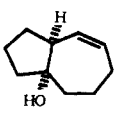
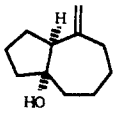
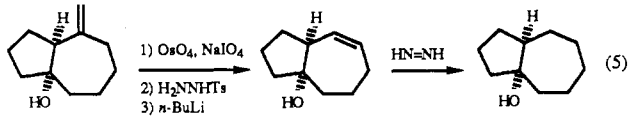
Table I. Chemical Shifts of the Bridgehead Allylic Hydrogens of 3a-b in $CDCl_3$ and Pyridine-d_5

	 3a	 3b
δ (pyridine-d_5)	2.95	2.87
δ ($CDCl_3$)	2.63	2.53
$\Delta\delta$	0.32	0.34

9 (4 equiv of KH, 0.4 equiv of I_2,[11] THF, 65 °C, 1.5 h, 75%) led to *cis*-cyclodecenone **10** (J_{alkene} = 10.7 Hz). Fluoride treatment of **10** (2 equiv of *n*-Bu_4NF, THF, 65 °C, 3.5 h, 95%) led to the same hydroazulenol **3a** previously obtained from the *trans*-cyclodecenone **2b**.

The cis stereochemistry of the ring fusion in bicyclo[5.3.0]decan-1-ols **3a-b** was ascertained both from spectroscopic data and by chemical transformations. In cyclic systems, it is known that the ^1H NMR chemical shifts of a hydrogen that is vicinal and syn to a hydroxyl group is deshielded and shifted downfield in pyridine-d_5 relative to the chemical shift of that same hydrogen in $CDCl_3$.[14] Such a deshielding for the allylic bridgehead hydrogen of **3a-b** would be observed for the cis ring fusion, but not for the trans ring fusion, since the deshielding is a through-space effect from the complexation of the pyridine with the hydroxyl group. A comparison of the ^1H NMR spectra taken in $CDCl_3$ and in pyridine-d_5 for **3a-b** revealed a greater than δ 0.3 shift for the bridgehead allylic hydrogen, which is consistent with a cis, but not a trans ring fusion for **3a-b**.

The cis stereochemistry of the ring fusion was further demonstrated by the conversion of **3b** into **3a**, and the reduction of **3a** into the known, fully saturated hydroazulenol **11** (eq 5). Oxidative cleavage of the alkene (0.01



(5)

3b **3a** **11**

equiv of OsO_4, 2.5 equiv of $NaIO_4$, 3:1 dioxane/H_2O, 0 °C → room temperature, 2 h, 88%) led to the corresponding ketone,[15] which was further subjected to the Shapiro reaction (1.1 equiv of H_2NNHTs, <0.01 equiv of *p*-TsOH, MeOH, room temperature 1 h; excess *n*-BuLi, -75 °C → -15 °C, 20 h, 25%) to give hydroazulenol **3a** that was identical by ^{13}C NMR spectroscopy with **3a** prepared from allylsilane cyclization of **2a**. **3a** itself could be reduced with diimide (3 equiv of $KO_2CN{=}NCO_2K$, 6 equiv of HOAc, 12 equiv of pyridine, MeOH, room temperature, 1 h, 95%) to the hydroazulenol **11**. Both the cis and trans ring fusion isomers of bicyclo[5.3.0]decan-1-ol are known compounds,[16] and the ^{13}C NMR spectrum of **11** was identical with that published for the cis isomer.

In conclusion, we have successfully demonstrated that our two-step methodology efficiently converts 1,2-divinylcyclohexanols into bicyclo[5.3.0]decan-1-ols. This methodology leads to one-carbon ring expansion of the cyclohexane nucleus with concomitant cyclopentane annulation. For the substrates so far examined, the use of fluoride-induced allylsilane cyclization results in formation of only the cis ring fusion in the hydroazulenols. The ease of preparation of the divinylcyclohexanols allows for both the synthesis of additional cyclodecenones and the study of their cyclization to hydroazulenols. Such studies are in progress, and will be reported in due course.

Acknowledgment. We thank the Robert A. Welch Foundation, the National Institutes of Health, and the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for their generous support for this research. Exact mass spectral data were obtained at the Michigan State University Mass Spectroscopy Facility, which is supported, in part, by a grant (DRR-00480) from the Biotechnology Research Branch, Division of Research Resources, National Institutes of Health. We also thank Dr. Whe-Narn Chou for obtaining the NMR spectroscopic data.

Supplementary Material Available: Complete spectroscopic data (IR, ^1H and ^{13}C NMR, and MS) for all compounds, HRMS on key intermediates, and complete experimental details plus NMR spectra (63 pages). Ordering information is given on any current masthead page.

(14) Demarco, P. V.; Farkas, E.; Doddrell, D.; Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480-6.

(15) This β-hydroxy ketone has been previously prepared, but no ^{13}C NMR data has been reported. The coupling constant observed in the ^1H NMR spectrum for the bridgehead hydrogen alpha to the ketone (t, J = 8 Hz) is the same as that reported by Warner, Jacobson, et al. for the isomer with the cis ring fusion. Warner, P. M.; Lu, S.-L.; Myers, E.; DeHaven, P. W.; Jacobson, R. A. *J. Am. Chem. Soc.* **1977**, *99*, 5102-18. See also: House, H. O.; Lee, J. H. C.; VanDerveer, D.; Wissinger, J. E. *J. Org. Chem.* **1983**, *48*, 5285-8.

(16) (a) Crandall, J. K.; Magaha, H. S.; Henderson, M. A.; Widener, R. K.; Tharp, G. A. *J. Org. Chem.* **1982**, *47*, 5372-80. (b) Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1986**, *51*, 1778-86.

1,4-Addition of Optically Active Transferable Ligands from Organocuprates. Generation and Reaction of Homochiral α-Alkoxyorganocuprates

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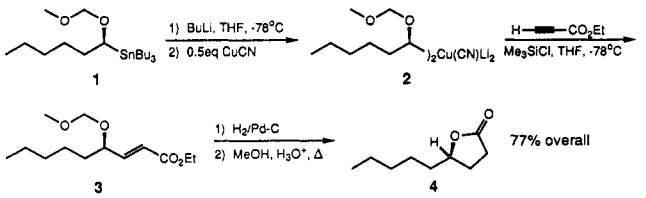
Summary: Homochiral higher order cyano α-alkoxyorganocuprate addition to ynoates and enones occurs with 0-97% retention of configuration; results that imply multiple reaction pathways may be operative in 1,4-addition reactions of these species.

Organocuprate reagents are now commonplace in synthetic organic chemistry as a method for the regioselective

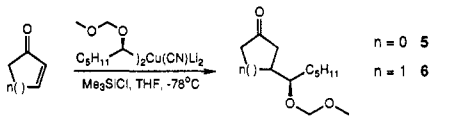
Scheme I



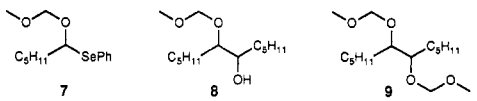
and stereoselective construction of carbon–carbon bonds.[1] In contrast, the basic understanding of cuprate structure and reaction mechanism remains limited.[2] Further knowledge of the reaction mechanism for 1,4-addition is of critical importance for the application of organocuprates in asymmetric synthesis. Enantioselective organocuprate addition reactions to enones rely on nontransferable asymmetric ligands[3] or on chirality elements present in the substrate.[2e,4] Previous studies have involved the transfer of racemic or nonchiral ligands from the cuprate to the electrophilic acceptor. Interestingly, no systematic studies of the transfer of optically active ligands from cuprates have been reported.[5] We would like to report herein our initial results on the generation and 1,4-addition reactions of homochiral α-alkoxyorganocuprate reagents as a probe for the study of organocuprate reaction mechanism.

α-Alkoxyorganostannanes are available in homochiral form by the asymmetric reduction of acyl stannanes.[6] Still and Sreekumar[7] and Chong and co-workers[8] have amply demonstrated that optically active α-alkoxyorganostannanes undergo transmetalation to the lithio species and subsequently react with a variety of electrophiles with retention of configuration. Racemic α-alkoxyorganocuprates have been prepared from secondary and tertiary α-alkoxyorganolithio anions and provide 1,4-addition reaction products in high yield.[9]

An asymmetric synthesis of (+)-γ-pelargonolactone[10] was carried out as illustrated in Scheme I. Chiral (*S*)-α-alkoxyorganostannane **1** (99% ee) was prepared as described.[11] Generation of the higher order cyano cuprate **2**[9] and 1,4-addition to ethyl propiolate in the presence of trimethylsilyl chloride[12] provided the unsaturated ester **3** in 85% yield. Hydrogenation and lactonization directly provided (+)-γ-pelargonolactone **4** in 77% overall yield. The lactone was obtained nearly optically pure (96% ee) as determined by optical rotation measurement.[13] Cuprate formation and 1,4-addition had occurred with 97% retention of configuration. Surprisingly, upon repetition of the sequence **4** was isolated with a much lower optical rotation, corresponding to only 60% retention of configuration for the cuprate transferred ligand. Further trials resulted in a range of 0–97% retention of configuration. Reactions of homochiral **2** with cyclohexenone and cyclopentenone were also carried out under the same reaction conditions.[9,12] The optical purity of the homoaldol type products **5** and **6** was determined by hydrolysis of the MOM protecting group and conversion of the alcohol to the Mosher ester.[14] ^{19}F NMR at 470 MHz achieved base-line resolution for the Mosher ester derivative of **6** but not for **5**. The ^{19}F NMR spectrum determined the diastereoselectivity for the 1,4-addition reaction (verified by GC) as well as the % ee for the alcohol chiral center. The 3-alkylated cyclohexanone **6** was obtained from several trials (chemical yields 65–98% with no trace of 1,2-addition) in only 0–20% ee!



The possibility of a simple radical 1,4-addition to provide **6** was ruled out by reaction of α-alkoxyalkyl phenyl selenide **7** with cyclohexenone.[15] The 1,4-addition product **6** was obtained from the radical addition reaction, albeit in 18% yield. More significantly, the diastereoselectivity of the radical addition was observed as 50:50 while the cuprate **2** reaction produces **6** with 70:30 selectivity in >90% yield. Examination of the crude reaction products from the cuprate additions to ethyl propiolate and cyclohexenone revealed the presence of traces of dimeric byproducts **8** and **9**.[9a] Although the chemical yield of **8** never



exceeded 5% in any reaction (<0.1% yield for **9**), an apparent correlation of an increasing dimer **8** to product (**3** or **6**) ratio with a decrease in the optical purity of the product was noted. The dimer does not arise by simple 1,1-reductive elimination from a cuprate species nor by fragmentation and radical coupling. An independent synthesis of dimer **9** and subjection of a sample of **9** to cuprate reaction and workup conditions[16] did not provide

(1) (a) Posner, G. H. *Org. React.* **1972**, *19*, 1–114. (b) Posner, G. H. *An Introduction to Synthesis Using Organocuprate Reagents*; Wiley: New York, 1980. (c) Lipschutz, B. H. *Synthesis* **1987**, 325–341.

(2) For lead references to organocuprate structures, see: (a) van Koten, G.; Jastrzebski, J. T. B. H. *Tetrahedron* **1989**, *45*, 569–578. (b) Olmstead, M. M.; Power, P. P. *J. Am. Chem. Soc.* **1989**, *111*, 4135–4136. For organocuprate mechanistic studies (1,4-addition), see: (c) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59–67. (d) Krauss, S. R.; Smith, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 141–148. (e) Corey, E. J.; Hannon, F. J.; Boaz, N. W. *Tetrahedron* **1989**, *45*, 545–555. (f) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015–6018. (g) Bertz, S. H.; Smith, R. A. *J. Am. Chem. Soc.* **1989**, *111*, 8276–8277. (h) Smith, R. A. J.; Vellekoop, A. S. *Tetrahedron* **1989**, *45*, 517–522. (i) Christenson, B.; Olsson, T.; Ullenius, C. *Tetrahedron* **1989**, *45*, 523–534.

(3) (a) Corey, E. J.; Naef, R.; Hannon, F. J. *J. Am. Chem. Soc.* **1986**, *108*, 7114–7116. (b) Bertz, S. H.; Dabbogh, G.; Sundararajan, G. *J. Org. Chem.* **1986**, *51*, 4953–4959. (c) Dieter, R. K.; Tokles, M. *J. Am. Chem. Soc.* **1987**, *109*, 2040–2046. (d) Villacorta, G. N.; Rao, C. P.; Lippard, S. J. *J. Am. Chem. Soc.* **1988**, *110*, 3175–3182. (e) Rossiter, B. E.; Eguchi, M. *Tetrahedron Lett.* **1990**, *31*, 965–968.

(4) For examples of asymmetric 1,4-addition reactions, see, inter alia: (a) Pan, Y.; Hutchinson, D. K.; Nantz, M. H.; Fuchs, P. L. *Tetrahedron* **1989**, *45*, 467–478. (b) Oppolzer, W.; Kingma, A. J.; Poli, G. *Tetrahedron* **1989**, *45*, 479–488 and references therein.

(5) To our knowledge there are few examples of optically active organocuprate reagents. One example of an optically active cuprate derived from glucose has been reported to undergo 1,4-addition to cyclohexenone with retention of configuration; Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1987**, *109*, 4930–4939.

(6) (a) Chan, P. C. H.; Chong, J. M. *J. Org. Chem.* **1988**, *53*, 5586–5588. (b) Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043–1052.

(7) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201–1202.

(8) (a) Chong, J. M.; Mar, E. K. *Tetrahedron* **1989**, *45*, 7709–7712. (b) Chong, J. M.; Mar, E. K. *Tetrahedron Lett.* **1990**, *31*, 1981–1984. (c) Chan, P. C. M.; Chong, J. M. *Tetrahedron Lett.* **1990**, *31*, 1985–1988.

(9) (a) Linderman, R. J.; Godfrey, A.; Horne, K. *Tetrahedron* **1989**, *45*, 495–506. (b) Linderman, R. J.; McKenzie, J. M. *Tetrahedron Lett.* **1988**, *29*, 3911–3914.

(10) Font, J.; Cardellach, J.; Ortuno, R. M. *J. Heterocycl. Chem.* **1984**, *21*, 327–331.

(11) Stannane **1** was prepared as described in ref 6. The optical purity of **1** was determined by ^{19}F NMR and GC analysis of the Mosher ester derivative.

(12) Linderman, R. J.; McKenzie, J. M. *J. Organomet. Chem.* **1989**, *361*, 31–42 and references therein.

(13) **4** $[\alpha]_D$ observed +42.98°, c = 2.4 (CH_2Cl_2) [lit.[10] +44.6°, c = 2.4 (CH_2Cl_2) and +45.52°, c = 1.0 (CH_3OH), lit.[10] +47.2°, c = 1.0 (CH_3OH).

(14) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.

(15) Selenide **7** was prepared from racemic **1** via (1) BuLi, THF, −78 °C; (2) PhSeBr. 1,4-Addition of **7** to cyclohexenone was carried out in refluxing benzene with Bu_3SnH (1.1 equiv) and catalytic AIBN.

(16) A sample of **9** was added to $Bu_2Cu(CN)Li_2$. Cyclohexenone and trimethylsilyl chloride were then added to the mixture at −78 °C. The reaction was quenched with aqueous NH_4Cl after 3 h.

any of the "MOM-OH" dimer 8. Therefore, 8 does not arise by partial hydrolysis of 9. Indeed, we were unable to prepare the "diMOM" dimer 9 by radical coupling of 7 using AIBN/Bu_3SnH, but instead had to resort to flash vacuum pyrolysis.[17] Traces of oxygen or Cu(II) salts are known to initiate dimerization of organocuprates.[1] Homochiral cuprate 2 was prepared in THF, and Cu(II) salts and oxygen were added in separate experiments. Upon aqueous quench, the Cu(II) addition reaction provided only protonated material while the oxygen addition reaction did provide 8 in 40% yield. GC analysis of 8 from the oxygen dimerization reaction determined that the % de corresponded to that obtained by simple condensation of the α-alkoxyorganolithio anion with hexanal. Mosher esterification and ^{19}F NMR analysis of 8 revealed that the dimer had been obtained with >90% retention of configuration! This unexpected result implies that racemization of the α-alkoxyalkyl ligand does not occur during cuprate formation (Li to Cu transmetalation), but most likely occurs during the 1,4-addition reaction. Equilibration of the cuprate and free RLi species is not a reasonable explanation for dimer formation given the fact that 1,2-addition to the enone is not observed.[18] In addition, the cuprate 2 does not add to aliphatic aldehydes even in the presence of trimethylsilyl chloride. The dimer 8 may arise by an oxygen-catalyzed decomposition pathway which produces hexanal and RLi. Rapid 1,2-addition of the lithio species to the aldehyde (perhaps mediated by a Cu template?) would then occur providing optically active 8. Single electron transfer processes were initially proposed as the mechanism of cuprate 1,4-addition.[2c] Previous studies have indicated that electron-transfer processes from cuprates are restricted in polar solvents such as THF and by the use of additives such as trimethylsilyl chloride.[2h] The reaction conditions employed in this study were therefore not optimal for electron transfer. Arguments favoring a stepwise process of d-π* complexation followed by a reversible β-Cu(III) intermediate have also been offered.[2d-i] Racemization of the transferable ligand observed in the 1,4-addition reactions of 2 during a direct oxidative addition of the cuprate to the enone or in a final reductive elimination step seems unlikely. Apparently, adventitious oxygen leads to the initiation of the racemization process (mechanism unknown) as well as dimerization. 1,4-Addition occurs at a faster relative rate than dimerization; however, racemization is extremely facile only for the 1,4-addition reaction. Even the small amounts of "MOM-OH" dimer 8 isolated from the 1,4-addition reactions to cyclohexenone exhibit a significant level of optical activity (≥80% retention of configuration).

Early work in cuprate chemistry revealed that cuprate reagents could undergo 1,4-addition reactions with retention of configuration (relative), and other more recent examples have also been reported.[19] The results presented in this paper indicate that more than one mechanism may be operative for organocuprate 1,4-addition.[2] The reaction pathway may be dependent on the type of cuprate[2h] and the transferable ligand as well as the substrate.[20] Secondary homochiral α-alkoxyorganocuprates can undergo 1,4-addition reactions with complete retention of configuration; however, this result is not readily reproducible. Further studies on the racemization of these organocuprate reagents and the novel formation of optically active dimeric species by oxidative dimerization processes are underway.

Acknowledgment. R.J.L. would like to thank the American Cyanamid Co. for an Academic Award (1989) and B.D.G. thanks the Burroughs-Wellcome Fund for fellowship support.

(17) Selenide 7 was subjected to flash vacuum pyrolysis conditions reported for alkyl, aryl selenides (650 °C, 0.5 mmHg); Misumi, S.; Higuchi, H.; Otsubo, T.; Ogura, F.; Yamaguchi, H.; Sakata, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 182–187.

(18) Lipshutz and co-workers have provided NMR evidence for equilibration processes in Gilman reagents: Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *J. Am. Chem. Soc.* **1985**, *107*, 3197–3204. Higher order (HO) cyano cuprates apparently do not exhibit the same characteristics in that free RLi is not present. For recent discussions on the solution structures of HO cyano cuprates, see: Lipshutz, B. H.; Sharma, S.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 4052–4054. Bertz, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 4051–4052.

(19) See, inter alia: (a) Whitesides, G. M.; Kendall, P. E. *J. Org. Chem.* **1972**, *37*, 3718–3725. (b) Morgans, D. J.; Feigelson, G. B. *J. Am. Chem. Soc.* **1983**, *105*, 5477–5479.

(20) For more recent mechanistic discussion, see: (a) Dorigo, A. E.; Morokuma, K. *J. Am. Chem. Soc.* **1989**, *111*, 6524–6536. (b) Corey, E. J.; Hannon, F. J. *Tetrahedron Lett.* **1990**, *31*, 1393–1396. Evidence for multiple reaction pathways has been presented by several research groups, see ref 2 and references cited therein.

Palladium-Catalyzed Reductive Coupling of Aromatic Acid Chlorides with Disilanes

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Summary: Electron-deficient aromatic acid chlorides are converted to biphenyl compounds by palladium-catalyzed reaction with disilanes.

Synthetic routes to biphenyl derivatives remain limited.[1] Ullmann coupling of aryl halides with copper or nickel and Gomberg–Bachman coupling of arenes with aromatic diazonium salts are often employed, but both methods have drawbacks. Other traditional approaches involve stoichiometric use of organometallic reagents, such as Grignards, arylthallium, arylmercury, and aryllithium compounds, or require forcing conditions as with Friedel–Crafts arylation. Limitations inherent in these and other routes have fostered continuing interest in a variety of new synthetic methods including modified Ullmann reactions, coupling of tellurium and bismuth reagents, aryltin reactions, cross-coupling reactions, and others.[2] In this context

(1) For overviews of this area, see: (a) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1985. (b) Sainsbury, M. *Tetrahedron* **1980**, *36*, 3327.

0022-3263/90/1955-5430$02.50/0