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Stereoselective Synthesis of Homochiral Alpha Substituted *o*-Methoxybenzyl Alcohols *via* Nucleophilic Additions to Kinetically Resolved Homochiral Tricarbonyl (η^6-*o*-anisaldehyde)chromium(0).

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Abstract: Tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) has been kinetically resolved *via* the selective hydrolysis of one of the L-valinol derived imine diastereoisomers in the presence of deactivated alumina An X-ray crystal structure analysis on the adduct formed between L-valinol and homochiral (+)-tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) unambiguously established the presence of the corresponding imine and not oxazolidine and confirmed the absolute configuration of the aldehyde complex Addition of Grignard reagents to homochiral tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) occurs completely stereoselectively to give, following decomplexation, homochiral alpha substituted *o*-methoxybenzyl alcohols

Introduction:

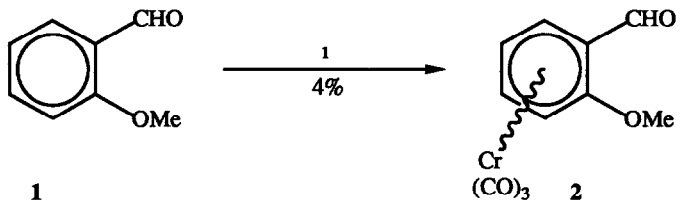
There have been several reported routes to optically active *ortho* substituted tricarbonyl(η^6-benzaldehyde)chromium(0) complexes utilising, for example, a classical separation of the diastereoisomeric semioxamazones derived from (S)-5-(1-phenethyl)semioxamazide[1] or a kinetic resolution *via* selective reduction of one aldehyde enantiomer with Baker's yeast.[2] However, the first method involves the preparation and use of an expensive chiral auxiliary, whilst the second method fails to produce homochiral material

The asymmetric synthesis of alpha substituted benzyl alcohols *via* the stereoselective addition of nucleophiles to *ortho* substituted tricarbonyl(η^6-benzaldehyde)chromium(0) or tricarbonyl(η^6-acetophenone)chromium(0) complexes, followed by decomplexation of the products has been well documented [3,4,5] Another approach has been the asymmetric addition of dialkylzinc reagents to benzaldehyde or *ortho* substituted benzaldehydes under homochiral alkaloid[6] or amino alcohol[7] catalysis, to give the corresponding substituted benzyl alcohol derivatives in moderate to good enantiomeric excesses.

We wished to investigate quick and convenient routes to homochiral *ortho* substituted tricarbonyl(η^6-benzaldehyde)chromium(0) complexes and to further improve the stereoselectivity of addition of nucleophiles to these complexes Some of the results shown below have been previously communicated.[8]

Results and Discussion:

In general, arenes possessing an aldehyde function cannot be complexed directly in good yield An attempt to complex *o*-anisaldehyde **1** under standard conditions and thus avoid two steps of the literature preparation of tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2**, gave a green solution Work up gave the required tricarbonylchromium(0) complex **2** in very low yield, as a red solid (Scheme 1) The ^{1}H n.m r spectrum of complex **2** contained an aldehyde proton singlet (δ10 05), two aromatic proton doublets (δ6.25-6 23 and 5 07-5 05) and two aromatic proton triplets (δ5 87-5 82 and 5 02-4 98) characteristic of four contiguous protons The spectroscopic data of complex **2** were identical with those in the literature [1]

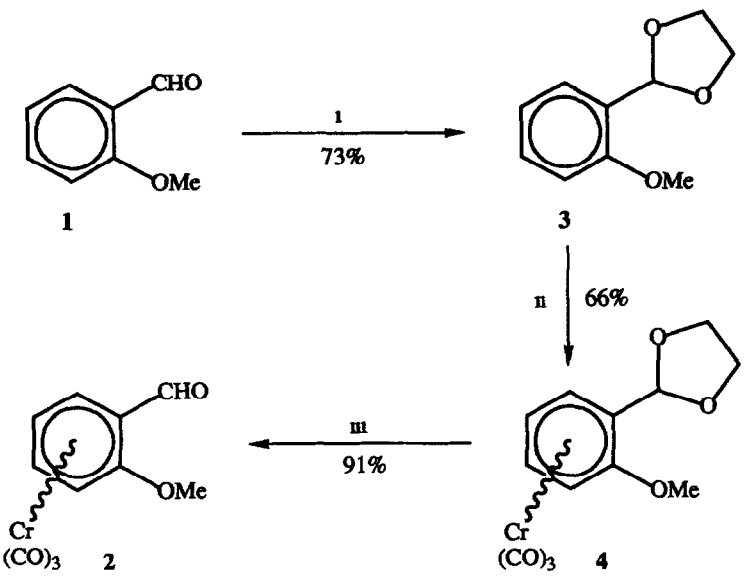


1 **2**

Scheme 1: *Reagents* i) $Cr(CO)_6$, Bu_2O, THF, Δ.

Repetition of the literature method overcame the low yield [1] *o*-Anisaldehyde **1** was treated with ethane-1,2-diol and a catalytic quantity of p-TsOH, and refluxed with benzene in a Dean-Stark trap (4h) Work up and distillation gave the corresponding acetal **3** in good yield The ^{1}H n m r spectrum of acetal **3** contained two multiplets (δ4 03-3 98 and 3 91-3 87) characteristic of the dioxolane ring protons Complexation of the protected aldehyde **3** under standard conditions gave the corresponding tricarbonylchromium(0) complex **4**, again in good yield The ^{1}H n.m r spectrum of complex **4** contained two aromatic proton doublets (δ5 95-5 92 and 5 04-5 02) and two aromatic proton triplets (δ5 59-5 55 and 4 90-4 86) The dioxolane ring protons appeared shifted downfield somewhat (δ4 20-4.03) A molecular ion *m/z* 316 (M^+) in the mass spectrum confirmed the identity of the product. Treatment of complex **4** with p-TsOH in aqueous THF gave, after stirring (4 5h) and work-up, large red needles of the required racemic complex **2** in excellent yield, spectroscopically identical to the sample previously prepared (Scheme 2)

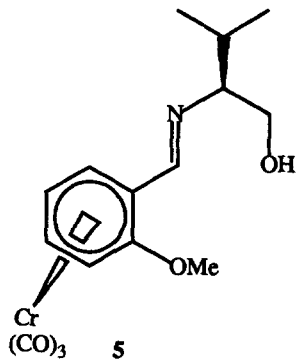
Treatment of a red Et_2O solution of racemic tricarbony(η^6-*o*-anisaldehyde)chromium(0) **2** with one equivalent of L-valinol, (prepared from L-valine by $LiAlH_4$ reduction in THF), gave an orange solution Absorption of this solution onto a column of deactivated alumina (Grade V) followed by slow elution with Et_2O and then CH_2Cl_2-MeOH, gave a red and a yellow band The first fraction (Et_2O) gave a red solid on evaporation of the solvent. The yellow second fraction (CH_2Cl_2·MeOH 10 1) was evaporated to a red oil Both fractions were briefly stirred in acidic, aqueous THF, the colour initially darkening and slowly turning crimson Work-up gave both products as red solids The ^{1}H n m r spectra of the compounds were identical with that of racemic starting material. The optical rotation of the first fraction clearly indicated the (-)-enantiomer (-)-**2** {$[\alpha]_D^{23}$ -1015 (c 0 06 in $CHCl_3$), Lit [1] $[\alpha]_D$ -1020 (c 0 09 in $CHCl_3$)}, whilst that of the second fraction indicated the (+)-enantiomer (+)-**2** {$[\alpha]_D^{23}$ +1016 (c 0 06 in $CHCl_3$) Lit [1] $[\alpha]_D$ +1015 (C 0 06 in $CHCl_3$)) The production of homochiral tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2** confirms that the sample of L-valinol used was also homochiral and thus the reduction of L-valine with $LiAlH_4$ proceeds with no racemisation at the α-centre This is in contrast to the reduction of L-valine esters to L-valinol, which under similar conditions gives partially racemised product.[9]

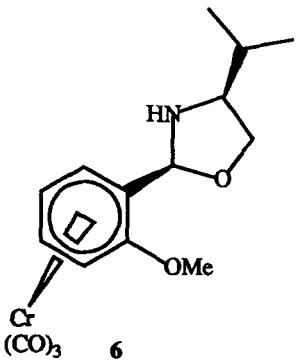


Scheme 2:

Reagents i) $HOCH_2CH_2OH$,p-TsOH, C_6H_6, Δ, ii) $Cr(CO)_6$, Bu_2O, THF, Δ, iii) H_3O^+, THF

Treatment of an ether solution of complex (+)-**2** with one equivalent of L-valinol gave a colour change from red to orange The ^1H n.m.r spectrum of an aliquot of the solution, contained only one set of peaks consistent with either the imine **5** or oxazolidine **6** The main features of the ^1H n m.r. spectrum (C_6D_6) were a benzylic proton singlet (δ8.34), two aromatic proton doublets (δ6.34-6 31 and 3 95-3.93) and two aromatic proton triplets (δ4 76-4 71 and 4 11-4 06). The orange colour of the product initially suggested the formation of the imine **5** Tricarbonyl(η^6-arene)chromium(0) complexes, such as complex **5**, possessing double bonds in a side-chain conjugated with the ring are generally orange to red, whilst nonconjugated complexes such as the oxazolidine **6** are generally yellow in colour





Evaporation of the remainder of the solution and crystallisation of the residue from Et_2O:light petroleum gave large orange blocks. The solution infrared spectrum of the complex (CH_2Cl_2) contained an absorption at 1633cm^{-1} characteristic of a C=N stretch This clearly indicated, in conjunction with the ^1H n.m.r spectoscopic data, which showed only a single compound, that the complex was the imine **5** and not oxazolidine **6** A single crystal X-ray structure analysis unambiguously confirmed the product as the imine **5**, Figure 1. Final atomic coordinates and selected torsional angles are presented in Tables 1 and 2 below * Note the coplanar arrangement of the C=N bond, aromatic ring and methoxy substituent

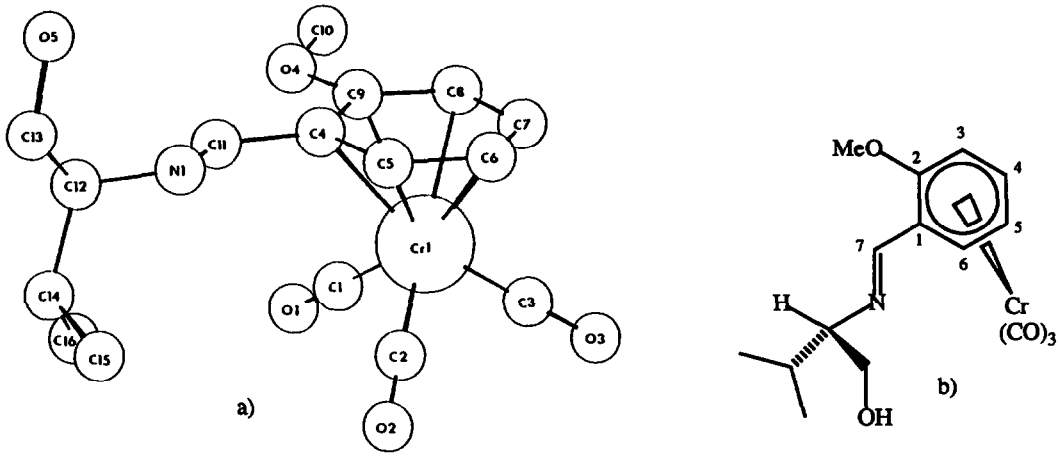
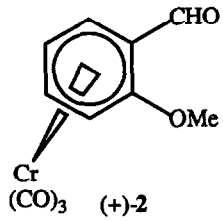
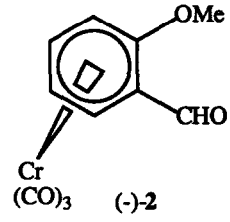


Figure 1: a) X-Ray crystal structure analysis of **5** the L-valinol derived imine of (+)-tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (+)-**2** with crystallographic numbering, b) Systematic numbering scheme.

Since the absolute configuration of the L-valinol is known, (as it is derived from L-valine),[10] the X-ray crystal structure analysis clearly establishes the absolute configuration of the tricarbonyl(η^6-arene)chromium(0) fragment of **5** to be (S)[11] and thus the absolute configuration of complex (+)-**2** must also be (S), as shown below



(+)-**2**



(-)-**2**

* Thermal parameters and bond lengths and angles are available on request from the Cambridge Crystallographic Data Centre

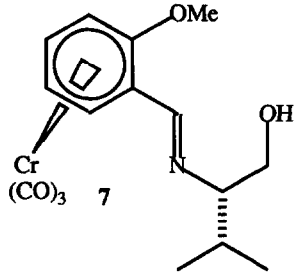
Table 1: Fractional atomic coordinates ($x10^4$) for complex (+)-**5** with estimated standard deviations in parentheses (The asymmetric unit consists of two crystallographically independent molecules each of which possess essentially the same conformation but in a different crystal environment)

Atom	x/a	y/b	z/c	U(iso)
Cr(1)	1602 6(9)	9641 5(7)	1305 1(6)	384
Cr(2)	1878 0(9)	3786 1(8)	9511.1(7)	424
C(1)	728(8)	8805(6)	939(5)	565
C(2)	685(6)	10466(6)	950(5)	508
C(3)	884(7)	9618(7)	2240(5)	681
C(4)	2965(5)	10508(4)	1473(4)	314
C(5)	3059(6)	9804(4)	1949(4)	426
C(6)	3062(7)	8963(4)	1652(5)	466
C(7)	2856(7)	8848(5)	863(5)	528
C(8)	2776(6)	9542(4)	367(4)	397
C(9)	2857(5)	10368(5)	646(4)	361
C(10)	2630(9)	10977(5)	-595(4)	582
C(11)	2938(6)	11383(4)	1766(4)	360
C(12)	2991(8)	12461(4)	2690(5)	477
C(13)	3920(9)	12714(6)	3199(5)	595
C(14)	1925(9)	12600(5)	3083(5)	586
C(15)	1764(11)	12002(7)	3773(6)	858
C(16)	1031(9)	12530(9)	2521(7)	987
C(17)	2849(6)	3493(6)	10286(5)	539
C(18)	2735(7)	3250(5)	8832(5)	587
C(19)	2621(6)	4753(5)	9350(5)	510
C(20)	496(6)	4126(5)	8805(4)	382
C(21)	541(6)	3220(5)	8886(5)	443
C(22)	565(7)	2858(6)	9624(6)	595
C(23)	586(8)	3399(8)	10270(5)	603
C(24)	529(7)	4277(6)	10210(4)	505
C(25)	460(5)	4654(6)	9462(4)	444
C(26)	465(9)	6074(7)	9982(5)	700
C(27)	582(5)	4541(5)	8034(4)	386
C(28)	779(7)	4590(6)	6704(4)	488
C(29)	-6(8)	4339(6)	6102(4)	603
C(30)	1907(8)	4443(5)	6439(5)	603
C(31)	2178(9)	3501(6)	6349(6)	822
C(32)	2685(8)	4855(7)	6980(6)	839
O(1)	231	8237	675	776
O(2)	147	10990	698	767
O(3)	486	9637	2833	805
O(4)	2779	11092	223	405
O(5)	4899(6)	12647(4)	2821(4)	674
O(6)	3454	3312	10751	535
O(7)	3275	2881	8392	883
O(8)	3075	5381	9246	708
O(9)	389	5498	9356	459
O(10)	-1064(5)	4515(4)	6326(3)	554
N(1)	3118	11566	2463	320
N(2)	560	4096	7408	378

Table 2: Selected torsional angles for complex (+)-**5** in degrees

C(8) - C(9) - O(4) - C(10)	-2
N(1) - C(11) - C(4) - C(5)	8
C(12) - N(1) - C(11) - C(4)	-176
O(5) - C(13) - C(12) - C(14)	-176
O(5) - C(13) - C(12) - N(1)	61

Treatment of complex (-)-**2** with one equivalent of L-valinol gave a pale orange solution An aliquot of the solution was evaporated to an orange oil and shown to contain only one compound, either the imine **7** or oxazolidine **8**, by ^{1}H n m.r spectroscopy The main features of the ^{1}H n m r spectrum (C_6D_6) were a benzylic proton singlet (δ8.28), two aromatic proton doublets (δ6 26-6 22 and 4 06-4 02) and two aromatic proton triplets (δ4 75-4 69 and 4 17-4 11) Recrystallisation of the product from Et_2O hexane failed, but the solution infrared spectrum (CH_2Cl_2) of the product contained an absorption at 1631cm^{-1} characteristic of an imine Consequently, since the ^{1}H n m r spectrum demonstrated only a single compound in solution and the infrared spectrum contained an imine absorption peak it follows that the product can again be identified as the imine **7** and not oxazolidine **8**



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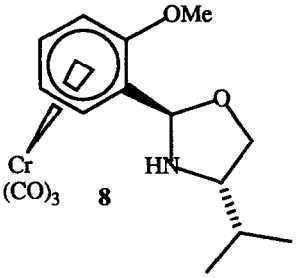
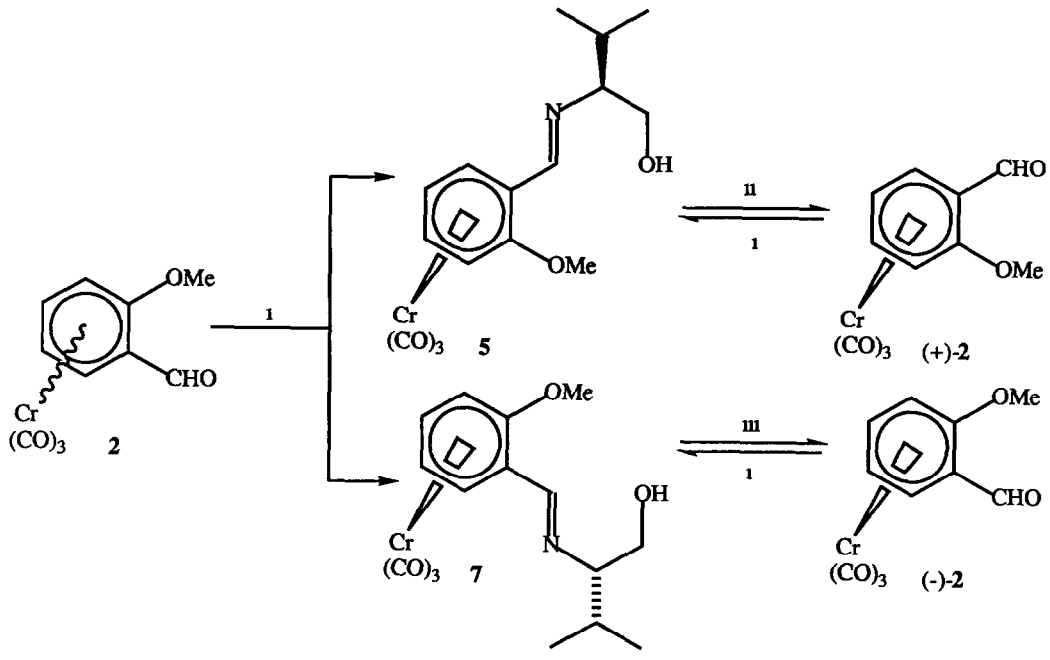


8

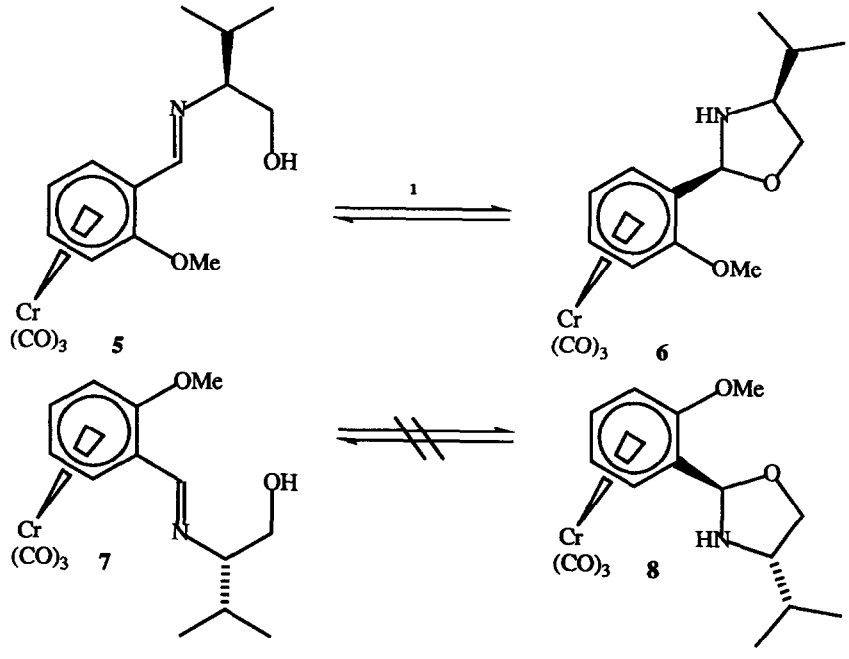
The presence of only imine products and no oxazolidines in the above reactions is consistent with a literature report on the effect of arene substituents on the position of the ring-chain tautomerism of these compounds [12] Placing electron-donating substituents on the ring of the tricarbonyl(η^6-arene)chromium(0) complex will favour the imine over oxazolidine, whilst the reverse is true for electron-withdrawing substituents Thus, in the case of an arene possessing an *o*-methoxy group, the presence of only the imine tautomer is consistent with the above trend

The exclusive production of a single diastereoisomeric compound upon treatment of resolved (+)-**2** or (-)-**2** with L-valinol clearly indicated that both samples of aldehyde were homochiral Acid hydrolysis of complex **5** regenerated homochiral (+)-**2** showing that no racemisation occurs on formation or hydrolysis of the imine (Scheme 3)

The above methodology represents a kinetic resolution procedure for the preparation of homochiral tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2** The method is based on the selective hydrolysis of imine **7** by deactivated alumina, associated with the large difference in R_f values between the aldehyde and imine complexes on deactivated alumina Presumably the imine group prefers to lie coplanar with the aromatic ring allowing maximum conjugation The orientation with respect to the *o*-methoxy group is *anti* for both electronic, dipole and steric reasons [13] Examination of molecular models indicates that closure of imine **5** by intramolecular *exo* attack of the hydroxyl onto the face of the imine away from the tricarbonylchromium(0) group gives rise to the *cis*-1,3-disubstituted oxazolidine **6**, whilst closure of imine **7** by a similar mechanism gives the *trans*-1,3-disubstituted oxazolidine **8** (Scheme 4) *cis*-1,3-Disubstituted oxazolidines have greater stability and are more easily formed that the corresponding *trans* isomers [14] In the presence of deactivated alumina imine **5** can undergo rapid reversible oxazolidine formation, thus protecting it from hydrolysis Under the same conditions imine **7**, however, can only undergo hydrolysis to give (-)-**2**



Scheme 3: *Reagents* i) L-valinol, Et_2O, ii) H_3O^+, THF, iii) Alumina (Grade V), Et_2O



Scheme 4: *Reagents* i) Alumina (Grade V)

Preparation of the diastereoisomeric mixture of imines **5** and **7** from complex **2** prior to column chromatography proved unnecessary for resolution. Thus, a deactivated alumina column was doped with one equivalent of L-valinol in both top and middle portions One equivalent of racemic aldehyde **2** in Et_2O solution was absorbed onto the column and allowed to stand Elution with Et_2O gave a red solution which was evaporated to a red solid The remaining yellow coloured bands were removed with Et_2O:MeOH (5 1) and evaporated to give an orange oil, Figure 2 Both fractions were separately treated with acidic, aqueous THF until no further colour change was observed and then isolated as red solids ^1H n m r. spectroscopy identified both compounds as tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2** whilst optical rotation measurements identified the first band as (-)-**2** {$[\alpha]_D^{25}$ -1006 (c 0 06 in $CHCl_3$)} and the second band as (+)-**2** {$[\alpha]_D^{24}$ +1020 (c 0 06 in $CHCl_3$)} Treatment of the first fraction with acidic, aqueous THF was necessary as a purification step Presumably a small quantity of L-valinol elutes through the column with the first fraction Once removed from alumina the amine may then recondense with the aldehyde to regenerate a small quantity of imine **7** Subsequent evaporation of the solvent gives (-)-tricarbony(η^6-*o*-anisaldehyde)chromium(0) **2** containing some imine impurity

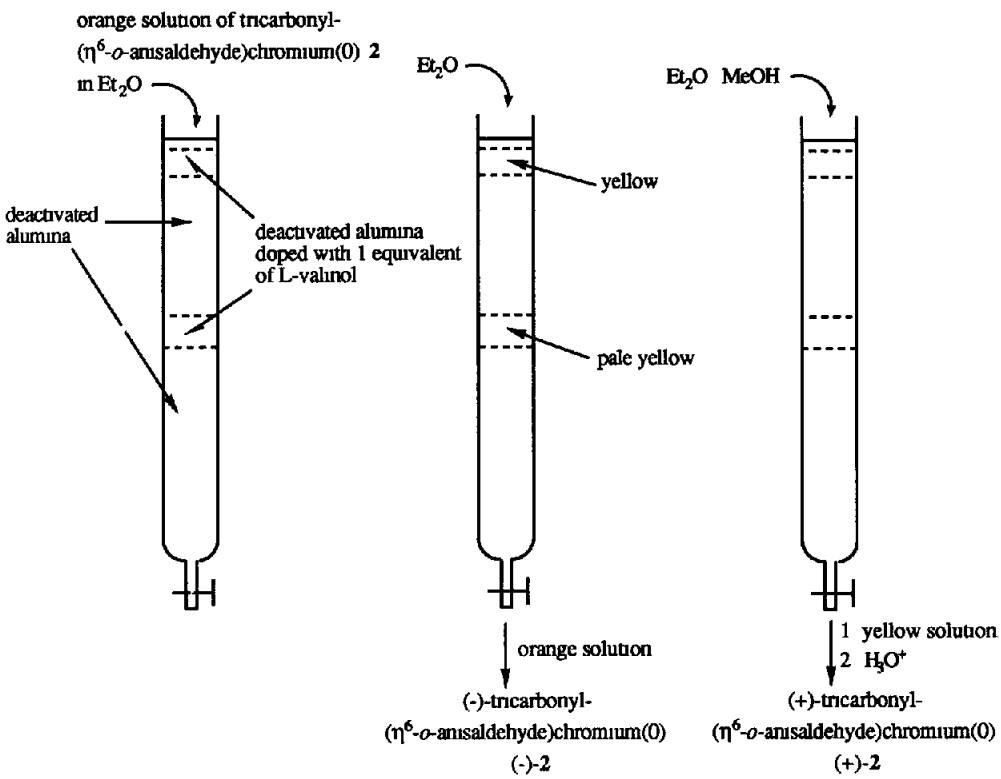
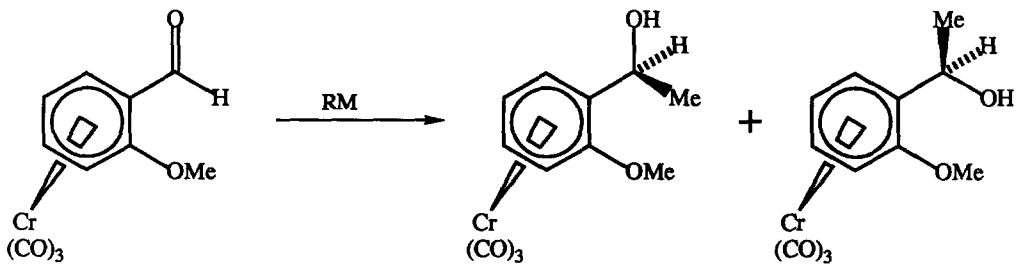


Figure 2:

Resolution of tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2** using a L-valinol doped alumina column

The use of two L-valinol doped bands of alumina proved necessary to produce products essentially homochiral Presumably quantitative production of imine **5** does not occur in the top doped band and any unreacted (+)-**2** complex is trapped out selectively by the second band This is consistent with the observation that the second doped band turns pale yellow as the first fraction elutes through, presumably due to formation of the L-valinol adduct with any remaining complex (+)-**2**

Addition of excess MeMgI to (+)-tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (+)-**2** in THF at -78°C gave an immediate colour change from red to yellow After work up, a yellow solid was isolated in essentially quantitative yield. ^{1}H n m r spectroscopy (C_6D_6) showed only a single set of peaks with a benzylic proton doublet of quartets (δ4 70, J_d 4 0Hz, J_q 6 4Hz) and three proton methyl doublet (δ1.15, J 6 4Hz) The product was assigned as a single diastereoisomer of the l-phenethanol derivative (-)-**9** A molecular ion *m/z* 288 (M^+) in the mass spectrum confirmed the identity of the product Repeating the reaction under similar conditions but using MeLi as the carbanion source, similarly gave a yellow solid in quantitative yield However, ^{1}H n m r spectroscopy clearly indicated a mixture of products in a ratio of 94 6 (Scheme 5) The major isomer was identical to complex **9** and the minor isomer was assigned as the epimer **10** by analogy with the previous literature reports [3,4,5]

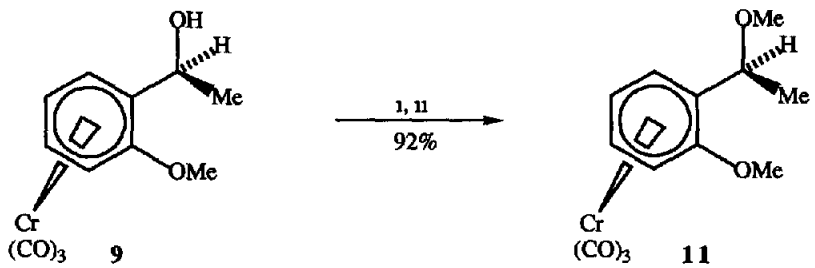


Scheme 5: *Reagents* MeMgI, THF, -78°C or MeLi, THF, -78°C

The unambiguous assignment of the relative configurations within complex **9** and hence absolute configuration of complex (-)-**9**, was achieved by O-methylation of a racemic sample of complex **9** and comparison with an authentic sample of racemic complex **11** A THF solution of complex **9** was treated with KH and stirred MeI was added and the orange solution turned yellow Work up and chromatography gave, after recrystallisation, complex **11** (Scheme 6) The ^{1}H n m r spectrum of complex **11** contained two aromatic proton doublets (δ5.87-5 84 and 5 04-5 01), two aromatic proton triplets (δ5 51-5 46 and 4 97-4 93), a benzylic proton quartet (δ4 41, J 6.4Hz) and two three proton methoxy singlets (δ3 74 and 3.57) Complex **11** was spectroscopically identical to an authentic sample of racemic complex **11**, the relative configuration within which had been confirmed by an X-ray crystal structure analysis [15]

The difference in observed stereoselectivities between the MeMgI and MeLi additions may arise as a result of the nature of the Lewis acidic species present in solution, Mg^{2+} is a stronger Lewis acid than Li^+ Thus in the case of the Grignard addition, the first step is presumably coordination of Mg^{2+} to the carbonyl oxygen atom This increases the effective bulk of the group and consequently only conformations with the

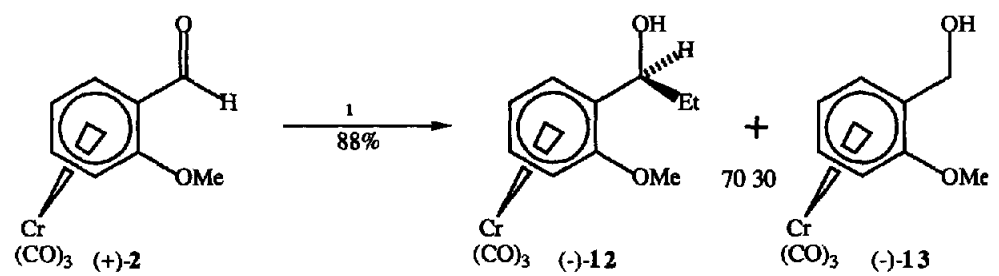
coordinated carbonyl group lying *anti* to the *o*-methoxy group and coplanar with the ring will be appreciably populated Thus, a strict *exo* attack of the nucleophile gives only a single diastereoisomer Presumably in the case of the alkyllithium, *exo* addition of the carbanion may occur on some non-Lewis acid coordinated aldehyde Whilst the preferred conformation of the free aldehyde is also *anti* to the *o*-methoxy group and coplanar with the ring (*vide supra*), there must be a small but significant population of the *syn* conformer



Scheme 6: *Reagents* i) KH, THF, ii) MeI, THF

Similar treatment of complex (+)-**2** with EtMgI gave three products separable by column chromatography The major fraction, isolated as a yellow solid was identified as a single diastereoisomer of the addition product (-)-**12** {$[\alpha]_D^{21}$ -201 (c 1 in $CHCl_3$)} The ^1H n m r spectrum clearly indicated the presence of an ethyl group with a two proton multiplet (δ1 79-1 59) and three proton triplet (δ1 01, *J* 7 4Hz) Also present were two aromatic proton doublets (δ5 90-5 88 and 5 06-5 04), two aromatic proton triplets (δ5 56-5 51 and 4 98-4 94) and a methoxy singlet (δ3 74)

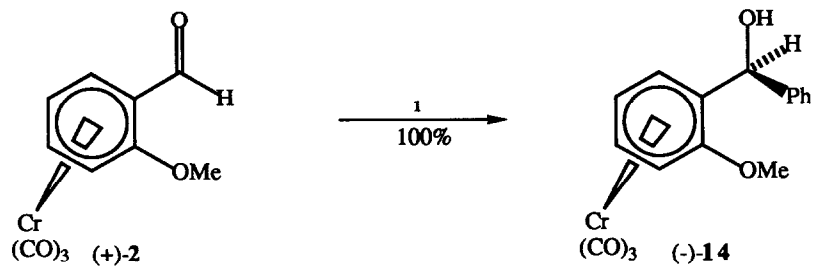
The remaining two fractions had ^1H n m.r spectra consistent with starting material (+)-**2** and the reduced complex (-)-**13** {$[\alpha]_D^{21}$ -216 (c 1 in $CHCl_3$)} Presumably the latter complex was produced by the Grignard reagent donating a β-hydride to the aldehyde function (Scheme 7) The ^1H n m.r spectrum of (-)-**13** contained a characteristic two proton benzylic AB system (δ4 64 and 4 38, J_{AB} 13 1Hz) and a broad one proton hydroxyl singlet (δ1 96)



Scheme 7: *Reagents* i) EtMgI, THF, -78°C

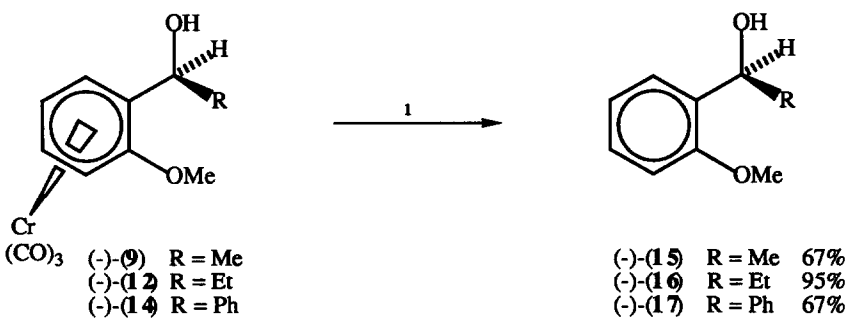
Addition of PhMgBr to complex (+)-**2**, in THF solution at -78°C, gave on work up a yellow solid (-)-**14** {$[\alpha]_D^{24}$ -178 (c 1 in $CHCl_3$)} The ^1H n m r spectrum contained a single set of peaks with two downfield aromatic proton multiplets characteristic of a non-complexed ring (δ7 48-7 44 and 7.40-7 29). A molecular ion

m/z 350 (M^+) in the mass spectrum and elemental microanalysis confirmed the identity of (-)-**14** as a single diastereoisomer of the addition product (Scheme 8)



Scheme 8: *Reagents* i) PhMgBr, THF, -78°C

The homochiral complexes (-)-**9**, (-)-**12** and (-)-**14** were decomplexed under standard conditions to give the free arenes (-)-**15** {$[\alpha]_D^{20}$ -59 (c 1 in toluene)}, (-)-**16** {$[\alpha]_D^{20}$ -57 (c 1 in toluene), Lit [6] $[\alpha]_D$ +47 (c 1 in toluene) for 87% ee opposite enantiomer} and (-)-**17** {$[\alpha]_D^{20}$ -34 (c 1 in $CHCl_3$)} respectively (Scheme 9) It follows that the absolute configuration of arenes (-)-**15**, (-)-**16** and (-)-**17** is (S), which in the case of (-)-**15** and (-)-**16** confirms the previous assignments based on Horeau's method [16]



Scheme 9: *Reagents* i) hυ, O_2, Et_2O

Enantiomeric purities of the free alcohols (-)-**15** and (-)-**16** were checked by ^1H n m r. spectroscopic analysis of their (R)-α-methoxy-α-(trifluoromethyl)phenylacetate esters [(R)-Mosher's esters] [17] Authentic racemic alcohols **15** and **16**, (prepared from o-anisaldehyde **1** and the corresponding alkyllithium or Grignard reagent), were similarly esterified, to show no kinetic resolution was occurring on esterification and used as standards Alcohols (-)-**15** and (-)-**16** were enantiomerically pure by this method (>99 5%) Arene (-)-**17** failed to generate the required ester under suitable conditions, but was assumed to be homochiral by analogy with alcohols (-)-**15** and (-)-**16**.

Conclusion:

Homochiral tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2** has been generated *via* a kinetic resolultion procedure involving the selective hydrolysis of the L-valinol derived imine of the (+)-enantiomer in the presence of deactivated alumina An X-ray crystal structure analysis confirmed the identity of the L-valinol adduct with complex (+)-**2** as the corresponding imine and not oxazolidine Complete asymmetric induction was achieved on addition of Grignard reagents to homochiral (+)-**2** at -78°C Decomplexation of the products gave the corresponding free alpha substituted benzyl alcohol derivatives, which were homochiral by ^{1}H n m r spectroscopic analysis of the (R)-Mosher's ester derivatives

Experimental:

All reactions involving the preparation or utilisation of tricarbonyl(η^6-arene)chromium(0) complexes were performed under an atmosphere of nitrogen.[18] All commercial reagents were purified according to standard techniques [19] THF was distilled from sodium benzophenone ketyl under an atmosphere of nitrogen Diethyl ether was peroxide free and dibutyl ether was dried over sodium and distilled under an atmosphere of nitrogen prior to use Hexacarbonylchromium(0) was steam distilled prior to use Grignard reagents were prepared according to the literature route[20] and used as diethyl ether solutions Methyllithium was used as a 1 4M or 1 1M solution and ethyllithium as a 1 43M solution in diethyl ether Potassium hydride was obtained as a 35% dispersion in oil, from which the oil was removed by repeated washings with light petroleum followed by drying *in vacuo* Methyl iodide was dried over 4Å molecular sieves Column chromatography was performed on alumina (Grade V Grade 1 deactivated with 10% v/v water) Melting points were obtained on a Kofler hot stage apparatus and are uncorrected Infrared spectra were obtained as solutions in dichloromethane ^{1}H n m r spectra were obtained at 200MHz unless otherwise stated Mass spectra were obtained using In Beam Electron Impact or Chemical Ionisation techniques

General procedure for preparation of tricarbonyl(η^6-arene)chromium(0) complexes - A deoxygenated 10 1 mixture of Bu_2O THF, arene and hexacarbonylchromium(0) was heated at reflux until the formation of the first trace of green precipitate was observed The cooled solution was filtered through celite and the solvent evaporated to give the crude complex

Tricarbonyl(η^6-o-anisaldehyde)chromium(0) **2** - Thermolysis of hexacarbonylchromium(0) (3 88g, 17 6mmol) with *o*-anisaldehyde (1) (2 00g, 14 7mmol) under standard conditions (55ml solvent, 5h) followed by work up and column chromatography (Al_2O_3, Et_2O), gave tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2** as a red solid (164mg, 4%), spectroscopically identical with the literature,[1] δ_H($CDCl_3$, 300MHz) 10 05 (lH, s, ArC*H*O), 6 25-6.23, 5 07-5 05 (2H, 2d, Ar*H*), 5 87-5 82, 5.02-4 98 (2H, 2t, Ar*H*), 3 87 (3H, s, ArOCH_3), δ_H(C_6D_6, 300MHz) 9 90 (lH, s, ArC*H*O), 5 91-5 88, 3 75-3.73 (2H, 2d, Ar*H*), 4 73-4 61, 3 92-3 88 (2H, 2t, Ar*H*), 2 79 (3H, s, ArOCH_3)

2-(o-Anisyl)-1,3-dioxolane **3** [1]- A mixture of *o*-anisaldehyde **1** (30.0g, 221mmol) and ethane-1,2-diol (15 0g, 242mmol) in benzene (250ml), containing a catalytic quantity of pTsOH H_2O (1 39g, 7 32mmol), was heated at reflux in a Dean-Stark trap until water ceased to be evolved (4h) Evaporation of the solvent followed by distillation of the crude oil gave 2-(*o*-anisyl)-1,3-dioxolane **3** as a clear, colourless oil (29 0g, 73%), b p 118-122°C (0 lmmHg), δ_H($CDCl_3$, 300MHz) 7 46-7 43, 6 80-6 77 (2H, 2d, Ar*H*), 7 24-7 19, 6 90-6 77 (2H, 2t, Ar*H*), 6 07 [lH, s, ArC*H*(OR)$_2$], 4 03-3 98, 3 91-3 87 (4H, 2m, -OCH_2CH_2O-), 3 73 (3H, s, ArOCH_3)

Tricarbonyl[η⁶-2-(o-anisyl)-1,3-dioxolane]chromium(0) **4**[1]. - Thermolysis of hexacarbonylchromium(0) (5 75g, 26.1mmol) with 2-(*o*-anisyl)-1,3-dioxolane **3** (3.92g, 21 8mmol) under standard conditions (110ml solvent, 40h) followed by work up and column chromatography (Al_2O_3, Et_2O), gave a yellow solid Recrystallisation from CH_2Cl_2 light petroleum gave the title compound **4** as yellow blocks (3 86g, 56%), δ_H($CDCl_3$, 300MHz) 5 95-5 92, 5 04-5 02 (2H, 2d, Ar*H*), 5 92 [lH, s, ArC*H*(OR)$_2$], 5.59-5 55, 4 90-4 86 (2H, 2t, Ar*H*), 4 20-4 03 (4H, m, -OCH_2CH_2O-), 3 80 (3H, s, ArOCH_3), *m/z* 316 (M^+)

Hydrolysis of tricarbonyl[η⁶-2-(o-anisyl)-1,3-dioxolane]chromium(0) **4**[1] -Tricarbonyl[η⁶-2-(*o*-anisyl)-1,3-dioxolane]chromium(0) **4** (2 00g, 6 33mmol) was dissolved in a 1·1 mixture of THF water (30ml) and p-TsOH H_2O (241mg, 1 27mmol) added. The solution was stirred (4 5h) and slowly turned red The mixture was concentrated and extracted with Et_2O (2 x 30ml). The organic extracts were combined, dried ($MgSO_4$) and evaporated to a red solid Recrystallisation from CH_2Cl_2 light petroleum gave tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) **2** as large red needles (1 57g, 91%), identified by comparison with an authentic sample

L-Valinol A suspension of L-valine (25 0g, 214mmol) in THF (250ml) was slowly added to a cooled (0°C), stirred suspension of $LiAlH_4$ (20 0g, 526mmol) in THF (250ml) The mixture was heated at reflux (17h), cooled (0°C) and water added dropwise to quench NaOH solution (5%, 40ml) was added and the mixture filtered through celite, washing with copious quantities of CH_2Cl_2 The filtrate was evaporated to a clear oil Distillation gave L-valinol as a low melting point white solid (18.6g, 84%), δ_H($CDCl_3$, 300MHz) 3 53, 3 22 (2H, ABX system, J_{AB} 9 7Hz, J_{AX} 7 6Hz, J_{BX} 10 4Hz, RCH_2OH), 2 50-2 44 (4H, m, br, RCH$_2$O*H*, RNH_2, RR^{1}C*H*NH$_2$), 1 50 [lH, m, RC*H*(CH$_3$)$_2$], 0 83, 0 82 [6H, 2d, J_1 6 8Hz, J_2 6 8Hz, RCH(CH_3)$_2$].

Kinetic resolution of tricarbonyl(η⁶-o-anisaldehyde)chromium(0) **2**. - L-Valinol (379mg, 3 68mmol) was added to a Et_2O (l0ml) solution of tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) **2** (1 00g, 3 68mmol) and the mixture stirred (4 5h), the initial red solution turning orange Column chromatography (Al_2O_3) of the crude solution without evaporation of the solvent, gave two fractions The first fraction (Et_2O) was evaporated to a red solid and the second fraction (MeOH CH_2Cl_2 1 10) to an orange oil Both products were separately dissolved in THF (8ml) Water (2ml) was added followed by c HCl (5 drops) and the darkened solutions stirred until they turned crimson (30min) Evaporation of the solvent followed by filtration of a Et_2O (l0ml) solution through a plug of alumina gave both products as red solids The first fraction was identified as (-)-tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) (-)-**2** (460mg, 46%) by comparison with an authentic racemic sample, $[\alpha]_D^{23}$ -1015 (c 0 06 in $CHCl_3$) Lit[1] $[\alpha]_D$ -1020 (c 0 09 in $CHCl_3$) The second fraction was identified as (+)-tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) (+)-**2** (380mg, 38%), also by comparison with an authentic racemic sample, $[\alpha]_D^{23}$ +1016 (c 0 06 in $CHCl_3$) Lit[1] $[\alpha]_D$ +1015 (c 0 06 in $CHCl_3$)

L-Valinol derived imine of (+)-tricarbonyl(η⁶-o-anisaldehyde)chromium(0) (+)-2, complex **5**. - (+)-Tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) (+)-**2** (250mg, 0 92mmol) was dissolved in Et_2O (12ml) and L-valinol (95mg, 0 92mmol) added After stirring (4 5h) a portion of the solution was evaporated to give an orange oil, δ_H(C_6D_6) 8 34 (lH, s, ArC*H*=NR), 6 34-6 31, 3 95-3.93 (2H, 2d, Ar*H*), 4 76-4 71, 4 11-4 06 (2H, 2t, Ar*H*), 3 67-3.61, 3 56-3 53 (2H, 2m, br, RCH_2OH), 2 92 (3H, s, ArOCH_3), 2 78-2 72 (lH, m, RR^{1}C*H*N=CHAr), 1.87-1 76 [lH, m, RC*H*(CH$_3$)$_2$], 1.06 (lH, s, br, RCH$_2$O*H*), 0 97, 0 86 [6H, 2d, J_1 6 8Hz, J_2 6.8Hz, RCH(CH_3)$_2$] The remainder of the solution was evaporated to an orange solid and recrystallised from Et_2O light petroleum to give the L-valinol derived imine of (+)-tricarbonyl(η⁶-*o*-

anisaldehyde)chromium(0) (+)-2, complex **5**, as orange blocks (295mg, 90%), m p 96-97°C, $[\alpha]_D^{21}$ +512 (c 0 204 in $CHCl_3$), (Found C, 54 1, H, 5.6, N, 3.9 $C_{16}H_{19}CrNO_5$ requires C, 53.8, H, 5.4, N, 3.9%), υ_{max} 1970, 1891br (-CO), 1633 (C=N), 1014 (C-O-C) cm^{-1}, *m/z* 325 (M^+-32) Treatment of a THF (5ml) solution of imine **5** (200mg, 0 56mmol) with water (2ml) and c.HCl (5 drops) with stirring (30min), gave, on evaporation of the solvent, followed by filtration of a Et_2O (10ml) solution through a plug of alumina, starting material (+)-2 as a red solid (145mg, 95%), identified by comparison with an authentic sample, $[\alpha]_D^{21}$ +1017 (c 0 06 in $CHCl_3$).

X-Ray crystal structure of the L-valinol derived imine of (+)-tricarbonyl(η^6-o-anisaldehyde)chromium(0) (+)-2, complex **5** - Cell parameters and reflection intensities were measured using graphite monochromated Cu-K_α radiation on an Enraf-Nonius CAD4-F 4-circle diffractometer operating in the $\omega/2\theta$ scan mode The scan range (ω) was calculated from $[1.00 + 0\ 14\tan\theta]^o$, and the scan speed varied from 1 7 to 6 7°/min depending upon the intensity. Reflections were measured in the range $0 < \theta < 60^o$ Four 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[21] and equivalent reflections were merged to give 3983 unique reflections of which 2220 were considered to be observed [$I > 3\sigma(I)$] and used in the structure analysis Scattering factors were taken from International Tables [22]

Crystal Data $C_{16}H_{19}CrNO_5$ M = 357 33 orthorhombic, space group $P2_12_12_1$ (established from systematic absences), *a* 12 743, b 15 673, c 17 383 Å *U* 3471 8Å^3, Z 8, D_{calc} 1 37 Mgm^{-3}, μ(Cu-Kα) 57 08 cm^{-1} The structure was solved by direct methods using the SHELXS-86[23] programme and electron density fourier synthesis Final full-matrix least-squares refinement included parameters for positional coordinates, anisotropic temperature factors (non-hydrogen atoms), an overall scale factor and an extinction parameter [24] 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* 0 049 (R_w 0 055) The weight for each reflection was calculated from the Chebyshev series $w = [7\ 768_{t0}(X)\ -3\ 010_{t1}(X) + 4\ 269_{t2}(X)]$ where $X = F_0/F_{max}$ [25] 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[26] on the Chemical Crystallography laboratory VAX 11/750 computer

L-Valinol derived imine of (-)-tricarbonyl(η^6-o-anisaldehyde)chromium(0) (-)-2, complex **7** (-)-Tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (-)-**2** (160mg, 0 59mmol) was dissolved in Et_2O (10ml) and L-valinol (61mg, 0 59mmol) added Excess 4Å molecular sieves (10g) were added to the solution and the mixture gently stirred (17h) After filtration through celite, the solution was evaporated to give the L-valinol derived imine of (-)-tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (-)-**2**, complex **7** as an orange oil (190mg, 90%), υ_{max} 1966, 1888br (-CO), 1631 (C=N), cm^{-1} $\delta_H(C_6D_6)$ 8 28 (IH, s, ArCH=NR), 6 16-6 22, 4 06-4 02 (2H, 2d, Ar*H*), 4 75-4.69, 4 17-4 11 (2H, 2t, Ar*H*), 3 69-3 58 (2H, m, RCH_2OH), 2 96 (3H, s, $ArOCH_3$), 2 82-2 74 (1H, m, RR^1CHN=CHAr), 1 87-1 72 [1H, m, $RCH(CH_3)_2$], 0 80, 0 77 [6H, 2d, J_1 6 6Hz, J_2 6 6Hz, $RCH(CH_3)_2$], *m/z* 358 (M^++1)

Kinetic resolution of tricarbonyl(η^6-o-anisaldehyde)chromium(0) 2 via an L-valinol doped alumina column - A slurry of L-valinol (400mg, 3 88mmol), deactivated alumina (40g) and Et_2O (15ml) was evaporated to give a free-flowing white powder A chromatography column was half packed with alumina (120g) in Et_2O and half the doped alumina (20g) added After further packing with alumina (120g), the remaining doped alumina was added to the top of the column A solution of tricarbonyl(η^6-*o*-

anisaldehyde)chromium(0) **2** (500mg, 1.84mmol) in Et_2O (10ml) was adsorbed onto the top of the column and allowed to stand (10min) Elution with Et_2O gave the first fraction as a red oil. The remaining two bands were eluted (MeOH Et_2O 1 5) and evaporated to give the second fraction as an orange oil Both products were separately dissolved in THF (8ml) Water (2ml) was added followed by c HCl (15 drops) and the darkened solutions stirred until they turned crimson (1h) Evaporation of the solvent followed by filtration of a Et_2O (10ml) solution through a plug of alumina gave both products as red solids The first fraction was identified as (-)-tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (-)-**2** (212mg, 42%), by comparison with an authentic sample, $[\alpha]_D^{25}$ -1006 (c 0 063 in $CHCl_3$) The second fraction was identified as (+)-tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (+)-**2** (171mg, 34%), also by comparison with an authentic sample, $[\alpha]_D^{24}$ +1020 (c 0 06 in $CHCl_3$)

General procedure for addition of nucleophiles to substituted tricarbonyl(η^6-benzaldehyde)chromium(0) complexes - A Et_2O solution of the nucleophile was added dropwise to a cooled (-78°C) THF solution of the complex and the mixture stirred (-78°C, 1h) Sufficient MeOH was slowly added to quench and the mixture warmed (20°C) and evaporated to gave a residue containing the crude product

Tricarbonyl(η^6-o-methoxy-1-phenethanol)chromium(0) **9** [3] Method 1. (+)-Tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (+)-**2** (960mg, 3 53mmol) in THF (20ml) was treated with MeMgI (4 0M, 1 77ml, 7 08mmol) under standard conditions Work up and column chromatography (Al_2O_3, Et_2O) gave (SS)-tricarbonyl(η^6-*o*-methoxy-1-phenethanol)chromium(0) (-)-**9** as a yellow solid (1.0lg, 99%), υ_{max} 3590 (-OH), 2860 (OCH_3), 1960, 1878br (-CO), 1021 (C-O-C) cm^{-1} $\delta_H(C_6D_6)$ 5 55-5 52, 3 95-3 91 (2H, 2d, Ar*H*), 4 70 [1H, d of q, J_d 4 0Hz, J_q 6 4Hz, ArC*H*(OH)CH_3], 4.59-4 51, 4 08-4 02 (2H, 2t, Ar*H*), 2 83 (3H, s, ArOCH_3), 1 49 [1H, d, J 3 8Hz, ArC*H*(OH)CH_3], 1 15 [3H, d, *J* 6 4Hz, ArCH(OH)CH_3], *m/z* 288 (M^+) Method 2. Racemic tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **2** (500mg, 1 84mmol) in THF (10ml) was treated with MeLi (1 40M, 2 63ml, 3 68mmol) under standard conditions Work up and column chromatography (Al_2O_3, Et_2O) gave a 94 6 mixture of (RR,SS)- and (RS,SR)-tricarbonyl(η^6-*o*-methoxy-1-phenethanol)chromium(0) complexes **9** and **10** respectively (530mg, 100%), the major product **9** being identified by comparison with an authentic sample, $\delta_H(C_6D_6)$ **10** 5 41-5 38, 4 25-4 22 (2H, 2d, Ar*H*), 4 50-4 45, 4 41-4 37 (2H, 2t, Ar*H*), 1 46 [1H, s, ArCH(O*H*)CH_3], 0 94 [3H, d, *J* 6 4Hz, ArCH(OH)CH_3] Recrystallisation of the mixture from CH_2Cl_2:light petroleum gave complex **9** as yellow needles

(RR,SS)-Tricarbonyl(η^6-o-methoxy-1-phenethyl methyl ether)chromium(0) **11** - (RR,SS)-Tricarbonyl(η^6-*o*-methoxy-1-phenethanol)chromium(0) **9** (325mg, 1 13mmol) was dissolved in THF (3ml) and added to a suspension of KH (79mg, 19 97mmol) in THF (3ml) and the mixture stirred (10 min) MeI (642mg, 4 52mmol) was added and the orange solution turned yellow After further stirring (30min), MeOH (1ml) was added and the solvent evaporated to give a yellow solid Column chromatography and recrystallisation from CH_2Cl_2·light petroleum gave the title complex **11** as yellow cubic crystals (315mg, 92%), identified by comparison with an authentic sample,[15] $\delta_H(CDCl_3)$ 5 87-5 84, 5 04-5 01 (2H, 2d, Ar*H*), 5 51-5 46, 4 97-4 93 (2H, 2t, Ar*H*), 4 41 [1H, q, *J* 6 4Hz, ArC*H*(OCH_3)CH_3], 3 74 (3H, s, ArOCH_3), 3 57 [3H, s, ArCH(OCH_3)CH_3], 1.37 [3H, d, *J* 6 4Hz, ArCH(OCH_3)CH_3]

(SS)-Tricarbonyl[η^6-1-(o-anisyl)propanol]chromium(0) (-)-**12** - (+)-(*o*-Anisaldehyde)chromium(0) (+)-**2** (300mg, 1 10mmol) in THF (10ml) was treated with EtMgI (0.79M, 2 53ml, 2 00mmol) under standard conditions Column chromatography (Al_2O_3, Et_2O) gave three fractions The first fraction was evaporated to give (SS)-tricarbonyl(η^6-1-(*o*-anisyl)propanol)chromium(0) (-)-**12** as a yellow solid (205mg, 62%), $[\alpha]_D^{21}$

-201 (c 1 17 in $CHCl_3$), δ_H($CDCl_3$) 5.90-5 88, 5.06-5 04 (2H, 2d, Ar*H*), 5 56-5 51, 4 98-4 94 (2H, 2t, Ar*H*), 4 80 [lH, s, br, ArC*H*(OH)R], 3 74 (3H, s, ArOCH_3), 1 80 [lH, s, br, ArCH(O*H*)R], 1 79-1 59 (2H, m, RCH_2CH$_3$), 1 01 (3H, t, *J* 7.4Hz, RCH$_2$CH_3) The second fraction was evaporated to give (+)-tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (+)-**2** (36mg, 12%) identified by comparison with an authentic sample The third fraction was evaporated to give (-)-tricarbonyl(η^6-*o*-methoxybenzylalcohol)chromium(0) (-)-**13** as a yellow solid (78mg, 26%), $[\alpha]_D^{21}$ -216 (c 1 03 in $CHCl_3$); δ_H($CDCl_3$) 5 78-5 76, 5 09-5 07 (2H, 2d, Ar*H*), 5 55-5 51, 4 95-4 91 (2H, 2t, Ar*H*), 4 64, 4.38 (2H, AB system, J_{AB} 13 1Hz, ArCH_2OH), 3 78 (3H, s, ArOCH_3), 1 96 (lH, s, br, ArCH$_2$O*H*)

(SS)-Tricarbonyl(η^6-α-phenyl-2-methoxybenzyl alcohol)chromium(0) (-)-**14** [3] - *(+)*-Tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) (+)-**2** (470mg, 1 73mmol) in THF (l0ml) was treated with PhMgBr (0 78M, 6 65ml, 5 19mmol) under standard conditions Work up and column chromatography (Al_2O_3, Et_2O) gave (SS)-tricarbonyl(η^6-α-phenyl-2-methoxybenzyl alcohol)chromium(0) (-)-**14** as a yellow solid (605mg, 100%), m p 113-114°C, $[\alpha]_D^{24}$ -178 (c 1 46 in $CHCl_3$), (Found C, 58 5, H, 4 2 $C_{17}H_{14}CrO_5$ requires C, 58 3, H, 4 0%), υ_{max} 1970, 1888br (-CO), 1608 (arene ring) cm^{-1}, δ_H($CDCl_3$) 7 48-7 44 (2H, m, Ar*H*), 7 40-7 29 (3H, m, Ar*H*), 6 06-6 02, 5 05-5 02 (2H, 2d, Ar*H*), 5 96 [s, lH, ArC*H*(OH)Ar^1], 5 58-5 50, 4 99-4 92 (2H, 2t, Ar*H*), 3 77 (3H, s, ArOCH_3), 2 19 [1H, d, *J* 2 3Hz, ArCH(O*H*)Ar^1], *m/z* 350 (M^+)

General procedure for decomplexation of tricarbonyl(η^6-arene)chromium(0) complexes - A Et_2O solution of the complex was stood in air and sunlight until a colourless solution with a green or brown precipitate resulted Filtration through celite followed by removal of the solvent by distillation or evaporation, gave the arene

(S)-o-Methoxy-1-phenethanol (-)-**15**. - (SS)-Tricarbonyl(η^6-*o*-methoxy-1-phenethanol)chromium(0) (-)-**9** (191mg, 0 66mmol) was dissolved in Et_2O (l00ml) and allowed to decomplex under standard conditions (48h) Work up and distillation gave the title componnd (-)-**15** as a clear, colourless oil (67mg, 67%), $[\alpha]_D^{20}$ -59 (c 1 18 in toluene), δ_H($CDCl_3$) 7 38-7 34, 6 93-6 89 (2H, 2d, Ar*H*), 7 32-7 23, 7 02-6 94 (2H, 2t, Ar*H*), 5 14-5 06 [lH, m, ArC*H*(OH)CH$_3$], 3 88 (3H, s, ArOCH_3), 2 70 [lH, s, br, ArCH(O*H*)CH$_3$], 1 53 [3H, d, *J* 6 5Hz, ArCH(OH)CH_3]

(S)-1-(o-Anisyl)propanol (-)-**16** - (SS)-Tricarbonyl[η^6-1-(*o*-anisyl)propanol]chromium(0) (-)-**12** (110mg, 0 36mmol) was dissolved in Et_2O (l00ml) and allowed to decomplex under standard conditions (48h) Work up and distillation gave the title compound (-)-**16** as a clear, colourless oil (57mg, 95%), $[\alpha]_D^{20}$ -57 (c 1 02 in toluene) Lit [6] $[\alpha]_D$ +47 (c 1 in toluene) for 87% ee opposite enantiomer; δ_H($CDCl_3$, 300MHz) 7 31-7 28, 6 90-6 87 (2H, 2d, Ar*H*), 7 27-7 21, 6 98-6 93 (2H, 2t, Ar*H*), 4 79 [lH, t, *J* 6 6Hz, ArC*H*(OH)R], 3 85 (3H, s, ArOCH_3), 2 53 [lH, s, br, ArCH(O*H*)R], 1 87-1 78 (2H, m, RCH_2CH$_3$), 0 96 (3H, t, *J* 7 4Hz, RCH$_2$CH_3)

(S)-α-Phenyl-2-methoxybenzyl alcohol (-)-**17** - (SS)-Tricarbonyl(η^6-α-phenyl-2-methoxybenzyl alcohol)chromium(0) (-)-**14** (297mg, 0 85mmol) was dissolved in Et_2O (l00ml) and allowed to decomplex under standard conditions (72h) Work up and distillation gave the title compound (-)-**17** as a clear, colourless oil (122mg, 67%), $[\alpha]_D^{20}$ -34 (c 1 2 in $CHCl_3$), δ_H($CDCl_3$) 7 49-7 23 (7H, m, Ar*H*), 7 00-6 89 (2H, m, Ar*H*), 6 08 [lH, s, ArC*H*(OH)Ar^1], 3 83 (3H, s, ArOCH_3), 3 74 (lH, s, br, RO*H*), *m/z* 197 (M^+-17)

(R,S)-o-Methoxy-1-phenethanol **15** - *o*-Anisaldehyde **1** (2 00g, 14 7mmol) in THF (20ml) was treated with MeLi (1 10M, 18 7ml, 20 6mmol) under standard conditions Work up gave a brown oil Water (100ml) was added and the aqueous mixture extracted with Et_2O (3 x 100ml) The organic extracts were

combined, dried ($MgSO_4$) and evaporated to a clear oil Distillation gave the title compound **15** as a clear, colourless oil (1 80g, 81%), identified by comparison with an authentic sample, b p. 72-76°C (0 1mmHg)

(R,S)-1-(o-Anisyl)propanol **16** - *o*-Anisaldehyde **1** (2 00g, 14 7mmol) in THF (20ml) was treated with EtLi (1 43M, 14 4ml, 20 6mmol) under standard conditions Work up gave a yellow oil Water (100ml) was added and the aqueous mixture extracted with Et_2O (3 x 100ml) The organic extracts were combined, dried ($MgSO_4$) and evaporated to a clear oil Distillation gave the title compound **16** as a clear, colourless oil (1 83g, 75%), identifed by comparison with an authentic sample, b p 78-80°C (0 1mmHg)

General procedure for preparation of (R)-α-methoxy-α-(trifluoromethyl)phenylacetate esters (Mosher's esters) [17] - A sample of homochiral or racemic alcohol (0 15mmol) was dissolved in CH_2Cl_2 (0 25ml) containing 4-dimethylaminopyridine (1 crystal) and pyridine (6 drops), and (R)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (1 55M in CH_2Cl_2, 0.17ml, 0 26mmol) added The solution was stirred (24h) and aqueous H_2SO_4 (1M, 2ml) added The mixture was extracted with Et_2O (3 x 2ml) and the organic extracts combined, dried ($MgSO_4$) and evaporated to give an oil A $CDCl_3$ (0 5ml) solution of the ester was filtered through a short plug of silica prior to ^1H n m r spectroscopy

(R)-α-Methoxy-α-(trifluoromethyl)phenylacetate esters of o-methoxy-1-phenethanol **15** *and 1-(o-anisyl)propanol* **16** - The (R)-α-Methoxy-α-(trifluoromethyl)phenylacetate esters of racemic and homochiral *o*-methoxy-1-phenethanol **15** and 1-(*o*-anisyl)propanol **16** were prepared under standard conditions The ^1H n m r chemical shifts used to check diastereoisomeric excesses of the esters, and hence enantiomeric excesses of the free alcohols, are presented below in Table 3

Table 3: ^1H n m r chemical shifts of the (R)-Mosher's esters of (S)-*o*-methoxy-1-phenethanol (-)-**15** and (S)-1-(*o*-anisyl)propanol (-)-**16**

	^1H n m r chemical shift					
(*R*)-α-methoxy-α-(trifluoro-methyl)phenylacetate ester	ROC*H*$_3$ (*RR*)	ROC*H*$_3$ ratio	ROC*H*$_3$ (*SR*)	RC*H*$_3$ (*RR*)	RC*H*$_3$ ratio	RC*H*$_3$ (*SR*)
(*R,S*)-*o*-methoxy-1-phenethanol (**15**)	δ3 86, s	50 50	δ3 83, s	δ1 56, d	50 50	δ1 61, d
(*S*)-*o*-methoxy-1-phenethanol (-)-(**15**)	--	0 100	δ3 83, s	--	0.100	δ1 61, d
(*R,S*)-1-(*o*-anisyl)propanol (**16**)	δ3 86, s	50 50	δ3 84, s	δ0 86, t	50 50	δ0 96, t
(*S*)-1-(*o*-anisyl)propanol (-)-(**16**)	--	0 100	δ3 85, s	--	0 100	δ0 98, t

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