Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 48 (2007) 2209–2211

Diastereoselective allylation of planar chiral substituted ferrocenecarboxaldehyde: an efficient entry to chiral ferrocenyl ligands

Hao Li, Hin-Soon Cheng, Ai-Hua Seow and Teck-Peng Loh*

Division of Chemistry and Biological Chemistry, Nanyang Technological University, Singapore 637616, Singapore

Received 3 November 2006; revised 16 December 2006; accepted 15 January 2007
Available online 18 January 2007

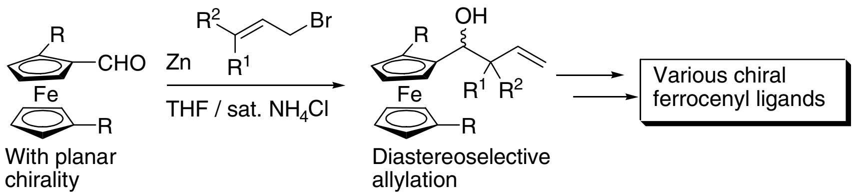
Abstract—2,2′-Disubstituted ferrocenecarboxaldehydes are subjected to zinc-mediated allylation to form homoallylic ferrocenyl alcohols. The effects of *ortho*-substituted functional groups on facial selectivities of planar chiral aldehydes were studied and it was found that the corresponding homoallylic alcohols were obtained as single diastereomers in excellent yields.

Ferrocene plays a significant role in many areas of synthetic and material chemistry owing to its stability and the wealth of methods for its derivatization. Chiral ferrocenyl derivatives have been utilized as chiral ligands in many asymmetric catalytic reactions.[1] In addition, the utility of the stable α-chiral carbenium of ferrocene alcohol may open up new areas of asymmetric catalysis.[2] In connection with our interest in the α-chiral ferrocene carbenium chemistry, we required efficient and practical methods to obtain α-chiral alcohols with high selectivities. There have been tremendous efforts directed towards the development of new methods to obtain optically pure ferrocenyl alcohols.[3] In this Letter, we report an efficient method utilizing the existing planar chirality of ferrocene to generate chiral ferrocenyl ligands cleanly (Scheme 1).

The 2,2′-substituted ferrocenecarboxaldehydes were prepared using the following general procedure.[4] Ferrocenecarboxaldehyde **1** was quantitatively converted into acetal **2** by heating with 1,3-propanediol in the presence of *p*-TSA in dichloromethane. Deprotonation of the acetal using *n*-BuLi (2.2 equiv) in THF at room temperature for 4 h, followed by quenching with different electrophiles (TMSCl or dibromoxylene) to intermediate **3** and finally deprotection furnished the respective desired 2,2′-substituted ferrocenecarboxaldehydes **4** (Scheme 2).

Phenylferrocenecarboxaldehyde (±)-**4d** was obtained using the Negishi coupling reaction.[5] After lithiation of ferrocenylacetal with *n*-BuLi, the *ortho* lithiated intermediate obtained was transmetallated with $ZnCl_2$ and cross-coupled with bromobenzene in the presence of a catalytic amount of $PdCl_2(Ph_3)_2$ to afford (±)-**4d** as shown in Scheme 3.

The 2,2′-disubstituted ferrocenecarboxaldehydes prepared were then subjected to allylation reactions.[6]

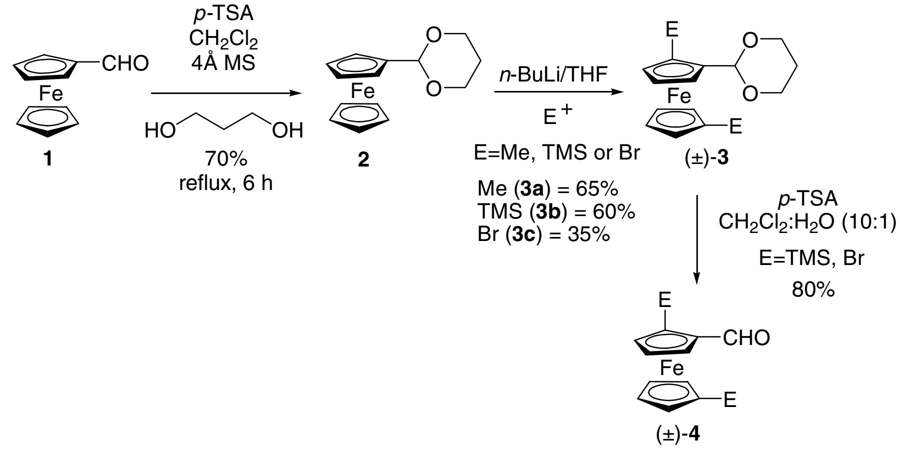


Scheme 1. Synthetic scheme to various chiral ferrocenyl ligands.

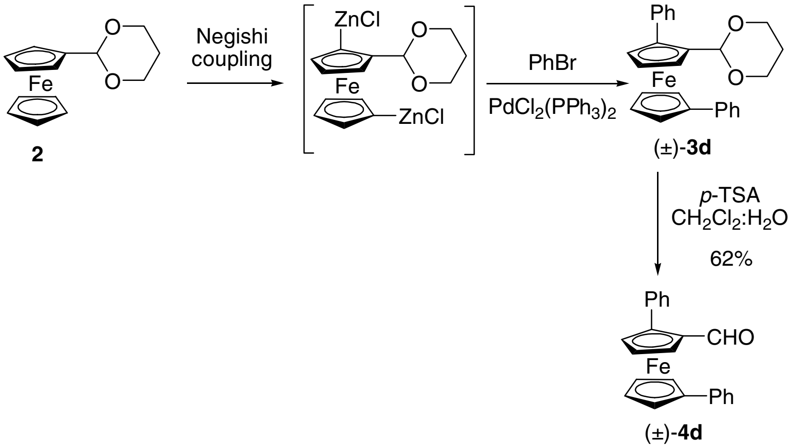
Keywords: 2,2′-Disubstituted ferrocenecarboxaldehydes; Allylation; Chiral ferrocenyl complexes.

* Corresponding author. Tel.: +65 63168899; fax: +65 67911961; e-mail: teckpeng@ntu.edu.sg

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.01.065

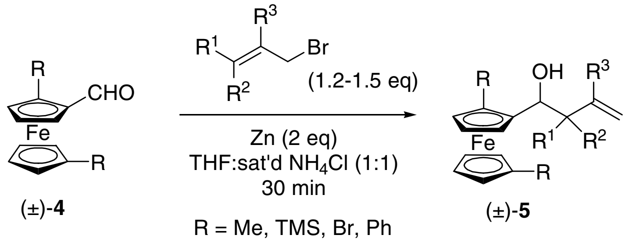


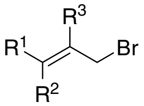
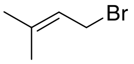
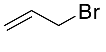
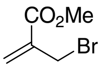
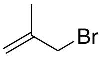
Scheme 2. Synthesis of 2,2′-disubstituted ferrocenecarboxaldehydes.



Scheme 3. Negishi coupling reaction.

Table 1. Allylation of 2,2′-disubstituted ferrocenecarboxaldehydes with various allyl bromides[a]



Entry	R		Yield[b]	Selectivity[c]
1	Me		83	75:25
2	TMS		92	67:33
3	Br		89	>99:1
4	Ph		85	>99:1
5	TMS		67	67:33
6	Br		84	>99:1
7	Ph		90	>99:1
8	TMS		94	52:48
9	Br		94	>99:1
10	Ph		76	>99:1
11	TMS		87	76:24
12	Br		90	>99:1
13	Ph		92	>99:1

[a] All reactions were carried out on a 0.5 mmol scale in an ice bath with 6 mL of solvent.

[b] Isolated yield.

[c] Diastereoselectivity was determined by ^1H and ^{13}C NMR spectroscopy.

Various allyl bromides were used in the presence of zinc powder and the results are summarized in Table 1.

In all cases, the zinc-mediated allylation proceeded smoothly to give the desired products in moderate to

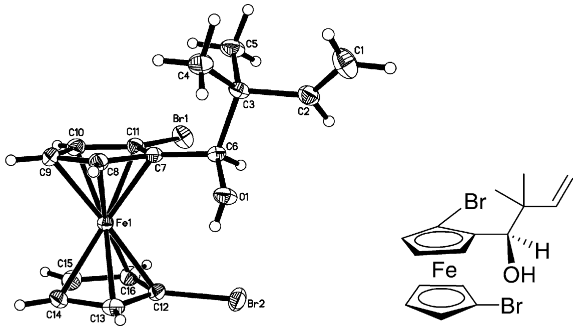
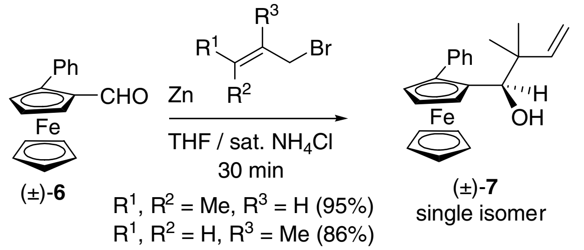


Figure 1. X-ray crystal structure of the allylation product.



Scheme 4. Allylation of 2-substituted ferrocenecarboxaldehyde with allyl bromide.

good yields (Table 1). When R = TMS or Me, the prenylated products were obtained with low selectivities (entries 1 and 2). This contrasts with the high facial selectivities for R = Br or Ph (entries 3 and 4). A similar trend was observed for allylation (entries 5–7), where TMS gave no preference in facial selectivity while Ph and Br gave the products essentially as single isomers. Furthermore, Ph and Br substituted ferrocenecarboxaldehyde also gave excellent selectivities with α-substituted bromide (entries 9, 10, 12 and 13). The relative stereochemistry of the alcohol product (entry 3, Table 1) was confirmed by X-ray crystallography (Fig. 1).

Furthermore, simple 2-substituted ferrocenecarboxaldehyde (±)-**6** was also subjected to the same zinc allylation conditions, giving similar yields and facial selectivities as shown in Scheme 4. This suggests that the key factor determining the diastereoselectivity of the allylation process is the substituted group on the upper cyclopentadienyl ring.

A transition state can be proposed to account for the observed stereochemistry. Organozinc reagents attack the formyl group from the less hindered side, away from the sterically hindered lower cyclopentadienyl ring to afford the product with the stereochemistry as shown in Scheme 5.

In conclusion, a series of 2,2′-disubstituted ferrocenecarboxaldehydes have been synthesized and were applied in allylation reactions using various allylic bromides. TMS and Me substituents did not give the good selectivity. However, Ph and Br substituents gave excellent diastereoselectivities (>99:1). A series of chiral ferrocenyl complexes are currently being derived from 2,2′-disubstituted ferrocenecarboxaldehydes.

Acknowledgement

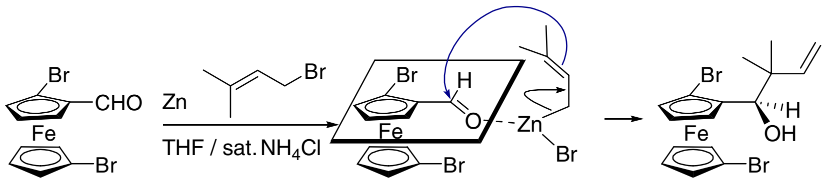
We are grateful to Nanyang Technological University for its generous financial support.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.01.065.

References and notes

1. For reviews, see: Hayashi, T. Asymmetric Catalysis with Chiral Ferrocenylphosphine Ligands. In *Ferrocenes*; Togni, A., Hayashi, T., Eds.; VCH: Weinheim, 1995; p 105; Togni, A. New Chiral Ferrocenyl Ligands for Asymmetric Catalysis. In *Metallocenes*; Togni, A., Halterman, R. L., Eds.; VCH: Weinheim, 1998; Vol. 2, p 689; Kagan, H. B.; Riant, O. *Adv. Asymmetric Synth.* **1997**, *2*, 189.
2. Taudien, S.; Riant, O.; Kagan, H. B. *Tetrahedron Lett.* **1995**, *36*, 3513.
3. Fukuzawa, S. I.; Tsuchiya, D.; Sasamoto, K.; Hirano, K.; Ohtaguchi, M. *Eur. J. Org. Chem.* **2000**, 2877.
4. Riant, O.; Samuel, O.; Kagan, H. B. *J. Am. Chem. Soc.* **1993**, *115*, 5835; Riant, O.; Samuel, O.; Flessner, T.; Tauben, S.; Kagan, H. B. *J. Org. Chem.* **1997**, *62*, 6733.
5. Mamane, V.; Fort, Y. *J. Org. Chem.* **2005**, *70*, 8220.
6. For a review, see: Loh, T. P.; Chua, G. L. *Yuki Gosei Kagaku Kyokaishi* **2005**, *63*, 1137.



Scheme 5. Proposed mechanism for the allylation of 2,2′-disubstituted ferrocenecarboxaldehyde with allyl bromide.