Conformational Studies of *ortho*-Substituted Benzaldehyde Chromium Tricarbonyl Complexes

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*Summary: The syn/anti conformational equilibrium of o-substituted benzaldehyde chromium tricarbonyl complexes was studied by CD and ^1H NMR (NOE). The preferred conformation of the o-methyl-, o-methoxy-, and o-iodobenzaldehyde complexes is anti, while those of the o-trimethyltin and o-trimethylsilyl benzaldehyde complexes is syn. The optical rotation values of (o-trimethylsilyl benzaldehyde)Cr(CO)$_3$ ((1S)-**2d**) vary from −174 (in ethanol) to +108 (in chloroform).*

Introduction

Planar chiral arene chromium tricarbonyl complexes are well established as chiral ligands and as building blocks for organic synthesis.[1,2] The complexes that have received most attention are the *o*-substituted benzaldehyde complexes and their derivatives.[1,3] Access to enantioenriched *o*-substituted benzaldehyde complexes is by resolution of racemates,[4] via diastereoselective complexation of chiral derivatives,[5] via diastereoselective[6] or enantioselective[7] *ortho*-lithiation, and via diastereoselective or enantioselective *ortho*-nucleopile addition/hydride abstraction.[8] Determination of enantiomeric purity and absolute configuration is of prime importance in all these methods. Enantiomeric purity can be accurately determined by chiral HPLC[9] or by ^1H NMR analysis using chiral derivatizing agents[5d] or shift reagents.[10] The absolute configuration is often deduced from chiroptical measurements (sign of optical rotation or CD spectra) by comparison with literature data of X-ray structure determination.[3a] The present note emphasizes that this method, albeit highly convenient, should be used with caution, especially in the case of *o*-substituted benzaldehyde complexes where conformational equilibria determine chiroptical properties.

In *o*-substituted benzaldehyde complexes, the aldehyde C═O bond is coplanar with the aromatic ring. It adopts either a *syn* or *anti* conformation with regard to the *o*-substituent (Scheme 1). The *anti* conformation is largely predominant, the driving force being A^{1,3} strain in the *syn* conformation.[11] The only documented exception is [(2-hydroxybenzaldehyde) Cr(CO)$_3$] (**1**), in which

(1) (a) Semmelhack, M. F. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon: Oxford, UK, 1995; Vol. 12, p 1039. (b) Davies, S. G.; MacCarthy, T. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: New York, 1995; Vol. 12, p 1039. (c) Schmalz, H.-G.; Siegel, S. In *Transition Metal Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH Verlag GmbH: Weinheim, Germany, 1998; Vol. 1, pp 550−559. (d) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*, 2nd ed.; University Science Books: Sausalito, California, 1999; p 287. (e) Pape, A. R.; Kaliappan, K. P.; Kündig, E. P. *Chem. Rev.* **2000**, *100*, 2917. (f) Rose-Munch, F.; Rose, E. *Eur. J. Inorg. Chem.* **2002**, *6*, 1269.

(2) (a) Bolm, C.; Muniz, K. *Chem. Soc. Rev.* **1999**, *28*, 51−59. Selected recent references: (b) Englert, U.; Haerter, R.; Vasen, D.; Salzer, A.; Eggeling, E. B.; Vogt, D. *Organometallics* **1999**, *18*, 4390. (c) Andrieu, J.; Baldoli, C.; Maiorana, S.; Poli, R.; Richard, P. *Eur. J. Org. Chem.* **1999**, 3095. (d) Vasen, D.; Salzer, A.; Gerhards, F.; Gais, H.-J.; Stuermer, R.; Bieler, N. H.; Togni, A. *Organometallics* **2000**, *19*, 539. (e) Weber, I.; Jones, G. B. *Tetrahedron Lett.* **2001**, *42*, 6983. (f) Gibson, S. E.; Ibrahim, H. *Chem. Commun.* **2001**, 1070.

(3) (a) Solladié-Cavallo, A. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; Jai Press: Greenwich, CT, 1989; Vol. 1, p 99. Selected recent references: (b) Taniguchi, N.; Hata, T.; Uemura, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 1232. (c) Baldoli, C.; Del Buttero, P.; Perdicchia, D.; Pilati, T. *Tetrahedron* **1999**, *55*, 14089. (d) Han, J. W.; Jang, H. Y.; Chung, Y. K. *Tetrahedron Asymmetry* **1999**, *10*, 2853. (e) Ratni, H.; Kündig, E. P. *Org. Lett.* **1999**, *1*, 1997; **2000**, *2*, 1983. (f) Kamikawa, K.; Watanabe, T.; Daimon, A.; Uemura, M. *Tetrahedron* **2000**, *56*, 2325. (g) Maiorana, S.; Baldoli, C.; Del Buttero, P.; Licandro, E.; Papagni, A.; Lanfranchi, M.; Tiripicchio, A. *J. Organomet. Chem.* **2000**, *593*−*594*, 380. (h) Moser, W. H.; Endsley, K. E.; Colyer, J. T. *Org. Lett.* **2000**, *2*, 717. (i) Kündig, E. P.; Ratni, H.; Crousse, B.; Bernardinelli, G. *J. Org. Chem.* **2001**, *66*, 1852.

(4) (a) Solladié-Cavallo, A.; Solladié, G.; Tsamo, E. *Inorg. Synth.* **1985**, *23*, 85. (b) Bromley, L. A.; Davies, S. G.; Goodfellow, C. L. *Tetrahedron: Asymmetry* **1991**, *2*, 139.

(5) Diastereoselective complexation, selected references: (a) Davies, S. G.; Goodfellow, C. L. *J. Organomet. Chem.* **1988**, *340*, 195. (b) Brocard, J.; Pelinski, L.; Lebibi, J.; Mahmoudi, M.; Maciejewski, L. *Tetrahedron* **1989**, *45*, 709. (c) Ohlsson, B.; Ullenius, C.; Jagner, S.; Grivet, C.; Wenger, E.; Kündig, E. P. *J. Organomet. Chem.* **1989**, *365*, 243. (d) Alexakis, A.; Mangeney, P.; Marek, I.; Rose-Munch, F.; Rose, E.; Semra, A.; Robert, F. *J. Am. Chem. Soc.* **1992**, *114*, 8288. (e) Schmalz, H. G.; Millies, B.; Bats, J. W.; Duerner, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 631. (f) Aubé, J.; Heppert, J. A.; Milligan, M. L.; Smith, M. J.; Zenk, P. *J. Org. Chem.* **1992**, *57*, 3563. (g) Baldoli, C.; Maiorana, S.; Carrea, G.; Riva, S. *Tetrahedron: Asymmetry* **1993**, *4*, 767. (h) Uemura, M.; Miyake, R.; Nakayama, K.; Shiro, M.; Hayashi, Y. *J. Org. Chem.* **1993**, *58*, 1238. (i) Tweddell, J.; Hoic, D. A.; Fu, G. C. *J. Org. Chem.* **1997**, *62*, 8286.

(6) Diastereoselective deprotonation, selected references: (a) Kondo, Y.; Green, J. R.; Ho, J. *J. Org. Chem.* **1993**, *58*, 6182. (b) Christian, P. W. N.; Gil, R.; Muniz-Fernandez, K.; Thomas, S. E.; Wierzchleyski, A. T. *J. Chem. Soc., Chem. Commun.* **1994**, 1569. (c) Davies, S. G.; Loveridge, T.; Clough, J. M. *J. Chem. Soc., Chem. Commun.* **1995**, 817. (d) Alexakis, A.; Kanger, T.; Mangeney, P.; Rose-Munch, F.; Perrotey, A.; Rose, E. *Tetrahedron: Asymmetry* **1995**, *6*, 2135. (e) Han, J. W.; Son, S. U.; Chung, Y. K. *J. Org. Chem.* **1997**, *62*, 8264. (f) Watanabe, T.; Shakadou, M.; Uemura, M. *Inorg. Chim. Acta* **1999**, *296*, 80. (g) Overman, L. E.; Owen, C. E.; Zipp, G. G. *Angew Chem. Int. Ed.* **2002**, *41*, 3884.

(7) Enantioselective lithiation, selected references: (a) Price, D. A.; Simpkins, N. S.; MacLeod, A. M.; Watt, A. P. *J. Org. Chem.* **1994**, *59*, 1961. (b) Kündig, E. P.; Quattropani, A. *Tetrahedron Lett.* **1994**, *35*, 3497. (c) Uemura, M.; Hayashi, Y.; Hayashi, Y. *Tetrahedron: Asymmetry* **1994**, *5*, 1427. (d) Schmalz, H.-G.; Schellhaas, K. *Tetrahedron Lett.* **1995**, *36*, 5515. (e) Siwek, M. J.; Green, J. R. *Chem. Commun.* **1996**, 2359. (f) Ewin, R. A.; MacLeod, A. M.; Price, D. A.; Simpkins, N. S.; Watt, A. P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 401. (g) Quattropani, A.; Bernardinelli, G.; Kündig, E. P. *Helv. Chim. Acta* **1999**, *82*, 90−104. (h) Pache, S.; Botuha, C.; Franz, R.; Kündig, E. P.; Einhorn, J. *Helv. Chim. Acta* **2000**, *83*, 2436.

(8) (a) Kündig, E. P.; Liu, R.; Ripa, A. *Helv. Chim. Acta* **1992**, *75*, 2657. (b) Fretzen, A.; Ripa, A.; Liu, R.; Bernardinelli, G.; Kündig, E. P. *Chem. Eur. J.* **1998**, *4*, 251. (c) Fretzen, A.; Kündig, E. P. *Helv. Chim. Acta* **1997**, *80*, 2023.

(9) (a) Bitterwolf, T. E.; Hubler, T. L. *J. Organomet. Chem.* **1995**, *487*, 119. (b) Villani, C.; Pirkle, W. H. *J. Chromatogr., A* **1995**, *693*, 63. (c) Pertici, P.; Borgherini, F.; Vitulli, G.; Salvadori, P.; Rosini, C.; Moise, C.; Besancon, J. *Inorg. Chim. Acta* **1998**, *268*, 323.

(10) (a) Solladié-Cavallo, A.; Suffert, J. *J. Magn. Reson. Chem.* **1985**, *23*, 735. (b) Ratni, H.; Jodry, J. J.; Lacour, J.; Kündig, E. P. *Organometallics* **2000**, *19*, 3997.

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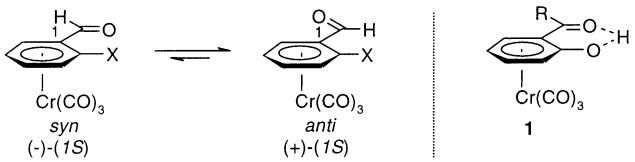
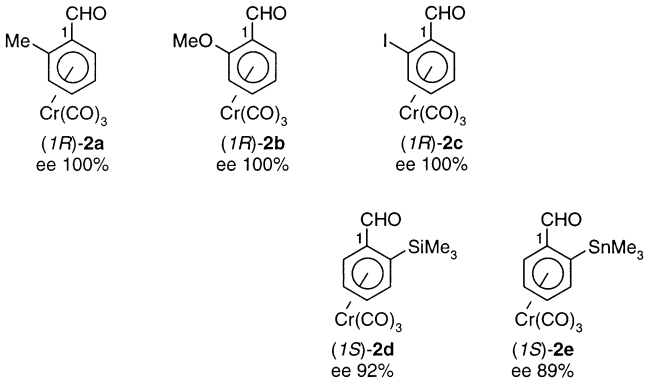
Scheme 1. Conformations of *o*-Substituted Benzaldehyde Chromium Tricarbonyl Complexes



Scheme 2. *o*-Substituted Benzaldehyde $Cr(CO)_3$ Complexes



the *syn* conformation is stabilized by an intramolecular hydrogen bond.[3a] In a series of complexes having the same absolute configuration, the conformation of the major rotamer can be deduced from the sign of the first Cotton effect in CD spectra (λ ~400−450 nm).

In the course of a study on enantioselective lithiation of prochiral complexes,[7h] we prepared a series of enantiomerically highly enriched *o*-substituted benzaldehyde complexes and realized that the equilibrium between *syn* and *anti* conformations is more complex than previously described. We here report a more detailed analysis of the situation.

Results and Discussion

The study was carried out with the five complexes **2a**−**e**, all previously described and synthesized in enantioenriched form (Scheme 2).[12] We probed their predominant conformation using CD spectroscopy, optical rotation measurement, and ^{1}H NMR (NOE) spectroscopy.

In all solvents tested (benzene, chloroform, tetrahydrofuran, ethanol), complexes (1*R*)-**2a**−**c** are levorotatory with rotation angles in the range −242° to −883° (Table 1). For **2a**, the CD absorptions are so weak that no reliable data could be obtained. The *anti* conformation could however be confirmed by measuring the ^{1}H NMR NOESY spectrum in C_6D_6. It shows interaction between the C*H*O and the *o*-Me group, whereas no interaction is found for C*H*O and the *o*-H_{Ar}. The CD spectra of **2b** and **2c** show a negative first Cotton effect. Thus, in full agreement with prior literature data and analyses the aldehyde group in complexes **2a**−**c** adopts a preferential *anti*-conformation with respect to the *ortho*-substituent for steric reasons ($A^{1,3}$ strain). In **2b** and **2c** electron pair repulsion in the *syn* conformer further contributes to this preference.

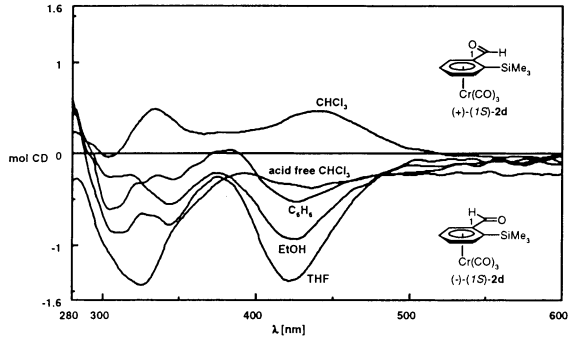
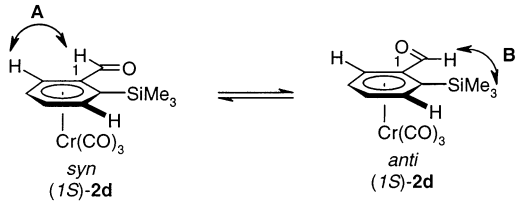


Figure 1. CD spectra of (1*S*)-**2d**.

Table 1. Optical Rotations and CD Measurements (first Cotton effect) for Complexes (1*R*)-2a−c

		solvent			
complex		C_6H_6	$CHCl_3$	THF	EtOH
(1*R*)-**2a**	$[\alpha]_D^{20}$	−505	−683	−480	−331
		(*c* 0.22)	(*c* 0.17)	(*c* 0.13)	(*c* 0.21)
(1*R*)-**2b**	$[\alpha]_D^{20}$	−534	−786	−883	−712
		(*c* 0.03)	(*c* 0.01)	(*c* 0.02)	(*c* 0.03)
	$\Delta\epsilon$	−20.8	−4.1	−4.5	−2.9
	λ_{max} [nm]	412	413	409	411
(1*R*)-**2c**	$[\alpha]_D^{20}$	−527	−664	−623	−242
		(*c* 0.03)	(*c* 0.04)	(*c* 0.03)	(*c* 0.04)
	$\Delta\epsilon$	−2.8	−2.4	−2.1	−2.4
	λ_{max} [nm]	430	426	427	434
solvent diel. constant		2.3	4.8	7.6	24.5
major conformation		*anti*	*anti*	*anti*	*anti*

Scheme 3. NOE in Complex 2d



The analyses for complexes **2d** and **2e** were carried out with the opposite (1*S*)-enantiomers. Complex (1*S*)-**2d** was reported to be dextrorotatory in $CHCl_3$.[13] The CD spectrum in $CHCl_3$ shows a positive Cotton effect, indicating a major *anti* conformation.[14] These characteristics thus suggest an analogous situation with that found for **2a**−**c**. We would like to point out that while chiroptical data are usually obtained in $CHCl_3$, the choice solvent for reactions involving these complexes is THF. Recording the CD spectrum of (1*S*)-**2d** in this solvent surprisingly showed a negative Cotton effect, indicating that the major conformation now is *syn*. This was also the case in benzene and ethanol (Figure 1) as well as in tetrachloromethane and methylene chloride. Suspecting acid impurities affecting the chloroform measurement, the spectrum was re-recorded in chloroform that had been passed through basic alumina immediately prior to the measurement. This indeed changed the spectrum drastically with now a negative first Cotton effect that indicates a preferred *syn* conformation as in the other solvents.

Syn and *anti* conformers coexist in solution. The ^{1}H NMR NOESY spectra of (1*S*)-**2d** attest to the solvent

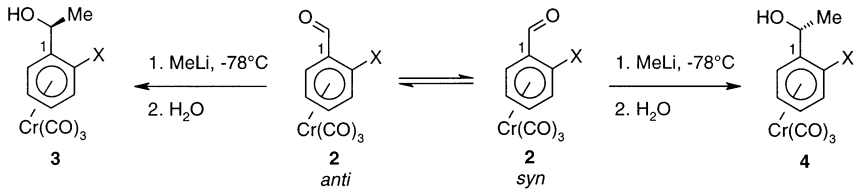
(11) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
(12) Complexes **2a** and **2b**: see ref 4a. Complex **2c**: see ref 3i. Complexes **2d** and **2e**: see ref 7h.
(13) Davies, S. G.; Goodfellow, C. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 393.
(14) The CD spectrum of (−)-(1*R*)-**2d** was reported previously but without solvent or concentration data: Meyer, A. *Ann. Chim.* **1973**, *8*, 315.

Table 2. Optical Rotations and CD Measurements (first Cotton effect) for (1*S*)-2d

	solvent						
	C_6H_6	$CHCl_3$	THF	EtOH	CCl_4	$CHCl_3$ [a]	CH_2Cl_2
$[\alpha]_D^{20}$	−86 (c = 0.11)	+105 (c = 0.12)	−160 (c = 0.10)	−174 (c = 0.19)	−60 (c = 0.02)	+108[b] (c = 0.02)	+91[b] (c = 0.03)
$\Delta\epsilon$	−0.5	+0.5	−1.5	−0.9	−1.8	−0.4	−0.4
λ_{max} [nm]	426	440	421	425	436	440	432
solvent dielectric constant	2.3	4.8	7.6	24.5	2.3	4.8	8.9
major conformation	*syn*	*anti*	*syn*	*syn*	*syn*	*syn*	*syn*

[a] Filtration of $CHCl_3$ over basic aluminum oxide before measurement. [b] The sign of the first Cotton effect in the CD spectrum and the sign of the $[\alpha]_D^{20}$ do not coincide.

Scheme 4. Addition of MeLi to *o*-Substituted Benzaldehyde $Cr(CO)_3$ Complexes



dependence of the position of the *syn*/*anti* aldehyde equilibrium. In C_6D_6, only interaction A (Scheme 3) is observed, whereas in THF-d_8 and $CDCl_3$, both interactions A and B were observed. The conformational changes associated with different *syn*/*anti* equilibria in different solvents strongly contribute to the sign and angles of the optical rotations. Changes of the angles and even of the sign of optical rotation of a given optically active compound in different solvents have much precedent.[15] The changes observed for (1*S*)-**2d** are, however, of a magnitude that is not usually encountered: the extremes are the rotations of +108 in $CHCl_3$ and of −174 in EtOH (Table 2)!

The $SnMe_3$ complex (1*S*)-**2e** is levorotatory and shows a negative Cotton effect in the CD spectrum in chloroform. This again is consistent with a *syn* conformation of the aldehyde group (Figure 2).

It is well established that in the absence of Lewis acids, complex (1*S*)-**2d** reacts with organolithium reagents to give as major product the chiral benzylic alcohol resulting from addition to the benzaldehyde Re-face.[13,16,17] With an *exo* approach of the nucleophile this corresponds to an addition to the *syn* conformer. Conversely, additions to complexes **2a**,**b** (and **2d** in the presence of Lewis acids) occur to the *anti* conformer.[3a,18] Both Hanaoka et al.[16] and Davies et al.[13] postulate oxygen Lewis base/silicon Lewis acid interactions to be at the origin of a different distribution of *syn* and *anti* conformers in **2d**. Davies and Goodfellow[13] attribute the

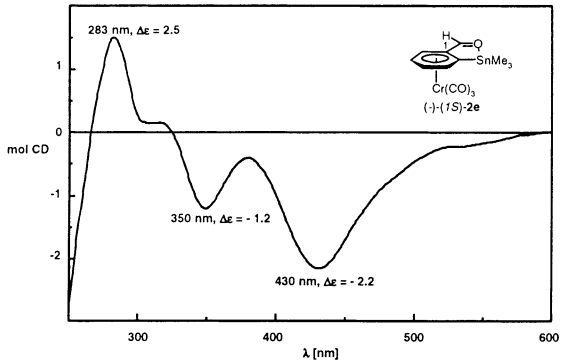


Figure 2. CD spectrum of (1*S*)-**2e** in $CHCl_3$ ($[\alpha]_D^{20}$ −354 (c 0.185, $CHCl_3$)).

Table 3. Addition of MeLi to *o*-Substituted Benzaldehyde $Cr(CO)_3$ Complexes

entry	starting complex	major conformer	dr (**3**:**4**)	additive	ref
1	**2b** (X = OMe)	*anti*	94:6	none	4b
2	**2d** (X = $SiMe_3$)	*syn*	12:88	none	13
3	**2e** (X = $SnMe_3$)	*syn*	0:100	none	this work
4	**2b** (X = OMe)	*anti*	100:1	$MgBr_2$	4b
5	**2d** (X = $SiMe_3$)	*anti*	87:13	$MgBr_2$	13
6	**2e** (X = $SnMe_3$)		50:50	$MgBr_2$	this work

stereochemical outcome of the addition reaction to steric hindrance in the nucleophile approach to the "major" *anti* conformer. While this argument is sound, the data presented here show that the *syn* conformer is dominant in THF and that RLi addition can therefore be expected to give as major diastereoisomer complex **4** as indeed found (Scheme 4). We have now extended the series of reactions of MeLi with *o*-substituted benzaldehyde complexes to the *o*-$SnMe_3$ complex **2e**. The reaction is detailed in Scheme 4 and in Table 3. Literature results for complexes **2b** and **2d** are included for comparison. MeLi addition to **2e** is highly diastereoselective and provides a single product **4** in keeping with an exo addition to the *syn* conformer as shown (Table 3, entry 3). Unlike in **2d** (entry 5), where $MgBr_2$ inverses the stereochemical outcome (from 12:88 to 87:13, entries 2 and 5), the weak Lewis acid merely shifts the ratio of products to an equimolar mixture (entries 3 and 6). We attribute this to the stronger intramolecular coordination of the carbonyl group to the adjacent Lewis acidic center in **2e** compared to that in **2d**.

Structural assignment of **4e** (X = $SnMe_3$) is based on its conversion to **4d** (X = $SiMe_3$) by transmetalation to Li/reaction with Me_3SiCl and hydrolysis of the ROSiMe ether. Spectral comparison (^{1}H NMR in $CDCl_3$) matched literature data for **4d**.[13]

(15) Eliel, E. L.; Wilen, S.; Mander, L. N. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994; pp 1076−1079.
(16) Mukai, C.; Cho, W.-J.; Kim, I. J.; Kido, M.; Hanaoka, M *Tetrahedron* **1991**, *47*, 3007.
(17) Moser, W. H.; Zhang, J.; Lecher, C. S.; Frazier, T. L.; Pink, M. *Org. Lett.* **2002**, *4*, 1981.
(18) Brocard, J.; Mahmoudi, M.; Pelinski, L.; Maciejewski, L. *Tetrahedron* **1990**, *46*, 6995.

Conclusions

o-Substituted benzaldehyde chromium tricarbonyl complexes fall into three groups: (a) the complexes of *o*-tolualdehyde (**2a**), *o*-anisaldehyde (**2b**), and *o*-halobenzaldehyde (e.g., **2c**) in which the conformation is *anti* because this minimizes $A^{1,3}$ strain and unfavorable dipole/dipole interactions; (b) the complexes of *o*-hydroxybenzaldehyde (**1**) and of *o*-trimethyltin benzaldehyde (**2e**) where the conformation is *syn* because of an intramolecular hydrogen bond (in **1**) or a Lewis acid/base interaction (in **2e**); and (c), the case where the two conformations coexist: [(*o*-trimethylsilyl benzaldehyde)-$Cr(CO)_3$] (**2d**). In this case, where neither of the two conformers is strongly favored, factors such as solvent polarity or acidity of the medium have a great influence on the conformational equilibrium and the sign and angle of optical rotation vary enormously. For the trimethyltin complex **2e** and for the trimethylsilyl complex **2d** this leads to a diastereoselectivity of nucleophile addition that is opposite that of the other *o*-substituted benzaldehyde complexes.

Experimental Section

General Procedures. Reactions were carried out under inert atmosphere using a N_2/vacuum double manifold and standard Schlenk techniques, with heat-dried glassware. THF and Et_2O were distilled prior to use from sodium-benzophenone ketyl. An Et_2O solution of $MgBr_2$ was freshly prepared from Mg/dibromoethane. All other reagents were obtained from Fluka or Acros and used without purification. IR spectra were measured on a Perkin-Elmer 1650 FT-IR spectrometer with a NaCl cell. NMR spectra were measured on Bruker 400 or 500 MHz spectrometers. Chemical shifts are given in ppm relative to the solvent signal; coupling constants are given in Hz. Optical rotations were measured on a Perkin-Elmer 241 polarimeter using a quartz cell ($l = 10$ cm) with high-pressure lamps of sodium ($\lambda = 589$ nm). Mass spectra were obtained on Varian CH 4 or SM 1 spectrometers; relative intensities are given in parentheses. High-resolution mass spectra were measured on a VG analytical 7070E instrument (data system 11250, resolution 7000). Melting points were determined on a Büchi 510 apparatus and are uncorrected. CD spectra were recorded on a Jasco J-700 spectrometer using a quartz cell ($l = 1$ cm). Elemental analyses were performed by H. Eder, Service de Microchimie, Institut de Chimie Pharmaceutique, Université de Genève.

MeLi Addition to [(Trimethyltin benzaldehyde)Cr(CO)$_3$] (2e). To a cold (−78 °C), magnetically stirred solution of complex **2e** (203 mg, 0.5 mmol) in THF (10 mL) was added dropwise MeLi (345 μL, 1.1 equiv, 1.6 M in Et_2O). After 1 h at −78 °C, the reaction was quenched by slow addition of MeOH (1 mL). The mixture was then warmed to RT and evaporated to dryness. ^{1}H NMR of the residue showed only one diastereoisomer. Purification by FC (SiO_2, pentane/Et_2O, 1:2) afforded 165 mg (0.39 mmol, 78%) of complex **4e** as a yellow solid.

Conversion 4e → 4d. To a solution of complex **4e** (X = $SnMe_3$) (63 mg, 0.15 mmol) in THF (3 mL) at −78 °C was added n-BuLi (206 μL of a 1.6 M solution in hexanes, 0.33 mmol). After stirring for 1 h, TMSCl (62 μL, 0.5 mmol) was added dropwise and the reaction mixture was slowly warmed to RT. Removal of volatiles afforded the trimethylsilyl ether of **4d** (50 mg, 83%). IR (film): 1956, 1866 cm^{-1}. ^{1}H NMR (C_6D_6): 5.04 (d, $J = 6.4$, 1H, H_{arom}), 4.95 (d, $J = 6.4$, 1H, H_{arom}), 4.80 (m, 2H, H_{arom}, H_{benz}), 4.52 (t, $J = 6.4$, 1H, H_{arom}), 1.47 (d, $J = 6.5$, 3H, CH_3), 0.37 (s, 9H, $SiMe_3$), 0.11 (s, 9H $SiMe_3$). ^{13}C NMR (C_6D_6): 233.5 (CO), 122.2 (C), 99.4 (C), 98.0 (CH), 93.2 (CH), 91.8 (CH), 91.1 (CH), 69.7 (CH_{benz}), 25.0 ($Si(CH_3)_3$), 0.8 ($Si(CH_3)_3$). MS, *m*/*z* (%): 402 (M, 18), 318 (56), 303 (26), 228 (78), 156 (22), 126 (57), 73 (30), 52 (100).

A solution of the trimethylsilyl ether of **4d** (20 mg, 0.05 mmol) in THF (3 mL) was treated with aqueous HCl (0.15 mL) at RT. TLC indicated complete reaction after 10 min. Extraction with ether was followed by washing with aqueous $NaHCO_3$ and water, and drying over $MgSO_4$ afforded **4d** (16 mg, 96%), identified by its ^{1}H NMR ($CDCl_3$) match to literature data.[13]

Reaction in the Presence of MgBr$_2$. Complex **2e** (203 mg, 0.5 mmol) was dissolved in Et_2O (10 mL). $MgBr_2$ (3.1 mL, 5 equiv, 0.8 M in Et_2O) was added, and the mixture was stirred for 10 min at RT, then cooled to −78 °C, and MeLi (345 μL, 1.1 equiv, 1.6 M in Et_2O) was added dropwise. After 1 h at 78 °C, the reaction was quenched by slow addition of MeOH (1 mL). The mixture was then warmed to RT and evaporated to dryness. ^{1}H NMR of the residue showed two diastereomers in a 1:1 ratio. Purification by FC (SiO_2, pentane/CH_2Cl_2, 1:2) afforded 90 mg (0.21 mmol, 43%) of complex **3e** as a yellow oil and 90 mg (0.21 mmol, 43%) of complex **4e** as a yellow solid.

Complex 3e: yellow oil. IR (CH_2Cl_2): 1962, 1884 cm^{-1}. ^{1}H NMR (C_6D_6): 4.85 (d, $J = 6.4$, 1H, H_{arom}); 4.82 (d, $J = 6.4$, 1H, H_{arom}); 4.69 (t, $J = 6.4$, 1H, H_{arom}); 4.30 (t, $J = 6.4$, 1H, H_{arom}); 4.10 (m, 1H, H_{benz}); 1.60 (d, $J = 6.5$, 1H, OH); 1.03 (d, $J = 6.4$, 3H, Me); 0.15 (s, 9H, $SnMe_3$). ^{13}C NMR (C_6D_6): 233.9 (CO), 125.1 (C), 124.6 (C), 101.2 (CH), 94.8 (CH), 91.2 (CH), 88.4 (CH), 68.7 (CH_{benz}), 24.9 (CH_3), −7.4 ($Sn(CH_3)_3$). MS, *m*/*z* (%): 422 (M, 21), 366 (10), 338 (45), 271 (31), 253 (80), 234 (100), 223 (30), 203 (30), 188 (49), 172 (20), 155 (30), 129 (25), 104 (11), 77 (11), 69 (19), 57 (22), 52 (92). HR-MS: calcd for $C_{14}H_{18}O_4CrSn^{120}$ 421.9632, found 421.9601; calcd for $C_{14}H_{18}O_4CrSn^{118}$ 419.9626, found 419.9577.

Complex 4e: yellow solid, mp 103−105°. IR (CH_2Cl_2): 1961, 1883. ^{1}H NMR (C_6D_6): 5.12 (td, $J = 6.4$, 6.3, 1H, H_{arom}); 4.68 (t, $J = 6.3$, 1H, H_{arom}); 4.27 (t, $J = 6.3$, 1H, H_{arom}); 4.01 (d, $J = 6.3$, 1H, H_{arom}); 3.90 (m, 1H, H_{benz}); 1.40 (d, $J = 4.6$, 1H, OH); 0.85 (d, $J = 6.6$, 3H, Me); 0.25 (s, 9H, $SnMe_3$). ^{13}C NMR (C_6D_6): 234.0 (CO), 128.4 (C), 122.3 (C), 102.4 (CH), 95.3 (CH), 90.1 (CH), 88.9 (CH), 69.5 (CH_{benz}), 25.2 (CH_3), −5.7 ($Sn(CH_3)_3$). MS, *m*/*z* (%): 422 (M, 21), 366 (11), 338 (45), 234 (95), 201 (27), 188 (52), 172 (22), 155 (31), 129 (25), 104 (18), 77 (13), 69 (18), 52 (100). HR-MS: calcd for $C_{14}H_{18}O_4CrSn^{120}$ 421.96322, found 421.96028; calcd for $C_{14}H_{18}O_4CrSn^{118}$ 419.9626, found 419.9673. Anal. Calcd: C 39.9, H 4.28. Found: C 39.9, H 4.32.

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Supporting Information Available: CD spectra of **2b** and **2c** in $CHCl_3$, THF, C_6H_6, and EtOH; CD spectra of **2d** in CCl_4 and CH_2Cl_2. This material is available free of charge via the Internet at http://pubs.acs.org.

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