to alcohols **20** and subsequent dehydration gave the desired enantiomerically pure 1-(benzyloxycarbonyl)-1,2-dihydropyridines **21a** [$[\alpha]^{23}_D$ −524 (*c* 0.42, $CHCl_3$)] and **21b** [$[\alpha]^{23}_D$ −696 (*c* 1.5, $CHCl_3$)] in 58 and 74% yield, respectively.[19,20]

The door has now been opened to the enantioselective synthesis of various alkaloids via chiral 1-acyl-1,2-dihydropyridine intermediates. Additional studies on the synthesis and synthetic utility of these chiral heterocycles are in progress.

Acknowledgment. We gratefully acknowledge support of this work by the National Institutes of Health and North Carolina State University.

Supplementary Material Available: Experimental details for the preparation of **7a** and **21a** and physical data for **7**, **15**, and **21a,b** (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(19) Dihydropyridines **21** of the opposite configuration can be prepared by using (+)-8-phenylmenthol as the chiral auxiliary. For a procedure on the preparation of 28 g of (+)-8-phenylmenthol, see: Buschmann, H.; Scharf, H.-D. *Synthesis* **1988**, 827.

(20) All new compounds were spectroscopically characterized and furnished satisfactory elemental analyses (C,H,N, ± 0.4%) or high-resolution mass spectra. Details are provided in the supplementary material.

The Asymmetric Metalation of Chiral Arylaldehyde Acetal Chromium Tricarbonyl Complexes

Yoshinori Kondo,[1a] James R. Green,*,[1b] and Jianwei Ho

Department of Chemistry and Biochemistry, University of Windsor, Windsor, Ontario N9B 3P4, Canada

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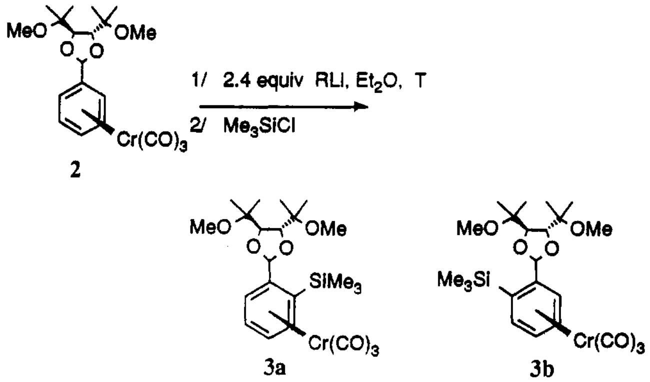
Summary: The chiral chromium tricarbonyl complex of benzaldehyde acetal **2**, derived from (+)-diethyl tartrate, can be metalated by *n*-BuLi and subsequently functionalized by various electrophiles with a minimum of 86% de.

The use of chromium tricarbonyl arene complexes in the synthesis of optically pure compounds has great potential.[2] Especially useful are the complexes of ortho-disubstituted arylaldehyde derivatives, as the chemistry of the carbonyl function in such molecules has been investigated in some depth and many highly asymmetric transformations have been revealed.[3] To this point, the field has been hampered by the limited availability of enantiomerically pure material. Preparation of enantiomerically enriched complexes of this type has been accomplished by classical or kinetic resolution of racemic mixtures.[4] Asymmetric synthesis of such compounds has been restricted to the α-phenethylamine- or ephedrine-derived substrates, which undergo highly diastereoselective ortho metalation[5–7] but where the chiral auxiliary is not readily removable.

Table I. Variation of Base and Conditions on Diastereoselectivity



base	*T* (°C)	yield (%)	**3a**:**3b**	de (%)
t-BuLi	−78	60	50:50	0
	−30	20	34:66	−32
MeLi[a]	−78	5	77:23	54
	−30	50	87:13	74
n-BuLi	−78	80	84:16	68
	−30	75	88:12	76
	−30[b]	90	93:7	86

[a] Low halide concentration (1.4 M MeLi, 0.05 M in halide). [b] Slow addition of *n*-BuLi (2.4 equiv over 1.5 h).

We were intrigued by the possibility of accomplishing asymmetric directed metalation of a monosubstituted arene–$Cr(CO)_3$ complex modified with a removable chiral

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(1) (a) Current address: Department of Heterocyclic Chemistry, Pharmaceutical Institute, Tokohu University. (b) NSERC (Canada) University Research Fellow 1989–1994.

(2) (a) Solladié-Cavallo, A.; Bencheqroun, M. *J. Organomet. Chem.* **1991**, *406*, C15. (b) Solladié-Cavallo, A., In *Advances in Metal-Organic Chemistry*; Liebeskind, L., Ed.; JAI: Greenwich, 1989; Vol. 1, pp 99–133. (c) Kalinin, V. N. *Usp. Khim.* **1987**, *56*, 1190; *Russ. Chem. Rev.* **1987**, *56*, 682 (Engl. trans.).

(3) (a) Solladié-Cavallo, A.; Quazzotti, S.; Colonna, S.; Manfredi, A. *Tetrahedron Lett.* **1989**, *30*, 2933. (b) Solladié-Cavallo, A.; Quazzotti, S. *Synthesis* **1991**, 177. (c) Brocard, J.; Mahmoudi, M.; Pelinski, L.; Maciejewski, L. *Tetrahedron* **1990**, *46*, 6995. (d) Baldoli, C.; Del Buttero, P.; Maiorana, S. *Tetrahedron* **1990**, *46*, 7823. (e) Solladié-Cavallo, A.; Bencheqroun, M. *J. Organomet. Chem.* **1991**, *403*, 159. (f) Mukai, C.; Cho, W.; Kim, I. J.; Kido, M.; Hanaoka, M. *Tetrahedron Lett.* **1990**, *31*, 6893. (g) Mukai, C.; Cho, W. J.; Kim, I. J.; Kido, M.; Hanaoka, M. *Tetrahedron* **1991**, *47*, 3007. (g) Roush, W. R.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 1143. (h) Harrington, P. J. *Transition Metals in Total Synthesis*; John Wiley and Sons: New York, 1990; Chapter 11.

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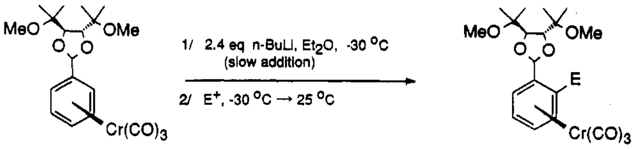
Table II. Electrophiles Incorporated in Lithiation of 2



electrophile	E	compd	yield[a] (%)	de[b] (%)	$[\alpha]^{26.5}_D$
$ClSiMe_3$	$SiMe_3$	**3a**	77	86	−25.0° (c 0.84, $CHCl_3$)
MeI	Me	**4a**	62	92	−63.7° (c 2.29, $CHCl_3$)
$ClSnBu_3$	$SnBu_3$	**5a**	73	91	+3.48° (c 2.01, $CHCl_3$)
$ClPPh_2$	PPh_2	**6a**	69	≥94	+166.4° (c 3.01, $CHCl_3$)
$BrCH_2CH_2Br$	Br	**7a**	64	88	−57.4° (c 0.94, $CHCl_3$)

[a] Yields of diastereomerically pure products. [b] Determined by ^1H NMR of crude reaction mixtures.

auxiliary. We chose to investigate acetal auxiliaries derived from C_2-symmetric diols[8] as directed metalation groups, including the diethyl tartrate derived **2**,[9] by virtue of the ready availability of both enantiomers of the chiral precursor and in anticipation of the ability to convert reaction products to the corresponding arylaldehyde complexes. In the event, chiral acetal **1**, prepared from (+)-diethyl tartrate and benzaldehyde diethyl acetal by a modification of the procedure of Matteson,[9a] could be converted into its chromium tricarbonyl complex, **2**, by standard methods (n-Bu_2O/THF/reflux/24 h) in 88% yield. Complex **2** could be deprotonated by various alkyllithium reagents under a wide range of reaction conditions (Table I) and subsequently functionalized with several electrophiles. We found that when 2.4 equiv of n-BuLi was added slowly (over a 1.5-h period) to a diethyl ether solution of **2** at −30 °C and the resulting anion quenched with Me_3SiCl an unequal mixture of diastereomers **3a**/**b** was formed in high yield. The two diastereomers could be distinguished in the ^1H NMR spectra by their different chemical shifts for hydrogen at the acetal carbon (δ 6.01 ppm versus 5.96 ppm for **3a** and **b**, respectively) and for the hydrogens of the trimethylsilyl function (δ 0.35 ppm versus 0.39 ppm for **3a** and **b**, respectively). Integration of the acetal hydrogen resonances of the diastereomeric mixture gave relative values of 93:7, or an 86% de. In the cases of the other electrophiles studied it was more convenient to compare the acetal hydrogen resonance of the major diastereomer with that of the lowest field arene hydrogen of the minor diastereomer. Integration of these signals revealed diastereomeric excesses of 92% (**4a**), 91% (**5a**), and 88% (**7a**) (Table II). In the case of chlorodiphenylphosphine (**6a**), the minor diastereomer could not be detected in the ^1H NMR of the crude product; we estimate a ≥94% de for **6a**. In all cases the major diastereomer could be isolated in a pure state following silica gel chromatography. In the trimethylsilyl substitution case, a small amount (4%) of the minor diastereomer **3b** was also isolated. Lower, and in some cases inverted, asymmetric induction was observed with other bases or under other conditions. The sense of chirality induced was deduced in two ways. The major trimethylsilyl-substituted product **3a** gave suitable crystals for X-ray structural analysis (Figure 1),[10] which revealed a $1R,2S$ configuration at the chiral centers on the arene ring. Also, when the incorporated electrophile was MeI, the purified major diastereomer **5a** could be hydrolyzed (10:1 benzene/60% aqueous H_2SO_4, 65% yield, 80% yield based on recovered starting material) to afford the known complex (−)-**8**.[11] Both pieces of information indicate

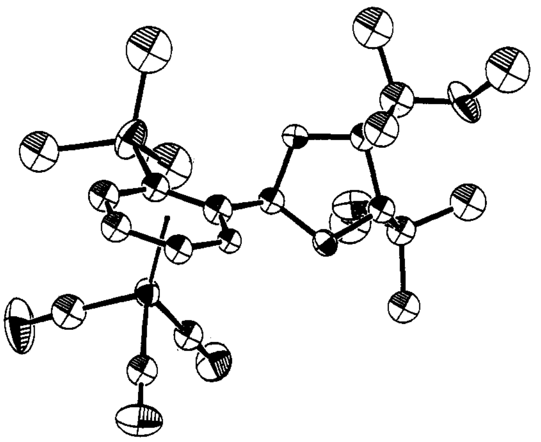
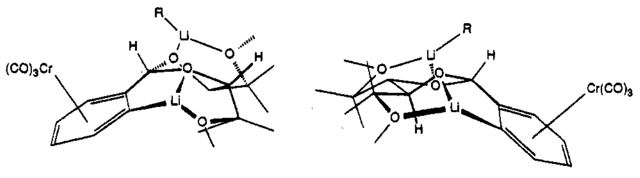


Figure 1. ORTEP drawing of **3a** based on X-ray coordinates.



favored
A (*pro-R*)

less favored
B (*pro-S*)

Figure 2. Competitive aryllithiums for *pro-R* versus *pro-S* abstraction.

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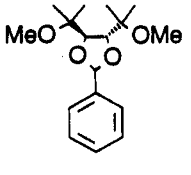
(8) (a) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581. (b) Alexakis, A.; Mangeney, P. *Tetrahedron: Asymmetry* **1990**, *1*, 477.

(9) For other uses of the diol from which **2** is derived, see: (a) Matteson, D. S.; Michnick, F. J. *Organometallics* **1990**, *9*, 3171. (b) Hoppe, I.; Schöllkopf, U.; Nieger, M.; Egert, E. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1067. (c) Nash, E. A.; Nelson, K. A.; Heidt, P. C. *Tetrahedron Lett.* **1987**, *28*, 1865. (d) Chapuis, C.; Jurczak, J. *Helv. Chem. Acta* **1987**, *70*, 436.

(10) Compound **3a** crystallized in the space group $P2_12_12_1$. The unit cell parameters were determined to be a = 11.868 (4) Å, b = 19.528 (7) Å, c = 11.431 (3) Å. The unit cell contains four asymmetric units of molecular formula $C_{23}H_{34}O_7SiCr$ in a volume of 2649 (3) $Å^3$ which produces a calculated density of 1.260 g/cm^3. A total of 2673 reflections were recorded in the range $2\theta < 50°$ with a Rigaku AFC6S diffractometer using the θ–2θ scan routine and Mo Kα radiation λ = 0.71069 Å). After Lorentz and polarization corrections and an empirical absorption correction, the structure was solved by the TEXSAN 9 package. The positions of all hydrogen atoms were calculated assuming a 0.95 Å C–H distance. The final agreement factors are R = 0.0644 and R_w = 0.0647 for 1039 unique, observed reflections $[F_0 > 3\sigma(F_0)]$ and 162 independent variables.

(11) (a) Solladié-Cavallo, A.; Solladié, G.; Tsamo, E. *J. Org. Chem.* **1979**, *44*, 4189. The observed optical rotation, $[\alpha]^{26.5}_D$ = −628° (c 0.25, $CHCl_3$), was slightly different from the literature value, $[\alpha]^{20}_D$ = −664° (c 0.26, $CHCl_3$). However, the presence of the minor enantiomer was not detectable using $Eu(hfc)_3$, the shift reagent employed by Solladié-Cavallo for the determination of the optical purity for this compound. (b) Solladié-Cavallo, A.; Suffert, J. *Magn. Res. Chem.* **1985**, *23*, 739.

preferential abstraction of the *pro-R* proton.



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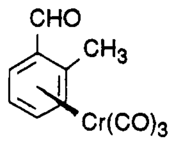

(-)-8

An understanding of the mechanistic reasoning for the observed selectivities is complicated by several facts. First, 2 equiv of base are required for complete arene deprotonation. Also, there is evidently both a kinetic and a thermodynamic diastereoselectivity of deprotonation, and they are in some cases quite dissimilar. Furthermore, the results vary greatly with the choice of base. Finally, it is well established that alkyl- and aryllithiums are rarely monomeric in solution.[12] Nevertheless, it is clear, in the most successful case, that the high diastereoselectivity observed is thermodynamic in origin. We envision that there is a competition between diastereomeric aryllithium species A and B (Figure 2), with the former having a cis-fused 5,5-ring system versus the trans-fused 5,5-system of the latter. Since a 6.0 kcal relative stabilization of the cis over the trans 5,5-fused ring system is known for the all-carbon framework,[13] A would be the preferred aryllithium. This corresponds to abstraction of the *pro-R* hydrogen, which is in agreement with experiment. We have included a second molecule of alkyllithium base, complexed to the remaining oxygen atoms of the auxiliary, in the aryllithium species. The reason for the necessity of this second equivalent is unknown at this time.

Acknowledgment. We are grateful for the Natural Sciences and Engineering Research Council (NSERC) of Canada for financial support.

Supplementary Material Available: Complete spectral details for compounds **2**–**8** (including experimental details) and crystallographic data for compound **3a** (including atomic coordinates, thermal parameters, bond distances, and bond angles) (12 pages). Ordering information is given on any current masthead page.

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[12] For a list of references on alkyllithium aggregation, see: (a) Fraenkel, G.; Chow, A.; Winchester, W. R. *J. Am. Chem. Soc.* **1990**, *112*, 6190. For aryllithium aggregation studies, see: (b) Harder, S.; Boersma, J.; Brandsma, L.; van Heterten, A.; Kanters, J. A.; Bauer, W.; Schleyer, P.v.R. *J. Am. Chem. Soc.* **1988**, *110*, 7802. (c) Setzer, W. N.; Schleyer, P.v.R. *Adv. Organomet. Chem.* **1985**, *24*, 353.

[13] Barrett, J. W.; Linstead, R. P. *J. Chem. Soc.* **1936**, 611.

Articles

Preparation and Isomerization of 1-Phenylseleno 1,3-Dienes

Michael D. Fryzuk,*,† Gordon S. Bates, and Charles Stone

Department of Chemistry, University of British Columbia, 2036 Main Mall,
Vancouver, British Columbia V6T 1Z1, Canada

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The preparation of a series of 1-phenylseleno 1,3-dienes is described starting from enyne derivatives via a hydrozirconation/transfer sequence. Hydrozirconation of a series of conjugated enynes having the general formula $HC{\equiv}CCR^1{=}CR^2R^3$ (**3a**: $R^1 = R^2 = R^3 = H$; **3b**: $R^1 = R^3 = H$, $R^2 = OMe$; **3c**: $R^1 = R^2 = H$, $R^3 = OMe$; **3d**: $\underbrace{R^1 = R^2} = -(CH_2)_4-$, $R^3 = H$) leads to the formation of zirconium dienyls of the formula $(\eta^5\text{-}C_5H_5)_2Zr(Cl){-}CH{=}CHCR^1{=}CR^2R^3$, **4a**–**d**, respectively; this reaction is both completely stereoselective and chemoselective. Use of the deuterium-substituted reagent $(\eta^5\text{-}C_5H_5)_2Zr(D)Cl$ generates the corresponding isotopomers $(\eta^5\text{-}C_5H_5)_2Zr(Cl){-}CH{=}CDCR^1{=}CR^2R^3$, **4a**–**d**-$d_1$. Addition of PhSeX (X = SePh, Cl, or *N*-phthalimido) to the zirconium dienyl derivatives **4a**–**d** at low temperature (−20 °C) and in the dark results in the formation of the 1-phenylseleno 1,3-dienes ($PhSeCH{=}CHCR^1{=}CR^2R^3$ (**5a**: $R^1 = R^2 = R^3 = H$; **5b**: $R^1 = R^3 = H$, $R^2 = OMe$; **5c**: $R^1 = R^2 = H$, $R^3 = OMe$; **5d**: $\underbrace{R^1 = R^2} = -(CH_2)_4-$, $R^3 = H$). This transfer of the dienyl unit from zirconium to selenium proceeds with complete stereoselectivity and with retention of configuration at the 1-position as long as light is excluded and the reaction is carried out at low temperatures. In the presence of room light (fluorescent), mixtures of stereoisomers are obtained for the seleno dienes **5a**–**c**; no apparent isomerization is observed for **5d**; similar results are obtained upon thermolysis (80 °C for 24–48 h). The mechanism of this isomerization process was determined to be intermolecular on the basis of crossover experiments; in addition, the use of radical traps established that the process was a radical chain mechanism, probably via addition of $PhSe^{\bullet}$ to the seleno diene followed by single-bond rotation.

Introduction

The synthesis of dienes for use in the Diels–Alder reaction[1,2] is still an important challenge in organic synthetic chemistry.[3,4] One particularly attractive approach has been the incorporation of heteroatom substituents[5] that can both activate the diene, thereby extending the range of workable dienophiles, and also provide a focal point for

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[†] E. W. R. Steacie Fellow, 1990–92.

[1] Wolliveber, H. *Diels-Alder Reaction*; Georg Thieme Verlag: Stuttgart, 1972.

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[3] March, J. *Advanced Organic Chemistry*; 2nd ed.; McGraw-Hill: Toronto, 1977.

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