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Regioselectivity of nucleophilic additions to (arene)chromium complexes: conformational effects of $Cr(CO)_3$ moieties and the nature of carbanions

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Abstract

Nucleophilic addition of some carbon nucleophiles to tricarbonyl(1-*exo*-isopropyl-5-methoxytetralin)-chromium (**4**), tricarbonyl(1-*endo*-isopropyl-5-methoxytetralin)chromium (**5**), and tricarbonyl(1-isopropyl-5-methoxy-3,4-dihydronaphthalene)chromium (**8**) has been investigated. The regioselectivity of the nucleophilic addition using 2-lithio-1,3-dithiane under kinetic control conditions is dependent on the conformation of the $Cr(CO)_3$ group for the arene ring. *exo*-Isopropyl complex **4** gives the *meta*-substituted compound with high regioselectivity in good yield, while the corresponding *endo*-isopropyl complex **5** yields predominantly the *ortho*-substituted arene. The crystal structure of the *endo*-complex **5** has been determined by X-ray crystallography, indicating that three CO ligands adopt the staggered conformation for the aromatic ring. On the other hand, the addition reaction with nitriles or cyanohydrin-stabilized carbanions under thermodynamic conditions provide the high *meta*-selectivity, regardless of the conformation of the $Cr(CO)_3$ moiety.

Introduction

The addition of carbon nucleophiles to η^6-(arene)chromium complexes has become a useful method for the introduction of substituents at proper positions not accessible by electrophilic substitution reactions [1]. High regioselectivity is often observed in substituted arene chromium complexes with strong electron donating substituents, such as methyl, alkoxy and dimethylamino groups, giving *meta* substitution products preferably [2,3]. However, the reaction mechanism is still complicated. The formation of anionic cyclohexadienyl intermediates can be reversible, and hence the interpretation of the regioselectivity is somewhat confusing. Herein we report the conformational effects of the $Cr(CO)_3$ moiety and the nature of nucleophiles that influence the regioselectivity in the nucleophilic addition.

Results and discussion

During the course of the investigation directed toward the total synthesis [4] of dihydroxyserrulatic acid (**1**) utilizing η^6-(arene)chromium complexes, it was required

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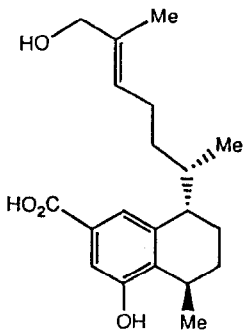
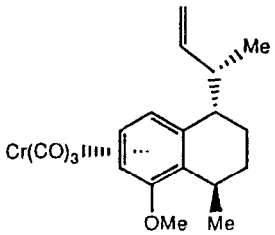


1
Dihydroxyserrulatic Acid



2

to introduce a carboxyl equivalent at the *meta* position for the methoxy group. Tricarbonyl(anisole)chromium is known to react with nucleophiles, giving *meta*-substituted anisole with high regioselectivity [1,2]. However, reaction of methoxytetralin-derived chromium complex **2** with 2-lithio-1,3-dithiane and subsequent oxidative demetallation gave an unexpected mixture of *ortho*- and *meta*-substituted compounds (ratio; 3 : 1) in less than 10% yield. In order to clarify the reason of this low yield and unusual formation of *ortho*-substituted isomer as the major product, we

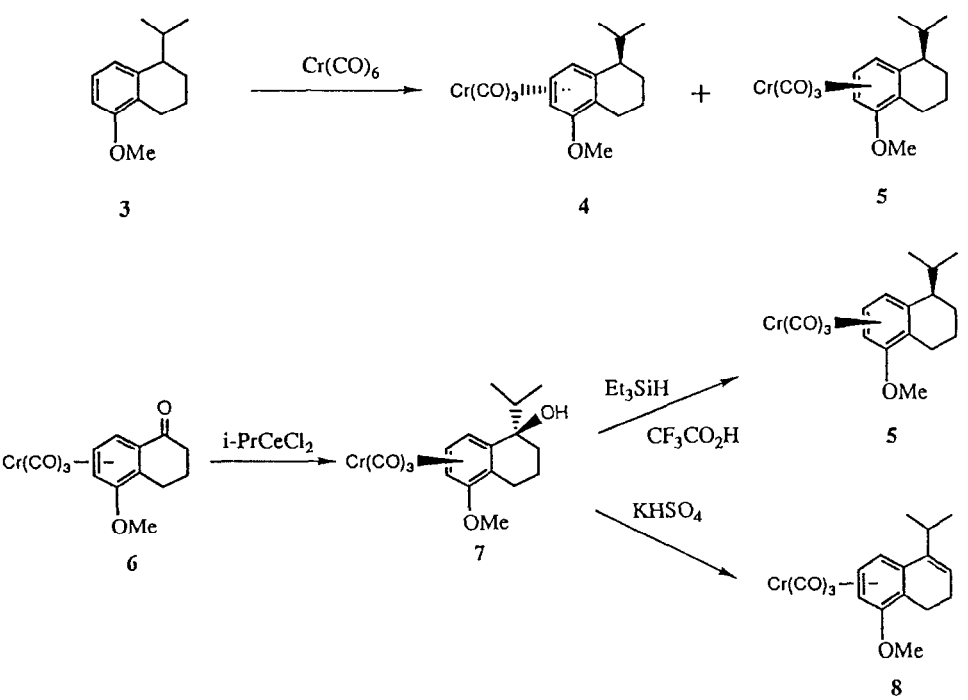
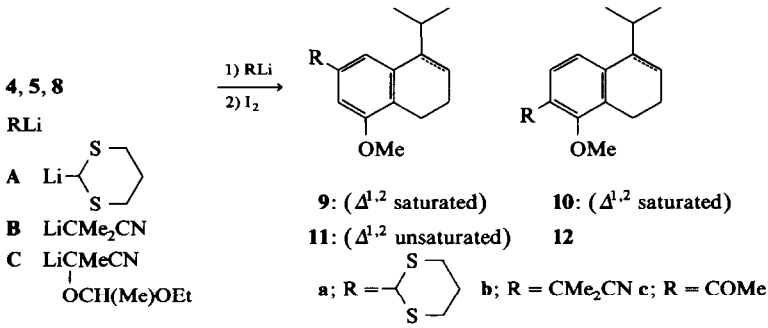


Table 1

Nucleophilic addition to (arene)chromium complexes



Entry	Complex	RLi	Reaction temp. (°C)	Reaction time (min)	Ratio of products *meta*: *ortho* (**9** or **11**:**10** or **12**)	Yield (%)
1 [a]	**4**	**A**	−78	30	93: 7	60
2 [a]	**5**	**A**	−78	30	35:65	28
3 [a]	**8**	**A**	−78	30	85:15	68
4 [a]	**4**	**B**	−78	30	94: 6	65
5	**4**	**B**	−78	5	97: 3	55
6	**4**	**B**	0	60	95: 5	15
7 [a]	**5**	**B**	−78	30	88:12	58
8 [a]	**5**	**B**	−20	30	84:16	60
9	**5**	**B**	−78	5	95: 5	40
10	**5**	**B**	−45	30	84:16	55
11	**5**	**B**	0	60	75:25	15
12 [a]	**8**	**B**	−78	30	90:10	70
13	**8**	**B**	−78	5	92: 8	70
14 [a,b]	**4**	**C**	−78	30	98: 2	62
15 [a,b]	**5**	**C**	−78	30	88:12	40
16 [a,b]	**8**	**C**	−78	30	95: 5	60

[a] In the presence of 10 mol% of HMPA. [b] Isolated as methyl ketone derivatives after hydrolysis.

have investigated the regiochemistry of the nucleophilic addition of carbon nucleophiles to three stereoisomeric chromium complexes, viz., **4**, **5** and **8**, of 1-isopropyl-5-methoxytetralin or dihydronaphthalene. The starting chromium complexes were synthesized as follows. The reaction of 1-isopropyl-5-methoxytetralin (**3**) with $Cr(CO)_6$ under thermal conditions gave (1-*exo*-isopropyl-5-methoxytetralin)-chromium complex (**4**) in 65% yield, along with 6% of the *endo*-isomer **5**. The *exo*-complex can be easily isolated by SiO_2 chromatography or recrystallization. The minor 1-*endo*-isopropyl chromium complex **5** is also prepared efficiently by ionic hydrogenolysis of (1-*exo*-isopropyl-5-methoxy-1-*endo*-tetralol)chromium (**7**) which was derived from (5-methoxy-1-tetralone)chromium (**6**) by the reaction with isopropylcerium dichloride. Dehydration of the complex **7** gave the dihydronaphthalene complex **8**.

The results of nucleophilic addition to these chromium complexes are summarized in the Table 1. The treatment of *exo*-isopropyl chromium complex **4** with 2-lithio-1,3-dithiane in HMPA/THF at −78°C followed by oxidative demetallation with I_2 produced two dithianylated products. ^1H NMR analysis indicated that

Table 2

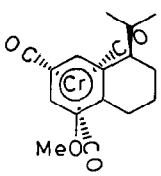
Bond lengths (Å) and angles (°)

Cr–C(5)	2.252(4)	Cr–C(6)	2.222(4)
Cr–C(7)	2.210(4)	Cr–C(8)	2.238(4)
Cr–C(9)	2.278(4)	Cr–C(10)	2.278(4)
Cr–C(15)	1.829(4)	Cr–C(16)	1.811(4)
Cr–C(17)	1.821(4)	O(1)–C(5)	1.366(5)
O(1)–C(14)	1.440(6)	O(2)–C(15)	1.154(5)
O(3)–C(16)	1.169(5)	O(4)–C(17)	1.161(5)
C(1)–C(2)	1.524(5)	C(1)–C(9)	1.537(5)
C(1)–C(11)	1.548(5)	C(2)–C(3)	1.528(6)
C(3)–C(4)	1.526(6)	C(4)–C(10)	1.515(5)
C(5)–C(6)	1.408(5)	C(5)–C(10)	1.422(5)
C(6)–C(7)	1.399(5)	C(7)–C(8)	1.409(5)
C(8)–C(9)	1.389(5)	C(9)–C(10)	1.431(5)
C(11)–C(12)	1.547(6)	C(11)–C(13)	1.505(6)
C(15)–Cr–C(16)	85.5(2)	C(15)–Cr–C(17)	89.5(2)
C(16)–Cr–C(17)	87.8(2)	C(5)–O(1)–C(14)	117.9(3)
C(2)–C(1)–C(9)	111.0(3)	C(2)–C(1)–C(11)	113.9(3)
C(9)–C(1)–C(11)	115.7(3)	C(1)–C(2)–C(3)	110.1(3)
C(2)–C(3)–C(4)	111.8(3)	C(3)–C(4)–C(10)	113.2(3)
O(1)–C(5)–C(6)	123.5(3)	O(1)–C(5)–C(10)	114.9(3)
C(6)–C(5)–C(10)	121.7(3)	C(5)–C(6)–C(7)	118.7(3)
C(6)–C(7)–C(8)	120.5(3)	C(7)–C(8)–C(9)	121.1(3)
C(1)–C(9)–C(8)	121.1(3)	C(1)–C(9)–C(10)	118.9(3)
C(8)–C(9)–C(10)	119.8(3)	C(4)–C(10)–C(5)	118.1(3)
C(4)–C(10)–C(9)	123.7(3)	C(5)–C(10)–C(9)	118.1(3)
C(1)–C(11)–C(12)	109.9(3)	C(1)–C(11)–C(13)	114.8(3)
C(12)–C(11)–C(13)	110.1(3)	Cr–C(15)–O(2)	177.1(3)
Cr–C(16)–O(3)	178.6(3)	Cr–C(17)–O(4)	179.1(3)

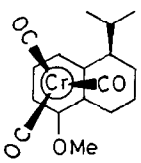
addition to the *meta*-position for the methoxy-group occurred with high regioselectivity (entry 1). Such high *meta*-selectivity appeared in the *exo*-complex **4** is consistent with that in (anisole)chromium complex. However, the corresponding *endo*-isopropyl complex **5** afforded predominantly the *ortho*-substituted compound (*ortho*:*meta*, 65 : 35), without the formation of the *para*-substituted compound, in 28% yield under the same conditions (entry 2). Major product in this reaction was chromium decomplexed 1-isopropyl-5-methoxytetralin. The results (lower yield and preference of the formation of the *ortho*-isomer) in the *endo*-isopropyl complex **5** are consistent with those in the complex **2**. In the reaction with dihydronaphthalene chromium complex **8**, the *meta*-substitution product was still predominant, where the addition product to the double bond was not formed. The addition to only the arene ring in complex **8** is in marked contrast to the results obtained in the reaction of the chromium complex of 5-methoxy-3,4-dihydronaphthalene which has no isopropyl group at C-1 position, a position at which nucleophiles (always) attack the double bond in a Michael-type reaction [5,6]. In any event, the regioselectivity in the nucleophilic reactions of these chromium complexes with 2-lithio-1,3-dithiane is quite dependent on the configuration of the isopropyl group to the $Cr(CO)_3$ moiety.

The reaction of (arene)chromium complexes with sulfur stabilized carbanions is known to be governed kinetically [7], and so regioselectivity is attributed to the

balance of charge and frontier orbital control [7,8]. The charge control is induced by a preferred conformation of the $Cr(CO)_3$ group for the arene ring, and the frontier orbital control is based on the magnitude of the coefficient in LUMO of the uncomplexed arenes. The *exo*-isopropyl complex **4** can adopt preferentially the *syn*-eclipsed conformation **13** as can the (anisole)chromium complex [9], and so the *meta*-carbon eclipsed by the CO ligand is exclusively attacked by the nucleophiles, because of the co-operation of the $Cr(CO)_3$ tripod and an electron-donating effect by the OMe group. However, the corresponding *endo*-isopropyl complex **5** exists in a staggered conformation **14** to avoid an adverse steric interaction between the *endo*-oriented isopropyl group and the CO ligand. This staggered conformation in the *endo*-substituted complex **5** would result in giving lower yield and regioselectivity in the nucleophilic addition reaction with 2-lithio-1,3-dithiane.



13
syn-eclipsed



14
staggered

The orientation of the $Cr(CO)_3$ tripod in these *exo*- and *endo*-isopropyl-substituted (arene)chromium complexes would be supported even in a solution by ^1H NMR of aromatic regions as follows. The aromatic protons eclipsed by the CO ligands are relatively deshielded, and thus resonate at lower magnetic field [10]. In the *exo*-isopropyl complex **4**, the *meta*-proton appeared at 5.44 ppm, and the *ortho*-, *para*-protons resonated at 4.97 ppm. On the other hand, the *meta*-proton in the corresponding *endo*-complex **5** appeared at δ 5.30, and the signals of the *ortho*- and *para*-protons occurred at δ 5.15 and 5.21. Thus, the *meta* proton in the *exo*-isopropyl complex is more deshielded than that in the *endo*-chromium complex, and, therefore, the *exo*-complex **5** should exist in solution in predominantly the *syn*-eclipsed conformation.

We have next examined the regioselectivity in the nucleophilic addition to these three chromium complexes with nitrile- or cyanohydrin-stabilized carbanions instead of the 2-lithio-1,3-dithiane. The *exo*-isopropyl complex **4** gave still *meta*-substitution products with high regioselectivity in good yields by the reaction with these carbanions in HMPA/THF at $-78°C$. Interestingly, the reaction of the corresponding *endo*-isopropyl complex **5** with these nucleophiles under the same conditions produced predominantly the *meta*-substitution products. Such regioselectivity is in contrast to that obtained in the reaction of the complex **5** with 2-lithio-1,3-dithane. Similarly, dihydronaphthalene chromium complex **8** afforded the *meta*-products with high selectivity.

It has been previously reported [7,8b] that the addition of 2-lithio-2-methylpropionitrile to some (arene)chromium complexes is a fast reaction, and the distribution of regioisomeric addition products depends on the reaction conditions such as reaction time, temperature and the presence (or absence) of HMPA. As seen from the Table 1, an increase in reaction time and/or temperature slightly changes the

product distribution in the reaction of *endo*-isopropyl complex **5** with 2-lithio-2-methylpropionitrile. Higher temperatures and longer reaction times increased the relative proportion of the *ortho*-substituted isomer, and lowered the yield of the addition products. The addition of HMPA to the reaction medium resulted in no drastic changes in the regioselectivity. In any event, the *meta*-substituted isomer was predominantly obtained from the chromium complexes such as **4**, **5** and **8** under thermodynamic conditions regardless of the configuration of the isopropyl group.

Equilibration of cyclohexadienyl $Cr(CO)_3$ anion intermediates has been demonstrated, and the distribution of products obtained from thermodynamically-controlled reactions are expected to reflect the relative stabilities of the regioisomeric η^5-cyclohexadienyl chromium anion intermediates; the charge distribution, electronic and steric interactions being major factors influencing the stability [7,8]. In (anisole)$Cr(CO)_3$, the OMe group would least destabilize the highest occupied cyclohexadienyl orbital when *meta* to the nucleophile, in which CO ligand eclipses sp^3-carbon of the cyclohexadienyl ligand. Therefore, the *meta*-substituted isomer was exclusively obtained even in the *endo*-isopropyl complex **5** under the thermodynamically controlled reactions due to the minimum destabilizing electronic interaction with the OMe group. Reversibility of the nucleophile in the addition to the complex **5** should be fast since the *meta*-selectivity was extremely high in a short time and at low temperature (entry 9). However, in this preferred cyclohexadienyl conformation with eclipsed *meta*-carbon derived from *endo*-complex **5**, the bulky isopropyl group is unfavorable since it interacts with the eclipsed CO ligand. So, longer reaction times and higher temperatures result in lower yields and selectivities, owing to the collapse of the *meta*-substituted cyclohexadienyl intermediate (entry 11).

In summary, the rgioselectivity is controlled by the conformation of the $Cr(CO)_3$ moiety for the arene under the kinetically controlled reactions, and the selectivity under the thermodynamic conditions is mainly affected by the position of the OMe group, regardless of the geometry of the $Cr(CO)_3$ tripod.

X-Ray diffraction study of (1-*endo*-isopropyl-5-methoxytetralin)chromium complex 5

Crystal data: $C_{17}H_{20}O_4Cr$, $f_w = 340.3$, monoclinic, space group $P2_1/c$, a 7.168(1), b 18.468(5), c 12.205(3) Å, β 100.95(2)°, U 1586.2(6) Å^3, D_c 1.425 g cm^{-1}, $Z = 4$, F(000) = 712, λ(Cu-K_α) 1.54178 Å, μ 63.66 cm^{-1}, T 25 °C, crystal size 0.5 × 0.1 × 0.1 mm. Unit cell parameters were refined with 2θ angles of 15 reflections ($40 \leqslant 2\theta \leqslant 45°$). Intensity data of 1997 unique reflections in the region of $2\theta \leqslant 110°$ were collected on a Rigaku AFC-5R diffractometer by the ω–2θ scan technique; scan speed 5° min^{-1} for ω, scan width $\Delta\omega = 0.8 + 0.2 \tan \theta°$, and background counting time 4s on each side. Three standard reflections monitored every 100 measurements showed no significant variation. A total of 1805 reflections were observed [$F_o > 3\sigma(F_o)$]. The structure was solved by the heavy-atom method and refined by the block-diagonal least squares method. Absorption corrections were applied after isotropic least squares refinement by an empirical method [11] based on the differences between the observed and calculated structure factors (relative transmission factors 0.732–1.318). H atoms were located in a difference electron density map. The positional parameters for all the atoms and the anisotropic thermal parameters for the non-H atoms were refined: the temperature factor of

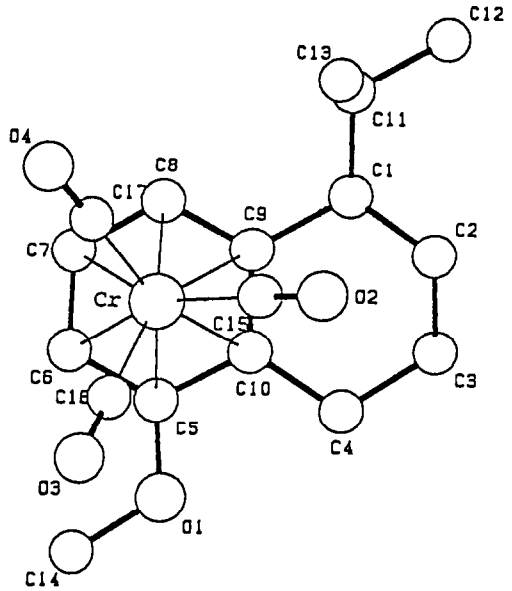


Fig. 1. Crystal structure of *endo*-isopropyl complex **5**.

each H atom was set equal to B_{eq} value of the bonded atom. Atomic scattering factors were calculated by $f = \Sigma[a_i \exp(-b_i\lambda^{-2} \sin^2\theta)] + c(i = 1 \ldots 4)$ [12]. Weights are estimated as $w = [\sigma^2(F_o) + 0.00614(F_o)^2]^{-1}$ for the reflections with $w^{1/2}|\Delta F| < 4$, and $w = 0$ otherwise. Final R, R_w and S (goodness of fit) were 0.041, 0.058 and 1.235 for 1764 reflections, respectively. Tables of atomic coordinates, anisotropic thermal parameters, and structure factors are available from the authors.

Experimental

All melting points were determined on a Yanagimoto Model MPJ-2 micro melting apparatus, and are uncorrected. IR spectra were recorded in $CHCl_3$ solution by a JASCO Model A-102 spectrometer, and ^1H NMR spectra were measured on JEOL GX-400 and Hitachi R-90H in $CDCl_3$ solution. NMR chemical shifts are in ppm downfield from Me_4Si, and coupling constants are in hertz. All reactions were carried out under a slightly-positive argon or nitrogen pressure. Tetrahedrofuran was freshly distilled from sodium benzophenone ketyl.

Preparation of tricarbonyl(1-exo-isopropyl-5-methoxytetralin)chromium (4)

A mixture of 1-isopropyl-5-methoxytetralin (**3**) (1.05 g, 5.15 mmol) and $Cr(CO)_6$ (2.26 g, 10.3 mmol) in a mixture of di-n-butyl ether (100 ml), heptane (10 ml) and THF (10 ml) was heated at 120 °C with stirring for 24 h under nitrogen. After being cooled to room temperature, the reaction mixture was evaporated under reduced pressure. The resulting yellow product was purified by SiO_2 (50 g) chromatography

with ether/hexane (1/5) as eluant. Two yellow fractions were collected. Recrystallization of the first fraction from hexane/ether afforded 1.20 g of *exo*-isopropyl complex **5**. M.p. 97 °C. IR ν_{max}: 1955, 1870, 1515 cm^{-1}. ^1H NMR δ: 0.76 (3H, d, $J = 7$ Hz), 1.02 (3H, d, $J = 7$ Hz), 1.40–2.82 (8H, m), 3.72 (3H, s), 4.97 (2H, t, $J = 7$ Hz), 5.44 (1H, t, $J = 7$ Hz). Anal. Found: C, 59.89; H, 5.97. $C_{17}H_{20}Cr$ calcd.: C, 60.00; H, 5.92%. The second fraction gave 120 mg of *endo*-isopropyl complex **5**.

*Preparation of tricarbonyl(1-*exo*-isopropyl-5-methoxy-1-*endo*-tetralol)chromium (7)*

Cerium chloride seven-hydrate, $CeCl_3 \cdot 7H_2O$, (3.20 g, 8.59 mmol) was placed in a 100 ml two-necked flask. The flask was evacuated and heated at 130–140 °C (ca. 0.1 Torr) and kept at that temperature for 1 h, and the cerium chloride was dried *in vacuo* with stirring at the same temperature for an additional hour. While the flask was still hot, argon gas was introduced and the the flask was cooled in an ice bath. Dry THF (20 ml) was added all at once with vigorous stirring, and the mixture was stirred for 2 h at room temperature. After the reaction mixture was cooled at −78 °C, isopropyllithium (0.62 *M* in pentane, 14.0 ml, 8.68 mmol) was added, and stirring was continued for 1 h. A solution of tricarbonyl(5-methoxy-1-tetralone)-chromium (**6**) (2.20 g, 7.05 mmol) in THF (20 ml) was added and the mixture was stirred for 1 h. The flask was warmed to 0 °C during 2 h, and the reaction mixture was quenched with aqueous saturated ammonium chloride. The mixture was extracted with ether, and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel chromatography with ether/hexane as eluant to give the chromium complex 7 (1.49 g, 59.4%) as yellow crystals. M.p. 114 °C. IR ν_{max}: 3350, 1955, 1880 cm^{-1}. ^1H NMR δ: 0.80 (3H, d, $J = 7$ Hz), 0.99 (3H, d, $J = 7$ Hz), 1.60–3.03 (8H, m), 3.67 (3H, s), 5.00–5.40 (3H, m). Anal. Found: C, 57.20; H, 5.69. $C_{17}H_{20}O_5Cr$ calcd.: C, 57.30; H, 5.66%.

*Preparation of tricarbonyl(1-*endo*-isopropyl-5-methoxytetralin)chromium (5)*

Boron trifluoride etherate (1.8 ml) was added to a mixture of (1-*exo*-isopropyl-5-methoxy-1-*endo*-tetralol)$Cr(CO)_3$ (**7**) (2.0 g, 5.62 mmol) and triethylsilane (2.61 g, 22.41 mmol) in dry CH_2Cl_2 (50 ml) at −78 °C under nitrogen. The reaction mixture was stirred at −45 °C, and quenched with saturated aqueous $NaHCO_3$, and was extracted with CH_2Cl_2. The extract was washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by SiO_2 chromatography with ether/hexane (1 : 10) as eluant to give 1.44 g (75%) of *endo*-isopropyl complex **5**. M.p. 104 °C. IR ν_{max}: 1950, 1867 cm^{-1}. ^1H NMR δ: 1.10 (3H, d, $J = 7$ Hz), 1.13 (3H, d, $J = 7$ Hz), 1.70–2.80 (8H, m), 3.75 (3H, s), 5.15 (1H, d, $J = 7$ Hz), 5.21 (1H, d, $J = 7$ Hz), 5.30 (1H, t, $J = 7$ Hz). Anal. Found: C, 59.92; H, 5.97. $C_{17}H_{20}O_4Cr$ calcd.: C, 60.00; H, 5.92%.

Preparation of tricarbonyl(1-isopropyl-5-methoxy-3,4-dihydronaphthalene)chromium (8)

A mixture of (1-*exo*-isopropyl-5-methoxy-1-*endo*-tetralol)$Cr(CO)_3$ (**7**) (800 mg, 2.25 mmol) and $KHSO_4$ (612 mg, 4.50 mmol) in dry benzene (50 ml) was refluxed for 1 h under argon. The mixture was poured into cold saturated aqueous $NaHCO_3$ (100 ml) and was extracted with benzene. The organic layer was washed with brine, dried over $MgSO_4$. The solvent was evaporated off *in vacuo*, the residue was purified by SiO_2 chromatography with ether/hexane (1 : 10) as eluant to afford the dihydro-

naphthalene complex **8** (733 mg, 96%). M.p. 77°C: IR ν_{max}: 1960, 1880, 1510, 1450 cm^{-1}. ^1H NMR δ: 1.10 (3H, d, $J = 7$ Hz), 1.21 (3H, d, $J = 7$ Hz), 2.16–2.95 (5H, m), 3.75 (3H, s), 4.98 (1H, d, $J = 7$ Hz), 5.05 (1H, d, $J = 7$ Hz), 5.57 (1H, t, $J = 5$ Hz), 6.05 (1H, d, $J = 7$ Hz). Anal. Found: C, 60.31; H, 5.40. $C_{17}H_{18}O_4Cr$ calcd.: C, 60.35; H, 5.36%.

*Addition of 2-lithio-1,3-dithiane to tricarbonyl(1-*exo*-isopropyl-5-methoxytetralin)chromium (4)*

n-Butyl lithium (1.6 *M* in hexane, 0.36 ml, 0.58 mmol) was added to a solution of 1,3-dithiane (70 mg, 0.58 mmol) in THF (5 ml) at −78°C under argon, and the reaction mixture was stirred for 20 min at −20°C. The mixture was again cooled to −78°C, followed by addition of HMPA (1 ml). To this mixture was added a solution of *exo*-isopropyl chromium complex **4** (100 mg, 0.29 mmol) in THF (5 ml) at −78°C, and stirred for 30 min before addition of a solution of I_2 (221 mg, 0.87 mmol) in THF (2 ml). After 1 h stirring, the mixture was added to an aqueous solution of Na_2SO_3. The mixture was extracted with ether, and the extract was washed with brine, dried over $MgSO_4$. Evaporation of the solvent produced a crude product. The ratio of regioisomeric products was determined by ^1H-NMR at 400 MHz; Ar*CH*$(S-)_2$; *meta*-product, 5.13 ppm: *ortho*-product, 5.59 ppm. The addition to the corresponding *endo*-complex **5** was achieved under the same conditions. Physical data of *meta*-substituted isomer **9a**. IR ν_{max}: 1600,, 1580, 1460, 1280, 1100, 915 cm^{-1}. ^1H NMR δ: 0.75 (3H, d, $J = 7$ Hz), 1.01 (3H, d, $J = 7$ Hz), 1.50–3.20 (14H, m), 3.82 (3H, s), 5.13 (1H, s), 6.76 (1H, d, $J = 2$ Hz), 6.94 (1H, d, $J = 2$ Hz). MS: *m/z* 322 (*M*), 279, 248, 205. ^1H NMR of *ortho*-isomer **10a**. δ: 0.80 (3H, d, $J = 7$ Hz), 1.01 (3H, d, $J = 7$ Hz), 1.50–3.20 (14H, m), 3.80 (3H, s), 5.59 (1H, s), 7.02 (1H, d, $J = 8$ Hz), 7.36 (1H, d, $J = 8$ Hz).

The addition to dihydronaphthalene chromium complex **8** with 2-lithio-1,3-dithiane was conducted as described above. The ratio of the two regioisomeric products was determined from the integrals of the proton signals of Ar*CH*$(S-)_2$; *ortho*, 5.57; *meta*, 5.08 ppm. Spectral data of the major *meta* isomer **11a**. IR ∂_{max}: 1600, 1570, 1420, 1275, 1130, 1035, 910 cm^{-1}. ^1H NMR δ: 1.13 (6H, d, $J = 7$ Hz), 1.80–3.20 (11H, m), 3.73 (3H, S), 5.08 (1H, s), 5.83 (1H, t, $J = 5$ Hz), 6.84 (1H, d, $J = 2$ Hz), 7.00 (1H, d $J = 2$ Hz). MS *m/z* 320 (M), 246, 203.

*Addition of 2-lithio-2-methylpropionitrile to tricarbonyl(1-*exo*-isopropyl-5-methoxytetralin)chromium (4)*

To a solution of 2-lithio-2-methylpropionitrile [prepared from isobutyronitrile (40 mg, 0.58 mmol), diisopropylamine (45 mg, 0.58 mmol) and n-BuLi (1.6 *M* in hexane, 0.36 ml, 0.58 mmol)] in THF (3 ml) was added HMPA (1 ml) at −78°C under argon. After the mixture was stirred for 5 min, a solution of *exo*-isopropyl complex **4** (100 mg, 0.29 mmol) in THF (5 ml) was added at once to the mixture at −78°C. The resulting mixture was stirred for 30 min at the same temperature, and was quenched with a solution of I_2 (147 mg, 0.58 mmol) in THF (2 ml). A crude product was obtained as an oil after the usual work-up. The relative ratio of two regioisomeric substitution products was determined by ^1H NMR (at 400 MHz). Physical data of *meta*-substituted compound **9b**. IR ν_{max}: 2215, 1605, 1580, 1420, 1280, 1100, 910 cm^{-1}. ^1H NMR δ: 1.70 (3H, d, $J = 7$ Hz), 0.98 (3H, d, $J = 7$ Hz), 1.50–2.80 (8H, m), 1.70 (6H, s), 3.85 (3H, s), 6.75 (1H, d, $J = 2$ Hz), 6.92 (1H, d,

$J = 2$ Hz). MS m/z 271 (M), 228, 160. ^{1}H NMR of *ortho*-substituted compound **10b**. δ 0.78 (3H, d, $J = 7$ Hz), 1.00 (3H, d, $J = 7$ Hz), 1.50–2.80 (8H, m), 1.70 (6H, s), 3.92 (3H, s), 6.98 (1H, d, $J = 8$ Hz), 7.10 ($J = 8$ Hz). This nucleophilic addition of 2-lithio-2-methylpropionitrile to the *endo*-isopropyl complex **5** was carried out similarly, and the experiments were repeated several times with different reaction temperatures, times and in the presence (or absence) of HMPA.

The addition to dihydronaphthalene complex **8** with 2-lithio-2-methylpropionitrile was achieved similarly. Spectral data of the *meta*-substituted compound **11b**. IR ν_{max}: 2220, 1600, 1575, 1460, 1280, 1040 cm^{-1}. ^{1}H NMR δ: 1.16 (6H, s), 1.75 (6H, s), 2.16–3.00 (5H, m), 3.87 (3H, s), 5.94 (1H, t, $J = 5$ Hz), 6.88 (1H, d, $J = 2$ Hz), 7.06 (1H, d, $J = 2$ Hz). MS m/z 269 (M), 226, 158.

Addition of lithio-protected acetaldehyde cyanohydrin acetal to tricarbonyl(1-exo-isopropyl-5-methoxytetralin)chromium (4)

To a solution of lithio-protected acetaldehyde cyanohydrin acetal **C** [prepared from protected acetaldehyde cyanohydrin (83 mg, 0.58 mmol), diisopropylamine (45 mg, 0.58 mmol) and n-BuLi (1.6 M in hexane, 0.36 ml, 0.58 mmol)] in THF (3 ml) was added HMPA (1 ml) at -78°C under nitrogen. After the mixture was stirred for 5 min, a solution of *exo*-isopropyl complex **4** (100 mg, 0.29 mol) in THF (5 ml) was added all at once. After the usual oxidative demetallation, a crude addition product was obtained (87 mg). The crude product was dissolved in a mixture of MeOH (8 ml) and 5% H_2SO_4 (2 ml), and the mixture was stirred for 30 min at room temperature. The organic solvent was removed under reduced pressure, and extracted with ether. The ether layer was shaken vigorously with aqueous solution of 0.5 M NaOH (20 ml). After the usual work-up and purification, the nucleophilic addition products were obtained as methyl ketone compounds (52 mg). Spectral data of *meta*-substituted compound **9c**. IR ν_{max}: 1680, 1580, 1280 cm^{-1}. ^{1}H NMR δ: 0.76 (3H, d, $J = 7$ Hz), 1.01 (3H, d, $J = 7$ Hz), 1.50–2.80 (8H, m), 2.58 (3H, s), 3.87 (3H, s), 7.24 (1H, d, $J = 2$ Hz), 7.44 (1H, d, $J = 2$ Hz). MS m/z: 246 (M), 203. ^{1}H NMR of *ortho*-substituted compound **10c**. δ: 0.73 (3H, d, $J = 7$ Hz), 1.00 (3H, d, $J = 7$ Hz), 1.50–2.80 (8H, m), 2.62 (3H, s), 7.05 (1H, d, $J = 8$ Hz), 7.42 (1H, d, $J = 8$ Hz).

The addition of protected acetaldehydecyanohydrin acetal to dihydronaphthalene complex **8** was conducted under the same conditions; spectral data of major *meta*-substituted compound **11c**. IR ν_{max}: 1680. ^{1}H NMR δ: 1.12 (6H, d, $J = 7$ Hz), 2.10–3.00 (5H, m), 2.55 (3H, s), 3.82 (3H, s), 5.90 (1H, t, $J = 5$ Hz), 7.30 (1H, d, $J = 2$ Hz), 7.51 (1H, d, $J = 2$ Hz). MS m/z: 242, 201.

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