Tricarbonylchromium Complexes of 2-Aminotetralin Derivatives. Part 2.[1] Regio- and Stereo-selective Reactions

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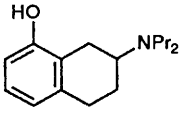
Methyl and trimethylsilyl substituents have been introduced in the C-7- and C-6-positions of tricarbonylchromium complexes of C-8-oxygenated 2-(dipropylamino)tetralin derivatives. The C-6-substituted regioisomers were produced from a complex with a bulky triisopropylsilyloxy C-8-substitutent whereas C-7-derivatives were produced from the C-8-methoxy substituted complex. The reactions proceed with high regioselectivities. Treatment of *endo*-tricarbonyl[2-(dipropylamino)-8-methoxytetralin]chromium with Bu^{t}OK and MeI in DMSO lead to introduction of a C-1-methyl group located *trans* to the C-2-substituent and *anti* to the tricarbonylchromium moiety. In contrast, a methyl group was introduced in the C-4-position, *cis* to the C-2-substituent and *anti* to the tricarbonylchromium moiety, when the diastereoisomeric *exo* complex was submitted to the same conditions.

Many derivatives of 2-aminotetralin (2-amino-1,2,3,4-tetrahydronaphthalene) possess impressive biological activities.[2] Particular interest has been devoted to 8-hydroxy-2-(dipropylamino)tetralin (8-OH DPAT; **1**)[3] due to its selectivity and high potency as a 5-HT_{1A}-receptor agonist.[4] We are currently interested in preparing derivatives of **1** in order to explore the structure–activity relationships of 5-HT_{1A}-receptor agonists and antagonists with the long-term objective of developing derivatives for use in the therapy of anxiety and depression.



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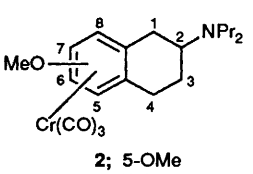
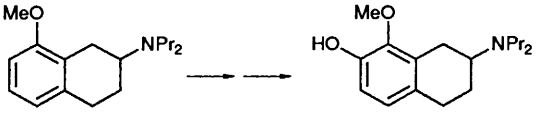
Tricarbonylchromium complexation of an aromatic ring may lead to a modified reactivity pattern of the ring as well as of its substituents.[5] Thus, the chemistry of arene-chromium complexes may be utilized to readily provide derivatives with odd substitution patterns. In addition, reactions with such complexes may proceed in a regio- and stereo-selective manner. Consequently, it was of interest to study the possibilities offered by tricarbonylchromium complexation in the synthesis of derivatives of **1**. Initially, we prepared stereochemically well-defined arene-chromium complexes of 5-, 7- and 8-methoxy-2-(dipropylamino)tetralin **2**–**4**.[1] In the present study we describe attempts to introduce substituents in the aromatic ring and in the benzylic positions of primarily C-8-oxygenated tricarbonylchromium complexes.



2; 5-OMe
3; 7-OMe
4; 8-OMe

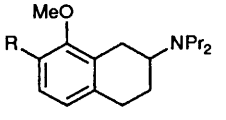
Results and Discussion

Introduction of Substituents in the C-7-*Position.*—The electron withdrawing ability of the tricarbonylchromium moiety in an arene chromium complex has been compared to that of a nitro group.[6] Consequently, the acidity of the aromatic hydrogens is increased in a tricarbonylchromiumium complex. Previously, Wikström *et al.*[7] have lithiated 8-methoxy-2-(dipropylamino)tetralin **5** in the C-7-position by using butyllithium (7 equiv.) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA; 3 quiv.) in Et_2O–hexane at 0 °C. They quenched the C-7 anion with nitrobenzene to obtain 7-hydroxy-8-methoxy-2-(dipropylamino)tetralin **6** in 20% yield. We generated the



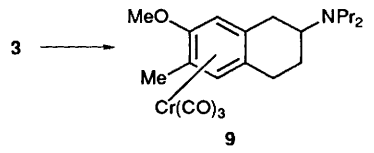
5 **6**

kinetic C-7-anions of a mixture of the arene-chromium complexes *endo*- and *exo*-**4** by treatment with butyllithium (3 equiv.) and TMEDA (3 equiv.) in THF at −78 °C. The carbanions were reacted with MeI or trimethylsilyl chloride and the resulting complexes were decomplexed to give the C-7-methylated and silylated derivatives **7** and **8** in 67 and 41% yield, respectively.



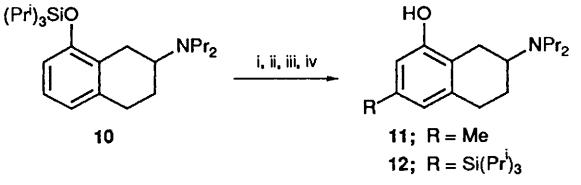
7; R = Me
8; R = TMS

The moderate yields in the reactions are mainly due to side reactions during the decomplexation since the lithiation–methylation sequence appears to proceed in about 90% yield. In contrast to lithiations of **5**, which did not proceed in the absence of TMEDA,[7] we could produce the anion of **4** without TMEDA. However, the addition of TMEDA considerably improved the yields. The reactions proceeded in an apparently regioselective manner since we only observed one substitution product from each reaction. Similarly, when applied to complex **3**, the only observed product from the lithiation–methylation procedure was the tricarbonylchromium complex of 7-methoxy-6-methyl-2-(dipropylamino)tetralin **9**.



9

Introduction of a methyl group in the C-6-*position of* **4**. Exchange of an aromatic methoxy group for bulky silyloxy groups such as *tert*-butyldimethylsilyloxy (TBDMSO) or triisopropylsilyloxy (TIPSO) groups block the *ortho*-directing effect of the oxygen substituent in tricarbonylchromium complexes. The silyl derived ethers direct anion formation to the *meta*-position of arene-chromium complexes,[8] the TIPSO group contributing to higher regioselectivities than the TBDMSO group.[9] We obtained the tricarbonylchromium complex of 2-(dipropylamino)-8-triisopropylsilyloxytetralin **10** in a good yield and generated the lithium anion (BuLi–TMEDA–THF) at −78 °C. The anion was methylated (MeI) and the complex was desilylated and decomplexed. GLC-analysis of the crude mixture indicated that only one methylated product had formed and that about 40% of the material has been methylated. The C-6-methylated **11** was separated from **1** by preparative HPLC. Treatment of the C-6-anion of the complex with trimethylsilyl chloride followed by decomplexation produced the analogous C-6-trimethylsilyl derivative **12**. GLC-analysis of the decomplexed mixture indicated that about 80% of the material had been trimethylsilylated in the C-6-position.



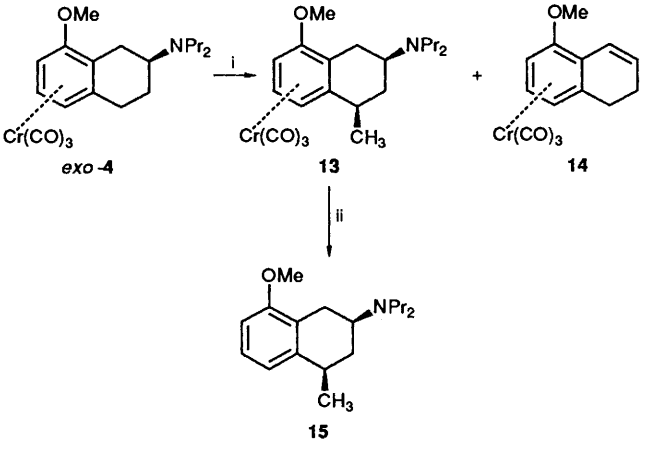
10 **11**; R = Me **12**; R = $Si(Pr^i)_3$

Reagents: i, $Cr(CO)_6$; ii, BuLi, TMEDA, MeI or TMSCl; iii, H^+; iv, air and sunlight

Alkylation of the benzylic positions of **4**. Not only aromatic but also benzylic hydrogens become more acidic in arene-chromium complexes.[10] This fact has been utilized synthetically, *e.g.* in syntheses of methylated derivatives of estradiol[11] and of nitrogen containing heterocyclic ring systems.[12] The observation that the hydrogens of a benzylic group *meta* to a methoxy group are more acidic than those on *para*-positioned benzylic alkyl groups[13] appeared useful since we were interested in introducing substituents in the C-4-position of **1** (*i.e.*, *meta* to the hydroxy group and not *ortho*). In addition, alkylation occurs *anti* to the tricarbonylchromium moiety.[14–17] This appeared particularly promising since we had been able to prepare the enantiomers of *endo*- and *exo*-**4**,[1] thereby opening up the possibility of utilizing the stereochemistry at C-2 (the nitrogen-bearing carbon) to control the absolute stereochemistry of substitution at the prochiral C-4 *via* the tricarbonylchromium moiety.

Treatment of tricarbonylchromium complexes *endo*- and *exo*-**4** with strong bases produces the initial *ortho*-lithiated anion which eventually forms a thermodynamically more stable benzylic anion. Unfortunately, due to the electron withdrawing ability of the dipropylamino substituent in the C-2-position, the acidity of the hydrogens at C-1 does not differ considerably from that of the C-4-hydrogens and when the C-1-anion is formed it readily eliminates dipropylamine.[18] Thus, ideal reaction conditions should convert the kinetically formed C-7 anion into the thermodynamically more stable anion at C-4 without forming an anion at C-1. In various preliminary experiments we attempted to circumvent part of this problem by removing the possibility of C-7-anion formation, *e.g.* by generating the anion from the *ortho*-trimethylsilylated complex (see above). However, this did not appear to lead to a regioselective anion formation and both aromatic and aliphatic substitution products were observed.

Generation of anions of *endo*- and *exo*-**4** with Bu^{t}OK in dry DMSO[16] produced the best results, even though a competitive elimination of dipropylamine occurred (Scheme 1). These

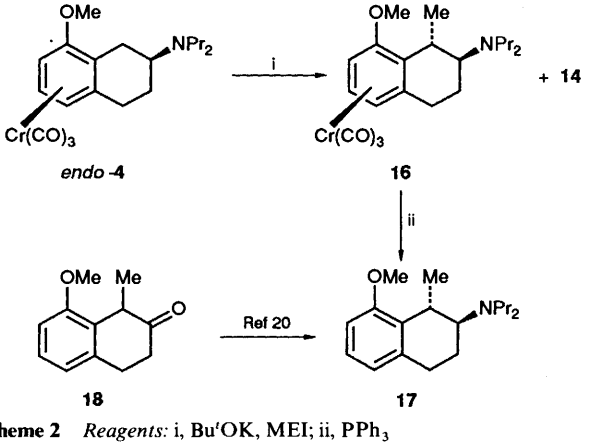


exo-**4** **13** **14** **15**

Scheme 1 *Reagents:* i, Bu^{t}OK, MeI; ii, PPh_3

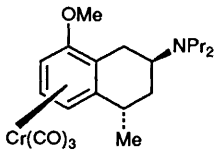
conditions do not lead to the *ortho*-anion but result in direct formation of a benzyl anion.[19] Alkylation of the anion of *exo*-**4** with MeI produced the methylated tricarbonylchromium complex **13** as a single diastereoisomer in 22% yield. In addition, quaternized ammonium derivatives and the elimination product, **14**, were formed but no regioisomers were observed. The ^1H NMR spectrum of the decomplexed material **15** established the expected stereochemistry of the product, the methyl group being introduced *anti* to the tricarbonylchromium moiety, that is, *cis* to the dipropylamino substituent: the observed vicinal coupling constants (large, diaxial, couplings between 2-H and 1-Hax and 3-Hax and from 4-H to 3-Hax) are consistent with a conformation in which the non-aromatic ring adopts a half-chair conformation with the C-2 and C-4 substituents assuming pseudoequatorial positions. Such a conformation corresponds to a minimum-energy conformer according to molecular mechanics (MM2) calculations.

Methylation of *endo*-**4** under the above conditions produced less quaternized products and more of the elimination product (**14**; Scheme 2). Unexpectedly, the only identified substitution product was the C-1-methylated **16** (isolated in 18% yield). Thus, we were not able to detect the regioisomeric C-4-methylated product **19**. The structures of **17** and, by analogy,



endo-**4** **16** **18** **17**

Scheme 2 *Reagents:* i, Bu^{t}OK, MEI; ii, PPh_3



19

that of **16** were initially assigned by use of 2-D NMR correlation spectroscopy. The structural assignments are unambiguous since **17** is identical with material previously prepared by us using 8-methoxy-1-methyltetralone (**18**) as starting material.[20]

Concluding Remarks.—Introduction of an aromatic substitutent *ortho* to a methoxy group *via ortho*-lithiation is facile in the tricarbonylchromium complexes but may also be achieved in the non-complexed compounds. However, derivatives substituted in the *meta*-position, which are readily obtained using arene-chromium complex-derived chemistry, are much more difficult to synthesize using traditional chemistry. The C-4-benzylic substitution proceeded in a low yield. Nevertheless, it may turn out to be quite competitive since other syntheses require longer synthetic routes. In fact, the methodology based on tricarbonylchromium complexation may be superior since it allows for regio- and stereo-specific introduction of a variety of electrophiles from a common intermediate.

The regiospecificity of the methylation reaction leading to C-4-substitution of *exo*-**4** and C-1-substitution of *endo*-**4** is intriguing. A speculative rationale for this observation might be that the amino substituent in *endo*-**4**, but not that in *exo*-**4**, would perturb the conformation of the tricarbonylchromium moiety in such a way that the stability/acidity of the C-1-hydrogens would change as compared to that of the C-4-hydrogens. It has been reported, however, that the conformation of the tricarbonylchromium moiety only slightly affects the stability of benzylic anions.[11]

Experimental

Routine ^1H and ^{13}C NMR spectra were recorded at 90 and 22.5 MHz, respectively, on a JEOL FX 90Q spectrometer. High resolution 270 MHz ^1H, 67.5 MHz ^{13}C and 2-D ^1H–^1H (COSY) and ^1H–^{13}C correlation NMR spectra were obtained on a JEOL JNM EX 270 spectrometer. All NMR spectra were referenced to internal tetramethylsilane. Coupling constants are given in Hz. For preparative HPLC a Hitachi L-4000 UV Detector (λ 245.5 nm) and a Hitachi L-6200 Intelligent Pump (10.5–12.0 cm^3 min^{-1}) were used and the chromatograms were recorded on a Shimadzu C-R4A Chromatopac integrator. The separation was performed on a Waters PrepPack 25 × 10 Cartridge (Bondapak C18, 125 Å. 10μ) in a 25 × 10 Compression Module. Capillary GLC was performed on a Carlo Erba 4200, by use of an SE 52 column (25 m), equipped with a flame ionization detector (FID-40) and a Milton Roy CI-10B integrator. M.p.s (uncorrected) were determined in open glass capillaries on a Thomas-Hoover apparatus. Elemental analyses were performed by Mikro Kemi AB, Uppsala, Sweden. Light petroleum refers to the fraction boiling in the range 40–60 °C. The concentration of BuLi in hexane was determined by titration on diphenyl acetic acid in THF (tetrahydrofuran). Throughout, the THF was freshly distilled from sodium and benzophenone, and all reactions were performed under an atmosphere of N_2. The glass equipment used was dried at 110 °C overnight and the syringes were kept in a dessicator for at least 12 h.

(±)-8-*Methoxy*-7-*methyl*-N,N-*dipropyl*-1,2,3,4-*tetrahydronaphthalen*-2-*ylamine Hydrochloride* (±)-**7**·HCl.—A mixture of *endo*- and *exo*-(±)-tricarbonyl[2-(dipropylamino)-8-methoxy-1,2,3,4-tetrahydronaphthalene]chromium **4**[1] (0.579 g, 1.46 mmol) and TMEDA (0.65 cm^3, 4.4 mmol) were dissolved in THF (30 cm^3). A solution of BuLi in hexane (3.00 cm^3, 4.38 mmol) was added dropwise at −70 °C and the reaction was stirred for 2 h at −78 °C. MeI (0.45 cm^3, 7.2 mmol) was added dropwise and the reaction was quenched with an excess of MeOH after 2 h. The solvent was evaporated and the reaction mixture was partitioned between aqueous NaOH (1 mol dm^{-3}) and Et_2O. The organic layer was dried (K_2CO_3) and concentrated. The residue was added to a solution of PPh_3 (8.07 g, 30.8 mmol) in 25 cm^3 of Bu_2O and the mixture was heated to reflux during 7 d. The mixture was partitioned between 1 mol dm^{-3} HCl and Et_2O. The aqueous layer was alkalinized and extracted with Et_2O. The combined organic layers were dried and concentrated. The oily residue was purified on a silica column by gradient elution (Et_2O–light petroleum 1:4 → Et_2O–light petroleum 1:1) to afford 0.27 g (67%) of pure **7** as an oil. The *oil* was dissolved in Et_2O and ethereal HCl was added. The resulting (±)-**7**·HCl was recrystallized from acetone–Et_2O, m.p. 130–131 °C; $\delta_H(CD_3OD)$ 7.00 (d, 6-H), 6.82 (d, 5-H), 3.75 (s, H-OMe), 3.70 (dddd, J_1 11.5, J_2 3.0, J_3 11.7, J_4 5.2, 2-H), 3.35–3.15 (6 H, m), 3.04–2.84 (m, obscured, 1ax-H), 3.3 (ddd, J_1 2.9, J_2 6.5, J_3 −15.6, 4eq-H), 2.96 (ddd, J_1 5.1, J_2 11.7, J_3 −15.6, 4ax-H), 2.29 (dddd, J_1 5.2, J_2 2.9, J_3 5.1, J_4 −11.9, 3eq-H), 2.24 (s, Me-7-H), 1.92 (dddd, J_1 11.7, J_2 11.7, J_3 6.5, J_4 −11.9, 3ax-H), 1.83 (m, β-H) and 1.05 (t, γ-H) $\delta_C(CD_3OD)$ 157.66 (C-8), 135.30 (C-4a), 130.45 (C-6), 129.28 (C-8a or C-7), 126.93 (C-7 or C-8a), 125.11 (C-5), 60.22 (C-OMe), 61.89 (C-2), 53.83 (C-α), 29.09, 25.26, 24.61 (cyclohexene Cs), 19.73 (C-β), 15.90 (C7-Me) and 11.36 (C-γ) (Found: C, 68.6; H, 9.6; N, 4.4. $C_{18}H_{29}NO$·HCl·$\frac{1}{4}H_2O$ requires C, 68.3; H, 9.7; N, 4.4%).

(±)-8-*Methoxy*-N,N-*dipropyl*-7-(*trimethylsilyl*)-1,2,3,4-*tetrahydronaphthalen*-2-*ylamine Hydrochloride* (±)-**8**·HCl.—Compound **8** was prepared by the above procedure from (±)-*endo*-**4** (0.304 g, 0.765 mmol), TMEDA (0.13 cm^3, 0.87 mmol), BuLi in hexane (0.80 cm^3, 1.2 mmol) and TMSCl (0.300 cm^3, 2.38 mmol). The product was purified on an alumina column by use of Et_2O–light petroleum 1:6 as eluent to give (±)-*endo*-*tricarbonyl*[2-(*dipropylamino*)-8-*methoxy*-7-(*trimethylsilyl*)-1,2,3,4-*tetrahydronaphthalene*]*chromium* (0.33 g, 0.703 mmol, 91.9%); $\delta_H(CDCl_3)$ 5.24 (d, 6-H), 4.91 (d, 5-H), 3.85 (s, OMe-H), 3.70 (s, 2-H), 2.90–1.20 (14 H, m), 0.90 (t, γ-H) and 0.36 (s, TMS-H); $\delta_C(CDCl_3)$ 232.77 (C-CrCO), 144.16 (C-8), 110.62 (C-4a), 101.26 (C-8a), 96.72 (C-6), 93.05 (C-7), 88.45 (C-5), 62.38 (C-OMe), 55.16 (C-2), 51.30 (C-α), 28.66, 25.26, 22.63 (cyclohexene Cs), 21.15 (C-β), 10.68 (C-γ) and 1.30 (C-TMS); ν(KBr)/cm^{-1} 1950 (CO), 1878sh and 1864 (Found: C, 58.7; H, 7.6; N, 2.9. $C_{23}H_{35}CrNO_4Si$ requires C, 58.8; H, 7.5; N, 3.0%).

Part of the tricarbonylchromium complex of **8** (0.69 g, 1.5 mmol) was added to a solution of PPh_3 (8.17 g, 31.2 mmol) in 25 cm^3 of Bu_2O. The mixture was heated to reflux over 7 d. Work-up as above (acid-base extraction and column chromatography on silica) gave pure **8** as an oil that was treated with ethereal HCl. The hygroscopic **8**·HCl (0.247 g, 41% from *endo*-**4**) was recrystallized from acetone–Et_2O, m.p. 95–97 °C; $\delta_H(CD_3OD)$ 7.24 (d, 6-H), 6.94 (d, 5-H), 3.77 (s, OMe-H), 3.7 (dddd, J_1 11.2, J_2 3.4, J_3 11.9, J_4 5.2, 2-H), 3.30–3.05 (7 H, m), 3.05–2.88 (m, obscured, 4ax-H), 2.30 (dddd, J_1 5.2, J_2 5.2, J_3 2.8, J_4 −12.1, 3eq-H), 1.95 (dddd, J_1 11.9, J_2 11.9, J_3 6.2, J_4 −12.1, 3ax-H), 1.82 (m, β-H), 1.05 (t, γ-H) and 0.27 (s, TMS-7-H); $\delta_C(CD_3OD)$ 164.98 (C-8), 139.84 (C-4a), 134.41 (C-6), 130.48 (C-7 or C-8a), 126.62 (C-8a or C-7), 125.20 (C-5), 61.92 (C-OMe), 61.74 (C-2), 53.89 (C-α), 29.25, 25.27, 24.49 (cyclohexene Cs), 19.80 (C-β), 11.33 (C-γ) and 0.0 (C-7-TMS) (Found: C,

63.6; H, 9.6; N, 3.8. $C_{20}H_{35}NOSi{\cdot}HCl{\cdot}\frac{1}{2}H_2O$ requires C, 63.4; H, 9.8; N, 3.7%).

(±)-*Tricarbonyl*[2-(*dipropylamino*)-7-*methoxy*-6-*methyl*-1,-2,3,4-*tetrahydronaphthalene*]*chromium* (±)-**9**.—An *endo*/*exo* mixture of (±)-tricarbonyl[2-(dipropylamino)-7-methoxy-1,2,-3,4-tetrahydronaphthalene]chromium (**3**; 0.134 g, 0.337 mmol)[1] was treated as above with BuLi in hexane (0.40 cm^3, 0.56 mmol), TMEDA (0.052 cm^3, 0.35 mmol) and MeI (0.080 cm^3, 1.3 mmol). Repeated column chromatography on alumina gave pure **9** (0.07 g, 50%) as a yellow oil; $\delta_H(CDCl_3)$ 5.42 (s, 5-H), 4.98 (s, 8-H), 3.71 (s, OMe-H), 3.17 (s, OMe-H), 3.20–1.20 (15 H, m) and 0.88 (t, γ-H); $\delta_C(CDCl_3)$ 234.38, 234.23 [$Cr(CO)_3$], 140.48, 140.20, 125.51, 108.75, 107.44, 103.43, 101.42, 97.75, 97.64, 97.23 (aromatic Cs), 52.54, 52.45, 56.46, 55.96, 55.87, 55.36, 31.43, 30.30, 30.06, 28.91, 27.20, 25.73, 24.10, 22.34, 21.71, 15.80, 15.70 and 11.82 (aliphatic Cs) (Found: C, 61.5; H, 7.3; N, 3.3. $C_{21}H_{29}CrNO_4$ requires C, 61.3; H, 7.1; N, 3.4%).

2-(*Dipropylamino*)-8-[(*triisopropyl*)*silyloxy*]-1,2,3,4-*tetrahydronaphthalene* **10**.—A mixture of 2-(dipropylamino)-8-hydroxy-1,2,3,4-tetrahydronaphthalene hydrobromide **1**[3] (0.94 g, 2.9 mmol), imidazole (0.78 g, 11 mmol) and triisopropylsilyl chloride (0.80 cm^3, 3.7 mmol) in 3 cm^3 of DMF was stirred at 40 °C for 18 h. The reaction mixture was partitioned between Et_2O and aqueous $NaHCO_3$. The combined organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by gradient elution (Et_2O–light petroleum 1:4→Et_2O) on a silica column to give pure (±)-**10** (1.14 g, 99%) as an oil; $\delta_H(CDCl_3)$ 6.95 (app t, 6-H), 6.68 (d, 7-H), 6.58 (d, 5-H), 3.13 (m, 2-H) and 3.0–0.7 (41 H, m); $\delta_C(CDCl_3)$ 154.10, 138.24, 127.62, 125.64, 120.91, 114.77 (aromatic Cs), 56.85, 52.72, 30.22, 26.94, 26.27, 21.87, 18.11, 17.72, 13.03 and 11.93 (aliphatic Cs) (Found: C, 73.8; H, 11.2; N, 3.4. $C_{25}H_{45}NOSi{\cdot}\frac{1}{4}H_2O$ requires C, 73.5; H, 11.2; N, 3.4%).

8-*Hydroxy*-6-*methyl*-N,N-*dipropyl*-1,2,3,4-*tetrahydronaphthalen*-2-*ylamine Hydrochloride* **11**·HCl.—A mixture of (±)-**10** (1.12 g, 2.77 mmol) and $Cr(CO)_6$ (0.98 g, 4.5 mmol) in Bu_2O and THF (9:1, 10.5 dm^3) was heated under reflux for 20 h. The hot reaction mixture was filtered through Celite and the THF was evaporated. The residue was applied onto a silica column, which was eluted with $CHCl_3$ followed by Et_2O. The resulting *endo*/*exo*-mixture of (±)-*tricarbonyl*{[2-(*dipropylamino*)-8-[(*triisopropyl*)*silyloxy*]-1,2,3,4-*tetrahydronaphthalene*}*chromium* (1.18 g, 2.19 mmol, 79%) was obtained as a yellow oil which crystallized in a refrigerator. The complex decomposed on storage; $\delta_H(CDCl_3)$ 5.45–4.74 (3 H, m, aromatic Hs) and 3.15–0.70 (42 H, m, aliphatic Hs); $\delta_C(CDCl_3)$ 234.0 (CrCO), 138.93 (C-8′), 137.86 (C-8), 112.14 (C-4a), 110.36 (C-4a′), 102.14 (C-8a′), 101.07 (C8a), 92.89 (C-6), 92.77 (C-6′), 87.15 (C-5), 86.94 (C-5′), 81.35 (C-7), 81.01 (C-7′), 56.43 (C-2), 55.36 (C-2′), 52.56 (C-α′), 52.47 (C-α), 29.93, 27.98, 27.28, 25.91, 25.85, 24.37, 21.14, 21.50, 18.00, 17.91, 12.86 and 11.79 (aliphatic Cs) (primes are used in cases where signals due to the *endo*- and *exo*-isomers could be assigned).

Part of the above complex (0.825 g, 1.53 mmol) and TMEDA (0.95 cm^3, 6.4 mmol) were dissolved in THF (50 cm^3) and a solution of BuLi in hexane (5.00 cm^3, 6.30 mmol) was added dropwise at −70 °C. MeI (0.60 cm^3, 9.6 mmol) was added after 2 h and the mixture was stired for an additional 2 h at −78 °C. Excess MeOH was added and the mixture was concentrated. The residue was added to 1 mol dm^{-3} aqueous HCl. The solution was stirred for 15 min and was then partitioned between saturated aqueous $NaHCO_3$ and Et_2O. The dried (Na_2SO_4) organic layer was exposed to daylight for 7 d. The resulting mixture was filtered and concentrated. According to GLC analysis, the oily residue consisted of a 56:44 mixture of **1** and **11**. Compound **11** was separated from **1** by preparative HPLC (retention values: t_R 12.8 min, **11**, and 24.0 min, **1**, at a flow rate of 10.5 cm^3 min^{-1}). The mixture of **1** and **11** was treated with ethereal HCl and the resulting hydrochlorides were dissolved in the mobile phase, MeOH–phosphate buffer (pH 6.0) 4:6. Fractions containing pure **11** were concentrated, alkalinized to pH 9 and extracted with Et_2O. The combined organic layers were dried (Na_2SO_4) and ethereal HCl was added to give 0.041 g (9%) of **11**·HCl which was recrystallized from MeOH–Et_2O and showed m.p. 206–207 °C; $\delta_H(CD_3OD)$ 6.45 (s, 7-H), 6.45 (s, 5-H), 3.70 (dddd, J_1 11.4, J_2 2.8, J_3 11.7, J_4 5.8, 2-H), 3.28–3.11 (6 H, m), 2.90 (ddd, J_1 9.4, J_2 3.6, J_3 −15.5, 4ax-H), 2.71 (dd, J_1 11.4, J_2 −16.1, 1ax-H), 2.25 (dddd, J_1 5.8, J_2 3.6, J_3 1.5, J_4 −12.6, 3eq-H), 2.19 (s, Me-6-H), 1.81 (m, β-H), 1.8 (m, obscured, 3ax-H) and 1.05 (t, γ-H); $\delta_C(CD_3OD)$ 156.21 (C-8), 138.18 (C-4a or C-6), 137.07 (C-6 or C-4a), 121.08 (C-5), 117.50 (C-8a), 113.80 (C-7), 62.21 (C-2), 53.90 (C-α), 29.49, 25.05, 24.95 (cyclohexene Cs), 19.83 (C-β), 12.21 (C6-Me) and 11.34 (C-γ) (Found: C, 67.2; H, 9.8; N, 4.4. $C_{17}H_{27}NO{\cdot}HCl{\cdot}\frac{1}{4}H_2O$ requires C, 67.5; H, 9.5; N, 4.6%).

8-*Hydroxy*-N,N-*dipropyl*-6-(*trimethylsilyl*)-1,2,3,4-*tetrahydronaphthalen*-2-*ylamine Hydrochloride* **12**·HCl.—Compound **12** was prepared by the above procedure *via* tricarbonylchromium complexation of **10** (0.226 g, 0.419 mmol) and subsequent treatment with TMEDA (0.25 cm^3, 1.7 mmol), a solution of BuLi in hexane (1.40 cm^3, 1.76 mmol) and TMSCl (0.35 cm^3, 2.8 mmol). GLC analysis of the desilylated and decomplexed mixture indicated the presence of **12** and **1** in a 81:19 ratio. The mixture was separated on an alumina column using Et_2O–light petroleum 1:4 as eluent. Fractions containing pure **12** were concentrated to give an oil which was treated with ethereal HCl to give 0.08 g (53%) of the hygroscopic **12**·HCl which was recrystallized from MeOH–Et_2O, decomp. 277–278 °C; $\delta_H(CD_3OD)$ 6.78 (s, 7-H), 6.77 (s, 5-H), 3.74 (dddd, J_1 11.2, J_2 3.0, J_3 11.5, J_4 5.7, 2-H), 3.28–3.14 (6 H, m), 2.96 (ddd, J_1 10.8, J_2 4.7, J_3 −12.1, 4ax-H), 2.77 (dd, J_1 11.2, J_2 −16.4, 1ax-H), 2.29 (dddd, J_1 5.7, J_2 4.7, J_3 2.1, J_4 −12.9, 3eq-H), 1.9 (m, obscured, 3ax-H), 1.82 (m, β-H), 1.05 (t, γ-H) and 0.20 (s, TMS-6-H); $\delta_C(CD_3OD)$ 155.89 (C-8), 140.31 (C-6 or C-4a), 136.84 (C-4a or C-6), 125.42 (C-5), 121.35 (C-8a), 117.38 (C-7), 62.09 (C-2), 53.91 (C-α), 25.13, 25.01, 24.48 (cyclohexene Cs), 19.82 (C-β), 11.34 (C-γ) and −1.04 (TMS-C-6) (Found: C, 64.0; H, 9.6; N, 4.0. $C_{19}H_{33}NOSi{\cdot}HCl$ requires C, 64.1; H, 9.6; N, 3.9%).

(±)-trans-8-*Methoxy*-1-*methyl*-N,N-*dipropyl*-1,2,3,4-*tetrahydronaphthalen*-2-*ylamine Hydrochloride* **17**·HCl.—A mixture of Bu^{t}OK (0.87 g, 7.7 mmol), *endo*-tricarbonyl[2-(dipropylamino)-8-methoxy-1,2,3,4-tetrahydronaphthalene]chromium (*endo*-**4**, 1.37 g, 3.46 mmol) and dry DMSO (15 cm^3) was stirred for 10 min. MeI (0.96 cm^3, 15 mmol) was added dropwise and the reaction mixture was cooled and maintained at room temperature. The progress of the reaction was followed by TLC. After 1 h, the reaction was quenched by addition of an excess of saturated aqueous NH_4Cl. The mixture was partitioned between 1 mol dm^{-3} aqueous NaOH and Et_2O and the organic layer was dried (K_2CO_3) and concentrated. The product was purified on a silica column by use of gradient elution (Et_2O–light petroleum 1:4→Et_2O) to give 0.26 g (18%) of endo-*tricarbonyl*[(cis)-2-(*dipropylamino*)-8-*methoxy*-1-*methyl*-1,2,3,4-*tetrahydronaphthalene*]*chromium* **16** as a yellow oil. In addition, elimination production **14** *tricarbonyl*[1,2-*dihydro*-5-*methoxynaphthalene*]*chromium* was isolated, $\delta_H(CDCl_3)$ 6.58 (1 H, d), 6.15–5.90 (1 H, m), 5.42 (t, 7-H), 5.04 (d, 6-H), 4.76 (d, 8-H), 3.76 (s, OMe-H), 2.90–2.20 (m, 2 H) and 1.60–1.10 (m, 2 H).

A solution of **16** and PPh_3 (2.33 g, 8.88 mmol) in 25 cm^3 of Bu_2O was heated to reflux for 6 d. The resulting mixture was partitioned between 1 mol dm^{-3} aqueous HCl and Et_2O. The water layer was alkalinized and extracted with Et_2O. The combined organic phases were dried (K_2CO_3) and concentrated. The oily residue was purified on a silica column with gradient elution (Et_2O–light petroleum 1:9→1:1) to give **17** as an oil. This oil was treated with ethereal HCl to give 0.16 g (92%) of **17**·HCl which could be recrystallized from MeOH–Et_2O. Compound (±)-**17**·HCl showed m.p. 124–125 °C (lit.,[20] m.p. 129–133 °C).

(±)-cis-8-*Methoxy*-4-*methyl*-N,N-*dipropyl*-1,2,3,4-*tetrahydronaphthalen*-2-*ylamine Hydrochloride* **15**·HCl.—Treatment of *exo*-tricarbonyl[2-(dipropylamino)-8-methoxy-1,2,3,4-tetrahydronaphthalene]chromium (*exo*-**4**) [1] (1.20 g, 3.02 mmol) with Bu^{t}OK (0.685 g, 6.10 mmol) and MeI (0.78 cm^3, 12 mmol) according to the above procedure gave, after work-up, the pure exo-*tricarbonyl*[cis-2-(*dipropylamino*)-8-*methoxy*-4-*methyl*-1,2,3,4-*tetrahydronaphthalene*]*chromium* **13** (0.27 g, 22%). Compound **13** was treated with PPh_3 (2.60 g, 9.91 mmol) to give pure **15** (0.11 g, 0.40 mmol) as an oil which was treated with ethereal HCl. (±)-**15**·HCl was recrystallized from acetone–Et_2O and showed m.p. 71–73 °C; $\delta_H(CD_3OD)$ 7.20 (app t, 6-H), 6.96 (d, 7-H), 6.81 (d, 5-H), 3.83 (s, OMe-H), 3.77 (dddd, J_1 11.6, J_2 2.7, J_3 11.9, J_4 5.3, 2-H), 3.34–2.98 (6 H, m), 2.80 (dd, J_1 11.6, J_2 −16.3, 1ax-H), 2.29 (dddd, J_1 5.3, J_2 2.5, J_3 2.5, J_4 −12.0, 3eq-H), 1.82 (m, β-H, one rotational isomer), 1.81 (m, β-H, other rotational isomer), 1.64 (dd, J_1 12.0, J_2 −12.0, 3ax-H), 1.41 (d, J 6.7, 4-H-ethereal HCl. (±)-**15**·HCl was recrystallized from acetone–Et_2O and showed m.p. 71–73 °C; $\delta_H(CD_3OD)$ 7.20 (app t, 6-H), 6.96 (d, 7-H), 6.81 (d, 5-H), 3.83 (s, OMe-H), 3.77 (dddd, J_1 11.6, J_2 2.7, J_3 11.9, J_4 5.3, 2-H), 3.34–2.98 (6 H, m), 2.80 (dd, J_1 11.6, J_2 −16.3, 1ax-H), 2.29 (dddd, J_1 5.3, J_2 2.5, J_3 2.5, J_4 −12.0, 3eq-H), 1.82 (m, β-H), one rotational isomer), 1.81 (m, β-H, other rotational isomer), 1.64 (dd, J_1 12.0, J_2 −12.0, 3ax-H), 1.41 (d, J 6.7, 4-H-Me), 1.05 (t, γ-H, one rotational isomer), 1.04 (t, γ-H, other rotational isomer); $\delta_C(CD_3OD)$ 158.36 (C-8), 142.23 (C-4a), 128.59 (C-6), 122.08 (C-8a), 119.55 (C-5), 108.71 (C-7), 61.33 (C2), 55.92 (C-OMe), 53.87 (C-α, one rotational isomer), 53.80 (C-α, other rotational isomer), 34.16, 33.87, 25.55, 21.49 (aliphatic Cs), 19.89 (β-C, one rotational isomer), 18.78 (C-β, other rotational isomer) and 11.32 (C-γ) (Found: C, 65.2; H, 9.4; N, 4.2. $C_{18}H_{29}NO$·HCl·H_2O requires C, 65.5; H, 9.8; N, 4.2%).

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