of 2a, and 0.33 mmol of Ph₃P.

^b Yield of isolated product after chromatography, calculated based on the reacted carbonylferrocenes **1a–f**.

^c The ratio of *E*- and *Z*-isomers was estimated by ¹H NMR of the crude product.

Table 3	Rh ₂ (OAc) ₄ /CeCl ₃ -Catalyzed Reaction of Ferrocenecarbox-
aldehyde	(1a) with Various Diazoacetates ^a

Fe	≻—СНО +	$R^2 \xrightarrow{N_2} CO_2 R^1$	Rh ₂ (OAc) ₄ , CeCl ₃ Ph ₃ P, DCE 80 °C	Fe U	→ R ²	-CO ₂ R ¹
	la	2b-h			4a–g	
Entry	2	\mathbb{R}^1	\mathbb{R}^2	4	Yield (%) ^b	E/Z^{c}
1	2b	Ph	Me	4 a	46	>20:1
2	2c	$2-ClC_6H_4$	Me	4b	48	>20:1
3	2d	$4-ClC_6H_4$	Me	4c	53	10:1
4	2e	$4-BrC_6H_4$	Me	4d	38	5:1
5	2f	$4-O_2NC_6H_4$	Me	4e	42	>20:1
6	2g	$3,4-(MeO)_2C_6H$	I ₃ Me	4f	d	_
7	2h	Ph	allyl	4g	48	>20:1

^a Reactions were carried out with 0.3 mmol of 1a, 0.45 mmol of 2b-h, and 0.33 mmol of Ph_3P

^b Yield of isolated product after chromatography, calculated based on the reacted ferrocenecarboxaldehyde (**1a**).

 $^{\rm c}$ The ratio of E- and Z-isomers was estimated by $^1{\rm H}$ NMR of the crude product.

^d Trace amount of product was detected by ¹H NMR of the reaction mixture.

Table 4 $Rh_2(OAc)_4/CeCl_3$ -Catalyzed Reaction of General Aldehydes with Ethyl Diazoacetate (2a)^a

RCHO 5a-c	+ H2	2 Rh ₂ (0 CO ₂ Et Ph ₃ 2a	DAc) ₄ , CeCl ₃ P, DCE 30 °C	R	CO₂Et 6a–c
Entry	5	R	6	Yield (%) ^b E/Z ^c
1	5a	Ph	6a	91	>20:1
2	5b	$4-ClC_6H_4$	6b	89	>20:1
3	5c	Pr	6с	81	>20:1

^a Reactions were carried out with 0.3 mmol of RCHO, 0.45 mmol of 2a, and 0.33 mmol of Ph_3P_1

^b Yield of isolated product after chromatography.

^c The ratio of E and Z isomers was estimated by ¹H NMR of the crude product.

Besides, it has been noted that this method is also applicable to the general aldehydes RCHO (R = aromatic and aliphatic group), as shown in Table 4. It was found that benzaldehyde, *p*-chlorobenzaldehyde, and butyraldehyde were all suitable for this transformation, and the corre-



Scheme 2 Reactions of ferrocenyl ketone derivatives



Scheme 3 Possible reaction pathway

sponding olefins were obtained in 91%, 89%, and 81% yields with excellent E stereoselectivity, respectively (Table 4, entries 1–3).

Finally, we tried to apply this novel method to the reaction of ferrocenyl ketone derivatives with EDA (Scheme 2). However, we were disappointed to find that no reactions occurred when acetylferrocene, propionylferrocene, and benzoylferrocene were used as the substrates under the above reaction condition. We attributed this result to the poor reactivity of ferrocenyl ketone derivatives.

A possible reaction pathway^{12c} to account for the formation of alkenylferrocenes is shown in Scheme 3. The reaction is initiated by diazo decomposition of EDA (**2a**) catalyzed by $Rh_2(OAc)_4$ to afford the metal carbene intermediate **A**, which is then converted to phosphorous ylide intermediate **B** in the presence of Ph_3P . Next, ferrocenecarboxaldehyde reacts with phosphorous ylide intermediate **B** to generate the product **3a**. The action of CeCl₃ may be act as Lewis acid to coordinate with the carbonyl group of carbonylferrocenes and increase the reactivity of this reactant.

In conclusion, we have developed a concise and efficient method for the preparation of alkenylferrocene derivatives based on the olefination of carbonylferrocenes with α -diazocarbonyl compounds using Rh₂(OAc)₄/CeCl₃ as efficient catalysts. This catalytic methodology is highly attractive and provides a valuable choice for the organic synthesis.

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(13) General Procedure

To a solution of carbonylferrocenes 1a-f (0.3 mmol), Ph₃P (0.33 mmol), CeCl₃ (0.15 mmol), and Rh₂ (OAc)₄ (0.5 mmol%) in anhyd DCE (3 mL) at 80 °C was added dropwise a solution of individual diazo compounds 2a-h (0.45 mmol)

in anhyd DCE (2 mL). The progress of the reaction was monitored by TLC. After completion of the reaction, solvent was removed by evaporation, and the residue was purified by column chromatography over silica gel to give the olefination products **3a–f** and **4a–g**.

Representative Spectroscopic Data

Compound **3f**: purple solid; mp 76–77 °C. IR (KBr): 3103, 3037, 1713, 1614, 1583, 1291, 1168, 1038, 1002 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): $\delta = 1.40$ (t, J = 7.0 Hz, 3 H), 4.22 (s, 5 H), 4.40 (q, J = 7.0 Hz, 2 H), 4.51 (t, J = 1.5 Hz, 2 H), 4.73 (t, J = 1.5 Hz, 2 H), 6.77 (d, J = 9.5 Hz, 1 H), 7.88 (s, 1 H), 8.81 (d, J = 9.5 Hz, 1 H). ¹³C NMR (125 MHz, CDCl₃): $\delta = 14.2, 62.0, 68.4, 68.6, 70.5, 71.6, 81.5, 116.8, 149.4,$ 151.3, 163.3, 164.7. Anal. Calcd for C₁₇H₁₇ClFeO₂: C, 59.25; H, 4.97. Found: C, 58.90; H, 5.17. Compound 4e: purple solid; mp 127–129 °C. IR (KBr): 3105, 1733, 1617, 1521, 1347, 1221, 1039 cm⁻¹. ¹H NMR $(500 \text{ MHz}, \text{CDCl}_3): \delta = 4.01 \text{ (s, 3 H)}, 4.24 \text{ (s, 5 H)}, 4.55 \text{ (s, })$ 2 H), 4.74 (s, 2 H), 7.96 (d, J = 5.0 Hz, 2 H), 8.28 (d, J = 5.0 Hz, 2 H), 8.59 (s, 1 H). ¹³C NMR (125 MHz, CDCl₃): δ = 52.2, 69.6, 69.7, 72.1, 72.4, 124.0, 128.0, 137.9, 149.0, 157.0, 165.6, 166.2. Anal. Calcd for C₂₀H₁₇FeNO₄: C, 61.40; H, 4.38; N, 3.58. Found: C, 60.11; H, 4.70; N, 3.79.

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