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NOTE

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Regioselective Addition of Various Heteronucleophiles to (Styrene)Cr(CO)$_3$ Complexes

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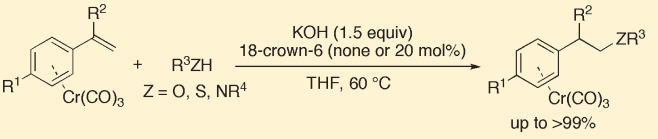
Supporting Information

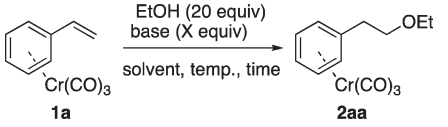
ABSTRACT: (Styrene)Cr(CO)$_3$ complexes underwent the addition of various heteronucleophiles such as alcohols, amines, and thiols, in the presence of KOH, and the β-addition products were selectively obtained in moderate to excellent yields. The structural details and features of the product complexes were also elucidated.



Arene chromium tricarbonyl ((arene)Cr(CO)$_3$) complexes are well known as useful intermediates for organic synthesis because they exhibit various types of reactivity not exhibited by free arenes.[1] For example, the Cr(CO)$_3$ moiety stabilizes benzylic carbanion(s); therefore, the (styrene)Cr(CO)$_3$ complexes are susceptible to nucleophilic attack exclusively at the β-position. Consequently, several examples of β-selective attack of carbon nucleophiles such as alkyl- and aryllithiums[2] and alkyl radicals[3] to the (styrene)Cr(CO)$_3$ complexes were reported. However, to the best of our knowledge, the nucleophilic addition of heteronucleophiles has rarely been examined.[4] Herein, we report the nucleophilic addition of oxygen, nitrogen, and sulfur nucleophiles to (styrene)Cr(CO)$_3$ complexes.

We first chose EtOH as an oxygen nucleophile and examined nucleophilic addition to the (styrene)Cr(CO)$_3$ complex **1a**. When complex **1a** and EtOH were heated in 1,4-dioxane, the reaction did not proceed at all, and complex **1a** was recovered (Table 1, entry 1). Next, we screened bases that improve the nucleophilicity of EtOH. We found that, in the presence of *t*-BuOK, K_2CO_3, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), no reaction proceeded even at the high temperatures (entries 2−4). On the other hand, the desired alkoxylation proceeded in the presence of KOH at 60 °C in THF, and the β-addition product **2aa** was obtained in 77% yield without formation of the α-addition product (entry 5).[5] We prolonged the reaction time (72 h) or increased the amount of KOH (3 equiv) for the complete consumption of the substrate, but complex **1a** remained in each case, and the yield was not improved (entries 6 and 7). When the reaction was conducted at a higher temperature (100 °C) in 1,4-dioxane, the yield drastically decreased presumably because of the decomposition of product **2aa** (entry 8). In the case of more polar solvents such as EtOH and CH_3CN, the yields decreased (entries 9 and 10). The addition of 18-crown-6, which improves the nucleophilicity of EtOH, did not affect the yield at all (entry 11). From these results, we concluded that the equilibrium between the starting material and the product hinders the complete consumption of complex **1a**.[6,7]

Table 1. Optimization of Nucleophilic Addition of EtOH to the (Styrene)Cr(CO)$_3$ Complex



1a **2aa**

entry	base (*X*)	solvent	temp (°C)	time (h)	yield (%)
1		1.4-dioxane	120	2	0
2	*t*-BuOK (1.2)	1.4-dioxane	120	2	0
3	K_2CO_3 (1.2)	1.4-dioxane	120	2	0
4	DBU (3)	THF	80	15	0
5	KOH (1.5)	THF	60	45	77
6	KOH (1.5)	THF	60	72	74
7	KOH (3)	THF	60	45	73
8	KOH (1.5)	1.4-dioxane	100	45	18
9	KOH (1.5)	EtOH	60	45	41
10	KOH (1.5)	CH_3CN	60	45	56
11[a]	KOH (1.5)	THF	60	45	72

[a] 18-Crown-6 (20 mol %) was added.

We then examined the scope of the oxygen nucleophile under the optimized conditions listed in entry 5 in Table 1. The desired regioselective reactions also proceeded when MeOH, *i*-PrOH, and allyl alcohol were used. In each reaction, chromium complex **1a** was not completely consumed even after 45 h, and the yields were moderate (Table 2, entries 1−3).

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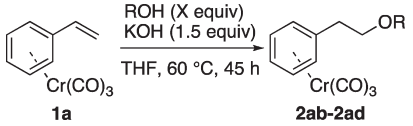
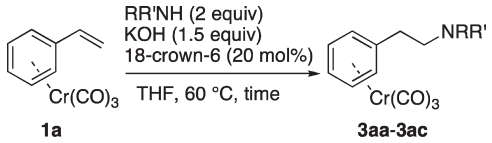
Table 2. Screening of Alcohols as Oxygen Nucleophiles



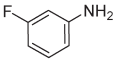
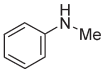
1a 2ab-2ad

entry	ROH (*X*)	product	yield (%)
1	MeOH (20)	**2ab**	50
2	*i*-PrOH (20)	**2ac**	56
3	CH_2=$CHCH_2$−OH (5)	**2ad**	45

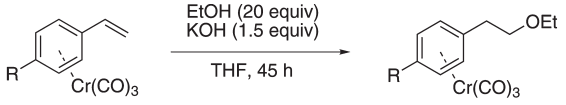
Table 3. Screening of Amines as Nitrogen Nucleophiles



1a 3aa-3ac

entry	RR'NH	product	time (h)	yield (%)
1		**3aa**	45	74
2		**3ab**	0.2	94
3		**3ac**	1	41

Styrene derivative−chromium tricarbonyl complexes were also submitted to the reaction with EtOH (eq 1). When the electron-withdrawing CF_3 group was installed on the benzene ring, the reaction proceeded at lower temperature (40 °C),[8] and β-addition product **2ba** was obtained in excellent yield. On the contrary, in the case of the electron-donating MeO group, the yield of **2ca** was low.



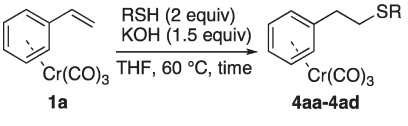
(1)

1b (R = CF_3) **2ba**: 94% (40 °C)
1c (R = OMe) **2ca**: 11% (60 °C)

Next we examined nitrogen nucleophiles. When the reaction was conducted using *N*-methyl-*p*-toluenesulfonamide in the presence of KOH at 60 °C in THF, the desired reaction did not proceed. However, when the reaction was promoted by adding a catalytic amount of 18-crown-6, the corresponding β-addition product **3aa** was obtained in 74% yield (Table 3, entry 1). This reaction was not complete because of the existence of the equilibrium between the starting material and the product. In contrast, the reaction of *m*-fluoroaniline was immediately complete in the same reaction conditions and gave the corresponding product **3ab** in excellent yield (entry 2). *N*-Methylaniline also underwent the desired reaction, and the reaction was complete in 1 h, but the yield was moderate, because addition product **3ac** without an electron-withdrawing group was thermally unstable, and the partial decomposition occurred (entry 3).

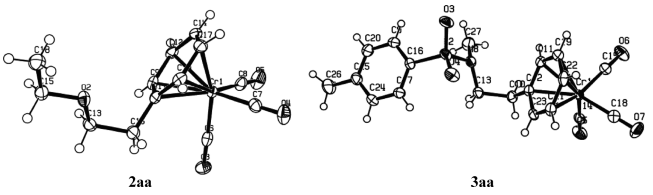
We further examined sulfur nucleophiles (Table 4). When ethanethiol (EtSH) was submitted to the reaction with complex **1a** in the presence of KOH at 60 °C in THF, complex **1a** was

Table 4. Screening of Thiols as Sulfur Nucleophiles



1a 4aa-4ad

entry	RSH	product	time (h)	yield (%)
1	EtSH	**4aa**	1	quant.
2	PhSH	**4ab**	4	quant.
3	*cyclo*-HexSH	**4ac**	5	97
4	HO-CH_2CH_2-SH	**4ad**	1.5	quant.

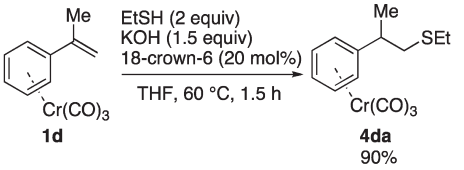


2aa 3aa

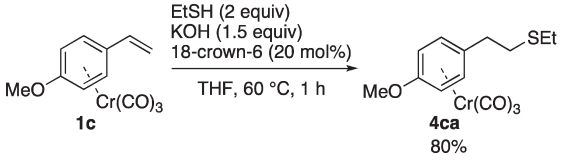
Figure 1. Molecular structure of complex **2aa** (left) and **3aa** (right). Selected bond lengths and angles are given in the Supporting Information.

completely consumed within 1 h, and the β-addition product **4aa** was obtained quantitatively (entry 1).[9] Thiophenol and cyclohexanethiol were also good substrates. The reactions were completed within 5 h, and the corresponding addition products **4ab** and **4ac** were obtained in excellent yields (entries 2 and 3, respectively). When 2-mercaptoethanol, which has both OH and SH groups, was examined, sulfur addition product **4ad** was exclusively obtained in excellent yield (entry 4). All reactions using sulfur nucleophiles smoothly proceeded along with complete conversion of the starting materials.

We found that thiols are the most reactive heteronucleophiles for the present reaction. The substrate scope of the styrene derivative−chromium tricarbonyl complex was examined using EtSH as a nucleophile. The reaction of (α-methylstyrene)$Cr(CO)_3$ (**1d**) proceeded in the presence of KOH, but it was much slower than that of complex **1a**. The addition of a catalytic amount of 18-crown-6 was effective, and the desired reaction was complete within 1.5 h to give complex **4da** in 90% yield (eq 2). In the reaction with EtSH, methoxy-substituted styrene complex **1c** efficiently underwent nucleophilic attack, and complex **4ca** was obtained in good yield (eq 3).



1d 4da 90% (2)



1c 4ca 80% (3)

We ascertained the structural details of complexes **2aa** and **3aa** by X-ray crystallographic analyses (Figure 1). The Cr−C bond

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lengths in both complexes did not change from those in complex **1a** itself,[10] and neither the oxygen nor nitrogen atom coordinated to the Cr atom. When complex **2aa** was exposed to sunlight in the air for a day, complete demetalation occurred, and ethyl 2-phenylethyl ether was quantitatively obtained.

In conclusion, we elucidated that the (styrene)$Cr(CO)_3$ complexes underwent regioselective nucleophilic addition of various heteronucleophiles such as alcohols, amines, and thiols, and the corresponding products were obtained in moderate to excellent yields. The structural details and features of the product complexes were also elucidated.

EXPERIMENTAL SECTION

Experimental Procedure for a Nucleophilic Addition of EtOH. (Styrene)$Cr(CO)_3$ (**1a**) (20.4 mg, 0.085 mmol), KOH (7.2 mg, 0.13 mmol), and EtOH (0.10 mL, 1.7 mmol) were dissolved in THF (0.20 mL) in a Schlenk tube. The solution was stirred at 60 °C for 45 h. After the volatiles were evaporated, the obtained crude products were purified by thin-layer chromatography (hexane/AcOEt, 5/1) to give analytically pure **2aa** (77%) as a yellow solid.

ASSOCIATED CONTENT

Supporting Information. Complete experimental procedures, spectral characterization for arene-$Cr(CO)_3$ as β-addition products, and X-ray structural details for complexes **2aa** and **3aa**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(3) Byers, J. H.; Janson, N. J. *Org. Lett.* **2006**, *8*, 3453.

(4) As far as we know, there is no example of the nucleophilic addition of oxygen and sulfur nucleophiles to (styrene)$Cr(CO)_3$ complexes. There are only a few examples of the addition of nitrogen nucleophiles to styrene derivative−$Cr(CO)_3$ complexes: (a) Blagg, J.; Davies, S. G. *J. Chem. Soc., Chem. Commun.* **1985**, 653. (b) Sainsbury, M.; Williams, C. S.; Naylor, A.; Scopes, D. I. C. *Tetrahedron Lett.* **1990**, *31*, 2763. (c) Sainsbury, M.; Mahon, M. F.; Williams, C. S.; Naylor, A.; Scopes, D. I. C. *Tetrahedron* **1991**, *47*, 4195.

(5) When complex-free styrene was tested under the conditions of entry 5 in Table 1, no reaction proceeded.

(6) We checked the inverse reaction: when complex **2aa** was submitted to the same reaction conditions of entry 5 in Table 1, (styrene)$Cr(CO)_3$ complex **1a** was obtained in 14% yield along with the recovery of complex **2aa** (78%).

(7) We examined the reaction under nonprotic conditions using EtONa as a nucleophile and MeI as a trapping agent of the carbanion, but no addition product was detected.

(8) The reaction of **1a** did not proceed at 40 °C.

(9) We also checked the inverse reaction of thiol-adduct **4aa**, but complex **1a** was not obtained at all.

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