

ZnI₂-promoted homologation of ferrocenylacetylene and aldehydes: an efficient synthesis of ferrocene-containing allenes

Shufeng Chen*, Jinxiang Shi, Binglong Wang, Haiying Zhao and Baoguo Li*



A concise and efficient protocol for the first synthesis of ferrocene-containing allenes based on the homologation reaction of ferrocenylacetylene and aldehydes promoted by ZnI₂ was developed. The present method was applicable to many kinds of substituted aldehydes, providing good to excellent yields of ferrocene-containing allenes. Copyright © 2012 John Wiley & Sons, Ltd.

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Keywords: ferrocenyl allenes; homologation; ferrocenylacetylene; aldehydes; catalysis

Introduction

Ferrocene and its derivatives are a class of important organometallic compounds^[1] and widely used in many areas such as material science,^[2] asymmetric catalysis,^[3] nonlinear optics,^[4] and bioorganometallic chemistry.^[5] It is well documented that introduction of ferrocene into organic molecules endows quite unique properties due to the special structure as well as electronic character of this novel ferrocenyl moiety.^[6] Undoubtedly, the design motif and synthesis strategy in ferrocene-based architectures play the most important role in delivering the targeted property. However, traditional methods for derivatization of aromatic compounds may not work for ferrocene owing to its specific geometric and electronic properties, although ferrocene derivatives are classical aromatic compounds.^[7]

On the other hand, allenes have recently attracted great attention from organic chemists.^[8,9] In addition, because they are useful structural motifs that can serve as substrates or intermediates in various transformations, development of synthetic methods of novel structural allene derivatives has been required. Over the past decades, enormous efforts have been devoted to the development of highly efficient allene synthesis.^[10,11] Among these, the Crabbé homologation reaction and its modifications are widely used in the synthesis of simple allenes because of the convenient availability of materials.^[12] Recently, Kuang and Ma disclosed a breakthrough based on the homologation reaction of aldehydes and terminal alkynes mediated by ZnI₂. This new method can be employed to synthesize a series of 1,3-disubstituted allenes.^[13] However, ferrocene-containing allene product was not found in their report.

Moreover, installation of ferrocenyl group to the framework of allenes would offer effective modification toward their original properties. However, to the best of our knowledge, there is only one example, reported by Bildstein *et al.*, allowing access to these types of ferrocene-containing allenes.^[14] Considering the potential applications and limited methods available for their preparation, further development of synthetically useful methodologies for these novel ferrocenyl allene derivatives is highly desirable. In this paper, we wish to report a modified method for the first

preparation of ferrocene-containing 1,3-disubstituted allene derivatives based on the homologation reaction of ferrocenylacetylene and aldehydes promoted by ZnI₂ (Scheme 1).

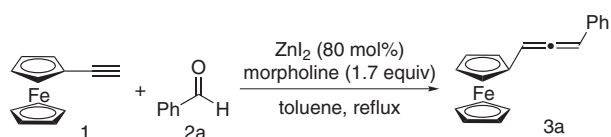
Results and Discussion

At the outset of this study, we employed ferrocenylacetylene **1** and benzaldehyde **2a** as substrates (Table 1). CuI, AgI and ZnI₂ were examined as catalysts with morpholine as base and toluene as solvent. CuI was found to be not effective and only a trace of ferrocenyl allene product was detected (entry 1). AgI led to the formation of ferrocenyl allene **3a** in 20% yield (entry 2) and, moreover, the isolated yield was improved to 56% when the reaction time was extended (entry 3). Furthermore, we were delighted to find that the isolated yield of **3a** was enhanced to 75% even in a short reaction time when ZnI₂ was used as the catalyst (entry 4). Encouraged by these results, we next carefully examined the effect of catalyst loading on this homologation reaction (entries 4–7). The result indicated that 80 mol% of ZnI₂ could give the best result under the same conditions (entry 4). After ZnI₂ was identified as the most efficient catalyst, the effect of base on this reaction was next examined. Bases such as ^tPr₂NH and Cy₂NH also led to the formation of ferrocenyl allene **3a** in moderate yields (entries 8 and 9). However, only a trace of ferrocenyl allene **3a** was detected when pyrrolidine was used in this reaction (entry 10). Therefore, ZnI₂ and morpholine were identified as the most efficient catalyst and base in this homologation reaction (entry 4).

With the optimized reaction conditions in hand, the scope of this homologation reaction was investigated by using a variety of aldehydes as substrates (Table 2). Various substitutions on

* Correspondence to: Shufeng Chen and Baoguo Li, College of Chemistry and Chemical Engineering, Inner Mongolia University, Hohhot 010021, China. E-mail: shufengchen@imu.edu.cn; baoguo@sohu.com

College of Chemistry and Chemical Engineering, Inner Mongolia University, Hohhot 010021, China

**Scheme 1.** Synthesis of ferrocene-containing allene derivative**Table 1.** Optimization of reaction conditions^a

Entry	Cat. (mol%)	Base	Time (h)	Yield (%) ^b
1	CuI (80)	Morpholine	12	Trace ^c
2	AgI (80)	Morpholine	6	20
3	AgI (80)	Morpholine	11	56
4	ZnI₂ (80)	Morpholine	4	75
5	ZnI ₂ (150)	Morpholine	4	68
6	ZnI ₂ (100)	Morpholine	4	70
7	ZnI ₂ (40)	Morpholine	4	69
8	ZnI ₂ (80)	ⁱ Pr ₂ NH	5.5	47
9	ZnI ₂ (80)	Cy ₂ NH	5.5	57
10	ZnI ₂ (80)	Pyrrolidine	5.5	Trace ^c

^aReactions were carried out with 0.24 mmol **1**, 0.43 mmol **2a**, and 0.40 mmol base in 3.0 ml toluene.

^bYield of isolated product after chromatography, calculated based on the reacted ferrocenylacetylene **1**.

^cTrace of the product was detected. The best result is highlighted in bold.

the phenyl ring could be tolerated, and the reaction gave moderate to good yields of the products **3a–h**. It was found that substrates with phenyl ring bearing a halogen group generally gave satisfactory yields (entries 2 and 3). The contrasting results obtained with *p*-NO₂ and *p*-MeO-substituted substrates indicated the important influence of electronic effects on this homologation reaction (entries 4 and 5). On the other hand, reactions with *ortho*-substituted aromatic aldehydes could only afford the corresponding ferrocenyl allene products in moderate yield, which showed that the reaction was also significantly affected by steric hindrance (entries 7 and 8). To our delight, when ferrocenecarboxaldehyde **2i** was used as the substrate in this reaction, the diferrocenyl-substituted allene product **3i** was obtained, albeit with slightly lower yield (entry 9). Moreover, it was noted that this approach was also applicable to substrates bearing heteroaromatic ring substituents to give novel allene products containing both ferrocene and heteroaromatic rings in good yield (entries 10 and 11). However, when aliphatic aldehydes were employed as substrates in this reaction, it was disappointing to find that the reaction gave a complex mixture and no desired allene products were detected (entries 12 and 13).

Next, we tried to apply this methodology to the reaction of ferrocenylacetylene with aromatic ketones (Scheme 2). However, we were disappointed to find that no reactions occurred when

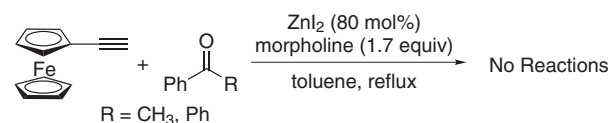
Table 2. ZnI₂-promoted homologation reaction of various aldehydes **2a–m** with ferrocenylacetylene **1**^a

Entry	2 , R	Reaction time (h)	3 , Yield (%) ^b
1	2a , Ph-	4	3a , 75
2	2b , <i>p</i> -BrC ₆ H ₄ -	3.5	3b , 62
3	2c , <i>p</i> -ClC ₆ H ₄ -	2	3c , 72
4	2d , <i>p</i> -CH ₃ OC ₆ H ₄ -	5.5	3d , 69
5	2e , <i>p</i> -NO ₂ C ₆ H ₄ -	1.5	3e , 84
6	2f , <i>m</i> -NO ₂ C ₆ H ₄ -	2.5	3f , 65
7	2g , <i>o</i> -NO ₂ C ₆ H ₄ -	5	3g , 42
8	2h , <i>o</i> -ClC ₆ H ₄ -	5	3h , 61
9	2i , Fc-	6	3i , 38
10	2j ,	2.5	3j , 65
11	2k ,	2	3k , 77
12	2l , CH ₃ CH ₂ CH ₂ -	3	nd ^c
13	2m , CH ₃ (CH ₂) ₅ -	6	nd ^c

^aReactions were carried out with 0.24 mmol **1**, 0.43 mmol **2a–n**, and 0.40 mmol morpholine in 3.0 ml toluene.

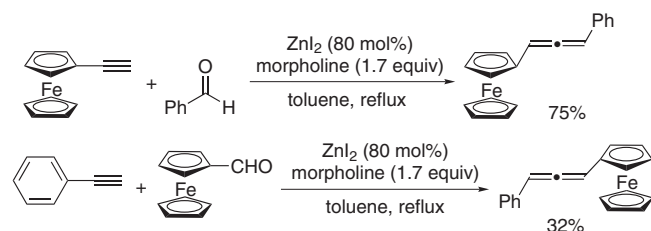
^bYield of isolated product after chromatography, calculated based on the reacted **1**.

^cNo ferrocenyl allene product was detected.

**Scheme 2.** Reactions of ferrocenylacetylene with aromatic ketones

acetophenone and benzophenone were used as substrates under the above reaction conditions. We attributed this result to the poor reactivity and steric hindrance of aromatic ketones.

Finally, for comparison, we employed this strategy in the reaction of ferrocenylacetylene with benzaldehyde and the reaction of phenylacetylene with ferrocenecarboxaldehyde, respectively (Scheme 3). Both reactions gave the same allene product under the same reaction conditions. The difference in the yield indicated that the reactivity of ferrocenecarboxaldehyde was poor, which is consistent with the result of entry 9 in Table 2.

**Scheme 3.** Comparable reactions using phenylacetylene and ferrocenylacetylene as substrates

Conclusions

We have developed a concise and efficient method for the preparation of ferrocene-containing allenes based on the homologation of ferrocenylacetylene with aromatic aldehydes using ZnI_2 as an efficient catalyst. The reaction is operationally simple and the conditions are mild with moderately high temperature, which provides a valuable choice for organic synthesis. Further studies on the applications as well as transformations of these novel ferrocenyl allenes are ongoing in our laboratory.

Experimental

General Procedure for the Homologation of Ferrocenylacetylene and Aldehydes

Under a nitrogen atmosphere at room temperature, ZnI_2 (63.8 mg, 0.2 mmol) was added to a mixture of ferrocenylacetylene **1** (50.4 mg, 0.24 mmol), morpholine (34.8 mg, 0.4 mmol), and *p*-bromobenzaldehyde **2b** (80.0 mg, 0.43 mmol) in toluene (5 ml) and the mixture was heated to reflux. The progress of reaction was monitored by thin-layer chromatography. After completion of the reaction, solvent was removed by evaporation, and the residue was purified by column chromatography over silica gel to afford 3-(4-bromo)phenylpropa-1,2-dienylferrocene **3b** as a purple solid (94 mg, 62% yield).

Representative spectroscopic data

3b: m.p. 177–179 °C; IR (KBr) 3087, 2924, 2851, 1651, 1595, 1487, 1456, 1069, 820 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.22 (s, 5 H), 4.61 (t, J = 4.0 Hz, 2 H), 4.91 (t, J = 4.0 Hz, 2 H), 7.11 (d, J = 15.5 Hz, 1 H), 7.51 (d, J = 8.5 Hz, 2 H), 7.56 (d, J = 8.5 Hz, 2 H), 7.72 (d, J = 15.5 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 69.9, 70.3, 73.1, 80.6, 123.7, 124.4, 129.8, 132.3, 134.3, 139.6, 192.8 ppm; MS (ESI) m/z = 377 $[\text{M}]^+$, 379 $[\text{M} + 2]^+$; Anal. Calcd for $\text{C}_{19}\text{H}_{15}\text{FeBr}$: C, 60.20; H, 3.99. Found: C, 60.58; H, 3.70. (The spectroscopic characterization of other compounds please see supporting information).

Acknowledgements

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