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Chelation-control in nucleophilic addition to $Cr(CO)_3$-complexed aryl aldehydes†

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One or more methoxy groups on the benzylic carbon at the *ortho*-position of tricarbonylchromium-complexed aryl aldehydes (**2**, **3** or **4**) permit chelation-controlled addition of nucleophiles to the carbonyl function in the presence of Lewis acids. In the absence of a Lewis acid additive, a complementary set of diastereomeric products are obtained.

In the case of nucleophilic addition to carbonyl functions, metal ion chelation plays a crucial organizational role by establishing a fixed stereochemical relationship between stereogenic centers and reaction sites, often reversing the sense of diastereoselectivity observed in the absence of such chelating cations.[1] Chelation usually involves a hard, Lewis acidic metal center like Mg^{2+} or Ti^{4+}, and a hard donor group like aliphatic –OR or $–NR_2$ on a neighboring stereogenic center for effective coordination and chiral induction.[2] An aromatic –OMe group on an achiral, planar arene ring may, in principle, participate in chelation but cannot induce asymmetric bias unless metal complexation renders the aromatic fragment chiral (Chart 1).

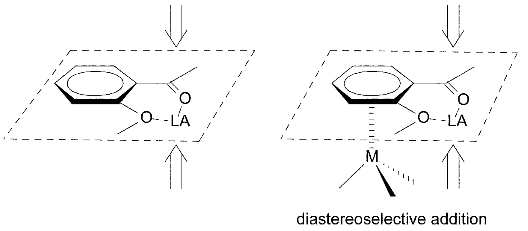

Chart 1

For instance, chiral *o*-methoxybenzaldehyde–$Cr(CO)_3$ complex, **1**, can adopt two possible conformations involving the carbonyl group: it is turned either towards (*syn*), or away from (*anti*), the *ortho*-substituent. Since nucleophilic addition is always *exo*-selective at the benzylic site (takes place preferentially from a face opposite the bulky $Cr(CO)_3$ group), configuration of the stereogenic center resulting from nucleophilic addition will then be governed by conformation of the carbonyl group.

Precedents suggest that an *o*-OMe group encourages *anti*-orientation of the adjacent carbonyl group on account of repulsion between the two oxygen atoms.[3] The *syn*-conformer could be enforced[4] if a Lewis acidic metal center formed a chelate involving the two oxygenated functions (Chart 2). In that case, participation of an aromatic methoxy group in chelate formation is critical to the steric outcome of nucleophilic addition. Crystal structures of anisole–$Cr(CO)_3$ complex[5a] and 4-fluoroanisole–$Cr(CO)_3$ complex[5b] reveal a near co-planarity of the OMe group with the aromatic ring and a shortening of the (*Ar*)C–O bond indicating that non-bonding electrons on oxygen strongly interact with the π-system of the complexed and electron-depleted aromatic ring. Such delocalization decreases the coordination ability of oxygen with metal cations.[5b] This is reflected in the failure of *o*-OMe-benzaldehyde–$Cr(CO)_3$ or *o*-OMe-acetophenone–$Cr(CO)_3$ complex to act as bidentate ligands to Lewis acidic metals and induce stereodivergence in nucleophilic addition.[6] Insertion of an extra carbon between the aromatic ring and the alkoxy group should restore the Lewis basicity of the oxygen and, if chelation can thus be facilitated, one can perform nucleophilic addition in a stereodivergent manner in the presence or absence of a Lewis acidic metal cation.[7] We report herein that stereodivergence can indeed be induced as envisaged above, with respectable diastereoselectivity.

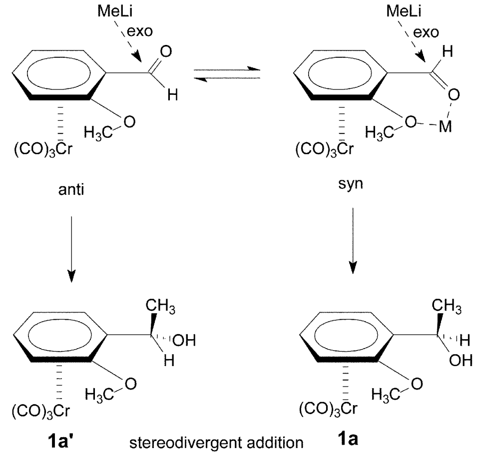

Chart 2

Results and discussion

Three substrates, **2**–**4**, were prepared in a straightforward manner as depicted in Scheme 1.

Substrate **2** was prepared from **3′** by lithiation,[8] followed by treatment with bromomethyl methyl ether and acid hydrolysis of acetal **2′** to aldehyde (*i*, Scheme 1). When DMF was used as the electrophile after the lithiation step, substrate **3** was obtained (*ii*, Scheme 1). Directed lithiation of complex **4′** followed by quenching with DMF afforded the substrate **4** (*iii*, Scheme 1). Of these, complex **2** is a liquid while complexes **3** and **4** are crystalline solids. All new complexes reported in this paper were characterized by IR, ^1H and ^{13}C NMR spectral data and elemental analyses. The number of oxygen atoms (as –OMe

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† Electronic supplementary information (ESI) available: 1) 200 and 300 MHz ^1H NMR spectra of selected compounds; 2) Crystallographic tables of bond angles, bond lengths, torsional angles *etc.* for compounds **3a** and **3a′**. See http://www.rsc.org/suppdata/ob/b3/b301426f/

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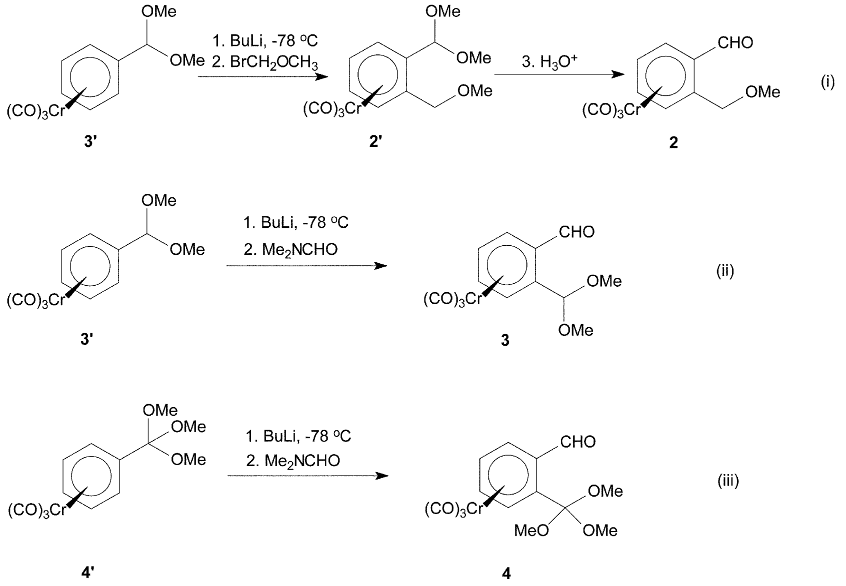
Table 1

Entry	Aldehyde	Reagent–Solvent	Yield (%)	Product (ratio)
1	**1**	MeLi–THF	100[a]	**1a** : **1a**′ = 1 : 15.7
2		MeLi–$MgBr_2$·OEt_2–DCM	98	**1a**′
3	**2**	MeLi–ether	91	**2a** : **2a**′ = 1 : 1.4
4		MeLi–$MgBr_2$·OEt_2–DCM	95	**2a**
5		*n*-BuLi–ether	98	**2b** : **2b**′ = 1 : 1.6
6		*n*-BuLi–$MgBr_2$·OEt_2–DCM	96	**2b** : **2b**′ = 8 : 1
7	**3**	MeLi–ether	90	**3a** : **3a**′ = 1 : 1.2
8		MeLi–THF	98	**3a** : **3a**′ = 1 : 1.6
9		MeLi–$MgBr_2$·OEt_2–DCM	91	**3a** : **3a**′ = 11 : 1
10		*n*-BuLi–ether	80	**3b** : **3b**′ = 1 : 1.2
11		*n*-BuLi–THF	98	**3b** : **3b**′ = 1 : 4.4
12		*n*-BuLi–$MgBr_2$·OEt_2–DCM	94	**3b**
13		PhLi–ether	92	**3c** : **3c**′ = 1 : 1.3
14		PhLi–THF	90	**3c** : **3c**′ = 1 : 1.3
15		PhLi–$MgBr_2$·OEt_2–DCM	77	**3c**
16	**4**	MeLi–ether	94	**4a** : **4a**′ = 1 : 18
17		MeLi–$MgBr_2$·OEt_2–DCM	91	**4a**
18		*n*-BuLi–ether	86	**4b**′
19		*n*-BuLi–$MgBr_2$·OEt_2–DCM	95	**4b**
20		PhLi–ether	96	**4c**′
21		PhLi–$MgBr_2$·OEt_2–DCM	93[b]	**4c** : **4c**′ = 7.2 : 1

[a] Ref. 3a. [b] Two eq. of $MgBr_2$·OEt_2 was used instead of four eq. to avoid side reactions.



Scheme 1

group) at the benzylic center increases from one to three on going from structures **2** to **4**: this was designed to address the entropy factor during chelation.

Nucleophilic additions were carried out using MeLi, *n*-BuLi and PhLi, both *without* Lewis acid in ether or THF and *with* $MgBr_2$·Et_2O (added as solid) in dichloromethane[9] at low temperature (−90 °C, methanol–slush-bath). Reactions were rapid in all cases accompanied by a clearly noticeable change of color from purple or dark red to yellow. The results are summarized in Table 1, with reference to structures in Chart 3. Isomers **2a**–**4c** are obtained from chelation-controlled addition, while isomers **2a**′–**4c**′ are products of nucleophilic addition without Lewis acid. Yields correspond to isolated yields of chromatographically pure products.

A clear trend emerges from the results. Lewis acid additives do bring about a reversal of diastereoselectivity:[10] major diastereomers obtained from *exo*-addition to the *anti*-conformer (entries 3, 5, 7, 8, 10, 11, 13, 14, 16, 18, 20) became minor isomers when Lewis acids were present in the reaction medium (entries 4, 6, 9, 12, 15, 17, 19, 21). For unambiguous assignment of relative stereochemistry, crystal structure solutions of a representative pair of products, **3a** and

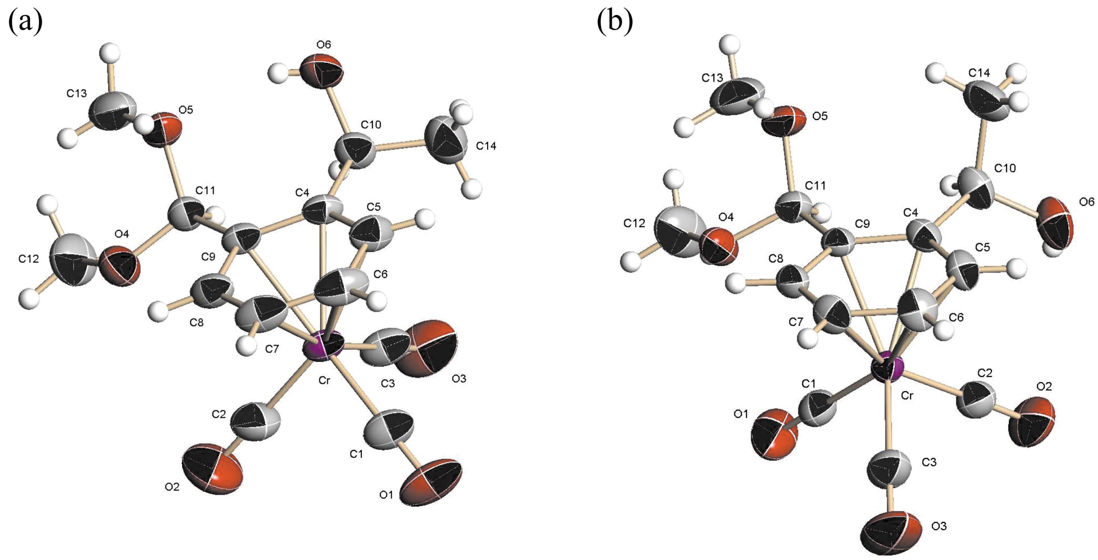
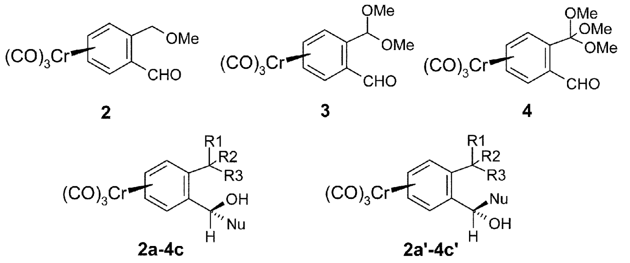


Fig. 1 (a) ORTEP diagram of complex **3a** (b) ORTEP diagram of complex **3a′**.



	R^1	R^2	R^3	Nu
2a, 2a′	H	H	OMe	Me
2b, 2b′	H	H	OMe	n-Bu
3a, 3a′	H	OMe	OMe	Me
3b, 3b′	H	OMe	OMe	n-Bu
3c, 3c′	H	OMe	OMe	Ph
4a, 4a′	OMe	OMe	OMe	Me
4b, 4b′	OMe	OMe	OMe	n-Bu
4c, 4c′	OMe	OMe	OMe	Ph

Chart 3

3a′ were performed§, and the ORTEP diagrams are displayed in Fig. 1.

The structures vindicate the assignment of the relative stereochemistry of the complexes. In the crystal lattice, four molecules of complex **3a′** are held together by intermolecular O—H—O type hydrogen bonds, while for complex **3a** two molecules are held together by two intramolecular O—H—O type hydrogen bonds and two intermolecular C—H—O type interactions[11] (Fig. 2). The average O–H(C) bond distance is 2.5 Å while the average O–H(O) distance is 2.1 Å. The presence of a center of inversion in both complexes is evident in the diagrams.

There was a consistent, recognizable pattern in the ^{1}H NMR spectra of the two sets of isomers down the series (**2a**, **2b**, **3a**–**3c** and **4a**–**4c** *vis-à-vis* **2a′**, **2b′**, **3a′**–**3c′** and **4a′**–**4c′**). For complexes **2a**–**2b**, the chemical shift difference between the diastereotopic Ar–CH_2–O protons is higher (about 0.9 ppm) than the difference observed for complexes **2a′**–**2b′** (about 0.45 ppm). The singlet around 5.5 ppm is assigned to the benzylic –CH signal for complex **3a**, while the same signal appears at 5.3 ppm for complex **3a′**. Similar differences are observed for complexes **3b** and **3b′** or **3c** and **3c′**. The proton signals for the complexed aromatic ring show comparable trends among **4a**–**c** and **4a′**–**c′**.

The reaction between complex **4** and PhLi went beyond the first step of nucleophilic addition in the presence of a Lewis acid, and formation of by-products[12] was avoided when only two molar equivalents (instead of usual four equivalents) of magnesium bromide was used.

Diastereoselectivity improved on going from substrates **2** to **4**, as the number of methoxy groups on the adjacent carbon increased (see Table 1), but the selectivity remained moderate in the absence of a Lewis acid additive. In the presence of a Lewis acid, diastereoselectivity was consistently very high. This would imply that the repulsive electrostatic field effect of the neighboring methoxy group or groups was not strong enough to restrict the orientation of the aldehyde function. Chelation held the groups in a relatively organized arrangement for better stereocontrol.

In summary, we reported the first definitive example of diastereoselective nucleophilic addition under chelation-control on arene–chromium complexes, and demonstrated its use in devising stereodivergent routes to products with predictable stereochemistry.

Experimental

All reactions were performed under an inert atmosphere of argon, using freshly distilled, degassed solvents. Diethyl ether and THF were freshly distilled over sodium benzophenone-ketyl. Dichloromethane was freshly distilled over P_2O_5. Melting points (recorded on a Thermonik Campbell melting point apparatus) are uncorrected and reported in the Celsius scale. IR spectra were recorded on a Shimadzu FTIR-8400 spectrometer. All ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC200, or MSL300. *J* values are given in Hz. Elemental analyses were performed on a Carlo-Erba 1100 automatic analyzer at NCL microanalysis facility. Metal complexes were crystallized from dichloromethane–hexane/dichloromethane–petroleum ether.

General procedure for the *ortho*-lithiation of tricarbonyl(η^6-arene)chromium(0) complexes

A solution of *n*-BuLi (1.6 M) was added dropwise to a cooled (−78 °C) THF solution of the complex and the mixture stirred (−78 °C, 2 h). The electrophile was added and stirring con-

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§ CCDC reference numbers 203336 and 203337. See http://www.rsc.org/suppdata/ob/b3/b301426f/ for crystallographic data in .cif or other electronic format.

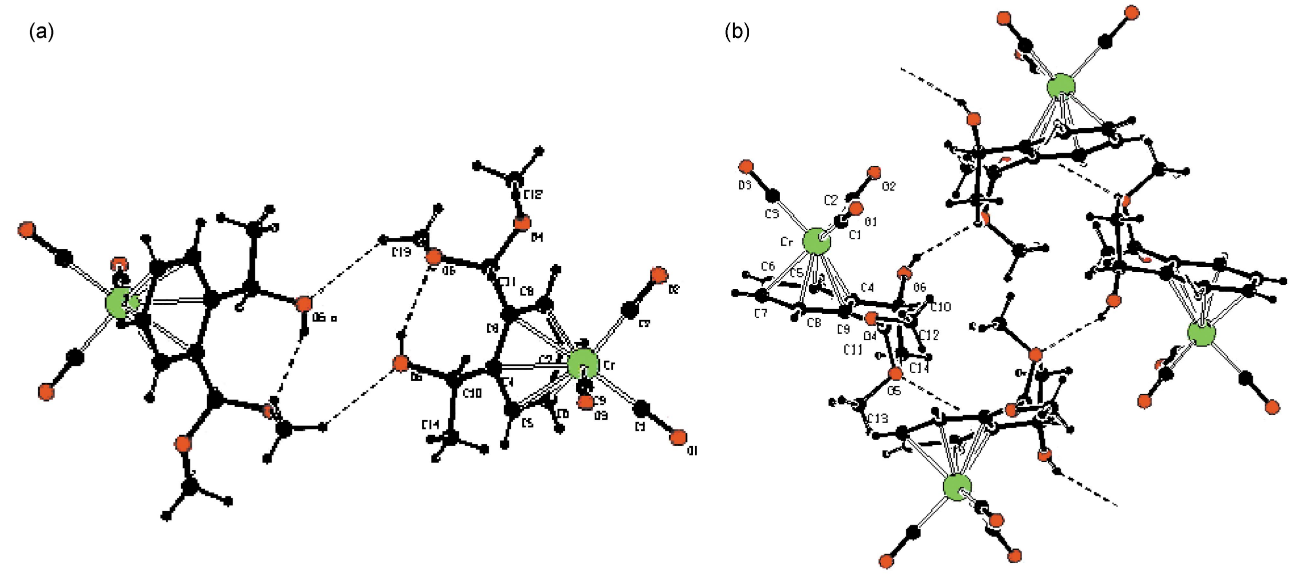

Fig. 2 (a) C–H–O interaction in complex **3a** (b) C–H–O interaction in complex **3a**′.

tinued (−78 °C, 2 h). After completion (TLC), the reaction was quenched slowly by dropwise addition of saturated ammonium chloride solution and allowed to warm to room temperature (20 °C). The reaction mixture was extracted with ether (3 × 10 cm^3), dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a residue containing the crude product.

Complex 2′. Complex **3′**^{8} (2.0 g, 6.94 mmol) in THF (40 cm^3) was treated with *n*-BuLi (1.66 M, 4.6 cm^3, 7.63 mmol) and bromomethyl methyl ether (1.3 g, 10.4 mmol) under standard conditions. Work-up and purification by flash column chromatography using petroleum ether and acetone (19 : 1) as eluent resulted in **2′** (1.5 g, 65%) as a yellow oil (Found: C, 50.98; H, 4.62. $C_{14}H_{16}CrO_6$ requires C, 50.61; H, 4.85%); ν_{max}(Nujol)/cm^{-1} 3094, 2935, 1963 and 1884; δ_H(200 MHz; $CDCl_3$) 3.24 (3 H, s, CH_2OCH_3), 3.50 (3 H, s, OCH_3), 3.58 (3 H, s, OCH_3), 4.24 (1 H, d, *J* 13, CH_2), 4.84 (1 H, d, *J* 13, CH_2), 5.24 (1 H, s, $CH(OMe)_2$), 5.31 (1 H, d, *J* 6, Ar*H*), 5.41 (1 H, t, *J* 6, Ar*H*), 5.54 (1 H, t, *J* 6, Ar*H*) and 5.78 (1 H, d, *J* 6, Ar*H*); δ_C(50.32 MHz; $CDCl_3$) 50.9, 56.4, 59.1, 69.5, 90.4, 91.1, 91.2, 91.5, 92.7, 99.7, 104.1, 107.3, 159.6 and 232.5.

Complex 2. Acetal complex **2′** (1.5 g, 4.52 mmol) dissolved in ethanol (15 cm^3) was hydrolyzed under mild conditions^{13} by the addition of activated silica gel (5 g) and dropwise addition of a saturated solution of oxalic acid at room temperature. Stirring for 20 minutes changed the color of the reaction mixture from yellow to deep red. Upon complete conversion (TLC), the reaction mixture was filtered and extracted with ether (3 × 5 cm^3). The combined organic fractions were dried over Na_2SO_4. Purification by flash column chromatography using petroleum ether and acetone (9 : 1) as eluent resulted in **2** (1.2 g, 96%) as a red oil (Found: C, 50.2; H, 3.14. $C_{12}H_{10}CrO_5$ requires C, 50.36; H, 3.52%); ν_{max}(Nujol)/cm^{-1} 3020, 1985, 1919 and 1691; δ_H(200 MHz; $CDCl_3$) 3.51 (3 H, s, OCH_3), 4.47 (1 H, d, *J* 13, CH_2), 4.84 (1 H, d, *J* 13, CH_2), 5.28 (1 H, dd, *J* 7 and 9, Ar*H*), 5.45 (1 H, d, *J* 7, Ar*H*), 5.76 (1 H, dd, *J* 6 and 5, Ar*H*), 6.0 (1 H, d, *J* 6, Ar*H*) and 9.67 (1 H, s, C*H*O); δ_C(50.32 MHz; $CDCl_3$) 58.9, 70.0, 88.4, 88.9, 92.7, 95.0, 95.5, 111.0, 188.0 and 230.1.

Complex 3. Complex **3′**^{8} (2.5 g, 8.68 mmol) in THF (50 cm^3) was treated with *n*-BuLi (1.66 M, 6 cm^3, 9.98 mmol) and *N,N*-dimethylformamide (0.95 g, 13.02 mmol) under standard conditions. Usual work-up and purification by flash column chromatography using petroleum ether and acetone (19 : 1) as eluent resulted in **3** (2.57 g, 94%) as a red solid; mp 72 °C; (Found: C, 49.91; H, 4.06. $C_{13}H_{12}O_6Cr$ requires C, 49.38; H, 3.83%); ν_{max}($CHCl_3$)/cm^{-1} 3020, 1988, 1923 and 1688; δ_H(200.13 MHz; $CDCl_3$) 3.29 (3 H, s, OCH_3), 3.60 (3 H, s, OCH_3), 5.32 (1 H, t, *J* 6, Ar*H*), 5.61 (1 H, d, *J* 6, Ar*H*), 5.72 (1 H, d, *J* 6, Ar*H*), 5.77 (1 H, s, $CH(OCH_3)_2$), 6.04 (1 H, d, *J* 7, Ar*H*) and 9.84 (1 H, s, C*H*O); δ_C(50.32 MHz; $CDCl_3$) 51.2, 56.3, 87.9, 89.1, 93.1, 93.4, 94.1, 99.3, 110.2, 121.7, 187.1 and 230.1.

Complex 4′. A deoxygenated mixture of Bu_2O–THF (10 : 1, 100 cm^3), trimethyl orthobenzoate (5 g, 27.4 mmol), and hexacarbonylchromium(o) (3 g, 13.6 mmol) was heated to reflux for about 20 hours until the first trace of green precipitate was observed. The cooled solution was then filtered through Celite and the solvent evaporated to give the crude complex. Purification by flash column chromatography using petroleum ether and acetone (19 : 1) as eluent resulted in **4′** (3.5 g, 91%, based on the recovered arene) as a yellow solid; mp 86–87 °C; (Found: C, 48.99; H, 4.26. $C_{13}H_{14}CrO_6$ requires C, 49.06; H, 4.43%); ν_{max}(Nujol)/cm^{-1} 1973, 1894 and 1892; δ_H(200.13 MHz; $CDCl_3$) 3.36 (9 H, s, 3 × OCH_3), 5.21 (2 H, t, *J* 6, Ar*H*), 5.47 (1 H, t, *J* 6, Ar*H*) and 5.70 (2 H, d, *J* 6, Ar*H*); δ_C(50.32 MHz; $CDCl_3$) 50.8, 89.0, 93.1, 94.3, 105.0, 112.5, 159.7 and 232.3.

Complex 4. Complex **4′** (2.5 g, 7.86 mmol) in THF (60 cm^3) was treated with *n*-BuLi (1.66 M, 5.7 cm^3, 9.43 mmol) and *N,N*-dimethylformamide (0.86 g, 11.79 mmol) under standard conditions. Usual work-up and purification by flash column chromatography using petroleum ether and acetone (19 : 1) as eluent resulted in **4** (2.53 g, 93%) as a red solid; mp 78 °C; (Found: C, 48.72; H, 3.78. $C_{14}H_{14}CrO_7$ requires C, 48.56; H, 4.08%); ν_{max}(Nujol)/cm^{-1} 1987, 1965, 1920 and 1676; δ_H(200.13 MHz; $CDCl_3$) 3.40 (9 H, s, 3 × OCH_3), 5.44–5.54 (2 H, m, Ar*H*), 5.67 (1 H, d, *J* 6, Ar*H*), 5.87 (1 H, d, *J* 6, Ar*H*) and 10.30 (1 H, s, C*H*O); δ_C(50.32 MHz; $CDCl_3$) 50.9, 89.6, 93.1, 94.3, 105.0, 112.5, 159.7 and 232.3.

General procedure for the chelation-controlled nucleophilic additions to aldehyde complexes 2–4

To a solution of aldehyde (*n* mmol) in dichloromethane (10*n* cm^3) cooled to −90 °C, the Lewis acid (4*n* mmol) was added and the mixture was stirred for 30 minutes during which the color of the reaction mixture turned to dark purple. Dropwise addition of alkyllithium (1.5*n* mmol) instantly resulted in a color change to yellow. After the reaction was complete (15–20 min, TLC) it was quenched slowly by dropwise addition of saturated ammonium chloride solution and warmed to room temperature. The crude product resulting after usual work-up was purified by flash column chromatography. The products were crystallised from dichloromethane and petroleum ether.

Complex 2a. Yellow solid; mp 55 °C; (Found: C, 51.27; H, 4.36. $C_{13}H_{14}O_5Cr$ requires C, 51.66; H, 4.67%); ν_{max}(Nujol)/cm^{-1} 3383, 1969 and 1892; δ_H(200.13 MHz; CDCl$_3$) 1.52 (3 H, d, *J* 6, CH_3), 3.50 (3 H, s, OCH_3), 3.80 (1 H, d, *J* 2, O*H*), 3.87 (1 H, d, *J* 11, CH_2), 4.76 (1 H, d, *J* 11, CH_2), 4.85 (1 H, dq, *J* 2 and 6, CH$_3$C*H*OH), 5.33–5.40 (2 H, m, Ar*H*) and 5.41–5.49 (2 H, m, Ar*H*); δ_C(50.32 MHz; CDCl$_3$) 19.0, 58.7, 65.3, 72.6, 90.1, 91.9, 94.5, 104.5, 113.5 and 232.0.

Complex 2b. Yellow solid; mp 55 °C; (Found: C, 55.5; H, 5.89. $C_{16}H_{20}CrO_5$ requires C, 55.81; H, 5.86%); ν_{max}(Nujol)/cm^{-1} 3420, 1970, 1969 and 1870; δ_H(300.13 MHz; CDCl$_3$) 0.97 (3 H, t, *J* 7, CH_3), 1.41–1.83 (6 H, m, (CH_2)$_3$), 3.5 (3 H, s, OCH_3), 3.60 (1 H, s, O*H*), 3.89 (1 H, d, *J* 12, CH_2), 4.54 (1 H, d, *J* 9, *n*-BuC*H*OH), 4.77 (1 H, d, *J* 12, CH_2) and 5.32–5.47 (4 H, m, Ar*H*); δ_C(50.32 MHz; CDCl$_3$) 13.9, 22.5, 28.7, 29.6, 33.3, 58.7, 69.7, 72.3, 91.0, 91.9, 94.3, 104.6, 113.7, 159.6 and 232.2.

Complex 3a. Yellow solid; mp 101 °C; (Found: C, 50.84; H, 5.17. $C_{14}H_{16}O_6Cr$ requires C, 50.61; H, 4.85%); ν_{max}(Nujol)/cm^{-1} 3406, 1960, 1886 and 1461; δ_H(300.13 MHz; CDCl$_3$) 1.52 (3 H, d, *J* 6, CH_3), 3.32 (3 H, s, OCH_3), 3.61 (3 H, s, OCH_3), 3.85 (1 H, s, O*H*), 4.86 (1 H, q, *J* 6, C*H*(CH$_3$)OH), 5.38 (1 H, d, *J* 3, Ar*H*), 5.41 (1 H, d, *J* 3, Ar*H*), 5.46 (1 H, t, *J* 3, Ar*H*), 5.5 (1 H, s, C*H*(OMe)$_2$) and 5.72 (1 H, t, *J* 3, Ar*H*); δ_C(50.32 MHz; CDCl$_3$) 19.1, 50.9, 57.2, 64.5, 89.5, 90.8, 91.2, 92.4, 100.1, 105.1, 111.4 and 232.1.

Complex 3b. Orange yellow solid; mp 64–65 °C; (Found: C, 54.21; H, 5.90. $C_{17}H_{22}CrO_6$ requires C, 50.54; H, 5.92%); ν_{max}(Nujol)/cm^{-1} 3475, 1973 and 1886; δ_H(300.13 MHz; CDCl$_3$) 0.97 (3 H, t, *J* 6, CH_3), 1.38–1.89 (6 H, m, (CH_2)$_3$), 3.32 (3 H, s, OCH_3), 3.61 (3 H, s, OCH_3), 3.72 (1 H, s, O*H*), 4.51–4.58 (1 H, m, C*H*(*n*-Bu)OH), 5.36–5.41 (3 H, m, Ar*H*), 5.54 (1 H, s, C*H*(OMe)$_2$) and 5.68–5.77 (1 H, m, Ar*H*); δ_C(50.32 MHz; CDCl$_3$) 14.0, 22.5, 28.9, 33.2, 50.8, 57.3, 68.8, 90.3, 90.9, 91.2, 92.6, 99.9, 104.9, 111.9, 121.8 and 232.2.

Complex 3c. Yellow solid; mp 98 °C; (Found: C, 58.1; H, 4.79. $C_{19}H_{18}CrO_6$ requires C, 57.87; H, 4.60%); ν_{max}(Nujol)/cm^{-1} 3489, 1965, 1886 and 1861; δ_H(300.13 MHz; CDCl$_3$) 3.41 (3 H, s, OCH_3), 3.68 (3 H, s, OCH_3), 4.51 (1 H, d, *J* 2, O*H*), 4.71 (1 H, d, *J* 6, Ar*H*), 5.14 (1 H, t, *J* 6, Ar*H*), 5.45 (1 H, t, *J* 6, Ar*H*), 5.62 (1 H, d, *J* 6, Ar*H*), 5.73 (1 H, s, C*H*(OMe)$_2$), 5.87 (1 H, d, *J* 2, Ar*H*), 7.34–7.46 (3 H, m, Ph) and 7.58 (2 H, d, *J* 7, Ph); δ_C(75.48 MHz; CDCl$_3$) 51.3, 57.4, 70.7, 88.8, 91.0, 92.8, 93.4, 100.5, 106.0, 111.5, 127.2, 128.2, 137.9 and 232.0.

Complex 4a. Yellow solid; mp 103–104 °C; (Found: C, 49.93; H, 4.76. $C_{15}H_{18}CrO_7$ requires C, 49.73; H, 5.0%); ν_{max}(Nujol)/cm^{-1} 3385, 1961, 1907 and 1894; δ_H(300.13 MHz; CDCl$_3$) 1.45 (3 H, d, *J* 6, CH_3), 4.40 (9 H, s, 3 × OCH_3), 3.86 (1 H, d, *J* 3, O*H*), 5.24 (1 H, t, *J* 6, Ar*H*), 5.33 (1 H, d, *J* 6, Ar*H*), 5.41 (1 H, doublet of quartet, *J* 3, 6, CH$_3$C*H*OH), 5.59 (1 H, t, *J* 6, Ar*H*) and 5.76 (1 H, d, *J* 6, Ar*H*); δ_C(75.48 MHz; CDCl$_3$) 19.4, 50.9, 64.2, 88.1, 94.5, 94.8, 112.9, 113.6 and 232.0.

Complex 4b. Yellow solid; mp 99–100 °C; (Found: C, 54.6; H, 5.92. $C_{18}H_{24}CrO_7$ requires C, 55.08; H, 5.85%); ν_{max}(CHCl$_3$)/cm^{-1} 3018, 1973 and 1902; δ_H(200.13 MHz; CDCl$_3$) 0.96 (3 H, t, *J* 6, CH_3), 1.23–1.84 (6 H, m, (CH_2)$_3$), 3.40 (9 H, s, 3 × OCH_3), 3.72 (1 H, d, *J* 3, O*H*), 5.10–5.18 (1 H, m, C*H*(*n*-Bu)OH), 5.23 (1 H, t, *J* 6, Ar*H*), 5.32 (1 H, d, *J* 6, Ar*H*), 5.56 (1 H, t, *J* 6, Ar*H*) and 5.75 (1 H, d, *J* 6, Ar*H*); δ_C(75.48 MHz; CDCl$_3$) 13.8, 22.3, 28.8, 33.6, 50.8, 67.9, 88.3, 89.2, 94.2, 94.5, 102.9, 113.5 and 232.0.

Complex 4c. Orange yellow solid; mp 131–132 °C; (Found: C, 56.71; H, 4.83. $C_{20}H_{20}CrO_7$ requires C, 56.61; H, 4.75%); ν_{max}(Nujol)/cm^{-1} 3474, 3018, 1973 and 1900; δ_H(200.13 MHz; CDCl$_3$) 3.51 (9 H, s, 3 × OCH_3), 4.49 (1 H, d, *J* 6, Ar*H*), 4.62 (1 H, d, *J* 2, O*H*), 5.26 (1 H, t, *J* 6, Ar*H*), 5.34 (1 H, t, *J* 6, Ar*H*), 5.58 (1 H, dd, *J* 6, 2, Ar*H*), 6.50 (1 H, d, *J* 2, PhC*H*OH) and 7.31–7.58 (5 H, m, Ph); δ_C(50.32 MHz; CDCl$_3$) 51.45, 71.08, 90.23, 92.4, 92.7, 92.8, 103.6, 111.6, 113.9, 127.3, 127.9, 128.1, 138.7 and 231.8.

General procedure for the non chelation-controlled nucleophilic additions to aldehyde complexes 2–4

To a solution of aldehyde (*n* mmol) in ether or THF (10*n* cm^3) cooled to −90 °C alkyllithium (1.5*n* mmol) was added dropwise. The color of the reaction mixture instantly turned from dark red to yellow. After the reaction was complete (15–20 min, TLC) it was quenched slowly by dropwise addition of saturated ammonium chloride solution and warmed to room temperature. The crude product resulting from the usual work-up was purified by flash column chromatography. The products were recrystallised from dichloromethane and petroleum ether.

Complex 2a′. Yellow solid; mp 79 °C; ν_{max}(Nujol)/cm^{-1} 3379, 1974 and 1880; (Found: C, 51.44; H, 4.41. $C_{13}H_{14}O_5Cr$ requires C, 51.66; H, 4.67%); δ_H(300.13 MHz; CDCl$_3$) 1.50 (3 H, d, *J* 6, CH_3), 1.95 (1 H, d, *J* 2, O*H*), 3.45 (3 H, s, OCH_3), 3.98 (1 H, d, *J* 12, CH_2), 4.41 (1 H, d, *J* 12, CH_2), 4.82 (1 H, dq, *J* 2, 6, C*H*(CH$_3$)OH), 5.29–5.50 (3 H, m, Ar*H*) and 5.72 (1 H, d, *J* 6, Ar*H*); δ_C(75.48 MHz; CDCl$_3$) 25.2, 58.7, 64.8, 71.0, 89.2, 92.1, 92.4, 93.6, 104.6, 117.5 and 232.7.

Complex 2b′. Yellow solid; mp 57 °C; (Found: C, 55.98; H, 5.48. $C_{16}H_{20}CrO_5$ requires C, 55.81; H, 5.86%); ν_{max}(Nujol)/cm^{-1} 3414, 1973, 1963 and 1874; δ_H(300.13 MHz; CDCl$_3$) 0.92 (3 H, t, *J* 7, CH_3), 1.33–1.74 (6 H, m, (CH_2)$_3$), 1.95 (1 H, s, O*H*), 3.45 (3 H, s, OCH_3), 3.99 (1 H, d, *J* 11, CH_2), 4.38 (1 H, d, *J* 11, CH_2), 4.58–4.65 (1 H, m, *n*-BuC*H*OH), 5.36–5.43 (3 H, m, Ar*H*) and 5.69 (1 H, d, *J* 6, Ar*H*); δ_C(50.32 MHz; CDCl$_3$) 13.9, 22.3, 28.2, 29.6, 38.9, 58.8, 68.3, 70.9, 89.5, 92.1, 92.4, 93.6, 104.6, 159.7 and 232.8.

Complex 3a′. Yellow solid; mp 115–116 °C; (Found: C, 50.61; H, 4.85. $C_{14}H_{16}O_6Cr$ requires C, 50.77; H, 4.67%); ν_{max}(Nujol)/cm^{-1} 3461, 1973 and 1880; δ_H(200.13 MHz; CDCl$_3$) 1.47 (3 H, d, *J* 6, CH_3), 2.0 (1 H, d, *J* 4, O*H*), 3.24 (3 H, s, OCH_3), 3.57 (3 H, s, OCH_3), 4.83 (1 H, dq, *J* 4, 6, C*H*(CH$_3$)OH), 5.30 (1 H, s, C*H*(OMe)$_2$), 5.36–5.46 (2 H, m, Ar*H*) and 5.66–5.75 (2 H, m, Ar*H*); δ_C(50.32 MHz; CDCl$_3$) 24.9, 50.6, 56.8, 64.3, 89.1, 90.6, 91.6, 93.0, 99.5, 105.1, 117.3 and 232.7.

Complex 3b′. Yellow solid; mp 86 °C; (Found: C, 54.59; H, 5.76. $C_{17}H_{22}CrO_6$ requires C, 54.54; H, 5.92%); ν_{max}(Nujol)/cm^{-1} 3336, 1969 and 1894; δ_H(300.13 MHz; CDCl$_3$) 0.92 (3 H, t, *J* 7, CH_3), 1.26–1.75 (6 H, m, (CH_2)$_3$), 1.91 (1 H, s, O*H*), 3.24 (3 H, s, OCH_3), 3.56 (3 H, s, OCH_3), 4.62 (1 H, d, *J* 9, C*H*(*n*-Bu)OH), 5.28 (1 H, s, C*H*(OMe)$_2$), 5.36–5.45 (2 H, m, Ar*H*), 5.64 (1 H, d, *J* 6, Ar*H*) and 5.74 (1 H, d, *J* 6, Ar*H*); δ_C(50.32 MHz; CDCl$_3$) 14.0, 22.5, 28.6, 38.7, 50.8, 57.0, 68.1, 89.3, 90.8, 91.6, 92.9, 99.7, 117.0 and 232.7.

Complex 3c′. Yellow solid; mp 68 °C; (Found: C, 57.65; H, 4.96. $C_{19}H_{18}CrO_6$ requires C, 57.87; H, 4.57%); ν_{max}(Nujol)/cm^{-1} 3369, 1975, 1894 and 1880; δ_H(300.13 MHz; CDCl$_3$) 2.41(1 H, d, *J* 3, O*H*), 2.90 (3 H, s, OCH_3), 3.55 (3 H, s, OCH_3), 5.37–5.45 (2 H, m, Ar*H*, C*H*(Ph)OH), 5.72 (1 H, dd, *J* 6, 3, Ar*H*), 5.76 (1 H, dd, *J* 6, 3, Ar*H*), 5.81 (1 H, d, *J* 3, Ar*H*) and 7.33–7.41 (5 H, m, Ph); δ_C(75.48 MHz; CDCl$_3$) 50.7, 56.4, 70.1, 90.4, 91.2, 91.6, 92.0, 99.7, 106.1, 114.3, 127.2, 128.2, 128.4, 141.4 and 232.5.

Complex 4a′. Orange yellow solid; mp 108 °C; (Found: C, 48.89; H, 5.12. $C_{15}H_{18}CrO_7$ requires C, 49.73; H, 5.0%); ν_{max}(Nujol)/cm^{-1} 3562, 1967, 1958 and 1884; δ_H(300.13 MHz; $CDCl_3$) 1.42 (3 H, d, *J* 6, C*H₃*), 2.09 (1 H, s, O*H*), 3.35 (9 H, s, 3 × OC*H₃*), 5.20 (1 H, d, *J* 6, Ar*H*), 5.41 (1 H, dq, *J* 3, 6, CH_3C*H*OH), 5.56 (1 H, d, *J* 6, Ar*H*), 5.63 (1 H, t, *J* 6, Ar*H*) and 5.79 (1 H, d, *J* 6, Ar*H*); δ_C(75.48 MHz, $CDCl_3$) 24.8, 50.5, 64.1, 87.5, 88.1, 94.5, 95.6, 103.0, 113.0, 119.6 and 232.6.

Complex 4b′. Yellow solid; mp 110 °C; (Found: C, 54.87; H, 5.67. $C_{18}H_{24}CrO_7$ requires C, 55.08; H, 5.85%); ν_{max}(Nujol)/cm^{-1} 3010, 1978 and 1900; δ_H(300.13 MHz; $CDCl_3$) 0.91 (3 H, t, *J* 6, C*H₃*), 1.26–1.77 (6 H, m, $(CH_2)_3$), 1.94 (1 H, s, O*H*), 3.36 (9 H, s, 3 × OC*H₃*), 5.20 (2 H, t, *J* 6, Ar*H*, C*H*(*n*-Bu)OH), 5.54 (1 H, d, *J* 6, Ar*H*), 5.61 (1 H, t, *J* 6, Ar*H*) and 5.78 (1 H, d, *J* 6, Ar*H*); δ_C(75.48 MHz; $CDCl_3$) 13.9, 22.4, 28.7, 38.5, 50.7, 67.9, 88.1, 88.3, 94.5, 95.2, 103.3, 113.1, 119.1 and 232.7.

Complex 4c′. Yellow solid; mp 108–109 °C; (Found: C, 57.14; H, 4.54. $C_{20}H_{20}CrO_7$ requires C, 56.61; H, 4.75%); ν_{max}(Nujol)/cm^{-1} 3483, 3016, 1971 and 1892; δ_H(300.13 MHz; $CDCl_3$) 2.55 (1 H, d, *J* 3, O*H*), 3.22 (9 H, s, 3 × OC*H₃*), 5.21 (1 H, t, *J* 6, Ar*H*), 5.55 (1 H, t, *J* 6, Ar*H*), 5.64 (1 H, dd, *J* 6, 1, Ar*H*), 5.75 (1 H, dd, *J* 6, 1, Ar*H*), 6.29 (1 H, d, *J* 3, PhC*H*OH) and 7.22–7.39 (5 H, m, Ph); δ_C(75.48; $CDCl_3$) 50.6, 69.6, 88.9, 90.0, 93.9, 104.1, 113.0, 116.9, 127.3, 127.6, 128.1, 142.0 and 232.0.

X-Ray structure determination of 3a and 3a′. Data for both the compounds were collected on a *MACH-3* diffractometer using MoK_α radiation with fine focus tube. All the data were corrected for Lorentzian, polarization and absorption effects. SHELX-97 (SHELXTL)[14] was used for structure solution and full matrix least squares refinement on F^2.

Crystal data for 3a. Cubic, yellow, single crystals were grown by slow evaporation of solvent from a mixture of dichloromethane and petroleum ether. $C_{14}H_{16}CrO_6$, M = 332.27. Crystals belong to monoclinic, space group *P*21/*c*°, $a = 8.099(1)$, $b = 8.084(6)$, $c = 23.252(2)$ Å, $\beta = 99.51(1)$ °, $V = 1501.4(3)$ Å^3, $Z = 4$, $D_c = 1.47$ mg m^{-3}, μ (MoK_α) = 0.785 mm^{-1}, T = 293(2) K, 2649 unique [$I > 2\sigma(I)$], $R_1 = 0.0350$, $wR_2 = 0.0889$.

Crystal data for 3a′. Rectangular pale yellow single crystals were grown by slow evaporation of solvent from a mixture of dichloromethane and petroleum ether. $C_{14}H_{16}CrO_6$, M = 332.27. Crystals belong to monoclinic, space group *P*21/*n*°, $a = 13.639(1)$, $b = 8.994(1)$, $c = 13.74(1)$ Å, $\beta = 113.594$ (7) °, $V = 1544.6$ (3) Å^3, $Z = 4$, $D_c = 1.429$ mg m^{-3}, μ (MoK_α) = 0.763 mm^{-1}, T = 293(2) K, 2710 unique [$I > 2\sigma(I)$], $R_1 = 0.0289$, $wR_2 = 0.0838$.

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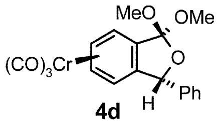
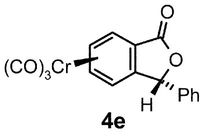


4d



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