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Stereoselective Synthesis of Both Enantiomers of *N*-Aryl Indoles with Axially Chiral N−C Bonds¶

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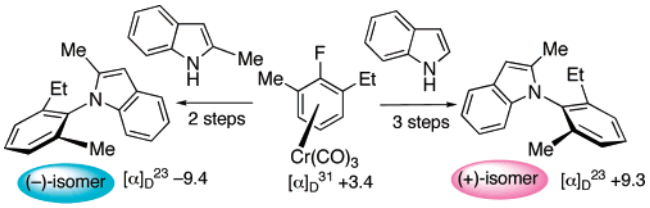

N-Aryl indoles with axially chiral N−C bonds were synthesized by stereoselective nucleophilic aromatic substitution reactions of planar chiral tricarbonyl(2,6-disubstituted-1-fluorobenzene)chromium complexes. The stereochemistry of the products is highly dependent on the position of the substituent in the indole. When indoles devoid of a substituent at the 2-position were used, *N*-aryl indole chromium complexes having anti orientation with respect to the tricarbonylchromium fragment were obtained diastereoselectively. In contrast, 2-substituted indoles gave the *N*-aryl indoles with syn orientation between the tricarbonylchromium fragment and the benzene ring of the indole. These results demonstrate that we have succeeded in synthesizing both enantiomers of *N*-aryl indoles utilizing an identical planar chiral arene chromium complex.

Introduction

Axially chiral N−C bonds are of potential importance in asymmetric reactions[1] and as intermediates for the synthesis of biologically active natural products, e.g., murrastifoline F[2] and ancisheynine.[3] Also, some compounds are used as agricultural herbicides and fungicides.[4] Thus, there is increasing attention on the development of an efficient synthetic route for enantiomerically pure compounds having an axially chiral N−C bond. Recently, asymmetric synthesis of axially chiral anilides among the chiral compounds with N−C bonds has been actively investigated. Simpkins[5] and we[6] reported the asymmetric desymmetrization of the ortho substituents in prochiral anilides with a stoichiometric amount of a chiral base. Kitagawa, Taguchi, and co-workers[7] and Terauchi and Curran[8] reported the catalytic asymmetric syntheses of atropisomeric anilides by N-arylation or allylation reactions. Tanaka and co-workers

¶ This paper is dedicated to Prof. Yoshihiko Ito in memoriam.

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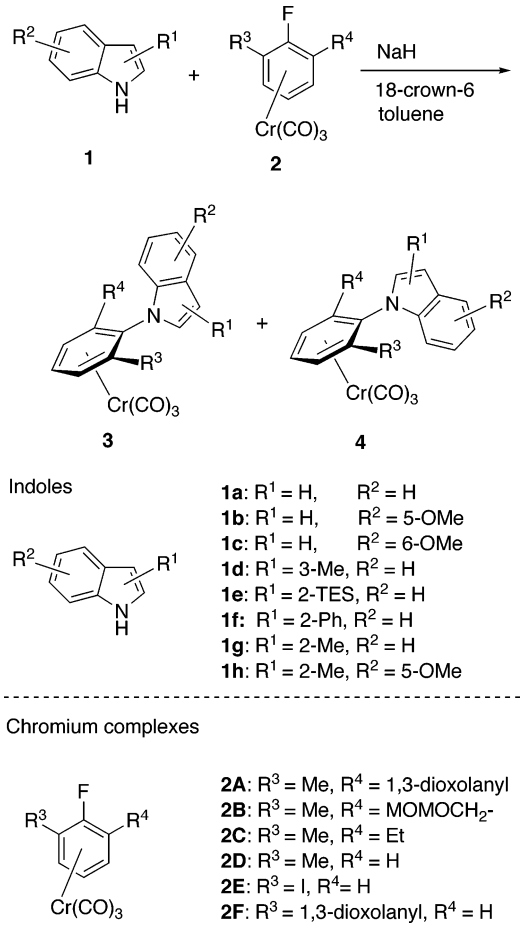
developed the catalytic asymmetric synthesis of axially chiral anilides by [2+2+2] cycloaddition reactions.[9] Asymmetric Friedel−Crafts-type amination of β-naphthol is also reported for the preparation of axially chiral naphthyl carbamate derivatives.[10] However, to our knowledge, there is no report on the direct asymmetric synthesis of axially chiral *N*-aryl amines without an amido bond, e.g., *N*-aryl pyrroles, indoles, carbazoles, and pyridines.[11] These types of compounds are mostly obtained as chiral compounds by optical resolution.[12] Herein, we report in detail the stereoselective synthesis of *N*-aryl indoles having axially chiral N−C bonds by nucleophilic substitution reactions utilizing planar chiral arene chromium complexes.

Results and Discussion

Stereoselective N−C Bond Formation by Nucleophilic Substitution Reactions. A coordination of an electron-withdrawing tricarbonylchromium fragment to the arene ring activates the ring toward additions of nucleophiles.[13] Semmelhack and co-workers reported the nucleophilic substitution reaction of tricarbonylchromium-coordinated indole with amine for the synthesis of teleocidin.[14] On the other hand, N−C(aryl) bond formation by nucleophilic aromatic substitution reactions of indoles with haloarene chromium complexes was conducted by Maiorana and co-workers.[15] However, the synthesis of *N*-aryl indoles having an axially chiral N−C(aryl) bond was not described. Thus, we initially examined the nucleophilic substitution reaction of an indolyl anion derived from indole (**1a**) with sodium hydride and tricarbonyl[2-(1,3-dioxolanyl)-6-methyl-1-fluorobenzene]chromium (**2A**) in the presence of 18-crown-6

SCHEME 1. Stereoselective Nucleophilic Substitution Reactions of Indoles 1 and Chromium Complexes 2



in toluene solution at 110 °C (Scheme 1; Table 1, entry 1). The reaction proceeded smoothly to give *N*-aryl indole chromium complex **3aA** as a single diastereomer in 76% yield.[16] The stereochemistry of **3aA** was confirmed by ^{1}H NMR analysis[17] to be anti configuration; i.e., the chromium tricarbonyl group and the benzene ring of the indole are in opposite directions with respect to the N−C bond. The structure was further tentatively confirmed by X-ray analysis.[18] However, the structure obtained was not of high quality owing to the fact that we were unable to obtain high quality crystals of **3aA** for use in the X-ray structure determination. When the chromium complex was changed to **2B** or **2C**, the *N*-aryl indole chromium complex **3aB** or **3aC** was obtained as a single diastereomer in a manner similar to that above (entries 2 and 3). Other nucleophiles having substituents at different positions were also examined, and all of them gave moderate to good yields with high diastereoselectivities (entries 4−7). Judging from the ^{1}H NMR chemical shifts of the proton at the C7 position of the indole fragment, the stereochemistry of these products was confirmed to be the thermodynamically stable anti configuration.[17]

Next the axial stereochemistry of *N*-aryl indole chromium complexes derived from the nucleophilic substitution reactions of the tricarbonyl(ortho-substituted fluorobenzene)chromium complex with 2-substituted indole was examined (Table 2). The

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(14) Semmelhack, M. F.; Rhee, H. *Tetrahedron Lett.* **1993**, *34*, 1399−1402.

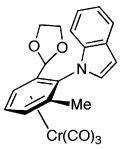
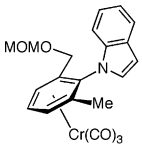
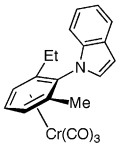
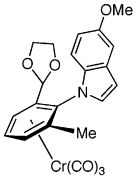
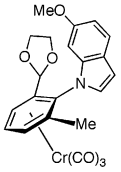
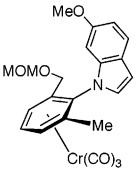
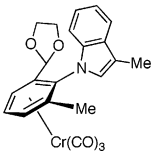
(15) Maiorana, S.; Baldoli, C.; Del Buttero, P.; Di Ciolo, M.; Papagni, A. *Synthesis* **1998**, 735−738.

(16) We confirmed that **3aA** was also prepared in an optically active form ($[\alpha]_D^{21}$ +68, *c* 0.04 in $CHCl_3$), and its demetalated *N*-aryl indole exhibited positive optical rotation ($[\alpha]_D^{24}$ +75, *c* 0.33 in $CHCl_3$) that did not change even after prolonged standing (24 h) at room temperature in chloroform solution. Furthermore, the optical purity of demetalated *N*-aryl indole did not decrease even after refluxing for 4 h by monitoring HPLC (HPLC conditions: Chiralcel OD; hexane/2-propanol = 9:1; flow rate 1.0 mL/min; column temperature 40 °C; UV detector 254 nm, retention time, racemate, 5.96 min for (+)-isomer, 6.74 min for (−)-isomer).

(17) Uemura, M.; Nishimura, H.; Kamikawa, K.; Shiro, M. *Inorg. Chim. Acta* **1994**, *222*, 63−70.

(18) For an X-ray structure for the corresponding complex, see Supporting Information.

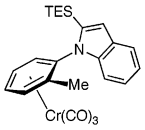
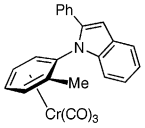
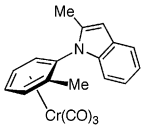
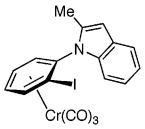
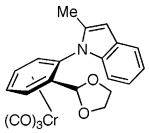
TABLE 1. Reaction of Tricarbonyl(2,6-disubstituted-1-fluorobenzene)chromium Complexes with Indoles

entry	1,2	major product	yield (%)	3 : 4[a]
1	**1a, 2A**	**3aA** 	76	>98 : <2
2	**1a, 2B**	**3aB** 	76	>98 : <2
3	**1a, 2C**	**3aC** 	94	>98 : <2
4	**1b, 2A**	**3bA** 	70	>98 : <2
5	**1c, 2A**	**3cA** 	86	>98 : <2
6	**1c, 2B**	**3cB** 	65	>98 : <2
7	**1d, 2A**	**3dA** 	77	>98 : <2

[a] Ratio of diastereomers was determined by ^{1}H NMR.

nucleophilic substitution reaction of tricarbonyl(2-methyl-1-fluorobenzene)chromium (**2D**) with 2-triethylsilylindole (**1e**)[19] under the same conditions as above gave complex **4eD** as a single diastereomer in 90% yield (entry 1). The stereochemistry of **4eD** was confirmed by X-ray analysis to be syn configuration; i.e., the chromium tricarbonyl group and the benzene ring of the indole are in the same direction.[18] A low-field shift of the C-7 proton signal of the indole fragment was observed (δ 7.97 ppm), which was caused by the anisotropic effect of the chromium tricarbonyl group.[17] In the case of 2-phenylindole (**1f**), the reaction gave product **4fD** as a single syn diastereomer (entry 2). On the other hand, when 2-methylindole (**1g**) was used as a nucleophile, the diastereoselectivity was dramatically decreased (entry 3). However, when this reaction was performed at 90 °C, the diastereoselectivity was improved to 17:83 for **3gD** and **4gD** (entry 4). These results indicate that **3gD** was formed as a result of the axial isomerization of **4gD** that initially formed predominantly. As the steric requirement of the ortho substituent on the fluorobenzene chromium complex increased, the axial isomerization would be suppressed to give good diastereoselectivity (entries 5 and 6).

TABLE 2. Reaction of Tricarbonyl(2-disubstituted-1-fluorobenzene)chromium Complexes with 2-Substituted Indoles

entry	1,2	major product	yield (%)	3 : 4[d]
1[a]	**1e, 2D**	**4eD** 	90	<2 : >98
2[a]	**1f, 2D**	**4fD** 	15[c]	<2 : >98
3[a]	**1g, 2D**	**4gD** 	88	33 : 67
4[b]	**1g, 2D**	**4gD**	87	17 : 83
5[b]	**1g, 2E**	**4gE** 	36[c]	5 : 95
6[a]	**1g, 2F**	**4gF** 	50	16 : 84

[a] Reaction was performed at 110°C. [b] Reaction was performed at 90°C. [c] The residual substance is the starting material. [d] Ratio of diastereomers was determined by ^{1}H NMR.

Stereoselective Synthesis of a 2,2′,6′-Trisubstituted *N*-Aryl Indole Chromium Complex. To investigate the stereoselective synthesis of highly hindered 2,2′,6′-trisubstituted *N*-aryl indoles, we next examined the nucleophilic substitution reaction of a 2,6-disubstituted fluorobenzene chromium complex with 2-methylindole as the nucleophile (Table 3). Initially, we examined the reaction of 2-methylindole (**1g**) and tricarbonyl[2-(1,3-dioxolanyl)-6-methyl-1-fluorobenzene]chromium (**2A**) (entry 1). Although it is a sterically hindered nucleophile, the reaction proceeded at 110 °C to give a product with high diastereoselectivity in 50% yield. The stereochemistry of the product was confirmed to be **4gA** by X-ray analysis.[18] A low-field shift of

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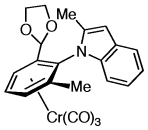
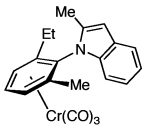
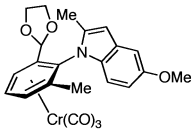
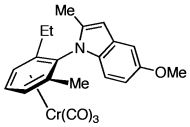
TABLE 3. Reaction of Tricarbonyl(2,6-disubstituted-1-fluorobenzene)chromium Complexes with 2-Substituted Indoles

entry	1,2	major product	yield (%)	3 : 4[c]
1[a]	**1g**, **2A**	**4gA** 	50	<2 : >98
2[b]	**1g**, **2C**	**4gC** 	38	<2 : >98
3[a]	**1h**, **2A**	**4hA** 	83	<2 : >98
4[a]	**1h**, **2C**	**4hC** 	52	4 : 96

[a] Reaction was performed at 110 °C. [b] Reaction was performed at 100 °C. [c] Ratio of diastereomers was determined by ^{1}H NMR.

TABLE 4. Relative Energy Difference Between Paths A and B [kJ/mol]

	TS1	Meisenheimer complex	TS2
path A	66.5	1.3	84.5
path B	67.7	0	79.6

the C-7 proton signal of the indole fragment was observed (δ 8.08 ppm), which was caused by the anisotropic effect of the chromium tricarbonyl group.[17] It is worth noting that the difference in bulkiness between the methyl group and the benzene ring of the indole was completely discriminated for the formation of the N−C bond. Furthermore, axial isomerization was exhibited by the steric bulkiness between ortho substituents with respect to the axis. The tricarbonyl(2-ethyl-6-methyl-1-fluorobenzene)chromium complex (**2C**) also promoted the nucleophilic substitution reaction with 2-methylindole (entry 2). When 2-methyl-5-methoxyindole (**1h**) was used as a nucleophile, **4hA**, which has the same stereochemical relationship as **4gA**, was obtained as a single diastereomer in good yield (entry 3). The improved yield could be attributed to the increase in nucleophilicity due to the introduction of an electron-donating MeO group. The combination of 2-methyl-5-methoxyindole (**1h**) and the tricarbonyl(2-ethyl-6-methyl-1-fluorobenzene)chromium complex (**2C**) gave a product with high diastereoselectivity (entry 4). In contrast, other 2-substituted indoles such as 2-iodo, bromo, and triethylsilylindole gave unsuccessful results with recovery of the starting material.

Stereochemical Outcome of Nucleophilic Substitution Reactions. It is recognized that the formation of complex **3** with the anti configuration is due to the steric repulsion between the tricarbonylchromium fragment and the benzene ring of the indole. On the other hand, 2-substituted indoles gave the products with the opposite configuration; i.e., the tricarbonyl-

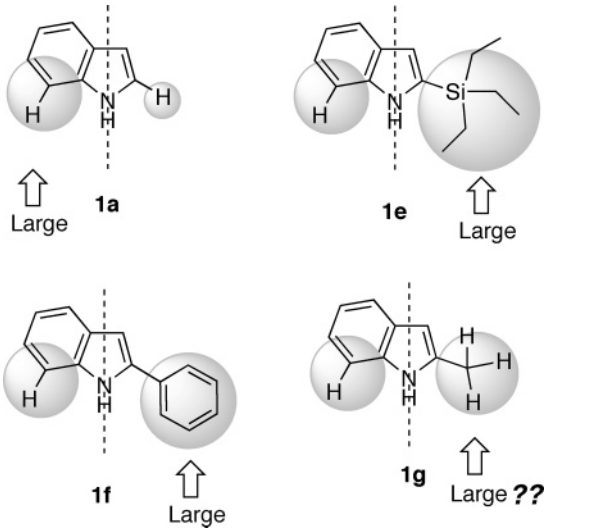


FIGURE 1. Approximate bulkiness with respect to chiral axes.

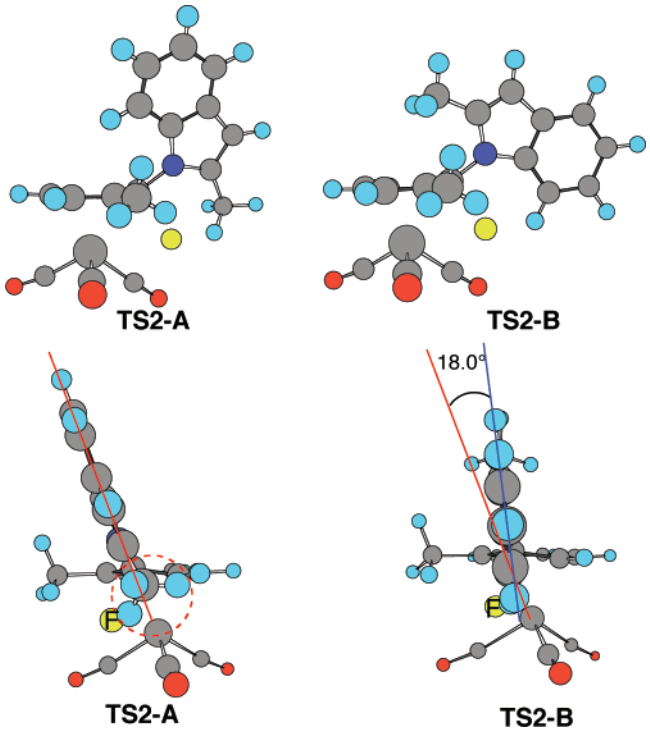


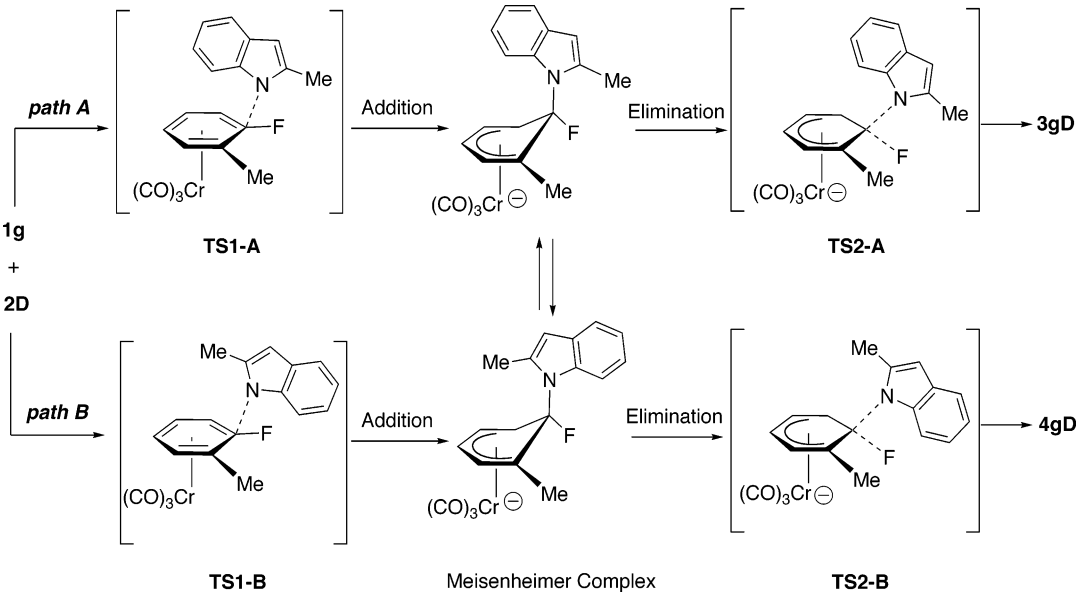
FIGURE 2. Plausible structures in TS2. The red and blue lines indicate the central axis of an indole plane in TS2-A and TS2-B, respectively.

chromium fragment and the benzene ring are in the same direction. As depicted by shaded circles of different sizes in Figure 1, the difference in steric bulkiness between the two sides with respect to the chiral axis may determine the axial chirality. In general, it is predicted that the large substituent directs the chromium tricarbonyl group to the opposite side to avoid steric repulsion.

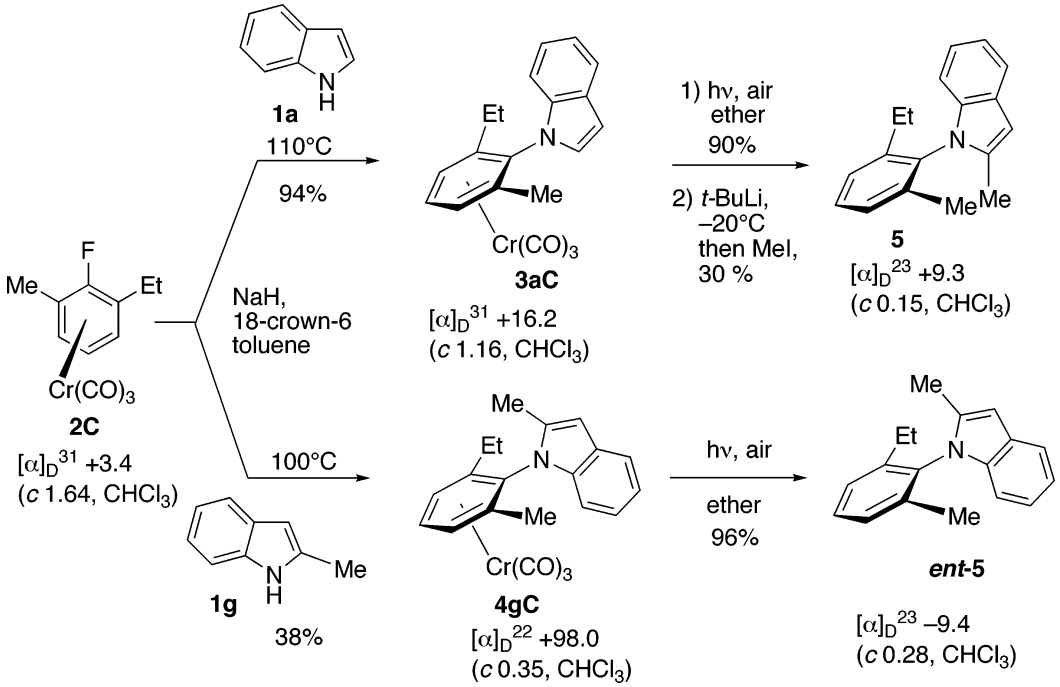
However, these considerations are inapplicable to the case of 2-methylindole (**1g**), whose bulkiness at both sides (methyl vs the C7 position of indole) with respect to the axis is almost the same. To gain insight into this stereochemical outcome, we next examined the theoretical calculation.

Nucleophilic aromatic substitution reactions have been proposed to proceed through an addition−elimination mechanism

SCHEME 2. Possible Reaction Pathways for the Formation of *N*-Aryl Indole

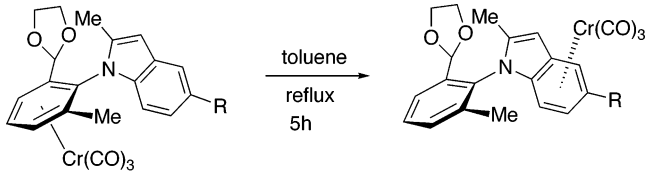


SCHEME 3. Stereoselective Synthesis of Both Enantiomers from an Identical Planar Chirality



involving the formation of an intermediate Meisenheimer complex[20] (Scheme 2), and some theoretical studies have been reported.[21] In this case, the theoretical calculation also finds these generally accepted steps (Table 4). In the initial step, 2-methylindole attacks almost perpendicular to the arene face of the fluorobenzene chromium complex. Then, it is possible to consider two pathways for the nucleophilic attack: one is path A in which the methyl group of an indole faces the fluorine atom (TS1-A), and the other is path B that shows an opposite orientation (TS1-B). However, it was revealed that the rate-

SCHEME 4. Stereoselective Tricarbonylchromium Migration

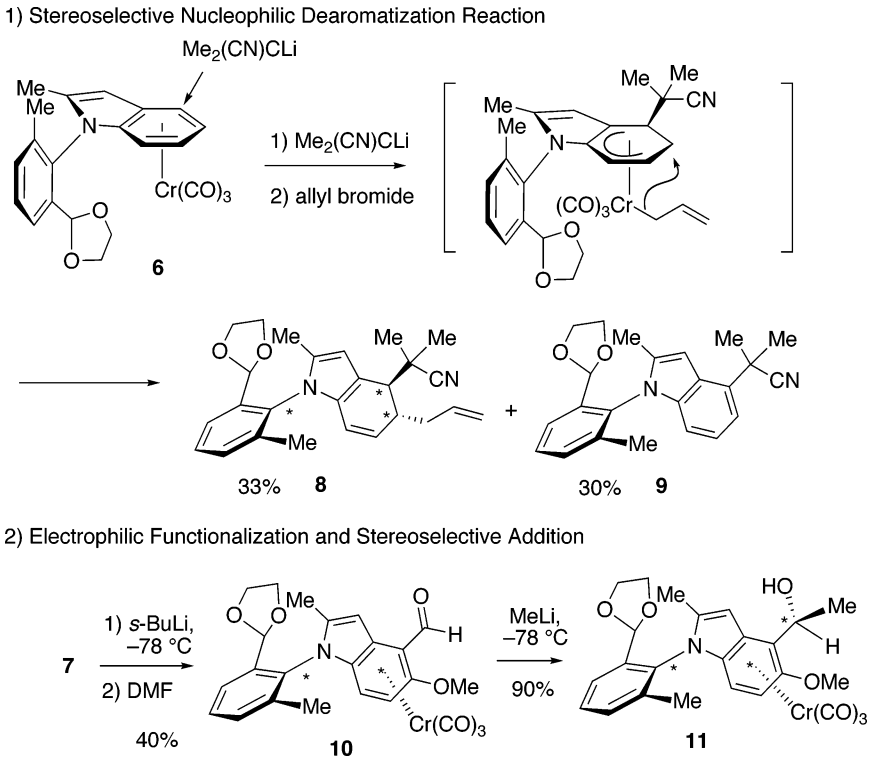


R = H: **4gA** — **6** 60 %
R = OMe: **4hA** — **7** 40 %

(20) η^5-Cyclohexadienyltricarbonylchromium complexes from addition of carbon nucleophiles to arene tricarbonylchromium complexes were characterized by X-ray analysis: Semmelhack, M. F.; Hall, H. T.; Farina, R.; Yoshifuji, M.; Clark, G.; Bargar, T.; Hirotsu, K.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535−3544.

(21) (a) Acevedo, O.; Jorgensen, W. L. *Org. Lett.* **2004**, *6*, 2881−2884. (b) Vayner, G.; Houk, K. N.; Jorgensen, W. L.; Brauman, J. I. *J. Am. Chem. Soc.* **2004**, *126*, 9054−058. (c) Lozano, A. E.; Jimeno, M. L.; de Abajo, J.; de la Campa, J. G. *Macromolecules* **1994**, *27*, 7164−7170. (d) Nudelman, N. S.; Palleros, D. R. *J. Chem. Soc., Perkin Trans. 2* **1985**, *6*, 805−809.

SCHEME 5. Stereoselective Transformations of Indole Complexes



determining step is the elimination step (TS2) that has the highest-energy barrier of all the steps. Thus, the stereochemistry of the product would be determined by the conformation at this step. Theoretical calculation showed that TS2-B was 4.9 kJ/mol more stable than TS2-A, in agreement with the stereochemical outcome of the reactions. Comparing the conformations of TS2-A and TS2-B, the arene face of 2-methylindole in TS2-A leans 18.0° with respect to the horizontal arene chromium face, compared to that in TS2-B (Figure 2). These results indicate that the methyl group in TS2-A might interfere more with the fluoride anion elimination than the flat benzene ring of indole in TS2-B. As a result, TS2-B would be a more preferable conformation than TS2-A.

Stereoselective Synthesis of Both Enantiomers of *N*-Aryl Indole. These results enabled us to synthesize both enantiomers of *N*-aryl indole from an identical planar chiral arene chromium complex (Scheme 3).[22] Enantiomerically pure (+)-tricarbonyl-(2-ethyl-6-methylfluorobenzene)chromium (**2C**) ($[\alpha]_D^{31}$ +3.4, *c* 1.64 in $CHCl_3$)[23] was reacted with indole (**1a**) in the presence of NaH and 18-crown-6 in toluene at 110 °C. *N*-Aryl indole complex **3aC** ($[\alpha]_D^{31}$ +16.2, *c* 1.16 in $CHCl_3$) with anti configuration was stereoselectively obtained in 94% yield. Oxidative demetalation and subsequent methylation at the C2 position of indole gave (+)-**5** ($[\alpha]_D^{23}$ +9.3, *c* 0.15 in $CHCl_3$).[24] On the other hand, (+)-**2C** was reacted with 2-methylindole (**1g**) to give the indole complex **4gC** ($[\alpha]_D^{22}$ +98.0, *c* 0.35 in $CHCl_3$) with opposite axial chirality. Subsequent oxidative demetalation gave ***ent*-5** ($[\alpha]_D^{23}$ −9.4, *c* 0.28 in $CHCl_3$).

Stereoselective Tricarbonylchromium Migration Reactions. Metal migration from one site of a coordinated organometallic ligand to another is a well-known process occurring in oligocyclic fused π−arene complexes due to the haptotropic ring slippage from the η^6 to η^4 coordination mode.[25] On the other hand, the migration of a tricarbonylchromium group between two different and nonadjacent six-membered rings is rare.[26] We previously reported the stereoselective migration of chromium to another arene face in biaryl chromium complexes.[27] The same type of transformation could be observed in sterically hindered *N*-aryl indole chromium complexes. For instance, reflux in toluene of complex **4gA** for a long time (5 h) induced the stereoselective migration of the chromium tricarbonyl group to the arene ring of the indole to give **6** in 60% yield as a single diastereomer (Scheme 4). X-ray analysis revealed that the

(22) (a) Uemura, M.; Kamikawa, K. *J. Chem. Soc., Chem. Commun.* **1994**, 2697−2698. (b) Kamikawa, K.; Watanabe, T.; Uemura, M. *J. Org. Chem.* **1996**, *61*, 1375−1384. (c) Kamikawa, K.; Uemura, M. *Synlett* **2000**, 938−949.

(23) Enantiomerically pure (+)-complex **2C** was prepared from optically resolved (+)-tricarbonyl(2-fluoro-3-methylbenzaldehyde)chromium ($[\alpha]_D^{22}$ +844, *c* 0.036 in $CHCl_3$) by reaction with MeMgBr and subsequent reduction by Et_3SiH in the presence of $BF_3{\cdot}Et_2O$ (see Supporting Information for details). Resolution of racemic tricarbonyl(2-fluoro-3-methylbenzaldehyde)chromium was achieved by the Davies method.[32] The optical purity of resolved tricarbonyl(2-fluoro-3-methylbenzaldehyde)chromium was determined by HPLC with Chiralpak AS: hexane/2-propanol = 9:1; flow rate 1.0 mL/min; column temperature 40 °C; UV detector 254 nm, retention time, racemate, 9.14 min for (+)-isomer, 14.70 min for (−)-isomer. The absolute stereochemistry of **2C** has not been determined.

(24) We confirmed that the optical rotation of (+)-**5** ($[\alpha]_D^{30}$ +9.3, *c* 0.15 in $CHCl_3$) did not change even after prolonged standing (24 h) at room temperature in chloroform solution. Our attempts to find the chiral HPLC condition of compound **5** were unsuccessful.

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(26) (a) Pan, J.; Kampf, J. W.; Ashe, A. J., III *Organometallics* **2006**, *25*, 197−202. (b) Oprunenko, Y. F.; Shaposhnikov, I. A.; Ustynyuk, Y. A. *Metalloorg. Khim.* **1991**, *4*, 1377−1390. (c) Cunningham, S. D.; Öfele, K.; Willeford, B. R. *J. Am. Chem. Soc.* **1983**, *105*, 3724−3725. (d) Traylor, T. G.; Goldberg, M. J. *Organometallics* **1987**, *6*, 2531−2536.

(27) (a) Kamikawa, K.; Sakamoto, T.; Tanaka, Y.; Uemura, M. *J. Org. Chem.* **2003**, *68*, 9356−9363. (b) Kamikawa, K.; Sakamoto, T.; Uemura, M. *Synlett* **2003**, 516−518.

chromium tricarbonyl group was directed toward the 1,3-dioxolane group.[18] On the other hand, **4hA** having a 1,3-dioxolane group was transformed into **7** as a single diastereomer. When the substituent was changed from the 1,3-dioxolane group to the methyl group, the migration did not proceed. Thus, the 1,3-dioxolane group might play a role in assisting the transfer of the tricarbonyl chromium group by coordinating to a chromium atom.

Because tricarbonyl chromium coordinated indole derivatives exhibit unique properties due to the selective activation of a six-membered ring, chemo- and stereoselective transformations are possible utilizing the planar chiral indole fragment. For the selective transformation of the chromium-coordinated arene ring, (1) nucleophilic dearomatization reactions[28] and (2) electrophilic functionalizations[29] are widely utilized. Therefore, the stereoselective (1) nucleophilic dearomatization was initially examined. Chromium complex **6** was treated with 2-lithio-2-methylpropionitrile and subsequently trapped with allyl bromide. Nucleophilic addition occurred at the 4-position from the exo side of the tricarbonylchromium group, and subsequent electrophilic addition occurred from the endo side to give **8** possessing two newly generated chiral centers *inside* the indole diastereoselectively utilizing the planar chirality of the indole.[28a,c] As a byproduct, **9** was formed by aromatization without trapping with allyl bromide. On the other hand, (2) electrophilic functionalization was also examined. Complex **7** was functionalized by treatment with *sec*-BuLi and subsequent trapping with DMF to give complex **10**, which was transformed at the C4 position of the indole fragment, as the major product.[30] The stereoselective addition reaction of **10** with methyl lithium at −78 °C gave complex **11** as a single diastereomer, and we could introduce a chiral center *outside* the indole (Scheme 5). Therefore, we succeeded in *controlling not only the axial chirality but also the central chiralities from a single mobile chiral auxiliary*.

Conclusions

We have demonstrated the stereoselective synthesis of axially chiral *N*-aryl indoles by nucleophilic substitution reaction with high diastereoselectivities. Together, the results indicate that we can control both the C−N axial chirality and the chirality at the side chain from a single chiral source. Application to the stereoselective synthesis of natural products having axially chiral N−C bonds is underway in our laboratory.

Experimental Section

General Procedure for Nucleophilic Substitution Reaction. To a solution of indole (**1a)** (20 mg, 0.17 mmol) in toluene (5.0 mL) were added 18-crown-6 (63 mg, 0.24 mmol) and NaH (6 mg, 0.24 mmol) at 0 °C under argon. The resulting mixture was stirred for 30 min at 25 °C, and then a toluene solution of arene chromium complex **2A** (50 mg, 0.16 mmol) was added to the solution and refluxed for 2 h. The reaction mixture was quenched with H_2O at 0 °C, extracted with ethyl acetate, and washed with brine. The organic layer was dried over anhydrous $MgSO_4$, and filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography to give *N*-aryl indole chromium complex **3aA** (50 mg, 76%). Other *N*-aryl indoles were prepared in a similar way.

Tricarbonyl[1-(η^6-2-dioxolanyl-6-methylphenyl)-1*H*-indole]-chromium (3aA): mp 105 °C; $[\alpha]_D^{21}$ +68.2 (*c* 0.044 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.75 (3H, s), 3.71−4.00 (4H, m), 5.21 (1H, d, *J* = 6.3 Hz), 5.30 (1H, s), 5.45 (1H, d, *J* = 6.3 Hz), 5.63 (1H, t, *J* = 6.3 Hz), 6.61 (1H, d, *J* = 3.2 Hz), 6.98 (1H, dd, *J* = 1.7, 6.3 Hz), 7.15−7.18 (2H, m), 7.26 (1H, m), 7.65 (1H, dd, *J* = 1.7 Hz, 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 16.7, 65.8, 66.0, 85.0, 90.0, 94.4, 99.4, 103.2, 110.1, 110.4, 111.0, 111.7, 120.5, 121.1, 122.5, 129.1, 132.4, 138.2, 231.3; IR ($CHCl_3$) 2253, 1977, 1908, 1462 cm^{-1}. Elemental analysis calcd (%) for $C_{21}H_{17}NO_5Cr$ (415.36): C, 60.72; H, 4.13. Found: C, 60.97; H, 3.95.

Tricarbonyl[1-(η^6-2-methoxymethoxymethyl-6-methylphenyl)-1*H*-indole]chromium (3aB): mp 83 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.85 (3H, s), 3.12 (3H, s), 4.06 (1H, d, *J* = 13.0 Hz), 4.12 (1H, d, *J* = 13.0 Hz), 4.34 (1H, d, *J* = 6.6 Hz), 4.47 (1H, d, *J* = 6.6 Hz), 5.18 (1H, d, *J* = 6.3 Hz), 5.44 (1H, d, *J* = 6.3 Hz), 5.69 (1H, t, *J* = 6.3 Hz), 6.64 (1H, d, *J* = 3.2 Hz), 6.96 (1H, dd, *J* = 3.2, 5.9 Hz), 7.16−7.19 (3H, m), 7.66 (1H, dd, *J* = 3.2, 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 16.8, 55.3, 64.3, 86.3, 89.0, 95.4, 96.4, 103.5, 109.3, 109.8, 111.3, 112.2, 120.5, 121.3, 122.6, 129.2, 131.8, 137.3, 231.5; IR ($CHCl_3$) 3020, 1974, 1903 cm^{-1}. Elemental analysis calcd (%) for $C_{21}H_{19}NO_5Cr$ (417.38): C, 60.43; H, 4.59. Found: C, 60.10; H 4.78.

Tricarbonyl[1-(η^6-2-ethyl-6-methylphenyl)-1*H*-indole]chromium (3aC): mp 93 °C; $[\alpha]_D^{31}$ +16.2 (*c* 1.16 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 0.94 (3H, t, *J* = 7.5 Hz), 1.84 (3H, s), 2.21 (2H, q, *J* = 7.5 Hz), 5.12 (1H, d, *J* = 6.3 Hz), 5.13 (1H, d, *J* = 6.3 Hz), 5.66 (1H, t, *J* = 6.3 Hz), 6.63 (1H, d, *J* = 2.7 Hz), 6.94 (1H, dd, *J* = 2.4, 6.3 Hz), 7.16−7.21 (3H, m), 7.68 (1H, dd, *J* = 2.4, 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 14.0, 17.1, 23.9, 86.6, 88.7, 96.1, 103.3, 109.4, 111.3, 112.9, 117.7, 120.5, 121.5, 122.6, 129.3, 132.4, 137.5, 232.2; IR ($CHCl_3$) 2981, 2930, 1971, 1900 cm^{-1}; MS (70 eV) *m*/*z* (%) 371 (51) [M^+], 315 (32) [M^+ − 2CO], 287 (100) [M^+ − 3CO]; HRMS calcd for $C_{20}H_{17}NO_3Cr$ 371.0613, found 371.0613.

Preparation of 1-(6-Ethyl-2-methylphenyl)-2-methyl-1*H*-indole (5). Complex **3aC** (150 mg, 0.40 mmol) in ether (70 mL) was exposed to sunlight for 30 min until the yellow solution became colorless. The precipitate was filtrated, and the filtrate was evaporated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 5:1) to give the de-chromium product (85 mg, 90%). To the solution of de-chromium product (40 mg, 0.17 mmol) in THF (2.0 mL) was added *t*-BuLi (0.13 mL, 0.20 mmol), warming to −20 °C for 3 h. Subsequently, methyl iodide (13 μL, 0.20 mmol) was added and stirred for 18 h, warming to ambient temperature. The resulting solution was quenched with aqueous NH_4Cl, extracted with ether, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel chromatography (hexane/benzene = 50:1) to give compound **5** as a colorless oil (13 mg, 30%): $[\alpha]_D^{23}$ +9.3 (*c* 0.15 in $CHCl_3$) (***ent*-5**: $[\alpha]_D^{23}$−9.4 (*c* 0.28 in $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.00 (3H, t, *J* = 7.6 Hz), 1.82 (3H, s), 2.11 (3H, s), 2.14−2.22 (2H, m), 6.43 (1H, s), 6.74 (1H, d, *J* = 7.8 Hz), 7.03 (1H, t, *J* = 7.3 Hz), 7.09 (1H, t, *J* = 7.3 Hz), 7.20 (1H, d, *J* = 7.3 Hz), 7.26 (1H, d, *J* = 7.3 Hz), 7.35 (1H, t, *J* = 7.8 Hz), 7.58 (1H, d, *J* = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 12.7, 14.5, 17.4, 23.8, 100.3, 109.7, 119.5, 119.6, 120.8,

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126.6, 128.3, 128.7, 135.0, 136.7, 137.2, 137.8, 143.6; IR ($CHCl_3$) 2253, 2857, 2931,2989 cm^{-1}; MS (70 eV) *m/z* (%) 249 (100) [M^+], 234 (88) [$M^+ - CH_3$]; HRMS calcd for $C_{18}H_{19}N$ 249.1518, found 249.1519.

General Procedure for Stereoselective Tricarbonylchromium Migration Reaction. A solution of the *N*-aryl indole complex (0.25 mmol) in toluene (5.0 mL) was degassed by three freeze/vacuum/thaw cycles and stirred at 110 °C under nitrogen for 5 h. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give the migrated product.

Tricarbonyl[η^6-1-(2-dioxolanyl-6-methylphenyl)-2-methyl-1*H*-indole]chromium (6): mp 130 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.69 (3H, s), 2.10 (3H, s), 3.92−4.20 (4H, m), 4.97 (1H, t, J = 6.6 Hz), 5.29 (1H, t, J = 6.6 Hz), 5.58 (1H, s), 5.75 (1H, d, J = 6.6 Hz), 6.06 (1H, d, J = 6.6 Hz), 6.22 (1H, s), 7.37 (1H, d, J = 7.6 Hz), 7.50 (1H, t, J = 7.6 Hz), 7.75 (1H, d, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 13.3, 16.8, 65.3, 65.4, 77.2, 81.7, 84.4, 86.5, 91.5, 99.0, 100.9, 105.7, 126.0, 130.2, 132.1, 133.4, 137.1, 137.7, 146.7, 235.3; IR ($CHCl_3$) 2253, 1953 cm^{-1}. Elemental analysis calcd (%) for $C_{22}H_{19}NO_5Cr$ (429.39): C, 61.54; H, 4.46. Found: C, 61.78; H, 4.22.

Tricarbonyl[η^6-1-(2-dioxolanyl-6-methylphenyl)-2-methyl-5-methoxy-1*H*-indole]chromium (7): mp 170 °C (decomposition); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.79 (3H, s), 2.09 (3H, s), 3.75 (3H, s), 3.82−3.94 (1H, m), 3.96−4.08 (2H, m), 4.11−4.19 (1H, m), 4.77 (1H, d, J = 6.8 Hz), 5.38 (1H, s), 5.81 (1H, d, J = 6.8 Hz), 5.89 (1H, s), 6.20 (1H, s), 7.38 (1H, d, J = 8.8 Hz), 7.50 (1H, t, J = 8.8 Hz), 7.74 (1H, d, J = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 13.3, 16.9, 55.6, 65.2, 65.3, 70.4, 73.6, 80.8, 99.1, 100.0, 106.9, 110.8, 126.0, 130.2, 132.0, 133.4, 137.1, 137.8, 140.0, 147.9, 235.7; IR ($CHCl_3$) 2990, 2952, 1953, 1800 cm^{-1}; MS (70 eV) *m/z* (%) 459 (9) [M^+], 375 (30) [M^+ − 3CO], 323 (100) [$M^+ - Cr(CO)_3$]; HRMS calcd for $C_{23}H_{21}NO_6Cr$ 459.0774, found 459.0782.

Stereoselective Nucleophilic Addition to Indole Chromium Complex 6. To a solution of diisopropylamine (25 μL, 0.18 mmol) and hexamethylphosphoric triamide (0.1 μL) in THF (2.0 mL) was added *n*-BuLi (110 μL, 1.6 M in hexane, 0.18 mmol) at −78 °C under a nitrogen atmosphere. Then, the resulting solution was stirred for 15 min, and 2-methylpropionitrile (16 mL, 0.18 mmol) was added and stirred for another 15 min. A solution of chromium complex **6** (70 mg, 0.16 mmol) in THF (0.5 mL) was added to the solution mentioned above at −78 °C and stirred for 1 h. Then allyl bromide (70 μL, 0.80 mmol) was added at −78 °C and gradually warmed to ambient temperature. The solution was quenched with aqueous NH_4Cl, extracted with ether, washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 7:1) to give compound **8** as a colorless oil (19 mg, 33%) and compound **9** as colorless crystals (16 mg, 30%).

Compound 8: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.30 (3H, s), 1.34 (3H, s), 1.76 (3H, s), 1.89−1.94 (4H, m), 2.05−2.09 (1H, m), 2.99 (1H, s), 3.62 (1H, s), 3.86−3.94 (2H, m), 4.10−4.19 (2H, m), 6.44 (1H, s), 5.41−5.47 (1H, m), 5.51 (1H, s), 5.87 (2H, m), 6.24 (1H, s), 7.30 (1H, d, J = 7.8 Hz), 7.40 (1H, t, J = 7.8 Hz), 7.56 (1H, d, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 13.9, 86.2, 94.5, 95.8, 96.3, 103.5, 112.4, 119.9, 120.7, 121.5, 128.4, 137.7, 230.8; IR ($CHCl_3$) 2987, 2926, 1945 cm^{-1}; MS (70 eV) *m/z* (%) 402 (3) [M^+], 361 (73) [$M^+ - C_3H_5$], 334 (43) [$M^+ - C_3H_6N$], 293 (65) [$M^+ - C_3H_5 - C_3H_6N$], 206 (100) [$M^+ - C_3H_5 - C_2H_4O - C_3H_6N - OH - C_2H_2$]; HRMS calcd for $C_{26}H_{30}N_2O_2$ 402.2308, found 402.2312.

Compound 9: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.78 (3H, s), 1.94 (6H, s), 2.19 (3H, s), 3.75−3.81 (2H, m), 3.90−4.04 (2H, m), 5.20 (1H, s), 6.74 (1H, d, J = 7.6 Hz), 6.74 (1H, s), 7.02 (1H, t, J = 7.6 Hz), 7.09 (1H, d, J = 7.6 Hz), 7.40 (1H, d, J = 7.6 Hz), 7.48 (1H, t, J = 7.6 Hz), 7.62 (1H, d, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 12.8, 16.9, 27.8, 27.9, 36.0, 65.2, 65.4, 99.9, 100.2, 110.3, 115.7, 120.8, 125.1, 125.2, 125.3, 129.3, 131.0, 131.8, 135.2, 137.3, 138.1, 138.3; IR ($CHCl_3$) 3019, 3007 cm^{-1}; MS (70 eV) *m/z* (%) 360 (100) [M^+], 334 (8) [M^+ − CN]; HRMS calcd for $C_{23}H_{24}N_2O_2$ 360.1838, found 360.1838.

Preparation of Tricarbonyl[η^6-1-(2-dioxolanyl-6-methylphenyl)-2-methyl-4-formyl-5-methoxy-1*H*-indole]chromium (10). To a solution of complex **7** (75 mg, 0.15 mmol) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (75 μL, 0.49 mmol) in THF (10 mL) was added *s*-BuLi (0.50 mL, 0.99 M in cyclohexane, 0.50 mmol) at −78 °C, and the solution was stirred for 1 h. DMF (15 mL, 0.20 mmol) was added to the solution and stirred at −78 °C for 30 min. The resulting solution was gradually warmed to 0 °C and quenched with aqueous NH_4Cl, extracted with ether, washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 4:1) and then purified again and eluted with benzene to give complex **10** (30 mg, 40%) as red foam: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.83 (3H, s), 2.13 (3H, s), 3.77 (3H, s), 3.84 (1H, q, J = 6.8 Hz), 3.94 (1H, q, J = 6.8 Hz), 4.03 (1H, q, J = 6.8 Hz), 4.15 (1H, q, J = 6.8 Hz), 4.62 (1H, d, J = 7.1 Hz), 5.14 (1H, s), 6.07 (1H, d, J = 7.1 Hz), 7.13 (1H, s), 7.43 (1H, d, J = 7.6 Hz), 7.53 (1H, t, J = 7.6 Hz), 7.75 (1H, d, J = 7.6 Hz), 10.45 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 13.5, 17.0, 56.2, 65.3, 65.4, 67.2, 80.6, 99.0, 101.5, 105.9, 108.4, 120.2, 126.1, 130.4, 132.2, 133.1, 137.0, 137.6, 144.2, 150.1, 187.6, 233.4; IR ($CHCl_3$) 2990, 2253, 1966, 1899, 1795 cm^{-1}; MS (70 eV) *m/z* (%) 487 (5) [M^+], 403 (20) [M^+ − 3CO], 351 (100) [$M^+ - Cr(CO)_3$]; HRMS calcd for $C_{24}H_{21}NO_7Cr$ 487.0723, found 487.0727.

Preparation of Complex 11. To a solution of complex **7** (25 mg, 0.050 mmol) in ether (10 mL) was added methyl lithium (0.10 mL, 1.0 M in ether, 0.10 mmol) at −78 °C under nitrogen. The resulting solution was gradually warmed to 0 °C and quenched with aqueous NH_4Cl. The mixture was extracted with ether, washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 4:1) to give yellow crystals (23 mg, 90%): mp 168 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) δ = 1.66 (3H, d, J = 6.6 Hz), 1.81 (3H, s), 2.10 (3H, s), 3.69 (3H, s), 3.89−3.93 (1H, m), 4.00−4.18 (3H, m), 4.63 (1H, d, J = 6.9 Hz), 5.36 (1H, s), 5.45 (1H, q, J = 6.6 Hz), 5.75 (1H, d, J = 6.9 Hz), 6.69 (1H, s), 7.39 (1H, d, J = 7.5 Hz), 7.50 (1H, t, J = 7.5 Hz), 7.74 (1H, d, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 13.4, 17.0, 22.1, 56.0, 64.9, 65.2, 65.4, 68.3, 79.3, 98.7, 99.0, 99.9, 100.8, 106.0, 111.3, 126.0, 130.2, 132.1, 133.3, 137.1, 137.9, 139.1, 148.1, 244.7; IR ($CHCl_3$) 3155, 2904, 2849, 2253, 1949, 1868 cm^{-1}; MS (70 eV) *m/z* (%) 503 (6) [M^+], 419 (25) [M^+ − 3CO], 367 (59) [$M^+ - Cr(CO)_3$], 306 (100) [$M^+ - Cr(CO)_3 - C_2H_5O_2$]; HRMS calcd for $C_{25}H_{25}NO_7Cr$ 503.1036, found 503.1040.

Computational Methods. Geometry optimizations were carried out with the RHF level of theory and 3-21G(d) basis sets for all atoms. Vibrational frequency analysis was performed by using RHF/3-21G* level calculations to confirm the stationary points as either minima (no imaginary frequencies) or transition structures (only one imaginary frequencies). The calculated zero-point energies were added to the total energy as a zero-point energy correction. All calculations were performed with the Gaussian 98[31] suite of programs on a Linux-based PC.

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Supporting Information Available: The procedures for the synthesis of indole chromium complexes, their characterization and NMR spectra, and CIF files of complexes **3aA** (CCDC number 286550), **4eD** (CCDC number 627417), **4gA** (CCDC number 286551), and **6** (CCDC number 286552). This material is available free of charge via the Internet at http://pubs.acs.org.

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