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Catalytic Cu(I) Assisted Polyfunctionalization of Zirconacyclopentenes

Bruce H. Lipshutz* and Masahito Segi

Department of Chemistry

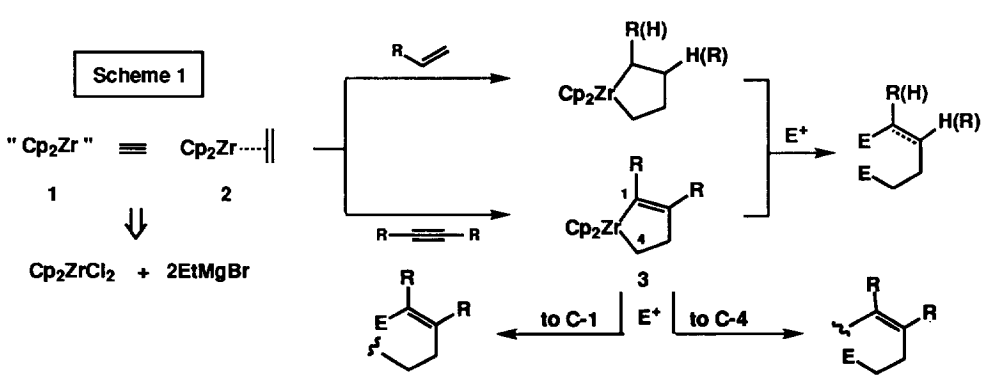
University of California, Santa Barbara, CA 93106

Fax: 805/893-4120

Abstract. *Using a catalytic quantity of CuCl•2LiCl, zirconacyclopentenes can be regiospecifically transmetallated and subsequently induced to undergo 1,4-additions to enones. Further manipulations of the presumed zirconium enolates are also presented, including three- and four-component couplings.*

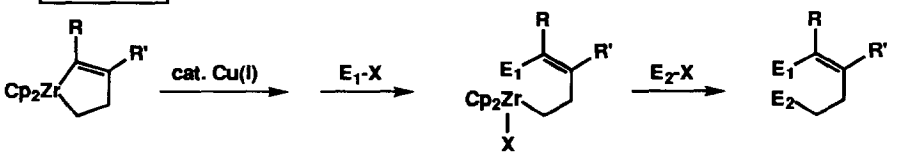
The synthetic chemistry of zirconium(II) compounds, most notably "Cp_2Zr" (**1**) or its equivalent (**2**), has blossomed since these species became readily available some years ago.[1] Indeed, it was the original report by the Editor of this Symposium-in-Print that provided an experimentally straightforward method for the *in situ* generation of this reactive carbene-like complex.[2] Reactions of **1**, in π-complexed form **2**, with alkenes and alkynes produce zirconacyclo-pentanes and -pentenes, respectively.[3] These intermediates are prone toward further manipulations which can lead overall to significant increases in molecular complexity *via* alkene/alkyne exchange for ethylene, or simultaneous electrophilic trapping at each carbon-zirconium bond (Scheme 1).[4] Curiously, selective C-C bond-forming transformations which occur at C-1 in **3** are rare,[5]

Scheme 1



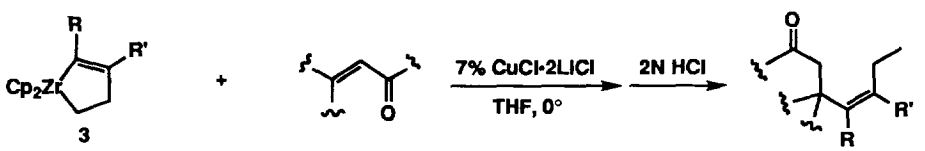
and only recently has progress been made along these lines involving regio- and chemoselective (*i.e.*, reagent-controlled) halogenations.[6] The corresponding process which results in site-selective C-C bond formations, to our knowledge, has not been reported. We now describe chemospecific transmetallations of zirconacyclopentenes **3** initiated by catalytic amounts of copper (I) salts that permit subsequent polyfunctionalizations of the basic four carbon skeleton (Scheme 2).

Scheme 2



2-Component Couplings. Zirconacyclopentenes **3** were prepared in standard fashion from Cp_2ZrCl_2, EtMgBr (2 eq), and the corresponding alkynes.[2b] Initial attempts to effect transmetallation of the vinylic zirconocene portion[7] of **3** to copper using higher order cuprate technology[8] was completely unsuccessful, as subsequent introduction of an enone afforded none of the desired 1,4-adduct. Use of catalytic quantities of a copper(I) salt, however, converted **3** to a reactive (halo?) cuprate[9] intermediate, which in the presence of an enone underwent remarkably smooth conjugate additions. Aqueous acid workup provided the Michael adducts **4** (Scheme 3). Several examples of these couplings are illustrated in Table 1. Using zirconacyclopen-

Scheme 3



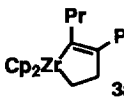
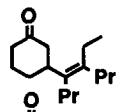
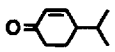
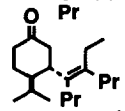
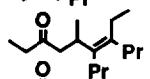
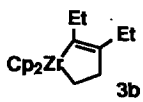
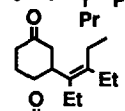
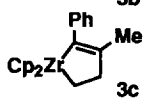
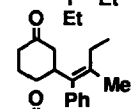
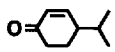
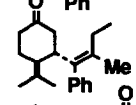
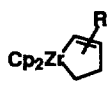
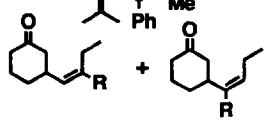
a: R=R'=Pr **b:** R=R'=Et **c:** R=Ph, R'=Me **d:** R=H, R'=Hex **d':** R=Hex, R'=H **e:** R=H, R'=Ph **e':** R=Ph, R'=H

tene **3a** as a test case, Michael additions to cyclohexenone under the influence of CuOTf (91%), CuCN•2LiCl (73%), CuI•2LiCl (88%), CuI•2LiI (82%), and $CuBr•SMe_2$ (71%) were all examined. Best results were realized using 7 mol % CuCl, solubilized by the presence of 2LiCl. Although clearly other copper salts give comparable yields, the CuCl•2LiCl catalyst system appears to give more rapid reactions, and is likely the least expensive alternative. Particularly intriguing among the examples studied are entries 7 and 8 involving a regioisomeric mix of *mono*substituted zirconacyclopentenes. Both **3d** and **3e** reacted at -40° (rather than at the standardized temperature of 0°) to afford adducts in ratios that were quite different from educt values. This was accomplished by taking advantage of the observation that the 1-substituted isomer reacts at a far slower rate than the 2-hexyl or 2-phenyl zirconacyclopentene, and hence by adjustment of stoichiometry (see Experimental Section), product mixes rich in one isomer could be obtained.

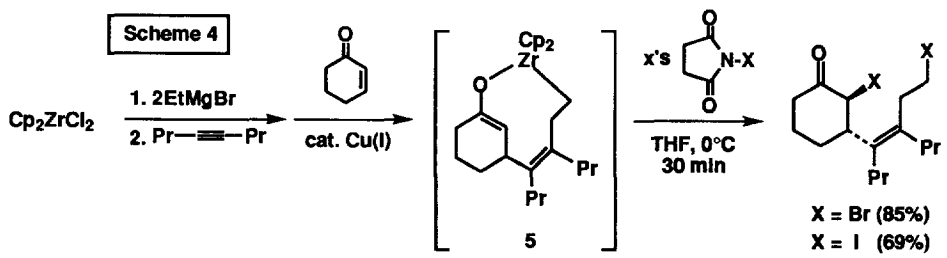
Given the catalytic presence of copper, the presumed zirconium enolate **5** should be susceptible to quenching with electrophiles other than protons. When **5** was treated with excess N-halosuccinimide (*i.e.*,

NBS or NIS) prior to workup, halogenation at both the α and carbon-bearing-zirconium sites occurred (Scheme 4).

Table 1. Cu(I)-Catalyzed Conjugate Additions of Zirconacyclopentenes in THF at 0°C.[a]

Entry	3	Enone	Time (min)	Product(s)	Yield (%)[b]
1	 3a		40		90
2			90		74[c]
3			90		73
4	 3b		40		83
5	 3c		90		90
6			120		94[c]
					
7	R=Hex (3d + 3d')[d]		120	88 : 12	80[f]
8	R=Ph (3e + 3e')[e]		120	85 : 15	73[f]

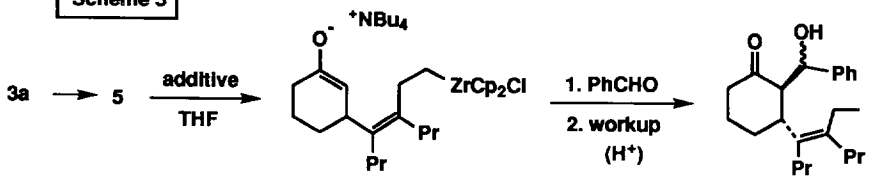
[a]7 mol % of CuCl•2LiCl was used. [b]Isolated. [c]Trans isomer by ^{1}H NMR. [d]Proton quenching immediately before the reaction with an enone showed a 7:3 mixture of **3d** and **3d'**. [e]A 2:3 mixture of **3e** and **3e'**. [f]Run at -40°C.



3-Component Couplings. In addition to halogenation of enolate **5**, quenching with an aldehyde would further elaborate the carbon framework, constituting a novel 3-component coupling.[10] Using zirconocene **3a** as a test case, introduction of benzaldehyde led to slow consumption of educt at 0°, ultimately providing the aldol product as a (78:22) mix of diastereomers. The rates in several of these condensations could be enhanced dramatically, however, upon addition of *n*-Bu_4NCl (1.5 eq), which may act to convert **5** to the

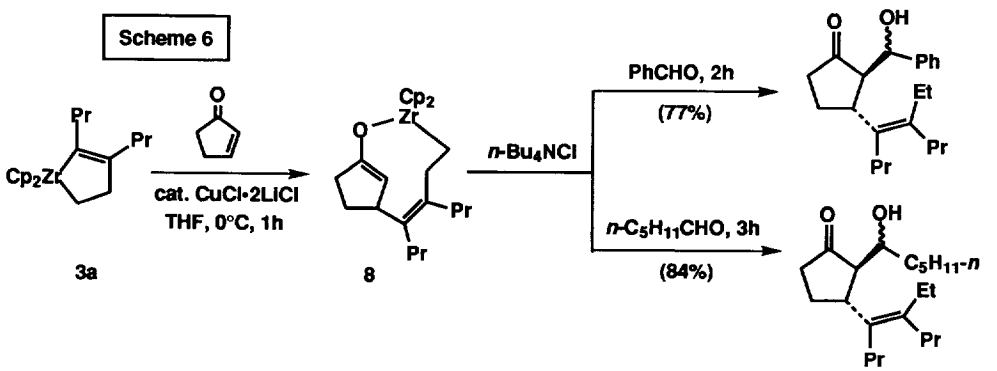
corresponding tetrabutylammonium (or "bare") enolate **6** (Scheme 5). Two additional examples are shown in Scheme 6.

Scheme 5



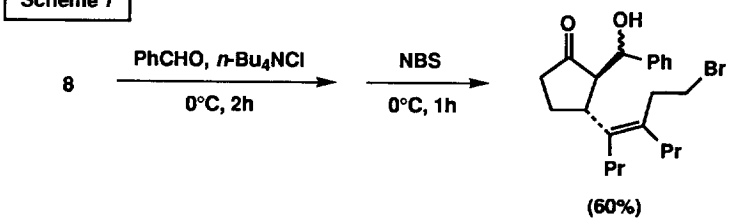
additive	time (h)	yield, 7 (%)
n-Bu_4NCl	1.5	78
none	17	63

Scheme 6

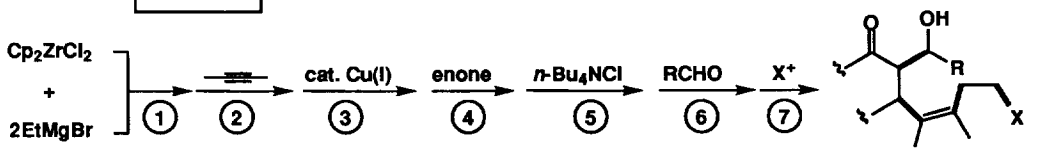


The aldol reaction that eventually converts **6** to products **7** after aqueous workup proceeds without affecting the C_{sp^3}-$ZrCp_2Cl$ bond, which is susceptible to yet one additional trapping with an electrophile such as NBS. This final carbon-halogen bond forming step, which has indeed been accomplished (Scheme 7), represents the culmination of a 1-pot, seven step sequence starting with Cp_2ZrCl_2 *(i.e.*, zirconocene formation, conversion to the zirconacyclopentene, transmetallation to the cuprate, 1,4-addition to an enone, transenolization to the tetrabutylammonium enolate, aldol condensation, and halogenation; Scheme 8). Thus, from an alkyne, one C-X and three C-C bonds were created (highlighted in Scheme 8) by organozirconium and copper chemistry working together in tandem.

Scheme 7

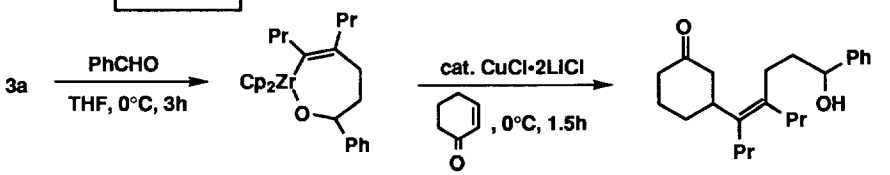


Scheme 8



Finally, the prospects for extension of these transmetallation-initiated couplings to *oxa*zirconacyclopentenes[1c,11] have been tested using the carbonyl of benzaldehyde which at low temperatures inserts into the zirconacyclopentene (rather than replacing ethylene; *cf.* **9**, Scheme 9).[12] Upon treatment of **9** with an enone, conjugate addition does indeed occur to efficiently produce secondary alcohol-containing adduct **10** upon workup. Additional examples of these, as well as the corresponding *aza*zirconacyclo-pentenes (and -pentanes)[13] are currently under study and will be described in due course.

Scheme 9



Conclusions. The facile ligand exchange between a vinylic zirconocene and a Cu(I) salt has led to a novel method for the regiospecific functionalization of zirconacyclopentenes. Michael additions of the transmetallated organometallics, as well as subsequent aldol couplings and halogenations, can all be effected in this 1-pot process.

Acknowledgements. We warmly thank the NSF (CHE 93-03883) for financial support of our programs. We are also pleased to acknowledge the helpful background information and unpublished data provided by Prof. Negishi and Dr. Takahashi.

Experimental Section

General. All reactions were carried out in a dry reaction vessel under an inert atmosphere of argon. NMR spectra were obtained on a Varian Gemini-200 spectrometer (^1H at 200 MHz, ^{13}C at 50 MHz). All spectra were taken in $CDCl_3$ with tetramethylsilane as an internal standard. Chemical shifts are given in ppm downfield of the reference. IR spectra were measured on a Perkin-Elmer 1330 IR spectrophotometer. Mass spectra were obtained at the Mass Spectrometry Facility, University of California, Los Angeles. Gas chromatographic analyses were performed on a Hewlett-Packard 5890A gas chromatograph equipped with a 60 m fused silica J & W DB-5 capillary column. Flame ionization detection was employed with H_2 as the carrier gas. The standard program to analyze reaction mixtures was as follows: initial temperature, 40°C; initial time, 2 minutes; rate, 20°C/min; final temperature, 300°C; final time, 20 minutes. Thin layer chromatography was carried out on Silica Gel 60 F_{254} plates (0.25 mm, Merck, #5715) which were

visualized by ultraviolet light (254 nm) and by staining with a 20% ethanolic solution of phosphomolybdic acid followed by development with heat. Flash column chromatography was performed using ICN Silica Gel 60A.

Materials. THF was distilled from sodium benzophenone ketyl under an atmosphere of dry N_2 immediately prior to use. Ethylmagnesium bromide was prepared from ethyl bromide plus Mg metal in THF and titrated according to the method of Watson and Eastham.[14] Copper(I) chloride, copper(I) bromide-dimethyl sulfide complex, copper(I) iodide, copper(I) cyanide, lithium chloride, and lithium iodide were obtained from Aldrich, and copper(I) triflate was obtained from Fluka. Zirconocene dichloride was purchased from Boulder Scientific. 1-Octyne, phenylacetylene, and 1-phenyl-1-propyne were obtained from Aldrich, and 4-octyne and 3-hexyne were bought from Lancaster. 2-Cyclohexen-1-one, 2- cyclopenten-1-one, 4-isopropyl-2-cyclohexen-1-one, and 4-hexen-3-one were purchased from Aldrich. N-Bromosuccinimide was obtained from Fluka and N-iodosuccinimide from Lancaster. Benzaldehyde and *n*-hexanal were purchased from Aldrich. All compounds were purified by standard techniques.[15]

Preparation of a 0.5 M THF Solution of CuCl•2LiCl. A mixture of CuCl (49.5 mg, 0.5 mmol) and dry LiCl (42.4 mg, 1.0 mmol) was dried by heating *in vacuo* with a heat gun. The flask was then filled with argon. Evacuation and filling with argon were each repeated twice. THF (1.0 mL) was injected, and the mixture was stirred for 5 minutes to yield a pale yellow, homogeneous solution. This solution was used as the CuCl•2LiCl source for these copper(I)-catalyzed reactions.

Preparation of THF Solutions of CuI•2LiCl, CuI•2LiI, and CuCN•2LiCl. These Cu(I) solutions were prepared in the same manner as CuCl•2LiCl. The following amounts of reagents were used: for CuI•2LiCl, CuI (95.2 mg, 0.5 mmol), LiCl (42.4 mg, 1.0 mmol), and THF (1.0 mL); for CuI•2LiI, CuI (95.2 mg, 0.5 mmol), LiI (134 mg, 1.0 mmol), and THF (1.0 mL); for CuCN•2LiCl, CuCN (44.8 mg, 0.5 mmol), LiCl (42.4 mg, 1.0 mmol), and THF (1.0 mL).

Typical Procedure for the Cu(I)-Catalyzed Conjugate Addition of *in situ* Prepared Zirconacyclopentenes to α,β-Unsaturated Ketones (Table 1, entry 1): (E)-3-(5-Ethyl-4-octen-4-yl)cyclohexanone. Zirconocene dichloride (149.8 mg, 0.512 mmol) was placed in an oven-dried 10 mL round bottom flask equipped with a magnetic stir bar and septum. The flask was evacuated and purged with argon, the process being repeated three times. THF (3 mL) was injected, and the stirred homogeneous solution was then cooled to -78°C, to which was added EtMgBr (1.20 mL, 0.857 M in THF, 1.025 mmol) *via* syringe. After 1 h of stirring at -78°C, 4-octyne (64 μL, 0.436 mmol) was added neat *via* syringe, followed by 5 minutes of additional stirring. The solution was then warmed to 0°C and stirred for 2 h at this temperature. Addition of 2-cyclohexen-1-one (24 μL, 0.25 mmol) was followed by injection of a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol). After 40 minutes at 0°C, the reaction was quenched with 2N HCl and extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Flash column chromatography on silica gel (10:1, hexane-ethyl acetate) afforded 52.9 mg of the desired product (90% yield) as a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.90 (t, J=7.4 Hz, 3H), 0.91 (t, J=7.4 Hz, 3H), 0.93 (t, J=7.4 Hz, 3H), 1.23-1.48 (m, 4H), 1.60-1.74 (m, 3H), 1.88- 2.45 (m, 11H), 2.78-2.96 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.16, 136.86, 134.18, 47.15, 41.79, 41.22, 34.10, 30.37, 30.19, 25.82, 24.34, 23.87, 21.93, 14.78, 14.31, 14.19; IR (neat) cm^{-1} 2958, 2930, 2868, 1715, 1468, 1456, 1426, 1265, 1222, 1060, 738; EIMS, m/e (relative intensity) 236 (32.7, M^+), 207 (35.4), 194 (13.0),

193 (55.8), 151 (19.5), 149 (20.4), 135 (16.1), 109 (10.5), 107 (11.4), 97 (22.5), 95 (21.1), 93 (14.9), 91 (11.5), 88 (15.1), 86 (86.6), 84 (100), 83 (13.1), 81 (16.9); HREIMS calculated for $C_{16}H_{28}O$ (M^+) 236.2140, found 236.2146.

(Table 1, entry 2): *trans*-(E)-3-(5-Ethyl-4-octen-4-yl)-4-isopropylcyclohexanone. The zirconacyclopentene was prepared as described above with the following quantities of reagents: Cp_2ZrCl_2 (150.4 mg, 0.514 mmol), THF (3 mL), EtMgBr (1.128 mL, 0.912 M in THF, 1.029 mmol), and 4-octyne (64 μL, 0.436 mmol). 4-Isopropyl-2-cyclohexen-1-one (35 mg, 0.25 mmol) and a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol) were added at 0°C and the mixture stirred for 90 minutes at this temperature. Quenching and extractive (Et_2O) workup followed by chromatography on silica gel with 10:1 hexane/ethyl acetate afforded 51.3 mg (74% yield) of product as a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.70 (d, J=6.8 Hz, 3H), 0.90 (t, J=7.4 Hz, 3H), 0.91 (t, J=7.4 Hz, 3H), 0.94 (d, J=6.8 Hz, 3H), 0.94 (t, J=7.4 Hz, 3H), 1.24-1.54 (m, 5H), 1.62-2.52 (m, 13H), 2.83 (ddd, J=4.1, 10.6, 12.8 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.37, 138.58, 132.84, 47.48, 44.35, 44.25, 41.24, 33.66, 27.49, 24.57, 24.36, 23.69, 21.95, 21.71, 16.03, 15.09, 14.26, 14.02; IR (neat) cm^{-1} 2958, 2924, 2866, 1719, 1467, 1430, 1389, 1375, 1342, 1328, 1267, 1206, 1080, 1063, 918, 736; EIMS, m/e (relative intensity) 279 (19.9), 278 (97.3, M^+), 250 (18.0), 249 (93.7), 236 (18.4), 235 (100), 217 (38.8), 208 (17.2), 193 (64.0), 179 (18.6), 177 (28.8), 165 (21.1), 139 (16.6), 123 (18.3), 95 (28.6), 93 (13.6), 91 (14.8), 83 (15.9), 81 (22.0); HREIMS calculated for $C_{19}H_{34}O$ (M^+) 278.2609, found 278.2604.

(Table 1, entry 3): (E)-7-Ethyl-5-methyl-6-propyl-6-decen-3-one. The zirconacyclopentene was prepared as described above with the following amounts of reagents: Cp_2ZrCl_2 (150.4 mg, 0.515 mmol), THF (3 mL), EtMgBr (1.128 mL, 0.912 M in THF, 1.029 mmol), and 4-octyne (64 μL, 0.436 mmol). 4-Hexen-3-one (29 μL, 0.25 mmol) was added neat, followed by injection of a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol). The solution was stirred at 0°C for 90 minutes, then quenched with 2N HCl, and worked up in the usual fashion. Chromatographic purification on silica gel with 10:1 hexane/ethyl acetate yielded 43.4 mg (73% yield) of the desired product as a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, J=7.4 Hz, 6H), 0.93 (t, J=7.4 Hz, 3H), 0.97 (d, J=7.0 Hz, 3H), 1.02 (t, J=7.4 Hz, 3H), 1.23-1.46 (m, 4H), 1.80-2.20 (m, 6H), 2.38 (q, J=7.4 Hz, 2H), 2.38 (d, J=7.0 Hz, 2H), 3.23 (hex, J=7.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.41, 136.28, 135.41, 48.64, 36.58, 34.13, 31.79, 30.34, 24.51, 23.99, 22.01, 19.77, 14.94, 14.45, 14.08, 7.7; IR (neat) cm^{-1} 2958, 2926, 2870, 1717, 1460, 1416, 1379, 1356, 1274, 1118, 1063, 1029, 984, 880, 736; EIMS, m/e (relative intensity) 238 (26.6, M^+), 220 (19.6), 209 (23.5), 195 (28.1), 191 (15.9), 167 (22.2), 166 (100), 153 (20.4), 137 (40.9), 125 (12.4), 124 (30.9), 123 (36.0), 109 (22.7), 99 (19.2), 97 (48.2), 96 (11.5), 95 (38.2), 91 (13.2), 83 (55.0); HREIMS calculated for $C_{16}H_{30}O$ (M^+) 238.2296, found 238.2292.

(Table 1, entry 4): 3-(4-Ethyl-3-hexen-3-yl)cyclohexanone. The zirconacyclopentene was prepared as described above with the following amounts of reagents: Cp_2ZrCl_2(150.3 mg, 0.514 mmol), THF (3 mL), EtMgBr (1.127 mL, 0.912 M in THF, 1.028 mmol), and 3-hexyne (50 μL, 0.437 mmol). 2-Cyclohexen-1-one (24 μL, 0.25 mmol) was added neat *via* syringe, followed by addition of a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol) and the mixture stirred at 0°C for 40 minutes. Quenching, extractive workup, and chromatography on silica gel (10:1, hexane/ethyl acetate) afforded 43.2 mg (83% yield) of the desired 1,4-adduct as a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (t, J=7.4 Hz, 3H), 0.97 (t, J=7.4 Hz, 3H), 0.98 (t, J=7.4 Hz, 3H), 1.60-1.75 (m, 3H), 1.99 (q, J=7.4 Hz, 2H), 2.02 (q, J=7.4 Hz, 4H), 2.08-2.46 (m, 5H),

2.79-2.96 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.24, 138.09, 134.85, 47.10, 41.84, 41.25, 30.34, 25.84, 24.66, 23.49, 20.15, 15.62, 14.20, 13.39; IR (neat) cm^{-1} 2956, 2922, 2864, 1714, 1468, 1453, 1426, 1380, 1347, 1319, 1270, 1221, 1184, 1057, 733; EIMS, m/e (relative intensity) 208 (37.5, M^+), 179 (59.7), 165 (23.5), 161 (20.5), 151 (11.2), 137 (19.5), 135 (13.5), 121 (41.8), 109 (19.8), 97 (21.3), 95 (22.1), 93 (15.3), 91 (10.2), 88 (10.9), 86 (66.6), 84 (100), 81 (22.6); HREIMS calculated for $C_{14}H_{24}O$ (M^+) 208.1827, found 208.1829.

(Table 1, entry 5): (E)-3-(2-Methyl-1-phenyl-1-butenyl)cyclohexanone. The zirconacyclopentene was prepared as described above with the following amounts of reagents: Cp_2ZrCl_2 (149.2 mg, 0.51 mmol), THF (3 mL), EtMgBr (1.12 mL, 0.912 M in THF, 1.021 mmol), and 1-phenyl-1-propyne (54 μL, 0.433 mmol). 2-Cyclohexen-1-one (24 μL, 0.25 mmol) was added as a neat liquid *via* syringe, followed by injection of a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol). The mixture was stirred at 0°C for 90 minutes, then quenched with 2N HCl, and worked up in the usual manner. Chromatographic purification on silica gel with 10:1 hexane/ ethyl acetate gave 54.2 mg (90% yield) of the desired 1,4-adduct as a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 1.06 (t, J=7.6 Hz, 3H), 1.36 (s, 3H), 1.29-1.85 (m, 3H), 2.18 (q, J=7.6 Hz, 2H), 1.95-2.36 (m, 5H), 3.12 (tt, J=12.5, 3.6 Hz, 1H), 6.97 (bd, J=6.1 Hz, 2H, aromatic), 7.25-7.39 (m, 3H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.99, 140.36, 136.88, 134.53, 129.97, 127.91, 126.22, 47.47, 40.95, 30.71, 26.30, 25.56, 19.88, 13.46; EIMS, m/e (relative intensity) 243 (21.9), 242 (100, M^+), 213 (61.6), 199 (24.5), 195 (18.1), 185 (14.1), 184 (20.0), 169 (31.6), 157 (18.9), 155 (49.7), 143 (48.7), 131 (17.6), 130 (18.0), 129 (67.9), 128 (31.8), 117 (12.5), 115 (42.7), 105 (17.5), 103 (12.1), 91 (40.2); HREIMS calculated for $C_{17}H_{22}O$ (M^+) 242.1670, found 242.1677.

(Table 1, entry 6): *trans*-(E)-4-Isopropyl-3-(2-methyl-1-phenyl-1-butenyl)cyclohexanone. The zirconacyclopentene was prepared as described above with the following amounts of reagents: Cp_2ZrCl_2 (149.1 mg, 0.51 mmol), THF (3 mL), EtMgBr (1.065 mL, 0.958 M in THF, 1.02 mmol), and 1-phenyl-1-propyne (54 μL, 0.433 mmol). 4-Isopropyl-2-cyclohexen-1-one (35 mg, 0.25 mmol) and a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol) were added at 0°C and the mixture stirred for 2 h at this temperature. Quenching and extractive (Et_2O) workup followed by chromatography on silica gel with 10:1 hexane/ethyl acetate yielded 66.8 mg (94% yield) of the desired 1,4-adduct as a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (d, J=6.8 Hz, 3H), 0.98 (d, J=6.8 Hz, 3H), 1.04 (t, J=7.4 Hz, 3H), 1.36 (s, 3H), 1.30-1.55 (m, 2H), 1.82-1.93 (m, 1H), 2.00-2.45 (m, 7H), 3.17 (dt, J=7.3, 12.5 Hz, 1H), 6.95 (br, 2H, aromatic), 7.26-7.40 (m, 3H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.54, 140.21, 136.57, 135.23, 127.95, 126.34, 46.86, 43.57, 42.78, 40.75, 27.52, 26.49, 24.21, 21.64, 19.99, 16.44, 13.25; IR (neat) cm^{-1} 3052, 3008, 2953, 2922, 2864, 1717, 1462, 1442, 1373, 1250, 1205, 1192, 1075, 912, 733, 706; EIMS, m/e (relative intensity) 284 (62.3, M^+), 255 (24.6), 199 (26.7), 183 (33.5), 157 (34.3), 146 (22.7), 145 (21.4), 142 (24.8), 141 (30.4), 131 (22.2), 129 (65.8), 128 (53.4), 117 (41.3), 116 (22.7), 115 (69.2), 105 (34.6), 91 (100), 83 (28.0); HREIMS calculated for $C_{20}H_{28}O$ (M^+) 284.2140, found 284.2133.

(Table 1, entry 7): (E)-3-(2-Ethyl-1-octenyl)cyclohexanone. To a solution of Cp_2ZrCl_2 (148.8 mg, 0.509 mmol) in THF (3 mL) was added EtMgBr (1.12 mL, 0.912 M in THF, 1.018 mmol) *via* syringe at -78°C. After 1 h of stirring at -78°C, 1-octyne (68 μL, 0.458 mmol) was added as a neat liquid, followed by 5 minutes of additional stirring. The mixture was then warmed to room temperature and stirred for 18 h at this temperature. The ratio of regioisomers for the zirconacyclopentenes formed was determined after

protonolysis of small aliquots with 2N HCl. GC analysis indicated formation of a 7:3 mixture of **3d** and its regioisomer (**3d'**). After the solution was cooled to -40°C, 2-cyclohexen-1-one (21 μL, 0.22 mmol) and a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol) were introduced and the mixture stirred at -40°C for 2 h. The solution was then quenched with 2N HCl and extracted with Et_2O. Normal handling and chromatography on silica gel with 10:1 hexane/ethyl acetate afforded 41.7 mg (80% yield) of the desired 1,4-addition product. ^1H NMR analysis of the product indicated formation of a 88:12 regioisomeric mixture of (E)-3-(2-ethyl-1-octenyl)cyclohexanone and (Z)-3-(3-decen-4-yl)cyclohexanone; Major isomer: ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (bt, J=6.8 Hz, 3H), 0.95 (t, J=7.4 Hz, 3H), 1.21-1.36 (m, 8H), 1.34-1.55 (m, 1H), 1.64-1.87 (m, 2H), 1.92-2.21 (m, 6H), 2.25-2.42 (m, 3H), 2.59-2.80 (m, 1H), 4.95 (d, J=9.3 Hz, 1H, vinylic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.73, 141.49, 127.04, 48.56, 41.21, 37.86, 36.17, 32.21, 31.71, 28.95, 27.94, 25.37, 23.15, 22.62, 14.08, 13.58; IR (neat) cm^{-1} 2956, 2922, 2853, 1712, 1460, 1424, 1379, 1348, 1314, 1259, 1221, 1190, 1053, 1029, 950, 912, 864, 731; EIMS, m/e (relative intensity) 237 (13.9), 236 (69.8, M^+), 207 (60.2), 193 (20.0), 179 (10.1), 178 (13.8), 152 (10.9), 151 (83.7), 133 (17.8), 123 (17.9), 110 (27.1), 109 (12.2), 108 (17.9), 107 (14.1), 97 (100), 95 (41.2), 93 (25.9), 91 (10.3), 81 (27.2); HREIMS calculated for $C_{16}H_{28}O$ (M^+) 236.2140, found 236.2143.

(Table 1, entry 8): (E)-3-(2-Phenyl-1-butenyl)cyclohexanone. The zirconacyclopentene was prepared as described above with the following amounts of reagents; Cp_2ZrCl_2 (150.0 mg, 0.513 mmol), THF (3 mL), EtMgBr (1.125 mL, 0.912 M in THF, 1.026 mmol), and phenylacetylene (48 μL, 0.436 mmol). GC analysis after protonolysis of small aliquots immediately before addition of an enone showed formation of a 2:3 mixture of **3e** and its regioisomer (**3e'**). After the mixture was cooled to -40°C, 2-cyclohexen-1-one (14 μL, 0.15 mmol) and a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol) were added and the mixture stirred at -40°C for 2 h. Quenching with 2N HCl and extractive (Et_2O) workup followed by chromatography on silica gel with 10:1 hexane/ethyl acetate afforded 3.8 mg (11% yield) of (E)-3-(1-phenyl-1-butenyl)cyclohexanone and 21.1 mg (62% yield) of (E)-3-(2-phenyl-1-butenyl)cyclohexanone as colorless oils; Major isomer: ^1H NMR (200 MHz, $CDCl_3$) δ 0.97 (t, J=7.4 Hz, 3H), 1.47-1.99 (m, 3H), 2.05-2.47 (m, 5H), 2.50 (q, J=7.4 Hz, 2H), 2.77-2.98 (m, 1H), 5.47 (d, J=9.3 Hz, 1H, vinylic), 7.23-7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.09, 142.30, 141.84, 130.62, 128.20, 126.87, 126.40, 48.14, 41.20, 38.54, 31.98, 25.35, 23.12, 13.95; IR (neat) cm^{-1} 3048, 3016, 2960, 2922, 2861, 1717, 1600, 1496, 1452, 1385, 1256, 1227, 916, 740, 702, 650; EIMS, m/e (relative intensity) 229 (18.1), 228 (100, M^+), 199 (52.9), 181 (25.9), 171, (41.1), 170 (50.1), 157 (34.8), 155 (23.3), 144 (13.6), 143 (35.7), 142 (13.4), 141 (39.0), 132 (16.9), 129 (95.5), 128 (44.5), 127 (14.3), 117 (27.1), 115 (41.3), 91 (73.8), 84 (19.2); HREIMS calculated for $C_{16}H_{20}O$ (M^+) 228.1514, found 228.1522.

Reaction with NBS: *trans*-2-Bromo-3-((Z)-5-(2-bromoethyl)-4-octen-4-yl)cyclohexanone. The copper-catalyzed conjugate addition was carried out as described above with the following amounts of reagents: Cp_2ZrCl_2 (149 mg, 0.51 mmol), THF (3 mL), EtMgBr (1.118 mL, 0.912 M in THF, 1.02 mmol), 4-octyne (64 μL, 0.434 mmol), 2-cyclohexen-1-one (24 μL, 0.25 mmol), and CuCl•2LiCl (72 μL, 0.5 M in THF, 0.036 mmol). N-Bromosuccinimide (408 mg, 2.29 mmol) in THF (5 mL) was added dropwise *via* syringe at 0°C. The mixture was stirred at 0°C for 30 minutes, followed by 1 h of additional stirring at room temperature. The reaction was then quenched with saturated aqueous NH_4Cl/concentrated NH_4OH solution (9:1) and extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*.

The oily residue was purified by chromatography on silica gel with 8:1 hexane/ethyl acetate to give 83.7 mg (85% yield) of the dibromide as a slightly yellowish liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.95 (t, J=7.4 Hz, 3H), 0.97 (t, J=7.4 Hz, 3H), 1.35-1.58 (m, 4H), 1.80-2.20 (m, 8H), 2.37-2.57 (m, 2H), 2.66-2.84 (m, 2H), 3.01-3.18 (m, 1H), 3.25 (dt, J=6.8, 9.8 Hz, 1H), 3.43 (dt, J=5.3, 9.8 Hz, 1H), 4.62 (d, J=12.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.16, 135.93, 134.71, 61.34, 51.15, 40.92, 34.71, 34.30, 31.80, 30.98, 29.98, 25.39, 24.31, 21.56, 14.98, 14.25; EIMS, m/e (relative intensity) 396 (11.3), 394 (23.1), 392 (12.5), 316 (16.7), 315 (93.6), 314 (20.3), 313 (93.7), 234 (13.4), 233 (24.0), 173 (14.2), 137 (16.9), 133 (22.9), 121 (14.8), 119 (23.9), 117 (46.5), 116 (15.1), 115 (18.0), 109 (18.9), 107 (24.9), 105 (35.6), 97 (38.1), 95 (45.1), 93 (35.1), 91 (54.0), 83 (100), 82 (19.4), 81 (36.1); HREIMS calculated for $C_{16}H_{26}{}^{79}Br_2O$ 392.0350, found 392.0339; calculated for $C_{16}H_{26}{}^{79}Br^{81}BrO$ 394.0330, found 394.0330; calculated for $C_{16}H_{26}{}^{81}Br_2O$ 396.0309, found 396.0307.

Reaction with NIS: *trans*-2-Iodo-3-((Z)-5-(2-iodoethyl)-4-octen-4-yl)cyclohexanone. The copper-catalyzed conjugate addition was carried out as described above with the following amounts of reagents: Cp_2ZrCl_2 (149.3 mg, 0.511 mmol), THF (3 mL), EtMgBr (1.12 mL, 0.912 M in THF, 1.021 mmol), 4-octyne (64 μL, 0.434 mmol), 2-cyclohexen-1-one (24 μL, 0.25 mmol), and CuCl•2LiCl (72 μL, 0.5 M in THF, 0.036 mmol). N-Iodosuccinimide (520 mg, 2.3 mmol) in THF (4 mL) was added dropwise *via* syringe and the mixture stirred at 0°C for 30 minutes, followed by 1 h of additional stirring at room temperature. Quenching with saturated aqueous NH_4Cl/concentrated NH_4OH solution (9:1), extractive (Et_2O) workup, and chromatography on silica gel with 10:1 hexane/ethyl acetate yielded 84.2 mg (69% yield) of the diiodide as a slightly reddish oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.96 (t, J=7.4 Hz, 3H), 0.97 (t, J=7.4 Hz, 3H), 1.36-1.57 (m, 4H), 1.65-2.22 (m, 8H), 2.35-2.60 (m, 2H), 2.70-2.90 (m, 2H), 3.01 (dt, J=6.8, 9.8 Hz, 1H), 2.99-3.18 (m, 1H) 3.23 (dt, J=5.3, 9.8 Hz, 1H), 4.83 (d, J=12.5 Hz, 1H).

Typical Procedure for Tandem Conjugate Addition-Aldol Reaction in the Presence of *n*-Bu_4NCl: *trans*-(E)-3-(5-Ethyl-4-octen-4-yl)-2-(1-hydroxy-1-phenylmethyl)cyclohexanone. The copper-catalyzed conjugate addition was carried out as described above with the following amounts of regents: Cp_2ZrCl_2 (149.7 mg, 0.512 mmol), THF (3 mL), EtMgBr (1.069 mL, 0.958 M in THF, 1.024 mmol), 4-octyne (64 μL, 0.436 mmol), 2-cyclohexen-1-one (24 μL, 0.25 mmol), and CuCl•2LiCl (72 μL, 0.5 M in THF, 0.036 mmol). To another 25 mL round bottom flask equipped with a stir bar and septum and cooled under argon was added dry *n*-Bu_4NCl (213.5 mg, 0.768 mmol) followed by THF (3 mL) and benzaldehyde (104 μL, 1.026 mmol). After the mixture was cooled to 0°C, the solution containing the zirconium enolate was then transferred dropwise over 10 minutes *via* canula into the flask containing the aldehyde, both at 0°C. After 1.5 h of stirring at 0°C, the reaction was quenched with 2N HCl and extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The oily residue was purified by chromatography on silica gel (8:1 hexane-ethyl acetate) to give two diastereomeric aldol products with a combined weight of 66.3 mg (78% yield). The isomer of higher R_f (9.2 mg, 11% yield, R_f 0.38, 8:1 hexane-ethyl acetate) was a slightly yellowish oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.92 (t, J=7.4 Hz, 3H), 0.96 (t, J=7.4 Hz, 3H), 1.00 (t, J=7.4 Hz, 3H), 1.23-1.57 (m, 4H), 1.62-2.39 (m, 11H), 2.44-2.66 (m, 1H), 2.87 (d, J=11.8 Hz, 1H), 3.31 (dt, J=4.4, 11.8 Hz, 1H), 4.34 (d, J=11.5 Hz, 1H, OH), 4.59 (d, J=11.5 Hz, 1H), 7.15-7.48 (m, 5H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 215.84, 144.61, 140.94, 131.65, 127.97, 126.32, 125.29, 71.92, 58.84, 46.22, 43.71, 34.48, 31.33, 27.04, 24.59, 23.98, 21.91, 15.01, 14.52, 14.14; IR (neat) cm^{-1} 3508, 3063, 3035, 2960,

2937, 2872, 1596, 1603, 1452, 1204, 1169, 1068, 913, 737, 700; EIMS, m/e (relative intensity) 342 (1.6, M^+), 324 (4.7), 236 (48.3), 207 (58.8), 194 (21.8), 193 (100), 162 (21.4), 151 (31.7), 149 (29.2), 135 (27.6), 109 (23.2), 107 (25.8), 105 (20.3), 97 (45.0), 95 (50.9), 93 (35.1), 91 (40.0), 83 (25.8); HREIMS calculated for $C_{23}H_{34}O_2$ (M^+) 342.2558, found 342.2571. The isomer of lower R_f (57.1 mg, 67% yield, R_f 0.27, 8:1 hexane-ethyl acetate) was a white solid; ^1H NMR (200 MHz, $CDCl_3$) δ 0.77 (t, J=7.4 Hz, 3H), 0.90 (t, J=7.4 Hz, 3H), 0.91 (t, J=7.4 Hz, 3H), 1.23-1.44 (m, 4H), 1.45-2.09 (m, 10H), 2.28-2.55 (m, 2H), 2.85 (dt, J=3.3, 11.5 Hz, 1H), 3.06 (dd, J=11.5, 4.2 Hz, 1H), 3.87 (d, J=8.0 Hz, 1H, OH), 4.83 (dd, J=8.0, 4.2 Hz, 1H), 7.23-7.25 (m, 5H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 215.40, 141.70, 139.05, 132.81, 127.82, 127.68, 126.92, 73.48, 58.46, 43,47, 42.38, 34.88, 32.06, 30.29, 25.12, 24.60, 23.91, 21.60, 14.98, 14.80, 13.87; IR (neat) cm^{-1} 3480, 3072, 3038, 2963, 2934, 2880, 1708, 1602, 1577, 1455, 1266, 1206, 1060, 914, 736; EIMS, m/e (relative intensity) 342 (11.8, M^+), 324 (32.0), 236 (53.6), 207 (66.0), 201 (26.8), 194 (21.4), 193 (100), 178 (26.3), 162 (22.4), 151 (22.6), 149 (37.1), 135 (33.1), 117 (32.3), 109 (20.7), 106 (46.6), 105 (66.7), 97 (26.2), 91 (25.6), 81 (41.8); HREIMS calculated for $C_{23}H_{34}O_2$ (M^+) 342.2558, found 342.2568.

***trans*-(E)-3-(5-Ethyl-4-octen-4-yl)-2-(1-hydroxy-1-phenylmethyl)cyclopentanone.** The reaction was carried out in the presence of *n*-Bu_4NCl as described above with the following amounts of reagents: Cp_2ZrCl_2 (149.5 mg, 0.511 mmol), THF (3 mL), EtMgBr (1.068 mL, 0.958 M in THF, 1.023 mmol), 4-octyne (64 μL, 0.436 mmol), 2-cyclopenten-1-one (21 μL, 0.25 mmol), CuCl•2LiCl (72 μL, 0.5 M in THF, 0.036 mmol), *n*-Bu_4NCl (213.5 mg, 0.768 mmol), and benzaldehyde (104 μL, 1.026 mmol). The reaction mixture was stirred for 2 h at 0°C and then quenched with 2N HCl. Extractive (Et_2O) workup followed by chromatography on silica gel with 8:1 hexane/ethyl acetate afforded the desired aldol product (63.2 mg, 77% yield, R_f 0.26, 8:1 hexane-ethyl acetate) as a single isomer; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, J=7.4 Hz, 3H), 0.88 (t, J=7.4 Hz, 3H), 0.89 (t, J=7.4 Hz, 3H), 1.20-1.82 (m, 4H), 1.55-2.18 (m, 9H), 2.37 (dd, J=18.5, 7.9 Hz, 1H), 2.67 (ddd, J=11.7, 4.1, 1.2 Hz, 1H), 3.16 (dt, J=11.7, 6.6 Hz, 1H), 3.60-3.90 (br s, 1H, OH), 5.01 (d, J=4.1 Hz, 1H), 7.20-7.28 (m, 5H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 221.87, 141.82, 139.07, 130.99, 128.00, 127.27, 126.28, 73.21, 57.79, 40.25, 38.80, 34.19, 30.17, 27.28, 24.25, 24.05, 21.85, 14.77, 14.55, 14.14; IR (neat) cm^{-1} 3458, 3076, 3040, 2982, 2948, 2890, 1743, 1604, 1460, 1120, 1032, 917, 743, 708; EIMS m/e (relative intensity) 328 (10.0, M^+), 222 (25.0), 193 (58.3), 179 (90.0), 164 (100), 135 (31.5), 131 (30.6), 107 (30.8), 106 (36.3), 105 (56.2), 95 (29.3), 93 (22.3), 91 (49.0), 83 (36.6), 81 (34.9); HREIMS calculated for $C_{22}H_{32}O_2$ (M^+) 328.2402, found 328.2405.

***trans*-(E)-3-(5-Ethyl-4-octen-4-yl)-2-(1-hydroxyhexyl)cyclopentanone.** The reaction was carried out in the presence of *n*-Bu_4NCl as described above with the following amounts of reagents: Cp_2ZrCl_2 (149.9 mg, 0.513 mmol), THF (3 mL), EtMgBr (1.07 mL, 0.958 M in THF, 1.026 mmol), 4-octyne (64 μL, 0.437 mmol), 2-cyclopenten-1-one (21 μL, 0.25 mmol), CuCl•2LiCl (72 μL, 0.5 M in THF, 0.036 mmol), *n*-Bu_4NCl (213.5 mg, 0.768 mmol), and hexanal (123 μL, 1.026 mmol). The reaction mixture was stirred for 3 h at 0°C and then quenched with 2N HCl. After the usual workup, chromatography on silica gel with 8:1 hexane/ethyl acetate gave two diastereomeric products with a combined weight of 67.8 mg (84% yield). The isomer of higher R_f (25.3 mg, 31% yield, R_f 0.34, 8:1 hexane-ethyl acetate) was a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, J=6.7 Hz, 3H), 0.93 (t, J=7.4 Hz, 6H), 0.97 (t, J=7.4 Hz, 3H), 1.20-2.49 (m, 23H), 2.90 (br s, 1H, OH), 3.20 (dt, J=6.4, 11.8 Hz, 1H), 3.49-3.62 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 221.81, 139.57, 131.72, 71.32, 56.51, 42.41, 38.67, 35.39, 34.39, 31.60, 30.14, 26.37, 25.73, 24.51, 24.13,

22.59, 21.89, 14.84, 14.49, 14.29, 14.02; IR (neat) cm^{-1} 3438, 2969, 2932, 2876, 1738, 1465, 1413, 1384, 1148, 1095, 1086, 1054, 919, 888, 741; EIMS, m/e (relative intensity) 322 (32.8, M^+), 304 (31.3), 275 (35.9), 261 (38.0), 193 (64.6), 181 (51.8), 179 (64.1), 169 (56.9), 166 (36.5), 165 (28.9), 164 (100), 156 (28.7), 135 (49.2), 123 (28.0), 99 (31.0), 95 (61.8), 93 (49.1), 91 (60.0), 83 (62.1), 82 (24.9); HREIMS calculated for $C_{21}H_{38}O_2$ (M^+) 322.2871, found 322.2875. The isomer of lower R_f (42.5 mg, 53% yield, R_f 0.29, 8:1 hexane-ethyl acetate) was a colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, J=6.7 Hz, 3H), 0.93 (t, J=7.4 Hz, 3H), 0.94 (t, J=7.4 Hz, 3H), 0.97 (t, J=7.4 Hz, 3H), 1.20-2.48 (m, 24H), 3.29 (dt, J=6.4, 11.8 Hz, 1H), 3.78-3.89 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 221.77, 139.03, 131.91, 71.05, 57.18, 40.54, 38.91, 34.25, 33.58, 31.62, 30.17, 26.64, 25.94, 24.63, 24.12, 22.53, 21.71, 14.87, 14.50, 14.34, 13.99; EIMS, m/e (relative intensity) 322 (36.5, M^+), 275 (25.8), 261 (29.9), 193 (28.4), 181 (69.7), 179 (62.2), 177 (22.3), 165 (27.6), 164 (100), 135 (29.7), 95 (28.7), 91 (25.2), 83 (31.8), 81 (42.1); HREIMS calculated for $C_{21}H_{38}O_2$ (M^+) 322.2871, found 322.2883.

***trans*-(Z)-3-(5-(2-Bromoethyl)-4-octen-4-yl)-2-(1-hydroxy-1-phenylmethyl)cyclopentanone.** The conjugate addition-aldol reaction was carried out as described above with the following amounts of reagents: Cp_2ZrCl_2 (150.1 mg, 0.513 mmol), THF (3 mL), EtMgBr (1.072 mL, 0.958 M in THF, 1.027 mmol), 4-octyne (64 μL, 0.437 mmol), 2-cyclopenten-1-one (21 μL, 0.25 mmol), CuCl•2LiCl (72 μL, 0.5 M in THF, 0.036 mmol), *n*-Bu_4NCl (203 mg, 0.72 mmol), and benzaldehyde (104 μL, 1.026 mmol). N-Bromosuccinimide (204 mg, 1.15 mmol) in THF (2.5 mL) was added dropwise *via* syringe into the solution containing the zirconium enolate at 0°C. After 1 h at 0°C, the reaction mixture was quenched with 2N HCl and extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Chromatography on silica gel with 6:1 hexane/ethyl acetate afforded 61.4 mg (60% yield) of the desired product as a single diastereomer; ^1H NMR (200 MHz, $CDCl_3$) δ 0.85 (t, J=7.4 Hz, 6H), 1.02-1.34 (m, 4H), 1.57-1.94 (m, 6H), 2.02-2.49 (m, 3H), 2.58-2.80 (m, 2H), 2.81-3.14 (br s, 1H, OH), 3.10-3.37 (m, 3H), 5.12 (d, J=3.5 Hz, 1H), 7.20-7.27 (m, 5H, aromatic); ^{13}C NMR (50 MHz, $CDCl_3$) δ 220.76, 141.90, 135.72, 133.87, 128.09, 127.21, 125.73, 72.20, 58.11, 39.82, 38.50, 35.12, 34.50, 31.42, 30.20, 27.02, 24.05, 21.68, 14.75, 14.46; IR (neat) cm^{-1} 3444, 3065, 3036, 2960, 2938, 2878, 1736, 1606, 1497, 1455, 1406, 1270, 1210, 1154, 1032, 745, 702; EIMS, m/e (relative intensity) 408 (1.6), 406 (2.2), 310 (27.4), 309 (100), 281 (28.6), 259 (45.7), 257 (47.8), 193 (37.1), 163 (76.3), 131 (23.0), 107 (64.0), 105 (28.0), 91 (52.2); HREIMS calculated for $C_{22}H_{31}{}^{79}BrO$ 406.1507, found 406.1517, calculated for $C_{22}H_{31}{}^{81}BrO$ 408.1486, found 408.1494.

(Z)-3-(1-Hydroxy-1-phenyl-4-propyl-4-octen-5-yl)cyclohexanone. The zirconacyclopentene was prepared as described above with the following amounts of reagents: Cp_2ZrCl_2 (149.1 mg, 0.51 mmol), THF (3 mL), EtMgBr (1.065 mL, 0.958 M in THF, 1.02 mmol), and 4-octyne (64 μL, 0.436 mmol). Benzaldehyde (56 μL, 0.548 mmol) was added to the mixture at 0°C. After 3 h of stirring at 0°C, addition of 2-cyclohexen-1-one (24 μL, 0.25 mmol) was followed by injection of a THF solution of CuCl•2LiCl (72 μL, 0.5 M, 0.036 mmol). The reaction mixture was stirred for 1.5 h at 0°C and then quenched with 2N HCl and extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Chromatography on silica gel with 3:1 hexane/ethyl acetate gave 68.4 mg (80% yield) of the desired product as an about 1:1 mixture of diastereomers that were not resolved by TLC; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, J=7.4 Hz, 3H), 0.91 (t, J=7.4 Hz, 3H), 1.20-2.40 (m, 21H), 2.57-2.79 (m, 1H), 4.54-4.69 (m, 1H), 7.20-

7.40 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.21, 211.99, 144.61, 144.53, 135.50, 135.36, 134.61, 134.53, 128.41, 127.47, 125.88, 125.76, 74.29, 74.21, 46.89, 41.62, 41.56, 41.10, 38.83, 38.70, 34.28, 34.19, 30.22, 26.86, 26.76, 25.61, 24.27, 21.86, 14.75, 14.22; IR (neat) cm^{-1} 3440, 3082, 3036, 2995, 2973, 2897, 1708, 1457, 1426, 1383, 1348, 1322, 1267, 1228, 1063, 916, 738, 704; EIMS, m/e (relative intensity) 342 (11.2, M^+), 325 (11.4), 324 (19.7), 246 (27.5), 227 (45.6), 220 (26.8), 207 (11.0), 191 (14.6), 177 (16.1), 133 (36.9), 120 (100), 107 (45.9), 105 (27.0), 97 (90.7), 95 (23.2), 93 (23.0), 91 (79.2), 81 (27.3); HREIMS calculated for $C_{23}H_{34}O_2$ (M^+) 342.2558, found 342.2574.

Note Added in Proof: After submission of this manuscript, a related study on the use of CuCl to effect Zr-to-Cu transmetalations/*alkylations* appeared; *cf.* Takahashi, T., Kotora, M., Kasai, K., Suzuki, N., *Tetrahedron Lett.*, **1994**, *35*, 5685.

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