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Note

The Regioselective Methylation of Polycyclic Aromatic Hydrocarbons through Tricarbonylchromium Coordination

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Deprotonation, methylation, and air oxidation of polycyclic arenes coordinated to chromium(0), (η^6-arene)$Cr(CO)_3$, produced ring-methylated products with high selectivity and in good yield. This procedure gave 3-methylbenz[*a*]anthracene from (η^6-benz[*a*]anthracene)$Cr(CO)_3$, 3-methylphenanthrene from (η^6-phenanthrene)$Cr(CO)_3$, 2-acetyl-6-methylphenanthrene from (η^6-2-acetylphenanthrene)$Cr(CO)_3$, and 3,7,12-trimethylbenz[*a*]anthracene from (η^6-7,12-dimethylbenz[*a*]anthracene)$Cr(CO)_3$.

INTRODUCTION

Since 1957, (η^6-arene)tricarbonylchromium complexes have drawn the attention of organic and organometallic chemists.[1-4] Intensive research in this field has led to the development of new techniques for the synthesis of organic compounds.[5-6] The chromium withdraws electron density from the coordinated arene, as evidenced by the high dipole moment (5.08D for benzene chromium tricarbonyl), the increase in acidity of benzoic acid upon complexation (pK_a = 4.77 for the benzoic acid complex vs. 5.75 for free benzoic acid) and the decrease in basicity for complexed aniline (pK_b = 13.31 vs. 11.70 for aniline itself) (Fig. 1). This fact is expected to increase the rate of nucleophilic substitutions on the aromatic ring.[7] As a consequence, the arene ring becomes activated towards electrophilic attack, rather than the normal nucleophilic attack. In addition, the electron deficient arene ring is better able to stabilize a negative charge, thus its deprotonation becomes more favorable. Finally, the chromium tricarbonyl fragment completely blocks one face of the arene, and directs incoming reagents to the ring further away from the metal. All of these effects have been used to an advantage in organic synthesis. In particular, a variety of nucleophilic substitutions on the arene ring can be carried out on the aromatic system with stereospecific reactions on the functional groups that are attached to the aromatic ring.

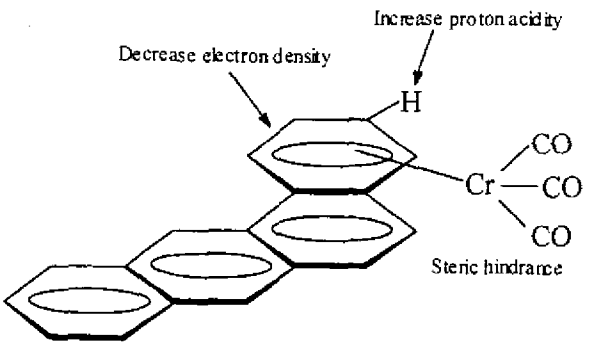


Fig. 1. Effect of $Cr(CO)_3$ moiety to the coordination ring.

Polycyclic aromatic hydrocarbons (PAHs) and their derivatives are widespread as environmental pollutants. Alkylated PAHs demonstrate strong carcinogenic and/or mutagenic activities.[8-10] Preparation of these compounds for biological studies and environmental protection are highly important and significant. The synthesis of methylated PAHs using organic methodology requires many steps and yields are frequently poor. The selective synthesis of 3-methylbenz[*a*]anthracene requires 5-steps[14] or 11-steps,[11] depending on the precursor.

In this work, the selective methylation of four polycyclic aromatic hydrocarbons is accomplished using (η^6-arene)$Cr(CO)_3$ intermediates. The electron-withdrawing nature of the $Cr(CO)_3$ group alters the properties of the complexed arenes. Reactions of complexed and uncomplexed arenes are compared.

RESULTS

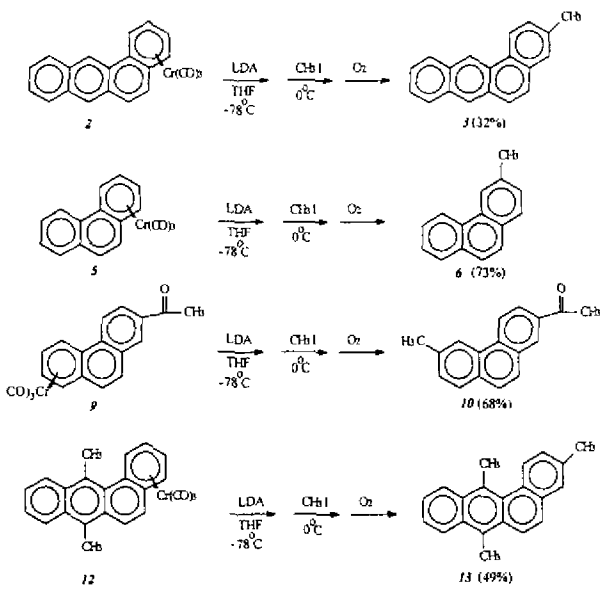
Preparation of (η^6-arene)tricarbonylchromium complexes

The complexes were prepared from refluxing the solutions of the PAH and chromium hexacarbonyl in a solution of *n*-butyl ether and tetrahydrofuran under an atmosphere of nitrogen for a period of 2-4 h depending on the arene used. The purity of these (η^6-arene)tricarbonylchromium complexes was characterized by UV-visible, mass, ^{1}H NMR spectra, and melting point.

Methylation

Deprotonation of **2**, **5**, **9**, and **12** with either *n*-butyl lithium or lithium diisopropylamide (LDA) at -78 °C gave the corresponding lithiated arene. These were not isolated. Addition of CH_3I at 0 °C produced the methylated arene complex. The free arenes were generated by air oxidation of the chromium complexes.

Scheme I Methylation of $(\eta^6\text{-PAH})Cr(CO)_3$ **2**, **5**, **9**, **12**



Methylation of free arenes

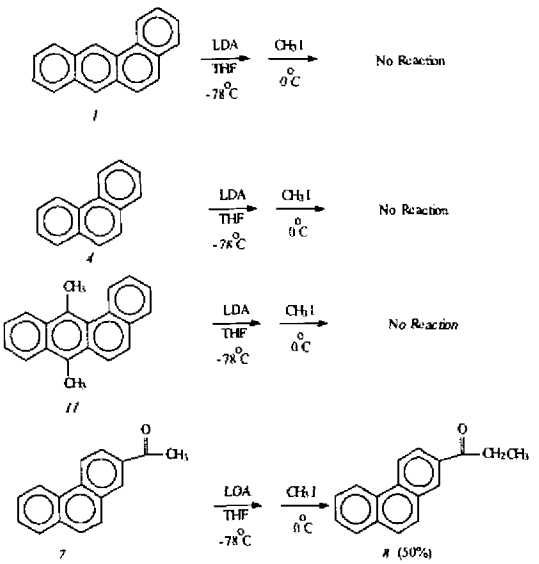
Deprotonation of **1**, **4**, **11** with either *n*-butyl lithium or lithium diisopropylamide (LDA) at -78 °C and addition of CH_3I at 0 °C for 24 hours, resulted in no reaction based on ^1H NMR analysis. However deprotonation of 2-acetylphenanthrene (**7**) with lithium diisopropylamide (LDA) at -78 °C, addition of CH_3I at 0 °C, stirring at 25 °C and then quenching with water, followed by work-up procedure, yielded a yellow solid obtained from CH_3CN/hexane which was identified as 2-propanoylphenanthrene (**8**).

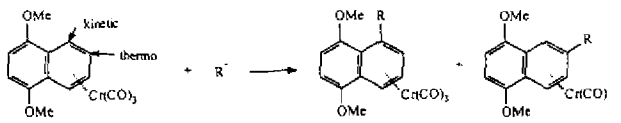
DISCUSSION

In this study, we synthesized four $(\eta^5$-arene)tricarbonylchromium complexes by the reflux of $Cr(CO)_6$ and *n*-butyl ether solution of arenes. The position of chromium moiety on the ring of the coordinated PAH had been characterized in our previous report.[8]

The first step of our reaction is a lithiation of the complexing arenes. The ring-lithiated arenechromium tricarbonyl complexes are readily prepared and are generally reactive towards electrophiles. This lithiation is possibly a reversible process like the nucleophilic reaction of the $(\eta^6$-1,4-dimethoxynaphthalene)tricarbonylchromium complexes, which leads to a kinetic alkylation at the α-position, but a thermodynamic alkylation at the β-position.[19]

Scheme II Methylation of PAH **1**, **4**, **7**, **11**





The $Cr(CO)_3$ moiety activated the C-H bond of the coordinated benzene ring for the Li-H exchange. Our reactions for Li-H exchange using a less active base (LDA) were performed at -78 °C. Our products are expected to be the thermodynamic resultants. The products from compound **2**, **5** and **12** are lithiated at C(3) position, which is the most thermodynamic by stable. Another important reason for this selectivity might be the steric effect of the $Cr(CO)_3$ moiety along with another part of the fused ring during the transition state. This novel process yielded compounds **3**, **6**, and **13** as a sole product, respectively. Compared with the normal synthetic procedure of eleven-steps from anthracene[11] or five-steps from benzyl p-tolyl ketone,[14] this is, without a doubt, a valuable route for the organic synthesis of the derivatives of polycyclic aromatic hydrocarbons.

With the presence of an acetyl group on the uncoordinated PAH (i.e., **7**), the methylation of lithiated intermediate took place at the methyl group of the acetyl group, yielding compound **8**. During addition of LDA, the hydrogen of the methyl can undergo an exchange with lithium. The lithium

in this resultant can bind with an oxygen of the carbonyl group of the methyl group for further reaction. Under the same reaction conditions, methylation of coordinated compound **9** resulted in C(6)-Me product (**10**). This might be because a hydrogen of the coordinated ring is more acidic than a hydrogen of the acetyl group for a Li-H exchange and methylation to yield compound **10**.

CONCLUSION

According to this work, we found that the product distributions from reacting the PAH systems (free or coordinated with tricarbonylchromium) and LDA followed by treatment with CH_3I are divergent. A $Cr(CO)_3$ moiety activated the C-H bond of the coordinated benzene ring for the Li-H exchange in the initial process, resulting in highly positional selectivity for alkylation of (η^6-arene)tricarbonylchromium. An electronic effect of the metal carbonyl moiety is responsible for this highly selective reaction.

EXPERIMENTAL SECTION

General Procedures

All mp were taken on a Yanagimoto melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 883 spectrophotometer. Ultraviolet and visible absorption spectra were recorded on a Shimadzu UV-260 spectrophotometer. Mass spectra were obtained using a JEOL JMS-DX300 spectrometer, with a solid probe inlet, by electron impact with electron energy of 70 eV and a source temperature at 250 °C. ^{1}H NMR spectra were recorded on a Bruker AC-250 spectrometer. The chemical shifts for samples in deuteriochloroform are reported in δ units relative to tetramethylsilane.

(η^6-Arene)tricarbonylchromium

The tricarbonylchromium complexes of benz[*a*]anthracene (**1**), phenanthene (**4**), 2-acetylphenanthrene (**7**), and 7,12-dimethyl benz[*a*]anthracene (**11**) were prepared according to the literature[16] and verified by comparison of the mp, ^{1}H NMR spectra with that of the authentic samples (**2**, **5**, **9**, **12**).

Typical Procedure for Methylation of Either (η^6-Arene)tricarbonylchromium or Polycyclic Aromatic Hydrocarbon

To a THF solution containing polycyclic aromatic hydrocarbons (0.8 mmol) at -78 °C, lithium diisopropylamide (LDA) (0.2 mL) was slowly added with stirring. After 20 min, the temperature of the solution was raised to 0 °C followed by addition of excess CH_3I. After another 15 min, the temperature was raised to 25 °C and then quenched with water (50 mL). The aqueous solution obtained from filtrations through a celite layer was extracted with CH_2Cl_2 (70 mL × 3). The organic fraction were combined, dried over $MgSO_4$, evaporated and then crystallized from CH_3CN/hexane to afford the crystals of polycyclic aromatic hydrocarbon derivatives.

Methylation of 2-Acetylphenanthrene (7)

After the work-up process, the yellow resultant was identified as 2-propanoylphenanthrene (**8**) (94 mg, 50% yield); mp 100-102 °C (lit.[17] 99-102 °C); UV-visible (CH_2Cl_2) λ_{max} 267 (ε = 19000), 293 (ε = 5800) nm; MS *m/z* (relative intensity) 234 ([M]$^+$, 6), 220 ([M-CH_2]$^+$, 83), 205 ([M-C_2H_5]$^+$, 20), 177 ([M-C_3H_5O]$^+$, 76); ^{1}H NMR δ 1.10 (t, 3H, *J* = 0.02 Hz, -CH_3), 2.81 (q, 2H, *J* = 0.02 Hz, -CH_2), 7.47 (dd, 1H, *J* = 8.3, 6.9 Hz, H_7), 7.54 (dd, 1H, *J* = 8.3, 6.9 Hz, H_6), 7.77 (d, 1H, *J* = 8.3 Hz, H_8), 7.90 (d, 1H, *J* = 8.6 Hz, H_9), 7.90 (d, 1H, *J* = 8.6 Hz, H_{10}), 7.95 (d, 1H, *J* = 8.8 Hz, H_3), 8.41 (s, 1H, H_1), 8.44 (d, 1H, *J* = 8.5 Hz, H_5), and 8.63 (d, 1H, *J* = 8.8 Hz, H_4).

Methylation of Benz[*a*]anthracene (1)

After work-up, there was no reaction, based on NMR analysis.

Methylation of Phenanthrene (4)

After work-up, there was no reaction, based on NMR analysis.

Methylation of 7,12-Dimethylbenz[*a*]anthracene (11)

After work-up, there was no reaction, based on NMR analysis.

Methylation of Benz[*a*]anthracenetricarbonylchromium (2)

After the work-up process, the orange solid was identified as 3-methylbenz[*a*]anthracene (**3**) (62 mg, 32% yield); mp 160-161 °C (lit.[12] 160 °C); MS *m/z* (relative intensity) 242 ([M]$^+$, 100), 227 ([M-CH_3]$^+$, 54), 214 ([M-C_2H_4]$^+$, 48); ^{1}H NMR δ 2.55 (s, 3H, -CH_3), 7.35 (d, 1H, *J* = 8.8 Hz, H_2), 7.45 (dd, 1H, *J* = 8.3, 6.9 Hz, H_9), 7.53 (s, 1H, H_4), 7.53 (d, 1H, *J* = 8.6 Hz, H_5), 7.66 (d, 1H, *J* = 8.6 Hz, H_6), 7.69 (d, 1H, *J* = 8.3 Hz, H_8), 7.74 (dd, 1H, *J* = 8.3, 6.9 Hz, H_{10}), 7.95 (d, 1H, *J* = 8.3 Hz, H_{11}), 8.10 (s, 1H, H_7), 8.38 (d, 1H, *J* = 8.8

Hz, H_1), and 8.59 (s, 1H, H_{12}).

Methylation of Phenanthrenetricarbonylchromium (5)

After the work-up process, the orange solid was identified as 3-methylphenanthrene (**6**) (111 mg, 73% yield); UV-visible (CH_2Cl_2) λ_{max} 255 (ε = 49000), 229 (ε = 50000) nm; mp 63-64 °C (lit.[16] 62-63 °C); MS *m/z* (relative intensity) 192 ([M]$^+$, 31), 177 ([M-CH_3]$^+$, 83); ^{1}H NMR δ 2.6 (m, 3H, -CH_3), 7.33 (d, 1H, J = 8.2 Hz, H_2), 7.5 (dd, 1H, J = 8.3, 6.9 Hz, H_7), 7.54 (dd, 1H, J = 8.5, 6.9 Hz, H_6), 7.61 (d, 2H, J = 8.6 Hz, $H_{9,10}$), 7.78 (d, 1H, J = 8.3 Hz, H_8), 8.23 (s, 1H, H_4), 8.39 (d, 1H, J = 8.5 Hz, H_5), and 7.7 (d, 1H, J = 8.2 Hz, H_1).

Methylation of 2-Acetylphenanthrenetricarbonylchromium (9)

After work-up process, the yellow resultant was identified as 2-acetyl-6-methylphenanthrene (**10**) (126 mg, 68% yield); UV-visible (CH_2Cl_2) λ_{max} 293 (ε = 2800), 267 (ε = 9300), 202 (ε = 2600) nm; MS *m/z* (relative intensity) 234 ([M]$^+$, 6), 205 ([M-C_2H_5]$^+$, 100), 177 ([M-C_3H_5O]$^+$, 76); ^{1}H NMR δ 2.45 (s, 3H, -$COCH_3$), 2.6 (m, 3H, -CH_3), 7.33 (d, 1H, J = 8.2 Hz, H_7), 7.67 (d, 1H, J = 8.6 Hz, H_9), 7.7 (d, 1H, J = 8.2 Hz, H_8), 7.71 (d, 1H, J = 8.6 Hz, H_{10}), 8.00 (d, 1H, J = 8.8 Hz, H_3), 8.56 (d, 1H, J = 8.8 Hz, H_4), 8.31 (s, 1H, H_5), and 8.46 (s, 1H, H_1); Anal. Calcd for $C_{17}H_{14}O$: C, 90.85; H, 9.15. Found: C, 90.69; H, 9.11.

Methylation of 7,12-Dimethylbenz[*a*]anthracenetricarbonylchromium (12)

After the work-up procedure, the orange solid was identified as 3,7,12-trimethyl benz[*a*]anthracene (**13**) (100 mg, 49% yield); mp 121-122 °C (lit.[13] 122 °C); MS *m/z* (relative intensity) 270 ([M]$^+$, 100), 255 ([M-CH_3]$^+$, 54), 240 ([M-C_2H_6]$^+$, 48), 225 ([M-C_3H_9]$^+$, 54); ^{1}H NMR δ 2.54 (s, 3H, 3-CH_3), 3.10 (s, 3H, 7-CH_3), 3.24 (s, 3H, 12-CH_3), 7.04 (dd, 1H, J = 8.9, 6.9 Hz, H_{10}), 7.05 (dd, 1H, J = 8.9, 6.9 Hz, H_9), 7.29 (q, 1H, J = 8.5 Hz, H_2), 7.47 (s, 1H, H_4), 7.62 (d, 1H, J = 8.8 Hz, H_{11}), 7.63 (d, 1H, J = 8.6 Hz, H_8), 7.64 (d, 1H, J = 9.0 Hz, H_5), 7.77 (d, 1H, J = 9.0 Hz, H_6), and 8.07 (d, 1H, J = 8.8 Hz, H_1).

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Key Words

Polycyclic aromatic hydrocarbons (PAHs); Benz[*a*]anthracene; Phenanthrene; 2-Acetyl-phenanthrene; 7,12-Dimethylbenz[*a*]anthracene; (η^6-Arene)tricarbonylchromium complex; Methylation.

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