

Arene-Metal Complexes. 13. Reaction of Substituted (Benzene)tricarbonylchromium Complexes with *n*-Butyllithium¹

Roger J. Card and Walter S. Trahanovsky*

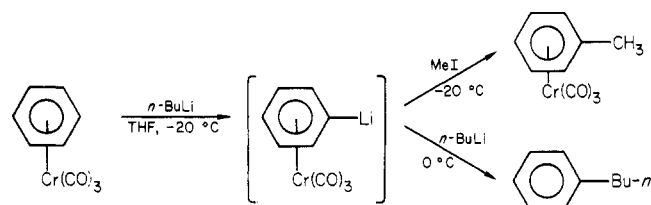
Department of Chemistry, Iowa State University, Ames, Iowa 50011

Received January 9, 1979

Reaction of a series of substituted (benzene)tricarbonylchromium complexes with *n*-butyllithium has been examined. The reaction appears to proceed via proton abstraction to yield an (aryllithium)tricarbonylchromium intermediate which may then be quenched by the addition of primary alkyl halides, usually methyl iodide. New, alkylated complexes may be obtained, or the material may be decomplexed to yield alkylated benzene derivatives. In this manner, (monoalkylbenzene)tricarbonylchromium complexes yield mainly *m*-dialkylbenzenes; (fluorobenzene)tricarbonylchromium yields *o*-fluorotoluene; (anisole)tricarbonylchromium yields mainly 2,6-dimethylanisole; and (*N,N*-dimethylaniline)tricarbonylchromium yields several isomeric *N,N*-dimethyltoluidines. (Iodobenzene)tricarbonylchromium undergoes metal-halogen exchange with *n*-butyllithium and may be converted to either toluene or *n*-butylbenzene depending on the reaction conditions. Comparison with known chemistry of the uncomplexed analogues demonstrates the strongly activating effect of the tricarbonylchromium moiety on these reactions. It is especially interesting that under these conditions reaction of (fluorobenzene)tricarbonylchromium with *n*-butyllithium results in proton abstraction rather than net nucleophilic displacement, as observed when less basic nucleophiles are used.

Reaction of substituted benzene-transition-metal complexes with nucleophiles and bases has received considerable attention over the past two decades. Because of the ease of its addition to and removal from the aromatic nucleus, the tricarbonylchromium group appears to be a very attractive means of temporarily altering the reactivity of aromatic systems. Recently, several reviews of work in this area have appeared.²

Contributions from this laboratory include the initial reports of thermodynamically controlled, stereoselective abstraction of protons α to the π -complexed ring of (arene)tricarbonylchromium complexes³ and of net nucleophilic displacement of ring hydride by base.^{1b} More recently, we have demonstrated that the reaction of (benzene)tricarbonylchromium with *n*-butyllithium proceeds to form (phenyllithium)tricarbonylchromium, which is con-



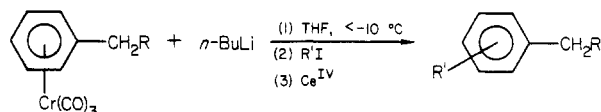
sistent with the work of others,⁴ and that (phenyllithium)tricarbonylchromium may then be alkylated either by the addition of primary alkyl iodides or by further reaction with *n*-butyllithium.^{1a} The rather mild conditions under which these reactions are observed suggest that they may prove to be of synthetic importance.

In order to establish the generality of these reactions we have studied the reaction of *n*-butyllithium with a variety of substituted (benzene)tricarbonylchromium complexes.

This work allows evaluation of both the regioselectivity of the proton abstraction process and the importance of potential competing reaction pathways.

Results and Discussion

A. (Arene)tricarbonylchromium Complexes. The reaction of (arene)tricarbonylchromium complexes with *n*-butyllithium was conducted in dry THF at less than -10°C . The reaction solution was quenched by the addition of methyl iodide, or another alkyl halide, and then oxidized to yield a mixture of alkylated products. Yields were determined by GLC (Table I).



Since α -proton abstraction from (arene)tricarbonylchromium complexes is the thermodynamically favored process,³ the high yield of ring-substituted products clearly demonstrates that proton abstraction by *n*-butyllithium is kinetically controlled and that transmetalation is not important.

A comparison of the difference in conditions required for proton abstraction from the arenes and their tricarbonylchromium complexes is provided by the competitive reaction of equimolar quantities of *p*-xylene and (toluene)tricarbonylchromium with an excess of *n*-butyllithium. Under conditions similar to those above, $3 \pm 1\%$ of the (toluene)tricarbonylchromium was recovered as toluene whereas $84 \pm 4\%$ of the *p*-xylene was recovered unchanged. No products resulting from the methylation of *p*-xylene were observed by GLC.

Also, metalation of toluene requires interaction with the *n*-butyllithium-tetramethylethylenediamine adduct and results in an 89% yield of products derived from α -metalation.⁵

The decreased importance of α -proton abstraction from (toluene)tricarbonylchromium relative to that from toluene (14% vs. 89%) might be due in part to the large steric bulk of the tricarbonylchromium moiety, which effectively blocks one face of the arene from attack. This steric bulk

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Table I. Products and Yields Obtained from the Alkylation of (Arene)tricarbonylchromium Complexes via the Addition of an Alkyl Halide to the Solution Resulting from the Reaction of the (Arene)tricarbonylchromium Complex with *n*-Butyllithium

| arene | alkyl halide | yield of alkylated product, % | |
|---------------------------|---|-------------------------------|--|
| | | α | ring (position) |
| toluene | CH ₃ I | 14 ± 2 | 6 ± 1 (<i>o</i>); 41 ± 1 (<i>m</i>); 22 ± 4 (<i>p</i>) |
| | C ₂ H ₅ Br | ~8 | 10 ± 1 (<i>o</i>); 34 ± 3 (<i>m</i>); ~13 (<i>p</i>) |
| ethylbenzene | CH ₃ I | <1 | 5 ± 0 (<i>o</i>); 49 ± 1 (<i>m</i>); 26 ± 2 (<i>p</i>) |
| <i>tert</i> -butylbenzene | CH ₃ I | -- | 32 ± 2 (<i>m</i>); 22 ± 1 (<i>p</i>) |
| <i>o</i> -xylene | CH ₃ I | 28 ± 2 | 8 ± 2 (3); 50 ± 7 (4) |
| <i>m</i> -xylene | CH ₃ I | 45 ± 1 | 10 ± 2 (4); 33 ± 4 (5) |
| <i>p</i> -xylene | CH ₃ I | 20 ± 3 | 44 ± 3 |
| mesitylene | CH ₃ I | 75 ^a | |
| | <i>n</i> -C ₃ H ₇ I | 71 ^a | |

^a Isolated yield of alkylated complex.

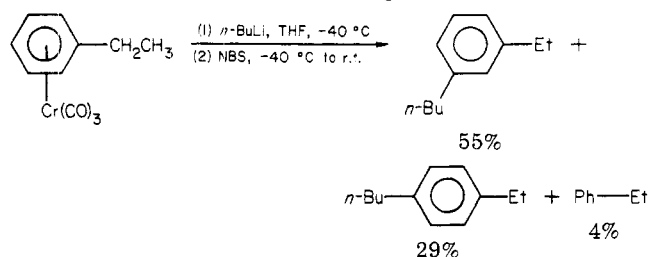
should be more effective in hindering α -proton abstraction than ring-proton abstraction.

It is also possible that proton abstraction is preceded by formation of an adduct involving coordination of the alkyl lithium to an oxygen of a carbonyl ligand. Similar adduct formation has been suggested in the reaction of methyl lithium with (benzene)tricarbonylchromium.⁵ Such an adduct might prefer an orientation where the alkyl group and the carbonyl-butyllithium adduct are as far apart as possible. This is consistent with the observation of products resulting mainly from meta and para proton abstraction.

From the data in Table I, it can be seen that α -substitution of (toluene)tricarbonylchromium by alkyl groups results in a decreased importance of α -proton abstraction; addition of ring methyl substituents increases the importance of α -proton abstraction, which becomes the only process observed for (mesitylene)tricarbonylchromium; and, in general, regioselectivity of proton abstraction is consistent with abstraction of the sterically most accessible protons.

The use of ethyl iodide as the alkylating agent resulted in slightly lower yields than the analogous methyl iodide sequence. Attempted alkylations with isopropyl iodide or *tert*-butyl chloride were unsuccessful.

The reaction of (ethylbenzene)tricarbonylchromium with an excess of *n*-butyllithium was allowed to proceed at -40 °C for 2 h, and then the oxidant *N*-bromosuccinimide (NBS) was added to the resulting solution. A 55 ± 1%



yield of *m*-ethyl-*n*-butylbenzene was obtained. Other products include *p*-ethyl-*n*-butylbenzene (29 ± 6%) and ethylbenzene (4 ± 1%). The reaction of (ethylbenzene)tricarbonylchromium with *tert*-butyllithium under similar conditions results in formation of *m*-ethyl-*tert*-butylbenzene and *p*-ethyl-*tert*-butylbenzene in 58 ± 1 and 5 ± 1% yields, respectively.

Ethylbenzene was recovered unchanged (>95%) after interaction with *tert*-butyllithium at 0 °C for 30 min. A 36% yield of *m*-ethyl-*tert*-butylbenzene was obtained from the reaction of *tert*-butyllithium with (ethylbenzene)tricarbonylchromium at -40 °C for 25 min. These results demonstrate, again, the strong activating influence of the tricarbonylchromium substituent and that NBS is not

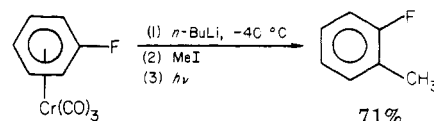
required for the net alkylation by base.

The observation of identical regioselectivity in the methylation and *n*-butylation of ethylbenzene is consistent with the formation of (phenyllithium)tricarbonylchromium as a common intermediate in these reactions.^{1a} In contrast, Semmelhack observes only minor amounts of para alkylation in the reaction of (toluene)tricarbonylchromium with less basic nucleophiles.^{2,7} This difference in regioselectivity is consistent with the postulation of different mechanisms in these reactions—apparently controlled by the nature of the nucleophile. It is therefore of interest that reaction of ethylbenzene with *tert*-butyllithium results in 5% para alkylation. This value lies between that of *n*-butyllithium and those of Semmelhack's bases and suggests that *tert*-butyllithium is a borderline example and that both mechanisms are operative. This is not totally surprising as *tert*-butyllithium is often observed to be more nucleophilic than *n*-butyllithium.⁸

B. (Halobenzene)tricarbonylchromium Complexes.

The reaction of (iodobenzene)tricarbonylchromium with *n*-butyllithium at -30 °C may be quenched by the addition of methyl iodide and the resulting product oxidized to produce toluene in 78 ± 5% yield. If the solution resulting from the reaction of (iodobenzene)tricarbonylchromium and *n*-butyllithium is allowed to warm to 0 °C, or if the reaction is performed initially at 0 °C, *n*-butylbenzene is obtained in 67 ± 3% yield. This chemistry is very similar to that of (benzene)tricarbonylchromium^{1a} and is consistent with the formation of a common intermediate, (phenyllithium)tricarbonylchromium, in these reactions. The reaction of iodobenzene with *n*-butyllithium results in a good yield of phenyllithium,⁹ and the reaction of (iodobenzene)tricarbonylchromium with magnesium produces the corresponding Grignard reagent.¹⁰

The reaction of *n*-butyllithium with (fluorobenzene)tricarbonylchromium at -40 °C was quenched by the addition of methyl iodide, and the products were decomposed on exposure to ultraviolet radiation. *o*-Fluorotoluene was obtained in 71 ± 3% yield. No butylbenzene



was observed by GLC. This result is especially interesting

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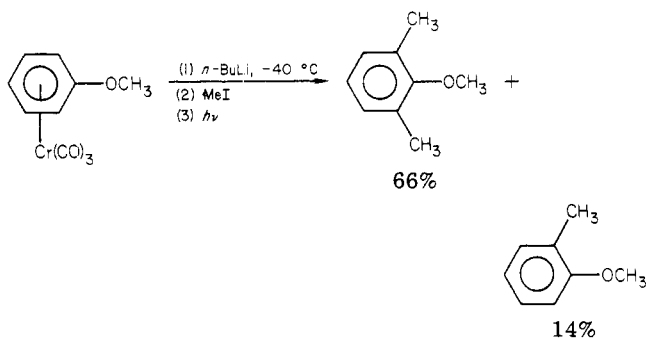
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in light of the very facile displacement of the fluoro group from (fluorobenzene)tricarboxylchromium by a wide variety of less basic nucleophiles.¹¹ Thus, even with this excellent leaving group, nucleophilic addition of *n*-butyllithium to the complexed benzene π system does not compete with proton abstraction. Fluorobenzene undergoes facile ortho metalation upon reaction with *n*-butyllithium.¹²

C. (Anisole)tricarboxylchromium. The reaction of (anisole)tricarboxylchromium with *n*-butyllithium at -40°C was quenched by the addition of methyl iodide, and the resulting products were decomplexed on exposure to ultraviolet radiation. 2,6-Dimethylanisole and 2-

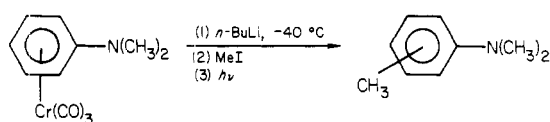


methylanisole were obtained in 66 ± 9 and $14 \pm 0\%$ yields, respectively. The addition of NBS to the reaction mixture at -40°C led to nearly quantitative recovery of anisole after photolytic decomplexation.

The dimetalation of (anisole)tricarboxylchromium occurs under conditions where THF does not appear to be affected. Cleavage of THF occurs more readily than proton abstraction from anisole by *n*-butyllithium.¹³ The observation of selective ortho proton abstraction is consistent with the known regioselectivity of proton abstraction from anisole by alkylolithium reagents.¹²

The observation of dimetalation under these mild conditions is interesting and may prove to be useful in the synthesis of otherwise difficult to obtain materials.

D. (*N,N*-Dimethylaniline)tricarboxylchromium. The reaction of (*N,N*-dimethylaniline)tricarboxylchromium with *n*-butyllithium at -40°C was quenched by the addition of methyl iodide and the resulting solution photolyzed. *N,N*-Dimethyltoluidines were produced in



a combined yield of 62%. The ortho isomer was obtained in 19% yield, and the remainder was a mixture of meta and para isomers which were not separated under the GLC conditions used. The mixture was collected and identified on the basis of its NMR spectrum, which was nearly identical with that of a 1:3 mixture of commercial *p*- and *m*-dimethyltoluidines. Mass spectral data are also consistent with this assignment. Addition of NBS or NCS to the reaction mixture at -40°C resulted in a very poor mass

balance, and no significant amounts of butylated materials were observed.

Reaction of *N,N*-dimethylaniline with *n*-butyllithium results in mainly ortho metalation.¹² The metalation of (*N,N*-dimethylaniline)tricarboxylchromium results in considerably less ortho metalation than its uncomplexed analogue, but more ortho metalation than (ethylbenzene)tricarboxylchromium. The increased ortho metalation relative to (ethylbenzene)tricarboxylchromium demonstrates that the amino group does possess some ortho directing ability. The decreased ortho metalation relative to *N,N*-dimethylaniline itself could be the result of competition between the carbonyl oxygens and the nitrogen to complex the *n*-butyllithium. This is consistent with the fact that the trisubstituted nitrogen is a weaker Lewis base than the oxygen or fluorine substituents of (anisole)tricarboxylchromium and (fluorobenzene)tricarboxylchromium, where exclusive ortho metalation is observed.

Recently Kozikowski and Isobe reported that (*N*-methylindole)tricarboxylchromium undergoes nucleophilic substitution reactions with generation of 7-substituted indoles.¹⁴

Conclusions

These results demonstrate that the reaction of *n*-butyllithium with a variety of substituted (benzene)tricarboxylchromium complexes proceeds by initial proton abstraction. Proton abstraction is observed even in the presence of ring fluorine substituents, which have been shown to be readily displaced by a number of less basic nucleophiles.¹¹

The (aryllithium)tricarboxylchromium complexes are formed in a kinetically controlled process, and the regioselectivity is, in general, very similar to that of the uncomplexed analogues. The exceptions include the decreased importance of alpha relative to ring proton abstraction from (arene)tricarboxylchromium complexes, and a lower ortho selectivity for (*N,N*-dimethylaniline)tricarboxylchromium. The tricarboxylchromium moiety exerts a strong stabilizing influence on the anionic intermediate formed in these reactions and, therefore, allows the reactions to be conducted under very mild conditions.

The $\text{Cr}(\text{CO})_3$ group is a unique substituent for organic aromatic systems in that it can stabilize intermediates with either a positive¹⁵ or negative^{1,2,3,7,11} charge. Moreover, it has the amazing ability to vary the extent of charge donation to an electron-deficient center.¹⁶ This uniqueness, together with the facility of attachment and removal of the $\text{Cr}(\text{CO})_3$ group from aromatic systems, makes it potentially attractive in certain synthetic pathways. However, the wide range of chemistry observed complicates the picture, and further work is necessary to allow an understanding of the controlling factors in these interesting reactions.

Experimental Section

Most equipment and methods have been previously described.¹⁷ The reaction of benzene derivatives with hexacarbonylchromium was performed in glyme-diglyme solvent mixtures as previously described.^{1a} Standard methods of purification were used. Yield data and physical properties are presented in Table II.^{1a,11b,18-21}

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Table II. Yields and Physical Properties of Prepared (Substituted Benzene)tricarbonylchromium Complexes

| substituted benzene | yield, % | melting point, °C | | | NMR data (CCl ₄), δ |
|--|----------|-------------------|-------------|-----|---------------------------------------|
| | | obsd | lit. | ref | |
| toluene | 65 | 79-81 | 82.5-83.5 | 18 | 5.18 (m, 5), 2.20 (s, 3) |
| ethylbenzene | 50, 70 | 47-49 | 48-49 | 19 | 5.20 (m, 5), 2.48 (m, 2), 1.15 (m, 3) |
| <i>tert</i> -butylbenzene | 54 | 79.5-80 | 83.5-84.5 | 18 | 5.22 (m, 5), 1.30 (s, 9) |
| <i>o</i> -xylene | 52 | 88-89 | 90-91.4 | 18 | 5.03 (s, 4), 2.11 (s, 6) |
| <i>m</i> -xylene | 82 | 104-106 | 107-108.5 | 18 | 5.20 (m, 1), 4.79 (m, 3), 2.40 (s, 6) |
| <i>p</i> -xylene | 60 | 95.5-97 | 99-100 | 18 | 5.15 (s, 4), 2.10 (s, 6) |
| mesitylene | 68 | 166-168 | ~165 | 20 | 4.75 (s, 3), 2.18 (s, 9) |
| anisole | 64 | 82-83 | 86-87 | 18 | 5.60-4.60 (m, 5), 3.66 (s, 3) |
| <i>N,N</i> -dimethylaniline ^a | 61, 85 | 142-143 | 145.8-146.5 | 18 | 5.52 (m, 2), 4.75 (m, 3), 2.85 (s, 6) |
| 2,6-dimethylanisole ^{a,b} | 46 | 63-64 | | | 5.03 (m, 3), 3.68 (s, 3), 2.22 (s, 6) |
| fluorobenzene ^c | 20, 25 | 116-118 | 116-117 | 11b | 5.27 (m, 4), 4.70 (m, 1) |
| iodobenzene ^{a,d} | 23, 28 | 110-111 | 111 | 21 | 5.57 (m, 2), 5.21 (m, 3) |

^a Chloroform was the NMR solvent. ^b Exact mass calcd for C₁₂H₁₂CrO₄, 272.0141; found, 272.0135. ^c Freshly sublimed hexacarbonylchromium was used. ^d Prepared as described in ref 1a.

Decomplexation Methods. Method A or B was used for all hydrocarbon arene work. Method C was used when the organic substrate contained fluoro, methoxy, or amino groups.

Method A. The material to be decomplexed (ca. 50 mg) was added to 2 mL of acetonitrile. A 0.2 N CAN solution (1 g of CAN dissolved in 2 mL of water and 8 mL of acetonitrile) was added dropwise until the solution turned nearly colorless and then slightly yellow. The solution was allowed to stand for 10 min and was then extracted with 10 mL of pentane. The pentane solution was washed with water and dried (MgSO₄).

Method B. This method is identical with method A except that an aqueous 0.2 N solution of CAN was added dropwise to an ethereal solution of the complex to be oxidized. This method involves a two-phase oxidation and is free of acetonitrile.

Method C. An ethereal solution (50 mg/10 mL) was irradiated using a sun lamp and water filter. After 1 h the green solution was filtered.

Methylation of Substituted (Benzene)tricarbonylchromium Complexes. Three examples of the general procedure used in the methylation of substituted (benzene)tricarbonylchromium complexes are presented. The reaction of (toluene)tricarbonylchromium presents the general manner in which the alkylation of the (arene)tricarbonylchromium complexes was conducted. The reaction of (anisole)tricarbonylchromium presents the general conditions for the methylation of the heteroatom substituted (benzene)tricarbonylchromium complexes. The reaction of (iodobenzene)tricarbonylchromium is presented because it is unique. The conditions and products from all these runs are presented in Table III. Several products were collected by GLC, and spectral data were obtained. These compounds and their spectral data are presented in Table IV.²³⁻²⁵ In cases where the NMR spectral data are published, the reference is provided without repeating the data. In each of these cases the NMR spectrum obtained from GLC collected material is very nearly identical with the published spectrum. The mass spectra of these products were used only to indicate that a variety of collected products were isomers. For this reason, only the molecular ion region and other characteristic peaks are reported.

Methylation of (Toluene)tricarbonylchromium. (Toluene)tricarbonylchromium (50 mg, 0.22 mmol) was added to 3 mL of cold THF in an argon atmosphere. The temperature was maintained with a dry ice-ethanol-water bath, in this case at -20 °C. *n*-Butyllithium (1 mL, 1.6 M in hexane, 1.6 mmol) was added

by syringe. The resulting solution was stirred at -20 °C for 10 min before 1 mL (10 mmol) of methyl iodide was added. In this case, 13 mg (0.11 mmol) of mesitylene was added. The resulting solution was added to ether, washed with aqueous sodium chloride, dried (MgSO₄), and filtered, and the solution was reduced in volume under reduced pressure. The resulting solution was decomplexed by either method A or B and then analyzed by GLC. Product assignment is consistent with retention times. Ethylbenzene and the xylenes were collected, and spectral data were obtained (Table IV). The identification of *m*-xylene is based on NMR and mass spectral data.

Methylation of (Anisole)tricarbonylchromium. (Anisole)tricarbonylchromium (50 mg, 0.20 mmol) was added to 3 mL of cold THF at -40 °C under an argon atmosphere. *n*-Butyllithium (0.5 mL, 1.6 M in hexane, 0.8 mmol) was added, and the solution was stirred at -40 °C for 25 min. Methyl iodide (1 mL, 10 mmol) was added, and the resulting solution was stirred at -40 °C for 25 min. The solution was poured into ether-water, worked up in the usual manner, and decomplexed by method C. The products were collected by GLC and identified on the basis of spectral data (Table IV).

In addition, the crude reaction product was chromatographed on silica gel using pentane-ether as the eluent. This led to the isolation of (2,6-dimethylanisole)tricarbonylchromium. This material was nearly identical by NMR and IR spectroscopy with the complex obtained on interaction of commercial 2,6-dimethylanisole with hexacarbonylchromium. The NMR data have been presented in Table II. The melting point of the material obtained from the chromatography (42-50 °C) was lower than that of the material prepared by direct complexation. Addition of pure material resulted in an increase in the melting point.

Conversion of (Iodobenzene)tricarbonylchromium to Toluene. Toluene was obtained from (iodobenzene)tricarbonylchromium in a manner very similar to the methylation of (benzene)tricarbonylchromium.^{1a} (Iodobenzene)tricarbonylchromium (70 mg, 0.2 mmol) was added to 3 mL of THF at -30 °C under an argon atmosphere. *n*-Butyllithium (0.8 mL, 1.6 M in hexane, 1.3 mmol) was added, and the resulting solution was stirred at -30 °C for 30 min. Methyl iodide (1 mL, 10 mmol) was added, and the resulting solution was stirred at -30 °C for 15 min. The solution was poured into ether-water and worked up in the usual manner. The resulting solution was decomplexed by method B and analyzed by GLC. A 78 ± 5% yield of toluene and a 2 ± 1% yield of butylbenzene were obtained. The products were identified on the basis of retention times.

Competition Study. (Toluene)tricarbonylchromium (54 mg, 0.24 mmol) and 23 mg (0.22 mmol) of *p*-xylene were added to 3.5 mL of THF. The solution was purged with argon and cooled to -20 °C. *n*-Butyllithium (0.5 mL of 1.6 M in hexane, 0.8 mmol) was added, and the resulting solution stirred at -15 °C for 10 min. Methyl iodide (1 mL, 10 mmol) was added, and the solution was stirred at -15 °C for 10 min and then worked up in the usual manner. Mesitylene (16 mg, 0.13 mmol) was added as standard. The solution was decomplexed by method A and analyzed by GLC (2 m 5% diisodecyl phthalate, 5% Bentone 34 on Chromosorb W at 50 °C). The following yields were obtained: ethylbenzene,

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Table III. Reaction Conditions, Products, and Yields for the Reactions of Substituted (Benzene)tricarboxylchromium Complexes with *n*-Butyllithium Which Were Quenched by the Addition of an Alkyl Halide

| substituted benzene (mmol; M) | temp, °C | alkyl halide ^a | concn of <i>n</i> -BuLi, M | standard | GLC conditions | | products ^c | yield, % |
|--|----------|--|----------------------------|-----------------------------|----------------------|----------|--|--|
| | | | | | col-umn ^b | temp, °C | | |
| toluene (0.22; 0.06) | -20 | | 0.4 | mesitylene | I | 40 | toluene ethylbenzene ^d <i>p</i> -xylene ^e <i>m</i> -xylene ^e <i>o</i> -xylene ^d | 5 ± 1 14 ± 2 22 ± 4 41 ± 1 6 ± 1 |
| toluene (0.22; 0.06) | -10 | C ₂ H ₅ Br | 0.4 | mesitylene | I | 70 | toluene <i>n</i> -propylbenzene <i>p</i> -ethyltoluene <i>m</i> -ethyltoluene <i>o</i> -ethyltoluene | 8 ± 3 ~ 8 ~ 13 34 ± 3 10 ± 1 |
| toluene (0.22; 0.06) | -10 | <i>i</i> -C ₃ H ₇ I | 0.4 | mesitylene | I | 70 | isopropyltoluenes | < 3 |
| toluene (0.22; 0.06) | -10 | <i>t</i> -C ₄ H ₉ Br | 0.4 | isopropylbenzene | I | 70 | <i>tert</i> -butyltoluenes | < 3 |
| ethylbenzene (0.21; 0.05) | -10 | | 0.4 | mesitylene | I | 70 | ethylbenzene <i>p</i> -ethyltoluene <i>m</i> -ethyltoluene <i>o</i> -ethyltoluene | 2 ± 1 26 ± 2 49 ± 1 5 ± 2 |
| <i>tert</i> -butylbenzene (0.40; 0.05) | -15 | C ₂ H ₅ Br | 0.2 | isopropylbenzene | II | 80 | <i>tert</i> -butylbenzene <i>m</i> -ethyl- <i>tert</i> -butylbenzene ^{e,f} <i>p</i> -ethyl- <i>tert</i> -butylbenzene ^{e,f} | 23 ± 5 32 ± 2 22 ± 1 |
| <i>o</i> -xylene (0.21; 0.05) | -20 | | 0.4 | durene | II | 75 | <i>o</i> -xylene <i>o</i> -ethyltoluene 1,2,3-trimethylbenzene 1,2,4-trimethylbenzene | 2 ± 1 28 ± 2 8 ± 2 50 ± 7 |
| <i>m</i> -xylene (0.21; 0.05) | -20 | | 0.2 | indan | II | 75 | <i>m</i> -xylene <i>m</i> -ethyltoluene 1,2,4-trimethylbenzene 1,3,5-trimethylbenzene | 2 ± 1 45 ± 1 10 ± 2 33 ± 3 |
| <i>p</i> -xylene (0.21; 0.05) | -10 | | 0.4 | <i>sec</i> -butylbenzene | II | 75 | <i>p</i> -xylene <i>p</i> -ethyltoluene 1,2,4-trimethylbenzene | 3 ± 1 20 ± 3 44 ± 3 |
| iodobenzene | -30 | | 0.4 | ethylbenzene | I | 65 | toluene | 78 ± 5 |
| fluorobenzene (0.21; 0.05) | -40 | | 0.4 | mesitylene | III | 55 | <i>o</i> -fluorotoluene ^e <i>n</i> -butylbenzene | 71 ± 3 < 1 |
| anisole (0.20; 0.05) | -40 | | 0.2 | <i>N,N</i> -dimethylaniline | II | 90 | 2-methylanisole ^e 2,6-dimethylanisole ^e | 14 ± 0 66 ± 9 |
| <i>N,N</i> -dimethylaniline (0.20; 0.05) | -40 | | 0.2 | anisole | II | 125 | <i>N,N</i> -dimethylaniline <i>o</i> - <i>N,N</i> -dimethyltoluidine ^e <i>m</i> - and <i>p</i> - <i>N,N</i> -dimethyltoluidine ^e | 8 ± 3 19 ± 0 42 ± 4 |

^a Methyl iodide was used unless otherwise indicated. ^b The following columns were used: (I) 2 m 5% diisodecyl phthalate, 5% Bentone 34 on Chromosorb W; (II) 2-m 10% Lac 446 on Chromosorb W; and (III) 4 m 5% diisodecyl phthalate, 5% Bentone 34 on Chromosorb W. ^c All products were identified on the basis of retention time and peak enhancement unless otherwise indicated. ^d Mass spectral data were obtained. ^e NMR and mass spectral data were obtained. ^f Exact mass was determined.

8 ± 0%; *p*-xylene, 93 ± 2%; *m*-xylene, 36 ± 1%; and *o*-xylene, 6 ± 2%. The yields of products listed are based on the consumption of 0.24 mmol of (toluene)tricarboxylchromium. The yields (omitting *p*-xylene) are somewhat lower than those in similar runs in the absence of initial *p*-xylene. If the ratio of *m*- to *p*-xylene formed from the (toluene)tricarboxylchromium is the same in both cases, a 19% yield of *p*-xylene is expected. Thus, unreacted *p*-xylene was recovered in 74% yield based on 0.24 mmol of starting material. Only 0.22 mmol of *p*-xylene was used, and correction for this results in an 84 ± 4% recovery of *p*-xylene. No products which could be due to the alkylation of *p*-xylene were observed by GLC.

(1-Ethyl-3,5-dimethylbenzene)tricarboxylchromium. (Mesitylene)tricarboxylchromium (199 mg, 0.78 mmol) was added to 12 mL of dry THF. The solution was cooled with stirring under argon to -30 °C. *n*-Butyllithium (1.5 mL, 1.6 M in hexane, 2.4 mmol) was added, and the resulting solution was stirred at -30 °C for 15 min. Methyl iodide (2 mL, 20 mmol) was added, and the resulting solution was stirred for 15 min and then taken up in ether. The ethereal solution was washed thoroughly with aqueous sodium chloride, dried (MgSO₄), and concentrated under reduced pressure. Sublimation afforded 158 mg (75%) of a yellow solid: mp 107–110 °C; after recrystallization, 109–110 °C; NMR

(DCCl₃) δ 4.82 (s, 3), 2.46 (q, 2, *J* = 7.5 Hz), 2.20 (s, 6), 1.34 (t, 3, *J* = 7.5 Hz).

Anal. Calcd for C₁₃H₁₄CrO₃: C, 57.78; H, 5.19. Found: C, 57.72; H, 5.08.

(1-Butyl-3,5-dimethylbenzene)tricarboxylchromium was obtained in 71% yield under the conditions described above with the exception that *n*-propyl iodide was used as the quenching agent: NMR (DCCl₃) δ 4.90 (s, 3), 2.30 (m, 2), 2.20 (s, 6), 1.52 (m, 4), 0.96 (m, 3); mp 80–82 °C.

Anal. Calcd for C₁₅H₁₆CrO₃: C, 60.40; H, 6.04. Found: C, 60.28; H, 6.18.

***m*-Ethyl-*tert*-butylbenzene.** (Ethylbenzene)tricarboxylchromium (50 mg, 0.21 mmol) was added to 3 mL of THF at -40 °C under argon. *tert*-Butyllithium (0.6 mL of 2.0 M in pentane, 1.2 mmol) was added, and the resulting solution was stirred for 2 h at -40 °C. *N*-Bromosuccinimide (200 mg, 1.1 mmol) was added and the resulting solution allowed to warm to room temperature over the period of 60 min. Mesitylene (13 mg, 0.11 mmol) was added as standard. The solution was taken up in ether, and the ethereal solution was washed successively with 0.3 N hydrochloric acid, saturated aqueous sodium bicarbonate, and three portions of saturated aqueous sodium chloride (the workup was accompanied by emulsion formation and the presence of a dark solid

Table IV. Spectral and Physical Data of GLC Collected Products Obtained from the Alkylation Sequence Involving the Addition of Alkyl Halides

| product | NMR (CCl ₄) | | mass spectral data (<i>m/e</i>) | | | other |
|---|---|-----|---|------------|-----|---|
| | δ | ref | 70 eV | 16 eV | ref | |
| <i>m</i> -xylene | 6.89 (m, 4) 2.38 (s, 6) | 23a | 106 105 91 | 106 105 | 24 | |
| <i>p</i> -xylene | 6.92 (s, 4) 2.30 (s, 6) | | 106 105 91 | | | solidified on standing at 0 °C lit. ²⁵ mp 13-14 °C |
| <i>o</i> -xylene | | | 106 105 | 106 105 | 24 | |
| ethylbenzene | | | 91 106 105 | 91 106 | 24 | |
| <i>m</i> -ethyl- <i>tert</i> -butylbenzene | 7.06 (s, 4) 2.62 (m, 2) 1.34 (s, 9) 1.26 (m, 3) | | 91 106 105 91 | 91 106 | | exact mass C ₁₂ H ₁₈ calcd 162.140843 obsd 162.138883 |
| <i>p</i> -ethyl- <i>tert</i> -butylbenzene | 7.08 (s, 2) 7.00 (s, 2) 2.57 (m, 2) 1.30 (s, 9) 1.18 (m, 3) | | 162 147 | 162 147 | | exact mass C ₁₂ H ₁₈ calcd 162.140843 obsd 162.138283 |
| <i>o</i> -fluorotoluene | 6.95 (m, 4) 2.27 (d, 3, <i>J</i> = 2.5 Hz) | 23b | 111 (08) 110 (100) 109 (03) | | | |
| <i>o</i> -methylanisole | 6.85 (m, 4) 3.78 (s, 3) 2.18 (s, 3) | 23c | 123 (10) 122 (100) 107 (04) | | | |
| 2,6-dimethylanisole | 6.86 (m, 3) 3.63 (s, 3) 2.23 (s, 6) | 23d | 137 (10) 136 (100) 121 (07) | | | |
| <i>o</i> - <i>N,N</i> -dimethyltoluidine | 7.0-6.75 (m, 4) 2.62 (s, 6) 2.26 (s, 3) | | 136 (11) 135 (100) 134 (06) 120 (06) 105 (06) | | | |
| <i>m</i> - and <i>p</i> - <i>N,N</i> -dimethyltoluidine | 7.1-6.3 (m) 2.86 (s) 2.80 (s) 2.27 (s) 2.21 (s) | | 136 (10) 135 (150) 134 (10) | | | |

insoluble in both the ethereal and aqueous solutions). The organic layer was dried (MgSO₄), filtered, concentrated under reduced pressure, and analyzed by GLC (Lac 446, 90 °C). *m*-Ethyl-*tert*-butylbenzene was obtained in 58 ± 1% yield (two runs). Other products included ethylbenzene (12 ± 1%) and *p*-ethyl-*tert*-butylbenzene (5 ± 1%). The retention times of the alkylated products were identical with those of *m*- and *p*-ethyl-*tert*-butylbenzenes, which had been characterized from the ethylation of (*tert*-butylbenzene)tricarbonylchromium. An NMR spectrum of the crude reaction mixture was consistent with this assignment. When this reaction was conducted at temperatures above -40 °C, low mass balance was received. When the reaction was conducted as above but without the addition of NBS, a 36% yield of *m*-ethyl-*tert*-butylbenzene was received.

***m*-Ethyl-*n*-butylbenzene** was obtained from (ethylbenzene)tricarbonylchromium in 55 ± 1% yield in the manner described above except that *n*-butyllithium (0.6 mL, 1.6 M in hexane, 1 mmol) was the base. Other products included *p*-ethyl-*n*-butylbenzene (29 ± 6%) and ethylbenzene (4 ± 1%). The alkylated products were collected by GLC. *m*-Ethyl-*n*-butylbenzene: NMR (CCl₄) δ 6.9 (m, 4), 2.55 (m, 4) and 1.8-0.8 (m, 10); mass spectrum, *m/e* (relative intensity, 16 eV) 163 (18), 162 (P, 100), 132 (10), 120 (68), 119 (38), 104 (14), and 91 (14). *p*-Ethyl-*n*-butylbenzene: NMR (CCl₄) 6.88 (m, 4), 2.54 (m, 4), 1.8-0.8 (m, 10); mass spectrum, *m/e* (relative intensity, 16 eV) 163 (14), 162 (P, 85), 132 (8), 120 (30), 119 (100), 104 (11) and 91 (11). The NMR spectrum was nearly identical with a published one for this material.²²

***n*-Butylbenzene** was obtained in 67 ± 3% yield from (iodobenzene)tricarbonylchromium in the manner described for the butylation of (benzene)tricarbonylchromium.^{1a}

Attempted Reaction of Ethylbenzene with *tert*-Butyllithium. This reaction was conducted in the manner described for the formation of *m*-ethyl-*tert*-butylbenzene from (ethylbenzene)tricarbonylchromium except that ethylbenzene was substituted for (ethylbenzene)tricarbonylchromium. Greater than 95% recovery of ethylbenzene was observed.

Attempted *n*-butylation of (anisole)tricarbonylchromium was conducted in a manner similar to that described for the *n*-butylation of (ethylbenzene)tricarbonylchromium. No evidence for formation of any butylated materials was observed. A good recovery of anisole was obtained from this reaction.

Attempted *n*-butylation of (*N,N*-dimethylaniline)tricarbonylchromium was conducted as described immediately above. After the usual aqueous workup, the solution was subjected to decomplexation by method C. GLC analysis did not indicate the presence of substantial amounts of either *N,N*-dimethylaniline or the expected alkylated products in the resulting solution.

Acknowledgment. We thank the donors of the Petroleum Research Foundation, administered by the American Chemical Society, for partial support of this research by Grant No. 6605-AC.

Registry No. Tricarbonylchromium toluene, 12083-24-8; tricarbonylchromium ethylbenzene, 12203-31-5; tricarbonylchromium *tert*-butylbenzene, 12110-51-9; tricarbonylchromium *o*-xylene, 12129-29-2; tricarbonylchromium *m*-xylene, 12129-28-1; tricarbonylchromium *p*-xylene, 12129-27-0; tricarbonylchromium mesitylene, 12129-67-8; methyl iodide, 74-88-4; ethyl bromide, 74-96-4;

(25) "Dictionary of Organic Compounds"; Oxford University Press: New York, 1965; Vol. 5, p 2366.

propyl iodide, 107-08-4; ethylbenzene, 100-41-4; *o*-xylene, 95-47-6; *m*-xylene, 108-38-3; *p*-xylene, 106-42-3; propylbenzene, 103-65-1; *o*-ethyltoluene, 611-14-3; *m*-ethyltoluene, 620-14-4; *p*-ethyltoluene, 622-96-8; isopropylbenzene, 98-82-8; *m*-*tert*-butyltoluene, 1075-38-3; *p*-*tert*-butyltoluene, 98-51-1; 3-methyl-*o*-xylene, 526-73-8; 4-methyl-*o*-xylene, 95-63-6; 5-methyl-*m*-xylene, 108-67-8; 5-ethyl-*m*-xylene, 934-74-7; 5-butyl-*m*-xylene, 98-19-1; toluene, 108-88-3; *tert*-butylbenzene, 98-06-6; anisole, 100-66-3; *N,N*-dimethylaniline, 121-69-7; 2,6-dimethylanisole, 1004-66-6; fluorobenzene, 462-06-6; iodobenzene, 591-50-4; tricarboxylchromium anisole, 12116-45-9; tri-

carbonylchromium *N,N*-dimethylaniline, 12109-10-3; tricarboxylchromium 2,6-dimethylanisole, 72207-21-7; tricarboxylchromium fluorobenzene, 12082-05-2; tricarboxylchromium iodobenzene, 12082-06-3; isopropyl iodide, 75-30-9; *tert*-butyl bromide, 507-19-7; *m*-ethyl-*tert*-butylbenzene, 14411-56-4; *p*-ethyl-*tert*-butylbenzene, 7364-19-4; *o*-fluorotoluene, 95-52-3; butylbenzene, 104-51-8; 2-methylanisole, 578-58-5; *o*-*N,N*-dimethyltoluidine, 609-72-3; *m*-*N,N*-dimethyltoluidine, 121-72-2; *p*-*N,N*-dimethyltoluidine, 99-97-8; tricarboxylchromium 1-ethyl-3,5-dimethylbenzene, 72207-22-8; tricarboxylchromium 1-butyl-3,5-dimethylbenzene, 72207-23-9.

Synthetic Applications of Metal Halides. Conversion of Cyclopropylmethanols into Homoallylic Halides

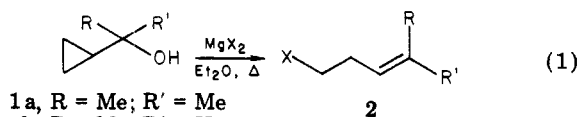
J. P. McCormick* and Donald L. Barton

Department of Chemistry, University of Missouri, Columbia, Missouri 65211

Received November 6, 1979

Magnesium and beryllium halides in refluxing diethyl ether effect the transformation of cyclopropylmethanols into homoallylic halides, in contrast to several other metal halides and Lewis acid/nucleophile combinations which were examined. Magnesium bromide and iodide are particularly effective: conditions are mild, yields are high, and little or no byproducts are formed. Tertiary and benzylic alcohols are more reactive than secondary alcohols, while the latter are converted into *E* homoallylic halides with high stereoselectivity. Cyclopropylmethanol itself fails to react. In the cases of magnesium halide reactions with bicyclo[3.1.0]-2-hexanol and bicyclo[4.1.0]-2-heptanol, addition of an equimolar amount of zinc halide not only caused substantial rate enhancement but also increased regioselectivity.

The transformation of cyclopropylmethanols into homoallylic halides is a useful reaction which has received considerable development and synthetic application,¹ including incorporation into a basic set of reactions for a recent approach to computer-assisted synthesis.^{1k} To date, the most commonly used procedures involve treatment of the appropriate cyclopropylmethanol with 48% hydrobromic acid^{1a,c} or conversion of the alcohol into the corresponding bromide, followed by reaction with zinc bromide.^{1e,f} We have described briefly the use of magnesium halides to effect this transformation (eq 1) directly and



- 1 a, R = Me; R' = Me
 b, R = Me; R' = H
 c, R = H; R' = H
 d, R = Ph; R' = H
 e, R = Me; R' = Et

cleanly in good yields.² This method, which is related to chemistry reported by others,³ offers advantages over other

Table I. Treatment of 2-Cyclopropyl-2-propanol with Metal Halides and with Lewis Acid/Nucleophile Combinations^a

| reagent/solvent ^b | reaction time, h (reflux) | % reaction ^c |
|---|---------------------------|-------------------------|
| MgI ₂ /Et ₂ O | 4 | 100 |
| MgBr ₂ /Et ₂ O | 8 | 100 |
| MgBr ₂ /THF | 2 | <4 |
| MgCl ₂ /Et ₂ O ^d | 71 | 95 |
| CaCl ₂ /Et ₂ O ^d | 16 | 0 |
| CaBr ₂ /Et ₂ O ^d | 48 | <3 |
| CaBr ₂ /THF ^d | 24 | <3 |
| LiI/Et ₂ O | 20 | 0 |
| LiI/THF | 36 | <7 |
| ZnBr ₂ /Et ₂ O | 12 | <1 |
| BeCl ₂ /Et ₂ O | 143 | 85 |
| BeBr ₂ /Et ₂ O | 45 | 95 |
| CuSO ₄ /I ⁻ /Et ₂ O ^d | 66 | 0 |
| MgSO ₄ /I ⁻ /Et ₂ O ^d | 52 | 0 |
| CaCl ₂ /I ⁻ /Et ₂ O ^d | 23 | 0 |

^a Reaction mixtures were sampled at regular intervals and examined by GC. ^b Iodide added as tetrabutylammonium iodide. ^c 2a was the only observed product; yields were determined by GC. ^d Heterogeneous reaction mixture.

procedures: intermediate cyclopropylmethyl halides need not be prepared, cyclobutyl compounds are not obtained as byproducts, and the use of strong mineral acids is avoided.⁴ We now report further on the possible synthetic scope and some mechanistic evidence regarding this transformation.

After initial experiments demonstrated that 2-cyclopropyl-2-propanol (1a) was converted cleanly into 5-

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(4) For some aspects of these difficulties, see ref 1e.