137. Enantioselective Synthesis of Planar Chiral [Cr(η^6-Arene)(CO)$_3$] Complexes *via* Nucleophilic Addition/Hydride Abstraction

Preliminary Communication

by **Angelika Fretzen** and **E. Peter Kündig***

Département de Chimie Organique, Université de Genève,
30 Quai Ernest Ansermet, CH-1211 Genève 4

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Non-racemic, planar chiral 1,2-disubstituted [Cr(η^6-arene)(CO)$_3$] complexes were obtained *via* external chiral ligand-controlled nucleophilic addition of alkyl-, vinyl-, and aryllithium reagents to monosubstituted complexes followed by an *endo*-hydride abstraction with trityl cation. The reactions with [Cr(CO)$_3$(η^6-phenyloxazoline)], [Cr(CO)$_3$(η^6-phenylmethaneimine)], and [Cr(CO)$_3$(η^6-phenylmethanehydrazone)] took place with complete *ortho*-selectivity and a high degree of enantioselectivity (up to 98% ee).

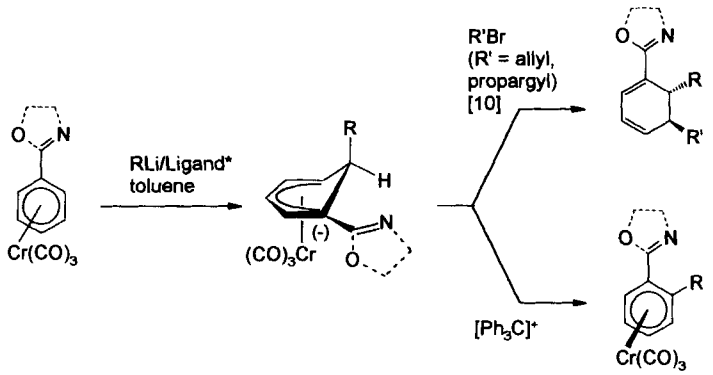
Unsymmetrically, 1,2-disubstituted [Cr(η^6-arene)(CO)$_3$] complexes are chiral molecules. They have emerged as important intermediates in asymmetric organic synthesis, the presence of the metal fragment facilitating regio- and diastereoselective reactions on or adjacent to the aromatic ring (for reviews, see [1]). Recent attention has focused on the preparation of complexes in enantiomerically enriched form. Available methods include chromatography on chiral supports [2], kinetic resolution of racemic complexes [3], diastereoselective complexation of arenes bearing chiral auxiliaries [4], and diastereoselective reactions on prochiral complexes. The most widely used reaction in the last category is the auxiliary directed *ortho*-lithiation followed by trapping with electrophiles [5]. A complementary approach, developed in this laboratory, and which is pertinent to this paper, is the diastereoselective nucleophilic addition/hydride abstraction with a SAMP-hydrazone complex [6].

Enantioselective approaches are scarce. Modest enantioselectivities (up to 69% ee) were reported in a *Suzuki* coupling reaction with a chiral Pd and a [Cr(CO)$_3$(1,2-dichlorobenzene)] complex [7] while higher selectivities (up to 90% ee) were realized in enantioselective deprotonations of prochiral complexes [8]. In related studies high enantioselectivities were also achieved in benzylic deprotonations [9].

In this paper, we detail our first results of a new enantioselective route to non-racemic [Cr(η^6-arene)(CO)$_3$] complexes. The first step of the one-pot procedure is an external chiral-ligand-controlled nucleophilic addition to mono-substituted arene complexes, a step that we have used previously in the transformation of arenes into enantiomerically enriched substituted cyclohexadienes [10]. The second step is an *endo*-hydride abstraction from the intermediate anionic cyclohexadienyl complex (*Scheme 1*).

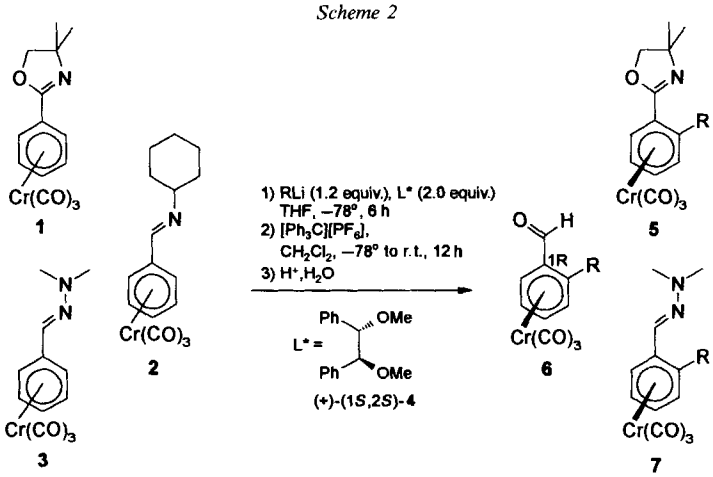
The reaction sequence was applied to the three [Cr(η^6-arene)(CO)$_3$] complexes **1**–**3**. Alkyl-, vinyl-, and phenyllithium reagents were used in the nucleophilic addition. Based

Scheme 1



on earlier findings [10], reactions were carried out in toluene in the presence of the chiral diether **4**[1])[2]). The subsequent re-aromatization was carried out in CH_2Cl_2 using $[Ph_3C][PF_6]$ as hydride-abstracting reagent[3]) (*Scheme 2*).

Scheme 2



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[1]) Ethers (+)-(1*S*,2*S*)-**4** and (−)-(1*R*,2*R*)-**4** were obtained in high yield (98%) from the corresponding diols by reaction with NaH and dimethyl sulfate [10]. The corresponding diols were obtained (in 100-g quantities) by asymmetric *Sharpless* dihydroxylation according to [11].

[2]) For previous application of (−)- and (+)-**4** as chiral ligands for organolithium additions to naphthalenes, see [12].

[3]) In a typical reaction procedure, 1.2-equiv. of the organolithium reagent was added dropwise to a toluene solution (0.2M) of the complex (1.0 equiv.) and the chiral ligand (2.0 equiv.) at −78°. The reaction mixture was stirred at this temperature for 6 h. Subsequently, volatiles were removed *in vacuo* at room temperature, the so obtained residue was taken up in a minimum of dry CH_2Cl_2 and 2.2 equiv. of $[Ph_3C][PF_6]$ were added as a saturated solution (*ca.* 0.4M in CH_2Cl_2) at −78°. Slow warm-up to room temperature, aqueous workup, and purification of the crude product by flash column chromatography yielded the pure [$Cr(CO)_3$(1,2-disubstituted arene)] complexes.

Table. *Enantioselective Nucleophilic Addition/Hydride Abstraction on [Cr(η⁶-Arene)(CO)₃] Complexes* **1**–**3**

Entry	Complex	R[a]		L*	Product	Yield [%][b]	ee [%]
1	**1**	Me[c]	**a**	(1*S*,2*S*)-**4**	(−)-(1*R*)-**5a**[d]	61	88[e]
2	**1**	Me	**a**	(1*R*,2*R*)-**4**	(+)-(1*S*)-**5a**	60	89
3	**1**	Bu[f]	**b**	(1*S*,2*S*)-**4**	(−)-(1*R*)-**5b**	65	58
4	**1**	Ph[g]	**c**	(1*S*,2*S*)-**4**	(+)-(1*R*)-**5c**	68	95
5	**1**	Ph	**c**	(1*R*,2*R*)-**4**	(−)-(1*S*)-**5c**	70	95
6	**2**	Me	**a**	(1*S*,2*S*)-**4**	(−)-(1*R*)-**6a**	58	86[h]
7	**2**	Ph	**c**	(1*S*,2*S*)-**4**	(−)-(1*R*)-**6c**	73	98[h]
8	**2**	Vinyl[i]	**d**	(1*S*,2*S*)-**4**	(−)-(1*R*)-**6d**	73	90[e][h]
9	**3**	Ph	**c**	(1*S*,2*S*)-**4**	(−)-(1*R*)-**7c**	67	90[j]

[a]) RLi was added to a solution of complex **1**, **2**, or **3** and the chiral ligand. [b]) Yield of isolated product after flash chromatography. [c]) Added as Et_2O solution (*Fluka*). [d]) The absolute configuration was assigned for the aldehyde complexes by comparison of the sign of $[\alpha]_D$ with literature data [6]. [e]) Determined by chiral HPLC analysis (*Chiralcel OD*: *e.g.*, **5c**): hexane/i-PrOH 80:20, 0.5 ml/min, t_R ((+)-(1*R*)-**5c**) 73.2 min; t_R ((−)-(1*S*)-**5c**) 65.4 min. [f]) Added as hexane solution (*Fluka*). [g]) Added as cyclohexane/Et_2O solution (70:30) (*Fluka*). [h]) Determined by chiral-shift ^{1}H-NMR experiments using [Eu(hfc)$_3$] as chiral shift reagent according to [13]. [i]) Prepared from tetravinyltin and MeLi in THF and used as a toluene solution after removal of THF *in vacuo*. [j]) Determined for the corresponding aldehyde after hydrazone hydrolysis.

The results are summarized in the *Table*. Obtained product yields were similar to those of the achiral version (carried out in THF). The chiral ligand, therefore, does not interfere with the hydride-abstracting step. In all experiments, a significant degree of enantioselectivity was obtained along with the already established 1,2-regioselectivity.

As observed previously in the sequential nucleophile/electrophile addition to complexes **1** and **2** [10], the reactions with PhLi gave the highest enantioselectivities (*Entries 4, 5, 7,* and *9*), while that with BuLi gave only modest induction (*Entry 3*).

As expected, the reaction using (*R*,*R*)-**4** as external ligand resulted in identical excesses of the opposite enantiomer to that obtained with (*S*,*S*)-**4** (*Entries 2* and *5*).

The enantioselective transformation of [Cr(CO)$_3$(η⁶-arene)] complexes **1**–**3** into enantiomerically enriched 1,2-disubstituted complexes has some advantages over the diastereoselective reactions developed earlier: the highly selective nucleophilic addition/hydride abstraction to imine complex **2** is of particular interest, because there are as yet no chiral imines which allow high *ortho*-regio- and stereocontrol in arene-addition reactions. The advantage of **2** over the use of SAMP-hydrazone lies in the straightforward hydrolysis of the imine function compared to the drastic conditions required for non-oxidative hydrolytic cleavage of the SAMP-hydrazone auxiliary [6]. This said, we note that inductions are not yet at the same level as those achieved with the SAMP-hydrazone [6] or of those involving chiral oxazolines [14], and that this calls for extending the search for more efficient ligands. Another potential advantage of the method described here, though this remains to be realized in the reaction under investigation, is the use of the chiral ligand in catalytic quantities[4]). Efforts in this direction and new applications of planar chiral complexes in diastereoselective synthesis (for recent examples, see [15]) are under active investigation in this laboratory.

[4]) Catalysis has already been achieved in additions to substituted naphthalenes [12].

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