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Asymmetric Synthesis of (*R*)-(+)-α-Methyl-*o*-methoxybenzyl Methyl Ether *via* the Stereoselective Benzylic Elaboration of Tricarbonyl (η^6-*o*-methoxybenzyl methyl ether)chromium(0)

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Abstract: Treatment of tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) with t-butyllithium followed by an electrophile gives a single diastereoisomer of the corresponding alpha substituted complex. The relative configuration within the product from methylation, tricarbonyl(η^6-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0), has been established *via* a single crystal X-ray structure analysis and found to be (*RS,RS*); the stereoselectivity thus arising from a non-chelation controlled mechanism. Repetition of the reaction on homochiral (+)-tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) gives, after decomplexation, homochiral (*R*)-(+)-α-methyl-*o*-methoxybenzyl methyl ether.

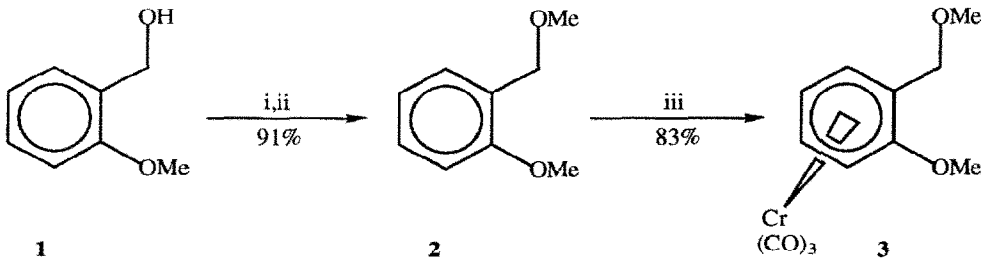
t-Butyllithium mediated deprotonations of tricarbonyl(η^6-benzyl alkyl ether)chromium(0) complexes occur exclusively at the alpha position to generate the corresponding lithio derivatives. These intermediates can undergo electrophilic quench with a variety of electrophiles, generally with suppression of the Wittig rearrangement,[1,2] to give the alpha alkylated derivatives.

The benzylic protons of tricarbonyl(η^6-benzyl methyl ether)chromium(0) are enantiotopic, thus, alpha alkylation will give rise to a racemic product. However, the benzylic protons are rendered diastereotopic when an *ortho* (and indeed a *meta*), substituent is introduced into the complex. Consequently, deprotonation followed by alpha alkylation could give rise to diastereoisomers. Deprotonation of tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) with strong bases could occur *ortho* to either ring substituent or at one of the two diastereotopic benzylic sites. If selective benzylic metallation occurred, opposing mechanisms involving either steric or chelation control could be suggested to account for any observed diastereoselectivity.[3,4] We describe herein that α-methylation of (+)-tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) occurs completely stereoselectively to yield after decomplexation, homochiral (*R*)-(+)-α-methyl-*o*-methoxybenzyl methyl ether. Part of this work has been previously communicated.[5]

Results and Discussion

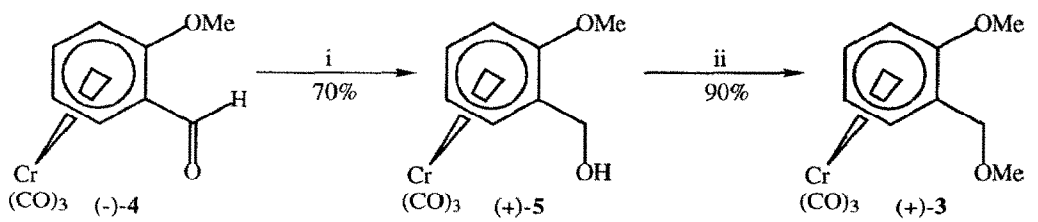
Treatment of *o*-methoxybenzyl alcohol **1** with potassium hydride in THF followed by the addition of methyl iodide gave, on work-up and distillation, *o*-methoxybenzyl methyl ether **2** as a clear oil in good yield. The ^{1}H n.m.r. spectrum of arene **2** contained the multiplets of four contiguous aromatic protons (δ7.47-6.89), a benzylic proton singlet (δ4.59) and two methoxy singlets (δ3.85, 3.49). A molecular ion *m/z* 152 (M^+) in the mass spectrum confirmed the identity of compound **2**. Thermolysis of hexacarbonylchromium(0) with arene **2** in a refluxing mixture of dibutyl ether:THF (10:1) under an inert atmosphere gave, on work-up, tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) **3** as a yellow oil in good yield (Scheme 1). The ^{1}H n.m.r.

spectrum of complex **3** contained four upfield shifted aromatic proton multiplets (δ5.76-4.91) characteristic of an arene complexed to the tricarbonylchromium(0) group. The two benzylic protons are diastereotopic and appeared as an AB system (δ4.53, 4.03, J_{AB} 12.0Hz). A high resolution mass spectrum confirmed the identity of complex **3**.



Scheme 1. *Reagents*: i, KH, THF; ii, MeI, THF; iii, $Cr(CO)_6$, Bu_2O, THF, Δ

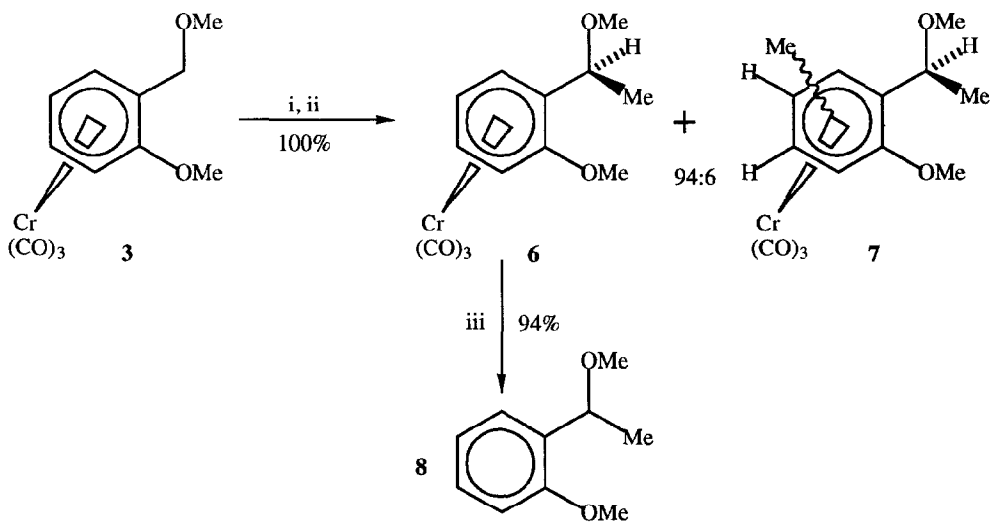
Preparation of homochiral (+)-**3** was achieved *via* a different route. Reduction of homochiral (*R*)-(-)-tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) (*R*)-(-)-**4**, [prepared *via* a kinetic resolution of tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) **4** with L-valinol][6] with sodium borohydride in THF:MeOH (3:1) gave a yellow solid identified as (+)-tricarbonyl(η⁶-*o*-methoxybenzyl alcohol)chromium(0) (+)-**5** {$[\alpha]_D^{22}$ +237 (c=1, $CHCl_3$)}. The ^1H n.m.r. spectrum of the product (+)-**5** contained a two proton AB system (δ4.64, 4.38, J_{AB} 13.1Hz) characteristic of two diastereotopic benzylic protons. A broad hydroxyl singlet (δ1.96) confirmed the identity of (+)-**5**. Conversion of compound (+)-**5** to (+)-**3** was achieved in good yield upon sequential treatment of (+)-**5** with sodium hydride and methyl iodide in THF. The product (+)-**3** {$[\alpha]_D^{22}$ +200 (c=1, $CHCl_3$)}, was spectroscopically identical to the racemic sample previously prepared (Scheme 2). Since the starting aldehyde complex (-)-**4** was homochiral[6,7] and subsequent transformations were only performed on the aldehyde group, it follows that complex (+)-**3** is homochiral. Also, since the absolute configuration of (-)-**4** is (*R*),[9] it follows that that of complex (+)-**3** is also (*R*).



Scheme 2. *Reagents*: i, $NaBH_4$, THF, MeOH; ii, NaH, THF; iii, MeI, THF

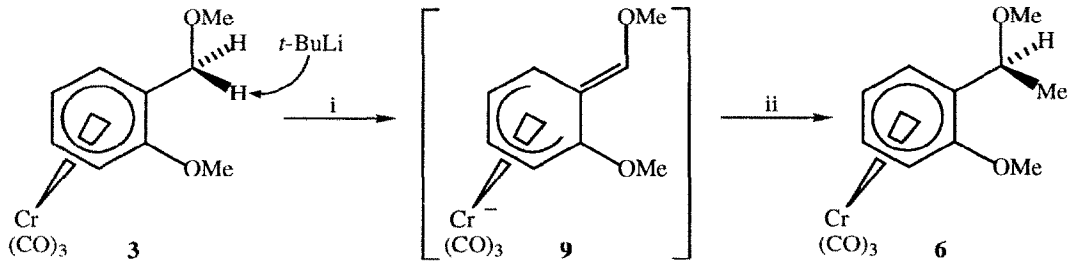
Addition of *t*-butyllithium to a cooled (-78°C) THF solution of racemic complex **3**, followed by methyl iodide gave, on work-up and chromatography, yellow crystals. The ^1H n.m.r. spectrum of the product clearly showed two compounds **6** and **7** in a ratio of 94:6. The major set of peaks comprised four contiguous aromatic

proton multiplets (δ5.86-4.93), a one proton benzylic quartet (δ4.41, *J* 6.3Hz), two three proton methoxy singlets (δ3.74, 3.57) and a three proton methyl doublet (δ1.37, *J* 6.3Hz) and was consistent with a single diastereoisomer of tricarbonyl(η⁶-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) **6**. The set of peaks corresponding to the minor product were similar to that of complex **6**, but contained three contiguous aromatic proton multiplets (δ5.42-5.15) and a new three proton singlet (δ2.24) characteristic of an aromatic methyl group. Compound **7** was identified as a dimethylated derivative. The multiplet splitting pattern of three contiguous aromatic protons in the ^{1}H n.m.r. spectrum indicated that the second methyl group was *ortho* to either the methoxy or alkyl side-chains. Recrystallisation of the mixture from CH_2Cl_2:light petroleum gave large yellow blocks of complex **6**. Complex **6** gave a molecular ion *m/z* 302 (M^+) in the mass spectrum and a correct elemental microanalysis. The dimethylated minor product **7** could not be isolated pure. Decomplexation of complex **6**, *via* exposure of a Et_2O solution to air and sunlight, gave the free racemic arene **8** in good yield (Scheme 3). The ^{1}H n.m.r. spectrum of arene **8** contained four aromatic proton multiplets (δ7.42-6.88), a benzylic proton quartet (δ4.78, *J* 6.4Hz) and a three proton methyl doublet (δ1.41, *J* 6.4Hz).



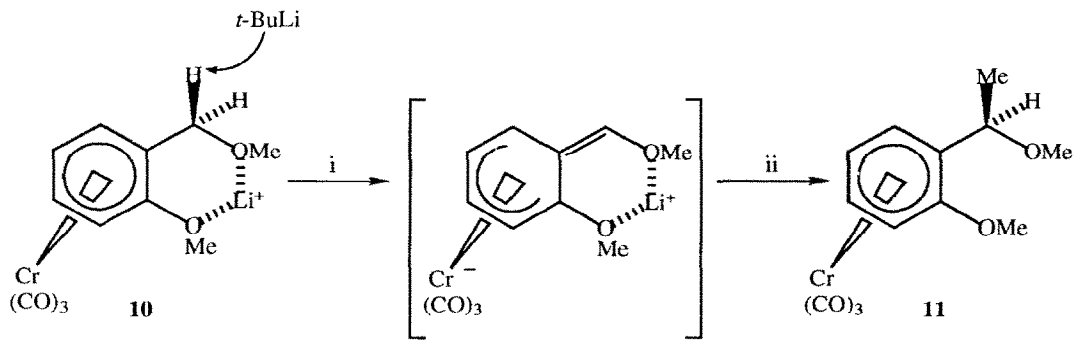
Scheme 3. *Reagents*: i, *t*-BuLi, THF; ii, MeI, THF; iii, hν, O_2, Et_2O.

Two mechanisms for this stereoselective benzylic alkylation are possible. In both, removal of a benzylic proton will occur preferentially from conformations which place the proton antiperiplanar to chromium, since delocalisation of the developing carbanion orbital over the ring and hence onto chromium will be maximised when the relevant orbitals have greatest overlap. In the first mechanism, the population of conformations which place the two methoxy groups *anti* are sterically favoured. The high energy dipolar interactions present between the lone pairs on the two oxygens will also favour the *anti* conformations over the *syn*.[10] Removal of a benzylic proton antiperiplanar to the metal moiety from these *anti* conformations gives the configurationally stable anion **9**. Subsequent *exo* alkylation would give rise to the product **6** (Scheme 4).



Scheme 4. *Reagents*: i, *t*-BuLi; ii, MeI

The second mechanism involves the formation of a Lewis acid chelated intermediate **10**, where the substrate **3** acts as a bidentate ligand towards Li^+. Benzylic deprotonation antiperiplanar to the chromium with a second molecule of base leads to loss of the other alpha proton. Subsequent *exo* alkylation in this case would give rise to the product **11** (Scheme 5).



Scheme 5. *Reagents*: i, *t*-BuLi; ii, MeI

The relative stereochemistry within the observed racemic product **6** was unambiguously confirmed by a single crystal X-ray structure analysis, Figure 1. Final atomic coordinates, and selected torsional angles are presented in Tables 1 and 2 respectively. The (*RS*,*RS*)† configuration within complex **6** is consistent with the operation of only the non-chelation control mechanism (Scheme 4).

Table 2.
Selected torsional angles for complex **6** in degrees (X-ray numbering scheme, Figure 1)

C(9) -	C(8) -	C(2) -	C(1)	77.74
C(8) -	C(2) -	C(1) -	O(1)	2.90
C(7) -	O(1) -	C(1) -	C(6) -	6.44
O(2) -	C(8) -	C(2) -	C(3)	20.88

† Throughout the descriptor for the configuration at the 1-position of the tricarbonyl(η^6-arene)chromium(0) fragment[9] is specified first followed by that for the benzylic stereogenic centre.

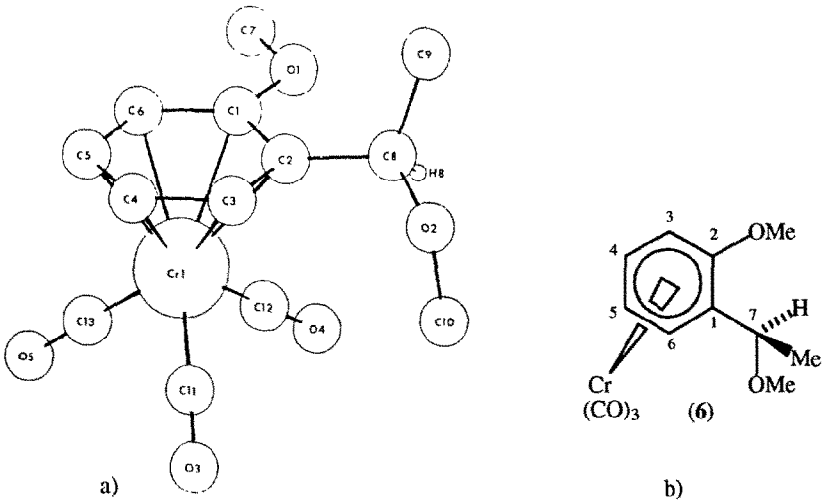
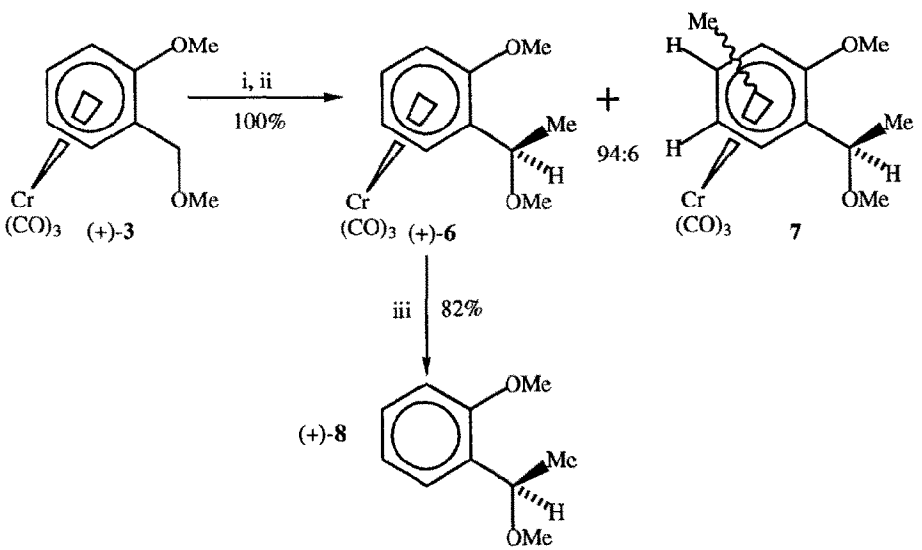


Figure 1.

a) X-Ray crystal structure of (*RS,RS*)-tricarbonyl(η^6-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) **6**; b) Systematic numbering scheme

Repetition of the stereoselective methylation reaction on homochiral (+)-**3** under the same conditions, similarly gave a 94:6 mixture of compounds (+)-**6** and **7**. Pure complex (+)-**6** {$[\alpha]_D^{22}$ +220 (c=0.8, $CHCl_3$)}, was isolated after a single recrystallisation from CH_2Cl_2:light petroleum. Decomplexation of (+)-**6** gave free homochiral (*R*)-(+)-α-methyl-*o*-methoxybenzyl methyl ether (+)-**8** {$[\alpha]_D^{22}$ +109 (c=1.19, $CHCl_3$)}, as a clear oil spectroscopically identical to the racemic sample previously prepared (Scheme 6).



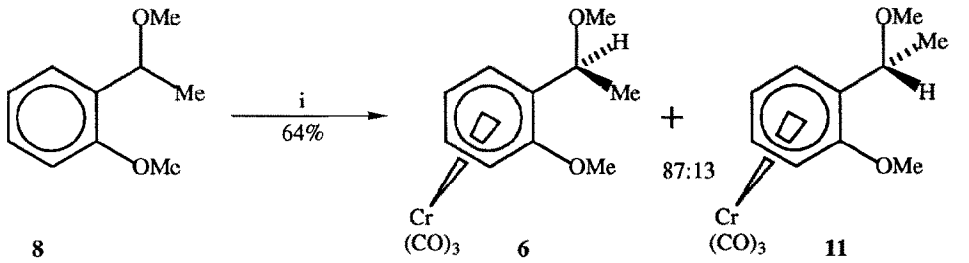
Scheme 6. *Reagents*: i, *t*-BuLi, THF; ii, MeI, THF; iii, hν, O_2, Et_2O

Table 1.

Atomic coordinates for complex **6** with estimated standard deviations in parentheses (X-ray numbering scheme)

Atom	x/a	y/b	z/c	U(iso)
Cr(1)	1922.0(4)	1700.7(8)	4415.4(6)	299
O(1)	3852(2)	-912(4)	1820(3)	399
O(2)	2872(2)	4500(4)	2667(3)	416
O(3)	915(3)	6093(5)	7067(4)	648
O(4)	4212(2)	4644(5)	7064(4)	619
O(5)	1601(3)	1245(7)	7002(5)	708
C(1)	2757(2)	-780(5)	1844(4)	335
C(2)	2399(2)	980(5)	1981(4)	313
C(3)	1270(3)	1183(6)	1961(4)	374
C(4)	493(3)	-263(6)	1844(5)	451
C(5)	860(3)	-1901(6)	1787(5)	470
C(6)	1994(3)	-2177(5)	1789(5)	405
C(7)	4298(4)	-2387(8)	1945(7)	508
C(8)	3236(3)	2422(5)	1990(4)	334
C(9)	3358(3)	867(6)	-89(5)	464
C(10)	3185(4)	6567(6)	4739(5)	552
C(11)	1312(3)	4406(6)	6038(5)	435
C(12)	3321(3)	3514(6)	6047(4)	387
C(13)	1718(3)	1373(6)	5966(5)	455
H(1)	1002(3)	2453(6)	2044(4)	702(35)
H(2)	-355(3)	-109(6)	1796(5)	702(35)
H(3)	291(3)	-2949(6)	1740(5)	702(35)
H(4)	2268(3)	-3405(5)	1756(5)	702(35)
H(5)	5151(4)	-2308(8)	1911(7)	702(35)
H(6)	4226(4)	-1743(8)	3266(7)	702(35)
H(7)	3853(4)	-4188(8)	754(7)	702(35)
H(8)	4002(3)	3053(5)	2974(4)	702(35)
H(9)	3942(3)	1857(6)	-77(5)	702(35)
H(10)	3632(3)	-701(6)	-661(5)	702(35)
H(11)	2570(3)	373(6)	-968(5)	702(35)
H(12)	2882(4)	8033(6)	5150(5)	702(35)
H(13)	4068(4)	7019(6)	5201(5)	702(35)
H(14)	2851(4)	6171(6)	5401(5)	702(35)

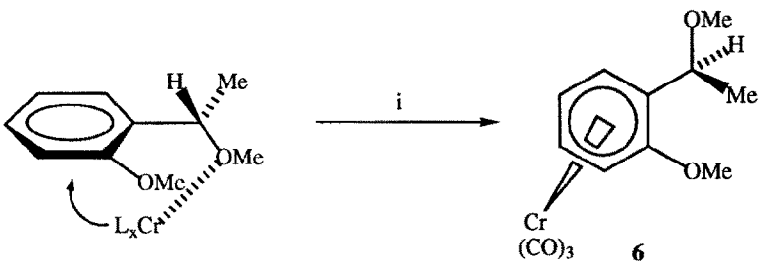
Complexation of the free racemic arene **8** with hexacarbonylchromium(0) in a refluxing mixture of dibutyl ether:THF (10:1) gave a mixture of products **6** and **11** in a ratio of 87:13. The major set of signals in the ^{1}H n.m.r. spectrum of the mixture was identical to that for pure complex **6**. The minor set of signals was similar to that of the major and contained four contiguous aromatic proton multiplets (δ5.93-4.87), a benzylic proton quartet (δ4.59, *J* 6.5Hz) and a three proton methyl doublet (δ1.52, *J* 6.5Hz). The minor product **11** was assigned therefore as the epimeric complex (Scheme 7).



8 **6** **11**

Scheme 7. *Reagents*: i, $Cr(CO)_6$, Bu_2O, THF, Δ

The formation the major compound **6** is consistent with an oxygen-chelate directing effect in the complexation reaction. The benzylic oxygen function directs the incoming chromium unit onto the proximate face of the arene in less crowded conformations which place the alpha proton and not the α-methyl group *syn* to the *o*-methoxy substituent (Scheme 8).[11]



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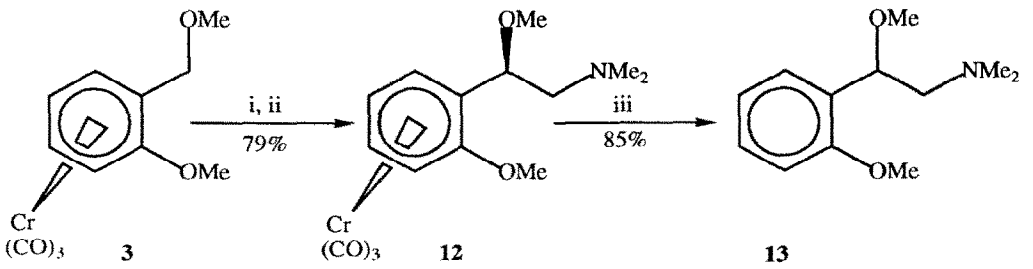
Scheme 8. *Reagents*: i, $Cr(CO)_6$, Δ

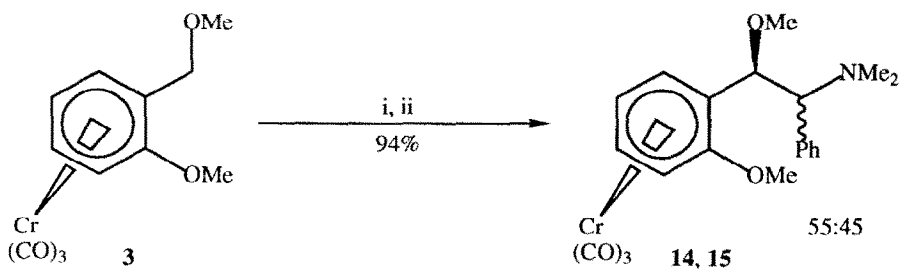
Addition of *t*-butyllithium to a cooled (-78°C) THF solution of racemic complex **3** followed by $CH_2{=}NMe_2^+$ I^- (Eschenmoser's salt), under standard conditions with warming to 0°C over 1h, gave on work-up, a single product the phenethanolamine derivative **12** as yellow needles. The ^{1}H n.m.r. spectrum of the product contained four contiguous aromatic proton multiplets (δ5.87-4.92), a benzylic proton doublet of doublets (δ4.50, J_{AX} 8.5Hz, J_{AY} 2.3Hz), a two proton ABX system (δ2.39, 2.52, J_{AB} 13.2Hz, J_{AX} 8.5Hz, J_{BX} 2.3Hz) and a six proton *N*-methyl singlet (δ2.33). Complex **12** gave a molecular ion *m/z* 346 (M^++1) in the mass spectrum and an elemental microanalysis confirmed the identity of the product. The relative stereochemistry within complex **12** was assigned by analogy with that observed in the stereoselective methylation reaction. Decomplexation of complex **12** under standard conditions gave the free racemic phenethanolamine **13** in good yield (Scheme 9). The ^{1}H n.m.r. spectrum of arene **13** was similar to that of its

tricarbonylchromium(0) complex **12** but with the four contiguous aromatic proton multiplets (δ7.38-6.85) shifted downfield.



Scheme 9. *Reagents*: i, *t*-BuLi, THF; ii, $CH_2=N^+Me_2\ I^-$, THF; iii, hv, O_2, Et_2O

Repeating the above reaction, using $PhCH=N^+Me_2\ I^-$ as the electrophile, gave a mixture of the two products **14** and **15** in a ratio of 55:45 identified by ^1H n.m.r. spectroscopy (Scheme 10). The presence of only two of the four possible diastereoisomeric products is consistent with complete stereocontrol at the α–centre, but with virtually no stereocontrol at the β-centre. The ^1H n.m.r. spectrum of the mixture contained two benzylic proton doublets [**14**, δ4.98, *J* 3.8Hz; **15**, δ4.68, *J* 6.1Hz], two beta proton doublets [**14**, δ3.15, *J* 3.2Hz; **15**, δ3.50, *J* 6.2Hz] and two six proton *N*-methyl singlets [**14**, δ2.28; **15**, δ2.26].



Scheme 10. *Reagents*: i, *t*-BuLi, THF; ii, $PhCH=N^+Me_2\ I^-$, THF

Conclusion

The completely stereoselective benzylic elaboration of tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) **3** has been achieved. The relative configuration within the product has been determined *via* a single crystal X-ray structure analysis and found to be (*RS,RS*). The ready access to homochiral complex **3**, *via* homochiral tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **4** potentially allows the synthesis of a wide range of homochiral alpha substituted benzyl methyl ethers. This methodology involves the selective removal of a benzylic proton followed by electrophilic quench and is complementary to the stereoselective additions to tricarbonyl(η^6-*o*-anisaldehyde)chromium(0) **4**[6,12] and tricarbonyl(η^6-*o*-trialkylsilylbenzaldehyde)chromium(0) complexes where nucleophilic species are used.[13]

Experimental

All reactions involving the preparation or utilisation of tricarbonyl(η^6-arene)chromium(0) complexes were performed under an atmosphere of nitrogen.[14] 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. *t*-Butyllithium was used as a solution in pentane. Potassium hydride and sodium hydride were obtained as 35% and 50% dispersions in oil respectively, from which the oil was removed by repeated washings with light petroleum followed by drying *in vacuo*. Methyl iodide was dried over 4A molecular sieves. Eschenmoser's salt ($CH_2{=}N^+Me_2\ I^-$) was recrystallised from dichloromethane: light petroleum and dried before use. All other commercial reagents were purified according to standard techniques.[15]

Column chromatography was performed on alumina (Grade V: Grade I 10% v/v deactivated). 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 300MHz and ^{13}C spectra at 62.9MHz. Mass spectra were obtained using In Beam Electron Impact or Chemical Ionisation techniques.

o-Methoxybenzyl methyl ether **2**. - A solution of *o*-methoxybenzyl alcohol **1** (8.73g, 63.3mmol) in THF (250ml) was added dropwise to a stirred suspension of potassium hydride (3.80g, 95.0mmol) in THF (250ml). The solution was stirred (21h) and methyl iodide (18.2g, 129mmol) added. After further stirring (1h), MeOH (5ml) was added cautiously and the solution filtered through celite and evaporated to a clear oil. Distillation gave the title compound **2** as a clear, colourless oil (8.72g, 91%), b.p. 54-58°C (0.1mmHg); ν_{max} 2838, 2824 (-OCH_3), 754 (disubstituted arene) cm^{-1}; δ($CDCl_3$) 7.47-7.44, 6.92-6.89 (2H, 2d, Ar*H*), 7.35-7.29, 7.05-7.00 (2H, 2t, Ar*H*), 4.59 (2H, s, ArCH_2OR), 3.85 (3H, s, ArOCH_3), 3.49 (3H, s, ROCH_3); *m/z* 152 (M^+).

General procedure for preparation of tricarbonyl(η^6-arene)chromium(0) complexes. - A deoxygenated 10:1 mixture of dibutyl ether: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-methoxybenzyl methyl ether)chromium(0) **3**. - Thermolysis of hexacarbonylchromium(0) (6.50g, 29.5mmol) with *o*-methoxybenzyl methyl ether **2** (3.00g, 19.7mmol) under standard conditions (110ml solvent, 68h) followed by work-up gave a brown oil. Column chromatography (Al_2O_3, Et_2O) gave the title compound (**3**) as a yellow oil (4.73g, 83%), ν_{max} ($CHCl_3$) 2850 (-OCH_3), 1971, 1891br (-CO) cm^{-1}; δ($CDCl_3$) 5.76-5.73, 5.08-5.06 (2H, 2d, Ar*H*), 5.54-5.49, 4.95-4.91 (2H, 2t, Ar*H*), 4.53, 4.03 (2H, AB system, J_{AB} 12.0Hz, ArCH_2OR), 3.77 (3H, s, ArOCH_3), 3.47 (3H, s, ROCH_3); [Found: *m/z* 288.0090. $C_{12}H_{12}CrO_5$ requires *m/z* 288.0090 (M^+)].

(+)-Tricarbonyl(η⁶-o-methoxybenzyl alcohol)chromium(0) (+)-**5**. - To a solution of (-)-tricarbonyl(η⁶-*o*-anisaldehyde)chromium(0) (-)-**4** (400mg, 1.47mmol) in THF (15ml) and MeOH (5ml) was added sodium borohydride (167mg, 4.41mmol) and the mixture stirred (30min). Saturated aqueous NH_4Cl (10 drops) was added and the solution evaporated to a yellow oily solid. Column chromatography (Al_2O_3, Et_2O) gave the title compound (+)-**5** as a yellow solid (280mg, 70%), $[\alpha]_D^{22}$ +237 (c=1.04, $CHCl_3$); δ($CDCl_3$) 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 (AB system, 2H, J_{AB} 13.1Hz, ArCH_2OH), 3.78 (3H, s, ArOCH_3), 1.96 (1H, s, br, ArCH_2OH).

(+)-Tricarbonyl(η⁶-o-methoxybenzyl methyl ether)chromium(0) (+)-**3**. - A solution of (+)-tricarbonyl(η⁶-*o*-methoxybenzyl alcohol)chromium(0) (+)-**5** (230mg, 0.85mmol) in THF (3ml) was added dropwise to a stirred suspension of sodium hydride (74mg, 3.08mmol) in THF (3ml). The solution was stirred (20min) and methyl iodide (477mg, 3.36mmol) added. After further stirring (40min), MeOH (0.5ml) was added cautiously and the solution evaporated to a yellow oily solid. Column chromatography (Al_2O_3, Et_2O:light petroleum 3:1) gave the title complex (+)-**3** as a yellow solid (220mg, 90%), identified by comparison with an authentic racemic sample, $[\alpha]_D^{22}$ +200 (c=1.26, $CHCl_3$).

General procedure for alkylation of tricarbonyl(η⁶-arene)chromium(0) complexes. - *t*-Butyllithium was added dropwise to a cooled (-78°C) THF solution of the complex and the mixture stirred (-78°C, 2h). The electrophile was added and stirring continued (-78°C, 2h). Sufficient MeOH was slowly added to quench and the mixture warmed (20°C) and evaporated to give a residue containing the crude alkylated complex.

(RS,RS)-Tricarbonyl(η⁶-α-methyl-o-methoxybenzyl methyl ether)chromium(0) **6**. - Tricarbonyl(η⁶-*o*-methoxybenzyl methyl ether)chromium(0) **3** (600mg, 2.08mmol) in THF (20ml) was treated with *t*-butyllithium (2.36M, 0.97ml, 2.29mmol) and methyl iodide (1.18g, 8.32mmol) under standard conditions. Work-up and column chromatography (Al_2O_3, Et_2O) gave a 94:6 mixture of (*RS,RS*)-tricarbonyl(η⁶-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) **6** and a dimethylated derivative **7** as yellow crystals (617mg, 100%), δ($CDCl_3$) **6**: 5.86-5.84, 5.04-5.02 (2H, 2d, Ar*H*), 5.51-5.47, 4.97-4.93 (2H, 2t, Ar*H*), 4.41 [1H, q, *J* 6.3Hz, ArCH(CH_3)OR], 3.74 (3H, s, ArOCH_3), 3.57 (3H, s, ROCH_3), 1.37 [3H, d, *J* 6.3Hz, ArCH(CH_3)OR], **7**: 5.42-5.41, 5.18-5.15 (2H, 2d, Ar*H*), 5.26-5.22 (1H, t, Ar*H*), 3.83 (3H, s, ArOCH_3), 3.54 (3H, s, ROCH_3), 2.24 (3H, s, ArCH_3), 1.45 [3H, d, *J* 6.3Hz, ArCH(CH_3)OR]. Recrystallisation of the mixture from CH_2Cl_2:light petroleum gave complex **6** as large yellow cubic crystals, m.p. 114-115°C; (Found: C, 51.75; H, 4.6. $C_{13}H_{14}CrO_5$ requires C, 51.7; H, 4.7%); ν_{max} ($CHCl_3$) 1969, 1888br (-CO) cm^{-1}; *m/z* 302 (M^+).

X-Ray crystal structure analysis of (RS,RS)-tricarbonyl(η⁶-α-methyl-o-methoxybenzyl methyl ether)chromium(0) **6**. 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 ω/2θ scan mode. The scan range (ω) was calculated from [1.00 + 0.14tanθ]°, and the scan speed varied from 1.3 to 5.5°/min depending upon the intensity. Reflections were measured in the range $0 < \theta < 60°$. 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[16] and equivalent reflections were merged to give 2364 unique

reflections of which 2336 were considered to be observed [$I > 3\sigma(I)$] and used in the structure analysis. Scattering factors were taken from International Tables.[17]

Crystal Data. $C_{13}H_{14}CrO_5$, M = 302.25 Triclinic, space group $P\bar{1}$ (established from systematic absences), *a* 12.246(1), *b* 8.169(1), *c* 10.164(1) Å, α 136.375(8), β 97.798(7), γ 92.420(10), U 680.2 Å^3, D_{calc} 1.48 Mgm^{-3}, μ(Cu-K_α) 71.59 cm^{-1}.

The structure was solved by Patterson 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 coordinates, anisotropic temperature factors (non-hydrogen atoms), an overall scale factor and an extinction parameter.[18] 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* 0.042 (R_ω 0.059). The weight for each reflection was calculated from the Chebyshev series $\omega = [217.58t_0(X) + 309.34_{t1}(X) + 116.56t_2(X) + 21.10t_3(X)]$ where $X = F_0/F_{max}$.[19] 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.

General procedure for decomplexation of tricarbonyl(η^6-arene)chromium(0) complexes. - An 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 crude arene.

α-Methyl-o-methoxybenzyl methyl ether **8**.[21] - (*RS,RS*)-Tricarbonyl(η^6-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) **6** (750mg, 2.48mmol) was dissolved in Et_2O (100ml) and allowed to decomplex under standard conditions (120h). Work-up and distillation gave the title compound **8** as a clear, colourless oil (385mg, 94%), b.p. 60-70°C (0.1mmHg); ν_{max} (neat) 2824, 2816 (-OCH_3), 1596 (arene ring), 1238, 1111 (C-O-C), 763 (disubstituted arene) cm^{-1}; δ($CDCl_3$) 7.42-7.40, 6.90-6.88 (2H, 2d, Ar*H*), 7.29-7.23, 7.03-6.98 (2H, 2t, Ar*H*), 4.78 [1H, q, *J* 6.4Hz, ArC*H*(CH_3)OR], 3.85 (3H, s, ArOCH_3), 3.28 (3H, s, ROCH_3), 1.41 [3H, d, *J* 6.4Hz, ArCH(CH_3)OR]; *m/z* 165 (M^+-1).

(R,R)-Tricarbonyl(η^6-α-methyl-o-methoxybenzyl methyl ether)chromium(0) (+)-**6**. - (+)-Tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) (+)-**3** (100mg, 0.35mmol) in THF (6ml) was treated with *t*-butyllithium (2.60M, 0.13ml, 0.35mmol) and methyl iodide (196mg, 1.38mmol) under standard conditions. Work-up and column chromatography (Al_2O_3, Et_2O) gave a 94:6 mixture of (*R,R*)-tricarbonyl(η^6-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) (+)-**6** and a dimethylated derivative **7** as a yellow solid (105mg, 99%), identified by comparison with an authentic racemic mixture. Recrystallisation of the mixture from CH_2Cl_2:light petroleum gave complex (+)-**6** as large yellow cubic crystals, identified by comparison with an authentic racemic sample, $[\alpha]_D^{22}$ +220 (c=0.795, $CHCl_3$).

(R)-α-Methyl-o-methoxybenzyl methyl ether (+)-**8**. - (*R,R*)-Tricarbonyl(η6-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) (+)-**6** (67mg, 0.22mmol) was dissolved in Et_2O (25ml) and allowed to decomplex under standard conditions (24h). Work-up and distillation gave the title compound (+)-**8** as a clear, colourless oil (30mg, 82%), identified by comparison with an authentic racemic sample, $[\alpha]_D^{22}$ +109 (c=1.19, $CHCl_3$).

Complexation of α-methyl-o-methoxybenzyl methyl ether **8**. - Thermolysis of hexacarbonylchromium(0) (421mg, 1.91mmol) with α-methyl-*o*-methoxybenzyl methyl ether **8** (212mg, 1.28mmol) under standard conditions (44ml solvent, 22h) gave after work-up and column chromatography (Al_2O_3, Et_2O) an 87:13 mixture of (*RS,RS*)-tricarbonyl(η^6-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) and (*RS,SR*)-tricarbonyl(η^6-α-methyl-*o*-methoxybenzyl methyl ether)chromium(0) **6** and **11** respectively as a yellow oil (246mg, 43%), δ($CDCl_3$) **6**: 5.88-5.85, 5.05-5.02 (2H, 2d, Ar*H*) 5.51-5.47, 4.98-4.94 (2H, 2t, Ar*H*), 4.42 [1H, q, *J* 6.4Hz, ArC*H*(CH_3)OR], 3.75 (3H, s, ArOCH_3), 3.58 (3H, s, ROCH_3), 1.38 [3H, d, *J* 6.4Hz, ArC*H*(CH_3)OR], (**11**): 5.93-5.91, 5.13-5.10 (2H, 2d, Ar*H*), 5.64-5.58, 4.91-4.87 (2H, 2t, Ar*H*), 4.59 [q, 1H, *J* 6.5Hz, ArC*H*(CH_3)OR], 3.79 (3H, s, ArOCH_3), 3.33 (3H, s, ROCH_3), 1.52 [3H, d, *J* 6.5Hz, ArCH(CH_3)OR]; *m/z* 302 (M^+).

(RS,RS)-Tricarbonyl(η^6-o-methoxy-N,O-dimethylhalostachine)chromium(0) **12**. - Tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) **3** (200mg, 0.69mmol) in THF (15ml) was treated with *t*-butyllithium (2.6M, 0.29ml, 0.75mmol) and $CH_2{=}N^+Me_2$ I^- (Eschenmoser's salt, 271mg, 1.47mmol) under standard conditions with warming (-78 to 0°C, 1h) prior to MeOH (1ml) quench. Work-up and column chromatography (Al_2O_3, Et_2O) gave, on evaporation of the solvent, a single compound as a yellow oil. Crystallisation from CH_2Cl_2:light petroleum gave the title compound **12** as yellow needles (189mg, 79%), m.p. 89-90°C; (Found: C, 52.15; H, 5.5; N, 3.6. $C_{15}H_{19}CrNO_5$ requires C, 52.2; H, 5.55; N, 4.1%); ν_{max} 2820 (-OCH_3), 2769 (-NCH_3), 1960, 1878br (-CO) cm^{-1}; δ($CDCl_3$) 5.87-5.84, 5.02-5.00 (2H, 2d, Ar*H*), 5.54-5.49, 4.96-4.92 (2H, 2t, Ar*H*), 4.50 [1H, d of d, J_{AX} 8.5Hz, J_{AY} 2.3Hz, ArC*H*(OCH_3)R], 3.75 (3H, s, ArOCH_3), 3.65 [3H, s, ArCH(OCH_3)R], 2.39, 2.52 (2H, ABX system, J_{AB} 13.2Hz, J_{AX} 8.5Hz, J_{BX} 2.3Hz, $R^1CH_2NR_2$), 2.33 [6H, s, RN(CH_3)$_2$]; *m/z* 346 (M^++1).

o-Methoxy-N,O-dimethylhalostachine **13**. - (*RS,RS*)-Tricarbonyl(η6-*o*-methoxy-N,O-dimethylhalostachine)-chromium(0) **12** (58mg, 0.17mmol) was dissolved in Et_2O (25ml) and allowed to decomplex under standard conditions (72h). Work-up gave the title compound as a clear, colourless oil (30mg, 84%), δ($CDCl_3$) 7.38-7.35, 6.88-6.85 (2H, 2d, Ar*H*), 7.26-7.21, 7.00-6.95 (2H, 2t, Ar*H*), 4.81 [1H, d of d, J_{AX} 9.1Hz, J_{AY} 2.3Hz, ArC*H*(OCH_3)R], 3.83 (3H, s, ArOCH_3), 3.26 [3H, s, ArCH(OCH_3)R], 2.60, 2.30 (2H, ABX system, J_{AB} 13.2Hz, J_{AX} 9.2Hz, J_{BX} 2.4Hz, $R^1CH_2NR_2$), 2.34 [6H, s, RN(CH_3)$_2$]; δC($CDCl_3$) 150.96, 128.85 (2s, Ar*C*), 128.32, 126.55, 120.73, 110.35 (4d, Ar*C*), 75.53 [d, ArC*H*(OCH_3)R], 65.33 (t, $R^1CH_2NR_2$), 56.91, 55.30 (2q, ArOCH_3, ROCH_3), 45.79 [q, RN(CH_3)$_2$].

Treatment of tricarbonyl(η^6-o-methoxybenzyl methyl ether)chromium(0) **3** *with t-butyllithium and PhCH=N$^+$Me$_2$ I$^-$*. - Tricarbonyl(η^6-*o*-methoxybenzyl methyl ether)chromium(0) **3** (546mg, 1.90mmol) in THF (12ml) was treated with *t*-butyllithium (2.6M, 0.74ml, 1.92mmol) and PhCH=N^+Me_2 I^- (1.14g, 4.37mmol) under standard conditions with warming (-78 to 0°C, 1h) prior to MeOH (1ml) quench. Work-up and column chromatography (Al_2O_3, Et_2O) gave, on evaporation of the solvent, a 55:45 mixture of (*RS,1RS,2RS*)- and (*RS,1RS,2SR*)-tricarbonyl(η^6-*o*-methoxy-2-phenyl-N,O-dimethylhalostachine)chromium(0) complexes **14** and **15** with unknown relative assignments, as a yellow solid (755mg, 94%), δ($CDCl_3$) **14**: 4.98 [1H, d, *J* 3.8Hz, ArC*H*(OCH_3)R], 3.78, 3.68 (6H, 2s, ArOCH_3, ROCH_3), 3.15 [1H, d, *J* 3.2Hz, $R^1CH(Ar^1)NR_2$], 2.28 [6H, s, RN(CH_3)$_2$], **15**: δ4.68 [1H, d, *J* 6.1Hz, ArC*H*(OCH_3)R], 3.66, 3.56 (6H, 2s, ArOCH_3, ROCH_3), 3.50

[1H, d, *J* 6.2Hz, $R^1CH(Ar^1)NR_2$], 2.26 [6H, s, $RN(CH_3)_2$], **14** and **15**: δ7.90-7.07 (10H, m, Ar*H*), 5.82-5.79, 5.74-5.72 (2H, 2d, Ar*H*), 5.45-5.38, 5.11-5.05, 4.81-4.76 (6H, 3m, Ar*H*).

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