

Comparison of (η^6 -Fluoroarene)tricarbonylchromium Complexes with Their Chloro-analogs in Radical Aromatic Substitutions[†]

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Reactions of fluoroarene-Cr(CO)₃ complexes with SmI₂ and carbonyl compounds in THF/HMPA at -40—-60 °C afforded the corresponding radical aromatic substitution products in high yield. Compared to the corresponding chloroarene-Cr(CO)₃ complexes, fluoroarene-Cr(CO)₃ complexes showed a higher efficiency and slightly lower regioselectivity.

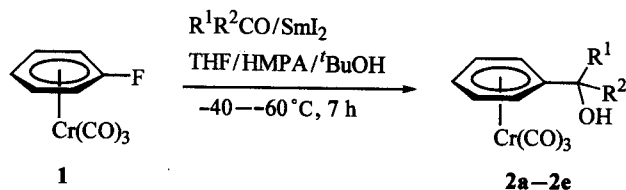
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Complexation of an arene ring by a transition metal dramatically alters its electronic nature, resulting in the remarkable enhancement in reactivity of the arene ring toward nucleophilic addition.¹ While nucleophilic addition to arene-metal complexes has been widely studied and utilized in organic synthesis, fewer works²⁻⁵ have been reported on the radical addition to arene-metal complexes and the chemistry is far from being well established. Schmalz *et al.*² first discovered the intramolecular ketyl or azaketyl radical addition and substitution reactions of methoxylated arene-Cr(CO)₃ complexes to give the corresponding demethoxylated products. Merlic and co-workers tested the competition between intramolecular addition to a Cr(CO)₃ complexed arene and intramolecular addition to a non-complexed arene using PhCH(CD₂I)Ph-Cr(CO)₃ as the model and observed a 2:1 preference for radical addition to the non-complexed arene.³ In contrast, they estimated from competition experiments that intermolecular ketyl radical addition to benzenetricarbonylchromium is faster than that attack on benzene by a factor of at least 100,000.³ Later, we successfully carried out the intermolecular radical aromatic substitutions on chloroarene-Cr(CO)₃ complexes by the reaction with SmI₂ and carbonyl compounds.⁵ To further explore the scope of the intermolecular radical substitutions, we here choose fluoroarene-Cr(CO)₃ complexes to substitute for chloroarene-Cr(CO)₃ complexes in reactions with SmI₂ and carbonyl compounds.⁶

Reaction of fluorobenzene-Cr(CO)₃ (**1**) with acetone (2 equiv.) and SmI₂ (4 equiv.) in THF/HMPA at

-40—-60 °C underwent smoothly to afford the corresponding substitution product **2a** in almost quantitative yield. Other ketones and even aldehydes showed similar behavior and the results are listed in Scheme 1. With ketones, excellent yields of substitution products **2** were achieved, while the yields with aldehydes were lowered. The reactions were very clean and no byproduct could be detected except that a small amount of starting material **1** was recovered in some cases.

Scheme 1



2a: R¹ = R² = Me (97%); **2b:** R¹R² = (CH₂)₄ (95%);
2c: R¹R² = (CH₂)₅ (94%); **2d:** R¹ = Et, R² = H (82%);
2e: R¹ = Pr, R² = H (81%)

While dechlorination always occurred in some extent in the reaction of chlorobenzene-Cr(CO)₃,⁵ there was no defluorination product observed in the reaction of **1**. Compared with chlorobenzene-Cr(CO)₃, the fluoro-analog **1** apparently showed a higher efficiency in the radical substitution reactions.⁷

In order to gain more information on the reaction pattern of fluoroarene-Cr(CO)₃ complexes, we chose *o*-, *m*- and *p*-fluorotoluene-Cr(CO)₃ (*o*, *m*, *p*-**3**)⁸ and complex **4**⁸ bearing an electron-withdrawing group as the model substrates and subjected them to the reactions with SmI₂ and a ketone or an aldehyde (Fig. 1). The results are summarized in Table 1.

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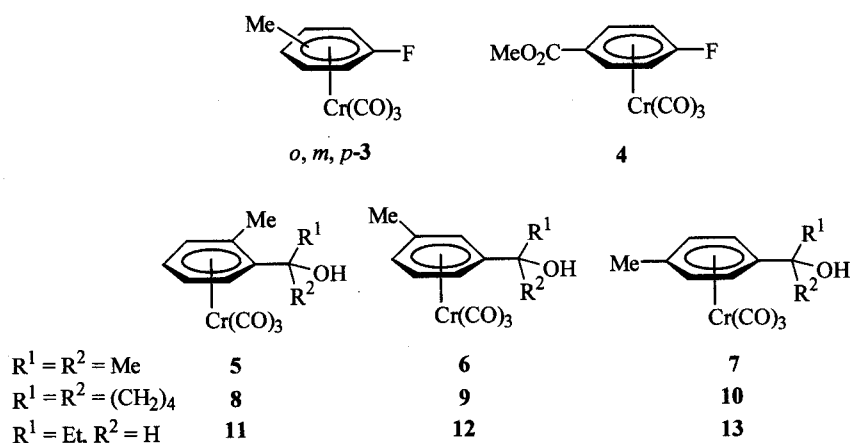


Fig. 1 Substrates **3** and **4** and their substitution products **5**—**13**.

Table 1 Reactions of fluorotoluene- Cr(CO)_3 complexes **3** with $\text{SmI}_2/\text{R}^1\text{R}^2\text{CO}$

| Entry | $\text{R}^1\text{R}^2\text{CO}$ | 3 | Yield ^a (%) | Products/Yields ^a (%) | | |
|-------|---------------------------------|---------------------|------------------------|----------------------------------|-----------|-----------|
| | Acetone | | | 5 | 6 | 7 |
| 1 | | <i>o</i> - 3 | 82 | 0 | 19 | 63 |
| 2 | | <i>m</i> - 3 | 96 | 0 | 89 | 7 |
| 3 | | <i>p</i> - 3 | 79 | 14 | 62 | 3 |
| | Cyclopentanone | | | 8 | 9 | 10 |
| 4 | | <i>o</i> - 3 | 79 | 0 | 24 | 55 |
| 5 | | <i>m</i> - 3 | 96 | 0 | 93 | 3 |
| 6 | | <i>p</i> - 3 | 75 | 9 | 64 | 2 |
| | Propionaldehyde | | | 11 | 12 | 13 |
| 7 | | <i>o</i> - 3 | 51 | 13 | 20 | 18 |
| 8 | | <i>m</i> - 3 | 61 | 9 | 52 | 0 |
| 9 | | <i>p</i> - 3 | 65 | 30 | 35 | 0 |

^a Isolated yield based on **3**.

The reactions of **3** with acetone were compared with those of chlorotoluene- Cr(CO)_3 complexes in the literature.⁵ The reaction of *o*-**3** with acetone afforded **6** (19%) and **7** (63%), similar to the reaction of *o*-chlorotoluene- Cr(CO)_3 which also produced **6** (32%) and **7** (43%). Treatment of *m*-**3** with acetone gave **6** (89%) and **7** (7%), while *m*-chlorotoluene- Cr(CO)_3 gave exclusively **6** (74%). For *p*-**3**, all the three substitution products **5** (14%), **6** (62%), **7** (3%) were isolated, while **5** (18%) and **6** (55%) but no **7** were achieved in the *p*-chlorotoluene- Cr(CO)_3 case. The above comparisons clearly demonstrate that the reactions of **3** with acetone closely parallel those of chloroarene- Cr(CO)_3 complexes, indicating that fluorine atom also shows *meta-tele*-directing effect in the radical substitution as chlorine atom does.⁵ The difference between chloro- and fluoro-complexes is that *ipso*-substitution (Entry 3, Table 1) and *cine-tele*-substitution (Entry 2, Table 1) were also observed in the reactions of fluoro-containing complexes, but in minor amounts. These results also indicate that the reactions of fluoroarene- Cr(CO)_3 complexes are less regioselective than those of chloro-substituted ones.

Cyclopentanone gave similar results as acetone.

When propionaldehyde was used, both the yield and the regioselectivity were lower.

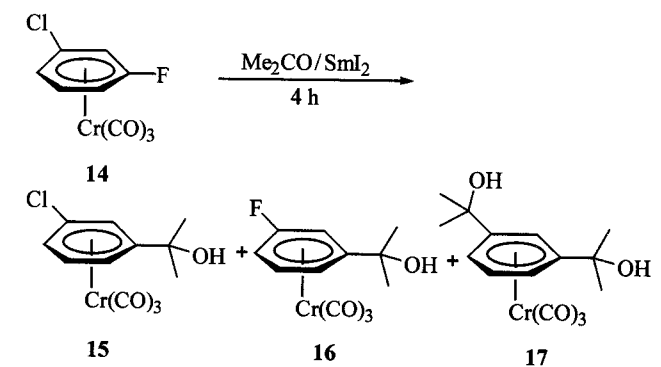
The reaction of *o*-**3** with propionaldehyde gave all the three substitution products **11**—**13** in about equal amount (Entry 7, Table 1). The reaction of *p*-**3** with propionaldehyde/ SmI_2 afforded the *meta-tele*- and *cine-tele*-substituted products in the ratio of 30:35 (Entry 9, Table 1), in which the *meta-tele*-substitution was significantly increased compared to that in acetone or cyclopentanone case. This might be attributed to the decreased steric hindrance of the radical in the reactions of propionaldehyde. The result also implies that the intensities of *meta-tele*-directing effects of methyl group and fluorine atom are at about the same level.

For substrate **4** bearing an electron-withdrawing group, its reaction with SmI_2 /acetone under the same experimental conditions was messy with no expected product isolated and the reason is still unknown.

To further compare the reactions of fluoro- and chloroarene complexes, we chose *m*-chlorofluorobenzene- Cr(CO)_3 (**14**)⁸ as the substrate. The reactions with SmI_2 /acetone were quenched before they were completed (35%—40% of **14** recovered in each case). The results

are presented in Scheme 2. When only one equivalent of acetone and two equivalents of SmI_2 were used, both the substitution for fluoride (product **15**) and the substitution for chloride (product **16**) occurred at 0 °C or lower temperature and the ratio was around 3 to 1 with the substitution for fluoride preferred. When the amounts of acetone and SmI_2 were doubled, further substitution also occurred to produce **17**, while the ratio of **15** to **16** was still 3 : 1 with 40% of **14** remained (Scheme 2).

Scheme 2 Reactions of complex **14** with SmI_2 /acetone



| Me_2CO (equiv.) | SmI_2 (equiv.) | Temp. (°C) | 15 ^a (%) | 16 ^a (%) | 17 ^a (%) |
|------------------------------------|----------------------------|---------------|-------------------------------|-------------------------------|-------------------------------|
| 1 | 2 | 0—4 | 23 | 8 | 4 |
| 1 | 2 | -40—-60 | 34 | 12 | trace |
| 2 | 4 | -40—-60 | 19 | 7 | 8 |

^a Isolated yield based on **14**.

Although no detailed kinetic studies have been done, it seems from the above results that the reaction rates of fluorobenzene- $\text{Cr}(\text{CO})_3$ complexes are only slightly higher than those of the corresponding chlorobenzene- $\text{Cr}(\text{CO})_3$ complexes, unlike the difference in their nucleophilic reactions.⁹

In conclusion, we have demonstrated that (η^6 -fluoroarene)-tricarbonylchromium complexes readily undergo radical aromatic substitution reactions with SmI_2 and an aldehyde or ketone. The reactions show similar behavior to the chloroarene- $\text{Cr}(\text{CO})_3$ complexes. The reactions proceed under milder conditions and in higher yield than the corresponding chloro-substituted complexes. However, competition experiments indicate that the relative reaction rates are very close, with the replacement of fluoride slightly faster.¹⁰

Experimental

THF were dried over sodium under nitrogen and freshly distilled prior to use. Melting points were not corrected. (η^6 -Fluoroarene) tricarbonylchromium complexes **1**, **3**, **4**, and **14** were prepared according to the reported methods.⁹ SmI_2 /THF were prepared from samarium and CH_2I_2 in THF.¹⁰

General procedure for radical substitution reactions

To a degassed HMPA (1 mL) was added the solution of SmI_2 in THF (16 mL, 1.6 mmol, 0.1 mol/L) resulting in a color change from blue to violet. The solution was cooled down to -60 °C and stirred for 5 min, and a thoroughly degassed THF (3 mL) solution of fluorobenzene-tricarbonylchromium (**1**) (92.8 mg, 0.4 mmol), acetone (58.7 μL , 0.8 mmol) and *t*-BuOH (59.2 mg, 0.8 mmol) was added via cannula. The solution was stirred at -40—-60 °C for 7 h. The resulting mixture was warmed up to r.t. and water (2 mL) was added. After stirring at r.t. for 2 h, the reaction mixture was extracted with ether (3 \times 35 mL) and the combined organic phase washed with aqueous NaHSO_3 (3 \times 40 mL) and then dried over anhydrous Na_2SO_4 . After removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with ethyl acetate/hexane (1/10, V/V) as the eluent to give pure **2a** as a yellowish solid. M.p. 76—77 °C.⁵

η^6 -[1-(1-Hydroxycyclopentyl)-3-methylbenzene] tricarbonylchromium (**9**) Yellowish oil; ¹H NMR (CDCl_3 , 300 MHz) δ : 1.80—2.08 (m, 9H), 2.22 (s, 3H), 5.19 (d, *J* = 4.5 Hz, 1H), 5.35—5.48 (m, 3H); ¹³C NMR (CDCl_3 , 300 MHz) δ : 20.8, 24.4, 42.3, 81.7, 88.1, 91.5, 92.5, 94.0, 109.3, 120.5, 233.7; IR (KBr) ν : 3580, 1954, 1872 cm^{-1} ; EIMS *m/z* (%): 312 (M^+ , 14), 256 (4), 228 (18), 210 (100), 159 (5), 105 (24), 91 (35), 52 (59). Anal. calcd for $\text{C}_{15}\text{H}_{16}\text{CrO}_4$: C 57.69, H 5.16; found C 57.61, H 5.34.

η^6 -[1-(1-Hydroxycyclopentyl)-4-methylbenzene] tricarbonylchromium (**10**) Yellowish oil; ¹H NMR (CDCl_3 , 300 MHz) δ : 1.79—2.05 (m, 9H), 2.20 (s, 3H), 5.15 (d, *J* = 6.0 Hz, 2H), 5.69 (d, *J* = 6.0 Hz, 2H); ¹³C NMR (CDCl_3 , 300 MHz) δ : 20.3, 24.1, 42.3, 81.6, 92.0, 92.9, 109.8, 115.5, 125.0, 128.9, 233.6; IR (KBr) ν : 3578, 1955, 1867 cm^{-1} . EIMS *m/z* (%): 312 (M^+ , 18), 256 (5), 228 (23), 210 (100), 159 (13), 105 (38), 91 (19), 52 (60). Anal. calcd for $\text{C}_{15}\text{H}_{16}\text{CrO}_4$: C 57.69, H 5.16; found C 57.60, H 5.31.

η^6 -[1-(1-Hydroxypropyl)-2-methylbenzene] tricarbonylchromium (**11**) Mixture of two isomers in about 1:1 ratio; yellowish oil; ¹H NMR (CDCl_3 , 300 MHz) δ : 1.04 (t, *J* = 7.2 Hz, 3H), 1.57—1.80 (m, 3H), 2.18 (s, 3H), 4.56—4.61 (m, 1H), 5.15 (d, *J* = 6.3 Hz, 1H), 5.27 (t, *J* = 6.0 Hz, 1H), 5.39 (t, *J* = 6.0 Hz, 1H), 5.75 (d, *J* = 6.3 Hz, 1H); ¹³C NMR (CDCl_3 , 300 MHz) δ : 10.1, 18.4, 31.2, 69.9, 90.7, 93.6, 93.9, 107.2, 115.2, 142.3, 233.4; IR (KBr) ν : 3594, 1960, 1876 cm^{-1} ; EIMS *m/z* (%): 286 (M^+ , 5), 230 (5), 202 (5), 187 (11), 132 (36), 121 (50), 91 (100), 52 (34). Anal. calcd for $\text{C}_{13}\text{H}_{14}\text{CrO}_4$: C 54.55, H 4.93; found C 54.66, H 5.11.

η^6 -[1-(1-Hydroxypropyl)-3-methylbenzene] tricarbonylchromium (**12**) Mixture of two isomers in about

1:1 ratio. Yellowish oil; ^1H NMR (CDCl_3 , 300 MHz) δ : 1.02 (t, $J = 7.5$ Hz, 3H), 1.57 (br, 1H), 1.66–1.79 (m, 2H), 2.20/2.22 (2s, 3H), 4.26–4.35 (m, 1H), 5.02/5.04 (2s, 1H), 5.14 (d, $J = 6.3$ Hz, 1H), 5.39–5.51 (m, 2H); ^{13}C NMR (CDCl_3 , 300 MHz) δ : 9.97/10.03, 20.7/20.8, 32.4, 73.3/73.4, 86.5/88.3, 89.8/91.5, 92.1/92.3, 94.3/94.5, 109.6/109.9, 117.8/117.9, 233.5; IR (KBr) ν : 3591, 1957, 1868 cm^{-1} ; EIMS m/z (%): 286 (M^+ , 56), 230 (39), 202 (38), 187 (90), 167 (30), 121 (49), 91 (67), 52 (100). Anal. calcd for $\text{C}_{13}\text{H}_{14}\text{CrO}_4$: C 54.55, H 4.93; found C 54.92, H 5.19.

η^6 -[1-(1-Hydroxypropyl)-4-methylbenzene] tricarbonylchromium (13) Mixture of two isomers in about 1:1 ratio; yellowish oil; ^1H NMR (CDCl_3 , 300 MHz) δ : 1.00 (t, $J = 7.8$ Hz, 3H), 1.57 (br, 1H), 1.63–1.78 (m, 2H), 2.20 (s, 3H), 4.17–4.26 (m, 1H), 5.16 (d, $J = 6.9$ Hz, 1H), 5.22 (d, $J = 6.6$ Hz, 1H), 5.36 (d, $J = 6.0$ Hz, 1H), 5.66 (d, $J = 6.3$ Hz, 1H); ^{13}C NMR (CDCl_3 , 300 MHz) δ : 10.0, 20.5, 32.2, 73.3, 91.2, 92.4, 92.6, 03.3, 113.7, 141.8, 233.3; IR (KBr) ν : 3594, 1960, 1876 cm^{-1} ; EIMS m/z (%): 286 (M^+ , 5), 230 (5), 202 (5), 187 (11), 132 (36), 121 (50), 91 (100), 52 (34). Anal. calcd for $\text{C}_{13}\text{H}_{14}\text{CrO}_4$: C 54.55, H 4.93; found C 54.69, H 5.17.

η^6 -[3-Chloro-1-(1-hydroxy-1-methylethyl)benzene] tricarbonylchromium (15) Yellowish oil; ^1H NMR (CDCl_3 , 300 MHz) δ : 1.52 (s, 3H), 1.57 (s, 3H), 1.92 (s, 1H), 5.27 (d, $J = 6.3$ Hz, 1H), 5.43 (t, $J = 6.3$ Hz, 1H), 5.50 (d, $J = 6.3$ Hz, 1H), 5.68–5.73 (m, 1H); ^{13}C NMR (CDCl_3 , 300 MHz) δ : 31.2, 31.3, 70.9, 86.8, 90.0, 91.3, 92.1, 112.0, 122.2, 232.0; IR (KBr) ν : 3594, 1967, 1893 cm^{-1} ; EIMS m/z (%): 306 (M^+ , 1), 288 (18), 256 (10), 232 (16), 204 (34), 152 (18), 115 (31), 52 (100). Anal. calcd for $\text{C}_{12}\text{H}_{11}\text{ClCrO}_4$: C 47.00, H 3.63; found C 47.10, H 3.82.

η^6 -[3-Fluoro-1-(1-hydroxy-1-methylethyl)benzene] tricarbonylchromium (16) Yellowish oil; ^1H NMR (CDCl_3 , 300 MHz) δ : 1.59 (s, 3H), 1.60 (s, 3H), 1.97 (s, 1H), 5.07 (d, $J = 6.0$ Hz, 1H), 5.36–5.42 (m, 1H), 5.48–5.60 (m, 2H); IR (KBr) ν : 3590, 1967, 1874 cm^{-1} ; EIMS m/z (%): 290 (M^+ , 4), 272 (18), 244 (4), 216 (16), 188 (40), 136 (100), 96 (74), 52 (79). HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{FCrO}_4$ 290.0046, found 290.0002.

η^6 -[1,3-Di-(1-hydroxy-1-methylethyl)benzene] tricarbonylchromium (17) Yellowish solid; m. p. 98–99 $^\circ\text{C}$. ^1H NMR (CDCl_3 , 300 MHz) δ : 1.56 (s, 12H), 1.77 (s, 2H), 5.24 (t, $J = 6.3$ Hz, 1H), 5.71 (d, $J = 6.3$ Hz, 2H), 5.96 (s, 1H); IR (KBr) ν : 3574, 1958, 1887, 1855 cm^{-1} ; EIMS m/z (%): 330 (M^+ , 3), 294 (10), 246 (5), 228 (13), 210 (82), 159

(94), 115 (57), 52 (79), 43 (100). HRMS calcd for $\text{C}_{13}\text{H}_{14}\text{CrO}_4$ 330.0559, found 330.0516.

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