

Aromatic Nucleophilic Substitution on Haloarene Chromium Tricarbonyl Complexes: Mild *N*-Arylation of Indoles

Stefano Maiorana,* Clara Baldoli, Paola Del Buttero, Michela Di Ciolo, Antonio Papagni

Dipartimento di Chimica Organica e Industriale, Università di Milano e CNR-Centro Studio Sintesi e Stereochimica Speciali Sistemi Organici. Via C. Golgi 19, I-20133 Milano, Italy

Fax +39(2)2364369. E-mail: maior@icil64.cilea.it

Received 5 August 1997; 17 October 1997

Abstract: A series of *N*-arylindoles were obtained in good yields and under mild conditions by nucleophilic substitution reaction of the sodium salt of indole on various haloarene chromium tricarbonyl complexes.

Key words: aromatic nucleophilic substitution, haloarene chromium tricarbonyl complexes, arylation, indole

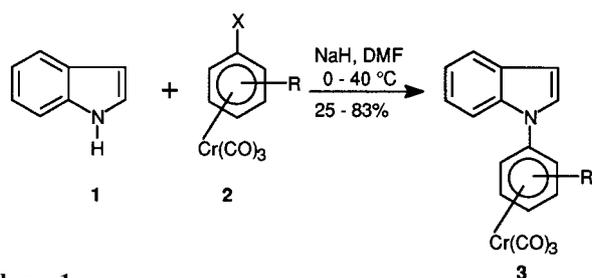
N-Arylindoles are present as heterocyclic subunits in a number of synthetically and medicinally relevant compounds.¹ One general method for their preparation is direct nitrogen arylation, including metal-mediated reactions,² Ullmann coupling³ and aromatic nucleophilic substitution.⁴ This last reaction seems to be a very useful strategy. Smith has recently reported the reaction of indole with some aryl electrophiles using 37% KF/Al₂O₃ as base in the presence of 18-crown-6 catalyst in DMSO at 120°C.⁵ The limitations of this method are the high temperature and the nature of the substituents on the aromatic ring (electron-withdrawing groups only).

The activation of haloarenes to aromatic nucleophilic substitution by complexation to Cr(CO)₃ group has been clearly demonstrated.⁶

Nevertheless, examples of the direct introduction of nitrogen substituents on Cr(CO)₃ complexed haloarenes are comparatively rare.⁷ A recent paper by Hong⁸ describes the nucleophilic substitution of *N*-lithium indole on (η^6 -4-fluorotoluene)Cr(CO)₃ and 2-, 3-, and 4-substituted (η^6 -fluoroanisole)Cr(CO)₃. Only four examples are reported and, although the yields are good, the reaction only works on fluoro-derivatives⁹ and requires a large amount of HMPA (6 equiv).

We here report the results of a study, in which we examined in more detail the reaction of the indole *N*-anion with a series of chloro- and fluoroarene complexes.

The 1-indolyl anion, generated from indole (**1**) with sodium hydride in DMF at 0°C, was reacted with the fluoro and chloroarene complexes **2a–m** to give the *N*-arylated indole complexes **3a–m** in generally good yields. (Scheme 1, Table 1).



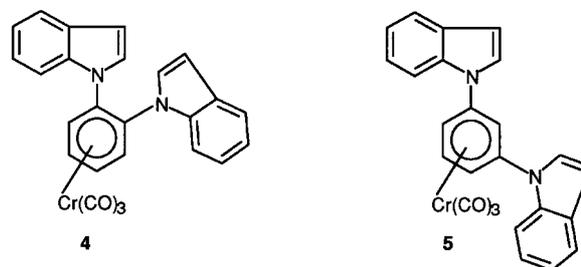
Scheme 1

Table 1. Reactions of Complexes **2** with Indoles **1** and **7**

2	X	R	T (°C)	Time (h)	Product	Yield (%) ^a
a	F	H	0	0.5	3a	76
b	F	2-Me	0	0.5	3b	79
c	F	3-Me	0	0.5	3c	75
d	F	4-Me	0	0.5	3d	81
e	F	2-OMe	0	0.75	3e	83
f	F	2-CH(OEt) ₂	0	0.5	3f	76
g	Cl	H	30	2	3a	73
h	Cl	2-Me	40	3	3b	75
i	Cl	2-CH(OEt) ₂	30	2	3f	76
l	Cl	2-Cl	0	1	3l	45
					4	28
m	Cl	3-Cl	0	1	3m	42
					5	25
a	F	H	0	0.5	8a	75
c	F	3-Me	0	0.5	8c	76

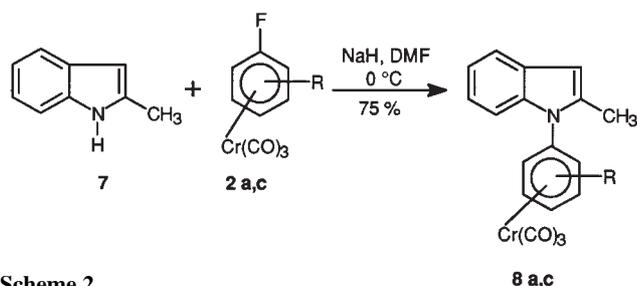
^a Yield of isolated product.

In line with the aromatic nucleophilic substitution mechanism¹⁰ the fluoroarenes were more reactive than the chloroarenes: the fluoro complexes **2a–f** reacted rapidly at 0°C giving complexes **3a–f** in good yields.¹¹ The chloro derivatives **2g–i** required 30–40°C and longer reaction times, but products **3a,b,f** were isolated in comparable yields: in contrast, the 1,2- and 1,3-dichlorobenzene complexes **2l,m** proved to be highly reactive and, even at 0°C, gave a mixture of the mono- and disubstituted products **3l,m**, **4** and **5**. We also ascertained that complexes **3l** and **3m** are quantitatively transformed into **4** and **5** by treatment with an equimolar amount of the indolyl anion generated with NaH at 0°C in DMF.



A further extension of the study was aimed at evaluating the general applicability of this arylation reaction to substituted indoles. Moreover, we were interested in verifying whether the presence of a stereogenic *ortho*-disubstituted chromium arene complex on the indole nitrogen could control the stereochemistry of a reaction at a

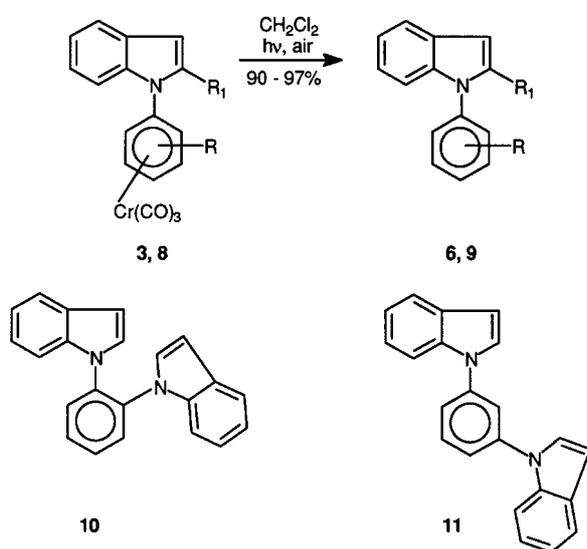
prostereogenic group present in position 2 of the indole ring. We considered indole rings bearing different groups in position 2, and studied the reaction of 2-ethoxycarbonyl-, 2-formyl-, 2-benzoyl-, and 2-methylindole with the fluoroarene complexes **2a–c**. Under our experimental conditions, only 2-methylindole (**7**) reacted with (fluorobenzene)Cr(CO)₃ (**2a**) and (3-fluorotoluene)Cr(CO)₃ (**2c**) and gave the expected *N*-derivatives **8a,c** in good yields (Scheme 2, Table 1).



Scheme 2

(2-Fluorotoluene)Cr(CO)₃ (**2b**) did not react with **7** even when heated at 60 °C for a long time: the *ortho* substitution in the complexed aromatic ring therefore seems to be incompatible with any substituent in position 2 of the indole ring, probably for steric reasons.

Finally, decomplexation of compounds **3** and **8** by means of air and sunlight gave indole derivatives **6** and **9** in quantitative yields (Scheme 3, Table 2). Similarly, compounds **4** and **5** were decomplexed to **10** and **11** respectively.



Scheme 3

In conclusion, the present study shows an efficient entry to *N*-arylated indoles, allowing the preparation of derivatives bearing a wide range of substituent on the phenyl ring. It is worth noting the possibility of introducing two indole rings on the same aromatic nucleus: 1,2- and 1,3-phenylenebis-1*H*-indoles **10** and **11** are not known. This class of compounds, although less represented, has found some interesting applications as electrophotographic

photoreceptors¹² and in colorimetric analysis.¹³ In addition, the possibility of substituting stepwise the two chlorine atoms in the dichlorobenzene complexes, represents a convenient method for the synthesis of arenes bearing two different indole rings. The potential of this latter reaction is currently under investigation.

All of the reactions involving organometallic reagents were carried out under dry N₂. Unless otherwise stated the ¹H and ¹³C NMR spectra were recorded in CDCl₃, using a Bruker AC300 spectrometer. Mp's were measured on a Buchi 510 M. P. apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 1725X FTIR. Solvents were purified and dried according to standard procedures. Reagents were purchased from commercial sources and used as obtained. Haloarene complexes **2a–m** were prepared as previously reported.¹⁴

Arylation of Indole; General Procedure:

A solution of indole (100 mg, 0.85 mmol) in anhyd DMF (1 mL) was added dropwise to a slurry of NaH (40 mg, 0.9 mmol, 55% suspension in oil) in DMF (2 mL) at 0 °C. After 5 min, a solution of complex **1a–e** (0.85 mmol) in DMF (1 mL) was added, and the mixture was stirred at the appropriate temperature (see Table 1). The mixture was then treated with sat. brine (10 mL) and extracted with Et₂O (3 × 15 mL). The organic layer was washed with water (2 × 15 mL), dried (Na₂SO₄) and evaporated to give the crude compounds **3**. Column chromatography (silica gel, light petroleum/CH₂Cl₂, 3:1) afforded complexes **3** as yellow solids. Compounds **4** and **5** were separated by column chromatography (light petroleum/CH₂Cl₂, 3:1, *R_f* ≅ 0.24) from the corresponding mono-substituted products **31** and **3m** (*R_f* ≅ 0.35) and recovered as yellow solids. A small amount (~5%) of the starting complexes **31** and **3m** were also isolated.

Tricarbonyl[1-(*η*⁶-phenyl)-1*H*-indole]chromium (**3a**): mp 99–101 °C (petroleum ether).

IR (Nujol): $\nu = 1961, 1908, 1864 \text{ cm}^{-1}$.

¹H NMR: $\delta = 5.2$ [t, 1H, *J* = 6.2 Hz, arom Cr(CO)₃], 5.6 [dd, 2H, *J* = 6.5, 6.2 Hz, arom Cr(CO)₃], 5.7 [d, 2H, *J* = 6.5 Hz, arom Cr(CO)₃], 6.7 (d, 1H, *J* = 3.4 Hz, H-3), 7.1–7.3 (m, 2H, arom), 7.32 (d, 1H, *J* = 3.4 Hz, H-2), 7.63 (m, 2H, arom).

¹³C NMR: $\delta = 87.5$ [d, 2C, arom Cr(CO)₃], 89.7 [d, arom Cr(CO)₃], 92.7 [d, 2C, arom Cr(CO)₃], 105.7 (d, C-3), 110.7 (d), 116.9 [s, arom Cr(CO)₃], 121.4 (d), 121.7 (d), 123.2, (d), 127.7 (d, C-2), 129.8 (s), 135.9 (s), 231.9 (s, 3C, CO).

Anal. Calcd for C₁₇H₁₁CrNO₃: C, 62.01; H, 3.37; N, 4.25. Found: C, 62.21; H, 3.39; N, 4.26.

Tricarbonyl[1-(*η*⁶-2-methylphenyl)-1*H*-indole]chromium (**3b**): mp 96–97 °C (petroleum ether).

IR (Nujol): $\nu = 1975, 1894 \text{ cm}^{-1}$.

¹H NMR: $\delta = 2.0$ (s, 3H, Me), 5.23 [t, 1H, *J* = 6.4 Hz, arom Cr(CO)₃], 5.26 [d, 1H, *J* = 6.2 Hz, arom Cr(CO)₃], 5.6 [t, 1H, *J* = 6.2 Hz, arom Cr(CO)₃], 5.7 [d, 1H, *J* = 6.4 Hz, arom Cr(CO)₃], 6.6 (d, 1H, *J* = 3.3 Hz, H-3), 7.1–7.25 (m, 3H, arom), 7.26 (d, 1H, *J* = 3.3 Hz, H-2), 7.7 (m, 1H, arom).

¹³C NMR: $\delta = 17.2$ (q), 87.6 [d, arom Cr(CO)₃], 90.7 [d, arom Cr(CO)₃], 94.9 [d, arom Cr(CO)₃], 96.4 [d, arom Cr(CO)₃], 103.6 (d, C-3), 109.8 (d), 110.5 [s, arom Cr(CO)₃], 112.2 [s, arom Cr(CO)₃], 120.7 (d), 121.4 (d), 122.7 (d), 131.4 (d, C-2), 129.2 (s), 137.8 (s), 231.8 (s, 3C, CO).

Anal. Calcd for C₁₈H₁₃CrNO₃: C, 62.97; H, 3.82; N, 4.08. Found: C, 62.89; H, 3.81; N, 4.06.

Tricarbonyl[1-(*η*⁶-3-methylphenyl)-1*H*-indole]chromium (**3c**): mp 94–95 °C (petroleum ether).

IR (Nujol): $\nu = 1950, 1872 \text{ cm}^{-1}$.

¹H NMR: $\delta = 2.6$ (s, 3H, Me), 5.0 [d, 1H, *J* = 6.1 Hz, arom Cr(CO)₃], 5.58–5.68 [m, 3H, arom Cr(CO)₃], 6.7 (d, 1H, *J* = 3.4 Hz, H-3), 7.1–7.3 (m, 2H, arom), 7.35 (d, 1H, *J* = 3.4 Hz, H-2), 7.6 (m, 2H, arom).

^{13}C NMR: δ = 20.7 (q), 84.8 [d, arom Cr(CO)₃], 88.1 [d, arom Cr(CO)₃], 89.5 [d, arom Cr(CO)₃], 93.6 [d, arom Cr(CO)₃], 105.6 (d, C-3), 109.2 [s, arom Cr(CO)₃], 110.8 (d), 118.2 [s, arom Cr(CO)₃], 121.4 (d), 121.7 (d), 123.1 (d), 127.6 (d, C-2), 129.9 (s), 135.8 (s), 232.3 (s, 3C, CO).

Anal. Calcd for C₁₈H₁₃CrNO₃: C, 62.97; H, 3.82; N, 4.08. Found: C, 62.90; H, 3.80; N, 4.07.

Tricarbonyl[1-(η^6 -4-methylphenyl)-1H-indole]chromium (3d):⁸ mp 100–102°C (pentane), (lit.⁸ not reported). Spectroscopic data is in agreement with that reported in the lit.⁸

Tricarbonyl[1-(η^6 -2-methoxyphenyl)-1H-indole]chromium (3e):⁸ mp 120–121°C (pentane), (lit.⁸ not reported). Spectroscopic data is in agreement with that reported in the lit.⁸

Tricarbonyl[1-(η^6 -2-(diethoxymethyl)phenyl)-1H-indole]chromium (3f): mp 100–101°C (petroleum ether).

IR (Nujol): ν = 1972, 1904 cm⁻¹.

^1H NMR: δ = 0.6 (br s, 3H, Me), 1.3 (t, 3H, J = 7 Hz, Me), 2.9–3.2 (m, 2H, CH₂), 3.6–3.8 (m, 2H, CH₂), 5.1 (s, 1H, CH), 5.4 [t, 1H, J = 6.3 Hz, arom Cr(CO)₃], 5.5 [t, 1H, J = 5.9 Hz, arom Cr(CO)₃], 5.6 [d, 1H, J = 5.9 Hz, arom Cr(CO)₃], 5.8 [d, 1H, J = 6.3 Hz, arom Cr(CO)₃], 6.6 (d, 1H, J = 3.3 Hz, H-3), 7.1–7.4 (m, 4H, arom+H-2), 7.6 (d, 1H, J = 7.4 Hz, arom).

^{13}C NMR: δ = 14.4 (q), 15.0 (q), 62.1 (t), 65.7 (t), 88.2, 89.8, 92.5, 92.54 [d, arom Cr(CO)₃], 97.8 (d, CH), 103.8 (d, C-3), 109.4 [s, arom Cr(CO)₃], 110.1 (d), 111.7 [s, arom Cr(CO)₃], 120.7, 121.2, 122.6 (d, arom), 129 (s), 130.9 (d, C-2), 131.2 (s), 231.6 (s, 3C, CO).

EI-MS: m/z = 431 (M⁺).

Tricarbonyl[1-(η^6 -2-chlorophenyl)-1H-indole]chromium (3l): mp 109–110°C (petroleum ether).

IR (CHCl₃): ν = 1986, 1923 cm⁻¹.

^1H NMR: δ = 5.2 [dd, 1H, J = 5.9, 6.4 Hz, arom Cr(CO)₃], 5.5 [dd, 1H, J = 5.9, 6.4 Hz, arom Cr(CO)₃], 5.6 [d, 1H, J = 5.9 Hz, arom Cr(CO)₃], 5.87 [d, 1H, J = 6.4 Hz, arom Cr(CO)₃], 6.65 (d, 1H, J = 3.3 Hz, H-3), 7.28–7.15 (m, 3H, arom), 7.32 (d, 1H, J = 3.3 Hz, H-2), 7.65 (d, 1H, J = 7.3 Hz, arom).

Anal. Calcd for C₁₇H₁₀ClCrNO₃: C, 56.13; H, 2.77; N, 3.85. Found: C, 56.32; H, 2.80; N, 3.87.

Tricarbonyl[1-(η^6 -3-chlorophenyl)-1H-indole]chromium (3m): mp 96–98°C (pentane).

IR (CHCl₃): ν = 1980, 1915 cm⁻¹.

^1H NMR: δ = 5.3 [d, 1H, J = 6.4 Hz, arom Cr(CO)₃], 5.5 [dd, 1H, J = 1.6, 6.4 Hz, arom Cr(CO)₃], 5.7 [t, 1H, J = 6.4 Hz, arom Cr(CO)₃], 5.9 [t, 1H, J = 1.6 Hz, arom Cr(CO)₃], 6.7 (d, 1H, J = 3.5 Hz, H-3), 7.2–7.32 (m, 2H, arom), 7.35 (d, 1H, J = 3.5 Hz, H-2), 7.7 (m, 2H, arom).

Anal. Calcd for C₁₇H₁₀ClCrNO₃: C, 56.13; H, 2.77; N, 3.85. Found: C, 56.22; H, 2.76; N, 3.84.

Tricarbonyl[1,1'-(η^6 -1,2-phenylene)bis-1H-indole]chromium (4): mp 198–200°C (pentane).

IR (CHCl₃): ν = 1981, 1914 cm⁻¹.

^1H NMR: δ = 5.54 [m, 2H, arom Cr(CO)₃], 5.92 [m, 2H, arom Cr(CO)₃], 6.4 [d, 2H, J = 3.4 Hz, H-3], 6.88 (d, 2H, J = 3.4 Hz, H-2), 7.1–7.0 (m, 4H, arom), 7.28 (m, 2H, arom), 7.4–7.5 (m, 2H, arom).

EI-MS: m/z = 444 (M⁺).

Anal. Calcd for C₂₅H₁₆CrN₂O₃: C, 67.57; H, 3.63; N, 6.3. Found: C, 67.65; H, 3.64; N, 6.26.

Tricarbonyl[1,1'-(η^6 -1,3-phenylene)bis-1H-indole]chromium (5): mp 158–160°C (pentane).

IR (CHCl₃): ν = 1981, 1914 cm⁻¹.

^1H NMR: δ = 5.65 [dd, 2H, J = 1.6, 6.5 Hz, arom Cr(CO)₃], 5.9 [t, 1H, J = 6.5 Hz, arom Cr(CO)₃], 6.15 [t, 1H, J = 1.6 Hz, arom Cr(CO)₃], 6.7 (d, 2H, J = 3.4 Hz, H-3), 7.2–7.35 (m, 4H, arom), 7.4 (d, 2H, J = 3.4 Hz, H-2), 7.65–7.75 (m, 2H, arom).

Anal. Calcd for C₂₅H₁₆CrN₂O₃: C, 67.57; H, 3.63; N, 6.3. Found: C, 67.60; H, 3.65; N, 6.31.

Tricarbonyl[2-methyl-1-(η^6 -phenyl)-1H-indole]chromium (8a): mp 158–160°C (petroleum ether).

IR (Nujol): ν = 1958, 1904, 1877 cm⁻¹.

^1H NMR: δ = 2.55 (s, 3H, Me), 5.3 [dd, 1H, J = 6.0, 6.21 Hz, arom Cr(CO)₃], 5.46 [dd, 2H, J = 6.3, 6.5 Hz, arom Cr(CO)₃], 5.58 [d, 2H, J = 6.5 Hz, arom Cr(CO)₃], 6.43 (s, 1H, H-3), 7.1–7.3 (m, 2H, arom), 7.55 (d, 1H, J = 7.67 Hz, arom), 7.65 (d, 1H, J = 8.18 Hz, arom).

^{13}C NMR: δ = 14.6 (q), 90.66 [d, arom Cr(CO)₃], 90.77 [d, 2C, arom Cr(CO)₃], 91.28 [d, 2C, arom Cr(CO)₃], 105.0 (d, C-3), 111.38 (d), 114.17 (s), 120.12 (d), 121.21 (d), 122.05 (d), 128.82 (s), 136.88 (s), 137.27 (s), 231.98 (s, 3C, CO).

Anal. Calcd for C₁₈H₁₃CrNO₃: C, 62.97; H, 3.82; N, 4.08. Found: C, 63.02; H, 3.80; N, 4.05.

Table 2. Yields and ^1H NMR Data of Compounds **6a–f**, **l**, **m**, **9a,c**

Product ^a	R ¹	R	Yield (%) ^b	^1H NMR (CDCl ₃) δ , J (Hz)
6a	H	H ¹⁵	96	6.7 (d, 1H, J = 3.3, H-3), 7.2–7.5 (m, 8H, arom.), 7.6 (d, 1H, J = 7.8, arom.), 7.7 (d, 1H, J = 7.8, arom.)
6b	H	2-Me ^{2d}	95	2.1 (s, 3H, Me), 6.7 (d, 1H, J = 3.2, H-3), 7.0–7.4 (m, 8H, arom.), 7.8 (m, 1H, arom.)
6c	H	3-Me ^{2d}	97	2.5 (s, 3H, Me), 6.7 (d, 1H, J = 3.3, H-3), 7.1–7.4 (m, 7H, arom.), 7.6 (d, 1H, J = 8.1), 7.7 (dd, 1H, J = 7.2, J = 1.4)
6d	H	4-Me ^{2d}	97	2.5 (s, 3H, Me), 6.7 (d, 1H, J = 3.2, H-3), 7.1–7.4 (m, 7H, arom.), 7.6 (d, 1H, J = 6.0, arom.), 7.7 (d, 1H, J = 7.6, arom.)
6e	H	2-OMe	93	3.8 (s, 3H, OMe), 6.7 (d, 1H, J = 2.7, H-3), 7.0–7.4 (m, 8H, arom.), 7.7 (m, 1H, arom.)
6f	H	2-CH(OEt) ₂	90	(C ₆ D ₆) 0.9 (br s, 3H, Me), 1.1 (br s, 3H, Me), 2.9–3.5 (m, 4H, CH ₂), 5.1 (s, 1H, CH), 6.7 (d, 1H, J = 3.1, H-3), 7.0–7.25 (m, 7H, arom.), 7.7 (d, 1H, J = 7.2, arom.), 8.0 (d, 1H, J = 7.7, arom.)
6l	H	2-Cl	95	6.7 (d, 1H, J = 3.3, H-3), 7.1–7.6 (m, 9H, arom.)
6m	H	3-Cl	95	6.7 (d, 1H, J = 3.3, H-3), 7.2–7.7 (m, 9H, arom.)
9a	CH ₃	H	94	2.4 (s, 3H, Me), 6.4 (s, 1H, H-3), 7.1–7.6 (m, 9H, arom.)
9c	CH ₃	3-Me	97	2.3 (s, 3H, Me), 2.5 (s, 3H, Me), 6.4 (s, 1H, H-3), 7.1–7.5 (m, 7H, arom.), 7.58–7.62 (m, 1H, arom.)

^a Satisfactory microanalyses obtained: C \pm 0.20, H \pm 0.30, N \pm 0.32.

^b Yield of isolated product.

Tricarbonyl[2-methyl-1-(η^6 -3-methylphenyl)-1H-indole]chromium (**8c**): mp 135–137°C (petroleum ether).

IR (Nujol): $\nu = 1956, 1865 \text{ cm}^{-1}$.

$^1\text{H NMR}$: $\delta = 2.3$ (s, 3H, Me), 2.55 (s, 3H, Me), 5.18 [d, 1H, $J = 5.55$ Hz, arom Cr(CO)₃], 5.5 [m, 3H, arom Cr(CO)₃], 6.4 (s, 1H, H-3), 7.1–7.3 (m, 2H, arom), 7.5 (d, 1H, $J = 7.6$ Hz, arom), 7.7 (d, 1H, $J = 8.17$ Hz, arom).

$^{13}\text{C NMR}$: $\delta = 14.7$ (q), 20.7 (q), 88.5 [d, arom Cr(CO)₃], 91.2 [d, arom Cr(CO)₃], 91.4 [d, arom Cr(CO)₃], 90.0 [d, arom Cr(CO)₃], 105.2 (d, C-3), 107.7 [s, arom Cr(CO)₃], 111.7 (d), 115.4 (s), 120.1 (d), 121.1 (d), 121.9 (d), 128.86 (s, C-2), 136.87 (s), 137.04 (s), 232.48 (s, 3C, CO).

Anal. Calcd for C₁₉H₁₅CrNO₃: C, 63.86; H, 4.23; N, 3.92. Found: C, 63.80; H, 4.25; N, 3.93.

Decomplexation of Compounds 3–5, 8; General Procedure:

A solution of complexes **3–5** and **8** in CH₂Cl₂ was exposed to air and sunlight until the yellow color (and therefore the starting complex) had completely disappeared. The solvent was evaporated and the residue, taken up with Et₂O, was filtered over a pad of Celite to yield indole derivatives **6** and **9** as nearly analytically pure colorless oils. Yields and $^1\text{H NMR}$ data of **6a–m** and **9a,c** are listed in Table 2. According to the same procedure compounds **10** and **11** were obtained as colorless oils.

1,1'-(1,2-Phenylene)bis-1H-indole (**10**): yield: 96%.

$^1\text{H NMR}$: $\delta = 6.4$ (d, 2H, $J = 3.3$ Hz, H-3), 7.1–7.7 (m, 14H, arom). Anal. Calcd for C₂₂H₁₆N₂: C, 85.69; H, 5.23; N, 9.08. Found: C, 85.50; H, 5.22; N, 9.10.

1,1'-(1,3-Phenylene)bis-1H-indole (**11**): yield: 97%.

$^1\text{H NMR}$: $\delta = 6.8$ (d, 2H, $J = 3.2$ Hz, H-3), 7.2–7.8 (m, 14H, arom). Anal. Calcd for C₂₂H₁₆N₂: C, 85.69; H, 5.23; N, 9.08. Found: C, 85.72; H, 5.23; N, 9.05.

Our thanks are due to the Italian MURST and CNR for their financial support.

- (1) Chapleo, R. B.; Fagan, G. P. *Ann. Drug Data Report* **1993**, *15*, 59.
Perregaard, J.; Arnt, J.; Bogeso, K. P.; Hyttel, J.; Sanchez, C. *J. Med. Chem.* **1992**, *35*, 1092.
Von Angerer, E.; Strohmeier, J. *J. Med. Chem.* **1987**, *30*, 131.
Glamkowsky, E. J.; Fortunato, J. M.; Spaulding, T. C.; Wilker, J. C.; Ellis, D. B. *J. Med. Chem.* **1985**, *28*, 66.
Unangst, P. C.; Carethers, M. E.; Webster, K.; Janik, G. M.; Robichaud, L. J. *J. Med. Chem.* **1984**, *27*, 1629.
- (2) (a) Barton, D. H. R.; Blazejewsky, J. C.; Charpiot, B.; Finet, J. P.; Motherwell, W. B.; Papoula, M. T. B.; Stanforth, S. P. *J. Chem. Soc., Perkin Trans. I* **1985**, 2667.
(b) Barton, D. H. R.; Finet, J. P.; Khansi, J. *Tetrahedron Lett.* **1988**, *29*, 1115.
(c) Brown, R. A.; Fernando, S. I.; Roberts, R. M. *J. Chem. Soc., Perkin Trans. I* **1994**, 197.
(d) Tokmakmov, G. P.; Grandberg, J. *Tetrahedron* **1995**, *51*, 2091.
- (3) Pozharskii, A. F.; Marsokha, B. K.; Simonov, A. M. *J. Gen. Chem. USSR* **1963**, *33*, 994.
- (4) Stabler, R. S.; Jahangir, *Synth. Commun.* **1994**, *24*, 123.
Seki, K.; Ohkura, K.; Terashima, M.; Kanaoka, Y. *Heterocycles* **1994**, *37*, 993.
- (5) Smith III, W. J.; Sawyer, S. *Tetrahedron Lett.* **1996**, *37*, 299.
- (6) Semmelhack, M. F. In *Comprehensive Organometallic Chemistry II*; Vol 12, Abel, E. W.; Stone, F. G. A.; Wilkenson, G., Eds.; Pergamon: New York, 1995; p 979.
Semmelhack, M. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed; Pergamon: Oxford, 1991; p 517.
Astruc, D.; Balas, L.; Jhurry, D.; Latxague, L.; Grelier, S.; Morel, Y.; Hamdani, M.; Ardoin, N. *Bull. Soc. Chim. Fr.* **1990**, 401.
- (7) Bunnet, J. F.; Hermann, H. *J. Org. Chem.* **1971**, *36*, 4081.
Houghton, R. P.; Voyle, M.; Price, R. *J. Organomet. Chem.* **1983**, *259*, 183.
Ghavshov, M.; Widdoson, D. A. *J. Chem. Soc., Perkin Trans. I* **1983**, 3065.
Keller, L.; Time-Marshall, K.; Behar, S.; Richards, K. *Tetrahedron Lett.* **1989**, *30*, 3373.
Baldoli, C.; Del Buttero, P.; Maiorana, S. *Tetrahedron Lett.* **1992**, *33*, 4049.
Perez, M.; Potier, P.; Halazy, S. *Tetrahedron Lett.* **1996**, *37*, 8487.
- (8) Hong, F. E.; Lo, S. H.; Liou, M. W.; Chou, L. F.; Lin, C. C. *J. Organomet. Chem.* **1996**, *516*, 123.
- (9) We ran the reaction on tricarbonyl(η^6 -chlorobenzene)chromium, as reported by Hong,⁸ but no arylation product was obtained. No products of *cine* or *tele* substitution were detected. For ref. see:
- (10) Rose-Munch, F.; Rose, E.; Semra, A.; Bois, C. *J. Organomet. Chem.* **1989**, *363*, 103.
Rose-Munch, F.; Rose, E.; Semra, A.; Mignon, L.; Garcia-Orikan, J. *J. Organomet. Chem.* **1989**, *363*, 297.
- (11) Reactions on fluoroarene complexes **2a–f** worked in comparable yields even using DME as solvent.
- (12) Toritsuka, K. Jpn Patent 04, 319, 959, 1992; *Chem. Abstr.* **1993**, *118*, 202029g.
- (13) Gerard-Monier, D.; Erdelmeier, I.; Chaudiere, J. R.; Yadan, J. C. Fr. Patent 2, 704, 947, 1993; *Chem. Abstr.* **1995**, *122*, 128088q.
- (14) Alemagna, A.; Cremonesi, P.; Del Buttero, P.; Licandro, E.; Maiorana, S. *J. Org. Chem.* **1983**, *48*, 3114.
- (15) *Dictionary of Organic Compounds*, 5th ed., Vol.V; Buckingham J., Ed.; Chapman and Hall: New York, 1982.
Begtrup, M.; Elguero, J.; Faure, R.; Camps, P.; Estopa, C.; Ilavsky, D.; Fruchier, A.; Marzin, C.; de Mendoza, J. *Magn. Res. Chem.* **1988**, *26*, 134.