Tetrahydroisoquinolines. Part 2.[1] Synthesis of 4-Substituted *N*-Methyl-1,2,3,4-tetrahydroisoquinolines *via* Regio- and Stereo-selective Elaboration of Tricarbonyl(*N*-methyl-1,2,3,4-tetrahydroisoquinoline)chromium

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Thermolysis of hexacarbonylchromium with *N*-methyltetrahydroisoquinoline generates the tricarbonyl-(*N*-methyltetrahydroisoquinoline)chromium complex (**4**). The 4-*exo* proton of complex (**4**) can be regio- and stereo-selectively removed with butyl-lithium and replaced stereoselectivity with retention of configuration by a variety of electrophiles [MeI, EtI, $PhCH_2Br$, CD_3OD, $Cr(CO)_3(PhF)$, MoOPH, Me_2CO]. Oxidative decomplexation generates quantitatively the corresponding 4-methyl, ethyl, benzyl, deuterio, phenyl, hydroxy, and (1-hydroxy-1-methylethyl)-*N*-methyltetrahydroisoquinolines.

The potent pharmacological activity of simple 4-substituted tetrahydroisoquinolines† has generated much interest in their synthesis and recently several new naturally-occurring compounds of this type have been isolated.[2] For example, the antidepressant drug Nomifensine (**1**)[3] has a close relationship to the alkaloid cherylline (**2**)[4] and 4-hydroxytetrahydroisoquinoline derivatives are of interest due to their involvement in alcohol addiction.[5]

Recently, a general synthetic route to optically active 1-substituted tetrahydroisoquinolines has been developed by Meyers *et al. via* the stereoselective alkylation of formamidine derivatives.[6] Methods for the introduction of substituents into the 4-position are, however, long and inefficient. It has been recognised for some time that co-ordination of an arene to tricarbonylchromium induces the stabilisation of benzylic carbanions.[7] We describe here the exploitation of the regio- and stereo-specific substitution of the 4-*exo*-hydrogen of tricarbonyl-(*N*-methyltetrahydroisoquinoline)chromium for the synthesis of a variety of 4-substituted *N*-methyltetrahydroisoquinolines. Part of this work has been the subject of a preliminary communication.[1]

Results

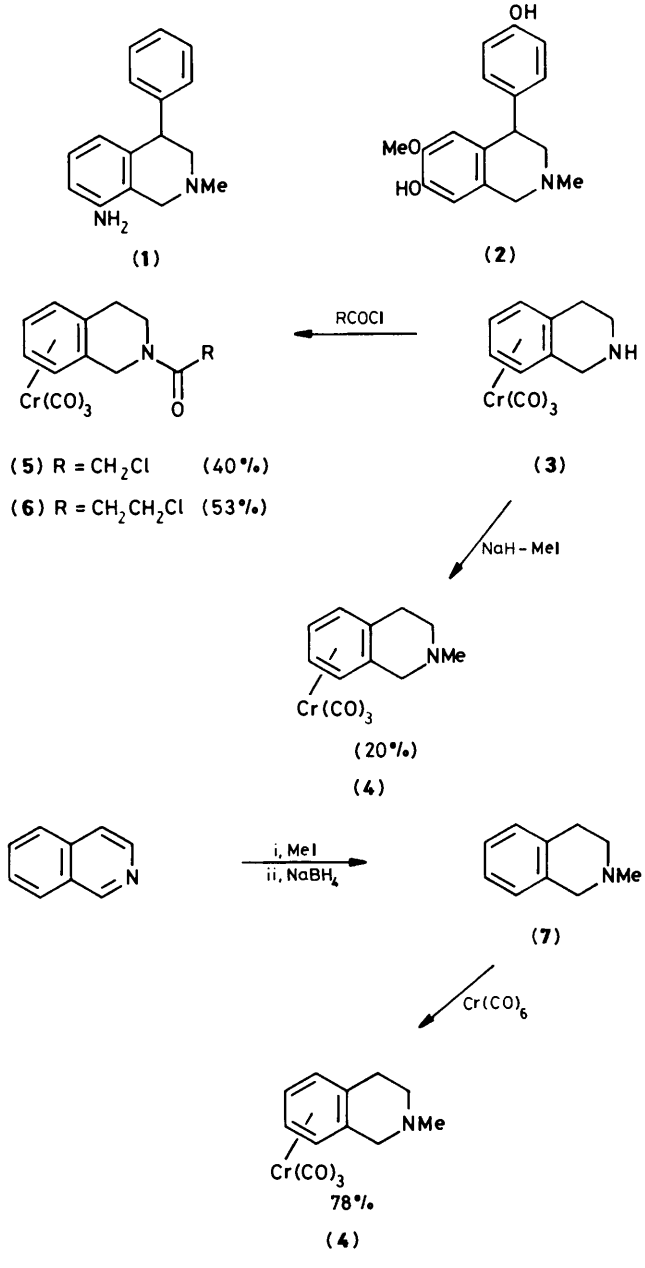
Thermolysis of hexacarbonylchromium with tetrahydroisoquinoline gave complex (**3**) which could be readily methylated or acylated to give the corresponding *N*-methyl (**4**) and *N*-acyl complexes (**5**) and (**6**) albeit in moderate yields.

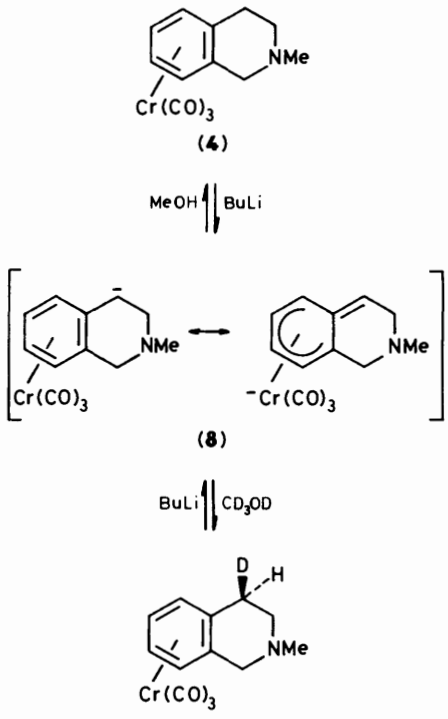
The complex (**4**) was best prepared as bright yellow plates in 78% yield *via* direct complexation of *N*-methyltetrahydroisoquinoline. (**7**).

Deprotonation of complex (**4**) with butyl-lithium at −78 °C gave an incarnadine solution of the 4-lithio derivative (**8**) which on quenching with deuteriomethanol produced the 4-*exo*-deuterio complex (**9**). Only one diastereoisomer of (**9**) could be detected by ^1H and ^2H n.m.r. spectroscopy and this was assigned as *exo* by analogy with all other benzylic substitutions carried out on complexed arene systems with the electrophile approaching the anion (**8**) from the unhindered *exo*-face.[8] That the deprotonation was also stereoselective was demonstrated by treating the complex (**9**) with butyl-lithium followed by methanol which completely removed the deuterium from (**9**) and regenerated the complex (**4**).

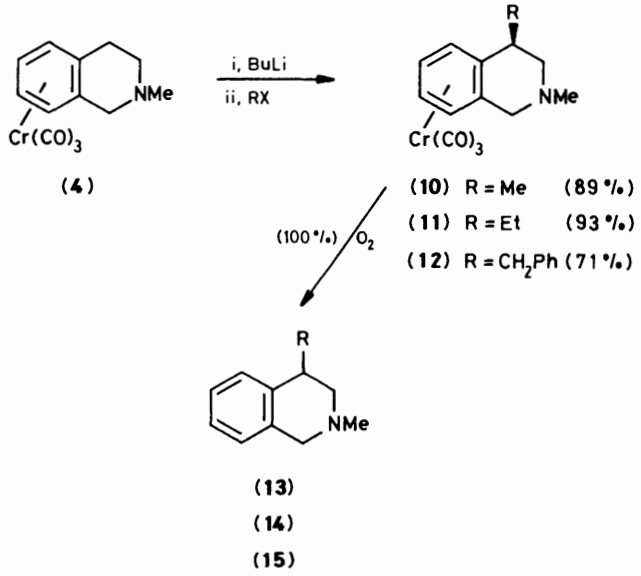
Alkyl halides also add stereoselectively to the anion (**8**). Thus addition of methyl iodide, ethyl iodide, or benzyl bromide to the

† For clarity the descriptors 1,2,3,4- are omitted.

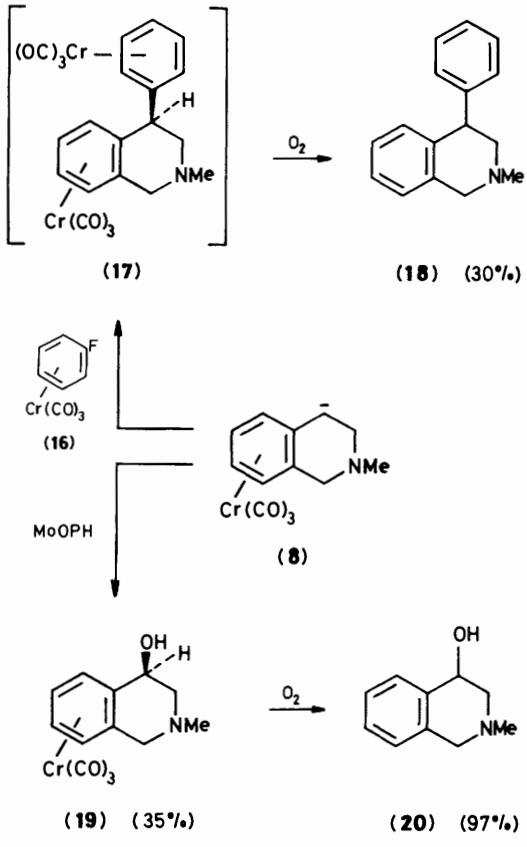




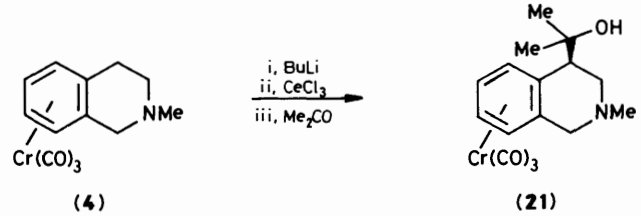
anion (**8**) gave the 4-*exo*-derivatives (**10**), (**11**), and (**12**) respectively in excellent yields with only one diastereoisomer being detected in each case. Although the anion (**8**) was also stable at ambient temperatures yields of the 4-alkylated products were generally not comparable with those obtained from the low temperature reactions. Essentially quantitative yields of free *N*-methyltetrahydroisoquinolines were obtained on removal of the tricarbonylchromium moiety by allowing solutions of the complexes to stand in air and sunlight.



Tricarbonyl(fluorobenzene)chromium (**16**) is known to undergo ready substitution, of fluoride by nucleophiles,[9] *via* an addition–elimination mechanism. Addition of a dilute solution of (**16**) to the anion (**8**) gave the unstable intermediate di(tricarbonylchromium) complex (**17**) which on decomplexation produced the known *N*-methyl-4-phenyltetrahydroisoquinoline (**18**).[10] Treatment of the anion (**8**) with MoOPH[11] allowed the introduction of a 4-*exo*-hydroxy substituent and isolation of the complex (**19**) again as a single diastereoisomer. Decomplexation of (**19**) gave 4-hydroxy-*N*-methyltetrahydroisoquinoline (**20**).



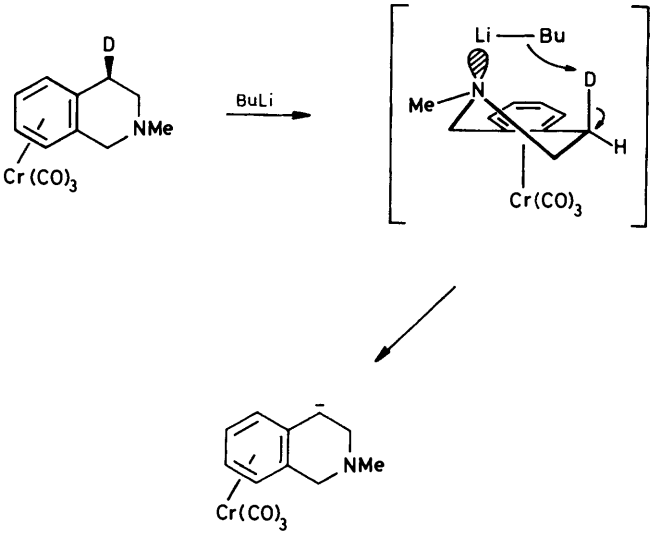
Previous work by Brocard *et al.* has suggested that the reaction of tricarbonylchromium stabilised benzylic anions with enolisable aldehydes and ketones leads to preferential self condensation of the carbonyl compound with concomitant protonation of the anion.[12] Only the intramolecular addition of ketones has previously been successful.[13] We found however that slow addition of a dilute solution of acetone to the anion (**8**) gave a moderate yield (36%) of the addition product (**21**). The use of anhydrous cerium(III) chloride to transmetallate[14] the initial lithium anion (**8**) improved the yield of (**21**) to 58%. In both cases only a single diastereoisomer of the product (**21**) could be detected.



Discussion

Deprotonation of tricarbonyl(*N*-methyltetrahydroisoquinoline)chromium (**4**) with butyl-lithium followed by trapping of the resultant anion by a variety of electrophiles leads in each case to a single product complex. That deprotonation occurs regioselectively in the 4-position is evidenced by the formation of the known 4-phenyl derivative (**18**).[10] Furthermore, both

diastereoisomers of 1,*N*- and of 3,*N*-dimethyltetrahydroisoquinoline were available[15] and since the complex (**10**) was distinct from these by ^{1}H n.m.r. spectroscopy, it must therefore be the 4-methyl derivative. The stereoselective formation of the 4-*exo* derivatives is consistent with the base and electrophiles being constrained to approach from the unhindered face *i.e.* away from the bulky tricarbonylchromium moiety. Both the regio- and stereo-selectivity of the deprotonation of the 4-*exo*-proton of (**4**) can be understood in terms of the axial nitrogen lone pair directing the butyl-lithium to remove the pseudo-axial 4-*exo*-proton by co-ordination as shown below.



Overall, the methodology described herein allows the stereoselective substitution with retention of configuration of the 4-*exo*-proton of tricarbonyl(*N*-methyltetrahydroisoquinoline)-chromium and provides a general synthesis of 4-substituted *N*-methyltetrahydroisoquinolines.

Experimental

All reactions involving the preparation or utilisation of tricarbonyl(arene)chromium(0) complexes were performed under an atmosphere of nitrogen. All commercial reagents were purified according to standard techniques.[16] THF was distilled from sodium diphenylketyl under an atmosphere of nitrogen. Dichloromethane was distilled from calcium hydride under nitrogen. Diethyl ether was peroxide free and hexane refers to that fraction of light petroleum boiling between 67 and 70 °C. Dibutyl ether was dried over sodium and distilled under an atmosphere of nitrogen prior to use. Hexacarbonylchromium was steam distilled prior to use. Flash chromatography was performed on SiO_2 (Merck; 40—60 μm). Infrared spectra were obtained as Nujol mulls (unless otherwise stated) and ^{1}H n.m.r. spectra were obtained in $CDCl_3$ at 300 MHz (unless otherwise stated). ^{13}C N.m.r. spectra were obtained in $CDCl_3$ at 62.90 MHz. Melting points were obtained on a Kofler hot-stage apparatus and are uncorrected.

Tricarbonyl(η^6-1,2,3,4-*tetrahydroisoquinoline*)*chromium*(0) (**3**).—A deoxygenated mixture of dibutyl ether (90 ml), tetrahydrofuran (9 ml), 1,2,3,4-tetrahydroisoquinoline (2.3 g, 17.3 mmol) and hexacarbonylchromium (4.2 g, 19.1 mmol) was heated at reflux under nitrogen (30 h). The cooled solution was filtered away from the excess hexacarbonylchromium and the solvents were removed. Column chromatography (Al_2O_3 Grade V–CH_2Cl_2) gave, after evaporation, an orange oil which was crystallised from dichloromethane–hexane to give the *title compound* as yellow-orange plates (4.18 g, 90%), m.p. 63—64 °C; $\nu_{max.}$ 1 980, 1 955, 1 890, and 1 850 (C≡O) cm^{-1}; δ_H (90 MHz) 5.30 (4 H, m, ArH), 3.85 (2 H, s, 1-H_2), 3.10 (2 H, t, *J* 6 Hz, 3-H_2), 2.65 (2 H, t, *J* 6 Hz, 4-H_2), and 1.75 (1 H, br, NH); *m/z* 269 (M^+) (Found: C, 53.5; H, 4.3; N, 5.4. $C_{12}H_{11}CrNO_3$ requires C, 53.5; H, 4.1; N, 5.2%).

Tricarbonyl(η^6-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)-*chromium*(0) (**4**).—A deoxygenated solution of tricarbonyl(η^6-1,2,3,4-tetrahydroisoquinoline)chromium(0) (**3**) (300 mg, 1.1 mmol) in tetrahydrofuran (10 ml) was added to a suspension of NaH (50% in oil; 265 mg, 5.5 mmol; previously washed with hexane) in tetrahydrofuran (25 ml). When no further gas was evolved the mixture was cooled (0 °C) and a solution of methyl iodide (0.8 g, 5.6 mmol) in tetrahydrofuran (10 ml) added. After the reaction had been stirred (2 h), diethyl ether (150 ml) was added and the resultant yellow solution filtered clear of sodium iodide. Evaporation followed by column chromatography (Al_2O_3 Grade V–Et_2O) gave the *title compound* as a yellow oil. Crystallisation from dichloromethane–hexane gave bright yellow needles (70 mg, 22%), m.p. 100—101 °C; $\nu_{max.}$ 2 795 (NMe), and 1 960, 1 883br, and 1 850br cm^{-1} (C≡O); δ_H 5.24—5.14 (4 H, m, ArH), 3.50 and 3.27 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 2.88—2.73 (1 H, m), 2.71—2.68 (1 H, m), 2.60—2.52 (1 H, m) and 2.49—2.41 (1 H, m, 3- and 4-H_2), and 2.35 (3 H, s, NMe); *m/z* 283 (M^+) (Found; C. 55.1; H, 4.7; N, 4.8. $C_{13}H_{13}CrNO_3$ requires C, 55.1; H, 4.6; N, 5.0%).

Tricarbonyl(η^6-2-*chloroacetyl*-1,2,3,4-*tetrahydroisoquinoline*)*chromium*(0) (**5**).—Tricarbonyl(η^6-1,2,3,4-tetrahydroisoquinoline)chromium(0) (**3**) (350 mg, 1.3 mmol) in dichloromethane (30 ml) was treated with chloroacetyl chloride (0.15 ml, 1.88 mmol) and heated at reflux (14 h). Filtration (Al_2O_3 Grade V–CH_2Cl_2) followed by evaporation and crystallisation from dichloromethane–hexane gave the *title compound* as yellow needles (180 mg, 40%), m.p. 120—122 °C, $\nu_{max.}$ 1 940 and 1 880br (C≡O) and 1 660 cm^{-1} (amide); δ 5.41—5.24 (4 H, m, ArH), 4.96 and 4.23 (2 H, AB system, J_{AB} 15 Hz, 1-H_2, major amide conformer), 4.63 and 4.49 (AB system, J_{AB} 15 Hz, 1-H_2, minor amide conformer), 4.19—3.97 (3 H, m), 3.60—3.51 (1 H, m), and 3.03—2.58 (2 H, m); *m/z* 345 [M^+, (^{35}Cl)] and 347 [M^+, (^{37}Cl)] (Found: C, 48.7; H, 3.7; N, 4.2. $C_{14}H_{12}ClCrNO_4$ requires C, 48.6; H, 3.5; N, 4.1%).

Tricarbonyl[η^6-2-(3-*chloropropionyl*)-1,2,3,4-*tetrahydroisoquinoline*]*chromium*(0) (**6**).—Tricarbonyl(η^6-1,2,3,4-tetrahydroisoquinoline)chromium(0) (**3**), (1.5 g, 5.58 mmol) in dichloromethane (50 ml) was treated with 3-chloropropionyl chloride (1 ml, 10.47 mmol) and heated at reflux (5 h). Filtration (Al_2O_3 Grade V–CH_2Cl_2) followed by evaporation and crystallisation from dichloromethane–hexane gave the *title compound* as yellow needles (1.05 g, 53%), m.p. 130—132 °C, $\nu_{max.}$ 1 940, 1 880, and 1 860br (C≡O), and 1 650 cm^{-1} (amide); δ 5.39—5.24 (4 H, m, ArH), 4.97 and 4.27 (2 H, AB system, J_{AB} 15 Hz, 1-H_2, major amide conformer), 4.57 and 4.43 (2 H, AB system, J_{AB} 15 Hz, 1-H_2, minor amide conformer), 3.97—3.80 (3 H, m), 3.57—3.47 (1 H, m), 3.91—3.81 (3 H, m), and 3.69—3.55 (1 H, m); *m/z* 359 [$^+$, (^{35}Cl)] and 361 [M^+ (^{37}Cl)] (Found: C, 50.3; H, 4.0; N, 3.7. $C_{15}H_{14}ClCrNO_4$ requires C, 50.1; H, 3.9; N, 3.9%).

2-*Methyl*-1,2,3,4-*tetrahydroisoquinoline* (**7**).[17]—Isoquinoline (30 g, 231 mmol) and methyl iodide (30 ml, 482 mmol) were added to ethanol (450 ml) and the mixture was heated at reflux (2 h). On cooling the reaction yellow needles were formed. Filtration gave 2-methylisoquinolinium iodide (59 g, 94%).

2-Methyl isoquinolinium iodide (30 g, 110.7 mmol) in methanol (100 ml) and water (100 ml) was treated with sodium borohydride (10 g, 263 mmol). When evolution of gas ceased the

mixture was heated at reflux (20 min). After the mixture had been cooled, water (400 ml) was added and the mixture was saturated with NH_4Cl. Diethyl ether extraction, evaporation and distillation gave the *title compound* as a clear oil (12.9 g, 79%), b.p. 50—52 °C (0.1 mmHg) [lit.,[17] 103—105 °C, 14 mmHg]; $\nu_{max.}$ (liquid film) 2 780 (NMe) and 740 cm^{-1} (1,2-disubstituted arene); δ_H (60 MHz; $CDCl_3$) 7.10 (4 H, s, ArH), 3.70 (2 H, s, 1-H_2), 3.10—2.70 (4 H, m, 3- and 4-H_2), and 2.55 (3 H, s, NMe); *m/z* 147 (M^+).

Tricarbonyl(η⁶-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)-*chromium*(0) (**4**)—A deoxygenated mixture of dibutyl ether (90 ml), tetrahydrofuran (9 ml), 2-methyl-1,2,3,4-tetrahydroisoquinoline (**4**) (2.4 g, 16.3 mmol) and hexacarbonylchromium (4.5 g, 20.5 mmol) was heated at reflux under nitrogen (29 h). The cooled solution was filtered and the solvents removed. Column chromatography [Al_2O_3, Grade V–light petroleum–Et_2O (1:1)] gave, after evaporation, a yellow solid which was recrystallised from dichloromethane–hexane to give the *title compound* as yellow needles (3.6 g, 78%). This compound was identical in all respects to the sample obtained from (**3**) above.

General Procedure for the Preparation of Tricarbonyl(η⁶-4-*lithio*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)*chromium*(0) (**8**).—Butyl-lithium (1.6M solution in hexane; 1.2 ml, 1.95 mmol) was added to a stirred solution of tricarbonyl(η⁶-2-methyl-1,2,3,4-tetrahydroisoquinoline)chromium(0) (**4**) (500 mg, 1.77 mmol) in tetrahydrofuran (30 ml) at −78 °C. The initial yellow solution rapidly became crimson. After the reaction had been stirred (−78 °C, 2 h), the electrophile (excess) was added (*vide infra*):

Tricarbonyl(η⁶-4-*deuterio*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)*chromium*(0) (**9**). A solution of the anion (**8**) prepared as above was treated with deuteriomethanol and allowed to stir (−78 °C, 2 h). The solution was warmed to room temperature and concentrated. Column chromatography [Al_2O_3 Grade V; hexane–Et_2O (1:1)] followed by evaporation and crystallisation from dichloromethane–hexane gave the *title compound* as yellow needles (371 mg, 74%, δ_H 5.24—5.14 (4 H, m, ArH), 3.50 and 3.27 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 2.71—2.68 (1 H, m), 2.60—2.52 (1 H, m) and 2.49—2.41 (1 H, m) (3- and 4-H), and 2.35 (3 H, s, NMe); δ_D ($CHCl_3$; referenced against internal $CDCl_3$) 2.89; *m/z* 284 (M^+).

Tricarbonyl(η⁶-2,4-*dimethyl*-1,2,3,4-*tetrahydroisoquinoline*)-*chromium*(0) (**10**).—A solution of the anion (**8**) prepared as above was treated with methyl iodide (>3 equiv.) and allowed to stir (−78 °C, 2 h). Methanol (1 ml), was added, the solution warmed to room temperature and evaporated. Column chromatography [Al_2O_3 Grade V; hexane–ether (3:1)] followed by evaporation and crystallisation from dichloromethane–hexane gave the *title compound* as yellow needles (467 mg, 89%), m.p. 74—75 °C; $\nu_{max.}$ 1 970, 1 940, and 1 900 cm^{-1} (C≡O); δ_H 5.52—5.34 (4 H, m, ArH), 3.57 and 3.25 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 2.84—2.78 (1 H, m, 4-H), 2.59 and 2.45 (2 H, AB system, J_{AB} 12 Hz, 3-H_2), 2.34 (3 H, s, NMe), and 1.36 (3 H, d, *J* 7 Hz, 4-Me); *m/z* 297 (M^+) (Found: C, 56.6; H, 5.2; N, 4.8. $C_{14}H_{15}CrNO_3$ requires C, 56.6; H, 5.1; N, 4.7%).

Tricarbonyl(η⁶-4-*ethyl*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)*chromium* (0) (**11**).—A solution of the anion (**8**) prepared as above was treated with ethyl iodide (>3 equiv.) and allowed to stir (−78 °C, 4 h). Methanol (1 ml) was added, the solution warmed to room temperature and evaporated. Column chromatography [Al_2O_3 Grade V; hexane–ether (3:1)] followed by evaporation and crystallisation from dichloromethane–hexane gave the *title compound* as yellow needles (515 mg, 93%), $\nu_{max.}$ 1 970, 1 900, and 1 860br cm^{-1} (C≡O); δ_H 5.37—5.22 (4 H, m, ArH), 3.61 and 3.22 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 2.68—2.43 (3 H, m, 3-H_2 and 4-H), 2.40 (3 H, s, NMe), 1.86—1.65 (2 H, m, CH_2Me), and 1.02 (3 H, t, *J* 7 Hz, CH_2Me); *m/z* 311 (M^+) (Found: M^+, 311.0615. $C_{15}H_{17}{}^{52}CrNO_3$ requires *M*, 311.0613).

(η⁶-4-*Benzyl*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)*tricarbonylchromium*(0) (**12**).—A solution of the anion (**8**) prepared as above was treated with benzyl bromide (0.3 ml, 2.52 mmol) and allowed to stir (−78 °C, 2 h). Methanol (1 ml) was added, the solution was warmed to room temperature and evaporated. Column chromatography [Al_2O_3 Grade V; hexane–ether (3:1)] followed by evaporation and crystallisation from dichloromethane–hexane gave the *title compound* as bright yellow needles (468 mg, 71%), m.p. 99—100 °C, $\nu_{max.}$ 1 970, 1 950, 1 900, and 1 860br cm^{-1} (C≡O); δ_H 7.36—7.18 (3 H, m, *Ph*CH_2), 5.34—5.1 (4 H, m, complexed arene protons), 3.68 and 3.30 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 3.12—2.94 (2 H, m, CH_2Ph) 2.79—2.75 (1 H, m, 4-H), 2.60 and 2.39 (2 H, ABX system, J_{AB} 11 Hz, 3-H_2), and 2.37 (3 H, s, NMe); *m/z* 373 (M^+) (Found: C, 64.2; H, 5.0; N, 4.1. $C_{20}H_{19}CrNO_3$ requires C, 64.3; H, 5.1; N, 3.8%).

2-*Methyl*-4-*phenyl*-1,2,3,4-*tetrahydroisoquinoline* (**18**).[10] A solution of the anion (**8**) prepared as above was allowed to warm to −40 °C. A solution of tricarbonyl(η⁶-fluorobenzene)chromium(0) (**16**)[18] (500 mg, 2.16 mmol) in tetrahydrofuran (10 ml) at −40 °C was added dropwise *via* a cannula (10 min). The crimson solution was allowed to warm (20 °C) and stirred overnight (16 h). Methanol (2 ml) was added and the solvent evaporated to leave a red oil. Chromatography (Al_2O_3 Grade V–Et_2O) gave, on evaporation of the solvent, a yellow gum which was dissolved in diethyl ether (50 ml) and allowed to stand in air and sunlight until colourless. Removal of the chromium residues by filtration (Celite) followed by evaporation gave a yellow oil. The latter was dissolved in ether (30 ml), extracted into 2M-HCl (3 × 25 ml) and the combined extracts were basified (2M-NaOH). Ether extraction (3 × 25 ml) followed by evaporation gave a clear oil. Chromatography [SiO_2; toluene–ethanol–ammonia (78:20:2)] collecting the first fraction gave the *title compound* (120 mg, 30%) as a clear oil, δ_H 7.33—6.86 (9 H, m, ArH) 4.31—4.26 (1 H, m, 4-H), 3.77 and 3.63 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 3.08—2.55 (2 H, m, 3-H_2), and 2.44 (3 H, s, NMe) [lit.,[10] δ_H (60 MHz; $CDCl_3$) 7.3—6.5 (9 H, m,), 4.19 (1 H, t, *J* 7 Hz), 3.88 (2 H, s), 3.12—2.45 (2 H, m), and 2.35 (3 H, s)]; δ $^{13}C\{^1H\}$ 144.8, 137.15, 135.25, 129.6, 129.4, 129.1 (2 × C), 128.31 (2 × C), 126.4, 126.3, 126.2, 126.0. 61.9, 58.5, and 46.0; *m/z* 223 (M^+); $C_{16}H_{17}N$·HCl m.p. 175—177 °C (lit.,[10] 178—179 °C).

Tricarbonyl(η⁶-4-*hydroxy*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)*chromium*(0) (**19**). A solution of the anion (**8**) prepared as above was allowed to warm to −40 °C. (Hexamethylphosphoric triamide)oxodi(peroxo)pyridinemolybdenum [MoOPh][11] (1.15 g, 2.65 mmol) was added and the crimson solution stirred until the reagent had dissolved (10—20 min). Saturated aqueous Na_2SO_3 (10 ml) was added, the mixture warmed to 20 °C, and treated with water (40 ml). The organic products were extracted with diethyl ether and the combined extracts concentrated and chromatographed [Al_2O_3 Grade V; Et_2O–CH_2Cl_2 (1:1)] to give a yellow oil. Crystallisation from dichloromethane–hexane gave the *title compound* as yellow needles (185 mg, 35%), m.p. 109—110 °C; $\nu_{max.}$ 3 100br (OH), 2 795 (NMe), and 1 950 and 1 890br cm^{-1} (C≡O); δ_H ($CDCl_3$–D_2O) 5.56—5.16 (4 H, m, ArH), 4.35 (1 H, br s, 4-H), 3.65 and 3.30 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 2.91 and 2.68 (2 H, AB system, J_{AB} 11 Hz, 3-H_2), and 2.44 (3 H, s, NMe); *m/z* 299 (M^+) (Found: C, 52.3; H, 4.4; N. 4.5. $C_{13}H_{15}CrNO_4$ requires C, 52.2; H, 4.4; N, 4.7%).

General Procedure for the Decomplexation of the Complexes (**10**), (**11**), (**12**), *and* (**19**).—A solution of the tricarbonylchromium complex (**10**), (**11**), (**12**), or (**19**) in diethyl ether (20 mg ml^{-1}) was allowed to stand in air and sunlight until the yellow solution became colourless. Chromium(III) residues were removed by filtration (Celite) and the ether evaporated to leave a clear oil. Where necessary, further purification was achieved by flash chromatography [SiO_2; toluene–ethanol–ammonia (78:20:2)]. Yields in each case were essentially quantitative.

2,4-*Dimethyl*-1,2,3,4-*tetrahydroisoquinoline* (**13**):[19] $\nu_{max.}$ (thin film) 2 795 (NMe) and 740 cm^{-1} (1,2-disubstituted arene); δ_H 7.27—6.97 (4 H, m, ArH), 3.57 and 3.53 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 3.12—3.04 (1 H, m, 4-H), 2.83—2.78 (1 H, m, 3-H), 2.45 (3 H, s, NMe), 2.36—2.29 (1 H, m, 3-H), and 1.33 (3 H, d, *J* 7 Hz, 4-Me); *m/z* 161 (M^+) (Found: M^+, 161.1204. Calc. for $C_{11}H_{15}N$: *M*, 161.1204).

4-*Ethyl*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline* (**14**): $\nu_{max.}$ (thin film) 2 795 (NMe) and 740 cm^{-1} (1,2-disubstituted arene); δ_H 7.23—7.0 (4 H, m, ArH), 3.64 and 3.45 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 2.83—2.76 (1 H, m, 4-H), 2.65 and 2.51 (2 H, AB system, J_{AB} 10 Hz, 3-H_2), 2.44 (3 H, s, NMe), 1.88—1.64 (2 H, m, CH_2Me), and 1.02—0.97 (3 H, t, *J* 7.5 Hz, CH_2*Me*); *m/z* 175 (M^+) (Found: M^+, 175.1360. $C_{12}H_{17}N$ requires *M*, 175.1361).

4-*Benzyl*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline* (**15**):[20] $\nu_{max.}$ (thin film) 2 780 (NMe), 1 600 (ArH), 750 (1,2-disubstituted arene), and 730 and 700 cm^{-1} (mono substituted arene); δ_H 7.37—7.07 (9 H, m, ArH), 3.77 and 3.42 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 3.15—2.91 (3 H, m), 2.60—2.55 (1 H, m), 2.41 (3 H, s, NMe), and 2.42—2.37 (1 H, m); δ $^{13}C\{^1H\}$ 140.8, 138.0, 134.9, 129.3 (2 × C), 128.6 (2 × C), 128.3, 126.3, 126.1, 126.0, 125.8, 58.6, 56.1, 46.2, 42.5, and 40.8; *m/z* 237 (M^+) (Found: C, 86.3; H, 8.2; N, 6.1. Calc. for $C_{17}H_{19}N$: C, 86.0; H, 8.1; N, 5.9%).

4-*Hydroxy*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline* (**20**): $\nu_{max.}$ (thin film) 3 100br (OH), 2 795 cm^{-1} (NMe); δ_H ($CDCl_3$–D_2O) 7.43—7.40 (1 H, m), 7.26—7.21 (2 H, m, ArH), 6.96—6.93 (1 H, m, ArH), 4.59—4.56 (1 H, br t, 4-H), 3.35 and 3.15 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 2.98—2.93 (1 H, m, 3-H), 2.52—2.47 (1 H, m, 3-H), and 2.35 (3 H, s, NMe); *m/z* 163 (M^+) (Found: M^+, 163.0997. $C_{10}H_{13}NO$ requires *M*, 163.0997).

Tricarbonyl[η^6-2-*methyl*-4-(1-*hydroxy*-1-*methylethyl*)-1,2,3,4-*tetrahydroisoquinoline*]*chromium*(0) (**21**).—A solution of the anion (**8**) prepared as above was treated with a solution of acetone (0.4 ml, 5.4 mmol) in tetrahydrofuran (20 ml) at −78 °C added dropwise *via* a cannula. After the reaction had been stirred (2 h, −78 °C), methanol (2 ml) was added to the resulting crimson solution, and the mixture was warmed to 20 °C and evaporated. Column chromatography (Al_2O_3 Grade V–Et_2O) followed by evaporation and crystallisation from dichloromethane–hexane gave the *title compound* as yellow needles (220 mg, 36%), m.p. 159—160 °C, $\nu_{max.}$ 1 950, 1 900, and 1 880 cm^{-1} (C≡O); δ_H 6.37 (1 H, br s, OH), 5.46—5.19 (4 H, m, ArH), 3.84 and 3.38 (2 H, AB system, J_{AB} 15 Hz, 1-H_2), 3.33 and 2.75 (2 H, AB system, J_{AB} 10 Hz, 3-H_2), 2.44 (3 H, s, NMe), 2.30 (1 H, br s, 4-H), 1.44 (3 H, s, *Me*COH), and 1.34 (3 H, s, *Me*COH); *m/z* 341 (M^+) (Found, C, 56.7; H, 5.4; N, 4.1. $C_{16}H_{19}CrNO_4$ requires C, 56.3; H, 5.6; N, 4.1%).

Tricarbonyl[η^6-2-*methyl*-4-(1-*hydroxy*-1-*methylethyl*)-1,2,3,4-*tetrahydroisoquinoline*]*chromium*(0) (**21**) via $CeCl_3$ *Transmetallation*.—A solution of the anion (**8**) prepared as above was added to a stirred suspension of anhydrous cerium(III) chloride (prepared from 900 mg $CeCl_3 \cdot 7H_2O$ according to the method of Imamoto[14]) in tetrahydrofuran (15 ml) at −78 °C. After 30 min a solution of acetone (0.4 ml, 5.4 mmol) in tetrahydrofuran (20 ml) at −78 °C was added dropwise *via* a cannula. After 2 h saturated aqueous ammonium chloride (20 ml) was added, the mixture allowed to warm to 20 °C and extracted with ethyl acetate (3 × 40 ml). Concentration of the combined organic layers followed by column chromatography (Al_2O_3 Grade V–Et_2O) evaporation and crystallisation from dichloromethane–hexane gave the *title compound* (350 mg, 58%) identical in all respects with the sample obtained above.

Tricarbonyl(η^6-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)*chromium*(0) (**4**) *from Tricarbonyl*(η^6-4-*deuterio*-2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*)*chromium*(0) (**9**).—The complex (**9**) (100 mg, 0.35 mmol) in tetrahydrofuran (20 ml) at −78 °C was treated with butyl-lithium (1.6M in hexane; 0.24 ml, 0.38 mmol). After the reaction had been stirred (2 h, −78 °C), methanol (1 ml) was added and the mixture was warmed (20 °C) and concentrated. Chromatography [Al_2O_3 Grade V; Et_2O–hexane (2:1)] gave, on evaporation, a yellow powder (89 mg, 89%) identical in all respects with an authentic sample of tricarbonyl(η^6-2-methyl-1,2,3,4-tetrahydroisoquinoline)-chromium(0) (**4**). ^2H N.m.r. spectroscopy showed no deuterium incorporation.

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