Acknowledgment. Financial support provided by the NSF (Grant CHE 87-03757), the donors of the Petroleum Research fund, administered by the American Chemical Society, and (in part) the Committee on Research, UCSB, is gratefully acknowledged. We are indebted to Otto Loeffler (Argus Chemical Co.) for supplying the Me_2SnCl_2[2a] used to prepare the initial precursor to **5** and **6**.

Registry No. **2**, 17955-46-3; **3a**, 80473-69-4; **3b**, 80473-70-7; **4**, 122539-76-8; **5**, 97877-91-3; **6**, 122539-75-7; **7**, 122539-77-9; **8**, 122539-78-0; $MeOC_6H_4$-*p*-$(CH_2)_2SnBu_3$, 122539-61-1; (*E*)-$Bu_3SnCH{=}CH(CH_2)_2OH$, 107399-01-9; $H_2C{=}C(SnBu_3)(CH_2)_2OH$, 122229-78-1; (*E*)-$HOCH_2CH{=}C(SnBu_3)CH_2OH$, 103223-42-3; (*E*)-$HOCH_2CH{=}CHSiMe_2$(*t*-Bu), 122539-65-5; (*E*)-$HOC(CH_3)_2CH{=}CHSiMe_2C(CH_3)_2CH(CH_3)_2$, 122539-66-6; (*E*)-$HO(CH_2)_2CH{=}CHSiMe_2C(CH_3)_2CH(CH_3)_2$, 122539-67-7; (*E*)-$HO(CH_2)_2C(CH_3){=}CHSiMe_2C(CH_3)_2CH(CH_3)_2$, 122539-68-8; (*E*)-(*t*-Bu)$SiMe_2CH_2CH{=}C(CH_3)CH_2OH$, 122539-69-9; (*Z*)-(*t*-Bu)$SiMe_2CH_2CH{=}C(CH_3)CH_2OH$, 122539-70-2; $MeOC_6H_4$-*p*-$(CH_2)_2Br$, 14425-64-0; $MeOC_6H_4$-*p*-$(CH_2)_2Cl$, 18217-00-0; $HC{\equiv}C(CH_2)_2OH$, 927-74-2; $HOCH_2C{\equiv}CCH_2OH$, 110-65-6; $HC{\equiv}CCH_2OH$, 107-19-7; $HC{\equiv}CC(CH_3)_2OH$, 115-19-5; (*E*)-$HO(CH_2)_2C(CH_3){=}CHI$, 78592-73-1; ethyl 1-(tributylstannyl)-1-cyclopentenecarboxylate, 122539-62-2; *trans*-4-isopropyl-3-(tributylstannyl)cyclohexanone, 122539-63-3; 3-methyl-3-(tributylstannyl)cyclopentanone, 122539-64-4; 3-(dimethylhexylsilyl)-3,5,5-trimethylcyclohexanone, 122539-71-3; *trans*-3-(dimethyl-*tert*-butylsilyl)-4-isopropylcyclohexanone, 122539-72-4; 3-(dimethyl-*tert*-butylsilyl)-3-methylcyclopentanone, 122539-73-5; trifluoromethyl 2-(ethoxycarbonyl)-1-cyclohexenesulfonate, 122539-74-6; 4-isopropylcyclohex-2-enone, 500-02-7; 3-methylcyclopent-2-enone, 2758-18-1; 2-methyl-2-vinyloxirane, 1838-94-4; 3,5,5-trimethylcyclohex-2-enone, 78-59-1.

Understanding Allylic Organocuprates: σ- or π-Bound Reagents?

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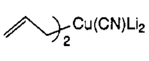
Summary: The nature of both lower and higher order cuprates containing allylic ligands has been investigated using variable-temperature, high-field ^{13}C NMR experiments. From these studies, the σ- vs π-bound state of these reagents has been unequivocally determined.

Sir: Notwithstanding the vast array of highly valued organocuprates composed of sp^2- and sp^3-based ligands,[2] there is a noticeable lack of successful examples involving Michael transfer of a simple allylic moiety.[3] Still fewer reports exist wherein carbon-substituted units (e.g., methallyl, prenyl, etc.) are effectively delivered.[4] Frustration over the noncharacteristic lack of chemospecificity of allylic cuprates, especially in conjugate addition schemes,[5a] has lead to the proposal that π-allyl rather than σ-bound reagents (Figure 1) account for their frequent non-cuprate-like behavior.[5b] We now report that by virtue of variable-temperature ^{13}C NMR spectroscopy, the precise nature of allyl ligand-containing cuprates, of both the lower order (L.O.) and higher order (H.O.) variety, has been ascertained. Moreover, the insight thereby provided has implications for synthetic uses of these reagents.[6]

Our studies began with the H.O. diallylcuprate **3**, prepared in THF from allyltributylstannane (**2**) via treatment with *n*-BuLi (1 equiv) at −78 °C followed by addition to LiCl-solubilized CuCN (0.5 equiv)[7] at −78 °C. ^{13}C NMR analysis (decoupled) of **3** at −95 °C revealed three major sharp peaks at δ 150, 91, and 23 ppm attributed to two olefinic carbons (CH and $C{=}CH_2$, respectively) and the methylene carbon attached to copper (Figure 2). The coupled spectrum showed the required multiplicities (doublet, triplet, triplet, respectively), confirming these assignments. Hence, whereas an $^3\eta$ π-allyl bound cuprate would show two signals, the presence of three distinct resonances establishes the σ-bound nature of **3**. Consistent with this trend, both **4** and **5** displayed the expected three key peaks, in addition to the vinylic methyl resonances.[8-10]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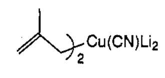
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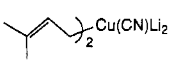
5

Warming **3** to −70 °C gave significant broadening of both the α- and γ-carbons almost into the base line, while the

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(1) A. P. Sloan Fellow, 1984–1988; Camille and Henry Dreyfus Teacher–Scholar, 1984–1989.

(2) Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, 1980. Posner, G. H. *Org. React.* **1972**, *19*, 1; **1975**, *22*, 253. Lipshutz, B. H.; Sengupta, S. *Ibid.*, in press.

(3) (a) House, H. O.; Fisher, W. F. *J. Org. Chem.* **1969**, *34*, 3615. (b) House, H. O.; Wilkins, J. M. *Ibid.* **1978**, *43*, 2443. (c) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *Ibid.* **1986**, *51*, 1745. (d) Whitesides, G. M.; Fischer, W. F.; San Filippo, J.; Bashe, R. W.; House, H. O. *J. Am. Chem. Soc.* **1969**, *91*, 4871. (e) Majetich, G.; Casares, A. M.; Chapman, D.; Behnke, M. *Tetrahedron Lett.* **1983**, *24*, 1909. (f) Corey, E. J.; Boaz, N. W. *Ibid.* **1985**, *26*, 6019. (g) Daviaud, G.; Miginiac, Ph. *Ibid.* **1972**, 997. (h) Drouin, J.; Leyendecker, F.; Conia, J. M. *Tetrahedron* **1980**, *35*, 1203. (i) Bertz, S. H.; Dabbagh, G. *Tetrahedron* **1989**, *45*, 425.

(4) Miginiac, Ph.; Daviaud, G.; Gerard, F. *Tetrahedron Lett.* **1979**, 1811. Corriu, R. J. P.; Guerin, C.; M'Boula, J. *Ibid.* **1981**, *22*, 2985. Enda, J.; Kuwajima, I. *J. Am. Chem. Soc.* **1985**, *107*, 5495. Hutchinson, D. K.; Fuchs, P. L., *Ibid.*, **1987**, *109*, 4755. Barbot, F., Kadib-Elban, A., Miginiac, Ph. *J. Organomet. Chem.* **1983**, *255*, 1; *Tetrahedron Lett.* **1983**, *24*, 5089.

(5) (a) See, for example: Bourgain-Commercon, M.; Foulon, J. P.; Normant, J. F. *J. Organomet. Chem.* **1982**, *228*, 321. (b) Hutchinson, D. K.; Fuchs, P. L. *Tetrahedron Lett.* **1986**, *27*, 1429.

(6) A reagent which successfully delivers a variety of allyl groups in a 1,4-sense has been developed: Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Smith, R. A. J., submitted.

(7) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

(8) Methallylcuprate **4** gives four key peaks at δ 157 (C-β, vinyl), 90 (terminal CH_2), 26 (C-α, CH_2) and 24 (CH_3) ppm, while prenylcuprate **5** displays signals at δ 136 (C-β, vinyl), 103 (C-γ), 26 (*E*-CH_3), 17.4, 17.2 (*Z*-CH_3 and C-α, or vice versa).

(9) From the spectra obtained we cannot unequivocally rule out the possibility that some of the mixed (1σ, 1π) bound system is present and that it is just not being observed in these ^{13}C NMR experiments. However, if such a mixed reagent was present to any appreciable degree, multiple signals would be expected for the carbons of the σ-bound allylic ligand as invariably seen with other mixed H.O.[12] and L.O.[15] cuprates in both their ^1H and ^{13}C spectra.

(10) For a discussion on the σ- vs π-bound nature of allylic compounds of lithium, magnesium, and potassium, see: Schlosser, M.; Stahle, M. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 487.

0022-3263/89/1954-4977$01.50/0 © 1989 American Chemical Society

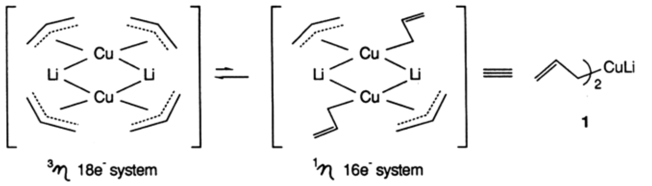

Figure 1.

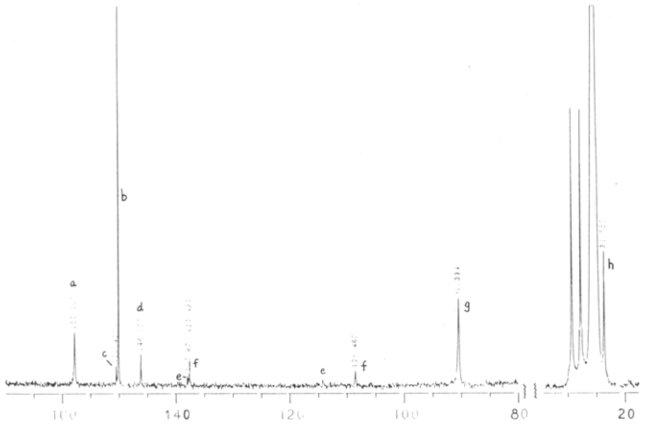

Figure 2. ^{13}C NMR spectrum of (allyl)$_2$Cu(CN)Li$_2$ (**3**) in THF at −95 °C. **a**, CN; **b**, C-β; **c**, C-β of mixed cuprate Me(allyl)Cu(CN)Li$_2$ due to incomplete transmetalation; **d**, C-2 of free allyllithium; **e**, C-1,6 and C-2,5 of 1,5-hexadiene; **f**, C-β and C-γ of allyltributyltin; **g**, C-γ of **3**; **h**, C-α of **3**.

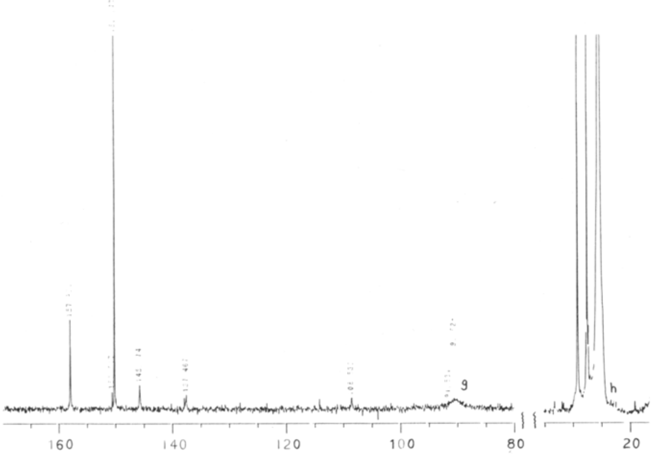

Figure 3. ^{13}C NMR spectrum of (allyl)$_2$Cu(CN)Li$_2$ (**3**) in THF at −65 °C. **g**, C-γ of **3**; **h**, C-α of **3**.

signal for the β-carbon remained unchanged (Figure 3). Recooling to −85 °C resharpened these peaks to a point reflecting this intermediate temperature.

Gilman-like cuprate **1** required extremely careful preparation and handling,[11] the ^{13}C NMR analysis of which at −95 °C clearly manifested its similar σ-bound status, as well as the products of its decomposition. The spectrum (Figure 4) contained three major peaks at essentially identical locations as with the H.O. analogue (δ 150, 91, 24 ppm), not totally unexpected from earlier ^{1}H NMR comparisons of dialkylcuprates.[12] Moreover, the spectra for both **1** and **3** contain a minor peak at 146 ppm, which corresponds to the central carbon of free allyllithium[13,14] and readily explains the observed positive Gilman test reported for **1**.[5b] The spectra are quite dissimilar, however, in one important respect: the relative amounts of decomposition which occur upon reagent generation and NMR inspection at elevated temperatures. Thus, while the spectrum of **1** shows an appreciable quantity of 1,5-hexadiene (in spite of sample manipulation at or below −78 °C),[11] **3** can be handled at 0 °C without buildup of this Wurtz-like product. Formation of **1** by adding allyllithium to CuI and warming to effect dissolution severely compromises cuprate formation, and by loss of an allyl ligand from (dimeric) **1**, other species (e.g., R$_3$Cu$_2$Li, R = allyl) are produced (see Figure 4), which undoubtedly have modified reactivities.[16]

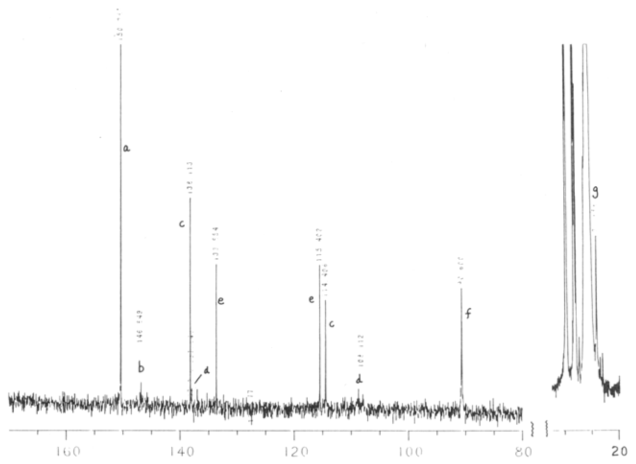

Figure 4. ^{13}C NMR spectrum of (allyl)$_2$CuLi (**1**) in THF at −95 °C. **a**, C-β; **b**, C-2 of free allyllithium; **c**, C-1,6 and C-2,5 of 1,5-hexadiene; **d**, C-β and C-γ of allyltributyltin; **e**, C-β and C-γ of (allyl)$_3$Cu$_2$Li; **f**, C-γ of **1**; **g**, C-α of **1**.

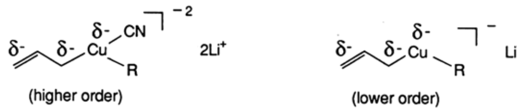

Figure 5.

Peak broadening in the spectra of **1** and **3** at temperatures commonly used for synthetic work[2] suggests that rapid α- to γ-exchange processes are ongoing within the cluster.[17] This phenomenon may be responsible for the atypical cuprate behavior observed with Michael acceptors.[3,5] Alternatively, there may be a "reactivity–selectivity" issue involved, as these reagents are extremely prone toward ligand release from copper,[6] perhaps due to an "α-effect"-like[18] buildup of adjacent negative charge (Figure 5). The contribution by the small component of allyllithium is not likely to be responsible for the chemistry observed.[5b]

In summary, ^{13}C NMR spectroscopy has unequivocally established the σ-bound nature of the bonding in both L.O. and H.O. allyl cuprates. It has also led to an appreciation

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[11] Samples of (allyl)$_2$CuLi were formed at ca. −105 °C and maintained at these low temperatures until placed in the probe, which had been precooled to −95 °C.

[12] Lipshutz, B. H.; Kozlowski, J. A.; Wilhelm, R. S. *J. Org. Chem.* **1984**, *49*, 3943 and references therein.

[13] Allyllithium itself gives peaks at δ 146 and 51 ppm in the ^{13}C NMR spectrum. The presence of both allyllithium and (allyl)$_3$Cu$_2$Li in the spectrum of [(allyl)$_2$CuLi]$_2$ is most atypical, since RLi and R$_3$Cu$_2$Li are normally incompatible (i.e., they would combine to form the Gilman-like dimeric cuprate R$_2$CuLi).[15]

[14] The possibility of free allyllithium in **1** was first raised by House; cf. ref 3b.

[15] Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *Tetrahedron Lett.* **1985**, *26*, 5911 and references therein.

[16] Lipshutz, B. H.; Ellsworth, E. L.; Siahaan, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 1351. Ashby, E. C.; Watkins, J. J. *Ibid.* **1977**, *99*, 5312. Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *Ibid.* **1985**, *107*, 3197. Ashby, E. C.; Lin, J. J. *J. Chem. Soc., Chem. Commun.* **1976**, 784.

[17] Changes in the spectrum of **5** begin to occur at ca. −30 °C.

[18] Hoz, S. *J. Org. Chem.* **1982**, *47*, 3545 and references therein.

for the limited thermal stability of $(allyl)_2CuLi$ and the products of its decomposition, while demonstrating that with $(allyl)_2Cu(CN)Li_2$ no such problem exists. The extent to which ligand reorganization between α- and γ-termini occurs is a function of temperature and substitution on the allyl unit. The understanding gained from these data now allows for the systematic development of allylic organocopper reagents, in essence, as "new" reagents for organic synthesis.[6]

Acknowledgment. Financial support provided by the NSF (Grant CHE 87-03757) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is greatly appreciated.

On the Mode of Conversion of Racemic, C_{14}–C_{19}, γ-Hydroxy Alkene Fatty Acids into C_7–C_{11}, Optically Active γ- and δ-Lactones in *Cladosporium suaveolens*

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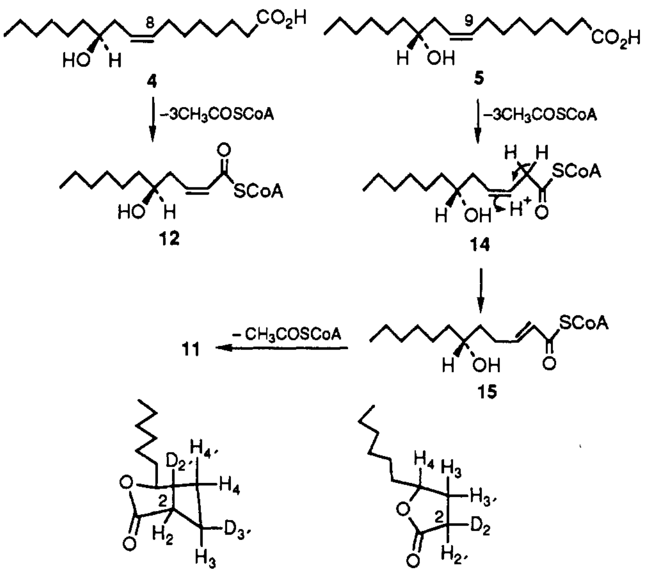
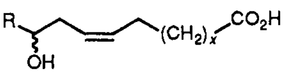
Summary: Growing cultures of *Cladosporium suaveolens* convert the fatty acid derivatives **1–6** either into (*S*)-**7** and -**8** or into (*R*)-**9**, -**10**, and -**11**, depending upon the position of the double bond. Experiments with deuterated substrates show that the hydrogen atom retained α to the carbonyl group in the two series hold the *pro-R* configuration.

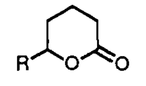
Sir: Optically active γ- and δ-lactones containing up to 12 carbon atoms are widely distributed in nature and play an important role in the flavor industry as aroma components.[1] However, current analytical studies[2,3] indicate that both optical purity and absolute configuration can vary for identical substances isolated from different sources. Moreover, the absolute configuration of the prevalent enantiomer can differ even within a homologous series in the same plant, e.g. the presence of *R* C_8 and C_{10} and *S* C_{12} δ-lactones in cocos meat.[3] These observations give support to the idea[4] that different biosynthetic pathways involving either anabolic or degradative processes can exist for these lipid-derived substances. Degradative processes include β-oxidation of suitably oxygenated intermediates which can be either chiral, such as those involved in the lipoxygenation cascade or those formed in enzymic hydration of methylene-interrupted polyunsaturated fatty acids, or racemic as those formed in photo- or autoxidation.[5] The former set of products is expected to lead to optically active lactones incorporating the chirality of the precursor, as for example in the manufacture of (*R*)-γ-decanolide (**11**) by microbial degradation of natural (*R*)-ricinoleic acid.[6,7] Conversely, racemic precursors are expected to generate educts whose optical purity and absolute configuration may depend upon the susceptibility of the degradative enzyme(s) to the stereochemistry of the hydroxy-bearing carbon atom located in the molecule far away from the place where the β-oxidation starts.

Scheme I

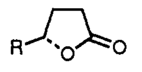




1: R = *n*-C_3H_7; *x* = 5
2: R = *n*-C_3H_7; *x* = 6
3: R = *n*-C_4H_9; *x* = 6
4: R = *n*-C_6H_{13}; *x* = 5
5: R = *n*-C_6H_{13}; *x* = 6
6: R = *n*-C_6H_{13}; *x* = 7



7: R = *n*-C_3H_7
8: R = *n*-C_6H_{13}



9: R = *n*-C_3H_7
10: R = *n*-C_4H_9
11: R = *n*-C_6H_{13}

In this context, we now describe the results of a study on the mode of degradation of the racemic C_{14}–C_{19} fatty acids **1–6**, all of which contain the structural unit (*Z*)-$CH{=}CHCH_2CH(OH)R$, to C_7–C_{11} lactones by growing cultures of *Cladosporium suaveolens*. The choice of the precursors **1–6** originates from the consideration that mid-chain hydroxy acids without conjugated unsaturation occur in nature[8] and that knowledge of the mode of their

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[1] Belitz, H. D.; Grosch, W. *Food Chemistry*; Springer Verlag: Berlin, 1987; p 270.

[2] Schuring, V. In *Bioflavour '87*; Schreier, P., Ed.; de Gruyter: Berlin, 1988; p 35.

[3] Mosandl, A.; Günther, C.; Gessner, M.; Deger, W.; Singer, G.; Heusinger, G. In *Bioflavour '87*; Schreier, P., Ed.; de Gruyter: Berlin, 1988; p 55.

[4] Tressl, R. In *Biogeneration of Aromas*; Parliment, T. H., Croteau, R., Eds.; ACS Symposium Series 317; American Chemical Society: Washington, DC, 1986; p 114.

[5] Gunstone, F. D. In *The Lipid Handbook*; Gunstone, F. D., Harwood, L. J., Padley, F. B., Eds.; Chapman and Hall: London, 1986; p 453.

[6] U.S. Patent 4,560,656 (to Fritzsche, Dodge, and Olcott); *Chem. Abstr.* 1983, *99*, 4080*t*.

[7] Ital. Appl. 67742 (to San Giorgio Flavors).

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