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A Conjugate Addition-Elimination Route to Alkenoyltrimethylsilanes

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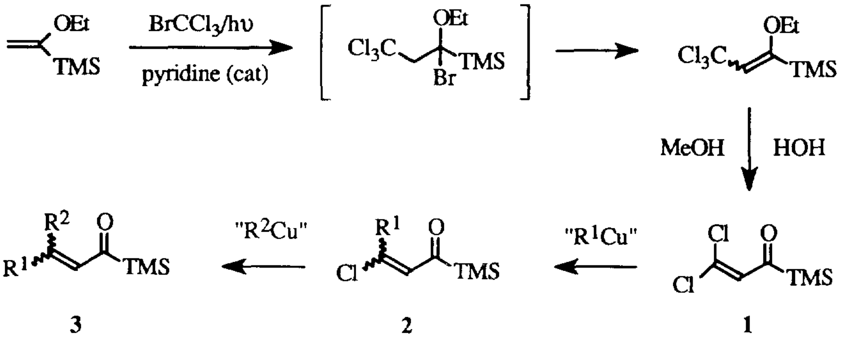
Abstract: Monosubstitution of 3,3-dichloro-1-(trimethylsilyl)-2-propenone (1) with organocuprates stereoselectively affords *E*-3-alkyl- and *Z*-3-phenyl-3-chloro-1-(trimethylsilyl)-2-propenones. Further substitution proceeds stereoselectively as a function of extant and incoming substituents. 1 was also reduced to *E*-3-chloro-1-(trimethylsilyl)-2-propenone and the latter converted to *E*-3-alkyl- and *E*-3-phenyl-1-(trimethylsilyl)-2-propenones.

A number of strategies are currently available for the synthesis of conjugated alkenoylsilanes[1], but none of these to our knowledge have been shown to afford differentially β,β-disubstituted-α,β-alkenoylsilanes in a stereoselective fashion. Here we wish to expand on our preliminary findings[2] which indicated that both **2**[3] and **3** could be obtained in a stereoselective fashion by sequential addition of organocopper reagents to dichloroketone **1**, which was itself readily available in the one-pot series of transformations shown in Scheme 1. When this project was initiated, only one example of the monoalkylation of a β,β-dichloroenone



Scheme 1

(4,4-dichloro-3-propen-2-one) was extant, a conversion which was observed to give the E isomer stereoselectively (95:5).[4] It was also subsequently shown that further treatment of this **2** with $nBu_2CuLi\cdot Me_2S$ afforded **3** (TMS = Me) with predominant inversion of configuration (E:Z = 2:3).[5]

RESULTS

Monosubstitution of 1

Organocuprates derived from CuCN were chosen for investigation because of their ease of preparation[6] and proven efficacy in conjugate addition reactions.[7,8] Trial experiments utilizing both $Me_2Cu(CN)Li_2$ and MeCu(CN)Li with **1** soon disclosed the highly reactive nature of these reagents towards not only **1**, but also towards the resulting substitution products **2** and **3** (Table 1, runs 1-3). The protocol finally employed to maximize the production of **2** (run 4) consisted of (a) use of a formal excess of MeCu(CN)Li in order to completely consume **1** (b) precooling both cuprate and **1** to -78 °C (c) slow addition of cuprate to **1** and (d) use of THF as solvent. However, extension of this procedure to other cuprates necessitated adaptations in stoichiometry and reagent on a case-by-case basis. For runs 5 and 6, a higher cuprate:**1** ratio was necessary for the complete consumption of **1**. This seemed related to a lower cuprate stability towards dimerization, since significant amounts of 3,4-dimethylhexane were found in the

Table 1. Treatment of **1** with Organocuprates[a]

Run	Cuprate	Mole Ratio (Cuprate:**1**)	Product Ratio[b] or Yield (%)[c]		
			1	**2**	**3**
1[d]	$Me_2Cu(CN)Li_2$	1.0	1	-	3
2[e]	$Me_2Cu(CN)Li_2$	1.0	-	-	(56)
3	MeCu(CN)Li	1.0	1	4	2
4	MeCu(CN)Li	1.2	-	(57)	-
5	tBuCu(CN)Li	1.5	-	(75)	-
6	sBuCu(CN)Li	1.5	-	(75)	-
7	nBuCu(CN)Li	1.2	6	33	1
8[f]	nBuCu(CN)MgCl	1.0	4	1	-
9[f]	$nBu_2Cu(CN)(MgCl)_2$	1.0	-	(80)	-
10[f]	$cPr_2Cu(CN)Li_2$	1.2	-	(75)	-
11	PhCu(CN)Li	1.5	3	2	2
12	$Ph_2Cu(CN)(MgCl)_2$	1.0	2	1	2
13[g]	PhCu(CN)Li	1.8	h		
14[i]	PhCu(CN)Li	1.8	1	1(65)[j]	-

[a]Except as noted, cuprate in THF at -78 °C added to **1** in THF at -78 °C. [b]Ratios from NMR analysis. [c]Isolated from chromatography [d]**1** in ether at 25 °C added to cuprate in ether at -78 °C; one-third of the product mixture consisted of neopentyl TMS ketone. [e]**1** in THF at 25 °C added to cuprate in THF at -78 °C. [f]In ether-THF. [g]In ether-1,2-dimethoxyethane. [h]No reaction. [i]TMSCl (5 eq.) was admixed with **1**. [j]Yield based on unrecovered **1**.

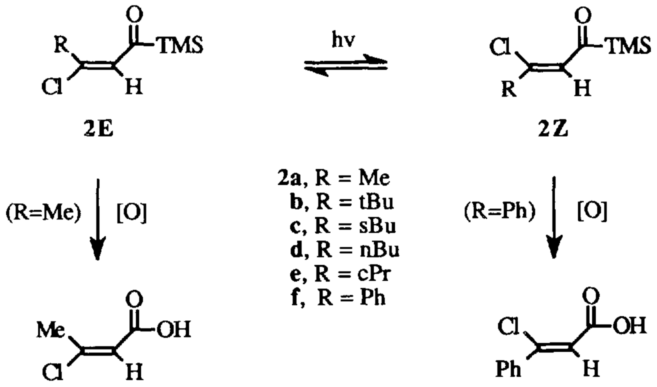
sBuCu(CN)Li experiments. Use of nBuCu(CN)Li afforded reasonable yields of the corresponding **2**, but the product contained small amounts of unreacted **1** (at lower cuprate:**1** ratios) or disubstituted **3** at higher ratios. A solution was finally found (run 9) by employing the dialkylcuprate derived from nBuMgCl. The cuprate cPrCu(CN)Li proved to be unreactive in either THF or ether, even at higher temperature (-20 °C), but the dialkyl(cyano)cuprate (run 10) afforded **2** in good yield and purity. Productive phenylation of **1** proved particularly difficult, with all previous protocols failing to afford clean **2**. It was finally noted (run 14) that inclusion of TMSCl in the reaction mixture inhibited formation of **3**, although conversion of **1** was then incomplete.[9] Nevertheless, since chromatographic separation of **2** from **1** (but not from **3**) was possible, this approach afforded pure monoadduct. All monoadducts (**2a-f**) could therefore be obtained in high (95+% by NMR analysis) isomeric and overall purity in the yields indicated in Table 1.

Structural Assignments for 2

The stereochemistry of the initial monoaddition products was determined by both chemical methods and comparative ^{1}H NMR spectral data. Oxidation[10] of **2a** (Scheme 2) afforded the known *E*-chloroacrylic acid[11] and UV irradiation provided a mixture containing the corresponding Z-ketone for spectral comparison (Table 2). In β-alkyl-β-chlorovinyl ketones, both the allylic (γ) hydrogens of the *cis* -β-alkyl group and the vinylic proton in the E isomer are deshielded relative to those of the Z- isomer.[12] These correlations allowed the assignment of E stereochemistry for **2a**. By extension, **2c-e** have also been assigned E stereochemistry based on the consistency of δ (=CH) values (δ 6.9) in the series **2a,c-e**. On standing, the initially obtained isomer of **2b** [δ (=CH) = 6.42] spontaneously isomerized completely to the stereoisomer exhibiting δ (=CH) = 6.24, thus identifying the initial isomer as E, in keeping with steric equilibrium expectations. This assignment is also consistent with the relative chemical shift values of the isomeric vinylic protons. The phenyl-substituted **2f** which was initially obtained displayed δ (=CH) = 6.94, and after photolytic isomerization, produced an isomer showing δ (=CH) = 6.71. Examination of literature data for an asilyl analogue (4-chloro-4-phenyl-3-propene-2-one), however, indicated that in contrast to β-alkylchlorovinylketones, it was the Z-isomer of β-phenylchlorovinylketones that exhibited lower-field vinylic proton absorption.[13] Additional NMR correlations for assigning Z configuration to **2f** lay in the upfield shift of TMS protons when positioned cis to a phenyl ring (see later). Finally, this assignment was confirmed by oxidation of **2f** to produce the known Z- carboxylic acid.[14] The α,β-unsaturated ketones **2c,d** were found to largely isomerize upon standing to their β,γ-isomers, consistent with reported observations on asilyl analogues.[15]

Disubstitution of 1

Homodisubstitution of **1** was first explored. Trial runs indicated that complete disubstitution required more forcing conditions than those employed for monosubstitution. The use of $R_2Cu(CN)Li_2$ reagents at more elevated temperatures (-20 to 0 °C) served to prepare the **3** listed in Table 3. An exception was $tBu_2Cu(CN)Li_2$, which led only to **5b** (*E*-4,4-dimethyl-1-(trimethylsilyl)-2-propenone), presumably by *in situ* reduction of **2b**.



Scheme 2

Table 2. ^{1}H NMR Data (δ) for **2a-f** and Asilyl Analogues

	TMS	γ-H	=CH	Other
2a (E)	0.22	2.47 (s, 3H)	6.88	
(Z)	0.22	2.21 (s, 3H)	6.46	
2a' (E) (TMS = Me)	-----	2.52 (s, 3H)	6.47	2.20 (s, 3H)
(Z) (TMS = Me)	-----	2.26 (s, 3H)	6.27	2.33 (s, 3H)
2b (E)	0.22		6.42	1.18 (s, 9H)
(Z)	0.22		6.24	1.20 (s, 9H)
2c (E)	0.22	3.73 (m, 1H)	6.89	1.4 (m, 2H), 1.07 (d, 3H), 0.80 (t, 3H)
2d (E)	0.20	2.81 (t, 2H)	6.88	1.55 (m, 2H), 1.3 (m, 2H), 0.90 (t, 3H)
2e (E)	0.20	3.37 (m, 1H)	6.92	1.05 (m, 2H), 0.93 (m, 2H)
2f (E)	-0.01		6.71	7.4 - 7.8 (m, 5H)
(Z)	0.29		6.94	7.4 - 7.8 (m, 5H)
2f' (E) (TMS = Me)	-----		6.42	2.20 (s, 3H)
(Z) (TMS = Me)	-----		6.74	2.33 (s, 3H)

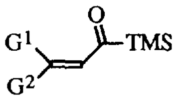
Table 3. Homodisubstitution of **1** by $R_2Cu(CN)Li_2$[a]

$R_2Cu(CN)Li_2$ R =	Cuprate/**1** mole ratio	Temp[b] (°C)	Product (% yield)
Me	2.4	0	**3a** (65)
tBu	3.0	0	**5b** (65)
sBu	3.0	-15	**3c** (75)
nBu	3.0	-20	**3d** (84)
Ph	3.0	-20	**3e** (73)

[a] Added at -78 °C, warmed to temperature indicated; protonated at -78 °C.

Heterodisubstitution of **1** was, where possible, carried out as a sequential *in situ* process for purposes of expedition and in order to avoid potential isomerization (Table 4). Exception was made in the case of **2f**, where isolation of the monosubstitution product was necessary in order to remove unreacted **1** (*vide supra*). In addition, a comparison was made between the *in situ* and "prior isolation" processes in runs 4-6 of Table 4. A change in (but not inversion of) the E:Z ratio of **3g** was noted when isolated **2c** was employed (run 5). Since under *in situ* conditions, an additional equivalent of LiCl results from the first addition-elimination before the addition of the second cuprate, these conditions were approximated in run 6 by adding one equivalent of LiCl during the second cuprate addition. The resulting E:Z ratio is closer to (but still smaller than) the *in situ* result, suggesting that the largest stereodifferentiation results from the *in situ* process. A similar addition of LiCl was made in all runs (10, 16, 19) where **2f** was islolated. The addition of $nBu_2Cu(CN)Li_2$ to **2f** resulted in a vigorous reaction from which no **3n** could be obtained, and dictated the use of nBuCu(CN)Li in run 19.

For a comparison of overall stereochemical change (**2**→**3**), the substrate-reagent combinations of Table 4 can be grouped into three regimes by type of first-introduced *vs* second-introduced organic group: (a) alkyl-alkyl (b) alkyl-phenyl and (c) phenyl-alkyl. All monoalkylated chlorovinyl ketones (**2a-d**) are of E configuration, and primarily give products of inverted configuration upon treatment with alkyl cuprates (a). The striking exceptions occur with the use of t-butyl cuprate, whereupon only **3** of retained configuration are produced. When phenyl cuprate was employed (b), complete retention of configuration resulted, except for the t-butyl-containing **2b** (run 15), where 90% inversion was observed. The monophenylated chloroketone **2f** has been established as the Z isomer, and subsequent treatment with alkyl cuprates (c) afforded products of retention.



3a G^1 = G^2 = Me
3c G^1 = G^2 = sBu
3d G^1 = G^2 = nBu
3e G^1 = G^2 = Ph

3f (E); G^1 = Me, G^2 = tBu
(Z); G^1 = tBu; G^2 = Me
3h (E); G^1 = Me, G^2 = nBu
(Z); G^1 = nBu, G^2 = Me
3j (E); G^1 =sBu, G^2 = tBu
(Z); G^1 = tBu, G^2 = sBu
3l (E); G^1 =tBu, G^2 = Ph
(Z); G^1 = Ph, G^2 = tBu
3n (E); G^1 = nBu, G^2 = Ph
(Z); G^1 = Ph, G^2 = nBu

3g (E); G^1 = Me, G^2 = sBu
(Z); G^1 =sBu, G^2 = Me
3i (E); G^1 = Me, G^2 =Ph
(Z); G^1 = Ph, G^2 = Me
3k (E); G^1 = nBu, G^2 = tBu
(Z); G^1 = tBu, G^2 = nBu
3m (E); G^1 = nBu, G^2 = sBu
(Z); G^1 = sBu, G^2 = nBu

Structural Assignments for 3

The stereochemistry of diadducts **3** was determined by ^{1}H NMR spectroscopy. (Table 5) It is well-established that in α, β - unsaturated aldehydes or ketones, γ - hydrogens which are cis to the carbonyl group appear downfield from those of an identical group which is trans-located.[15] In ambiguous cases where only one stereoisomer was generated upon sequential cuprate additions, UV-isomerization of the initial adduct afforded the other geometric isomer. Inspection of the data for **3i, l, n** leads to an additional correlation: compounds containing a cis (to carbonyl) phenyl group show TMS absorption at higher field than those with a trans-oriented phenyl group (this shift is also displayed by the *di*phenyl compound **3e** and by the E/Z isomers of **2f**).

Reduction of 1 and the Substitution of 4

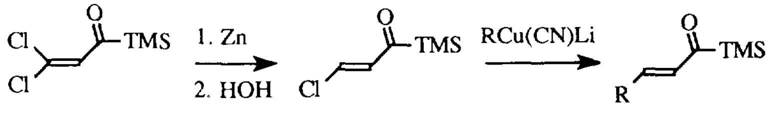
Rao and Knochel have shown that organozinc halides can be formed from β-(mono)halovinyl carbonyl compounds,[16] and that these species , or their cuprates, can be coupled with certain organic halides. The organozinc reagent derived from the dichloro substrate **1** formed readily, but attempts at elaborating this

Table 4. **3** Obtained From Sequential Cuprate Additions to **1**[a]

Run	Cuprate #1[b]	Cuprate #2[b]	**3**	Predominant
	(**1** : Cuprate mole ratio)		E:Z[c] (% yield)	Stereochemistry[d]
1	Me (1.2)	tBu$_2$ (1.5)[e]	**3f** 1:0 (72)	R
2	tBu (1.5)	Me$_2$ (1.5)[e]	**3f** 1:0 (97)	I
3	Me (1.2)	sBu$_2$ (1.5)[f]	**3g** 1:4 (69)	I
4	sBu (1.5)	Me$_2$ (1.5)[f]	**3g** 7:1 (67)	I
5	sBu (1.5)[g]	Me$_2$ (1.5)[f]	**3g** 3:2 (66)[i]	I
6	sBu (1.5)[g,h]	Me$_2$ (1.5)[f]	**3g** 4:1 (77)[i]	I
7	Me (1.2)	nBu$_2$ (1.5)[f]	**3h** 1:3 (67)	I
8	nBu$_2$ (1.0)[j]	Me$_2$ (1.5)[e]	**3h** 3:1 (70)	I
9	Me (1.2)	Ph$_2$ (1.5)[k]	**3i** 1:0 (70)	R
10	Ph (1.8)[gh]	Me$_2$ (1.5)[l]	**3i** 1:0 (74)[i]	R
11	tBu (1.5)	sBu$_2$ (2.0)[l]	**3j** 1:0 (79)	I
12	sBu (1.5)	tBu$_2$ (2.0)[l]	**3j** 1:0 (73)	R
13	tBu (1.5)	nBu$_2$ (2.0)[l]	**3k** 1:0 (61)	I
14	nBu$_2$ (1.0)[j]	tBu$_2$ (2.0)[l]	**3k** 1:0 (60)	R
15	tBu (1.5)	Ph$_2$ (2.0)[e]	**3l** 1:9 (77)	I
16	Ph (1.8)[g,h]	tBu$_2$ (2.0)[e]	**3l** 1:0 (75)[i]	R
17	sBu (1.5)	nBu$_2$ (2.0)[e]	**3m** 1:0 (75)	I
18	nBu$_2$ (1.0)[j]	sBu2 (2.0)[e]	**3m** 1:3 (73)	I
19	Ph (1.8)[g,h]	nBu (2.0)[e,m]	**3n** 1:0 (67)[i]	R
20	nBu$_2$ (1.0)[j]	Ph$_2$ (1.5)[e]	**3n** 1:0 (54)	R

[a]Each added at -78 °C; then held at -78 °C, 1 h, unless otherwise indicated. [b]"R" = RCu(CN)Li; "R$_2$" = R$_2$Cu(CN)Li$_2$ [c]E:Z ratio determined by NMR analysis of product obtained after workup but before chromatography. [d]Majority inversion (I) or retention (R) of configuration in the conversion of **2** to **3**. [e]0 °C, 0.5 h. [f]0 °C, immediate recool to -78 °C. [g]Monoadduct (**2f**) isolated. [h]One equivalent of LiCl added before second cuprate. [i]Yield of second step only. [j]nBu$_2$Cu(CN)(MgCl)$_2$; -10 °C, 1.0 h. [k]-10 °C, 0.5 h. [l]0° C, 1 h. [m]See experimental section.

species by coupling reactions were uniformly unsuccessful.[17] However, hydrolysis provided the monoreduction product **4** in good yield and high stereoselectivity. This allowed an entry to E-configured α,β-unsaturated acylsilanes **5a-e** by way of a stereoselective cuprate addition-elimination step (Scheme 3).



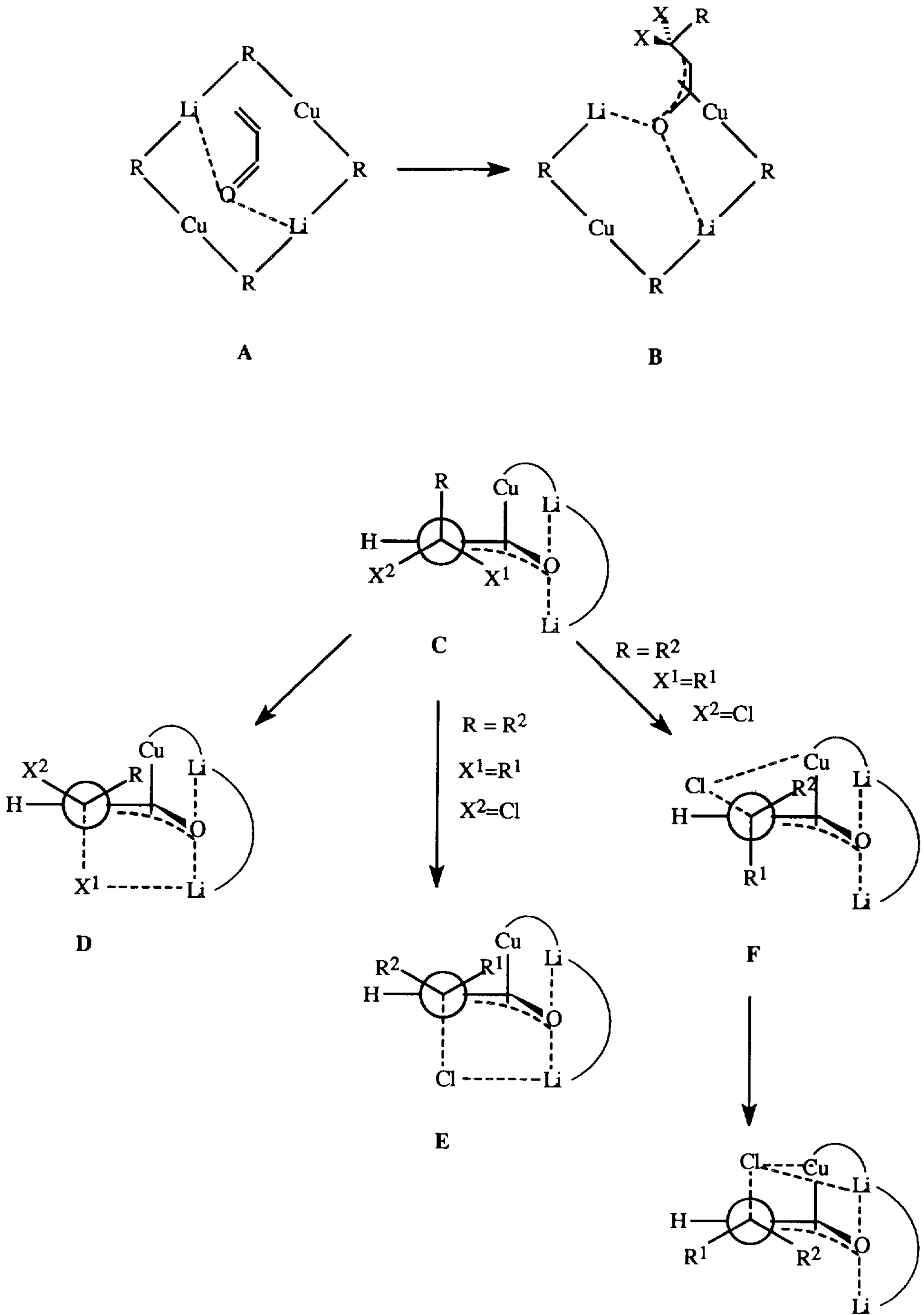
1 **4**

5a, R = Me
b, R = tBu
c, R = sBu
d, R = nBu
e, R = Ph

Scheme 3

Discussion

Dieter was the first to address the monosubstitution of α,β-unsaturated carbonyl compounds containing two good leaving groups [β,β-bis(thioalkyl)].[4] There is a strong parallel between these results [employing mainly RCu(SPh)Li in THF] and ours in that products of high E/Z ratios were obtained in each case. Further investigation by Dieter of the stereochemistry associated with the substitution of the second thioalkyl group indicated that for a given substrate, predominant retention or inversion was a function of the cuprate/solvent combination chosen.[5] However, in the two instances in which $Me_2Cu(CN)Li_2$ (in ether) was employed, a high degree of inversion occurred, in concert with our observation that inversion dominates the further substitution of *E*-**2a-d** with higher-order cyanocuprates (alkyl-alkyl cases; exceptions involve substitution by the tBu group and will be addressed below). With chloroenones, cyanocuprates as employed by us gave more inversion than other cuprates.[5] Rationalizations for the stereochemical outcomes of both the **1** to **2** and *Z*-**2** to **3** conversions for thioalkyl analogues have been given previously,[4,5].but although also in part applicable to present results, are not extendable to the predominant inversion of stereochemistry in the *E*-**2** to **3** transformations encountered herein. We suggest consideration of Scheme 4 as a unifying concept. Support exists for the initial chelation[18] of a planar cuprate dimer[19] with an enone substrate (**A**).[20] Upon transfer of the R group to the β-C atom of the enone, the enolate anion may assume same-face perpendicular coordination (90° rotation vs. the initial approach geometry) to the copper atom within a complex now exhibiting bifacial lithium coordination (**B**, TMS group omitted for clarity). A Newman projection view (**C**) of this complex suggests that for **1** ($X^1 = X^2 = Cl$) and *Z*-**2f** ($X^1 = Cl$, $X^2 = Ph$) a 60° clockwise rotation to attain the anti-periplanar geometry favored for elimination (**D**) will prevail over the counterclockwise alternative because of the proximate location of a (complexed?) lithium counterion which can ultimately accompany the expelled chloride ion. This process results in emplacement of R with retention of configuration relative to X^1, producing the observed *E*-**2a-e** from **1**, and **3** of retained configuration from *Z*-**2f**. The unique stereochemistry of **2f** formation is accommodated by this analysis if it is assumed that steric and electronic repulsion forces (vis a vis the enolate anion) are more inhibitory for clockwise motion of the phenyl group than for counter-clockwise movement of $X^1 = Cl$.[21] The *E*-**2** to **3** conversions are modeled by **C** ($X^1 = R^1$, $X^2 = Cl$), which is the initial rotamer formed upon introduction of R^2. Since this does not possess proximate metal and chlorine groups nor a periplanar geometry, it must undergo either a 60° counterclockwise rotation to give **E** or a 60° clockwise rotation to give **F** on the way to **G**. By traditional view, the most accessible activation energies for



Scheme 4

β-elimination have been limited to antiperiplanar (lower energy) and synperiplanar (higher energy) geometries. However, recent results indicate that in $E1_{cb}$-like systems, a gauch-syn arrangement between leaving group and developing carbanion (in **F**, chlorine and Cu-complexed enolate anion) may represent the transition state for elimination, with eventual double-bond geometry being attained later in the reaction profile.[22] The benefit of this view to the evolution of **C** by clockwise rotation is twofold: it requires the same least motion as in the attainment of **E**, and it obviates the necessity of eclipsing R^2 and the bulky enolate moiety required to arrive at the transition state (**G**) for synperiplanar elimination. Disposition of **C** by counterclockwise rotation to attain **E**, in contrast, necessitates eclipsing R^1 and the enolate substituent. Since **F** leads to inversion, and **E** to retention products, the inversion:retention values observed in the conversion of *E*-**2** to *E,Z*-**3** (Table 4) may be a reflection of a tradeoff between steric and stereoelectronic factors. By this reasoning, "large" groups which cannot relieve steric or electronic interactions with the enolate moiety by conformational adaptations (Ph, tBu) should strongly resist rotations within **C** which generate such compression. In fact, *E*-**2b** undergoes substitution (**C**, X^1 = tBu) with 100% inversion (Table 4, runs 2, 11, 13) except for run 15 (90% inversion), where phenyl is pitted against it. Similarly, introduction of tBu as R^2 leads to 100% retention (Table 4, runs 1, 12, 14, 16), as does introduction of the phenyl group (Table 4, runs 9, 20). These results are therefore in concert with the interpretation presented here. Parallel reasoning predicts that addition-elimination of **4** should proceed via **C** (X^1 = H, X^2 = Cl) to **E** (R^1 = H) and thence to *E*-**5**, as observed.

Experimental

General

NMR spectra were obtained at 200 MHz using $CDCl_3$ solutions ($CHCl_3$ taken as δ 7.24). IR spectra were taken on neat films. Gas chromatographic analyses utilized 2 ft and 5 ft (x 0.25 in) 20% SE-30 columns. All reactions were carried out under argon. THF and ether were distilled from sodium benzophenone ketyl immediately before use. Methyllithium (MeLi·LiBr), 1.5 M in ether, butyllithium (nBuLi), 1.6 M in hexane, *sec*-butyllithium (sBuLi), 1.3 M in cyclohexane, *tert*-butyllithium (tBuLi), 1.7 M in pentane, phenyllithium (PhLi), 1.8 M in 70-30 cyclohexane-ether, phenylmagnesium chloride (PhMgCl), 2M in THF, butylmagnesium chloride (nBuMgCl), 2.0 M in ether and CuCN were obtained from Aldrich Chemical Co. Enone cis-trans isomerizations were carried out in hexane solution employing a quartz vessel and a "Rayonet" apparatus at 265 nm. All compounds (**2-5**) were obtained as liquids from chromatography.

3,3-Dichloro-1-(trimethylsilyl)-2-propenone (1). A mixture of (1-ethoxyethenyl)trimethylsilane[23] (27 g, 0.19 mol), bromotrichloromethane (79 g, 0.40 mol), pyridine (1.6 g, 0.02 mol), and 100 mL of CCl_4 was placed in a flask equipped with a reflux condenser and irradiated with a 150 watt spotlight for 6 h. Methanol (100 mL) and water (20 mL) were added and the reaction mixture stirred for 1 h. After a water-pentane workup, the dried ($MgSO_4$) organic phase afforded 26 g (70%) of **1**, bp 60-65 °C (1 mmHg).[2] A smaller run was interrupted after 20 min irradiation and filtered. An NMR spectrum of the filtrate showed, besides absorptions attributable to unreacted (1-ethoxyethenyl)trimethylsilane, absorptions at δ 0.20 (s, 9H), 0.25 (s, 9H), 1.22 (t, J = 6 Hz, 3H), 1.26 (t, J = 6 Hz, 3H), 3.65-3.95 (overlapped m, 4H), 6.28 (s, 1H), 6.50 (s, 1H). These are assumed to arise from the E/Z isomers of $Cl_3CCH{=}C(OEt)SiMe_3$.

Preparation of 3-Chloro-1-(trimethylsilyl)-2-alkenones (2). The following procedure is representative of all preparations of **2** when the appropriate cuprate and stoichiometry indicated in Table 1 are employed.

***E*-3-Chloro-1-(trimethylsilyl)-2-butenone (2a).** Copper(I) cyanide (0.22 g, 2.4 mmol) was dried by air-gun heating under vacuum (1 mm), and the flask then back-filled with argon. After cooling, THF (10 mL) was added and the suspension cooled to -78 °C. MeLi (1.6 mL, 2.4 mmol) was added and the mixture allowed to warm to between -30 and -10 °C. After a clear solution had formed, it was recooled to -78 °C and quickly transferred by syringe to a precooled (-78 °C) addition funnel. This was attached to a flask containing a solution of 0.39 g (2.0 mmol) of **1** in 10 mL THF at-78 °C, and the cuprate was added dropwise with stirring. After 1 h at -78 °C, 2.4 mmol of acetic acid in THF was added and the solution allowed to warm to 25 °C. The mixture was poured into water-pentane, the layers cross-extracted, and the organic phase dried by passage through $MgSO_4$. The concentrate was immediately filtered through Florisil (pentane) and then subjected to flash chromatograpy on silica gel (hexane) to give 0.20 g (57%) of **2a**. Anal. calc for $C_7H_{13}ClOSi$: C, 47,58; H, 7.42. Found: C, 47.82; H, 7.46. IR: 1640(m), 1560(s) cm^{-1}. ^{13}C NMR: δ 236.1, 148.1, 128.0, 24.3, -3.2.

***E*- 3-Chloro-4,4-dimethyl-1-(trimethylsilyl)-2-pentenone (2b).** Anal. calc for $C_{10}H_{19}OSi$: C, 54.89; H, 8.75. Found: C, 54.88; H, 8.84. IR: 1640(m), 1610(s), 1565(m), cm^{-1}. ^{13}C NMR: ∂ 240.0, 150.9, 132.0, 40.2, 30.1, -2.7. Upon standing at 25 °C for 1 day, complete isomerization to the Z-isomer had occurred; Anal. Found: C, 55.10; H, 8.70. IR: 1630(m), 1600(s), 1565(sh) cm^{-1}. ^{13}C NMR: δ 242.0, 151.8, 126.0, 39.5, 28.5, -2.8.

***E*-3-Chloro-4-methyl-1-(trimethylsilyl)-2-hexenone (2c).** Obtained from chromatography on Florisil (8 in x 1 in). Anal. calc for $C_{10}H_{19}ClOSi$: C, 54.89; H, 8.75. Found: C, 54.79; H, 8.85. After standing 3 days at 25 °C, isomerization into a 2:1 mixture of β,γ-isomers had occurred, as evidenced by ^{1}H NMR absorptions at (in addition to δ 0.20): δ 0.97 (t, J = 7Hz,3H); 1.85 (s, 3H); 2.03 (q, J = 7Hz, 2H); 3.62 (s, 2H) and δ 1.01 (t, J = 7Hz, 3H); 1.68 (s, 3H); 2.27 (q, J = 7Hz, 2H); 3.60 (s, 2H).

***E*-3-Chloro-1-(trimethylsilyl) -2-heptenone (2d)**.[2] The cuprate $nBu_2Cu(CN)(MgCl)_2$ was unreactive towards **1** at -78 °C. After addition of the cuprate at -78 °C, the reaction mixture was allowed to warm to -10 °C, held at this temperature 0.5 h and recooled to -78 °C before the usual protonation. After isolation, **2d** slowly isomerized to the β,γ-isomer. Heating a neat sample at 90 °C for 1 h effected complete conversion to mostly (>9:1) one isomer with ^{1}H NMR: δ 0.21(s, 9H); 0.92 (t, J = 7Hz, 3H); 1.42 (m, J = 7Hz, 2H); 2.19 (m, J = 7Hz, 2H); 3.51 (s, 2H), 5.59 (t, J = 7Hz,1H).

***E*-3-Chloro-3-cyclopropyl-1-(trimethylsilyl)-2-propenone (2e).** Cyclopropyllithium was prepared by treating bromocyclopropane with two equivalents of tBuLi at -78 °C in ether and warming to 25 °C. The standard procedure then afforded **2e**. Anal. calc for $C_9H_{15}ClOSi$: C, 53.31; H, 7.46. Found: C. 53.23; H, 7.50. IR: 1628(s), 1542(s) , 1530(s) cm^{-1}. ^{13}C NMR: δ 233.9, 156.0, 127.3, 16.1, 9.1, -3.4.

Z-3-Chloro-3-phenyl-1-(trimethylsilyl)-2-propenone (2f). Anal. calc for $C_{12}H_{15}ClOSi$: C, 60.36; H, 6.33. Found: C, 60.55; H, 6.33. IR 1648, 1568, 1540 cm $^{-1}$. ^{13}C NMR: δ 237.5, 138.5, 137.0, 130.8, 129.6, 128.9, 128.1, -3.0.

Irradiation of 2 and 3. Samples of **2** or **3** were dissolved in pentane and irradiated in a quartz tube at 256 nm using a "Rayonet" apparatus until approximately an equal amount of each stereoisomer was present. Solvent was removed and ^1H NMR spectra obtained; the NMR spectra of new stereoisomers were then obtained by difference.

Preparation of Homosubstituted 3 ($G^1 = G^2$). The general procedure outlined for the preparation of **2** was followed, but the stoichiometries indicated in Table 3 were used. After the addition of cuprate, the reaction mixture was allowed to warm to the temperature stated in Table 3 and then recooled immediately to -78 °C before HOAc-THF protonation. Products were purified by chromatography on silica gel 60 (9:1 hexane-ether).

3-Methyl-1-(trimethylsilyl)-2-butenone (3a). Anal. calcd for $C_8H_{16}OSi$: C, 61.47; H, 10.32. Found: C, 61.57; H, 10.22. IR: 1642(m), 1568(s) cm^{-1}. ^{13}C NMR: δ 237.6, 150.1, 126.9, 27.4, 21.0, -3.3.

4-methyl-3-(1-methylpropyl)-1(trimethylsilyl)-2-hexene (3c). Anal. calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 70.00; H, 11.72. IR: 1630(m), 1570(s) cm^{-1}.

3-Butyl-1-(trimethylsilyl)-2-heptenone (3d). Anal. calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 70.05; H, 11.37. IR: 1632(m), 1570(s) cm^{-1}.

3,3-Diphenyl-1-(trimethylsilyl)-2-propenone (3e). Anal. calcd for $C_{18}H_{20}OSi$: C, 77.09; H, 7.19. Found: C, 77.16; H, 7.26. IR 1640(sh), 1580(br).

Preparation of 3 ($G^1 \neq G^2$). The general procedure outlined for the preparation of **2** was followed but the stoichiometries relative to **1** indicated in Table 4 were used. For R^1 = alkyl the monosubstituted product (**2**) was not isolated, but treated in situ with the second cuprate as indicated. For R^1 = Ph, *Z*-**2f** was isolated, combined with one equivalent of LiCl, and then treated with the second cuprate as indicated. E:Z ratios for **3** were determined from NMR spectra of products before chromatography (for any given E/Z set, those proton sets which were "in the clear" were chosen for comparison; see Table 5). Product isolation involved flash silica gel (230-400 mesh) chromatography with hexane eluant. Yields for individual runs are tabulated in Table 4. The IR spectra of all **3** showed bands at 1635-1640(m) cm^{-1} plus 1570-1580(s) cm^{-1} (dialkyl substitution) or 1630(m) cm^{-1} plus 1555(s) cm^{-1} (phenyl substitution).

***E*-3,4,4-Trimethyl-1-(trimethylsilyl)-2-pentenone (3f).** Anal. calcd for $C_{11}H_{22}OSi$: C, 66.59; H, 11.18. Found: C, 66.53; H, 11.20. ^{13}C NMR: δ 239.5, 160.2, 123.4, 37.5, 28.6, 15.9, -3.1.

Table 5. ^{1}H NMR Data (δ) for 3

	TMS	γ-H	=CH	Other
3a	0.15	1.83 (s, 3H) 2.05 (s, 3H)	6.52	
3c	0.16	2.21 (m, 1H) 3.45 (m, 1H)	6.47	0.81 (t, 3H), 0.89 (t, 3H), 0.98 (dd, 3H), 1.03 (d, 3H), 1.40 (m, 2H), 1.71 (m, 2H)
3d	0.17	2.09 (t, 2H) 2.41 (t, 2H)	6.47	0.88 (m, 6H), 1.34 (m, 8H),
3e	-0.12		6.54	7.1 (m, 4H), 7.3 (m, 6H)
3f (E)	0.17	2.02 (s, 3H)	6.58	1.09 (s, 9H)
(Z)	0.17	1.82 (s, 3H)	6.08	1.08 (s, 9H)
3g (E)	0.17	2.03 (m, 1H) 1.96 (s, 3H)	6.52	0.80 (t, 3H), 1.02 (d, 3H), 1.4 (m, 2H)
(Z)	0.16	3.48 (m, 1H) 1.73 (s, 3H)	6.47	0.80 (t, 3H), 0.96 (d, 3H), 1.3 (m, 2H)
3h (E)	0.17	2.08 (t, 2H) 2.04 (s, 3H)	6.51	0.90 (t, 3H), 1.36 (m, 4H)
(Z)	0.17	2.45 (t, 2H) 1.84 (s, 3H)	6.51	0.90 (t, 3H), 1.36 (m, 4H)
3i (E)	0.23	2.45 (s, 3H)	6.96	7.37-7.49 (m, 5H)
(Z)	-0.12	2.20 (s, 3H)	6.21	7.2-7.3 (m, 5H)
3j (E)	0.17	2.23 (m, 1H)	6.45	0.81 (t, 3H), 1.10 (s, 9H), 1.10 (d, 3H), 1.4-1.6 (m, 2H)
(Z)	0.18	1.5 (m, 1H)	5.78	0.90 (t, 3H), 1.04 (s, 9H), 1.05 (d, 3H), 1.4-1.6 (m, 2H)
3k (E)	0.17	2.37 (m, 2H)	6.62	0.87 (t, 3H), 1.10 (s, 9H), 1.35 (m, 4H)
3l (E)	0.21		6.06	1.10 (s, 9H), 7.1-7.3 (m, 5H)
(Z)	0.03		6.56	1.13 (s, 9H), 7.0-7.3 (m, 5H)
3m (E)	0.15	2.08 (s, 1H) 2.35 (m, 2H)	6.46	0.8-0.9 (m, 6H), 1.02 (d, 3H) 1.35 (m, 6H)
(Z)	0.16	3.42 (s, 1H) 2.04 (m, 2H)	6.46	0.8-0.9 (m, 6H), 0.95 (d, 3H) 1.35 (m, 6H)
3n (E)	0.14	2.83 (t, 2H)	6.78	0.80 (t, 3H), 1.26 (m, 4H) 7.3-7.4 (m, 5H)

3,4-Dimethyl-1-(trimethylsilyl)-2-hexenone (3g). *E*-isomer. Anal. calcd for $C_{11}H_{22}OSi$: C, 66.59; H, 11.18. Found: C, 66.41; H, 11.23. ^{13}C NMR: δ 240.2, 157.9, 125.8, 45.8, 27.3, 19.1, 16.0, 12.0, -2.1. *Z*-isomer. Anal. Found: C, 66.61; H, 11.28. ^{13}C NMR: δ 238.4, 157.4, 126.0, 45.6, 27.6, 18.9, 16.2, 12.0, -3.2.

3-Methyl-1-(trimethylsilyl)-2-heptenone (3h). *E*-isomer. Anal. calcd for $C_{11}H_{22}OSi$: C, 66.59; H, 11.18. Found: C, 66.57; H, 11.23. ^{13}C NMR: δ 237.9, 153.8, 126.3, 40.7, 29.7, 22.3, 19.5, 13.8, -3.2. *Z*-isomer. Anal. Found: C, 66.57; H, 11.23. ^{13}C NMR: δ 237.9, 155.0, 127.0, 33.9, 27.4, 19.5, 13.8, -3.2.

3-Methyl-3-phenyl-1(trimethylsilyl)-2-butenone (3i). *E*-isomer. Anal. calcd for $C_{13}H_{18}OSi$: C, 71.44; H, 8.31. Found: C, 71.70; H, 8.51. ^{13}C NMR: δ 238.9, 148.4, 142.8, 129.0, 128.5, 126.9, 126.7, 18.5, -3.1.

3-(1,1-Dimethylethyl)-4-methyl-1(trimethylsilyl)-2-hexenone (3j). *E*-isomer. Anal. calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 69.78; H, 11.68. ^{13}C NMR: δ 241.5, 165.8, 125.3, 38.7, 37.4, 28.9, 28.1, 19.2, 13.1, -3.0.

3-(1,1-Dimethylethyl)-1-(trimethylsilyl)-2-heptenone (3k). *E*-isomer. Anal. calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 70.08; H, 11.65. ^{13}C NMR: δ 237.9, 165.4, 122.7, 37.9, 33.2, 30.5, 28.9, 23.6, 13.8, -3.1.

4,4-Dimethyl-3-phenyl-1-(trimethylsilyl)-2-pentenone (3l). *E*-isomer. Anal. calcd for $C_{16}H_{24}OSi$: C, 73.78; H, 9.29. Found: C, 74.55; H, 9.53 (best analysis). ^{13}C NMR: δ 244.1, 157.6, 144.5, 133.6, 127.8, 127.5, 126.5, 36.7, 31.2, -3.0. *Z*-isomer. Anal. Found: C, 73.82; H, 9.28. ^{13}C NMR: δ 241.2, 158.3, 139.0, 129.1, 127.8, 127.3, 126.9, 36.8, 29.4, -3.1.

3-(1-methylpropyl)-1-(trimethylsilyl)-2-heptenone (3m). *E*-isomer. Anal. calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 70.01; H, 11.90. ^{13}C NMR: δ 237.4, 162.6, 124.8, 43.7, 32.5, 31.7, 28.4, 23.3, 19.5, 13.9, 11.9, -3.2. *Z*-isomer. Anal. Found: C, 69.83; H, 11.62. ^{13}C NMR: δ 237.6, 162.7, 124.8, 43.7, 32.5, 31.8, 28.5, 23.3, 19.5, 13.9, 11.9, -3.1.

3-Phenyl-1-(trimethylsilyl)-2-heptenone (3n). The use of $nBu_2Cu(CN)Li_2$ in run 19 of Table 4 led to a vigorous reaction from which no **3n** was obtained; nBuCu(CN)Li was then successfully employed. *E*-isomer. Anal. calcd for $C_{16}H_{24}OSi$: C, 73.78; H, 9.29. Found: C, 73.72; H, 9.15. ^{13}C NMR: δ 238.5, 153.7, 141.9, 128.8, 128.5, 127.2, 126.9, 31.6, 31.2, 22.9, 13.9, -3.1.

3-Chloro-1-(trimethylsilyl)-2-propenone (4). A flame-dried flask under argon flow was charged with 0.65 g (10 mmol) of zinc dust. 1,2-Dibromoethane (27μL, 59 mg, 0.3 mmol) and 0.4 mL of THF were then added. The flask was gently heated with a heat gun until bubbles appeared, then stirred for a few minutes and heated again. The process was repeated three times, after which chlorotrimethylsilane (67 μL, 57 mg, 0.52 mmol) was introduced. The suspension was stirred 15 min, and then 0.98 g (5.0 mmol) of **1** in 2.5 mL of THF was added. After 1 h, the mixture was cooled to -20 °C and treated with acetic acid (0.48 mL, 0.66 g, 10 mmol) in 1 mL THF. After warming to 25 °C, solids were filtered off (sintered glass frit), washed with pentane, and the filtrate washed with water. The dried ($MgSO_4$) concentrate was then dissolved in hexane and passed through a short Florisil column to give 0.61 g (75%) of **4** with a vpc purity of 98%. Anal. calcd for $C_6H_{11}ClOSi$: C, 44.40; H, 6.83. Found: C, 44.54; H, 6.88. IR: 1636(m), 1611(m), 1583(s), 1553(s). ^1H NMR: δ 0.21 (s, 9H), 6.69 (d, J = 15 Hz, 1H), 7.16 (d, J = 15 Hz, 1H). ^{13}C NMR: δ 233.1, 136.1, 136.5, -2.9

***E*-1-(Trimethylsilyl)-2-butenone (5a).** This procedure is typical of all preparations of **5**. MeCu(CN)Li (2.4 mmol in 10 mL of THF) at -78 °C was added dropwise over 45 min to a solution of 0.20 g (1.2 mmol) of **4** in 10 mL of THF at -78 °C. After an additional hour at -78 °C, one equivalent of acetic acid in THF was added, and the mixture allowed to warm to 25 °C. After a water-pentane workup, the product was isolated from silica gel chromatography (hexane) to give 0.13 g (91%) of **5a**. Anal. calcd for $C_7H_{14}OSi$ C, 59.09; H, 9.92. Found: C, 59.07; H, 9.91. IR: 1640(m), 1588(s) cm^{-1}. ^1H NMR: δ 0.23 (s, 9H), 1.91(dd, J = 7, 1.5 Hz, 3H), 6.20 (d, J = 16 Hz, 1H), 6.75 (dt, J = 16, 7 Hz, 1H). ^{13}C NMR: δ 237.1, 143.7, 138.2, 19.8, -1.9.

***E*-4,4-Dimethyl-1-(trimethylsilyl)-2-pentenone (5b).** Yield: 85%. Anal. calcd for $C_{10}H_{20}OSi$: C, 65.15; H, 10.94. Found: C, 65.17; H, 11.07. IR: 1652(m), 1638(m), 1559(s). ^1H NMR: δ 0.23 (s, 9H), 1.07 (s, 9H), 6.10 (d, J =16 Hz, 1H), 6.72 (d, J = 16 Hz, 1H). ^{13}C NMR: δ 237.2, 158.9, 131.4, 33.9, 28.7, -1.8.

***E*-4-Methyl-1(trimethylsilyl)-2-hexenone (5c).** Yield: 85%. Anal. calcd for $C_{10}H_{20}OSi$: C, 65.15; H, 10.94. Found: C, 65.14; H, 11.07. IR: 1650(m), 1637(m), 1594(s). ^1H NMR: δ 0.23 (s, 9H), 0.87 (t, 3H), 1.04 (d, 3H), 1.41 (q, 2H), 2.22 (m, 1H), 6.14 (d, J = 16 Hz, 1H), 6.37 (dd, J = 16, 8 Hz, 1H). ^{13}C NMR: δ 236.8, 154.1, 134.8, 38.5, 29.0, 19.0, 11.6, -1.9.

***E*-1-(Trimethylsilyl)-2-heptenone (5d).** Yield: 73%. Anal. calcd for $C_{10}H_{20}OSi$: C, 65.15; H, 10.94. Found: C, 64.91; H, 11.10. IR: 1647(m), 1636(m), 1590(s). ^1H NMR: δ 0.22 (s, 9H), 0.89 (t, 3H), 1.39 (m, 4H), 2.21 (q, 2H), 6.17 (d, J = 16 Hz, 1H), 6.73 (dt, J = 16, 7 Hz, 1H). ^{13}C NMR: δ 236.6, 148.9, 136.4, 32.4, 30.3, 22.2, 13.8, -1.9.

***E*-3-Phenyl-1-(trimethylsilyl)-2-propenone (5e).** Yield: 93%. Anal. calcd for $C_{12}H_{16}OSi$: C, 70.53;H, 7.89. Found: C, 70.61; H, 7.72. IR: 1648(m), 16219(m), 1580(s), 1572(s). ^1H NMR: δ 0.31 (s, 9H), 6.88 (d, J =16 Hz, 1H), 7.43 (m, 6H). ^{13}C NMR: δ 236.2, 142.8, 134.9, 131.2, 130.4, 128.9, 128.2, -2.1.

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