Synthesis of a Brominated Biphenyl Chromium Tricarbonyl Complex

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ABSTRACT

Hydroxycarbene complexes have been proposed as intermediates in industrial processes such as the Fischer-Tropsch process and hydroformylation. As part of the overall synthesis of an aryl-tethered version of a chromium hydroxycarbene complex we have examined three synthetic routes toward the brominated biphenyl chromium tricarbonyl compound (η^6-2'-bromobiphenyl)Cr(CO)$_3$, which is an immediate precursor of our target hydroxycarbene. A direct nucleophilic attack of 1,2-dibromobenzene by phenyllithium-chromium-tricarbonyl failed, and a successful Suzuki coupling route was abandoned due to difficulties in purification of the product. Surprisingly, simply refluxing 2-bromobiphenyl with chromium hexacarbonyl led to isolation of the desired intermediate in high purity, where only the non-brominated biphenyl ring had coordinated to the metal with no evidence of coordination of the brominated ring. This is a crucial intermediate, since metal-halogen exchange would convert it to a "locked" anion that, upon protonation, would provide the desired aryl-tethered hydroxycarbene complex.

INTRODUCTION

In 1995, the tethered rhenium complexes 1 and 2 were reported as the first hydroxycarbene/acyl hydride pair in equilibrium with each other (Figure 1).[1] Since the untethered version of 1 has been shown to exist only as the hydroxycarbene isomer it has been suggested that introduction of an alkyl tether causes strain in the otherwise more stable hydroxycarbene isomer, and relief of this strain is the driving force for the observed rearrangement from 1 to 2.[1-3] Our research efforts have been focused on finding other variations of these hydroxycarbene/acyl hydride pairs since ultimately, molecules that display this equilibrium may act as models for important industrial processes such as the Fischer-Tropsch process and hydroformylation.[4]
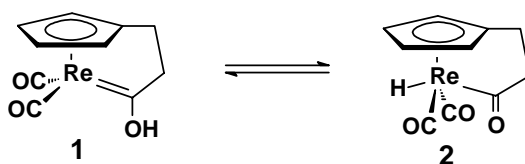

Figure 1. Rhenium hydroxycarbene/acyl hydride equilibrium

In 1992, Merlic synthesized the aryl-tethered methoxycarbene complex {[(1',2',3',4',5',6'-η)-1,1'-biphenyl-2-yl]methoxymethylene}-dicarbonyl-chromium (3).[5] Attempts by Czerwinski and Lueck to synthesize the hydroxycarbene version of this compound using Merlic's route failed, presumably due to the thermal instability of hydroxycarbene complexes.[6] As a result of this failed synthesis, the goal of the current research project became the synthesis of (η^6-2'-bromobiphenyl)Cr(CO)$_3$ (4), which would be a crucial intermediate in an alternate route to the synthesis of the desired aryl-tethered version of a chromium hydroxycarbene complex.
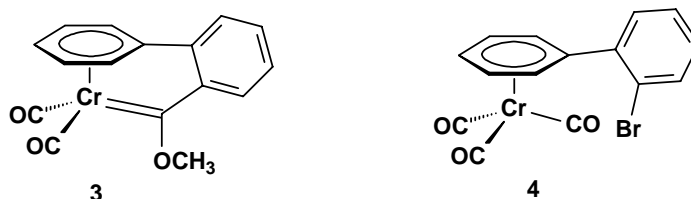
RESULTS AND DISCUSSION

Three routes were explored in an attempt to synthesize $(\eta^6\text{-}2'\text{-bromobiphenyl})Cr(CO)_3$ (**4**) from available starting materials: i) deprotonation of $(\eta^6\text{-}C_6H_6)Cr(CO)_3$ and nucleophilic attack of 1,2-dibromobenzene by the resulting anion, ii) palladium catalyzed Suzuki coupling of $(\eta^6\text{-}C_6H_5Br)Cr(CO)_3$ with 2-bromophenylboronic acid, and iii) heating $Cr(CO)_6$ with 2-bromobiphenyl.

First, to explore the deprotonation route, a series of experiments were performed to determine how coordination to chromium affects the acidity of arene hydrogens. Treatment of benzene with *n*-butyllithium (*n*-BuLi) in tetrahydrofuran solvent at -78 °C followed by quenching with methyl iodide resulted in only 6% conversion to toluene (Figure 2). Repeating the reaction sequence at 25 °C and in either tetrahydrofuran or diethyl ether gave no better conversion.
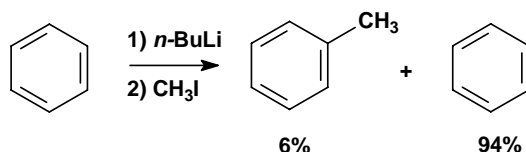

Figure 2. Deprotonation of benzene with *n*-BuLi. The reaction
was carried out in THF at -78 °C and 25 °C and in Et$_2$O at 25 °C

However, when the reaction sequence was repeated with benzene coordinated to chromium a 71% conversion of $(\eta^6\text{-}C_6H_6)Cr(CO)_3$ to $(\eta^6\text{-}C_6H_5CH_3)Cr(CO)_3$ was realized. This is due to the increased acidity of arene hydrogens when the ring is coordinated to the electron withdrawing $Cr(CO)_3$ fragment (Figure 3).
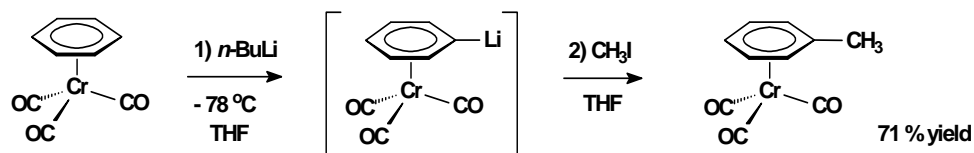

Figure 3. The acidity of the arene hydrogens is increased
when the benzene ring is coordinated to chromium

Although the arene hydrogens in $(\eta^6\text{-}C_6H_6)Cr(CO)_3$ are acidic enough to be removed by *n*-BuLi to form phenyllithium-chromium-tricarbonyl, a subsequent nucleophilic attack of 1,2-dibromobenzene by phenyllithium-chromium-tricarbonyl failed to lead to the desired product (Figure 4). This is not entirely unexpected, since the electron-withdrawing $Cr(CO)_3$ fragment makes the coordinated phenyllithium less basic than uncoordinated anions, and since aromatic compounds are usually poor substrates for nucleophilic substitution.
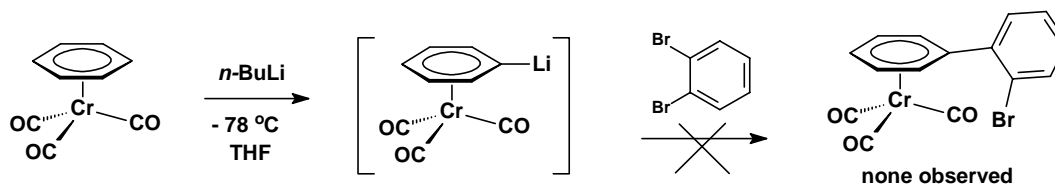

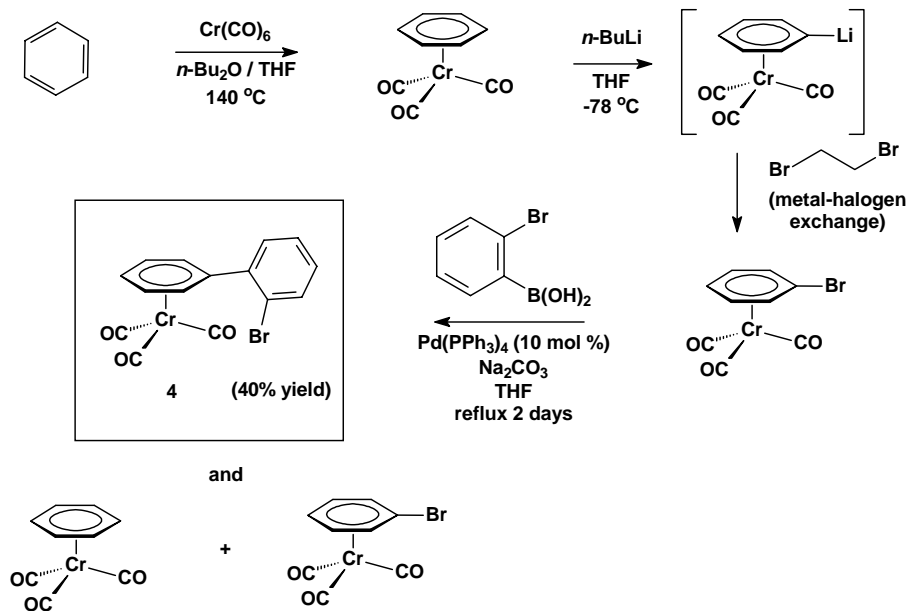**Figure 4.** Attempted synthesis of **4** by nucleophilic attack

Figure 5. Synthesis of **4** by Suzuki coupling

Before attempting to optimize chromatography or recrystallization conditions to purify **4** from the Suzuki coupling, we attempted a third route, the direct reaction of 2-bromobiphenyl with chromium hexacarbonyl. While two products might be expected in this reaction, one where the brominated ring is not coordinated to the metal (**4**) and one where the brominated ring is coordinated to the metal, refluxing 2-bromobiphenyl with chromium hexacarbonyl in 10:1 butyl ether:THF gave the desired **4** in 40% yield with no formation of the other isomer (Figure 6). Although the yield is equal in comparison with the yield from the Suzuki coupling reaction, there are no unreacted staring materials or other products to cause difficulty in isolation of **4**, which was collected as a yellow, air-stable solid after column chromatography.
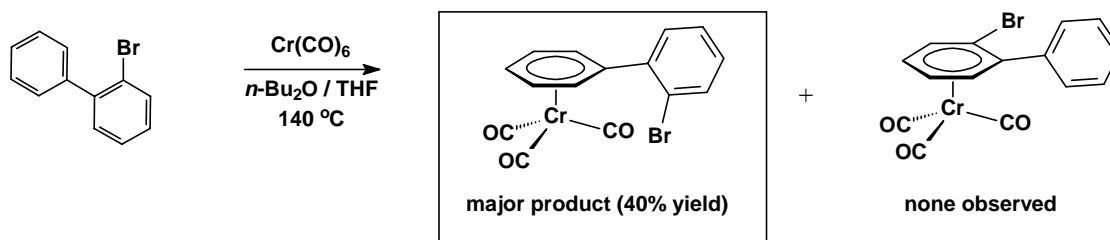

Figure 6. Synthesis of **4** by direct reflux

Molecular mechanics and semi-empirical calculations suggest at least a partial explanation for why only the non-brominated ring of 2-bromobiphenyl coordinates to chromium under these conditions. Figure 7 shows an electrostatic potential map of the minimized geometry of 2-bromobiphenyl. The difference in shading in the center portion of the two rings graphically illustrates that bringing a positively charged fragment such as $Cr(CO)_3$ close to 2-bromobiphenyl would result in a favorable *decrease* in energy for the *non-brominated* phenyl ring, but a disfavored *increase* in energy for the *brominated* benzene ring.
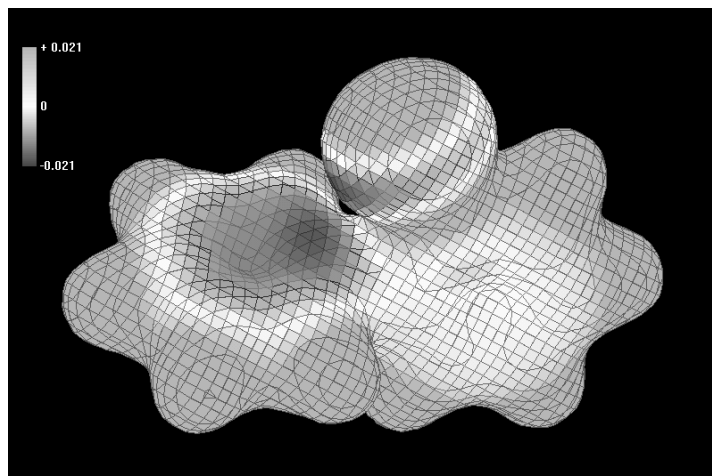
Figure 7. Electrostatic potential map of the minimized geometry of 2-bromobiphenyl

In light of these calculations it is not surprising that in a separate experiment, refluxing bromobenzene with $Cr(CO)_6$ led to only trace amounts of $(\eta^6\text{-}C_6H_5Br)Cr(CO)_3$ (Figure 8).

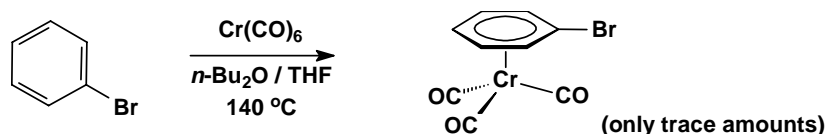**Figure 8.** Reduced reactivity of arene ring substituted with electronegative element.
Only trace amounts of $(\eta^6\text{-}C_6H_5Br)Cr(CO)_3$ were observed.

CONCLUSION

We have examined three potential synthetic routes in the synthesis of $(\eta^6\text{-}2'\text{-bromobiphenyl})Cr(CO)_3$. We have shown that while deprotonation of an arene ring coordinated to a $Cr(CO)_3$ fragment can lead to bromination or methylation in subsequent reactions, arylation was not possible. Bromination led to a product useful for the Suzuki coupling reaction, which was successful but led to difficulties at the purification stage. Suprisingly, simply heating chromium hexacarbonyl with 2-bromobiphenyl leads to the desired $(\eta^6\text{-}2'\text{-bromobiphenyl})Cr(CO)_3$ with only trace amounts of the brominated ring coordinating to the metal, a result that can be rationalized through molecular mechanics and semi-empirical calculations. Early attempts to use $(\eta^6\text{-}2'\text{-bromobiphenyl})Cr(CO)_3$ in a metal-halogen exchange reaction for the ultimate formation of an aryl-tethered hydroxycarbene complex have not been successful to this point, perhaps due to steric hindrance by the $Cr(CO)_3$ or perhaps due to electronic effects of the bromine atom. Currently we are studying steric effects in the reaction of $(\eta^6\text{-}2'\text{-bromobiphenyl})Cr(CO)_3$ with alkyllithium reagents and are pursuing similar reactions with the $(\eta^6\text{-}2'\text{-iodobiphenyl})Cr(CO)_3$ analog.

EXPERIMENTAL

General Methods. All reactions were performed under an inert atmosphere of nitrogen using standard Schlenk techniques. Benzene, dibutyl ether, and tetrhydrofuran were distilled prior to use. Proton NMR spectra were obtained using a Bruker AC MHz Spectrometer and GC/MS spectra were obtained using a Varian Saturn 2000.

$(\eta^6\text{-}C_6H_6)Cr(CO)_3$ [7]: In a 100 mL round-bottom flask under a nitrogen atmosphere a mixture of $Cr(CO)_6$ (2.000 g, 9.09 mmol), benzene (10 mL, 112.5 mmol), THF (5mL), and dibutyl ether (60 mL) was refluxed at 140 °C. After 40 h, the reaction solution was cooled in an ice bath for 10 min to precipitate unreacted $Cr(CO)_6$ and filtered

(sand, Celite, silica gel/benzene) through a glass frit. Solvents were removed under vacuum to give $Cr(CO)_6$ as a yellow solid (1.418 g, 6.62 mmol, 72.9% based on $Cr(CO)_6$).

Deprotonation and methylation of benzene:

    (A) Benzene (0.883 g, 11.3 mmol) and THF (20 mL) were combined in a Schlenk flask under a nitrogen atmosphere. At 0 °C, n-BuLi (7.78 mL, 12.4 mmol) was added via syringe. The solution was warmed to 25 °C and CH_3I (0.703 mL, 11.3mmol) was added via syringe. Analysis of the solution by gas-chromatography/mass spectrometry (GC/MS) showed 6% conversion of starting benzene to toluene**.**

    (B) Benzene (0.895 g, 11.5 mmol) and Et_2O (20 mL) were combined in a Schlenk flask under a nitrogen atmosphere. At 0 °C, n-BuLi (7.78 mL, 12.4 mmol) was added via syringe. The solution was warmed to 25 °C and CH_3I (0.703 mL, 11.3mmol) was added via syringe. Analysis of the solution by gas-chromatography/mass spectrometry (GC/MS) showed only benzene and no toluene.

    (C) Benzene (0.500 g, 6.41 mmol) and THF (20 mL) were combined in a Schlenk flask under a nitrogen atmosphere. At -78 °C, n-BuLi (4.40 mL, 7.05 mmol) was added via syringe. After 2 h of stirring at –78 °C, CH_3I (2.00 mL, 32.1mmol) was added via syringe. Analysis of the solution by gas-chromatography/mass spectrometry (GC/MS) to showed only benzene and no toluene.

(η^6-$C_6H_5CH_3$)Cr(CO)_3 In a Schlenk flask a yellow solution of (η^6-C_6H_6)Cr(CO)_3 (0.500 g, 2.34 mmol) in THF (20 mL) at –78 °C was treated with *n*-BuLi (1.61 mL, 2.57 mmol, added via syringe) resulting in the solution turning orange-yellow in color. After 2 h of stirring, CH_3I (1.45 mL, 23.4 mmol) was added to the solution via syringe turning the solution yellow-brown in color. The solution was warmed to room temperature and THF was evaporated under vacuum to give a liquid that was filtered (sand, Celite, silica gel/CH_2Cl_2) and purified by column chromatography (silica gel/CH_2Cl_2). The yellow band was collected and solvents were evaporated on a rotary evaporator to give of (η^6-$C_6H_5CH_3$)Cr(CO)_3 as a yellow solid (0.356 g, 1.56 mmol, 71.1% based (η^6-C_6H_6)Cr(CO)_3).

Attempted synthesis of (η^6-2'-bromobiphenyl)Cr(CO)_3 (4) through deprotonation/nucleophilic attack route. In a Schlenk flask a yellow solution of (η^6-C_6H_6)Cr(CO)_3 (0.500 g, 2.34 mmol) and THF (20 mL) at –78 °C was treated with n-BuLi (1.76 mL, 2.81 mmol, added via syringe) resulting in the solution turning orange-brown in color. After 2 h of stirring at –78 °C, 1,2-dibromobenzene (0.558 mL, 4.68 mmol) was added to the solution via syringe. The solution was warmed to room temperature and THF was evaporated under vacuum to give crude product as a brown liquid. Celite (3 small scoops) and CH_2Cl_2 (5 mL) were added to the Schlenk flask and the solvent was evaporated under vacuum to leave crude product absorbed onto Celite. The crude product was placed onto a pre-wetted (hexanes) silica gel chromatography column. Unreacted 1,2-bromobenzene was eluted using hexanes, then 1:1 hexanes/ether was used to elute a yellow band. Solvents were removed under vacuum and a ^{1}H NMR (CDCl$_3$) showed only (η^6-C_6H_6)Cr(CO)_3 and no **4**.

(η^6-C_6H_5Br)Cr(CO)_3. In a Schlenk flask, a yellow solution of (η^6-C_6H_6)Cr(CO)_3 (0.500 g, 2.34 mmol) and THF (20 mL) at –78 °C, was treated with n-BuLi (1.76 mL, 2.81 mmol, added via syringe) resulting in the solution turning orange-brown in color. After 2 h of stirring at –78 °C, 1,2-dibromoethane (0.403 mL, 4.68 mmol) was added to the solution via syringe. After 30 min, the reaction solution was warmed to 25 °C and the solvents were removed under vacuum to give a brown solid. Celite (3 small scoops) and CH_2Cl_2 (6 mL) were added to the Schlenk flask and the solvent was evaporated under vacuum to leave crude yellow-green **6** absorbed onto Celite. Crude **6** was further purified by silica gel column chromatography (1:1 hexanes/ether) to give **6** as a yellow liquid. Solvents were removed using a rotary evaporator to give **6** as a yellow solid (0.285 g, 0.973 mmol, 41.6%).

Attempted synthesis of (η^6-2'-bromobiphenyl)Cr(CO)_3 (4) through the Suzuki coupling route. In a 10 mL round-bottom flask (η^6-C_6H_5Br)Cr(CO)_3 (0.285 g, 0.973 mmol), 2-bromophenylboronic acid (0.195 g, 0.973 mmol), tetrakis(triphenylphosphine)-palladium (0.0523 g, 0.0973 mmol), Na_2CO_3 (0.206 g, 1.95 mmol) and THF (5 mL) were heated at reflux for 48 hours. Solvents were evaporated under vacuum to give a brown solid. Celite (3 small scoops) and CH_2Cl_2 (6 mL) were added to the flask and the solvent was evaporated under vacuum to leave crude brown product absorbed onto Celite. Column chromatography (1:1 hexanes/benzene) gave a mixture of products shown by ^{1}H NMR to contain (η^6-C_6H_5Br)Cr(CO)_3, (η^6-C_6H_6)Cr(CO)_3 and (η^6-2'-bromobiphenyl)Cr(CO)_3.

(η^6-2'-bromobiphenyl)Cr(CO)$_3$ (4). In a 100 mL round-bottom flask under a nitrogen atmosphere Cr(CO)$_6$ (0.524 g, 2.36 mmol), 2-bromobiphenyl (1.283 g, 5.50 mmol), THF (3.0 mL), and dibutyl ether (30 mL) were reflux at 140 ^{o}C. After 20 min, the solution began to turn clear yellow. After 40 h, the yellow solution was cooled in an ice bath for 10 min to precipitate unreacted Cr(CO)$_6$. The yellow solution was filtered (sand, Celite, silica gel/CH$_2$Cl$_2$) and solvent was evaporated under vacuum to leave crude **5** as a yellow solid. Celite (3 small scoops) and CH$_2$Cl$_2$ (5 mL) were added to the Schlenk flask and the solvent was evaporated under vacuum to leave crude product absorbed onto Celite that was placed on top of a silica gel chromatography column and eluted with hexanes to remove unreacted 2-bromobiphenyl. Further elution with 1:1 hexanes/ether gave a yellow band. Evaporation of solvents under vacuum gave **5** as a yellow solid (300 mg, 0.81 mmol, 35%). ^{1}H NMR (CDCl$_3$) δ 5.35 (2H, t); 5.5 (1H, t); 5.65 (2H, d); 7.25, 7.40, 7.50, 7.65 (4H, m).

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