linear optics since it would require the refractive index to change sign.

In conclusion, we have shown that a chiral discotic nematic liquid crystal in the absence of an orienting electric field is apolar and has only one second-order NLO susceptibility component. In the presence of an orienting electric field, it becomes polar and displays four significant susceptibility components. In the unoriented state, there are no CD effects on second-harmonic efficiency, even though the linear circular dichroisms and optical rotations are large. In the oriented state, such CD effects are seen, and they change sign when the polarity of the orienting field is reversed.

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Diastereoselective Lithiation of (η^6-Arene)dicarbonyltriphenylphosphane Chromium(0) Oxazoline Complexes—Direct Preparation of Enantiopure Complexes Having Planar Chiral Fragments of Either Configuration[**]

Larry E. Overman,[*] Carolyn E. Owen, and G. Greg Zipp

Planar chiral η^6-arene chromium(0) complexes are finding increasing application in the synthesis of enantioenriched compounds by serving as enantiopure starting materials or ligands for catalytic asymmetric processes.[1,2] Whereas early methods of generating enantiopure 1,2-disubstituted η^6-arene chromium(0) complexes relied on resolution of racemates,[3] many methods have been developed recently for asymmetric synthesis of these molecules.[1] One powerful strategy employs an enantiopure chiral lithium reagent (or an achiral lithium reagent plus a chiral additive) to elaborate a prochiral complex by either enantioselective ring lithiation followed by trapping with an electrophile,[4] or enantioselective nucleophilic addition followed by abstraction of hydride.[5] Another strategy involves diastereoselective lithiation of a monosubstituted η^6-arene chromium(0) complex containing a chiral, nonracemic substituent that is capable of directing *ortho* lithiation.[6]

We recently introduced chiral ferrocenyl oxazoline palladacycles as catalysts for the asymmetric addition of external (that is, not bound to a metal) nucleophiles to prochiral alkenes.[7] To further explore this general catalyst architecture, we became interested in the synthesis of related η^6-arene chromium(0) complexes. The precursors of the ferrocenyl catalysts were prepared by diastereoselective *ortho* lithiation of enantiopure chiral ferrocenyl oxazolines with alkyl lithium reagents.[8] Unfortunately, this convenient approach cannot be used to prepare (η^6-arene)tricarbonylchromium(0) complexes, as lithium reagents are known to add to such complexes containing strong acceptor substituents such as imines or oxazolines.[1e,5,9] Herein we report that less electron deficient (η^6-arene)dicarbonyl(triphenylphosphane) chromium(0) oxazoline complexes undergo *ortho* lithiation, rather than addition, upon exposure to either *sec*- or *n*-butyllithium, and that, depending on the presence or absence of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA), either diastereomer

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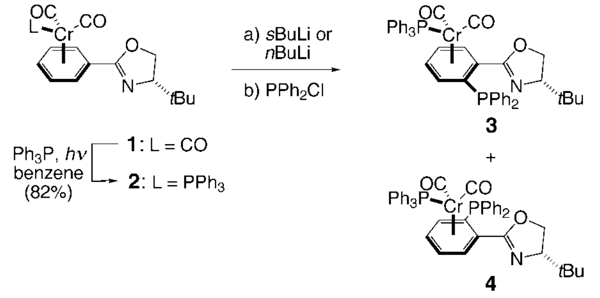
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

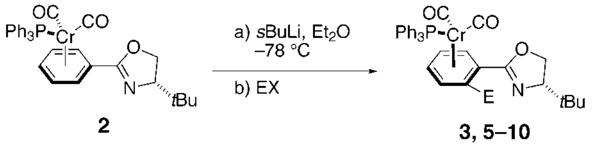
of the 1,2-disubstituted arene chromium(0) complex can be prepared with high selectivity.[10]

Photolytic replacement of a carbonyl ligand[11] of complex **1**[12] by triphenylphosphane provided complex **2** as a crystalline red solid in good yield (Scheme 1). Reaction of **2** with 1.5 equiv of *n*-butyllithium at −78 °C in Et_2O, followed by warming to −30 °C and quenching with chlorodiphenylphosphane provided the chromium(0)-complexed aryl phosphane oxazolines **3** and **4** in a 10:1 ratio. The diastereoselectivity of this transformation was improved when the lithiation was conducted with *sec*-butyllithium at −78 °C and the intermediate organolithium species was trapped at this temperature. By this procedure, diastereomers **3** and **4** were produced in an 18:1 ratio and 59% yield.[13,14] As summarized in Table 1, varying the electrophile allows a variety of related 1,2-disubstituted η^6-arene chromium(0) complexes to be prepared in useful chemical yields and high diastereoselectivities (18–50:1).



Scheme 1. Synthesis of oxazolines **3** and **4** by metalation of **2** and quenching with PPh_2Cl. Diastereoselectivity (**3**:**4**): in Et_2O (−78 °C), 18:1; in Et_2O/TMEDA (−78 °C), 1:50.

Table 1. Metalation of **2** with *s*BuLi in Et_2O.

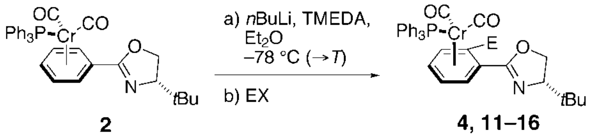


Product	E	EX	yield [%]	d.r.
3	PPh_2	Ph_2PCl	59	18:1
5	SePh	PhSeSePh	59	22:1
6	CO_2Me	MeO_2CCl[a]	56	18:1
7	I	$I(CH_2)_2I$	66	20:1
8	CH(OH)Ph	PhCHO	68	13:1[b]
9	Me	MeI	48	50:1[c]
10	TMS	TMSCl	63	25:1[c]

[a] The ketone product resulting from double aryl lithium addition was not observed. [b] A 1:1 mixture of alcohol epimers was obtained. [c] Reaction was maintained at 4 °C for 18 hours before quenching.

Complexes possessing a planar chiral moiety of the opposite absolute configuration can be formed with high selectivity by a simple modification of the lithiation conditions. Thus, addition of 1.5 equiv of *n*-butyllithium to a solution of oxazoline **2**, TMEDA (1.5 equiv), and Et_2O at −78 °C, followed by quenching at this temperature with chlorodiphenylphosphane provided **4** and **3** in a 50:1 ratio and 81% yield.[13] By using this procedure, various 1,2-disubstituted (η^6-arene)chromium(0) complexes were prepared in excellent chemical yield and diastereoselectivity (10:1–50:1) (Table 2). In some cases, diastereoselection was improved slightly when the reaction mixture was warmed to −30 °C prior to adding the electrophile. Interestingly, although benzylic alcohol **8** was generated as a 1:1 mixture of alcohol epimers (Table 1), diastereomer **14** was produced as a single alcohol epimer (Table 2).

Table 2. Metalation of **2** with *n*BuLi·TMEDA in Et_2O.



Product	E	EX	*T* [°C]	yield [%]	d.r.
4	PPh_2	Ph_2PCl	−78	81	50:1
			−30	86	25:1
11	SePh	PhSeSePh	−78	82	16:1
			−30	78	22:1
12	CO_2Me	MeO_2CCl[a]	−78	60	13:1
			−30	75	17:1
13	I	$I(CH_2)_2I$	−78	69	20:1
			−30	76	13:1
14	CH(OH)Ph	PhCHO	−30	78	10:1[b]
15	Me	MeI	4	38	15:1
16	TMS	TMSCl	4	81	14:1

[a] The ketone product resulting from double aryl lithium addition was not observed. [b] Produced as a single alcohol epimer.

The relative configuration of (η^6-arene)chromium(0) complex **7** was determined by single-crystal X-ray analysis[15] (Figure 1) and that of **10** and **16**[16] by chemical correlation of the latter with the dextrorotatory *S*p enantiomer of tricarbonyl(η^6-2-trimethylsilylbenzaldehyde)chromium(0).[17,18] The relative configurations of other complexes reported in Tables 1 and 2 were assigned by analogy.

Steric interactions between the oxazoline *tert*-butyl substituent, the chromium tripod, and the base should determine

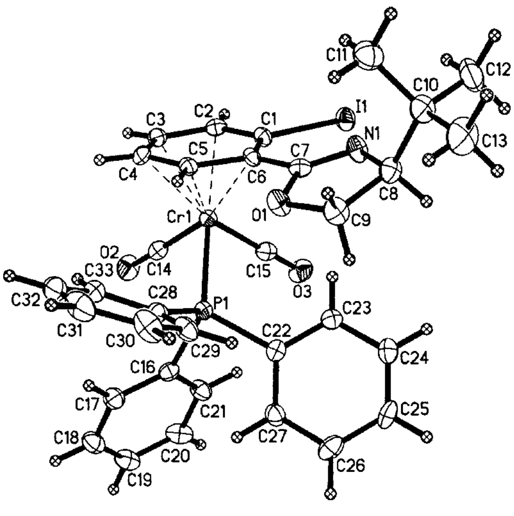
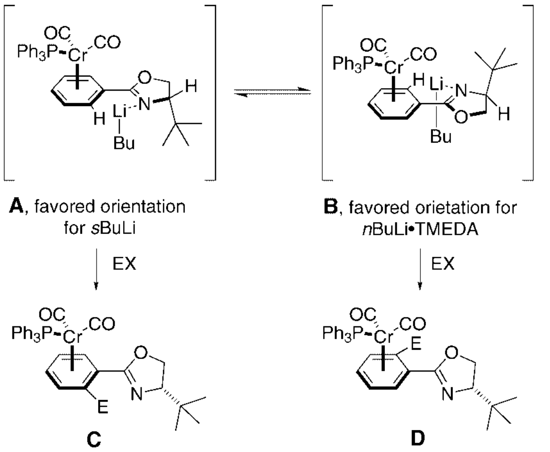


Figure 1. ORTEP representation of the molecular structure of iodide **7**. Torsion angle C6–center of arene-Cr1-P1: 53.9°.

which of the diastereotopic *ortho* hydrogen atoms of **2** is abstracted by lithiation (Scheme 2).[12,19–21] When deprotonation is performed with an alkyl lithium base in Et_2O, destabilizing interactions between the bulky chromium tripod and the *tert*-butyl group apparently favor lithiation in the sense depicted in ensemble **A**.[22] The solid-state structure of iodide **7** provides some indication of the considerable steric bulk of the $\{CrPPh_3(CO)_2\}$ unit (Figure 1).[23] If, as has been suggested, the addition of TMEDA increases the effective size of the base,[21a] deprotonation by the *n*BuLi·TMEDA complex might preferentially proceed via ensemble **B**, in which orientation of the oxazoline substituent towards the chromium tripod allows the bulky nitrogen-coordinated base to approach unhindered from the opposite direction.



Scheme 2. Proposed interactions governing the diastereoselectivity of the metalation reactions.

In summary, (η^6-arene)dicarbonyltriphenylphosphane chromium(0) oxazoline complexes, in contrast to (η^6-arene)-tricarbonyl chromium(0) oxazoline complexes, undergo *ortho* lithiation, rather than addition, upon reaction with alkyl lithium bases in Et_2O. As diastereoselection in this deprotonation can be regulated by the presence or absence of TMEDA, either diastereomer of a variety of enantiopure 1,2-disubstituted (η^6-arene)chromium(0) oxazoline complexes can be prepared in one simple synthetic step. Numerous potential applications of this now readily available family of chiral enantiopure (η^6-arene)chromium(0) complexes are readily envisaged.

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[13] a) Diastereomeric ratios were determined by HPLC analysis of crude reaction mixtures (Alltech Alltima 5 μ SiO_2 column); b) nearly identical stereoselectivity was realized by using 1 equiv of the organolithium reagent; thus, the formation of a small amount of dianion[10] (5–15 % by D_2O quench) when 1.5 equiv of *s*BuLi or *n*BuLi·TMEDA was employed is not critical in obtaining the stereoselectivities we report. On the scale the reactions reported herein were conducted, multiple runs were more reproducible (both in terms of yield and d.r.) when 1.5 equiv of the base was employed.

[14] a) At −78 °C, *n*-butyllithium does not deprotonate **2** at a convenient rate. Stereoselectivity in forming **3** and **4** was unchanged when **2** was was deprotonated with *s*-butyllithium at −78 °C and the reaction warmed to −30 °C prior to quenching; b) deprotonation of **1** with *sec*-butyllithium at −78 °C followed by trapping with Ph_2PCl gave a complex product mixture; the product of lithiation–trapping was not

detected by ESMS analysis of this mixture. Deprotonation of **1** with *n*-butyllithium/TMEDA at −78 °C followed by trapping with Ph_2PCl at −30 °C provided the product of *ortho* lithiation–trapping in low yield.

[15] Crystal structure analysis of **7**: Bruker CCD platform diffractomer, 168(2) K, $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, the structure was solved by direct methods (SHELXTL; G. M. Sheldrick, SHELXTL Version 5.10, Bruker Analytical X-Ray Systems, Inc.; Madison, WI, **1999**); full-matrix least-squares refinement on F^2 (SHELXTL), structure presentation: crystal dimensions $0.22 \times 0.18 \times 0.08$ mm^3, orange crystals, space group $P2_12_12_1$, orthorhombic, $a = 10.0557(5)$ Å, $b = 17.7209(8)$ Å, $c = 19.4695(9)$ Å, $V = 3469.4(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.481$ Mg m^{-3}, $2\theta_{max} = 56.58°$, 42399 measured, 8460 independent reflections, $R = 0.0343$, $wR = 0.0667$, residual electron density = 0.652 e Å^{-3}, hydrogen atoms were included using a riding model. CCDC-187068 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

[16] Diastereomers **10** and **16** could be separated by silica gel chromatography.

[17] Sequential treatment of **16** with a) MeOTf, b) $NaBH_4$, and c) aqueous oxalic acid[18a] provided (*S*p)-tricarbonyl(η^6–2-trimethylsilylbenzaldehyde)chromium(0), $[\alpha]_D^{23} = +151$ ($c = 0.14$ in $CHCl_3$).[18b,c]

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[19] Control experiments established that the selectivities reported in Tables 1 and 2 are largely the result of kinetic control in the lithiation step. For example, generation of the arenyllithium by reaction of iodide **7** with *s*BuLi in Et_2O followed by addition of 10 mol % of **2** and warming to −30 °C in the presence or absence of added TMEDA did not result in significant equilibration. Similarly, treatment of arene **2** with 0.7 equiv *s*BuLi in Et_2O followed by addition of TMEDA (1.5 equiv) also did not result in significant equilibration.

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[21] a) T. Sammakia, H. A. Latham, *J. Org. Chem.* **1995**, *60*, 6002; b) T. Sammakia, H. A. Latham, *J. Org. Chem.* **1996**, *61*, 1629.

[22] Although the lithium aggregate is depicted in **A** to be on the face of the *t*Bu substituent, it alternatively could be oriented towards the chromium tripod.

[23] The effective size of this fragment would obviously depend on the orientation of the Ph_3P ligand. It is interesting to note that the torsion angle measured from the center of the arene to C6 and Cr1 to P1 is 53.9° (see Figure 1).

Enantioselective Synthesis of Substituted Pyrrolidines by Dynamic Resolution**

Iain Coldham,* Samuel Dufour,
Thomas F. N. Haxell, Steven Howard, and
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The formation of enantiomerically enriched products from chiral organolithium species is a highly efficient and selective approach for organic synthesis.[1] The majority of examples involve the selective asymmetric deprotonation of a prochiral hydrogen atom adjacent to an oxygen or nitrogen atom, such as the method developed by the groups of Hoppe and Beak in which *sec*-butyllithium and (−)-sparteine is used as the chiral base.[2] However, an alternative mode of asymmetric induction exists, in which the chiral, racemic organolithium species is formed and complexed with a chiral ligand to promote asymmetric substitution. We report here the first highly enantioselective substitution of nonactivated organolithium species at ambient temperature.

Asymmetric substitution requires, for high yields, a dynamic resolution[3] in which the reacting chiral center can invert under the reaction conditions. Success has been achieved with lithiated allylic or benzylic substrates in the presence of a chiral ligand through either a dynamic thermodynamic or a dynamic kinetic resolution pathway.[4–7] Examples with α-thio and α-seleno organolithium species have also been reported,[8] however, to our knowledge there are no reports of dynamic resolution, followed by addition of an electrophile, of other nonactivated lithiated species. This may be a consequence of the common perception that organolithium species should be generated and treated at low temperature (typically −78 °C); under these conditions, although allylic, benzylic, α-thio and α-seleno organolithium species undergo racemization,[9] nonactivated chiral organolithium species do not normally racemize. For example, α-amino organolithium species display configurational stability at low temperature.[10] We have found, however, that the formation of α-amino organolithium species and their racemization is possible at room temperature.[11] We therefore set out to substitute racemic α-amino organolithium species asymmetrically in the presence of a chiral ligand.

Extending our work on intramolecular carbolithiation,[11,12] we studied the dynamic resolution of chiral 2-lithiopyrrol-

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