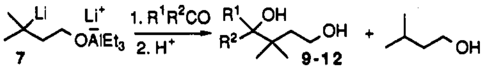
Table I. Reactions of 7 with Aldehydes and Ketones



R^1, R^2	diol, yield (%)[a]	yield of 3-methylbutanol (%)
i-Pr, H	9, 52 (59)	16 (15[b])
t-Bu, H	10, 56	15[b]
$-(CH_2)_5-$	11, (43)	40[b]
Ph, H	12, 38[c]	20[b]

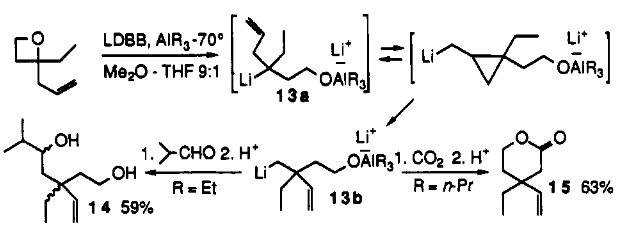
[a] Isolated yields; yields in parentheses refer to 9:1 Me_2O–THF system. [b] GC yields. [c] $PhCH_2OH$ (30%) and $CH_2{=}C(CH_3)CH_2CH_2OH$ (31%) were also isolated.

2,2-Dimethyloxetane[10] undergoes reductive lithiation by LDBB at 0 °C for 2 h to form lithium 4-lithio-2-methyl-2-butoxide (5), which was trapped with (*E*)-2-methyl-2-butenal to give, after acidic treatment, the natural product, (±)-ocimenoyl oxide (6)[11] in 57% yield. The same oxetane, however, when subjected to reductive cleavage in the Et_3Al–LDBB system followed by treatment with this aldehyde gave the expected diol 8 at first in only 27% yield along with 3-methylbutanol (50%) resulting from the protonation of the tertiary organolithium 7. The yield of 8 and analogues in the latter process could be improved by changing both the solvent and the electrophile,[12] since both were determined to be proton sources. Dimethyl ether–THF (9:1) was found to be advantageous over pure THF particularly when easily enolizable carbonyl compounds were employed, as exemplified by the increase in the ratio of 8 to 3-methylbutanol from 0.5 to 1.5 and in the yield of 8 to 45% (Scheme IV).

Table I lists the yields of the diols 9–12 and 3-methylbutanol obtained by trapping the organolithium 7 with some carbonyl compounds.

The moderate yields of the diols 9–12 could result not only from the protonation of 7 but also from other side reactions such as the reduction of the carbonyl compound by 7 to an alcohol which effectively competes with the nucleophilic attack at the carbonyl group in the case of benzaldehyde. The delivery of the β-hydride to the carbonyl carbon has previously been observed for lithium 2-lithioethoxide and is well known for Grignard reagents.[1b]

Scheme V



2-Allyl-2-ethyloxetane[13] in the LDBB–R_3Al system (R = Et or *n*-Pr, −70 °C/Me_2O–THF 9:1) gave an interesting result. It instantaneously underwent the expected exclusive cleavage of the most substituted C–O bond. However, the diol 14 and lactone 15 that were generated by immediate quenching of the intermediate with isobutyraldehyde and CO_2, respectively, followed by the acidic workup, did not result from the reaction of these electrophiles with the initially formed tertiary organolithium 13a but rather with the rearranged primary organolithium 13b (Scheme V). All reported cases of homoallylic rearrangements of organolithiums[14] require many hours at room temperature or higher.[15] A systematic study of this unusual rate acceleration is in progress.

Acknowledgment. We thank the National Science Foundation for financial support.

Supplementary Material Available: Sample procedures for the reductive cleavages of 2,2-disubstituted oxetanes in the LDBB–R_3Al system and the spectral data of the products (3 pages). Ordering information is given on any current masthead page.

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(10) Prepared in 65% yield by sequential treatment of 2-chloropropionyl chloride with MeMgBr (2 equiv in ether) and NaH in DMSO, condensing the product in a cold trap in vacuo.

(11) Strickler, H.; Kovacs, E. *Helv. Chim. Acta* **1966**, *49*, 2055.

(12) Since reaction of *t*-BuLi with (*E*)-2-methyl-2-butenal in THF gave a high yield of the addition product, we conclude that triethylaluminum, by complexing the aldehyde oxygen atom, significantly enhances the acidity of its γ-proton.

(13) Prepared in 72% overall yield by addition of allylmagnesium bromide to commercial 1-chloro-3-pentanone followed by cyclization of the tertiary alcohol in the NaH/Et_2O–DMSO 95:5 system.

(14) Review: Grovenstein, E., Jr. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 313–332. Recent examples: Grovenstein, E., Jr.; Black, K. W.; Goel, S. C.; Hughes, R. L.; Northrop, J. H.; Streeter, D. L.; VanDerveer, D. *J. Org. Chem.* **1989**, *54*, 1671.

(15) Maercker, A.; Weber, K. *Liebigs Ann. Chem.* **1972**, *756*, 43.

Carboalumination/Transmetalation/Conjugate Addition: A New Catalytic Cu(I)-Induced Process for the 1,4-Delivery of Vinylic Groups to Enones

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Department of Chemistry, University of California, Santa Barbara, California 93106

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Summary: Exposure of vinylalanes, derived from carbometalations of 1-alkynes, to catalytic amounts of $CuCN{\cdot}2LiCl$ in the presence of an α,β-unsaturated carbonyl group affords products of vinylic ligand transfer in a 1,4-manner.

Transmetalations of a variety of organometallic intermediates, mediated by preformed higher order cyanocuprates, have only recently begun to expand the scope of the intrinsic chemistry of various metals.[1] Thus, vinylic stannanes,[2] tellurides,[3] and zirconates[4] readily exchange

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(1) For some examples, see: Lipshutz, B. H. *Synlett* **1990**, 119.

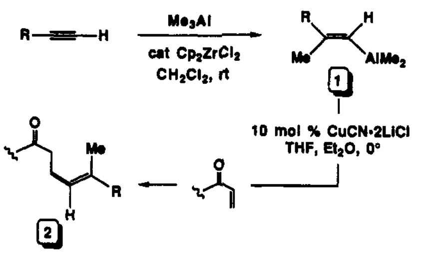
(2) Behling, J. R.; Babiak, K. A.; Ng, J. S.; Campbell, A. L.; Moretti, R.; Koerner, M.; Lipshutz, B. H. *J. Am. Chem. Soc.* **1988**, *110*, 2641.

(3) Comasseto, J. V., Berriel, J. N. *Synth. Commun.* **1990**, *20*, 1681.

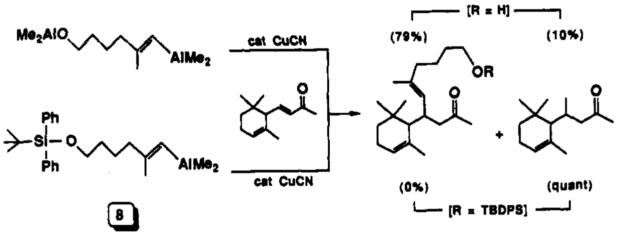
(4) Lipshutz, B. H.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 7440. Babiak, K. A.; Behling, J. R.; Dygos, J. H.; McLaughlin, K. T.; Ng, J. S.; Kalish, V. J.; Kramer, S. W.; Shone, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 7441.

0022-3263/91/1956-5761$02.50/0

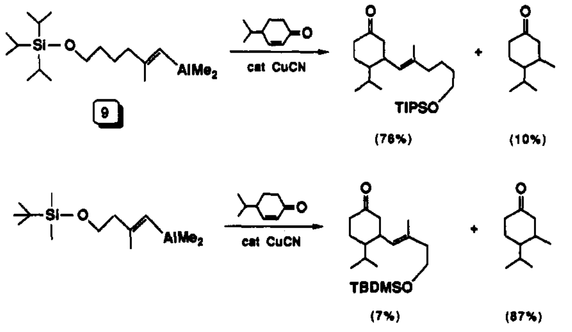
Scheme I



Scheme II



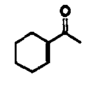
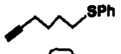
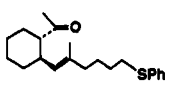
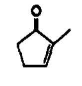
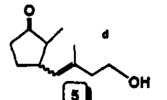
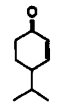
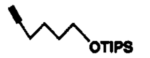
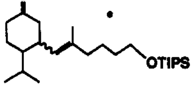
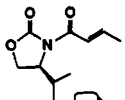
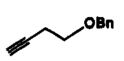
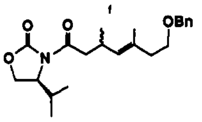
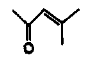
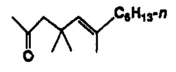
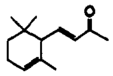
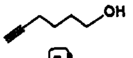
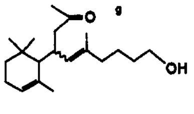
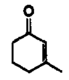
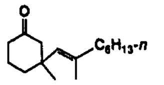
Scheme III



their vinylic ligands for alkyl groups on copper. Vinylic alanes, formed via Negishi-type carbometalations with Me_3Al/catalytic Cp_2ZrCl_2[5] have also been converted to mixed higher order cyanocuprates, which transfer vinylic residues in a Michael sense to enones.[6] This latter process, which is stoichiometric in copper, we viewed as potentially realizable using catalytic quantities of a Cu(I) *salt*, rather than stoichiometric amounts of a *bis*-acetylenic higher order cuprate. We now report that a new, experimentally simple procedure has been developed to effect this type of valuable C–C bond formation under *catalytic* conditions.

Treatment of a 1-alkyne with Me_3Al + catalytic Cp_2ZrCl_2 in CH_2Cl_2 at ambient temperatures affords the expected vinylic alane 1.[5] Dropwise addition of this solution to 10 mol % of $CuCN{\cdot}2LiCl$[7] in THF/Et_2O at 0 °C over the course of 1 h in the presence of a substrate leads to the 1,4-adducts 2 in good isolated yields (Scheme I).[8]

Table I. Carboalumination/*Catalytic* Cu(I)-Induced Conjugate Addition Reactions

enone	acetylene	product(s)[a]	yield (%)[b]
	 **3**		67(90)[c]
	 **4**	 [d] **5**	82
		 [e]	76
 **6**		 [f]	74
	$\equiv$—C_6H_{13}-*n*		74
	 **7**	 [g]	66(79)[c]
	$\equiv$—C_6H_{13}-*n*		71

[a] Fully characterized by IR, NMR, MS, and HRMS data. [b] Isolated following column chromatography. [c] Yield obtained by vacuum removal of excess Me_3Al prior to exposure of the vinylalane to Cu(I). [d] Ratio (of isomers): 2.8:1 trans:cis. [e] Ratio: 25:1 trans:cis. [f] Ratio of diastereomers: 3.5:1. [g] Ratio of diastereomers: 5.7:1.

Several examples are illustrated in Table I from which the following points emerge: (1) neither the rate nor percent conversion of the coupling was affected by the presence of the sulfide function in acetylene 3; (2) unprotected alcohols (e.g., 4 and 7), undoubtedly as their alanates,[5] readily participate and suggest that hydroxyl protecting group chemistry is not required when part of the 1-alkynyl educt; (3) various substitution patterns associated with the Michael acceptor seem amenable, including an Evans chiral auxiliary (6).[9]

Quite unexpectedly, the nature of a silyl protecting group present in the acetylene associated with a *primary* hydroxyl can significantly alter the course of the transmetalation. As illustrated in Schemes II and III, use of either the TBDMS or TBDPS groups led to predominant methyl, as opposed to vinyl, ligand transfer, irrespective of the fact that the silyl group (in, e.g., 8) is nine atoms removed from the "business end" of the chemistry. Chelation via the ether oxygen may well play a role, and hence its blockage in this capacity via the corresponding TIPS ether (as in 9) appears to reverse this trend.[10] When the

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(5) Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333.

(6) Ireland, R. E., Wipf, P. *J. Org. Chem.* **1990**, *55*, 1425.

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

(8) The desired 1,4-addition is usually accompanied by somewhat competitive delivery of a methyl ligand (due to the excess Me_3Al present),[5] which accounts for the majority of the mass balance. To minimize this side product, the residual Me_3Al can be removed under vacuum prior to exposure of the vinylalane to the enone/CuCN (see Table I, entries 1 and 6).

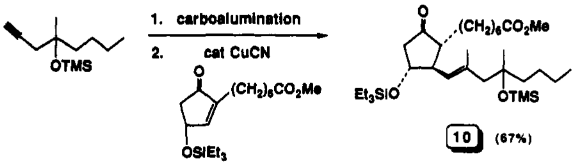
(9) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1984**, *106*, 4261.

(10) Magnus, P.; Mugrage, B. *J. Am. Chem. Soc.* **1990**, *112*, 462. Frye S. V.; Eliel, E. *J. Am. Chem. Soc.* **1988**, *110*, 484. Chen, X.; Hortelano, E. R.; Eliel, E. L.; Frye, S. V. *J. Am. Chem. Soc.* **1990**, *112*, 6130. Frye, S. V.; Eliel, E. L. *Tetrahedron Lett.* **1986**, *27*, 3223.

(11) Collins, P. W. *Med. Res. Rev.* **1990**, *10*, 149; *J. Med. Chem.* **1986**, *29*, 437.

(12) For other representative procedures involving vinylic alanes and catalytic Cu(I), see: Ziegler, F. E.; Mikami, K. *Tetrathedron Lett.* **1984**, *25*, 131. Sharma, S.; Oehlschlager, A. *Tetrahedron Lett.* **1986**, *27*, 6161.

silyl ether relates to, e.g., a teriary hydroxyl, the "normal" sequence of events occurs. This was demonstrated by the preparation of prostanoid **10**, the 14-methyl analogue of misoprostol.[11]



$\boxed{10}$ (67%)

In summary, a new method is described that combines the virtues of a carboalumination together with a *catalytic* Cu(I)-based transmetalation scheme[12] for vinyl ligand addition to α,β-unsaturated carbonyl derivatives.[13] Highly basic reagents (e.g. RLi, RMgX) normally involved in cuprate formation[14] play no role at any stage. Moreover, solvent exchange from chlorinated to ethereal media is not necessary,[6] further streamlining the process. Further advances in the transmetalation chemistry of Cu(I) reagents will be reported in due course.

Acknowledgment. Financial support provided by the NSF (CHE 90-05758) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. We are indebted to Boulder Scientific Co. for providing generous amounts of Cp$_2$ZrCl$_2$ used in this study.

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(13) A representative procedure for the preparation of **5** is as follows. A solution of zirconocene dichloride[15] (84.0 mg, 0.287 mmol) in 2.25 mL of CH$_2$Cl$_2$ was treated with 1.75 mL (3.0 mmol) of a 2.0 M solution of trimethylaluminum in hexane at 0 °C followed by the careful dropwise addition of 3-butyn-1-ol (80.6 mg, 1.15 mmol) dissolved in 1.0 mL of CH$_2$Cl$_2$. The resulting solution was allowed to warm to room temperature with stirring and then taken up into a gas-tight 5-mL motor-driven syringe[16] with a 0.50-mL CH$_2$Cl$_2$ wash. A 1.0 M solution of CuCN·2LiCl was prepared by dissolving a flame-dried admixture of CuCN (85.0 mg, 0.949 mmol) and LiCl (81.7 mg, 1.93 mmol) in 0.95 mL of THF at room temperature with stirring. The contents of the syringe were added slowly, dropwise, to 4.0 mL of dry Et$_2$O with stirring at 0 °C. When the solution became visibly yellow, 0.10 mL of the 1.0 M CuCN·2LiCl solution was added dropwise followed by the dropwise addition of a solution of 2-methylcyclopentenone (95.9 mg, 0.998 mmol) in 1.0 mL of Et$_2$O. The vinylalane was added over 1 h and the resulting suspension stirred at 0 °C for an additional 1.5 h. The reaction mixture was then poured into a solution of 20 mL of 1.0 M tartaric acid and 20 mL of Et$_2$O at 0 °C. The biphasic suspension was allowed to warm to room temperature with vigorous stirring, which was continued until the solids had dissolved. The layers were then separated and the aqueous phase was extracted three times with Et$_2$O. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and chromatographed (silica gel, CH$_2$Cl$_2$/EtOAc, 17:3) to yield 148.8 mg (82%) of the desired keto alcohol as a 2.8:1 mixture of diastereomers by capillary GC: R_f 0.16 (9:1 CH$_2$Cl$_2$/EtOAc); IR (film) 3435, 1740, 1457, 1166, 1058 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 5.16 (d, 1 H, J = 8.6 Hz, major), 5.07 (d, 1 H, J = 10.0 Hz, minor), 3.71 (t, 2 H, J = 6.3 Hz, major), 3.67 (t, 2 H, J = 8.3 Hz, minor), 3.24–3.18 (m, 1 H, minor), 2.59–2.51 (m, 1 H, major), 2.43–2.33 (m, 1 H), 2.34–2.26 (m, 1 H), 2.32 (t, 2 H, J = 6.3 Hz, major), 2.27 (t, 2 H, J = 6.1 Hz, minor), 2.20–2.03 (m, 2 H), 1.86–1.77 (m, 1 H), 1.71 (d, 3 H, J = 1.0 Hz, major), 1.69 (s br, 3 H, minor), 1.60–1.51 (m, 1 H), 0.97 (d, 3 H, J = 7.0 Hz, major), 0.91 (d, 3 H, J = 7.3 Hz, minor); ^{13}C NMR (CDCl$_3$) δ 220.09, 133.61, 130.17, 126.23, 60.35, 60.23, 51.05, 47.73, 43.94, 42.82, 42.70, 37.20, 35.64, 27.94, 27.29, 16.35, 16.23, 14.14, 12.00; mass spectrum (EI) *m/z* (rel intensity) 182 (M$^+$, 16.5), 152 (31.2), 149 (11.5), 138 (11.5), 137 (58.0), 135 (11.2), 123 (14.3), 121 (10.2), 111 (15.9), 110 (100), 109 (50.2), 108 (11.1), 107 (25.0), 97 (51.5), 96 (30.6), 95 (82.4), 94 (11.2), 93 (50.9), 91 (21.9), 84 (10.7), 83 (11.1), 82 (16.5), 81 (52.7), 80 (13.6), 79 (39.2), 77 (25.0), 69 (23.0), 68 (12.7), 67 (46.7), 57 (18.2), 56 (12.3), 55 (51.2), 53 (20.6); HRMS (EI) calcd for C$_{11}$H$_{18}$O$_2$ 182.1307, found 182.1287.

(14) Lipshutz, B. H.; Sengupta, S. *Org. React.* In press. Posner, G. H. *Org. React.* **1975**, *22*, 253; **1972**, *19*, 1.

(15) Material of excellent quality was obtained from Boulder Scientific Company, Mead, CO.

(16) Use of a gas tight dropping funnel will also suffice; half of the examples in Table I were carried out with this alternative technique.