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Stereoselective [3,3]-Sigmatropic Rearrangement Promoted by the Metal [1,3]-Shift of Binuclear Fischer Carbene Complexes

Ken Kamikawa,[†] Atsushi Tachibana,[†] Yasunori Shimizu,[†] Kazuya Uchida,[†] Masaru Furusho,[‡] and Motokazu Uemura*,[†]

Department of Chemistry, Faculty of Integrated Arts and Sciences, Osaka Prefecture University, Sakai, Osaka 599-8531, Japan, and Analysis Technology Research Center, Sumitomo Electric Industries, Ltd., 1-1-1, Koyakita, Itami, Hyogo, 664-0016, Japan

uemura@ms.cias.osakafu-u.ac.jp

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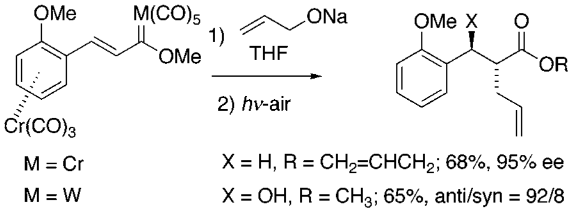
ABSTRACT



Reaction of chiral homobinuclear Fischer chromium carbene complexes with allyl alcohol in the presence of NaH and the following oxidative demetalation gave α-allyl esters in up to 97% ee via [3,3]-sigmatropic rearrangement reaction promoted by the metal 1,3-shift. On the other hand, chiral heterobinuclear tungsten carbene complexes with arene chromium complexes afforded α-allyl-β-hydroxy esters as a major product in up to 92/8 dr by the same reaction sequence.

Fischer carbene complexes are among the most versatile organometallic reagents for organic synthesis.[1] Furthermore, optically active Fischer carbene complexes have attracted increasing attention as powerful tools for asymmetric synthesis, and various chiral carbene complexes have been developed to date. Most of these chiral α,β-unsaturated Fischer carbene complexes belong to a class in which chiral alcohols or amines are incorporated at the carbene carbon atom as a stabilizing substituent due to their easy preparation. On the other hand, there are few examples of other types of chiral α,β-unsaturated Fischer carbene complexes, in which a chiral auxiliary is directly attached to the α,β-unsaturated bond.[2] We expected that these chiral Fischer carbene complexes would become promising chiral reagents, since a reactive site is located close to the chiral auxiliary. As a synthetic development of the planar chiral arene chromium complexes, we have investigated the reaction of chiral α,β-unsaturated binuclear Fischer carbene complexes[3] with allyl alcohols in the presence of base.

Barluenga et al. reported[4] that α,β-unsaturated Fischer carbene complexes **1** were treated with allyl alcohol in the presence of a base to give β-allyl arylpropionate **4** via

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[†] Osaka Prefecture University.

[‡] Sumitomo Electric Industries, Ltd.

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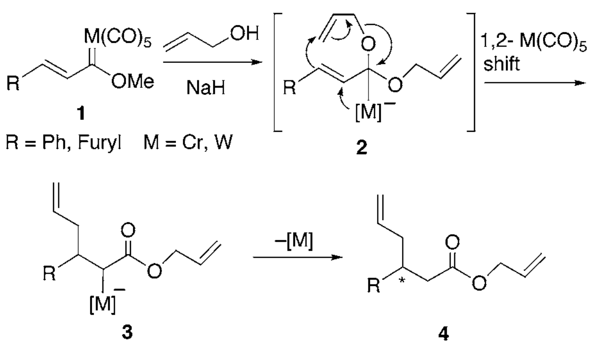
Scheme 1. [3,4]-Sigmatropic Rearrangement Promoted by [1,2]-Metal Shift Reported by Barluenga[4]



concerted 1,2-M(CO)$_5$ shift followed by [3,4]-sigmatropic rearrangement as shown in Scheme 1. The allyl group was introduced at the β-carbon to the ester carbonyl group. Therefore, β-allyl arylpropionates **4** would be obtained as optically active compounds by utilizing planar chiral arene chromium complexes as a chiral auxiliary.

Binuclear α,β-unsaturated Fischer carbene complexes **5** as starting materials were easily prepared by aldol condensation of benzaldehyde chromium complexes with methylmethoxycarbene complexes in the presence of triethylamine and trimethylsilyl chloride in reasonable yields.[5] We initially investigated the synthesis of **4** by using the binuclear carbene complex **5a** according to Barluenga's procedure. The carbene complex **5a** in allyl alcohol was treated with NaH under inert gas in a balloon and subsequently exposed to sunlight. Surprisingly, α-allyl β-phenyl propionate **6a** was obtained in 75% yield without formation of β-allyl β-phenyl propionate **4** (Table 1, entry 1). Thus, the allyl group was regioselectively introduced at the α-position to the ester. The structure of α-allyl β-phenyl propionate **6a** was absolutely confirmed by comparison with both authentic samples **6a** and **4** (R = Ph).[6] This result is in sharp contrast to Barluenga's report, in which the allyl group was introduced at the β-position. We initially imagined that the distinct reaction path of α,β-unsaturated Fischer carbene complexes with allyl alkoxide might be attributed to the strong electron-withdrawing ability of the tricarbonylchromium fragment. However, we were surprised that the chromium-uncomplexed α,β-unsaturated chromium carbene complex **1** (R = Ph, M = Cr) gave only α-allyl β-phenyl propionate **6a** in 68% yield without β-allyl β-phenyl propionate **4** (R = Ph) by the reaction with allyl alkoxide. Also, the corresponding tungsten carbene complex **1** (R = Ph, M = W) afforded α-allyl β-phenyl propionate **6a** in 55% yield without detection of β-allyl β-phenyl propionate. In this way, we obtained only α-allyl β-phenyl propionate by reaction with allyl alkoxide in both cases of α,β-unsaturated Fischer carbene complexes **1** and the corresponding tricarbonylchromium-coordinated α,β-unsaturated Fischer carbene complexes **5**.

We next extended this interesting reaction to the asymmetric synthesis of α-allyl β-phenyl propionate by using planar chiral binuclear carbene complexes. When enantiomerically pure binuclear Fischer carbene complex **5b** ($[\alpha]^{24}_{D}$ −3400 (*c* 0.001, CHCl$_3$)), derived from a planar chiral (−)-(*R*)-*o*-methoxybenzaldehyde chromium complex, was reacted with allyl alkoxide at 25 °C, an α-allyl *o*-methoxyphenyl propionate (**6b**) ($[\alpha]^{23}_{D}$ −25.2 (*c* 0.09, CHCl$_3$)) was obtained in 68% yield with 95% ee[7] (entry 2).

Expectedly, the α-allyl phenyl propionate **6b** was obtained with high enantiomeric excess despite severe basic conditions. The absolute stereochemistry of **6b** was determined as (*R*)-configuration by comparison of an optical rotation of authentic (*S*)-configurated allyl 2-allyl *o*-methoxyphenylpropionate ($[\alpha]^{23}_{D}$ +27.1 (*c* 0.38, CHCl$_3$)) prepared from Evans' oxazolidone derivative.[8] When the reaction was performed at 0 °C, the corresponding α-allyl methyl ester **7b** was obtained in 40% yield with 97% ee along with formation of α-allyl-β-hydroxy ester **8b** as an easily separable diastereomeric mixture in 40% yield (entry 3).

The stereochemistry of the major α-allyl-β-hydroxy ester **8b** ($[\alpha]_{D}^{30}$ −36.0 (*c* 0.23, CHCl$_3$)) was determined to possess the anti-(2*R*,3*S*)-configuration by comparison with authentic compound.[9] Similarly, with 2-methyl-2-propen-1-ol at 25 °C, the corresponding product **6c** was obtained in 85% yield with 72% ee (entry 4). On reaction of **5b** with 2-methyl-2-propen-1-ol at 0 °C, the corresponding α-allyl-β-hydroxy ester **8c** was only obtained with 83/17 dr (entry 5). Similarly, with *o*-methyl-substituted arene chromium complex **5c**, the reaction products were controlled by reaction temperature. Thus, α-allyl-β-hydroxy ester **6d** was obtained at 25 °C (entry 6), while the corresponding α-allyl methyl ester **7d** and diastereomeric α-allyl-β-hydroxy ester **8d** were obtained at lower reaction temperature (entries 7 and 8). The optical yield of **7d** increased to 97% ee in the reaction at −30 °C (entry 8). When the ortho substituent of the arene chromium complex was changed to an isopropoxy group, aldol-type product **8e** was obtained as a major product in 51% yield with 85/15 dr (entry 9). In this way, binuclear α,β-unsaturated chromium carbene complexes with planar chiral arene chromium complexes were reacted with allyl alcohols in the presence of a base to give 2-allyl *o*-substituted phenyl propionate esters with high ee. Furthermore, when the reaction was performed at lower temperature, methyl α-allyl-β-hydroxy arylpropionates **8** were obtained with high anti

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[6] Authentic samples **4** (R = Ph) and **6a** were prepared by allyl esterification of 3-phenyl-hex-5-enoic acid and α-allylation of β-phenyl propionate, respectively. See Supporting Information.

[7] Enantiomeric excess was determined by chiral HPLC with Chiralcel OD; hexane/2-propanol = 100/1; flow rate 1.0 mL/min; column temperature 40 °C; UV detector 254 nm, retention time, racemate, 14.3 min, 16.9 min: **6b**, 16.9 min.

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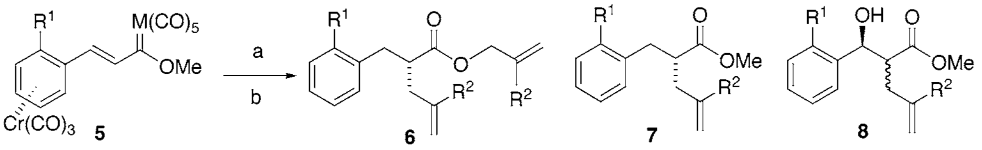
Table 1. Reaction of Binuclear Carbene Complexes **5** with Allyl Alcohols[a]



5a; R^1 = H, M = Cr
5b; R^1 = OMe, M = Cr
5c; R^1 =Me, M = Cr
5d; R^1 = OPr-*i*, M = Cr
5e; R^1 = H, M = W
5f; R^1 = OMe, M = W
5g; R^1 = Me, M = W
5h; R^1 = OPr-*i*, M = W

Alphabetical numbering for compounds **6**, **7** and **8** is as follows;
a: R^1 = R^2 = H; b: R^1 = OMe, R^2 = H; c: R^1 = OMe, R^2 = Me; d: R^1 = Me, R^2 = H;
e: R^1 = O^iPr, R^2 = H

entry	complex	temp (°C)	yield of **6** (%)	yield of **7** (%)	yield of **8** (%)	% ee[b] of **6** or **7**	anti/syn ratio[c] of **8**
1	**5a**	25	75				
2	**5b**	25	68			95	
3	**5b**	0		40	40	97	78/22
4	**5b**	25	85			72	
5	**5b**	0			45		83/17
6	**5c**	25	83			77	
7	**5c**	0		55	40	93	83/17
8	**5c**	−30		33	30	97	80/20
9	**5d**	0		10	51		85/15
10	**5e**	25		10	71		63/37
11	**5e**	−30			75		92/8
12	**5f**	−30			65		92/8
13	**5g**	−30			70		92/8
14	**5h**	−30			31		75/25

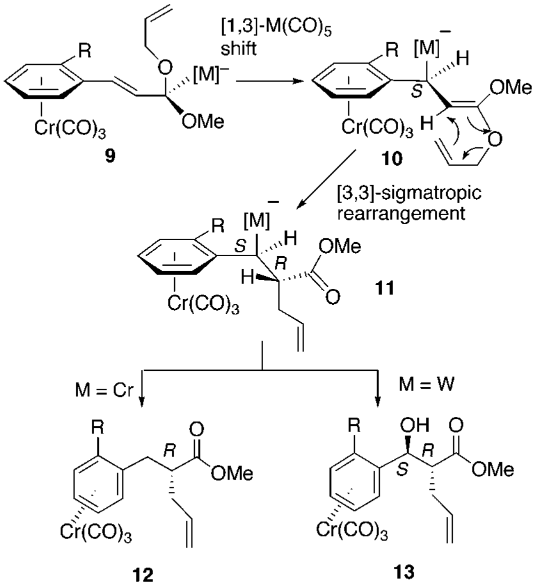
[a] Reagents and conditions: (a) $CH_2{=}C(R^2)CH_2OH$, NaH, THF, under inert gas in a balloon; (b) *hν*−air, ether. [b] Determined by chiral HPLC (see Supporting Information for details). [c] Determined by integration of representative signals by ^{1}H NMR of the crude product.

selectivity in moderate yield. To further extend this reaction, we next turned our attention to the reaction of heterobinuclear tungsten carbene complexes with planar chiral arene chromium complexes. A heterobinuclear tungsten carbene complex **5e** was reacted with allyl alkoxide to give α-allyl-substituted esters, **7a** and **8a**, in analogy with homobinuclear chromium carbene complexes. But, in the case of binuclear tungsten carbene complex, methyl α-allyl-*β*-hydroxy arylpropionate **8a** was predominantly obtained even at room temperature (entry 10). In the reaction at −30 °C, the aldol-type product **8a** was obtained as the sole product with higher diastereoselectivity (entry 11). Similarly, optically active tungsten carbene complexes with planar chiral arene chromium complexes **5f** and **5g** gave the corresponding α-allyl-*β*-hydroxy arylpropionates **8b** and **8d** in good yields with high diastereoselectivity by reaction with allyl alkoxide at −30 °C (entries 12 and 13). Compared with homobinuclear chromium complexes, heterobinuclear tungsten carbene complexes with a planar chiral arene chromium complex gave *anti*-α-allyl-*β*-hydroxy arylpropionates with high diastereoselectivity. With a sterically bulky *ortho*-isopropoxy substituent of the arene chromium complex, the diastereomeric ratio decreased to 75/25 (entry 14). In conclusion, tricarbonylchromium-coordinated binuclear α,*β*-unsaturated carbene complexes afforded α-allyl arylpropionates and *anti*-α-allyl-*β*-hydroxy arylpropionates as optically enriched compounds depending on the nature of carbene metal and reaction conditions.

The origin of the benzylic oxygen of α-allyl-*β*-hydroxy arylpropionates **8** in the reaction of binuclear carbene complexes **5** is significant for clarification of the reaction mechanism. Although the reaction was carried out under an inert atmosphere in a balloon, trace amounts of oxygen might be present in the solvent and/or inert gas. Therefore, the mixture of **5**, allyl alcohol, and NaH in dry THF was carefully degassed by an inert gas/freeze/vacuum technique, and the reaction was carried out in a well-degassed glovebox. Consequently, it was found that the aldol-type product **8** decreased to 15% yield, and the α-allyl product **7** was obtained in 50% yield. This result indicates obviously that the benzylic hydroxy group was introduced from oxygen in the solvent and/or inert gas. Higher yields of the oxygenated product **8** in the reaction with the heterobinuclear tungsten carbene complexes than with chromium complexes are attributed to the strong nucleophilicity of tungsten.

On the basis of these results, we propose a reaction mechanism of α,*β*-unsaturated Fischer carbene complexes with allyl alkoxide in Scheme 2. Nucleophilic addition of allyl alkoxide at the metal carbene fragment is initiated to give a tetrahedral intermediate **9**. The formation of (*S*)-configured α-allyl arylpropionates **6** and **7** starting from planar chiral carbene complexes **5** would be explained by a

Scheme 2. Proposed Mechanism



1,3-metal shift[10,11] and a subsequent [3,3]-sigmatropic rearrangement reaction. 1,3-Metal shift from the tetrahedral intermediate **9** generates an intermediate **10** with an anti conformation between the tricarbonylchromium fragment and the pentacarbonylmetal group due to steric repulsion. Consequently, the benzylic position of the resulting σ-allyl chromium complex **10** is (*S*)-configured. Subsequent [3,3]-sigmatropic rearrangement from the intermediate **10** produced (*R*)-configured α-allyl aryl propionate complex **11** by approach from the less hindered *si*-face. In the case of the chromium carbene complexes, protonation of **11** and the following reductive elimination occur to give complex **12** as the major product. On the other hand, with tungsten carbene complexes, an anionic tungsten species was easily trapped with oxygen followed by reductive elimination to give *anti*-aldol-type products **13**. Similarly, even in the chromium-uncomplexed α,β-unsaturated Fischer carbene complexes **1**, a 1,3-metal shift and subsequent [3,3]-sigmatropic rearrangement occurred to give α-allyl arylpropionates.

In conclusion, we have demonstrated a stereoselective [3,3]-sigmatropic rearrangement of chiral binuclear α,β-unsaturated Fischer carbene complexes promoted by a 1,3-metal shift. The characteristics of this reaction utilizing binuclear carbene complexes are as follows: reaction of chiral homobinuclear Fischer carbene complexes with allyl alcohol in the presence of base gave α-allyl esters in up to 97% ee, and chiral heterobinuclear carbene complexes afforded *anti*-aldol-type products, α-allyl-β-hydroxy esters, in up to 92/8 dr. Further exploration of the synthetic utility and clarification of the precise mechanism of these reactions is in progress.

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Supporting Information Available: Experimental procedures and characterization data of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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