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Radical Additions to (η^6-Styrene) Chromium Tricarbonyl

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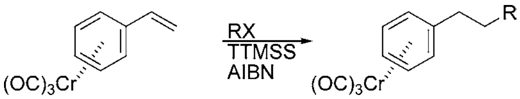
ABSTRACT



Alkyl radical addition reactions to styrene chromium tricarbonyl can be accomplished using alkyl halides and tris(trimethylsilyl)silane in the presence of AIBN in refluxing benzene. The ketyl generated from acetone with SmI_2 in THF/HMPA also underwent successful addition. These addition reactions are believed to proceed through intermediates in which the radical is interacting with an adjacent arene chromium tricarbonyl functionality and do not appear to be complicated by polymerization.

Arene chromium tricarbonyl complexes, first reported nearly 50 years ago,[1] have long proven to be valuable intermediates for organic synthesis due to the significant ways in which the $Cr(CO)_3$ fragment alters reactivity on the arene ring itself, as well as on the vicinal functionality.[2] Over the past few years, significant attention has been directed at the radical activity of these arene−Cr complexes. Reactions involving direct attack of nucleophilic radicals such as SmI_2-ketyls[3] and their imine derivatives[4] have illustrated the activating effect of the $Cr(CO)_3$ fragment toward these additions. Radical intermediates α to arene chromium tricarbonyl complexes have also been observed. The SmI_2-ketyl of benzaldehyde chromium tricarbonyl and its simple derivatives have been trapped with acrylate esters, leading to butyrolactones in high stereoselectivity.[5] Several theoretical studies have concluded that the $Cr(CO)_3$ fragment offers only little, if any, additional stability relative to that observed with the relevant free arene, the benzyl radical,[6] although there is some contradictory data in this regard. Only two reactions proceeding through the intermediacy of a $Cr(CO)_3$-complexed alkyl-substituted benzylic radical have been noted,[3a,6a] and no attempts to develop synthetic methodology arising from this intermediate have been reported.

The ways in which other common transition-metal complexes interact with adjacent radicals have been studied. For example, experimental[7] and theoretical[8] studies have indicated a significant radical stabilizing effect by ferrocene. Radicals stabilized by iron−diene complexes, formally pentadienyl radicals, have been implicated in electrochemical studies,[9] as well as in radical additions to the uncomplexed alkene in iron−triene complexes.[10] Cyclizations of radicals mediated by (alkyne)$Co(CO)_6$[11] and reductive dimerizations of radicals derived from (alkyne)$Co_2(CO)_6$-stabilized cations[12] have also been studied.

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[1] Fisher, E. O.; Ofele, K. *Chem. Ber.* **1957**, *90*, 2532.

[2] Pape, A. R.; Kaliappan, K. P.; Kundig, E. P. *Chem. Rev.* **2000**, *100*, 2917.

[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) Lin, H.; Yang, L.; Li, C. *Organometallics* **2002**, *21*, 3848. (d) Lin, H.-C.; Yang, L.; Li, C.-Z. *Chin. J. Chem.* **2003**, *21*, 797. (e) Schmalz, H.-G.; Kiehl, O.; Gotov, B. *Synlett* **2002**, 1253. (f) Merlic, C. A.; Miller, M. M.; Hietbrink, B. N.; Houk, K. N. *J. Am. Chem. Soc.* **2001**, *123*, 4904.

[4] Hoffmann, O.; Schmalz, H.-G. *Synlett* **1998**, 1426.

[5] (a) Merlic, C. A.; Walsh, J. C. *Tetrahedron Lett.* **1998**, *39*, 2083. (b) Taniguchi, N.; Uemura, M. *Tetrahedron Lett.* **1997**, *38*, 7199.

[6] (a) Merlic, C. A.; Walsh, J. C.; Tantillo, D. J.; Houk, K. N. *J. Am. Chem. Soc.* **1999**, *121*, 3596. (b) Pfletschinger, A.; Dargel, T. K.; Bats, J. W.; Schmalz, H.-G.; Koch, W. *Chem.−Eur. J.* **1999**, *5*, 537. (c) Merlic, C. A.; Hietbrink, B. N.; Houk, K. N. *J. Org. Chem.* **2001**, *66*, 6738.

[7] Creary, X.; Mehrsheikh-Mohammadi, M. E.; McDonald, S. *J. Org Chem.* **1989**, *54*, 2904.

[8] Creary, X. *Org. Lett.* **2000**, *2*, 2069.

[9] Hwang, W.-S.; Liao, R.-L.; Ong, C. W. *Polyhedron* **1989**, *8*, 479.

[10] Wei, L. L.; Lai, M. C.; Ong, C. W. *Tetrahedron Lett.* **2000**, *41*, 3407.

[11] (a) Salazar, K. L.; Nicholas, K. M. *Tetrahedron* **2000**, *56*, 2211. (b) Salazar, K. L.; Khan, M. A.; Nicholas, K. M. *J. Am. Chem. Soc.* **1997**, *119*, 9053.

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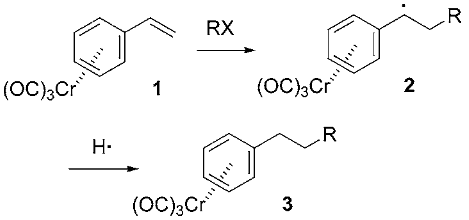
Styrene has long proven to be a classic "test olefin" for radical additions. Nonetheless, it is invariably used in significant excess under radical conditions such as tin hydride additions[13] due, at least in part, to its proclivity for polymerization. On the other hand, styrene chromium tricarbonyl has been demonstrated to diminish the rate of copolymerization with styrene[14] and, in fact, is immune to homopolymerization upon radical initiation with AIBN or benzoyl peroxide.[15] This behavior is somewhat puzzling in light of evidence suggesting little energetic difference between the benzyl radical and its $Cr(CO)_3$-complexed counterpart.[6] Nonetheless, this difference in reactivity might be put to useful ends.

Thus, we sought to examine radical additions to styrene chromium tricarbonyl (**1**), which would presumably proceed through the intermediacy of a radical modified by benzene chromium tricarbonyl (**2**). We envisioned that a process of this type could prove complementary to the existing methodology involving radical additions to free styrene and might prove particularly valuable should circumstances demand that the styrene-based reagent be used as a limiting reagent. This approach would also provide added synthetic value by allowing for direct access to a variety of novel arene chromium tricarbonyl complexes (**3**), as illustrated in Scheme 1. Because **1** is known to be reactive with nucleophiles,[16] we reasoned that it would be most reactive with nucleophilic (electron-rich) radicals.

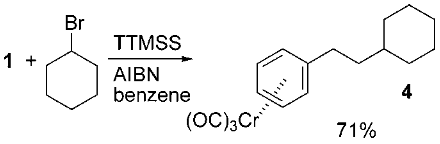
Scheme 1. General Alkyl Radical Addition



The literature procedures for the synthesis of (η^6-styrene) chromium tricarbonyl (**1**) include reaction of styrene with $(NH_3)_3Cr(CO)_3$[17] and $(CH_3CN)_3Cr(CO)_3$[15b] as well as the Wittig reaction with benzaldehyde chromium tricarbonyl.[17,18] We found that **1** could be more conveniently synthesized from styrene in an appropriate scale from commercially available $Cr(CO)_6$ in refluxing *p*-dioxane, albeit in mediocre yield (29%).

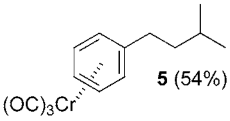
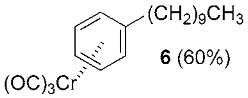
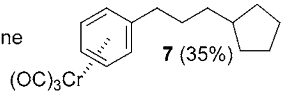
We initially chose to make use of the well-known tin hydride-promoted radical addition conditions[13] to achieve these goals. Initial radical addition attempts involved refluxing a benzene solution of cyclohexyl bromide and **1** in the presence of catalytic AIBN, yielding addition product **4** in only 10% yield. Reasoning that the modest yields were due in part to a slow radical−olefin reaction leading to cyclohexyl radical reduction prior to addition, we modified the reaction conditions by adding Bu_3SnH over 12 h with a syringe pump, which improved the addition product yield to 39%. The best results were eventually obtained with the less-reactive reducing agent tris(trimethylsilyl)silane (TTMSS).[19] This silane can be advantageous when intercepting radicals with olefins because of its slower rate of hydrogen atom donation, diminishing simple reduction of the alkyl halide. Under these conditions, the addition of a cyclohexyl radical to **1** led to formation of **4** in 71% yield (Scheme 2). Unfortunately, synthetically useful yields of **4** could only be obtained when a significant excess of alkyl halide (10 equiv) and TTMSS (5 equiv) was employed. When these conditions were employed using styrene, rather than **1**, only minute traces of the addition product, 2-(cyclohexyl)ethylbenzene, could be detected in the GC/MS of the crude reaction mixture.

Scheme 2. TTMSS-Promoted Radical Addition[a]



[a] Conditions: 0.83 mmol of **1**, 8.3 mmol of cyclohexylbromide, 4.15 mmol of TTMSS, and 0.09 mmol of AIBN, in 12 mL of refluxing benzene, for 18 h.

Table 1. TTMSS-Promoted Radical Reactions

alkyl halide	addition product
2-iodopropane	 **5** (54%)
1-iodooctane	 **6** (60%)
6-bromo-1-hexene	 **7** (35%)

Other successful additions are shown in Table 1. All yields reported are for isolated products, pure by NMR.

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(12) (a) Melikyan, G. G.; Khan, M. A.; Nicholas, K. M. *Organometallics* **1995**, *14*, 2170. (b) Melikyan, G. G.; Combs, R. C.; Lamirand, J.; Khan, M.; Nicholas, K. M. *Tetrahedron Lett.* **1994**, *35*, 363.

(13) Giese, B.; González-Gómez, J. A.; Witzel, T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 69.

(14) Grishin, D. F.; Semyonycheva, L. L.; Illichev, I. S.; Artemov, A. N. *Appl. Organomet. Chem.* **2001**, *15*, 169.

(15) (a) Pittman, C. U., Jr.; Marlin, G. V. *J. Polym. Sci., Part A-1* **1973**, *11*, 2753. (b) Knox, G. R.; Leppard, D. G.; Pauson, P. L.; Watts, W. E. *J. Organomet. Chem.* **1972**, *34*, 347.

(16) Semmelhack, M. F.; Seufert, W.; Keller, L. *J. Am. Chem. Soc.* **1980**, *102*, 6584.

(17) Rausch, M. D.; Moser, G. A.; Zaiko, E. J.; Lipman, A. L. *J. Organomet. Chem.* **1970**, *23*, 185.

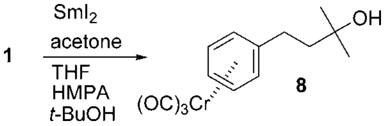
(18) Bitterwolf, T. E.; Dai, X. *J. Organomet. Chem.* **1992**, *440*, 103.

(19) (a) Giese, B.; Kopping, B. *Tetrahedron Lett.* **1989**, *30*, 681. (b) Ballestri, M.; Chatgilialoglu, C.; Clark, K. B.; Griller, D.; Giese, B.; Kopping, B. *J. Org. Chem.* **1991**, *56*, 678.

Addition of the 5-hexenyl radical led only to product **7**, illustrating that radical addition is slower than the hexenyl radical cyclization ($k = 10^6$ s^{-1} at 60 °C).[20] This was not surprising, in light of previous observations that simple reduction of radicals prior to olefin addition was problematic. Attempted addition of the electron-deficient malonate radical generated from diethyl bromomalonate failed as expected, given the electron-deficient character of the olefin in **1**. The attempted addition of phenyl radicals derived from iodobenzene failed, probably because of the very fast rates of H abstraction often seen with the phenyl radical,[21] which precluded olefin addition in this case. Addition of *tert*-butyl radicals from *tert*-butyl bromide showed evidence of success in the crude ^{1}H NMR, but the addition product could not be readily isolated due to its chromatographic mobility, which was identical to that for the excess reagent, TTMSS.

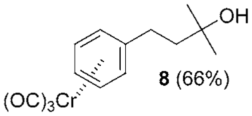
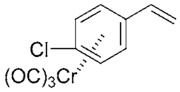
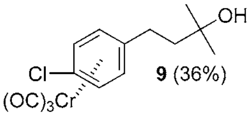
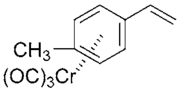
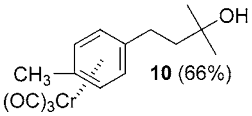
Conjugate intramolecular addition of a SmI_2-ketyl to a dihydronaphthalene chromium tricarbonyl derivative has been observed,[3a] but treatment of styrene chromium tricarbonyl with SmI_2 under aqueous conditions has been shown to lead to olefin reduction.[22] With this in mind, we examined the intermolecular addition of acetone to **1**, as well as to two other similar olefins, upon treatment with SmI_2 in THF/HMPA/*t*-BuOH (Scheme 3).

Scheme 3. SmI_2-Promoted Additions[a]



[a] Conditions: 0.83 mmol of **1**, 4.2 mmol each of acetone, *t*-BuOH, HMPA, and SmI_2 (0.1 M in THF) in 10 mL of refluxing THF, for 18 h.

Table 2. SmI_2-Promoted Additions to Complexed Olefins

Cr-complexed olefin	product
1	 **8** (66%)
	 **9** (36%)
	 **10** (66%)

These conjugate additions proved quite feasible, and successful examples of this process are shown in Table 2. The 4-chloro[23] and 4-methyl[24] styrene chromium tricarbonyl complexes employed were synthesized via the same procedure as that used for **1**, and their NMR spectra matched the literature data. It is interesting to note that although direct addition of SmI_2-ketyls of acetone to benzene chromium tricarbonyl are known[6] no products arising from the conjugate arene addition of this reagent have been observed, illustrating the enhanced reactivity of the exocyclic olefin relative to the arene itself under these conditions.

In summary, we have demonstrated the effectiveness of radical addition to $Cr(CO)_3$ complexes of styrene or substituted styrenes. This approach could prove complementary to known methodology involving radical additions to styrene and is most likely to be useful in cases where it might prove impractical to use excess olefin or when the $Cr(CO)_3$ complex is required for subsequent transformations. In addition, this study sheds further light on the generation and reactivity of radicals modified by benzene chromium tricarbonyl substitution.

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Supporting Information Available: Experimental procedures for **1** and **4**−**10** and spectral data for **4**−**10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317.
(21) Scaiano, J. C.; Stewart, L. C. *J. Am. Chem. Soc.* **1983**, *105*, 3609.
(22) Schmalz, H.-G.; Siegal, S.; Bernicke, D. *Tetrahedron Lett.* **1998**, *39*, 6683.
(23) Khand, I. U.; Murphy, E.; Pauson, P. L. *J. Chem. Res. (M)* **1978**, 4434.
(24) Wilhelm, R.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3808.