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Conjugate Additions of a Simple Monosilylcopper Reagent with Use of the CuI·DMS Complex: Stereoselectivities and a Dramatic Impact by DMS

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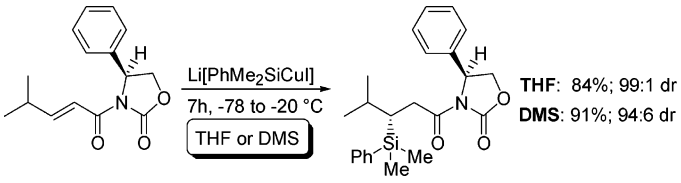

Conjugate additions utilizing the simple monosilylcuprate reagent Li[$PhMe_2SiCuI$] to α,β-unsaturated carbonyl compounds are described. The presence of dimethyl sulfide (DMS), either as a component originating from the $(CuI)_4(DMS)_3$ complex or as a solvent added, has an amazing influence on both chemical yield and the level of diastereomeric ratio (dr) of the products. Gilman-type silylcyanocuprates {$Li(Ph_2MeSi)_2Cu/LiCN$} have previously been used to guarantee good results in conjugate addition reactions. External additives such as HMPA, tributylphosphine, or dialkylzinc are not necessary in conjunction with the simple Li[$PhMe_2SiCuI$] reagent. It is demonstrated that the monosilylcuprate reagent with DMS as the solvent is very useful with sterically hindered (β,β-disubstituted) enones, and provides very high yields of the β-silylated 1,4-addition products. Since there is no oligomerization problem associated with the simple monosilylcuprate reagent, this reagent should be considered as a very useful 1,4-silyl donor to enals, enones, and enoates in conjugate addition reactions.

Introduction

Organosilanes have fundamental roles in organic chemistry and synthesis, particularly as control moieties for stereochemistry in chemical transformations,[1] or as key intermediates to introduce the hydroxy function.[2] Formation of the silicon−carbon bond from the conjugate addition of a suitable silyl cuprate reagent to an α,β-unsaturated carbonyl compound is an excellent surrogate for the acetate aldol reaction. Although there are various silyl substituents available, the dimethylphenylsilyl (Me_2PhSi) group is probably one of the most useful because the carbon−silicon bond can be replaced under mild oxidative conditions (Tamao−Fleming)[2,3] to make the corresponding alcohols with complete retention of stereochemistry.[2a] Thus, creating a carbon−silicon bond with a predominantly high asymmetric induction at the β-carbonyl position serves as a complementary synthetic tool in the making of enantiomerically pure acetate aldol products.[4]

Since the pioneering work by Fleming in the early 1980s,[5] the dimethylphenylsilylcyanocuprate reagent, depicted either as $(PhMe_2Si)_2CuLi{\cdot}LiCN$[6] or $(PhMe_2Si)_2Cu(CN)Li_2$, has been used extensively in the majority of conjugate additions to make β-silylated carbonyl compounds.[5b] The corresponding monosilylcuprate reagents, represented either as $PhMe_2SiCu/LiX$ or Li[$PhMe_2SiCuX$],[7] possess a better economy of group

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(1) (a) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, UK, 1981. (b) Webber, W. P. *Silicon Reagents in Organic Synthesis*, Springer: Berlin, Germany, 1983. (c) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: Orlando, FL, 1988. (d) Brook, M. A. *Silicon in Organic, Organometallic and Polymer Chemistry*; Wiley: New York, 2000. (e) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev*. **1997**, *97*, 2063-2192.

(2) (a) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun., I* **1984**, 29−31. (b) Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett*. **1987**, *28*, 4229−4232. (c) Fleming, I.; Henning, R.; Parker, D. C.; Plaut, H. E.; Sanderson, P. E. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 317−337.

(3) (a) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694−1696. (b) Tamao, K.; Tanaka, T.; Nakajima, T.; Sumiya, R.; Arai, H.; Ito, Y. *Tetrahedron Lett*. **1986**, *27*, 3377−3380. (c) Tamao, K.; Kawachi, A.; Ito, Y. *J. Am. Chem. Soc*. **1992**, *114*, 3989−3990.

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transfer, but their inherent lower stability, solubility, and reactivity have limited their widespread use as reliable reagents for the formation of β-silylated carbonyl products. Such problems are sometimes solved by taking advantage of additives such as tributylphosphine[8a] or HMPA.[8b] Dialkylzinc[9] has also been used to form the milder discrete silylzincates from the corresponding lithium reagents, which allows for catalytic quantities of CuCN to be used.[10a] The "Gilman-type" cyanocuprates utilize 2 equiv of the silyllithium reagent, as opposed to 1 equiv relative to CuCN in the monosilylcuprate. Examples of the monosilylcuprate reagents used in conjugate additions are rare,[11] and most accounts support the idea that these reagents are not as useful as "Gilman-type" silylcyanocuprates.[12]

In contrast to these notions, quite recently we introduced a very versatile monosilylcuprate reagent, Li[$PhMe_2SiCuI$],[13] based on 1 equiv of $PhMe_2SiLi$ and 1 equiv of the $(CuI)_4(SMe_2)_3$ complex (CuI·0.75DMS) in THF. Specifically, we reported that dimethyl sulfide purified CuI is an instrumental component in obtaining very high yields as well as exceptional levels of stereoselectivity compared to what has previously been reported with the $(PhMe_2Si)_2CuLi$·LiCN reagent. We also demonstrated that external additives such as tributylphosphine, HMPA, or dialkylzinc are unnecessary, even though less of the silyllithium reagent was needed[14] to obtain high yields as well as diastereoselectivities of the β-silylated carbonyl products. Similar asymmetric studies with the $(PhMe_2Si)_2CuLi$·LiCN system in conjugate additions have been carried out to α,β-unsaturated esters,[15a] *N*-enoylsultams,[8a,15b] α-alkylidenelactones,[16] α,β-unsaturated oxazolidines,[15a] and *N*-enoyl pyrrolidinones,[9b,15ac] most commonly in conjunction with additives to increase the magnitude of π-facial selectivity. In support of our asymmetric additions to chiral *N*-enoyloxazolidinones[17a] or pyrrolidinones,[17b] we found that the less complex reagent, Li[$PhMe_2SiCuI$], needs no external additives or Lewis acids, other than the dimethyl sulfide derived from the CuI·0.75DMS complex, to generate very high yields and diastereomeric ratios.[13]

We now extend the scope of the CuI·0.75DMS promoted conjugate additions of the monosilylcuprate reagent to α,β-unsaturated substrates. Most importantly, with regard to applications in asymmetric synthesis, we present a variety of highly diastereoselective reactions applying the Li[$PhMe_2SiCuI$] reagent, followed by the Tamao−Fleming mild oxidation protocol[2,3] for the preparation of acetate aldol products in excellent optical purities. Finally, we introduce a nice solution to previous problems associated with sterically congested β,β-disubstituted enones and their reactivity in 1,4-additions of the Li[$PhMe_2SiCuI$] reagent.

Results and Discussion

Conjugate addition reactions with the Li[$PhMe_2SiCuI$] reagent have been shown[13] to work perfectly on a variety of α,β-unsaturated substrates, including ketones, aldehydes, esters, imides, and even a primary amide to provide extraordinarily good yields as well as high stereoselectivities of the products. The Li[$PhMe_2SiCuI$] reagent is prepared from 1 equiv of the dark red $PhMe_2SiLi$ reagent[18] and 1.2 equiv[19] of the CuI·0.75DMS complex[20]

(4) Reviews on asymmetric acetate aldol reactions, see: (a) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1−30. (b) Braun, M. *Angew. Chem., Int. Ed. Engl*. **1987**, *26*, 24−37. Articles on auxiliary based asymmetric acetate aldol reactions, see: (c) Oppolzer, W.; Starkemann, C. *Tetrahedron Lett*. **1992**, *33*, 2439−2442. (d) Helmchen, G.; Leikauf, U.; Taufer-Knöpfel, I. *Angew. Chem., Int. Ed. Engl*. **1985**, *24*, 874−875. (e) Bond, S.; Perlmutter, P. *J. Org. Chem*. **1997**, *62*, 6397−6400. (f) Palomo, C.; González, A.; García, J. M.; Landa, C.; Oiarbide, M.; Rodríguez, S.; Linden, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 180−182. Articles on chiral metal complexes in acetate aldol reactions, see: (g) Masamune, S.; Sato, T.; Kim, B.-M.; Wollman, T. A. *J. Am. Chem. Soc*. **1986**, *108*, 8279−8281. (h) Duthaler, R. O.; Herold, P.; Lottenbach, W.; Oertle, K.; Riediker, M. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 495−497. (i) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc*. **1989**, *111*, 5493−5495. Articles on tin-enolates in acetate aldol reactions, see: (j) Nagao, Y.; Yamada, S.; Kumagai, T.; Ochiai, M.; Fujita, E. *J. Chem. Soc., Chem. Commun*. **1985**, 1418−1419. (k) Ryu, I.; Murai, S.; Sonoda, N. *J. Org. Chem*. **1986**, *51*, 2391−2393. Articles on lithium-enolates in acetate aldol reactions, see: (l) Braun, M.; Devant, R. *Tetrahedron Lett*. **1984**, *25*, 5031−5034. (m) Devant, R.; Mahler, U.; Braun, M. *Chem. Ber*. **1988**, *121*, 397−406. (n) Saito, S.; Hatanaka, K.; Kano, T.; Yamamoto, H. *Angew. Chem., Int. Ed*. **1998**, *37*, 3378−3381. Articles on boron-enolates in acetate aldol reactions, see: (o) Yan, T.-H.; Hung, A.-W.; Lee, H.-C.; Chang, C.-S. *J. Org. Chem*. **1994**, *59*, 8187−8191. (p) Zhang, Y.; Phillips, A. J.; Sammakia, T. *Org. Lett*. **2004**, *6*, 23−25. Articles on titanium-enolates in acetate aldol reactions, see: (q) Yan, T.-H.; Hung, A.-W.; Lee, H.-C.; Chang, C.-S.; Liu, W.-H. *J. Org. Chem*. **1995**, *60*, 3301−3306. (r) González, Á.; Aiguadé, J.; Urpí, F.; Vilarrasa, J. *Tetrahedron Lett*. **1996**, *37*, 8949−8952. (s) Guz, N. R.; Phillips, A. J. *Org. Lett*. **2002**, *4*, 2253−2256. (t) Hodge, M. B.; Olivo, H. F. *Tetrahedron* **2004**, *60*, 9397−9403.

(5) (a) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2520−2526. (b) Fleming I. in *Organocopper Reagents−A Practical Approach*; Taylor, R. J. K., Ed.; Oxford University Press: Oxford, UK, 1994; pp 267−292 and references therein. (c) Perlmutter P. *Conjugate Addition Reactions in Organic Synthesis*: Pergamon Press: Oxford, UK, 1992.

(6) The silylcyanocuprate should be indicated as the "Gilman-type" reagent, see: Bertz, S. H.; Miao, G.; Eriksson, M. *Chem. Commun*. **1996**, 815−816. See also: Lipshutz, B. H.; James, B. *J. Org. Chem*. **1994**, *59*, 7585−7587.

(7) Although there is no evidence for a Cu−X bond, the silylhalocuprate reagent is tentatively depicted as the favorable "Gilman-type" reagent: Li[$PhMe_2CuX$].

(8) (a) Palomo, C.; Aizpurua, J. M.; Iturburu, M.; Urchegui, R. *J. Org. Chem*. **1994**, *59*, 240−244. (b) Takaki, K.; Maeda, T.; Ishikawa, M. *J. Org. Chem*. **1989**, *54*, 58−62.

(9) (a) Tückmantel, W.; Oshima, K.; Nozaki, H. *Chem. Ber*. **1986**, *119*, 1581−1593. (b) Crump, R. A. N. C.; Fleming, I.; Urch, C. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 701−706. (c) MacLean, B. L.; Hennigar, K. A.; Kells, K. W.; Singer, R. D. *Tetrahedron Lett*. **1997**, *38*, 7313−7316.

(10) (a) Lipshutz, B. H.; Sclafani, J. A.; Takanami, T. *J. Am. Chem. Soc*. **1998**, *120*, 4021−4022. For some other developments of 1,4-additions of silyl groups, see: (b) Hale, M. R.; Hoveyda, A. H. *J. Org. Chem*. **1994**, *59*, 4370−4374. (c) Ito, H.; Ishizuka, T.; Tateiwa, J.-I.; Sonada, M.; Hosomi, A. *J. Am. Chem. Soc*. **1998**, *120*, 11196−11197. (c) Lee, T. W.; Corey, E. J. *Org. Lett*. **2001**, *3*, 3337−3339.

(11) (a) Sharma, S.; Oehlschlager, A. C. *Tetrahedron* **1989**, *45*, 557−568. (b) Sharma, S.; Oehlschlager, A. C. *J. Org. Chem*. **1991**, *56*, 770−776.

(12) Dieter, R. K. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, Germany, 2002; pp 79−144.

(13) Dambacher, J.; Bergdahl, M. *Chem. Commun*. **2003**, 144−145.

(14) Typically, 1.4−2.0 equiv of Li[$PhMe_2SiCuI$] (∼60 mM in THF) was employed.

(15) (a) Fleming. I.; Kindon, N. D. *J. Chem. Soc., Perkin Trans. 1* **1995**, 303−315. (b) Oppolzer, W.; Mills, R. J.; Pachinger, W.; Stevenson, T. *Helv. Chim. Acta* **1986**, *69*, 1542−1545. (c) Fleming, I.; Kindon, N. D. *J. Chem. Soc., Chem. Commun*. **1987**, 1177−1179.

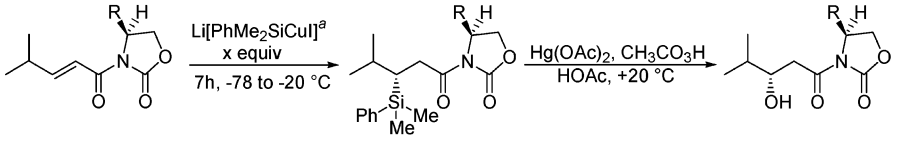
(16) (a) Amberg, W.; Seebach, D. *Angew. Chem., Int. Ed. Engl*. **1988**, *27*, 1718−1719. (b) Amberg, W.; Seebach, D. *Chem. Ber*. **1990**, *123*, 2439−2444.

(17) (a) Nicolás, E.; Russel, K. C.; Hruby, V. J. *J. Org. Chem*. **1993**, *58*, 766−770. (b) Tomioka, K.; Suenaga, T.; Koga, K. *Tetrahedron Lett*. **1986**, *27*, 369−372.

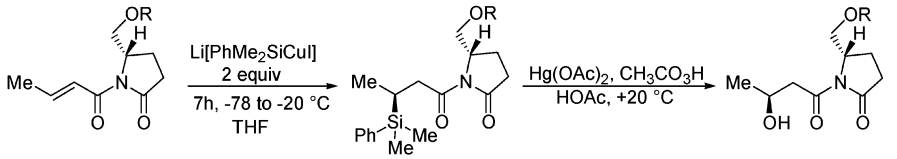
(18) See ref 5b, p 260.

(19) Molar equivalents calculated for pure $(CuI)_4(Me_2S)_3$, so as to avoid formation of the corresponding homocuprate $(PhMe_2Si)_2CuLi$/LiI. For a discussion on trialkylsilylcuprate formation, see: Sharma, S.; Oehlschlager, A. C. *J. Org. Chem*. **1989**, *54*, 5383−5387.

TABLE 1. Influence by DMS and THF on Asymmetric 1,4-Additions



Entry	Substrate	Equiv; Solvent	Prod; Yield,[b] dr[c]	Prod.;Yield,[d] dr
1	**1**; R = Ph	x = 2.0; THF	**5**; 84%, 99:1	**9**; 77%, >99:1
2	**1**;	x = 2.0; DMS	**5**; 94%, 94:6	
3	**1**;	x = 1.6; DMS	**5**; 93%, 94:6	
4	**1**;	x = 1.4; DMS	**5**; 91%, 94:6	
5	**1**;	x = 1.2; DMS	**5**; 51%, 94:6	
6	**2**; R = *t*-Bu	x = 2.0; THF	**6**; 87%, 96:4	**10**; 77%, >99:1



Entry	Substrate	Cu(I) source	Prod.; Yield,[b] dr[c]	Prod.; Yield,[d] dr
7	**3**; R = Trityl	CuI•0.75DMS	**7**; 92%, 96:4	
8	**3**;	CuI[e]	**7**; 63%, 1:1	
9	**3**;	CuI[e] + DMS[f]	**7**; 76%, 85:15	
10	**4**; R = TBDPS[g]	CuI•0.75DMS	**8**; 93%, 95:5	**11**; 53%, >99:1
11	**4**;	CuBr•DMS	**8**; 95%, 94:6	

[a] Obtained from 1 equiv of $PhMe_2SiLi$ and 1.2 equiv of CuI·0.75DMS. [b] Based on isolated, purified, and characterized material. [c] Diastereomeric ratio measured on crude material, using ^1H NMR, 500 MHz. [d] Yield and dr based on isolation of the major diastereomer. [e] 99.999% reagent purity CuI (Aldrich). [f] 0.75 equiv added to 99.999% CuI. [g] TBDPS = *tert*-butyldiphenylsilyl.

in an appropriate solvent at −78 °C. Although the Li[$PhMe_2SiCuI$] reagent is sensitive to elevated temperatures, the presence of DMS seems to have a stabilizing effect[21] on the silylcopper reagent. Thus, the substrates are exposed to the Li[$PhMe_2SiCuI$] reagent at −78 °C, and subsequently the reaction temperature is increased to −20 °C during 5−8 h. The efficiency of the heterogeneous brown Li[$PhMe_2SiCuI$] reagent in THF is dramatically improved at low temperatures. The loss of activity of silylcopper reagent is clearly visible when the color of the reagent turns gray-black, accentuated at higher temperatures. The active Li[$PhMe_2SiCuI$] reagent is stable for many hours at −78 °C. Once the reaction temperature has reached approximately −20 °C, the organocopper reaction is quenched by the addition of aqueous NH_4Cl/NH_3. Results of the asymmetric conjugate additions of the Li[$PhMe_2SiCuI$] reagent to various optically active imides employing THF or DMS as a medium are illustrated in Table 1.

Several research groups have utilized organocopper reagents in asymmetric 1,4-additions to optically active imides, such as the *N*-enoyl-substituted oxazolidinones[17a,22] and pyrrolidinones.[15c,17b] Recently we reported the Li[RCuI]/TMSI combination to the same substrates where it was found that the sense of stereochemistry obtained was extremely dependent on Lewis acids as well as the medium.[22i] Although TMS−halides are very popular additives for increasing the rate of 1,4-addition reactions using organocopper reagents, we specifically found that this additive is not a participant in the critical steps in Et_2O. The role of TMSI in THF, on the other hand, is tremendously important. The same sense of π-facial stereochemistry is obtained in THF by using Li[BuCuI] as the Li[$PhMe_2SiCuI$] reagent, using the same chiral imide. The level of diastereomeric ratio (dr) with Li[$PhMe_2SiCuI$] in THF is 99:1 (entry 1) while the dr with Li[BuCuI] in the same medium was significantly lower (3:1).[22j] Intuitively it appears the size of the copper reagent might play a crucial role on the stereochemical outcome, but the reactivity of the reagent is equally important. While 2 equiv of the Li[$PhMe_2SiCuI$] reagent to imide **1** initially was used, it is feasible to use much less silylcopper reagent (∼1.3 equiv versus imide) in THF and still maintain a high yield and good stereoselectivity. It is also possible to use DMS as a solvent in the conjugate addition of the Li[$PhMe_2SiCuI$] reagent to imide **1**. The presence of DMS has remarkable effects on the rate, stability, and selectivity of the conjugate addition of the monosilylcuprate reagent (Table 1).[23] In

(20) For a discussion on the stability of the CuI/DMS complex, see: Eriksson, M.; Hjelmencrantz, A.; Nilsson, M.; Olsson, T. *Tetrahedron* **1995**, *51*, 12631−12644. See also: Eriksson, M.; Iliefski, T.; Nilsson, M.; Olsson, T. *J. Org. Chem*. **1997**, *62*, 182−187.

(21) Bertz, S.; Dabbagh, G. *Tetrahedron* **1989**, *45*, 425−434.

(22) (a) Wipf, P.; Xu, W.; Smitrovich, H.; Lehmann, R.; Venanzi, L. M. *Tetrahedron* **1994**, *50*, 1935−1954. (b) Lou, B.-S.; Li, G.; Lung, F.-D.; Hruby, V. J. *J. Org. Chem*. **1995**, *60*, 5509−5514. (c) Qian, X.; Russel, K. C.; Boteju, L. W.; Hruby, V. J. *Tetrahedron* **1995**, *51*, 1033−1054. (d) Wipf, P.; Takahashi, H. *Chem. Commun*. **1996**, 2675−2676. (e) Andersson, P. G.; Schink, H. E.; Österlund, K. *J. Org. Chem*. **1998**, *63*, 8067−8070. (f) Williams, D. R.; Kissel, W. S.; Li, J. J. *Tetrahedron Lett*. **1998**, *39*, 8593−8596. (g) Schneider, C.; Reese, O. *Synthesis* **2000**, 1689−1694. (h) Pollock, P.; Dambacher, J.; Anness, R.; Bergdahl, M. *Tetrahedron Lett*. **2002**, *43*, 3693−3697. (i) Dambacher, J.; Bergdahl, M. *Org. Lett*. **2003**, *5*, 3539−3541. (j) Dambacher, J.; Anness, R.; Pollock, P.; Bergdahl, M. *Tetrahedron* **2004**, 60, 2097−2110. (k) Williams, D. R.; Nold, A. L.; Mullins, R. J. *J. Org. Chem*. **2004**, *69*, 5374−5382.

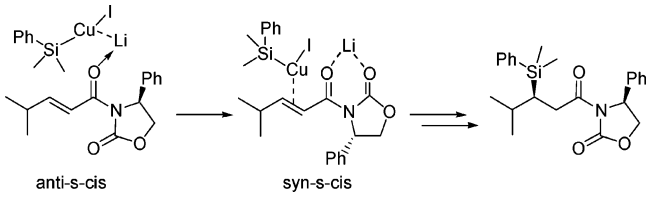
(23) A similar observation has been reported by Bertz using the Li[BuCuI] reagent in the conjugate addition to 2-cyclohexenone, see ref 21.

contrast to THF and Et_2O, the CuI·0.75DMS dissolved in DMS and gave a homogeneous dark brown color of Li[$PhMe_2SiCuI$] after the addition of $PhMe_2SiLi$ at −78 °C. The Li[$PhMe_2SiCuI$] reagent in DMS reacts faster with the imides than in THF. Thus, product **5** was obtained in 94% (dr = 94:6) if the silylcuprate addition to imide **1** was conducted in DMS at −78 °C for 12 h. Due to the favorable Li-THF coordination, the reaction temperature was slowly increased to −20 °C over 7 h. Employing 1.4 equiv of the Li[$PhMe_2SiCuI$] reagent in DMS gave 91% yield of product **5** (dr = 94:6) (entry 4) while a considerably higher dr is obtained in THF (entry 1). In comparison, the phenylglycine-derived oxazolidinone (**1**) is considerably more efficient in blocking one π-face during the conjugate addition of the Li[$PhMe_2SiCuI$] reagent than the corresponding *tert*-leucine-derived oxazolidinone **2** (entry 6). The absolute stereochemistry of the created β-silyl carbon was determined by using the optical rotation of the corresponding β-silyl carboxylic acid[15a] obtained after removal of the chiral auxiliary with LiOH in THF.

The influence of the DMS, derived from the CuI·0.75DMS complex, in the conjugate addition of Li[$PhMe_2SiCuI$] is instrumental. Thus, the CuI purified via its DMS complex is of fundamental importance for the Li[$PhMe_2SiCuI$] reagent to undergo an efficient conjugate addition. The influence of DMS on yield as well as stereoselectivity is demonstrated for the 1,4-additions of Li[$PhMe_2SiCuI$] to Koga's 2-pyrrolidinone (Table 1).[13] Employing imide **3** and the Li[$PhMe_2SiCuI$] reagent obtained from ultrapure grade CuI,[24] in the absence of DMS, not only drastically reduced the yield of **7** from 92% to 63%, it also completely degraded the dr from 92%[25] to an insignificant level (entry 8). Once DMS was introduced with ultrapure grade CuI (entry 9), the yield as well as the ratio of the β-silylated product increased significantly. As it was impossible to restore the level of dr (96:4) by adding DMS, it is likely that the Cu(I) quality is indeed also a variable. DMS remaining from the purification of CuI is partly a constituent responsible for the higher yield, probably due to a more soluble and increasingly reactive silylcopper species. Although we have reported monumental differences between CuI·0.75DMS and CuBr·DMS complex applied in promoting catalytic 1,4-additions of alkenyl groups from vinylzirconocenes relative to the transfer of the corresponding alkyl groups,[26] the difference between iodide and bromide ligands in this study utilizing $PhMe_2SiLi$ in THF is less important. Thus, conjugate addition of Li[$PhMe_2SiCuX$] to the silyl protected 2-pyrrolidinone **4**, using either CuI·0.75DMS (entry 10) or the CuBr·DMS complex (entry 11), provided excellent yields as well as matching diastereomeric ratios of product **8**.

Because of the uncertainty of many variables in organocopper reactions (e.g., cuprate structures, additives, solvents, reaction conditions, and substrate, as well as the cuprate cluster at each stage of the reaction pathway), a detailed mechanistic explanation has not yet emerged. However, it is generally accepted that the initial lithium−carbonyl coordination is a first critical step in conjugate additions of organocuprate reagents.[27] Although the mechanistic details of the organocopper reactions are very elusive, a qualitative pattern with the Li[$PhMe_2SiCuI$] reagent in asymmetric 1,4-additions is becoming apparent. Thus, a lithium species is proposed to initially chelate the carbonyl groups preceding the formation of the copper π-complex, allowing the silyl addition to occur to the most available π-face of the imide while adopting a syn-s-cis conformation (Scheme 1). Since the nature of the responsible silylcopper species depicted that forms the π-complex[28] is unknown, there is the possibility for dimer[29] and higher oligomer formations.[30]

SCHEME 1



The distinctive power of the Li[$PhMe_2SiCuI$] as a reagent in asymmetric conjugate additions to various *N*-enoyl-2-oxazolidinones is illustrated (Table 2). The conjugate addition of the "$PhMe_2Si$" group is proposed to proceed via the syn-s-cis imide conformation based on the stereochemistry introduced as well as the built-in chirality of the 2-oxazolidinone moiety. Not only is the chemical yield almost quantitative for the 1,4-additions employing the monosilylcopper reagent, but also the diastereomeric ratios are very high. Specifically the phenylglycine-derived oxazolidinone (**12**) was most efficient in favoring one π-face for the 1,4-additions, using the silylcuprate reagent obtained from the CuI·0.75DMS complex (entry 12). Although the yield of **18** was excellent when employing the CuBr·DMS complex, the stereoselectivity decreased (entry 13). Oxazolidinone (**12**) has previously been found to be an excellent auxiliary for other organocopper systems.[16a,22] In contrast to our results, it has been reported that tributylphosphine was "imperative" for the Li[$PhMe_2SiCuI$] reagent to undergo a conjugate addition to imide **12**, even at 0 °C.[8a] In the same report, the corresponding Li[$(PhMe_2Si)_2Cu$]LiCN reagent was reported to give only ∼50% de to substrate **12** and ∼20% de employing imide **13**. In comparison, CuI·0.75DMS generated Li[$PhMe_2SiCuI$] reagent is very efficient with *tert*-leucine-derived imides (**14**−**16**) or with the phenylalanine derivative (**13**) without any external additives such as HMPA or tributylphosphine.

(24) Reagent purity grade (99.999%) CuI purchased from Aldrich.

(25) The absolute stereochemistry at the β-silyl carbon was determined by integration of the two methyl doublet peaks {δ 1.02 (minor isomer) and 0.94 ppm (major isomer)} in the ^{1}H NMR spectrum, see ref 15a.

(26) El-Batta, A.; Hage, T.; Plotkin, S.; Bergdahl, M. *Org. Lett*. **2004**, *6*, 107−110.

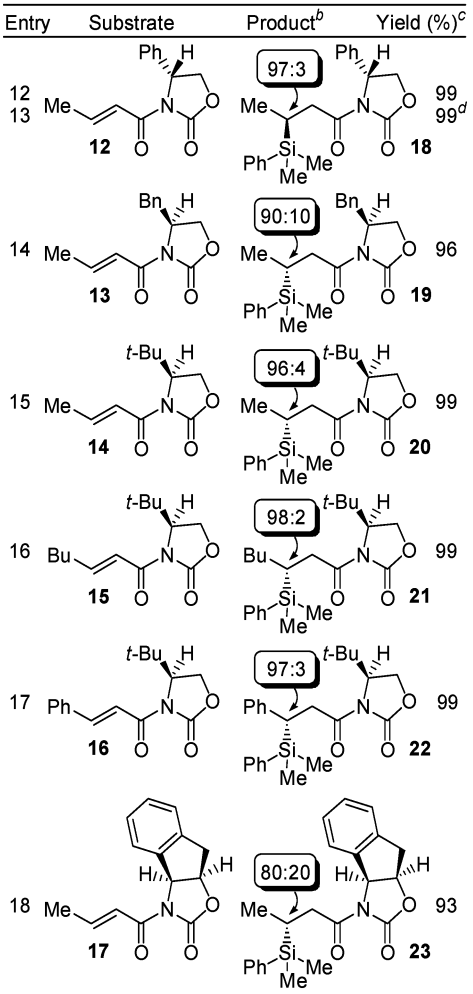
(27) The presence of powerful electrophiles (e.g., TMSI or TMSOTf) can compete with lithium as the initial "activator" in conjugate additions of Li[RCuI], see ref 22j. See also: (a) Bergdahl, M.; Lindstedt, E.-L.; Nilsson, M.; Olsson, T. *Tetrahedron* **1988**, *44*, 2055−2062. (b) Bergdahl, M.; Lindstedt, E.-L.; Olsson, T. *J. Organomet. Chem*. **1989**, *365*, c11−14. (c) Bergdahl, M.; Nilsson, M.; Olsson, T.; Stern, K. *Tetrahedron* **1991**, *47*, 9691−9702. (d) Bergdahl, M.; Iliefski, T.; Nilsson, M.; Olsson, T. *Tetrahedron Lett*. **1995**, *36*, 3227−3230.

(28) For a recent NMR study on π-complex formation, see: Bertz, S. H.; Carlin, C. M.; Deadwyler, D. A.; Murphy, M. D.; Ogle, C. A.; Seagle, P. H. *J. Am. Chem. Soc*. **2002**, *124*, 13650−13651.

(29) Nakamura, E.; Mori, S.; Morokuma, K. *J. Am. Chem. Soc*. **1998**, *120*, 8273−8274.

(30) Olmstead, M.; Power, P. P.; *J. Am. Chem. Soc*. **1990**, *112*, 8008−8014.

TABLE 2. Asymmetric Li[PhMe$_2$SiCuX] Additions



[a] Reactions were conducted in THF with purified CuI·0.75 DMS complex. [b] Characterized by NMR (^{1}H and ^{13}C), IR, and MS. Diastereomeric ratios determined on the crude material by high-resolution ^{1}H NMR (500 MHz). [c] Based on isolated and purified material. [d] Purified CuBr·DMS employed, dr = 93:7.

It has also been reported[8a] that Oppolzer's[31] *N*-enoylsultam provides very high diastereomeric ratios employing the Li[(PhMe$_2$Si)$_2$Cu]LiCN reagent. However, as a significant contrast, the same *N*-crotonylsultam exerted an extremely poor diastereoselectivity (~10%) in THF utilizing the Li[PhMe$_2$SiCuI] reagent obtained from DMS purified CuI.

Due to the efficiency of the phenylglycine-derived auxiliary (**12**) to differentiate between the two π-faces despite the ability for free rotation of the phenyl group, attention was also paid to the corresponding more rigid indanol auxiliary[32] (entry 18). Surprisingly, the indanol (**17**) auxiliary displays a less efficient π-face discrimination than the corresponding phenylglycine-, phenylalanine-, and *tert*-leucine-derived auxiliaries in the conjugate addition of Li[PhMe$_2$SiCuI] in THF.

The monosilylcuprate reagent, Li[PhMe$_2$SiCuI], is mild enough to work in the presence of fairly sensitive substrates. Our results employing the simple Li[PhMe$_2$SiCuI] reagent obtained from CuI·0.75DMS are exceptional, not only with respect to levels of stereoselectivity but also chemical yield. The fact that excellent chemical yields also were obtained with α,β-unsaturated aldehydes and ketones (Table 3) implies that there is little, if any, oligomerization occurring, which normally is a common side reaction associated with more reactive enals and enones with Gilman-type cuprate reagents. Moreover, the monosilylcuprate reagent underwent very efficient conjugate additions to enoates (entries 22 and 25). As the Li[PhMe$_2$SiCuI] reagent reacted with an α,β-unsaturated amide to give the product (**26**) in 60% yield (entry 21), it is feasible to conduct the 1,4-addition in the presence of fairly acidic moieties.

Large substituents surrounding the β-carbon in the enone are known to influence the rate of the addition of Li[PhMe$_2$SiCuI]. Thus, conjugate addition of the monosilylcuprate reagent conducted in THF to 3-methyl-2-cyclopentenone (entry 32) provided only 5% of product **35** with a significant amount of recovered enone. The 1,4-addition to 2-cyclopentenone, on the other hand, provided 99% of **34** (entry 31). Since it is recognized that coordinating media like THF decrease the rate of the conjugate additions and that DMS at the same time increases the rate, stability, and selectivity with use of alkylcopper reagents,[21] it was intuitive to assess the influence of DMS as a solvent on the conjugate addition of Li[PhMe$_2$SiCuI] to β,β-disubstituted enones. Indeed, it was possible to obtain very high yields of product **35** and **36** starting from β,β-disubstituted cyclic enones and Li[PhMe$_2$SiCuI] in DMS as the solvent. Similarly, mesityloxide (entry 28) provided an excellent yield of product **31** (entry 28) when the reaction was conducted in DMS, while the similar reaction in THF only provided 5% of **31** (entry 27) and a considerable amount of unconsumed enone.

The influence of DMS on the rate of the addition of Li[PhMe$_2$SiCuI] to a 2-ene-4-ynoate (**32**) was also scrutinized. Consequently, if the reaction of Li[PhMe$_2$SiCuI] and **32** was conducted in THF at −78 °C for 4 h, 45% of product **33** was obtained (entry 29). Despite the presence of the electron-rich alkyne attached on the β-position, the yield increased to 78% of the β-silylated product **33** if the reaction was conducted in DMS at −78 °C. In this context, it should be mentioned that Gilman-type cuprates (R$_2$CuLi/LiI and R$_2$CuLi/LiCN) have been reported[33] to prefer the 1,6-addition pathway instead of the 1,4-addition to a 2-ene-4-ynoate. In contrast, the conjugate addition with the Li[PhMe$_2$SiCuI] reagent in DMS to **32** has an extraordinary preference (entry 30) for the 1,4-addition pathway.[34]

The most desirable application of a β-SiMe$_2$Ph carbonyl compound comes from its subsequent oxidation to a hydroxyl group, a reaction sequence that proceeds via retention of configuration at the β-carbon. Thus, oxidation of the phenylsilane (Table 1) with mercuric ion in an acetic acid solution of peracetic acid[2b] provides excellent yields of the enantiomerically pure acetate aldol products **9**, **10**, and **11**. Fleming[5b] has described this powerful transformation in great detail. Hence the key phenylsi-

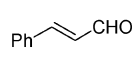
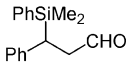
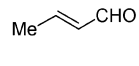
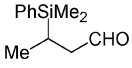
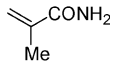
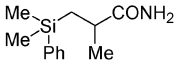
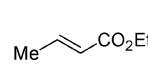
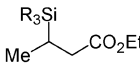
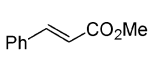
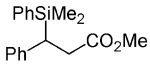
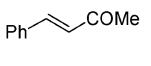
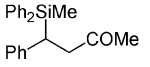
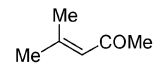
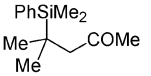
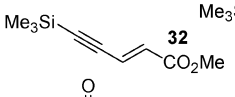
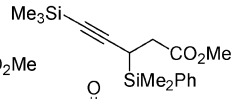
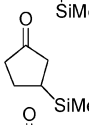
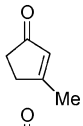
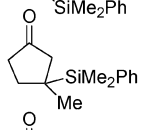
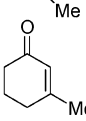
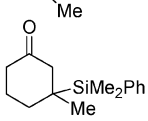
(31) (a) Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969−2004. (b) Oppolzer, W. *Pure Appl. Chem*. **1988**, *60*, 39−48.

(32) (a) Ghosh, A.; Duong, T.; McKee, S. *J. Chem. Soc., Chem Commun*. **1992**, 1673−1674. (b) Senanayake, C. H. *Aldrichim. Acta* **1998**, *31*, 3−15.

(33) Krause, N.; Thorand, S. *Inorg. Chim. Acta* **1999**, *296*, 1−11. See also: Gerold, A.; Krause, N. *Chem. Ber*. **1994**, *127*, 1547−1549.

(34) No 1,6-addition product could be detected.

TABLE 3. 1,4-Additions of Monosilylcopper Reagents

Entry	Reagent/Solvent[a]	Substrate	Product[b]		Yield(%)[c]
19	Li[PhMe$_2$SiCuI]/THF			**24**	71
20	Li[PhMe$_2$SiCuI]/THF			**25**	82
21	Li[PhMe$_2$SiCuI]/THF			**26**	60
22	Li[PhMe$_2$SiCuI]/THF			**27**; R$_3$=PhMe$_2$	95
23	Li[Ph$_2$MeSiCuI]/THF			**28**; R$_3$=Ph$_2$Me	45
24	Li[Ph$_2$MeSiCuI]/DMS			**28**; R$_3$=Ph$_2$Me	70
25	Li[PhMe$_2$SiCuI]/THF			**29**	91
26	Li[Ph$_2$MeSiCuI]/THF			**30**	85
27	Li[PhMe$_2$SiCuI]/THF			**31**	5
28	Li[PhMe$_2$SiCuI]/DMS				81
29	Li[PhMe$_2$SiCuI]/THF			**33**	45[d]
30	Li[PhMe$_2$SiCuI]/DMS				78[d]
31	Li[PhMe$_2$SiCuI]/THF			**34**	99
32	Li[PhMe$_2$SiCuI]/THF			**35**	5
33	Li[PhMe$_2$SiCuI]/DMS				85
34	Li[PhMe$_2$SiCuI]/THF			**36**	10
35	Li[PhMe$_2$SiCuI]/DMS				88

[a] Reactions conducted with purified CuI·0.75DMS complex. 1.4−2.0 equiv versus substrate. 1.2 equiv of "Cu" versus 1.0 equiv of silyl lithium reagent. Reaction temperature maintained at −78 °C for 4 h, increased toward 0 °C over 7 h. [b] Characterized by NMR (^{1}H and ^{13}C), IR, and MS. [c] Based on isolated and purified material. [d] Reaction quenched at −78 °C after 4 h.

lane has to first react with an electrophile, in which the resulting activated phenyl ring is removed by nucleophilic attack of a peracetate anion, followed by a rearrangement that resembles the well-known oxidation of a borane with a peroxide.

Regardless of the electrophile used in the initial attack of the PhMe$_2$Si group, alkenes present will react faster than the disconnection of the phenyl ring from the silyl group. In this scenario, synthesis of a propargylic alcohol from silane **33** utilizing the Tamao−Fleming protocol would be fruitless. Since other silanes have been found readily oxidized to the corresponding alcohols, and thus more applicable for synthesis, several attempts were made to differentiate the substituents attached on the silicon atom in the monosilylcuprate reagent utilizing the CuI·0.75DMS complex. Specifically the Li[(Et$_2$N)Ph$_2$SiCuI] reagent[3c,5b] was attempted because the silicon already has a nucleophilic group present that can be removed under basic oxidative conditions. Attempted monosilylcuprates generated from, e.g., Ph$_2$MeSiLi,[35] *t*-BuPh$_2$SiLi,[36] or (Et$_2$N)Ph$_2$SiLi[5b] in THF in conjunction with the CuI·0.75DMS complex either gave decomposition or low yields of the 1,4-addition products. The Li[Ph$_2$MeSiCuI] reagent reacts readily with an enone in THF (entry 26). Also in this case, utilizing the Li[Ph$_2$MeSiCuI] reagent and an enoate, a good yield of product **28** was obtained if the reaction was conducted in DMS (entry 24).

Conclusions

This paper illustrates that excellent yields and levels of stereoselectivity can be obtained by utilizing the monosilylcuprate reagent, Li[PhMe$_2$SiCuI], generated from the CuI·0.75DMS complex. It is highly recommended that the CuI be purified via its DMS complex prior to making the monosilylcuprate reagent in THF or DMS as solvents. This study also shows that the monosilylcuprate reagent is both more stable and more reactive with DMS as solvent. In this context, it is possible to utilize the monosilylcuprate reagent with sterically hindered (β,β-disubstituted) enones and still maintain a high

(35) Chen, H.-M.; Oliver, J. P. *J. Organomet. Chem.* **1986**, *316*, 255−260.

(36) Barbero, A.; Cuadrado, P.; González, A. M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2811−2816.

yield of the 1,4-addition products. We have clearly demonstrated that the presence of external additives such as tributylphosphine, HMPA, or dialkylzinc is unnecessary even though 1 equiv of the silyllithium reagent relative to the CuI·0.75DMS complex is employed. Although the corresponding silylzincates can be used to avoid oligomerization of β-silyl enolates, we have furthermore demonstrated that the monosilylcuprate reagent can be adopted successfully since there are no oligomerization problems observed during the 1,4-addition reactions. Employing the simple Li[$PhMe_2SiCuI$] reagent obtained from CuI·0.75DMS is an attractive alternative to CuCN. The monosilylcopper system is anticipated to be a very useful reagent in the formation of silicon−carbon bonds in organic synthesis. Further development of other monosilylcopper systems will be reported from our laboratory.

Experimental Section

Typical Procedure for 1,4-Additions of Monosilylcuprate Reagents: Preparation of Compounds 5−8, 18−31, 33−36. The Li[$PhMe_2SiCuI$] reagent was prepared from $PhMe_2SiLi$[5b] (0.986 mmol, 1 equiv) and purified CuI·0.75DMS[37] complex (1.2 equiv) at −78 °C in anhydrous THF (10 mL), or alternatively in anhydrous DMS (10 mL). The resulting dark brown slurry was stirred 20 min at −78 °C, and the appropriate substrate (0.5−0.8 equiv) dissolved in THF or DMS (7−10 mL) was added via the reaction flask wall at −78 °C, using a gastight syringe. In THF, the reaction mixture was stirred for 2 h at −78 °C and then allowed to rise to about −20 °C over the next 7 h before a saturated solution of NH_4Cl/NH_3 (pH ∼10) was added (5 mL). In DMS, depending on the reactivity of the substrate, the reaction temperature was maintained at −78 °C and subsequently quenched at this low temperature. After increasing the temperature to +20 °C and removing the septum, the resulting mixture was stirred until a homogeneous deep blue solution was obtained. The mixture was then poured out in mixture of Et_2O (25 mL) and water (25 mL) and transferred to a separation funnel. The aqueous phase was extracted with Et_2O (3 × 25 mL) and the combined organic layers dried over $MgSO_4$. After removal of the solvent, the crude material was dried and the diasteromeric ratio was determined with ^{1}H NMR spectroscopy. The crude product was subsequently purified with chromatography on a silica gel column.

Typical Procedure for Preparation of Acetate Aldol Products (9−11):[2c] **Oxidation of Silanes 5, 6, and 8.** The appropriate silane (400 μmol, 1 equiv) and $Hg(OAc)_2$ (420 μmol) in 32% peracetic acid in acetic acid (4 mL) was stirred at room temperature for 5 h. Ether (80 mL) was added and the mixture was transferred to a separation funnel. The organic layer was washed with sodium thiosulfate (1.0 M, 50 mL), water (50 mL), sodium bicarbonate (2.0 M, 50 mL), and brine (50 mL) and dried over anhydrous magnesium sulfate. The organic solvent was removed under vacuum and the diastereomeric ratio was determined on the crude material with ^{1}H NMR spectroscopy. Purification of the crude acetate aldol products and enrichment of the major diasteromer for compounds **9−11** were conducted by using flash chromatography on silica gel.

***N*-(4′-Methyl-2′-pentenoyl)-4*S*-phenyl-1,3-oxazolidin-2-one (1).**[38] **1** was obtained from an acylation reaction[39] with 4*S*-phenyl-1,3-oxazolidin-2-one, butyllithium, and *trans*-4-methyl-2-pentenoyl chloride in THF. The crude product was purified with flash chromatography (30% Et_2O in pentane, R_f 0.40) to give an 80% (943 mg) yield of **1** as a white solid; mp 99−102 °C; $[\alpha]^{20}_D$ +131.0 (*c* 1.0, CH_2Cl_2) {lit.[38] mp 103.0−104.0 °C; $[\alpha]^{20}_D$ +103.1 (*c* 1.0, $CHCl_3$)}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.31 (m, Ar-*H*, 5H), 7.23 (dd, CHC*H*CO, J = 15.4, 1.3 Hz, 1H), 7.07 (dd, C*H*CHCO, J = 15.4, 6.8 Hz, 1H), 5.50 (dd, NC*H*, J = 8.8, 3.9 Hz, 1H), 4.70 (t, OCH_2, J = 8.8 Hz, 1H), 4.28 (dd, OCH_2, J = 8.8, 3.9 Hz, 1H), 2.53 (m, $(CH_3)_2$C*H*, 1H), 1.09, 1.08 (2d, $(CH_3)_2$CH, J = 6.8 Hz each, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 158.1, 153.7, 139.2, 129.2 (2C), 128.6, 126.0 (2C), 117.7, 69.9, 57.8, 31.5, 21.2(2C); FTIR (cm^{-1}) 2964, 1771, 1686, 1635; MS *m/z* 259 (M^+, 63%), 216 (M − C_3H_7, 8%), 162 (M − C_6H_9O, 5%), 96 (100%), 77 (C_6H_5, 19%); HRMS (EI) calcd for [$C_{15}H_{17}NO_3$] 259.1208, found 259.1201.

***N*-(4′-Methyl-2′-pentenoyl)-4*S*-*tert*-butyl-1,3-oxazolidin-2-one (2).** Butyllithium (2.5 M in hexane, 0.92 mL, 2.3 mmol, 1.1 equiv) was added to a solution of 4*S*-*tert*-butyl-1,3-oxazolidin-2-one (2.1 mmol, 300 mg) in THF (10 mL) at −78 °C under argon. The resulting mixture was stirred for 45 min and a solution of freshly distilled *trans*-4-methyl-2-pentenoyl chloride (1.2 equiv, 2.5 mmol) in THF (5 mL) was added via syringe at −78 °C. The reaction mixture was stirred for an additional 30 min at −78 °C and then warmed to ambient temperature. Saturated aqueous ammonium chloride (1 mL) was added to the mixture and then diluted with water (30 mL). After extraction with ether (3 × 30 mL), the combined organics were dried over $MgSO_4$, filtered, and evaporated. The crude product was purified with flash chromatography (15% Et_2O in pentane, R_f 0.25) to give a 60% (301 mg) yield of **2** as a clear oil; $[\alpha]^{20}_D$ +85.0 (*c* 0.10, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (dd, CHC*H*CO, J = 15.4, 1.3 Hz, 1H), 7.09 (dd, C*H*CHCO, J = 15.4, 6.7 Hz, 1H), 4.50 (dd, NC*H*, J = 7.6, 1.7 Hz, 1H), 4.28 (dd, OCH_2, J = 9.3, 1.7 Hz, 1H), 4.23 (dd, OCH_2, J = 9.3, 7.6 Hz, 1H), 2.54 (m, $(CH_3)_2$C*H*, 1H), 1.10, 1.08 (2d, $(CH_3)_2$CH, J = 6.8 Hz each, 3H each), 0.94 (s, *t*-Bu, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 157.6, 154.7, 117.9, 65.2, 60.8, 35.9, 31.5, 25.6 (3C), 21.3 (2C); FTIR (film, cm^{-1}) 2965, 1782, 1689, 1635; MS *m/z* 239 (M^+, 11%), 224 (M − CH_3, 7%), 196 (M − C_3H_7, 8%), 97 (M − $C_7H_{12}NO_2$, 100%), 57 (C_4H_9, 12%); HRMS (EI) calcd for [$C_{13}H_{21}NO_3$] 239.1521, found 239.1514.

***N*-(2′*E*-Butenoyl)-5*S*-*tert*-butyldiphenylsilyloxymethyl-2-pyrrolidinone (4).** Butyllithium (2.5 M in hexane, 1.40 mL, 3.50 mmol, 1.2 equiv) was added to a solution of 5*S*-*tert*-butyldiphenylsilyloxymethyl-2-pyrrolidinone[40] (2.83 mmol, 1.0 g) in THF (10 mL) at −78 °C under argon. The resulting mixture was stirred for 45 min and a solution of freshly distilled *trans*-crotonyl chloride (2.83 mmol, 1.0 equiv) in THF (5 mL) was added via syringe at −78 °C. The reaction mixture was stirred for an additional 30 min at −78 °C and then warmed to ambient temperature. Saturated aqueous ammonium chloride (1 mL) was added to the mixture and then diluted with water (30 mL). After extraction with ether (3 × 30 mL), the combined organics were dried over $MgSO_4$, filtered, and evaporated. The crude product was purified with flash chromatography (30% Et_2O in pentane, R_f 0.40) to give an 87% (1.03 g) yield of **4** as a white solid; mp 115−117 °C, $[\alpha]^{20}_D$ −65.5 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66−7.62 (m, Ar-*H*, 2H), 7.57−7.55 (m, Ar-*H*, 2H), 7.46−7.37 (m, Ar-*H*, 4H), 7.36−7.32 (m, *partly hidden*, Ar-*H*, 2H), 7.32 (dq, *partly hidden*, C*H*CHCH$_3$, J = 15.2, 1.6 Hz 1H), 7.09 (dq, CHC*H*CH$_3$, J = 15.2, 7.0, 1H), 4.51 (m, NC*H*, 1H), 3.99 (dd, OCH_2, J = 10.6, 3.7 Hz, 1H), 3.74 (dd, OCH_2, J = 10.6, 2.3 Hz, 1H), 2.92 (ddd, J = 17.7, 10.5, 10.5 Hz, COCH_2-ring, 1H), 2.50 (m, COCH_2-ring, 1H), 2.13 (m, CH_2-ring, 2H), 1.98 (dd, CHCHCH_3, J = 7.0, 1.6 Hz, 3H), 1.05 (s, Si-*t*-Bu, 9H); ^{13}C NMR δ 176.4, 165.9, 145.5, 135.6 (2C), 135.5 (2C), 133.1, 132.8, 129.82, 129.80, 127.8 (2C), 127.7 (2C), 124.1, 64.7, 58.0, 33.4, 26.8 (3C), 21.0, 19.2, 18.5; FTIR (cm^{-1}) 2958, 1736, 1680, 1637, 1336, 1112, 704; MS *m/z* 422 (M^+, 1%), 406 (M − CH_3, 1%), 364 (M

(37) House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. *J. Org. Chem*. **1975**, *40*, 1460−1469. See also ref 20.

(38) Liao, S.; Shenderovich, M. D.; Lin, J.; Hruby, V. J. *Tetrahedron* **1997**, *53*, 16645−16662.

(39) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc*. **1981**, *103*, 2127−2129.

(40) Obtained in 92% yield from the silylation of the alcohol, using TBDPSCl and imidazole in DMF.

− C_4H_9, 100%), 296 (20%), 266 (17%), 236 (15%), 218 (40%), 181 (M − $C_{16}H_{19}Si$, 8%), 69 (C_4H_5O, 20%); HRMS (EI, DCI/NH_3) calcd for $[C_{25}H_{32}NO_3Si]^+$ (MH^+) 422.2151, found 422.2144.

***N*-(3′*S*-Dimethylphenylsilyl-4′-methylpentanoyl)-4*S*-phenyl-1,3-oxazolidin-2-one (5). 5** was obtained from a reaction between substrate **1** and Li[$Me_2PhSiCuI$] in THF. The crude product was purified with flash chromatography (15% Et_2O in pentane, R_f 0.25) to give 84% (163 mg, 99:1 dr) of **5** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.49−7.47 (m, Ar-*H*, 2H), 7.40−7.29 (m, Ar-*H*, 6H), 7.23−7.21 (m, Ar-*H*, 2H), 5.18 (dd, NC*H*, J = 8.7, 3.7 Hz, 1H), 4.55 (t, OCH_2, J = 8.8 Hz, 1H), 4.20 (dd, OCH_2, J = 8.8, 3.7 Hz, 1H), 3.13 (dd, COCH_2, J = 17.2, 7.3 Hz, 1H), 2.85 (dd, COCH_2, J = 17.2, 6.4 Hz, 1H), 1.86 (m, $(CH_3)_2$C*H*, 1H), 1.63 (m, SiC*H*, 1H), 0.88, 0.82 (2d, $(CH_3)_2$CH, J = 6.8 Hz, 3H each), 0.28, 0.27 (2s, Si$(CH_3)_2$, 3H each); ^{13}C NMR δ 173.4, 153.6, 139.2, 139.1, 134.0 (2C), 129.1 (2C), 128.7, 128.6, 127.6 (2C), 125.9 (2C), 69.9, 57.7, 33.2, 28.8, 27.8, 22.6, 21.1, −2.3, −3.1; FTIR (film, cm^{-1}) 1786, 1705; MS *m/z* 395 (M^+, 3%), 380 (M − CH_3, 40%), 352 (M − C_3H_7, 85%), 298 (60%), 135 ($PhSiMe_2$, 100%); HRMS (EI, DCI/NH_3) calcd for $[C_{23}H_{30}NO_3Si]^+$ (MH^+) 396.1995, found 396.1981.

***N*-(3′*S*-Dimethylphenylsilyl-4′-methylpentanoyl)-4*S*-*tert*-butyl-1,3-oxazolidin-2-one (6). 6** was obtained from a reaction between substrate **2** and Li[$Me_2PhSiCuI$] in THF. The crude product was purified with flash chromatography (15% Et_2O in pentane, R_f 0.40) to give an 87% (161 mg, 96:4 dr) yield of **6** as a white solid; mp 82−85 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.56−7.53 (m, Ar-*H*, 2H), 7.35−7.32 (m, Ar-*H*, 3H), 4.31 (dd, NC*H*, J = 7.7, 1.6 Hz, 1H), 4.21 (dd, OCH_2, J = 9.3, 1.6 Hz, 1H), 4.09 (dd, OCH_2, J = 9.3, 7.7 Hz, 1H), 3.17 (dd, COCH_2, J = 18.1, 7.2 Hz, 1H), 2.87 (dd, COCH_2, J = 18.1, 5.1 Hz, 1H), 1.95 (m, $(CH_3)_2$C*H*, 1H), 1.68 (m, SiC*H*, 1H), 0.92 (d, $(CH_3)_2$CH, J = 6.8 Hz, 3H), 0.86 (d, $(CH_3)_2$CH, "partly hidden", J = 6.8 Hz, 3H), 0.86 (s, *t*-Bu, 9H), 0.38, 0.37 (2s, Si$(CH_3)_2$, 3H each); ^{13}C NMR δ 173.9, 154.7, 139.3, 134.0 (2C), 128.8, 127.7 (2C), 65.2, 61.2, 35.7, 32.9, 29.0, 27.7, 25.7 (3C), 22.8, 21.4, −2.1, −2.9; FTIR (film, cm^{-1}) 1781, 1705; MS *m/z* 375 (M^+, 2%), 360 (M − CH_3, 40%), 332 (M − C_3H_7, 100%), 279 (80%), 135 ($PhMe_2Si$, 50%); HRMS (EI, DCI/NH_3) calcd for $[C_{21}H_{34}NO_3Si]^+$ (MH^+) 376.2308, found 376.2318.

***N*-(3′*S*-Dimethylphenylsilylbutanoyl)-5*S*-trityloxymethyl-2-pyrrolidinone (7).**[13,15c] **7** was obtained from a reaction between substrate **3**[17b,22j] and Li[$Me_2PhSiCuI$] in THF. The crude product was purified with flash chromatography (30% Et_2O in pentane, R_f 0.60) to give a 92% (255 mg, 96:4 dr) yield of **7** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.59−7.56 (m, Ar-*H*, 2H), 7.40−7.10 (m, Ar-*H*, 18H), 4.49−4.45 (br m, NC*H*, 1H), 3.50 (dd, OCH_2, J = 9.8, 4.0 Hz, 1H), 3.20 (dd, OCH_2, J = 9.8, 2.7 Hz, 1H), 2.98 (dd, SiCHCH_2, J = 16.2, 3.3 Hz, 1H), 2.95−2.85 (m, COCH_2-ring, 1H), 2.78 (dd, SiCHCH_2, J = 16.2, 11.3 Hz, 1H), 2.47 (ddd, COCH_2-ring, J = 17.8, 9.9, 1.8 Hz, 1H), 2.12−1.92 (2m, CH_2-ring, 1H each), 1.59−1.51 (m, SiC*H*, 1H), 0.94 (d, CH_3CHSi, J = 7.3 Hz, 3H), 0.36, 0.35 (2s, Si$(CH_3)_2$, 3H each); ^{13}C NMR δ 176.1, 173.9, 143.6, 137.8, 134.0, 128.6, 127.94, 127.86, 127.75, 127.1, 87.0, 64.1, 56.6, 39.0, 33.2, 21.2, 15.3, 14.4, −4.9, −5.1; FTIR (film, cm^{-1}) 1735, 1697; MS *m/z* 597 (M + Cl^-, 30%), 601 (M + K^+, 15%). HRMS or EA missing.

***N*-(3′*S*-Dimethylphenylsilylbutanoyl)-5*S*-diphenyl-*tert*-butylsilyloxymethyl-2-pyrrolidinone (8). 8** was obtained from a reaction between substrate **4** and Li[$Me_2PhSiCuI$] in THF. The crude product was purified with flash chromatography (15% Et_2O in pentane, R_f 0.40) to give a 93% (255 mg, 95:5 dr) yield of **8** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.62−7.50 (2m, Ar-*H*, 6H), 7.44−7.40 (3m, Ar-*H*, 9H), 4.40 (m, NC*H*, 1H), 3.89 (dd, OCH_2, J = 10.6, 3.7 Hz, 1H), 3.67 (dd, OCH_2, J = 10.6, 2.4 Hz, 1H), 3.00 (dd, SiCHCH_2, J = 16.0, 3.4 Hz, 1H), 2.84 (ddd, COCH_2-ring, J = 17.7, 10.7, 10.3 Hz, 1H), 2.69 (dd, SiCHCH_2, J = 16.0, 11.3 Hz, 1H), 2.44 (ddd, COCH_2-ring, J = 17.7, 9.2, 3.0 Hz, 1H), 2.05 (m, CH_2-ring, 2H), 1.52 (m, SiC*H*, 1H), 1.02 (s, Si-*t*-Bu, 9H), 0.90 (d, CH_3CHSi, J = 7.3 Hz, 3H), 0.32, 0.31 (2s, Si$(CH_3)_2$, 3H each); ^{13}C NMR δ 176.3, 174.3, 138.0, 135.7, 134.2, 133.4, 133.0, 130.0, 129.2, 128.0, 65.0, 58.0, 39.3, 33.4, 27.0, 21.3, 19.4, 15.6, 14.6, −4.7, −4.9; FTIR (film, cm^{-1}) 1736, 1690; HRMS (EI) calcd for $[C_{33}H_{44}NO_3Si_2]^+$ (MH^+) 558.2860, found 558.2838. Anal. Calcd for $C_{33}H_{43}NO_3Si_2$: C, 71.05; H, 7.77; N, 2.51. Found: C, 70.83; H, 8.04; N, 2.46.

***N*-(3′*S*-Hydroxy-4′-methylpentanoyl)-4*S*-phenyl-1,3-oxazolidin-2-one (9).**[46] Obtained from the oxidation of silane **5** using $Hg(OAc)_2$ and peracetic acid. The crude product was purified using flash chromatography (50% Et_2O in pentane, R_f 0.20 for the major diastereomer) to give a 77% (71 mg, >99:1 dr) yield of **9** as a white solid; mp 93−94 °C (lit.[46] mp 86.0 °C). ^1H NMR (500 MHz, $CDCl_3$) δ 7.42−7.33 (m, Ar-*H*, 3H), 7.32−7.28 (m, Ar-*H*, 2H), 5.46 (dd, NC*H*, J = 8.7, 3.6 Hz, 1H), 4.71 (dd, OCH_2, J = 8.9, 8.7 Hz, 1H), 4.28 (dd, OCH_2, J = 8.9, 3.6 Hz, 1H), 3.81 (m, HOC*H*, 1H), 3.15 (dd, COCH_2, J = 17.0, 2.7 Hz, 1H), 3.07 (dd, COCH_2, J = 17.0, 9.6 Hz, 1H), 2.70 (br s, O*H*, 1H), 1.74 (m, $(CH_3)_2$C*H*, 1H), 0.96 (2d, $(CH_3)_2$CH, J = 6.1 Hz, 6H); ^{13}C NMR δ 172.8, 153.8, 138.7, 129.3 (2C), 128.8, 125.7 (2C), 72.7, 70.1, 57.6, 39.9, 33.3, 18.4, 17.7; FTIR (cm^{-1}) 3522, 1782, 1703; MS *m/z* 259 (M − H_2O, 25%), 234 (M − C_3H_7, 83%), 164 (100%). HRMS (DEI) calcd for $[C_{15}H_{20}NO_4]^+$ (MH^+) 278.1392, found 278.1390.

***N*-(3′*S*-Hydroxy-4′-methylpentanoyl)-4*S*-*tert*-butyl-1,3-oxazolidin-2-one (10).** Obtained from the oxidation of silane **6** using $Hg(OAc)_2$ and peracetic acid. The crude product was purified using flash chromatography (30% Et_2O in pentane, R_f 0.20 for the major diastereomer) to give a 77% (74 mg, >99:1 dr) yield of **10** as a white solid; mp 77−78 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 4.46 (dd, NC*H*, J = 7.6, 1.6 Hz, 1H), 4.31 (dd, OCH_2, J = 9.3, 1.6 Hz, 1H), 4.26 (dd, OCH_2, J = 9.3, 7.6 Hz, 1H), 3.82 (m, C*H*OH, 1H), 3.15 (dd, COCH_2, J = 16,7 9.9 Hz, 1H), 3.03 (dd, COCH_2, J = 16.7, 2.6 Hz, 1H), 2.91 (br d, CHO*H*, J = 4.6 Hz, 1H), 1.77 (m, $(CH_3)_2$C*H*, 1H), 0.99, 0.97 (2d, $(CH_3)_2$CH, J = 6.7 Hz, 3H each), 0.95 (s, *t*-Bu, 9H); ^{13}C NMR δ 173.2, 154.9, 72.9, 65.5, 61.0, 39.8, 35.9, 33.5, 25.7(3C), 18.5, 17.7; FTIR (cm^{-1}) 3543, 1780, 1698. HRMS (DEI) calcd for $[C_{13}H_{24}NO_4]^+$ (MH^+) 258.1703, found 258.1705.

***N*-(3′*S*-Hydroxybutanoyl)-5*S*-diphenyl-*tert*-butylsilyloxymethyl-2-pyrrolidinone (11). 11** was obtained from the oxidation of silane **8** with $Hg(OAc)_2$ and peracetic acid. The crude product was purified with flash chromatography (50% Et_2O in pentane, R_f 0.30, major diasteromer) to give a 53% (75 mg, >99:1 dr) yield of **11** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.65−7.62 (m, Ar-*H*, 2H), 7.57−7.54 (m, Ar-*H*, 2H), 7.47−7.38 (m, Ar-*H*, 6H), 4.46 (m, NC*H*, 1H), 4.24 (m, HOC*H*, 1H), 3.98 (dd, OCH_2, J = 10.6, 3.6 Hz, 1H), 3.70 (dd, OCH_2, J = 10.6, 2.2 Hz, 1H), 3.22 (br s, O*H*, 1H), 3.19 (dd, HOCHCH_2, J = 17.9, 2.6 Hz, 1H), 2.98−2.88 (m, HOCHCH_2 and COCH_2-ring, "partly overlap", 2H), 2.50 (m, COCH_2-ring, 1H), 2.15 (m, CH_2-ring, 2H), 1.27 (d, CH_3CHOH, J = 6.5 Hz, 3H), 1.05 (s, Si-*t*-Bu, 9H); ^{13}C NMR δ 176.5, 173.9, 135.49 (2C), 135.47 (2C), 133.0, 132.5, 130.0, 129.9, 127.9 (2C), 127.8 (2C), 64.5, 64.0, 57.8, 45.5, 33.0, 26.8 (3C), 22.3, 21.2, 19.1; FTIR (film, cm^{-1}) 3470, 1741, 1690; HRMS (EI, DCI/NH_3) calcd for $[C_{25}H_{34}NO_4Si]^+$ (MH^+) 440.2257, found 440.2242.

***N*-(3′*S*-Dimethylphenylsilylbutanoyl)-4*R*-phenyl-1,3-oxazolidin-2-one (18).**[13] **18** was obtained from a reaction between substrate **12**[17a,22j] and Li[$Me_2PhSiCuI$] in THF. The crude product was purified with flash chromatography (30%

(41) Karlsson, S.; Han, F.; Högberg, H.-E.; Caldirola, P. *Tetrahedron: Asymmetry* **1999**, *10*, 2605−2616.
(42) Ager, D.; Fleming, I. *J. Chem. Soc., Chem. Commun*. **1978**, 177−178.
(43) Fleming, I.; Newton, T. W. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1805−1808.
(44) Compound **32** was obtained in 58% yield in a Horner−Wadsworth−Emmons reaction between TMS−acetaldehyde and methyl diethylphosphonoacetate, using BuLi in Et_2O.
(45) Engel, W.; Fleming, I.; Smithers, R. H. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1637−1641.
(46) Fukuzawa, S.-I.; Matsuzawa, H.; Yoshimitsu, S.-I. *J. Org. Chem*. **2000**, *65*, 1702−1706.

Et_2O in pentane, R_f 0.40) to give a 99% (179 mg, 97:3 dr) yield of **18** as a white solid; mp 73−75 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (m, Ar-*H*, 2H), 7.36−7.25 (m, Ar-*H*, 8H), 5.35 (dd, NC*H*, J = 8.7, 3.7 Hz, 1H), 4.63 (dd, OCH_2, J = 8.9, 8.7 Hz, 1H), 4.24 (dd, OCH_2, J = 8.9, 3.7 Hz, 1H), 3.00 (dd, COCH_2, J = 15.8, 3.7 Hz, 1H), 2.68 (dd, COCH_2, J = 15.8, 11.2 Hz, 1H), 1.50 (m, SiC*H*, 1H), 0.82 (d, CH_3CH, J = 7.3 Hz, 3H), 0.27, 0.26 (2s, SiCH_3, 3H each); ^{13}C NMR δ 173.5, 153.6, 139.5, 137.5, 134.2, 129.3, 129.2, 128.9, 127.9, 126.2, 70.1, 57.8, 38.1, 15.8, 14.4, −4.87, −4.89; FTIR (cm^{-1}) 1785, 1703; MS *m/z* 403 (M + Cl^-, 10%), 406 (M + K^+, 50%).

***N*-(3′*R*-Dimethylphenylsilylbutanoyl)-4*S*-phenylmethyl-1,3-oxazolidin-2-one (19). 19** was obtained from a reaction between substrate **13**[22j,39] and Li[Me_2PhSiCuI] in THF. The crude product was purified with flash chromatography (15% Et_2O in pentane, R_f 0.40) to give a 96% (178 mg, 9:1 dr) yield of **19** as a white solid; mp 87−90 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (m, Ar-*H*, 2H), 7.38−7.23 (m, Ar-*H*, 6H), 7.18 (m, Ar-*H*, 2H), 4.58 (m, NC*H*, 1H), 4.12 (m, OCH_2, 2H), 3.25 (dd, PhCH_2, J = 13.3, 3.4 Hz, 1H), 3.03 (dd, COCH_2, J = 16.1, 3.8 Hz, 1H), 2.74 (dd, COCH_2, J = 16.1, 10.8 Hz, 1H), 2.66 (dd, PhCH_2, J = 13.3, 9.8 Hz, 1H), 1.60 (m, SiC*H*, 1H), 1.00 (d, CH_3CH, J = 7.3 Hz, 3H), 0.34, 0.33 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR δ 173.5, 153.6, 137.7, 135.6, 134.2, 129.6, 129.3, 129.1, 128.0, 127.5, 66.4, 55.4, 38.2, 38.1, 15.8, 14.8, −4.7, −4.9; FTIR (cm^{-1}) 1790, 1697; MS *m/z* 417 (M + Cl^-, 70%), 421 (M + K^+, 40%); HRMS (EI) calcd for [$C_{22}H_{27}NO_3Si$] 381.1760, found 381.1756.

***N*-(3′*R*-Dimethyl(phenyl)silylbutanoyl)-4*S*-*tert*-butyl-1,3-oxazolidin-2-one (20). 20** was obtained from a reaction between substrate **14**[22f,j] and Li[Me_2PhSiCuI] in THF. The crude product was purified with flash chromatography (15% Et_2O in pentane, R_f 0.30) to give a 99% (175 mg, 96:4 dr) yield of **20** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (m, Ar-*H*, 2H), 7.35 (m, Ar-*H*, 3H), 4.39 (dd, NC*H*, J = 7.6, 1.6 Hz, 1H), 4.24 (dd, OCH_2, J = 9.2, 1.6 Hz, 1H), 4.16 (dd, OCH_2, J = 9.2, 7.6 Hz, 1H), 3.02 (dd, COCH_2, J = 15.8, 3.2 Hz, 1H), 2.69 (dd, COCH_2, J = 15.8, 11.3 Hz, 1H), 1.57 (m, SiC*H*, 1H), 0.97 (d, CH_3CH, J = 7.5 Hz, 3H), 0.90 (s, *t*-Bu, 9H), 0.33, 0.32 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR δ 173.5, 154.7, 137.5, 134.0, 129.0, 127.8, 65.3, 61.0, 37.6, 35.7, 25.7, 16.1, 14.4, −4.9, −5.1; FTIR (cm^{-1}) 1782, 1703; MS *m/z* 387 (M + K^+, 40%); HRMS (EI, DCI/NH_3) calcd for [$C_{19}H_{30}NO_3Si$]$^+$ (MH^+) 348.1995, found 348.1985.

***N*-(3′*R*-Dimethylphenylsilylheptanoyl)-4*S*-*tert*-butyl-1,3-oxazolidin-2-one (21). 21** was obtained from a reaction between substrate **15**[22j] and Li[Me_2PhSiCuI] in THF. The crude product was purified with flash chromatography (15% Et_2O in pentane, R_f 0.30) to give a 99% (192 mg, 98:2 dr) yield of **21** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.52 (m, Ar-*H*, 2H), 7.35−7.33 (m, Ar-*H*, 3H), 4.35 (dd, NC*H*, J = 7.7, 1.2 Hz 1H), 4.22 (dd, OCH_2, J = 9.1, 1.2 Hz, 1H), 4.12 (dd, OCH_2, J = 9.1, 7.7 Hz, 1H), 2.94 (m, COCH_2, 2H), 1.58 (m, SiC*H*, 1H), 1.48 (m, CH_2, 1H), 1.29 (m, CH_2, 1H), 1.22−1.12 (m, 2 × CH_2, 4H), 0.87 (s, *t*-Bu, 9H), 0.80 (t, CH_3CH$_2$, J = 6.9 Hz, 3H), 0.33, 0.32 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR δ 173.9, 154.9, 138.6, 134.2, 129.1, 128.0, 65.5, 61.3, 36.2, 35.9, 31.5, 30.3, 25.9, 23.1, 21.0, 14.1, −3.6, −3.8; FTIR (film, cm^{-1}) 1782, 1705; MS *m/z* 428.5 (M + K^+, 30%); HRMS (EI, DCI/NH_3) calcd for [$C_{22}H_{39}N_2O_3Si$]$^+$ (M + H_4N^+) 407.2730, found 407.2745.

***N*-(3′*S*-Dimethylphenylsilyl-3′-phenylpropanoyl)-4*S*-*tert*-butyl-1,3-oxazolidin-2-one (22). 22** was obtained from a reaction between substrate **16**[41] and Li[Me_2PhSiCuI] in THF. The crude product was purified with flash chromatography (30% Et_2O in pentane, R_f 0.40) to give a 99% (200 mg, 97:3 dr) yield of **22** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.30 (m, Ar-*H*, 5H), 7.15 (m, Ar-*H*, 2H), 7.05 (m, Ar-*H*, 1H), 6.94 (m, Ar-*H*, 2H), 4.18 (dd, NC*H*, J = 7.8, 1.6 Hz, 1H), 4.14 (dd, OCH_2, J = 9.2, 1.6 Hz, 1H), 3.97 (dd, OCH_2, J = 9.2, 7.8 Hz, 1H), 3.58 (dd, PhC*H*, J = 16.1, 12.2 Hz, 1H), 3.09 (dd, COCH_2, J = 16.1, 3.6 Hz, 1H), 3.05 (dd, COCH_2, J = 12.2, 3.6 Hz, 1H), 0.72 (s, *t*-Bu, 9H), 0.30, 0.24 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR δ 173.0, 155.0, 141.6, 136.7, 134.4, 129.5, 128.3, 128.1, 128.0, 125.2, 65.5, 61.2, 35.75, 35.70, 32.7, 25.6, −4.0, −5.0; FTIR (film, cm^{-1}) 1774, 1701; MS *m/z* 445.2 (M + Cl^-, 5%), 448.8 (M + K^+, 10%).

***N*-(3′*R*-Dimethylphenylsilylbutanoyl)-(4*S*,5*R*)-indano-[1,2-d]oxazolidin-2-one (23). 23** was obtained from a reaction between substrate **17**[32] and Li[Me_2PhSiCuI] in THF. The crude product was purified with flash chromatography (30% Et_2O in pentane, R_f 0.40) to give a 93% (166 mg, 4:1 dr) yield of **23** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, Ar-*H*, J = 7.7 Hz, 1H), 7.53 (m, Ar-*H*, 2H), 7.35 (m, Ar-*H*, 4H), 7.27 (m, Ar-*H*, 2H), 5.88 (d, NC*H*, J = 7.0 Hz, 1H), 5.24 (m, OC*H*, 1H), 3.37 (m, Ar−CH_2, 2H), 3.03 (dd, NCOCH_2, J = 15.9, 3.8 Hz, 1H), 2.72 (dd, NCOCH_2, J = 15.9, 11.1 Hz, 1H), 1.58 (m, SiC*H*, 1H), 0.99 (d, CHCH_3, J = 7.4 Hz, 3H), 0.33, 0.32 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR δ 174.0, 153.1, 139.7, 139.5, 137.7, 134.3 (2C), 130.0, 129.3, 128.3, 128.0 (2C), 127.5, 125.4, 78.2, 63.2, 38.3, 38.0, 15.9, 14.6, −4.82, −4.83; FTIR (film, cm^{-1}) 1770, 1701; HRMS (EI) calcd for [$C_{22}H_{25}NO_3Si$] 379.1604, found 379.1590.

3-(Dimethylphenylsilyl)-3-phenylpropanal (24).[13,42] **24** was obtained from the reaction of *trans*-3-phenylpropenal with Li[Me_2PhSiCuI] in THF as solvent. The crude product was purified with flash chromatography (5% ether in pentane; R_f 0.30) to give a 71% (94 mg) yield of **24** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (dd, C*H*O, J = 2.4, 1.5 Hz, 1H), 7.42−7.29 (m, Ar-*H*, 5H), 7.24−7.19 (m, Ar-*H*, 2H), 7.14−7.09 (m, Ar-*H*, 1H), 6.98−6.94 (m, Ar-*H*, 2H), 2.92−2.84 (m, α-CH_2, 2H), 2.68−2.60 (m, C*H*Si, 1H), 0.28, 0.25 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 141.4, 136.4, 134.3 (2C), 129.7, 128.5 (2C), 128.1 (2C), 127.9 (2C), 125.4, 43.8, 30.3, −4.0, −5.3; FTIR (film, cm^{-1}) 2956, 1721, 1251, 700; MS *m/z* 267 (M^+ − H, 4%), 253 (M n -CH_3, 10%), 190 (M − H, C_6H_6, 52%), 175 (M − C_7H_9, 30%), 135 (M − C_9H_9O).

3-(Dimethylphenylsilyl)butanal (25).[2c,13] **25** was obtained from the reaction of *trans*-propenal with Li[Me_2PhSiCuI] in THF as solvent. The crude product was purified with flash chromatography (5% ether in pentane; R_f 0.30) to give a 82% (82 mg) yield of **25** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 (dd, C*H*O, J = 3.2, 1.2 Hz, 1H), 7.52−7.49 (m, Ar-*H*, 2H), 7.40−7.35 (m, Ar-*H*, 3H), 2.44 (ddd, α-CH_2, J = 16.4, 3.7, 1.2 Hz, 1H), 2.16 (ddd, α-CH_2, J = 16.4, 10.9, 3.2 Hz, 1H), 1.51 (m, C*H*Si, 1H), 1.00 (d, CH_3, J = 7.3 Hz, 3H), 0.32, 0.31 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.4, 137.3, 134.1 (2C), 129.5, 128.1 (2C), 46.2, 14.8, 14.1, −4.7, −5.2; FTIR (film, cm^{-1}) 3070, 2957, 1708, 1427, 1251, 701; MS *m/z* 191 (M^+ − CH_3,70%) 135 (M − C_4H_7O, 100%).

3-(Dimethylphenylsilyl)-2-methylpropionamide (26).[13] **26** was obtained from the reaction of 2-methylacrylamide with Li[Me_2PhSiCuI] in THF as solvent. The crude product was purified with flash chromatography (100% ether; R_f 0.20) to give a 60% (63 mg) yield of **26** as a white solid; mp 58−60 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55−7.50 (m, Ar-*H*, 2H), 7.38−7.35 (m, Ar-*H*, 3H), 5.60, 5.32 (2br s, NH_2, each 1H), 2.33 (m, C*H*, 1H), 1.26 (dd, CH_2, J = 14.7, 6.5 Hz, 1H), 1.15 (d, CH_3, J = 6.9 Hz, 3H), 0.94 (dd, CH_2, J = 14.7, 7.8 Hz, 1H), 0.34, 0.32 (2s, Si(CH_3)$_2$, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.2, 139.0, 133.8 (2C), 129.3, 128.1 (2C), 37.0, 21.4, 21.3, −2.0, −2.4; FTIR (cm^{-1}) 3192, 2961, 1647, 1250, 800; MS *m/z* 221 (M^+, 3%), 220, (M − H, 16%), 205 (M − NH_2), 177 (M − $CONH_2$, 22%). Anal. Calcd for $C_{12}H_{19}NOSi$: C, 65.11; H, 8.55; N, 6.33. Found: C, 64.81; H, 8.68; N, 6.10.

3-(Dimethylphenylsilyl)butanoic Acid Ethyl Ester (27).[13,42] **27** was obtained from the reaction of *trans*-butenoic acid ethyl ester with Li[Me_2PhSiCuI] in THF as solvent. The crude product was purified with flash chromatography (5% ether in pentane; R_f 0.35) to give a 95% (128 mg) yield of **27** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.49 (m, Ar-*H*, 2H), 7.39−7.34 (m, Ar-*H*, 3H), 4.09 (q, OCH_2CH$_3$, J = 7.2 Hz, 2H), 2.39 (dd, α-CH_2, J = 15.1, 4.0 Hz, 1H), 2.06 (dd, α-CH_2, J = 15.1, 11.2 Hz, 1H), 1.46 (m, C*H*Si, 1H), 1.24 (t,

OCH_2CH_3, J = 7.2 Hz, 3H), 0.99 (d, $CHCH_3$, J = 7.3 Hz, 3H), 0.30 (s, $Si(CH_3)_2$, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 137.6, 134.2 (2C), 129.3, 128.0 (2C), 60.4, 37.1, 16.7, 14.7, 14.5, −4.8, −5.1; FTIR (film, cm^{-1}) 2956, 1732, 1251, 701; MS *m/z* 250 (M^+, 7%), 235 (M − CH_3, 57%), 205 (M − OCH_2CH_3, 100%), 173 (M − C_6H_5, 65%), 135 (M − $C_6H_{11}O_2$, 50%), 105 (12%), 75 (26%).

3-(Methyldiphenylsilyl)butanoic Acid Ethyl Ester (28). 28 was obtained from the reaction of *trans*-butenoic acid ethyl ester with Li[$MePh_2SiCuI$] in dimethyl sulfide as solvent. The crude product was purified with flash chromatograpy (5% ether in pentane; R_f 0.30) to give a 70% (98 mg) yield of **28** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.58−7.54 (m, Ar-*H*, 4H), 7.43−7.35 (m, Ar-*H*, 6H), 4.09 (q, OCH_2CH_3, J = 7.2 Hz, 2H), 2.49 (dd, α-CH_2, J = 15.3, 3.4 Hz, 1H), 2.12 (dd, α-CH_2C, J = 15.3, 11.6 Hz, 1H), 1.93 (m, C*H*Si, 1H), 1.24 (t, OCH_2CH_3, J = 7.2 Hz, 3H), 1.06 (d, CH_3CHSi, J = 7.3 Hz, 3H), 0.58 (s, $SiCH_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 135.7, 135.6, 135.04 (2C), 135.02 (2C), 129.59, 129.56, 128.13 (2C), 128.12 (2C), 60.5, 37.2, 15.3, 14.9, 14.5, −6.3; FTIR (film, cm^{-1}) 3069, 2957, 1733, 1428, 1254, 1210, 1110, 700; MS *m/z* 312 (M^+, 3%), 297 (M − CH_3, 11%), 267 (M − C_2H_5O, 18%), 236 (M − C_6H_6, 100%), 197 (Ph_2MeSi, 12%); HRMS (EI, DCI/NH_3) calcd for $[C_{19}H_{28}NO_2Si]^+$ (M + H_4N^+) 330.1889, found 330.1893.

3-(Dimethylphenylsilyl)-3-phenylpropanoic Acid Methyl Ester (29).[13,43] **29** was obtained from the reaction of *trans*-3-phenylpropenoic acid methyl ester with Li[$Me_2PhSiCuI$] in THF as solvent. The crude product was purified with flash chromatography (10% ether in pentane; R_f 0.60) to give a 91% (133 mg) yield of **29** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.45−7.33 (m, Ar-*H*, 5H), 7.24−7.19 (m, Ar-*H*, 2H), 7.14−7.09 (m, Ar-*H*, 1H), 7.00−6.95 (m, Ar-*H*, 2H), 3.49 (s, OCH_3, 3H), 2.88 (dd, C*H*Si, J = 11.1, 4.9 Hz, 1H), 2.78 (dd, α-CH_2, J = 15.8, 11.1 Hz, 1H), 2.67 (dd, α-CH_2, J = 15.8, 4.9 Hz, 1H), 0.28, 0.24 (2s, $Si(CH_3)_2$, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 142.0, 136.7, 134.3 (2C), 129.5, 128.3 (2C), 127.9 (2C), 127.7 (2C), 125.2, 51.6, 35.0, 32.5, −3.9, −5.3; FTIR (film, cm^{-1}) 3024, 2953, 1732, 1252, 835; MS *m/z* 298 (M^+, 78%), 283 (M − CH_3, 20%), 267 (M − OCH_3, 58%), 222 (18%), 208 (38%), 193 (39%), 135 (M − $C_{10}H_{11}O_2$, 87%), 104 (100%).

4-(Methyldiphenylsilyl)-4-phenyl-butan-2-one (30). 30 was obtained from the reaction of 4-phenyl-3-buten-2-one with Li[$MePh_2SiCuI$] in THF as solvent. The crude product was purified with flash chromatography (15% ether in pentane; R_f 0.40) to give an 85% (125 mg) yield of **30** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.55−6.90 (m, Ar-*H*, 15H), 3.37 (dd, C*H*Si, J = 11.4, 3.6 Hz, 1H), 2.99 (dd, α-CH_2, J = 16.9, 11.4 Hz, 1H), 2.77 (dd, α-CH_2, J = 16.9, 3.6 Hz, 1H), 1.95 (s, CH_3, 3H), 0.46 (s, $SiCH_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.0, 141.7, 135.5 (2C), 135.3, 135.1 (2C), 134.7, 129.8, 129.6, 128.34 (2C), 128.32 (2C), 128.1 (2C), 128.0 (2C), 125.3, 44.7, 30.4, 30.1, −5.2; FTIR (film, cm^{-1}) 3069, 3024, 2885, 1717, 1252, 790, 700; HRMS (EI) calcd for $[C_{23}H_{24}OSi]$ 344.1596, found 344.1608.

4-(Dimethylphenylsilyl)-4-methyl-pentan-2-one (31).[42] **31** was obtained from the reaction of 4-methyl-3-penten-2-one with Li[$Me_2PhSiCuI$] in dimethyl sulfide as solvent. The crude product was purified with flash chromatography (10% ether in pentane; R_f 0.70) to give a 81% (93 mg) yield of **31** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.53−7.49 (m, Ar−H, 2H), 7.40−7.34 (m, Ar-*H*, 3H), 2.30 (s, CH_2CO, 2H), 2.04 (s, $COCH_3$, 3H), 1.05 (s, $(CH_3)_2C$, 6H), 0.33 (s, $Si(CH_3)_2$, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.7, 137.2, 134.8 (2C), 129.2, 127.8 (2C), 51.3, 32.8, 23.5 (2C), 20.5, −5.5 (2C); FTIR (film, cm^{-1}) 2957, 2862, 1716, 1427, 1357, 1251, 815, 703; MS *m/z* 234 (M^+, 3%), 219 (M − CH_3, 100%), 157 (M − C_6H_5, 30%), 135 (M − $C_6H_{11}O$, 30%), 83 (C_6H_{11}, 50%).

3-(Dimethylphenylsilyl)-5-trimethylsilylpent-4-ynoic Acid Methyl Ester (33). 33 was obtained from a reaction of 5-trimethylsilyl-pent-2-ene-4-ynoic acid methyl ester (**32**)[44] with Li[$Me_2PhSiCuI$] in DMS as solvent. The crude product was purified with flash chromatography (2% ether in pentane; R_f 0.30) to give a 78% (122 mg) yield of **33** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.57−7.54 (m, Ar-*H*, 2H), 7.41−7.31 (m, Ar-*H*, 3H), 3.62 (s, OCH_3, 3H), 2.46−2.29 (m, $COCH_2$ and SiC*H*, "*partly overlap*", 3H), 0.41, 0.40 (2s, $Si(CH_3)_2$, 3H each), 0.12 (s, $Si(CH_3)_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 135.7, 134.1, 129.6, 127.8, 107.4, 86.0, 51.6, 34.7, 17.7, 0.19, −4.5, −5.4; FTIR (film, cm^{-1}) 2957, 2160, 1743, 1250, 842; HRMS (EI) calcd for $[C_{17}H_{26}O_2Si_2]$ 318.1471, found 318.1477.

3-(Dimethylphenylsilyl)cyclopentanone (34).[13,45] **34** was obtained from the reaction of 2-cyclopenten-1-one with Li[$Me_2PhSiCuI$] in THF as solvent. The crude product was purified with flash chromatography (30% ether in pentane; R_f 0.50) to give a 99% (106 mg) yield of **34** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.53−7.50 (m, Ar-*H*, 2H), 7.41−7.35 (m, Ar-*H*, 3H), 2.32−2.19 (m, CH_2, 2H), 2.17−2.06 (m, CH_2, 2H), 1.91 (dd, CH_2, J = 18.1, 13.1 Hz, 1H), 1.75−1.62 (m, CH_2, 1H), 1.61−1.51 (m, C*H*Si, 1H), 0.34 (s, $Si(CH_3)_2$, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 221.0, 137.2, 134.0(2C), 129.5, 128.1(2C), 40.3, 39.5, 25.2, 24.2, −4.7, −4.8; FTIR (film, cm^{-1}) 3458, 3069, 2957, 1736, 1251, 700; MS *m/z* 217 (M^+ − H, 5%), 203 (M − CH_3, 2%), 135 (M − C_5H_7O, 30%), 67 (C_5H_7, 100%).

3-(Dimethylphenylsilyl)-3-methylcyclopentanone (35).[42] **35** was obtained from the reaction of 3-methyl-2-cyclopenten-1-one with Li[$Me_2PhSiCuI$] in dimethyl sulfide as solvent. The crude product was purified with flash chromatography (15% ether in pentane; R_f 0.40) to give a 85% (97 mg) yield of **35** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.53−7.50 (m, Ar-*H*, 2H), 7.41−7.35 (m, Ar-*H*, 3H), 2.32−2.18 (2m, CH_2, each 1H), 2.11−1.98 (m, CH_2, 2H), 1.90 (d, CH_2, J = 18.0 Hz, 1H), 1.72−1.65 (m, CH_2, 1H), 1.04 (s, CCH_3, 3H), 0.36, 0.35 (2s, $Si(CH_3)_2$, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.8, 136.3, 134.3 (2C), 129.4, 127.9 (2C), 48.3, 35.2, 31.1, 25.6, 22.1, −5.99, −6.05; FTIR (film, cm^{-1}) 2955, 1740, 1427, 1251, 854, 702; MS *m/z* 232 (M^+, 2%), 231 (M − H, 12%), 217 (M − CH_3, 30%), 154 (M − C_6H_6, 12%), 135 (M − C_6H_9O, 30%), 83 (C_6H_{11}, 50%).

3-(Dimethylphenylsilyl)-3-methylcyclohexanone (36).[42] **36** was obtained from the reaction of 3-methyl-2-cyclohexen-1-one with Li[$Me_2PhSiCuI$] in dimethyl sulfide as solvent. The crude product was purified with flash chromatography (15% ether in pentane; R_f 0.40) to give a 88% (106 mg) yield of **36** as a clear oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.52−7.48 (m, Ar-*H*, 2H), 7.42−7.35 (m, Ar-*H*, 3H), 2.36 (d, α-CH_2, J = 13.4 Hz, 1H), 2.31−2.25 (2m, α′-CH_2, 1H), 2.24−2.16 (ddd, α′-CH_2, J = 13.9, 7.0, 1.0 Hz, 1H), 2.01−1.89 (2m, *partly hidden*, CH_2, 2H), 2.00 (d, *partly hidden*, α-CH_2, J = 13.4 Hz, 1H), 1.76 (ddd, CH_2, J = 13.5, 12.3, 4.4 Hz, 1H), 1.52 (2m, CH_2, 1H), 0.94 (s, CCH_3, 3H), 0.33 (2s, $Si(CH_3)_2$, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.3, 136.1, 134.8 (2C), 129.5, 128.0 (2C), 48.5, 41.8, 31.0, 26.5, 23.1, 19.1, −6.36, −6.43; FTIR (film, cm^{-1}) 2954, 1709, 1427, 1252, 816, 703; MS *m/z* 246 (M^+, 2%), 245 (M − H, 10%), 231 (M − CH_3, 100%), 135 (M − $C_7H_{10}O$, 85%), 95 (C_7H_{11}, 50%).

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Supporting Information Available: General and chemical information plus copies of ^1H and ^{13}C NMR spectra of compounds **1**−**2**, **4**−**11**, **18**−**31**, and **33**−**36**. This material is available free of charge via the Internet at http://pubs.acs.org.

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