Radical Aromatic Substitutions on (η^6-Chloroarene)tricarbonylchromium Complexes

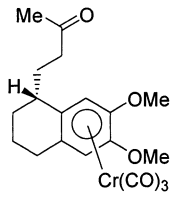
Hechun Lin,[‡] Li Yang,[‡] and Chaozhong Li*[,†]

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, People's Republic of China, and State Key Laboratory of Applied Chemistry, Lanzhou University, Gansu, Lanzhou 730000, People's Republic of China

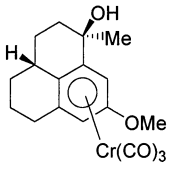
Received June 12, 2002

Summary: Successful radical aromatic substitutions on chloroarene−Cr(CO)$_3$ complexes were carried out by reaction with SmI$_2$ and a carbonyl compound in THF/HMPA at −30 to −40 °C to afford the corresponding products in 66−89% yield. Deuterated experiments revealed that the mechanism was preferably meta-tele-substitution.

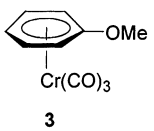
Nucleophilic aromatic substitutions on halogenated arene metal complexes are one of the unique characteristics of organometallic chemistry and have attracted considerable interest in organic synthesis.[1] However, successful free radical substitutions on haloarene metal complexes have never been reported, although attempts to carry out such transformations could be traced back to the 1950s.[2] Recently, a few examples of intramolecular radical substitutions on (η^6-methoxybenzene)−Cr(CO)$_3$ derivatives were reported by Schmalz et al. which led to the demethoxylated products (e.g., **1** and **2**).[3] However, the general picture of the intermolecular radical substitution chemistry remains obscure. We report here the first examples of radical substitutions on chloroarene−Cr(CO)$_3$ complexes by reaction with SmI$_2$ and ketones or aldehydes.[4]



1

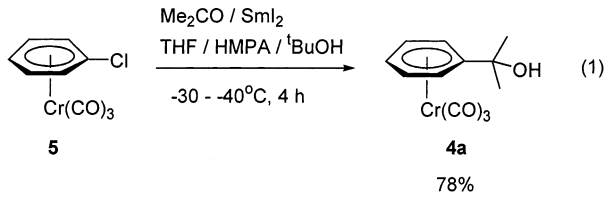


2



3

Reaction of anisole−Cr(CO)$_3$ complex (**3**) with SmI$_2$ and acetone at various reaction conditions yielded no product or only a trace amount of PhC(OH)Me$_2$−Cr(CO)$_3$ (**4a**), while more than 90% of the starting material **3** was recovered. However, when we treated chlorobenzene−Cr(CO)$_3$ (**5**) with SmI$_2$ (4 equiv) and acetone (2 equiv) in THF/HMPA with t-BuOH (2 equiv) as the proton source at 0 °C for 4 h, 63% of the substitution product **4a** was obtained. When the reaction was carried out at lower temperature (−30 to −40 °C) for 4 h, **4a** was achieved in 78% yield along with 14% of the dechlorination product benzene−Cr(CO)$_3$ and 7% of **5** was recovered (eq 1). Other ketones and even aldehydes underwent similar reactions, and the results are listed in Table 1.



5 **4a** 78% (1)

To gain more information on the radical substitution pattern, we chose *o*-, *m*-, and *p*-chlorotoluene−Cr(CO)$_3$ complexes to subject to the reaction with SmI$_2$/acetone, and the results are presented in Table 2. The reaction of *m*-chlorotoluene−Cr(CO)$_3$ complex **6** with Me$_2$CO/SmI$_2$ afforded **7** in 74% yield as the only product, while *o*-chlorotoluene−Cr(CO)$_3$ (**8**) yielded two substitution products, **7** (32%) and **9** (43%). For *p*-chlorotoluene−Cr(CO)$_3$ (**10**), the reaction was slightly slower, and only 36% yield of substitution products were isolated within 4 h while 53% of the starting **10** was recovered. However, when the reaction was carried out for a longer period of time (12 h), the substitution products **11** (18%) and **7** (55%) were achieved in satisfactory overall yield (73%).

As can be seen in Table 2, complexes **8** and **10** gave both *cine*- and *tele*-substitution products, while no *ipso*-substitution products could be detected. This regioselectivity is different from that in ordinary homolytic aromatic substitutions[5] or that in nucleophilic aromatic substitutions on chloroarene−Cr(CO)$_3$ complexes,[1] in which *ipso*-substitutions are observed in many cases. The results prompted us to check the reactions of **5** and **6** that appear to proceed via the *ipso*-substitution process. Thus, *p*-D-chlorobenzene−Cr(CO)$_3$ complex (**12**)[6]

* Corresponding author. E-mail: clig@pub.sioc.ac.cn.
† Shanghai Institute of Organic Chemistry.
‡ State Key Laboratory of Applied Chemistry.

(1) (a) Semmelhack, M. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 4, p 517. (b) Semmelhack, M. F. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: New York, 1995; Vol. 12, p 979. (c) Pape, A. R.; Kaliappan, K. P.; Kundig, E. P. *Chem. Rev.* **2000**, *100*, 2917.

(2) Nicholls, B.; Whiting, M. C. *J. Chem. Soc.* **1959**, 551.

(3) (a) Schmalz, H.-G.; Siegel, S.; Bats, J. W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2383. (b) Schmalz, H.-G.; Siegel, S.; Schwarz, A. *Tetrahedron Lett.* **1996**, *37*, 2947. (c) Hoffmann, O.; Schmalz, H.-G. *Synlett* **1998**, 1426. (d) Schwarz, O.; Brun, R.; Bats, J. W.; Schmalz, H.-G. *Tetrahedron Lett.* **2002**, *43*, 1009.

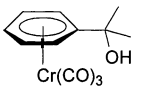
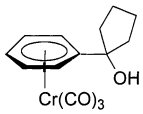
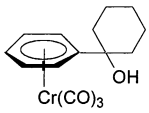
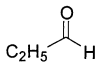
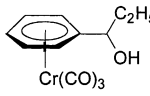
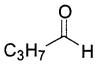
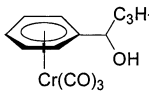
(4) For reviews on SmI$_2$-mediated radical reactions, see: (a) Molander, G. A. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: New York, 2001; Vol. 1, p 153. (b) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307.

(5) Studer, A.; Bossart, M. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: New York, 2001; Vol. 2, p 62.

(6) Takamuku, S.; Hori, H. M. A.; Sakurai, H. *J. Am. Chem. Soc.* **1980**, *102*, 1441.

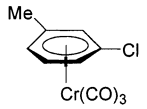
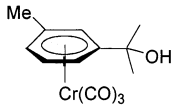
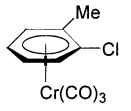
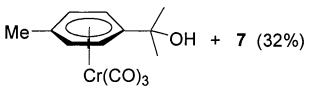
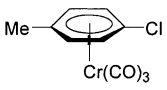
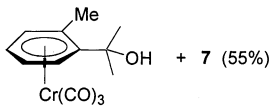
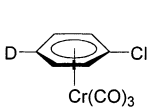
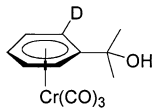
10.1021/om020466l CCC: $22.00
Publication on Web 08/22/2002

Table 1. Reactions of Chlorobenzene−$Cr(CO)_3$ Complex 5 with SmI_2/R^1R^2CO

carbonyl comound	product[a]		yield (%)[b]
		**4a**	78
		**4b**	89
		**4c**	66
		**4d**	70
		**4e**	75

[a] Reaction conditions: SmI_2 (4 equiv), a carbonyl compound (2 equiv), t-BuOH (2 equiv) in THF/HMPA, −30 to −40 °C, 4 h. [b] Isolated yield based on **5**. Dechlorination products were also formed in 5-15% yield along with the starting complexes recovered (6−15%).

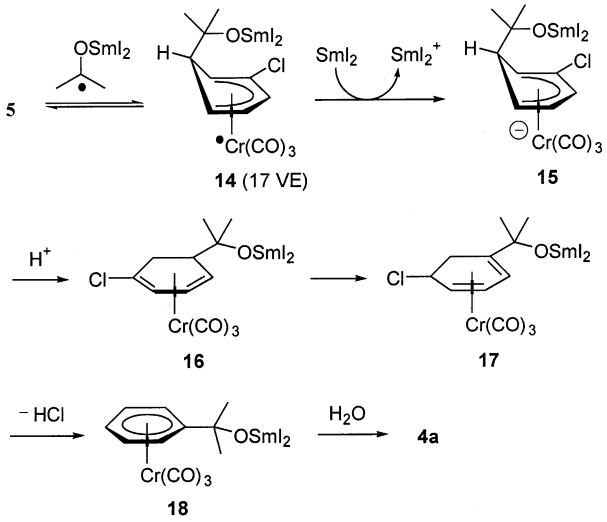
Table 2. Reactions of Chloroarene−$Cr(CO)_3$ Complexes with SmI_2/Me_2CO

substrate	products (yield)[a,b]
 **6**	 **7** (74%)
 **8**	 **9** (43%)
 **10**[c]	 **11** (18%)
 **12**	 **13** (77%)

[a,b] See Table 1. [c] Reaction time: 12 h.

was subjected to the reaction with SmI_2/Me_2CO under the same experimental conditions above and *o*-D-PhC-$(OH)Me_2$−$Cr(CO)_3$ (**13**) was achieved in 77% yield as the sole product, demonstrating that the substitution on **5** occurred at the *meta*-position exclusively. This result, along with the formations of **7** (from **6**), **9**, and **11**, indicates that *meta-tele*-substitution is the preferred mode in the radical aromatic substitution reactions of chloroarene−$Cr(CO)_3$ complexes. The formation of **7** in all the chlorotoluene cases also implies the strong directing effect of the methyl group on radical addition at the *meta*-position.

Scheme 1. Proposed Mechanism for *meta-tele*-Substitution



On the basis of the above results, a plausible mechanism could be drawn for the aromatic substitution reactions as outlined in Scheme 1. The probably reversible radical addition to the arene ring generates the 17-VE intermediate **14**, which is then reduced by SmI_2 to give the 18-VE intermediate **15**.[3,7,8] Acidification of **15** to **16** followed by rearrangement to **17** and subsequent elimination of HCl affords the product **4a**, which resembles the mechanism of nucleophilic aromatic substitutions.[9] The *cine*-substitution might follow a similar mechanism.

In conclusion, we demonstrate that chloroarenetricarbonylchromium complexes readily undergo radical aromatic substitution reactions with SmI_2 and an aldehyde or ketone. The reactions exhibit a unique regioselectivity in that *meta-tele*-substitution is strongly preferred, while no *ipso*-substitution can be observed. The methyl substitution on the phenyl ring shows the *meta*-directing effect on the radical addition. Detailed investigations of the above radical substitution mechanism and its implications in organic synthesis are currently in progress.

Acknowledgment. This project is supported by the Hundreds of Talent program of the Chinese Academy of Sciences, by the National Natural Science Foundation of China, and by the QiMingXing program of the Shanghai Municipal Scientific Committee.

Supporting Information Available: Typical experimental procedure for the synthesis of **4**, **7**, **9**, and **11**, characterization of **4**, **7**, **9**, **11**, and **13**, and X-ray crystal structures of **4a**, **7**, **9**, and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM020466L

(7) Merlic, C. A.; Miller, M. M.; Hietbrink, B. N.; Houk, K. N. *J. Am. Chem. Soc.* **2001**, *123*, 4904.
(8) Lin, H.; Zhang, H.; Yang, L.; Li, C. *Org. Lett.* **2002**, *4*, 823.
(9) For examples, see: (a) Rose-Munch, F.; Rose, E.; Semra, A. *J. Chem. Soc., Chem. Commun.* **1987**, 942. (b) Rose-Munch, F.; Rose, E.; Semra, A.; Jeannin, Y.; Robert, F. *J. Organomet. Chem.* **1988**, *353*, 53. (c) Rose-Munch, F.; Rose, E.; Semra, A.; Mignon, L.; Garcia-Oricain, J.; Knobler, C. *J. Organomet. Chem.* **1989**, *363*, 297.