The Diastereoselective Functionalisation of Arene Tricarbonylchromium Complexes Containing a Benzylic Heteroatom Substituent

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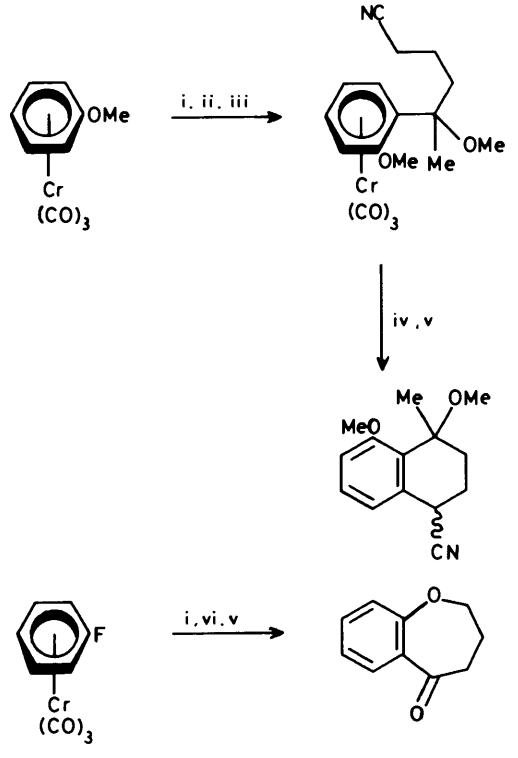
Treatment of (*S*)-tricarbonyl(α-methylbenzyldimethylamine)chromium (**4**) with n-butyl-lithium or t-butyl-lithium gives rise to a highly regioselective *ortho* deprotonation *via* co-ordination of the base to the benzylic nitrogen atom. In the latter case a highly diastereoselective substitution is observed consistent with reaction *via* the least hindered transition state. Determination of the stereochemistry of the product (*S*)-tricarbonyl(2,α-dimethylbenzyldimethylamine)chromium (**5**) by single crystal *X*-ray analysis is described. The regioselectivity of metallation of tricarbonyl(α-methylbenzyl methyl ether)chromium (**14**) and tricarbonyl(ethyl α-methylbenzyl sulphide)chromium (**20**) is also described. Treatment of compound (**14**) with t-butyl-lithium gives regioselective α-deprotonation with concomitant suppression of the Wittig rearrangement.

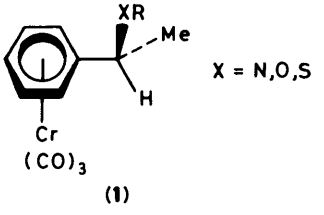
Following the discovery that benzenetricarbonylchromium could be deprotonated as a consequence of the activation imparted by the tricarbonylchromium entity,[1] several studies have been made on the regioselectivity of this deprotonation when applied to substituted arenes.[2] Semmelhack and Trahanovsky have investigated the strong *ortho* directing effect of methoxy and fluoro substituents and thereby effected a number of synthetically useful transformations (Scheme 1).[3]



Scheme 1. *Reagents:* i, Bu^{n}Li; ii, Ac(CH$_2$)$_3$CN; iii, MeI; iv, LDA; v, I$_2$; vi, tetrahydrofuran-2-one

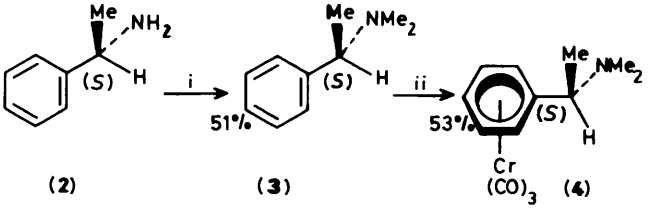
Monosubstituted achiral arene tricarbonylchromium complexes have enantiotopic *ortho* protons. When a chiral centre is present in the substituent, however, the *ortho* protons becomes diastereotopic. Little attempt has been made to extend the high degree of regioselectivity displayed above such that only one of the two diastereotopic *ortho* positions of a suitably monosubstituted arene is functionalised. This would provide a method of transferring side-chain chirality onto the co-ordinated arene.

Our initial studies in this area focussed on the chiral benzylic heteroatom functionalised complexes (**1**).†



Results and Discussion

Treatment of (*S*)-α-methylbenzylamine (**2**) with aqueous formic acid and formaldehyde according to the literature method gave (*S*)-α-methylbenzyldimethylamine (**3**).[4] Thermolysis of compound (**3**) with hexacarbonylchromium gave (*S*)-tricarbonyl(α-methylbenzyldimethylamine)chromium (**4**) as a yellow crystalline solid, $[\alpha]_D^{22} = -14.9°$ (*c* 0.99, $CHCl_3$) (Scheme 2).



Scheme 2. *Reagents:* i, HCO$_2$H, HCHO; ii, Cr(CO)$_6$, Bu^n$_2$O, THF

Treatment of complex (**4**) in THF at −78 °C with Bu^{t}Li followed by methyl iodide gave (*S*)-tricarbonyl(2,α-dimethylbenzyldimethylamine)chromium (**5**) (Scheme 3). Only a single diastereoisomer could be detected in the crude reaction product. Crystallisation gave (**5**) as yellow cubic crystals in 77% yield, $[\alpha]_D^{19} = -39°$ (*c* 1.03, $CHCl_3$). The relative configuration of the new arene centre to the original (*S*)-α-centre of complex (**4**) was

† Where X = N all complexes were prepared as single enantiomers, whereas for X = O, and X = S, a racemic mixture of the starting complex (**1**) was used.

Table 1. Atomic co-ordinates for non-hydrogen atoms

Atom	*x/a*	*y/b*	*z/c*
Cr(1)	0.845 0(1)	0.320 4(2)	0.117 6(1)
O(1)	1.171 2(7)	0.345(1)	−0.023 6(9)
O(2)	0.772(1)	0.143 5(8)	−0.155(1)
O(3)	0.973(1)	0.124 0(6)	0.329(1)
C(1)	0.641 3(5)	0.351 5(4)	0.290 1(6)
C(2)	0.781 4(6)	0.409 9(5)	0.360 9(9)
C(3)	0.864(1)	0.489 3(6)	0.263(1)
C(4)	0.811(1)	0.514 4(7)	0.094(2)
C(5)	0.677(1)	0.459 0(9)	0.023(1)
C(6)	0.592 4(7)	0.375 4(6)	0.122 3(8)
C(7)	0.549 7(6)	0.267 0(5)	0.398 7(7)
C(8)	0.452(1)	0.173 1(7)	0.301(1)
C(9)	0.841 3(7)	0.384 4(7)	0.536 8(8)
C(10)	1.043 9(7)	0.337(1)	0.028 9(8)
C(11)	0.800(1)	0.215 8(9)	−0.049(1)
C(12)	0.923(1)	0.200 4(7)	0.246(1)
C(13)	0.329 3(8)	0.407 8(8)	0.444(1)
C(14)	0.401(1)	0.264(1)	0.656(1)
N(1)	0.459 6(5)	0.338 0(7)	0.519 0(6)

Table 2. Selected torsional angles

C(6)–C(1)–C(7)–C(8)	+25	C(14)–N(1)–C(7)–C(1)	−165
C(6)–C(1)–C(7)–N(1)	−105	C(9)–C(2)–Cr(1)–C(12)	+17
C(13)–N(1)–C(7)–C(1)	+68		

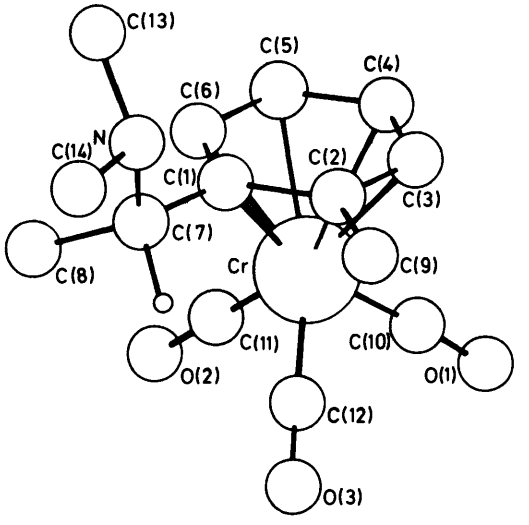
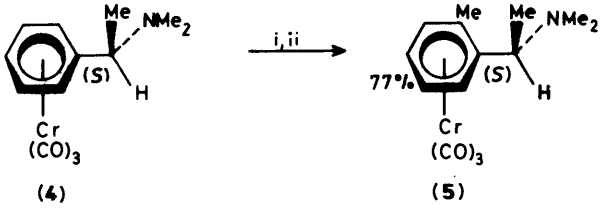


Figure 1.



Scheme 3. *Reagents:* i, Bu^{t}Li, −78 °C; ii, MeI, −78 °C

established by single crystal *X*-ray analysis (Figure 1) and indicated that exclusive removal of the *pro-S ortho* hydrogen had occurred. Selected bond lengths and bond angles are given in Table 1 and final atomic co-ordinates are listed in Table 2.†

Presumably the reaction proceeds *via* initial co-ordination of Bu^{t}Li to the nitrogen atom. The Newman projections along the C_α–C_{ipso} bond (Figure 2) reveal that transition states leading to the removal of the *pro-S ortho* proton have the α-proton *syn* to the bulky tricarbonylchromium moiety, whereas those leading to removal of the *pro-R ortho* proton have the α-methyl group *syn* to the metal unit. The transition states leading to removal of the *pro-S ortho* hydrogen are therefore favoured, resulting in complex (**5**) after subsequent methylation.

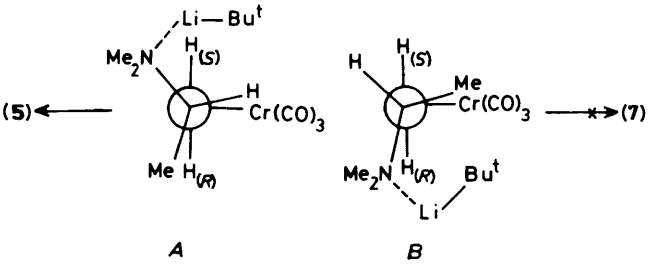
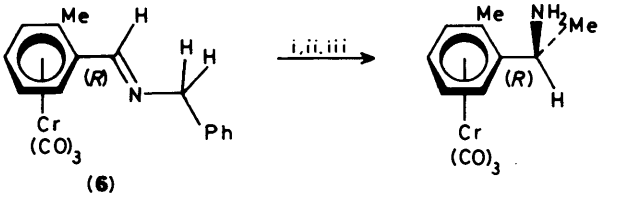


Figure 2.

The product of this reaction (**5**) is the opposite diastereoisomer of the complex obtained by Solladie-Cavallo from metallation of the chiral imine complex (**6**).[5] (Scheme 4).

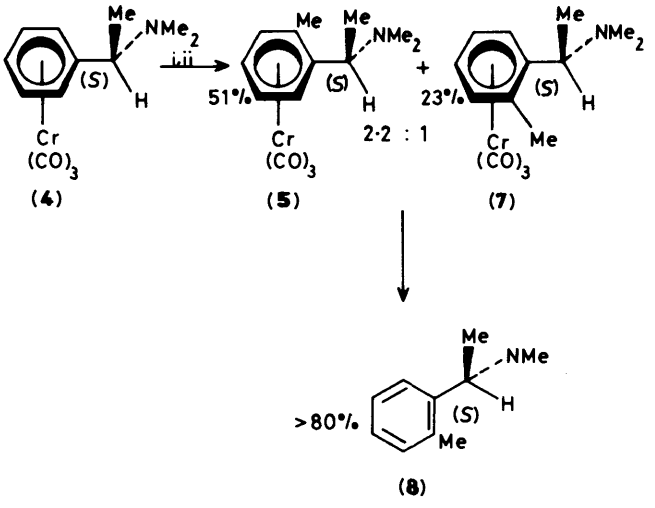


Scheme 4. *Reagents and conditions:* i, LDA, HMPT, THF, −78 °C; ii, MeI; iii, H$^+$

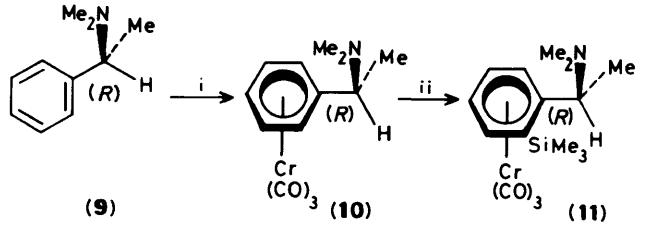
Treatment of complex (**4**) with n-butyl-lithium under identical conditions to those above gave a *ca.* 2:1 mixture of diastereoisomers, the major one of which was identical with complex (**5**). To confirm that both diastereoisomers corresponded to *ortho* methylated products the mixture of diastereoisomers was allowed to decomplex by exposing an ether solution in air and sunlight. Filtration followed by evaporation gave a single compound (**8**) as a clear oil, identified by comparison with an authentic sample of (*R*,*S*)-2,α-dimethylbenzyldimethylamine prepared according to the literature method.[6] (Scheme 5).

Although high *ortho* regioselectivity has been demonstrated with both Bu^{n}Li and Bu^{t}Li only the latter gives rise to high diastereoselectivity enabling complete transfer of side chain chirality onto the arene ring. To demonstrate the generality of this process (*R*)-tricarbonyl(α-methylbenzyldimethylamine)-chromium (**10**) [prepared in an analogous manner to the (*S*) analogue (**4**)] was treated with Bu^{t}Li followed by Me_3SiCl. A single diastereoisomer of the *ortho* functionalised complex (**11**) was isolated in 56% yield, $[\alpha]_D^{21} = -33.9°$ (*c* 7.06%, $CHCl_3$) (Scheme 6). Assuming that the diastereoselectivity is determined in the deprotonation step the stereochemistry of the product complex (**11**) was assigned as below by analogy with the conversion of complex (**4**) into (**5**), *i.e.* with the *pro-R ortho* proton of (**10**) replaced by the trimethylsilyl group. The fluoride

† Thermal parameters and other bond lengths and angles are available on request from the Cambridge Crystallographic Data Centre. See Instructions for Authors (1987), para. 5.6.3, *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1.



Scheme 5. *Reagents and conditions:* i, Bu^{n}Li, −78 °C; ii, MeI, −78 °C



Scheme 6. *Reagents and conditions:* i, $Cr(CO)_6$, THF, Bu$^n{}_2O$; ii, Bu^{t}Li, −78 °C; iii. Me_3SiCl, −78 °C

catalysed removal of trimethylsilyl groups from co-ordinated arenes has previously been demonstrated[7] and therefore a temporary transfer of chirality from side chain to co-ordinated arene is feasible.

We have previously demonstrated that complexation of benzyl alkyl ethers to the tricarbonylchromium unit facilitates benzylic functionalisation *via* a stabilised carbanion with suppression of the Wittig rearrangement.[8] The regio- and diastereo-selectivity of subsequent metallations of the resultant α-substituted (benzyl alkyl ether)$Cr(CO)_3$ complexes has not been determined, however.

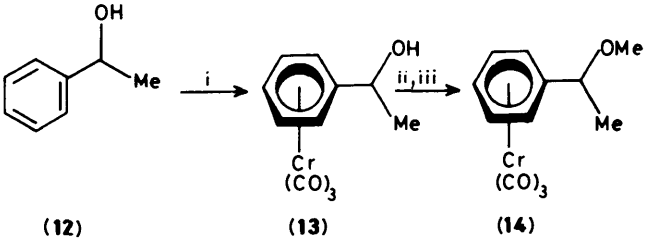
Thermolysis of (±)-α-methylbenzyl alcohol (**12**) with hexacarbonylchromium gave tricarbonyl(α-methylbenzyl alcohol)chromium (**13**).[9] Treatment of a dichloromethane solution of (**13**) containing methanol with HBF_4·OMe_2 at −30 °C gave tricarbonyl(α-methylbenzyl methyl ether)chromium (**14**) as a racemate.[8,10] (Scheme 7).

Treatment of a solution of complex (**14**) in THF at −78 °C with Bu^{t}Li followed by an electrophile gave the benzylically disubstituted species (**15**; E = Me) and (**16**; E = Me_3Si) (Scheme 8).

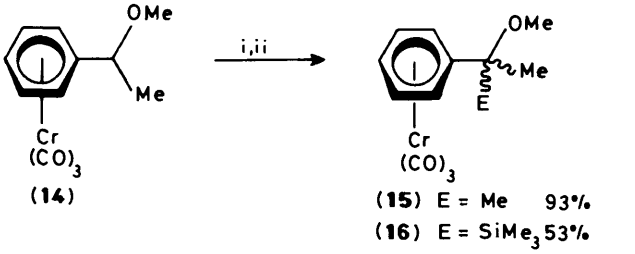
That complete suppression of the Wittig rearrangement was occurring was demonstrated by treatment of complex (**14**) with Bu^{t}Li followed by methanol under identical conditions. No Wittig rearranged product could be detected consistent with formation of the stable benzylic carbanion (**17**) (Scheme 9).

Treatment of complex (**14**) with Bu^{n}Li followed by MeI lowered regioselectivity however, and a mixture of three products was obtained. The minor product was identical in all respects with complex (**15**) obtained above whilst the remaining products were identified as the two diastereoisomers of tricarbonyl(2,α-dimethylbenzyl methyl ether)chromium (**18**) and (**19**) (Scheme 10).

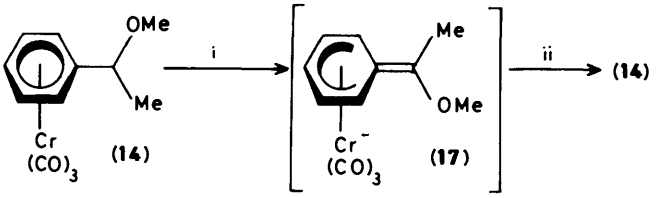
Presumably the strong base Bu^{t}Li removes the most acidic α-proton without appreciable co-ordination to oxygen whilst



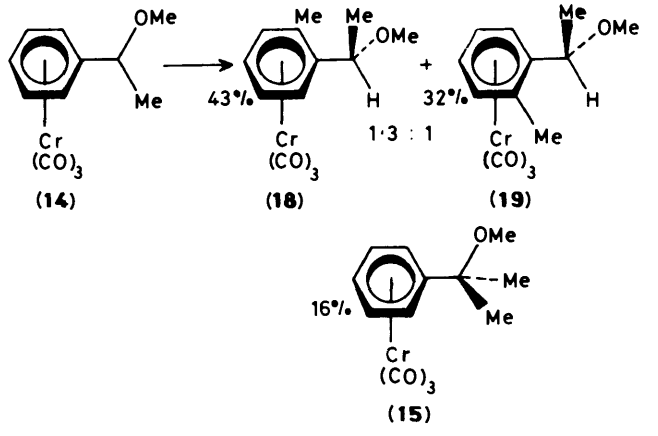
Scheme 7. *Reagents and conditions:* i, $Cr(CO)_6$, THF, Bu$^n{}_2O$; ii, HBF_4·OMe_2, MeOH–CH_2Cl_2, −30 °C



Scheme 8. *Reagents and conditions:* i, Bu^{t}Li, −78 °C; ii, E^+, −78 °C



Scheme 9. *Reagents and conditions:* i, Bu^{t}Li, −78 °C; ii, MeOH

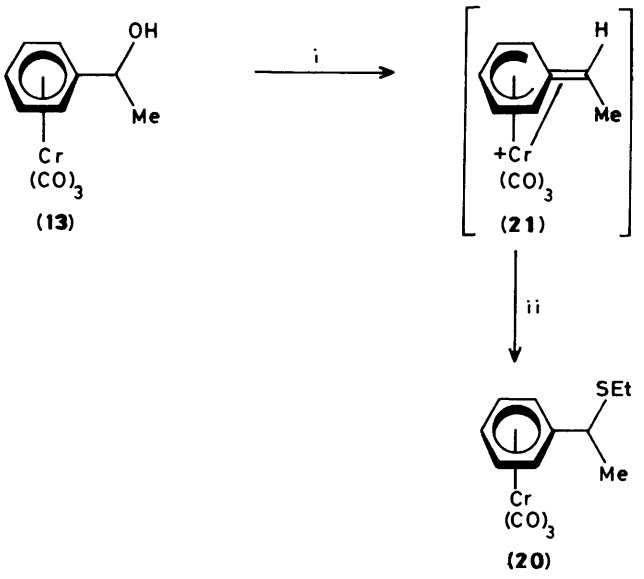


Scheme 10. *Reagents and conditions:* i, Bu^{n}Li, −78 °C; ii, MeI, −78 °C

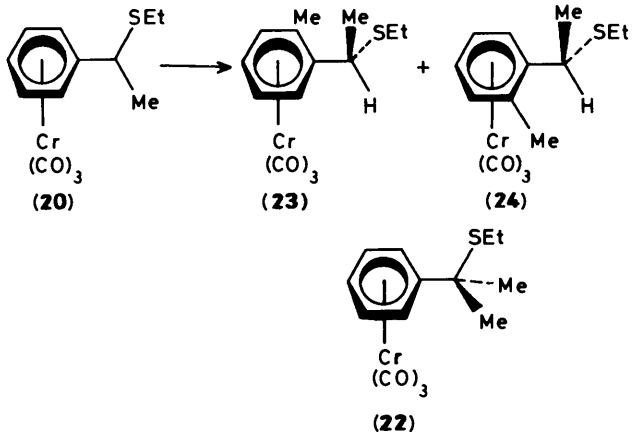
the lower basicity of Bu^{n}Li renders the rates of α-deprotonation and co-ordination to oxygen comparable. Once the base is co-ordinated to oxygen, regioselective *ortho* metallation occurs with the major isomer (**18**) resulting from reaction *via* the least encumbered transition state (*vide supra*). An example of the preference of Bu^{n}Li over Bu^{t}Li for co-ordination to oxygen has been demonstrated in the literature.[11]

Treatment of a dichloromethane solution of tricarbonyl(α-methylbenzylalcohol)chromium (**13**) containing ethanethiol with HBF_4·OMe_2 at −30 °C gave tricarbonyl(ethyl α-methylbenzyl sulphide)chromium (**20**) *via* the stabilised carbonium ion (**21**) (Scheme 11).

Metallation of complex (**20**) with Bu^{t}Li at −78 °C followed by the addition of methyl iodide gave a mixture of three diastereoisomers (**22**), (**23**), and (**24**) in the ratio *ca.* 6:7:4. Treatment of complex (**20**) with Bu^{n}Li under identical



Scheme 11. *Reagents and conditions:* i, HBF_4·OMe_2; ii, EtSH



Scheme 12. *Reagents and conditions:* i, Bu^nLi, −78 °C; ii, MeI, −78 °C

conditions again gave a mixture of the diastereomeric products (**22**), (**23**), and (**24**) as well as the *meta* or *para* substituted product (**25**) in the ratios *ca.* 10:9:6:8 respectively. The ethyl α-methylbenzyl sulphide complex (**20**) therefore, shows properties intermediate between those of its oxygen analogue (**14**) and nitrogen analogue (**4**) where treatment with Bu^tLi gives rise to regiospecific benzylic and *ortho* deprotonation respectively. Presumably the rate of co-ordination of Bu^tLi to the sulphur of complex (**20**) is comparable to the rate of benzylic deprotonation. Once the base is co-ordinated to the sulphur, however, regioselective *ortho* deprotonation occurs with the major diastereoisomer (**23**) resulting from reaction *via* the least hindered transition state. These results are in contrast to the reported reaction of ethyl α-methylbenzyl sulphide with alkyllithium reagents to give products derived from cleavage of the sulphide bond.[12]

The strong co-ordination of both Bu^nLi and Bu^tLi to the nitrogen atom of (*S*)-tricarbonyl(α-methylbenzyldimethylamine)chromium (**4**) gives rise to regioselective *ortho* deprotonation. In both cases a preference for reaction *via* the least hindered transition state is observed; in the latter case only the major diastereoisomer could be detected after trapping of the anion with methyl iodide. Treatment of tricarbonyl(α-methylbenzyl methyl ether)chromium (**14**) with Bu^tLi, however, gives regioselective α-deprotonation presumably *via* fast removal of the most acidic proton without co-ordination of base to the heteroatom substituent. With the weaker base Bu^nLi the rates of α-deprotonation and co-ordination to oxygen become comparable and products derived from α-deprotonation and *ortho* deprotonation are observed. Treatment of tricarbonyl(ethyl α-methylbenzylsulphide)chromium (**20**) with Bu^tLi provides an intermediate case where the rate of α-deprotonation and co-ordination of base to sulphur are comparable leading to a mixture of products.

Experimental

All reactions involving the preparation or utilisation of (arene)tricarbonylchromium(0) complexes were performed under an atmosphere of nitrogen. All commercial reagents were purified according to standard techniques.[13] THF was distilled from sodium benzophenone ketyl under an atmosphere of nitrogen. Dichloromethane was distilled from calcium hydride under nitrogen. Diethyl ether was peroxide free and hexane refers to light petroleum (b.p. 67—70 °C). Di-n-butyl ether was dried over sodium and distilled under an atmosphere of nitrogen prior to use. Hexacarbonylchromium was steam distilled prior to use. n-Butyl-lithium was used as a 1.55M solution in hexane and t-butyl-lithium as a 2M solution in pentane unless otherwise stated.

I.r. spectra were obtained as solutions in chloroform unless otherwise stated and ^1H n.m.r. spectra were obtained in [^2H]chloroform at 300 MHz unless otherwise stated. Optical rotations were obtained on a Perkin-Elmer 241 polarimeter and m.p.s were obtained on a Kofler hot-stage apparatus and are uncorrected.

(S)-α-*Methylbenzyldimethylamine* (**3**).[4]—Formaldehyde solution (37% aqueous solution; 14.0 ml) followed by formic acid (100% aqueous solution; 31.2 ml) were added dropwise to (*S*)-α-methylbenzylamine (**2**) (5.00 g, 41.3 mmol) at 0 °C. The solution was heated under reflux (24 h), cooled, basified (NaOH pellets), and extracted with diethyl ether (3 × 50 ml). The combined organic extracts were dried ($MgSO_4$) and then evaporated and finally distilled under reduced pressure to give the title compound (**3**) as a colourless oil (3.12 g, 51%), b.p. 40—42 °C, 0.1 mmHg; *m/z* 149 (M^+); $\nu_{max.}$ (liquid film): 2 764 (NMe_2), 756 and 701 (monosubstituted arene); $[\alpha]_D^{20}$ −61.1° (neat oil), [lit.[14] $[\alpha]_D^{26}$ −61.8° (neat oil)]; δ 7.32—7.21 (5 H, m, ArH), 3.22 (1 H, q, *J* 6.7 Hz, ArC*H*MeNMe$_2$), 2.17 (6 H, s, RN*Me*$_2$), and 1.35 (3 H, d, *J* 6.8 Hz, ArCH*Me*NMe$_2$).

(S)-*Tricarbonyl*(η^6-α-*methylbenzyldimethylamine*)*chromium*(0). (**4**).—(*S*)-α-Methylbenzyldimethylamine (**3**) (2.00 g, 13.4 mmol) and hexacarbonylchromium (3.54 g, 16.1 mmol) were added to di-n-butyl ether (40 ml) containing THF (5 ml) and heated under reflux (24 h). The cooled solution was filtered and the solvent removed. Column chromatography (Al_2O_3, Grade V, Et_2O) gave, after evaporation of the solvent and recrystallisation from dichloromethane–hexane solution, the title compound (**4**) as yellow needles (2.01 g, 53%) (Found: C, 54.55; H, 5.45; N, 4.75. $C_{13}H_{15}CrNO_3$ requires C, 54.74; H, 5.30; N, 4.91%); *m/z* 285 (M^+); $\nu_{max.}$(Nujol): 2 782 [N(Me)$_2$], 1 977, 1 965, 1 907, and 1 858br cm^{-1} (C≡O); $[\alpha]_D^{22}$ −14.9° (*c* 0.99, $CHCl_3$); δ 5.47—5.32 (5 H, m, ArH), 3.46 [1 H, q, *J* 6.9 Hz, ArC*H*(Me)N(Me)$_2$], 2.23 [6 H, s, RN*Me*$_2$], and 1.29 [3 H, d, *J* 6.9 Hz, ArCH(*Me*)NMe$_2$].

(S)-*Tricarbonyl*(η^6-2,α-*dimethylbenzyldimethylamine*)*chromium*(0) (**5**).—Bu^tLi (1.1 ml, 2.22 mmol) was added to a stirred solution of (*S*)-tricarbonyl(η^6-α-methylbenzyldimethylamine)chromium(0) (575 mg, 2.02 mmol) in THF (15 ml) at

−78 °C. The orange solution was stirred at −78 °C for 2 h, after which methyl iodide (0.20 ml, 3.03 mmol) was added and stirring continued for a further 2h at −78 °C. Methanol (2 ml) was then added and the mixture evaporated to give a deep red oil. Column chromatography (Al_2O_3, Grade V, Et_2O) of this gave, after removal of the solvent and recrystallisation from dichloromethane–light petroleum solution a single diastereoisomer of the title compound (**5**) as yellow cubic crystals (464 mg, 77%), m.p. 116—117 °C (Found: C, 56.2; H, 5.7; N, 4.55; $C_{14}H_{17}CrNO_3$ requires C, 56.18; H, 5.73; N, 4.68%); *m/z* 299 (M^+); $\nu_{max.}$ 2 790 (NMe_2), 1 966, and 1 888br cm^{-1} (C≡O); $[\alpha]_D^{19}$ −38.8° (*c* 1.03, $CHCl_3$); δ 5.52—5.50, 5.16—5.13 (2 H, 2 × d, ArH, and 6-H), 5.43—5.39, 5.22—5.17 (2 H, 2 × t, 4-ArH,5-ArH), 3.66 [1 H, q, *J* 6.8 Hz, ArC*H*(Me)NMe_2] 2.28 (3 H, s, Ar*Me*), 2.23 (6 H, s, $RNMe_2$), and 1.27 [3 H, d, *J* 6.8 Hz, ArCH(*Me*)N_2Me_2].

X-*Ray Crystal Structure Analysis of* (S)-*Tricarbonyl*(η⁶-2,α-*dimethylbenzyldimethylamine*)*chromium*(0) (**5**).—Cell parameters and reflection intensites were measured using graphite-monochromated Cu-K_α radiation on an an Enraf-Nonius CAD-4 diffractometer operating in the ω/2θ scan mode for a crystal having approximate dimensions 0.61 × 0.52 × 0.20 mm. The scan range (ω) was calculated from [0.80 + 0.14 tan θ]°, and the scan speed varied from 1.0 to 6.7° min^{-1} depending upon the intensity. Reflections were measured in the range 0 < θ < 75°. Three standard reflections measured every hour were used to scale the data and correct for crystal decomposition. The data were corrected for Lorentz-polarisation and absorption effects[15] (relative transmission factors 1.00—2.26) and equivalent reflections were merged to give 1 517 unique reflections (R_m 0.059) of which 1 274 were considered to be observed [$I > 3\sigma(I)$] and used in the structure analysis. Scattering factors were taken from International Tables.[16]

Crystal data. $C_{14}H_{17}NO_3Cr$, M = 299.29. Monoclinic, space group $P2_1$ (established from systematic absences), *a* 8.330(1), *b* 11.229(3), *c* 7.925(1) Å, β 91.73(1)°, *U* 740.9 Å³, *Z* = 2, D_{calc} = 1.34 Mg m^{-3}, μ(Cu-K_α) 64.8 cm^{-1}, *F*(000) = 312.

The structure was solved by direct methods and electron density Fourier synthesis, and refined by full-matrix least-squares methods. Parameters in the final cycles of refinement included those for positional co-ordinates, anisotropic temperature factors (non-hydrogen atoms), an overall scale factor, and an extinction parameter.[17] Hydrogen atoms were included in calculated positions and were allowed to 'ride' on their respective carbon atoms. The refinement was terminated when all shifts were less than 0.001σ with *R* 0.044 (R_w 0.050, GOF 0.98). The weight for each reflection was calculated from the Chebyshev series $w = [3.453\ t_0(X) + 4.697t_1(X) + 0.166\ t_2(X)]$ where $X = F_o/F_{max.}$.[18] Refinement of an enantiomorph-polarity estimation parameter *x* in the expression $F_o^2 = (1 - x)\ F_c(h)^2 + x\ F_c(-h)^2$, according to the method of Flack,[19] converged to a near-zero value indicating that the structure solution was of the correct handedness. Final difference electron-density Fourier synthesis revealed no significant features and a detailed analysis failed to reveal any systematic errors. All calculations were performed using the CRYSTALS package[20] on the Chemical Crystallography Laboratory VAX 11/750 computer.

Methylation of (S)-*Tricarbonyl*(η⁶-α-*methylbenzyldimethylamine*)*chromium*(0) (**4**), via *Treatment with* Bu^nLi.—Bu^nLi (0.77 ml, 1.15 mmol) was added to a stirred solution of compound (**4**) (300 mg, 1.05 mmol) in THF (20 ml) at −78 °C upon which the yellow solution rapidly turned red. The solution was stirred at −78 °C for 2 h, after which methyl iodide (0.21 ml, 3.15 mmol) was added and stirring was continued at −78 °C for a further 5 h. Methanol (1 ml) was then added and the reaction mixture warmed to 20 °C and evaporated. Column chromatography (Al_2O_3, Grade V, Et_2O) of the residue obtained after evaporation, gave a mixture of the two diastereoisomers (**5**) (159 mg, 51%) and (**7**) (72 mg, 23%) as a yellow oil; *m/z* 299 (M^+); $\nu_{max.}$ (Nujol): 2 781 [$N(Me)_2$], 1 973 and 1 905br cm^{-1} (C≡O); for compound (**5**) δ 5.44—5.20 (4 H, m, ArH), 3.67 [1 H, q, *J* 6.7 Hz, ArC*H*(Me)NMe_2], 2.28 (3 H, s, Ar*Me*), 2.24 (6 H, s, $RNMe_2$), and 1.28 [3 H, d, *J* 7.0 Hz, ArCH(*Me*)NMe_2]; for compound (**7**) δ 5.84—5.02 (4 H, m, ArH), 3.19 [1 H, q, *J* 6.6 Hz, ArC*H*(Me)NMe_2], 2.39 [6 H, s, $RN(Me_2)$], 2.27 (3 H, s, ArMe), and 1.33 [3 H, d, *J* 6.8 Hz, ArCH(*Me*)NMe_2]. The data for complex (**5**) was identical with that of an authentic sample.

(S)-2,α-*Dimethylbenzyldimethylamine* (S)-(**8**).—A mixture of the two diastereoisomers (**5**) and (**7**) of (*S*)-tricarbonyl(η⁶-2,α-dimethylbenzyldimethylamine)chromium(0) (60 mg, 0.20 mmol) was dissolved in diethyl ether (20 ml) and allowed to decomplex in air and sunlight (24 h). The solution was filtered twice through alumina (Grade V) and evaporated to give (*S*)-(**8**) as a clear oil (26 mg, 80%), identified by comparison with an authentic sample.[6]

(R)-α-*Methylbenzyldimethylamine* (**9**).—Formaldehyde solution (37% aqueous solution; 21.0 ml) followed by formic acid (23.4 ml, 100% aqueous solution) were added dropwise to (*R*)-α-methylbenzylamine (10.0 g, 82.5 mmol). The solution was heated under reflux (24 h), cooled (20 °C), basified (NaOH pellets) and extracted with diethyl ether (3 × 50 ml). The combined organic extracts ($MgSO_4$) were evaporated and distilled under reduced pressure to give the title compound (**9**) as a colourless oil (8.15 g, 66%), b.p. 40—42 °C, 0.1 mmHg; *m/z* 149 (M^+); $\nu_{max.}$ (liquid film): 2 765 (NMe_2), 756 and 702 (monosubstituted arene); $[\alpha]_D^{20}$ +61.0° (neat oil) [lit.,[14] $[\alpha]_D^{26}$ +61.8° (neat oil)]; δ 7.32—7.21 (5 H, m, ArH), 3.22 [1 H, q, *J* 6.7 Hz, ArC*H*(Me)NMe_2], 2.18 (6 H, s, $RNMe_2$), and 1.35 [3 H, d, *J* 6.7 Hz, ArCH(*Me*)NMe_2].

(R)-*Tricarbonyl*(η⁶-α-*methylbenzyldimethylamine*)-*chromium*(0) (**10**).—*R*-α-Methylbenzyldimethylamine (**9**) (2.00 g, 13.4 mmol) and hexacarbonylchromium (3.54 g, 16.1 mmol) were added to di-n-butyl ether (40 ml) containing THF (5 ml) and heated under reflux (24 h). The cooled solution was filtered and the solvent removed. Column chromatography (Al_2O_3, Grade V, Et_2O) gave, after evaporation of the solvent, a dark yellow oil which was recrystallised from diethyl ether–hexane solution to give the title compound (**10**) as yellow needles (2.47 g, 65%), m.p. 59—60 °C; *m/z* 285 (M^+); $\nu_{max.}$ (Nujol mull): 2 781 (NMe_2), 1 977, 1 907br cm^{-1} (C≡O); $[\alpha]_D^{22}$ +13.8° (*c* 0.96, $CHCl_3$); δ 5.48—5.34 (5 H, m, ArH), 3.48 [1 H, q, *J* 6.8 Hz, ArC*H*(Me)NMe_2], 2.25 (6 H, s, $RNMe_2$), and 1.31 [3 H, d, *J* 6.9 Hz, ArCH(*Me*)NMe_2].

(R)-*Tricarbonyl*(η⁶-α-*methyl*-2-*trimethylsilylbenzyldimethylamine*)*chromium*(0) (**11**).—Bu^tLi (1.16 ml, 2.32 mmol) was added to a stirred solution of (*R*)-tricarbonyl(η⁶-α-methylbenzyldimethylamine)chromium(0) (**10**) (600 mg, 2.10 mmol) in THF (15 ml) at −78 °C. The orange solution was stirred at −78 °C for 2 h after which chlorotrimethylsilane (1.06 ml, 8.40 mmol) was added. Stirring was continued for a further 2 h at −78 °C, after which methanol (1 ml) was added and the solution evaporated to leave an orange foam. Column chromatography (Al_2O_3, Grade I, Et_2O) of this gave, after removal of the solvent and recrystallisation from dichloromethane–light petroleum solution, the title compound (**11**) as a yellow plates (418 mg, 56%), m.p. 70—71 °C (Found: C, 53.5; H, 6.6; N, 3.75. $C_{16}H_{23}NO_3$ requires C, 53.76; H, 6.49; N, 3.92%); *m/z* 357 (M^+); $\nu_{max.}$ 2 780 [$N(Me)_2$], 1 967 and 1 890br cm^{-1} (C≡O); $[\alpha]_D^{21}$ −33.9° (*c* 1.06, $CHCl_3$); δ 5.60—5.55, 5.22—5.18 (2

H, 2 × t, 4-,5-ArH), 5.52—5.50, 5.20—5.18 (2 H, 2 × d, 3-,6-ArH), 3.83 [1 H, q, *J* 6.7 Hz, ArC*H*(Me)NMe_2], 2.14 (6 H, s, RNMe_2), 1.16 [3 H, d, *J* 6.7 Hz, ArCH(*Me*)NMe_2], and 0.34 (9 H, s, $ArSiMe_3$).

Tricarbonyl(η⁶-α-*methylbenzyl alcohol*)*chromium*(0) (**13**).[9]—α-Methylbenzyl alcohol (**12**) (3 g, 24.6 mmol) and hexacarbonylchromium (5.9 g, 26.8 mmol) were added to di-n-butyl ether (90 ml) containing THF (9 ml) and the solution was heated under reflux for 48 h. The cooled mixture was filtered and concentrated to give a yellow oil. Column chromatography (Al_2O_3, Grade V, Et_2O) of this gave, after evaporation, the title compound (**13**) as a yellow oil (5.5 g, 86.7%); *m/z* 258 (M^+); $\nu_{max.}$ (liquid film); 3 590 (OH, non H-bonded), 3 420br (OH, H-bonded) and 1 959 and 1 869br cm^{-1} (C≡O); δ 5.56—5.27 (5 H, m, ArH), 4.53 [1 H, q, *J* 6.1 Hz, ArC*H*(Me)OH] 2.78 (1 H, s, br, ROH), and 1.44 [3 H, d, *J* 6.3 Hz, ArCH(*Me*)OH].

Tricarbonyl(η⁶-α-*methylbenzyl methyl ether*) *chromium*(0) (**14**).[17]—Tricarbonyl(η⁶-α-methylbenzyl alcohol)chromium(0) (**13**) (311 mg, 1.98 mmol) in dichloromethane (20 ml) and methanol (2 ml) was cooled to −30 °C, and the dimethyl ether complex of tetrafluoroboric acid (900 mg, 6.80 mmol) was added dropwise. After being stirred for 10 min, the reaction mixture was warmed to 20 °C and water (5 ml) was added. The solution was extracted with diethyl ether and the extracts were combined and evaporated. Column chromatography (Al_2O_3, Grade V, Et_2O) of the residue gave, after removal of the solvent, and recrystallisation from dichloromethane–hexane, the title compound (**14**) as yellow needles (320 mg, 59%) (Found: C, 52.6; H, 4.4. $C_{12}H_{12}CrO_4$ requires C, 52.95; H, 4.4%); *m/z* 272 (M^+); $\nu_{max.}$(CH_2Cl_2) 2 820 (OMe), 1 970 and 1 890br (C≡O), and 1 108 (COMe); δ 5.53—5.31 (5 H, m, ArH), 4.05 [1 H, q, *J* 6.5 Hz, ArC*H*(Me)OMe], 3.46 (3 H, s, RO*Me*), and 1.45 [3 H, d, *J* 6.5 Hz, ArCH(*Me*)OMe].

Tricarbonyl(η⁶-α,α-*dimethylbenzyl methyl ether*)*chromium*(0) (**15**).—Bu^{t}Li (0.66 ml, 1.32 mmol) was added to tricarbonyl(η⁶-α-methylbenzyl methyl ether)chromium(0) (**14**) (327 mg, 1.20 mmol) in THF (12 ml) at −78 °C. The solution was stirred at −78 °C for 2 h after which methyl iodide (0.37 ml, 6.00 mmol) was added and stirring was continued at −78 °C for 2 h. Methanol (2 ml) was added and the solution evaporated to provide an orange oil. Column chromatography (Al_2O_3, Grade V, 1:1 Et_2O–light petroleum) of this gave, on removal of the solvent and recrystallisation, the title compound (**15**) as fine yellow needles (321 mg, 93%); m.p. 74—76 °C (Found: C, 54.45; H, 5.0. $C_{13}H_{14}CrO_4$ requires C, 54.55; H, 4.9%); *m/z* 286 (M^+); $\nu_{max.}$ 2 814 (OMe), 1 981 and 1 893br (C≡O), and 1 131 cm^{-1} (COMe); δ 5.64—5.21 (5 H, m, ArH), 3.28 (3 H, s, RO*Me*), and 1.51 [6 H, s, ArC(Me_2)OMe].

Tricarbonyl(η⁶-α-*methyl*-α-*trimethylsilylbenzyl methyl ether*)*chromium*(0) (**16**).—Bu^{t}Li (0.46 ml, 0.92 mmol) was added to tricarbonyl(η⁶-α-methylbenzyl methyl ether)chromium(0) (**14**) (263 mg, 0.97 mmol) in THF (12 ml) at −78 °C and the solution stirred for 2 h. Chlorotrimethylsilane (0.37 ml, 2.76 mmol) was added and stirring was continued at −78 °C for 3 h. Methanol (1 ml) was added and the mixture evaporated to give an orange oil which, after column chromatography (Al_2O_3, Grade V, 1:10 Et_2O–light petroleum) and recrystallisation from pentane, afforded the title compound (**16**) as yellow needles (176 mg, 53%), m.p. 106—108 °C (Found: C, 52.6; H, 5.9. $C_{15}H_{20}CrO_4Si$ requires C, 52.3; H, 5.85%); *m/z* 344 (M^+); $\nu_{max.}$ 2 822 (OMe), 1 967 and 1 890br (C≡O), 1 600 (arene ring), and 1 098 cm^{-1} (COMe); δ 5.69—5.08 (5 H, m, ArH), 3.43 (3 H, s, RO*Me*), 1.62 [3 H, s, ArC(*Me*)(OMe)$SiMe_3$], and −0.04 (9 H, s, RSiMe_3).

Attempted Wittig Rearrangement of Tricarbonyl(η⁶-α-*methylbenzyl methyl ether*)*chromium*(0) (**14**).—Bu^{t}Li (0.55 ml, 1.10 mmol) was added to compound (**14**) (272 mg, 1.00 mmol) in THF (2 ml) at −78 °C. The solution was stirred at −78 °C for 2 h, after which methanol (1 ml) was added and the solution warmed and evaporated to provide an orange solid. Column chromatography (Al_2O_3, Grade V, Et_2O) of this gave, on removal of the solvent, starting material (**14**) (202 mg, 74%) identified by comparison of spectroscopic data with that of an authentic sample.

Methylation of Tricarbonyl(η⁶-α-*methylbenzyl methyl ether*)*chromium*(0) (**14**).— via *Treatment with* Bu^{n}Li. Bu^{n}Li (0.71 ml, 1.10 mmol) was added to compound (**14**) (150 mg, 0.55 mmol) in THF (10 ml) at −78 °C and the solution stirred at −78 °C for 1 h. Methyl iodide (0.14 ml, 2.20 mmol) was added and stirring was continued at −78 °C for a further 1 h. Methanol (5 ml) was added and the mixture evaporated to leave a red oil. Column chromatography (Al_2O_3, Grade V, 1:3 Et_2O–light petroleum) of this gave, after removal of the solvent, a mixture of tricarbonyl(η⁶-α,α-dimethylbenzyl methyl ether)-chromium(0) (**15**) (25 mg, 16%) and the two diastereoisomers of tricarbonyl(η⁶-2,α-dimethyl benzyl methyl ether)chromium(0) (**18**) (68 mg, 43%) and (**19**) (51 mg, 32%), as a yellow solid; *m/z* 286 (M^+); $\nu_{max.}$ 2 813 (OMe), 1 969 and 1 887br (C≡O), and 1 090 cm^{-1} (COMe); for compound (**15**), δ 5.64—5.21 (5 H, m, ArH), 3.28 (s, RO*Me*), and 1.51 [6 H, s, ArC(Me)$_2$OMe]; for compound (**18**), 5.74—5.08 (4 H, m, ArH), 4.30 [1 H, q, *J* 6.4 Hz, ArC*H*(Me)OMe], 3.34 (3 H, s, RO*Me*), 2.26 (3 H, s, ArMe), and 1.51 [3 H, d, *J* 6.4 Hz, ArCH(*Me*)OMe]; for compound (**19**) 5.74—5.08 (4 H, m, ArH), 4.20 [1 H, q, *J* 6.4 Hz, ArC*H*(Me)OMe], 3.54 (3 H, s, RO*Me*), 2.17 (3 H, s, Ar*Me*), and 1.37 [3 H, d, *J* 6.3 Hz, ArCH(*Me*)OMe]. The data for complex (**15**) were identical with those of an authentic sample.

Tricarbonyl(η⁶-*ethyl* α-*methylbenzyl sulphide*)*chromium*(0) (**20**).[8,10]—Tricarbonyl(η⁶-α-methylbenzyl alcohol)chromium-(0) (**13**) (580 mg, 2.25 mmol) in dichloromethane (30 ml) and ethanethiol (0.75 ml, 10.1 mmol) was cooled at −30 °C. The dimethyl ether complex of tetrafluoroboric acid (0.4 ml) was added dropwise and the solution stirred for 20 min at −30 °C. Water (2 ml) was added, and the mixture warmed to room temperature and concentrated. Chromatography (Al_2O_3, Grade I, Et_2O) of the residue gave the title compound (**20**) as a yellow oil (505 mg, 74%); *m/z* 302 (M^+); $\nu_{max.}$ (liquid film) 1 965 and 1 865 (C≡O); δ 5.42—5.27 (5 H, m, ArH), 3.62 [1 H, q, *J* 7.0 Hz, Ar*CH*(Me)SEt], 2.55 (2 H, m, SCH_2Me), 1.60 [3 H, d, *J* 7.0 Hz, ArCH(*Me*)SEt], and 1.25 (t, *J* 7.4 Hz, 3 H, RSCH_2Me).

Methylation of Tricarbonyl(η⁶-*ethyl* α-*methylbenzyl sulphide*)*chromium*(0) (**20**) via *Treatment with* Bu^{t}Li.—Bu^{t}Li (0.69 ml, 1.39 mmol) was added to compound (**20**) (441 mg, 1.46 mmol) in THF (12 ml) at −78 °C and the solution stirred at −78 °C for 2 h. Methyl iodide (0.27 ml, 4.4 mmol) was added and stirring was continued at −78 °C for a further 2 h. Methanol (1 ml) was added and the mixture warmed to room temperature and evaporated to give an orange oil. Column chromatography (Al_2O_3, Grade V, 1:1 Et_2O–light petroleum) of this gave, after removal of the solvent, a mixture of the two diastereoisomers of tricarbonyl(η⁶-ethyl 2,α-dimethylbenzyl sulphide)chromium(0) (**23**) and (**24**) and compound (**22**) (333 mg, 72%) in the ratio *ca.* 7:4:6; *m/z* 316 (M^+); $\nu_{max.}$ (liquid film) 1 965 and 1 865 cm^{-1} (C≡O); compound (**23**): δ 5.65—5.11 (4 H, m, ArH), 3.65 [1 H, q, *J* 6.8 Hz, Ar*CH*(Me)SEt], 2.66—2.50 (2 H, m, SCH_2Me), 2.21 (3 H, s, Ar*Me*), 1.62 [3 H, d, *J* 6.8 Hz, ArCH(*Me*)SEt], and 1.26 (3 H, t, *J* 7.6 Hz, SCH_2Me). Compound (**24**): δ 5.65—5.11 (4 H, m, ArH), 3.57 [1 H, q, *J* 7.0 Hz, Ar*CH*(Me)SEt], 2.66—2.50 (2 H, m, SCH_2Me), 2.20 (3 H, s,

Ar*Me*), 1.60 [3 H, d, *J* 7.1 Hz, ArCH(*Me*)SEt], and 1.26 (3 H, t, *J* 7.61 Hz, SCH_2Me); compound (**22**): δ 5.65—5.11 (5 H, m, ArH), 2.42 (2 H, q, *J* 7.5 Hz, SCH_2Me), 1.68 (s, 6 H, $ArCMe_2$), and 1.13 (3 H, t, *J* 7.5 Hz, SCH_2Me).

Methylation of Tricarbonyl(η⁶-*ethyl α-methylbenzyl sulphide*)*chromium*(0) (**20**) via *Treatment with* Bu^nLi.—Bu^nLi (1.17 ml, 1.87 mmol) was added to compound (**20**) (283 mg, 0.94 mmol) in THF (10 ml) at −40 °C and the solution stirred at −40 °C for 1 h. Methyl iodide (0.19 ml, 3.06 mmol) was added and stirring was continued at −40 °C for 1 h. Addition of methanol (1 ml), warming to room temperature, and evaporation gave an orange oil. Column chromatography (Al_2O_3 Grade V, 1.5 Et_2O–light petroleum) of this gave, after removal of the solvent, a mixture of the two diastereoisomers of tricarbonyl-(η⁶ ethyl 2,α-dimethylbenzyl sulphide)chromium(0) (**23**) and (**24**) and compounds (**22**) and (**25**) (275 mg, 93%) in the ratio *ca.* 9:6:10:8; *m*/*z* 316 (M^+); $\nu_{max.}$ (liquid film) 1 965 and 1 865 (C≡O); compound (**25**): δ 5.65—5.04 (4 H, m, ArH), 3.67 [1 H, q, *J* 7.0 Hz, ArC*H*(Me)SEt], 2.18 (3 H, s, Ar*Me*), and 1.68 [3 H, d, *J* 7.0 Hz, ArCH(*Me*)SEt]. Data for complexes (**22**), (**23**), and (**24**) was consistent with that given previously.

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References

1 A. N. Nesmeyanov, N. E. Kolobova, K. N. Anisimov, and Y. U. Makarov, *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 1968, 2665; M. D. Rausch and R. E. Gloth, *J. Organomet. Chem.*, 1978, **153**, 59; J. Bisaha, M. Czarny, and M. F. Semmelhack, *J. Am. Chem. Soc.*, 1979, **101**, 768.

2 R. J. Card and W. S. Trahanovsky, *J. Org. Chem.*, 1980, **45**, 2560; G. Nechvatal, D. A. Widdowson, and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1981, 1260; G. Nechvatal and D. A. Widdowson, *ibid.*, 1982, 467; L. M. Sandilands, C. J. L. Lock, R. Faggiani, N. Hao, B. G. Sayer, M. A. Quillam, B. E. McCarry, and M. J. McGlinchey, *J. Organomet. Chem.*, 1982, **224**, 267; Y. Hayashi, T. Higuchi, K. Hirotsu, N. Nishikawa, M. Ohnishi, K. Take, and M. Uemura, *J. Org. Chem.*, 1983, **48**, 2349; M. Fukui, T. Ikeda, and T. Oishi, *Chem. Pharm. Bull.*, 1983, **31**, 466; N. F. Masters and D. A. Widdowson, *J. Chem. Soc., Chem. Commun.*, 1983, 955; M. Ghavshou and D. A. Widdowson, *J. Chem. Soc., Perkin Trans. 1*, 1983, 3065; Y. Hayashi, K. Isobe, T. Minami, K. Take, and M. Uemura, *Tetrahedron*, 1985, **41**, 5771.

3 J. Bisaha, M. Czarny, and M. F. Semmelhack, *J. Am. Chem. Soc.*, 1979, **101**, 768; R. J. Card and W. S. Trahanovsky, *J. Org. Chem.*, 1980, **45**, 2560.

4 H. R. Snyder and J. H. Brewster, *J. Am. Chem. Soc.*, 1949, **71**, 291.

5 D. Farkhani and A. Solladie-Cavallo, *Tetrahedron Lett.*, 1986, 1331.

6 Y. Ito, M. Nakatsuka, and T. Saegusa, *J. Am. Chem. Soc.*, 1982, **104**, 7609.

7 F. Effenberger and K. Schollkopf, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 266; *Chem. Ber.*, 1985, **118**, 4356; *Chem. Ber.*, 1985, **118**, 4377; J. Blagg and S. G. Davies, *J. Chem. Soc., Chem. Commun.*, 1986, 492.

8 S. G. Davies, N. J. Holman, C. A. Laughton, and B. E. Mobbs, *J. Chem. Soc., Chem. Commun.*, 1983, 1316; J. Blagg, S. G. Davies, N. J. Holman, C. A. Laughton, and B. E. Mobbs, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1581.

9 S. Top and G. Jaouen, *J. Org. Chem.*, 1981, **46**, 78.

10 B. Caro, G. Jaouen, and S. Top, *Tetrahedron Lett.*, 1978, 787.

11 A. I. Meyers and R. F. Spohn, *J. Org. Chem.*, 1985, **50**, 4872.

12 S. Cabiddu, C. Floris, S. Melis, P. P. Piras, and F. Sotgin, *J. Organomet. Chem.*, 1982, **236**, 149.

13 D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, 'Purification of Laboratory Chemicals,' Pergamon Press, Oxford, 1966.

14 'Dictionary of Organic Compounds,' J. Buckingham and S. M. Donaghy eds., Chapman and Hall, London, 1982, vol. 5, p. 4623.

15 A. C. T. North, D. C. Phillips, and F. S. Mathews, *Acta Crystallogr., Sect. A*, 1968, **24**, 351.

16 'International Tables for *X*-Ray Crystallography,' Kynoch Press, Birmingham, England, 1974, vol. IV, p. 99—101 and 149—150.

17 A. C. Larson, in 'Crystallographic Computing,' ed. F. R. Ahmed, Munksguard, 1970, p. 170.

18 J. R. Carruthers and D. J. Watkin, *Acta Crystallogr., Sect A*, 1979, **35**, 698.

19 H. D. Flack, *Acta Crystallogr., Sect. A*, 1983, **39**, 876.

20 J. R. Carruthers and D. J. Watkin, 'CRYSTALS User Guide,' Chemical Crystallography Laboratory, University of Oxford, 1984, Issue 8.

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