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Article

Enantioselective Addition-Alkylation of α,β-Unsaturated Carbonyls via Bisguanidinium Silicate Ion Pair Catalysis

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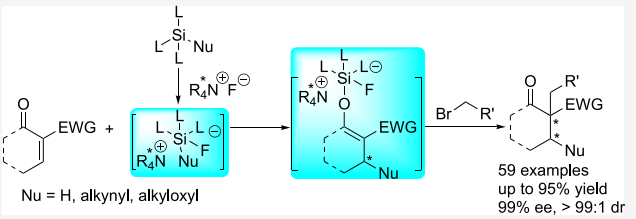
ABSTRACT: Silicon hydrides, alkynylsilanes, and alkoxylsilanes were activated by fluoride in the presence of bisguanidinium catalyst to form hypervalent silicate ion pairs. These activated silicates undergo 1,4-additions with chromones, coumarins, and α-cyanocinnamic esters generating enolsilicate intermediates, for a consequent stereoselective alkylation reaction. The reduction-alkylation reaction proceeded under mild conditions using polymethylhydrosiloxane, a cheap and environmentally friendly hydride source. The addition-alkylation reactions with alkynylsilanes and alkoxylsilanes resulted in the construction of two vicinal chiral carbon centers with excellent enantioselectivities and diastereoselectivities (up to 99% ee, >99:1 dr). Density functional theory calculations and experimental NMR studies revealed that penta-coordinated silicates are crucial intermediates.



INTRODUCTION

Penta- and hexacoordinated hypervalent silicates are known to be crucial intermediates in chiral Lewis base catalyzed stereoselective reactions.[1] Neutral organosilanes are also known to be activated by fluoride for the reduction of carbonyl compounds.[2a−c] In 1997, Kagan and co-worker reported the use of a monolithium salt of (*R*)-binaphthol as an activator of trimethoxysilane for the reduction of ketones.[2d] *N*-Formylproline derivatives[2e] and dilithium salt of histidine[2f] were reported as promoters as well. In addition, enantioselective reduction of imines[2g,h] as well as phosphine-catalyzed conjugate reduction of α,β-unsaturated ketones or β-enamino esters using trichlorosilane as the hydride source were also reported (Figure 1a).[3a−f] As silyl enol ethers were formed during the reduction of α,β-unsaturated ketones, enantioselective tandem reduction-aldol reaction have been developed (Figure 1a).[3c,4a,b] Despite such advances and the tremendous amount of chemistry relating to silyl enol ether, the generation of this useful intermediate by reduction with hydrides and further reaction have not been fully explored.

Phase transfer and ion-pairing catalysis, in which chiral cations work synergistically with anions, were reported for many enantioselective transformations.[5] We have previously reported enantioselective reactions using dicationic bisguanidinium **BG** (Table 1) to direct various metal-centered anions.[6] We have also proposed bisguanidinium hypervalent silicates as key intermediates in enantioselective alkylations using silyamides (Figure 1b)[6d] and enantioselective 1,2-anionotropic rearrangement of acylsilanes (Figure 1c).[6e]

In this report, we demonstrate that silicon hydride can be activated with fluoride in the presence of bisguanidinium **BG** catalyst to form a hypervalent hydridosilicate ion pair (Figure 1d). This is followed by an enantioselective conjugate reduction of chromones, coumarins, or α-cyanocinnamic esters to generate a hypervalent enolsilicate intermediate, followed by a stereoselective alkylation reaction. Similarly, alkynylsilanes and alkoxylsilanes can also lead to the formation of hypervalent alkynylsilicate and alkoxylsilicate ion pairs. The addition-alkylation with alkynylsilanes and alkoxylsilanes resulted in the construction of two vicinal chiral carbon centers with excellent enantioselectivities and diastereoselectivities.

RESULTS AND DISCUSSION

Enantioselective Reduction-Alkylation of Chromones. Asymmetric phase-transfer alkylation of β-keto esters is an attractive approach to obtain chiral quaternary carbon centers. Because of its low pK_a, it is difficult to avoid background reactions.[7] A tandem reduction-alkylation is a useful strategy to circumvent this difficulty. Conjugate reduction-alkylation of α,β-unsaturated aldehydes with alcohols was reported using chiral secondary amines through enamine, iminium, and acid pathways.[8a] Another reduction-alkylation route through Cu-catalyzed conjugate reduction and Pd-catalyzed arylation led to α-arylated cycloalkanones.[8b] Using 4-oxochroman-3- carbonitrile **1a** as a model, we

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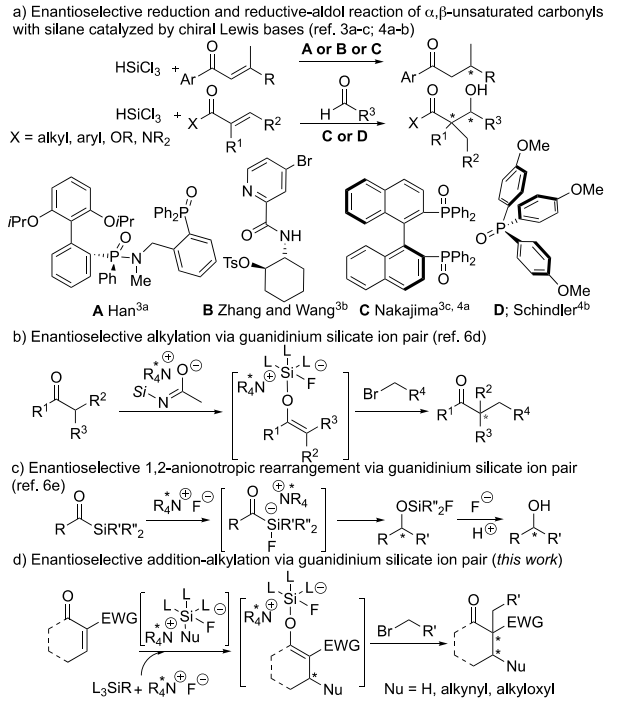
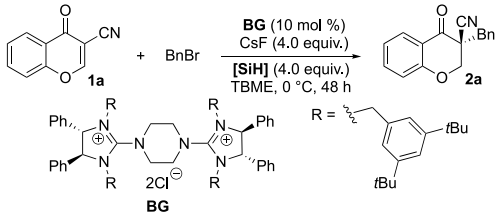


Figure 1. Stereoselective reactions with hypervalent silicate as intermediates.

Table 1. Optimization of Reaction Conditions[a]



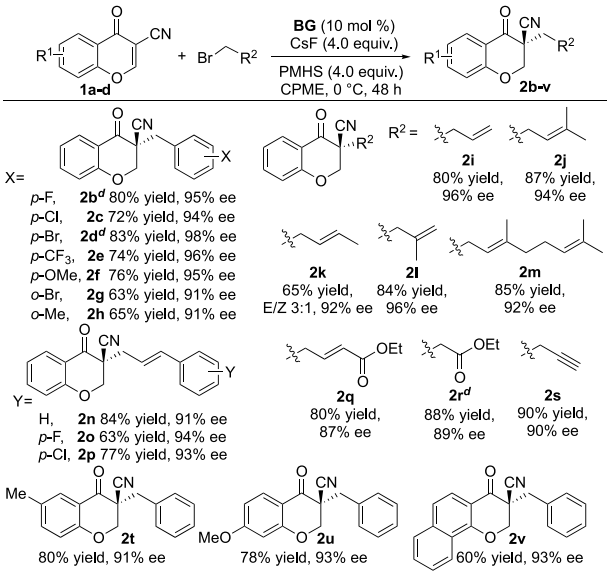
entry	[SiH]	yield[b]	ee[c]
1	$PhSiH_3$	24	75
2	$PhMeSiH_2$	30	78
3	Ph_3SiH	75	76
4	Ph_2MeSiH	68	90
5	$PhMe_2SiH$	41	96
6	Et_3SiH	10	97
7	$(MeO)_3SiH$	77	89
8	$(EtO)_3SiH$	60	60
9	$(EtO)_2MeSiH$	50	67
10	$(EtO)Me_2SiH$	trace	
11	PMHS	76	90
12[d]	PMHS	84	98

[a]Reaction was conducted with **1a** (0.1 mmol, 1.0 equiv), BnBr (0.4 mmol, 4.0 equiv) in 0.5 mL of *tert*-butyl methyl ether (TBME) in the presence of 10 mol % **BG** at 0 °C for 48 h. [b]Isolated yields. [c]Determined by HPLC analysis on a chiral stationary phase. [d]Cyclopentyl methyl ether (CPME) was used as solvent.

investigated our approach with a variety of silanes (Table 1, entries 1−10).

We found that both trisubstituted arylsilane and trisubstituted trialkoxylsilane furnished good yields and enantioselectivities (entries 3 and 7). We were delighted to find that polymethylhydrosiloxane (PMHS), which is an attractive reagent because of its low price, stability against air and moisture, and easy handling,[2c] can also provide the reduced chromone **2a** with excellent results (entries 11 and 12). With suitable conditions in hand, we next investigated the substrate scope of the reduction-alkylation using different chromones **1a−1d** (Scheme 1). Benzyl bromides, bearing both electron-

Scheme 1. Reduction-Alkylation of Chromones[a,b,c]



[a]Reaction was carried out with **1a−1d** (0.1 mmol), electrophile (0.4 mmol), PMHS (0.4 mmol), CsF (0.4 mmol), and catalyst **BG** (10 mol %) in 0.5 mL of CPME at 0 °C for 48 h. [b]Unless otherwise noted, yields are isolated yields. [c]ee was determined by HPLC analysis on a chiral stationary phase. [d]Absolute configuration was determined by X-ray analysis.

withdrawing and electron-donating groups, delivered the desired products **2b−2h** in good yields and excellent enantioselectivities. We further examined different electrophiles **2i−2s** and found that different activated bromides, including allylic-, propargylic-, and ester-substituted ones gave good results. Different chromones were also investigated and good yields and excellent enantioselectivities were obtained: **2t−2v**. Remarkably, changing the aryl group to a naphthalene ring also provided reduced chromone **2v** with satisfactory results.

Enantioselective Reduction-Alkylation of Coumarins. Dihydrocoumarin compounds have attracted much attention because of their desirable biological activities. Generation of an α-quaternary carbon center of hydrocoumarins is nontrivial and there are few known examples of catalytic enantioselective synthesis.[9a−d,6d] Using similar conditions developed previously (Scheme 1), we found that coumarins **3a−3d** underwent reduction-alkylation smoothly with various bromides to give the corresponding products with good yields and excellent enantioselectivities (Scheme 2).

We found that it was necessary to change the fluoride source from cesium fluoride to potassium fluoride for the enantioselectivities to be satisfactory (Scheme 2, **4a**). Residual moisture in the salts was unlikely the cause for the difference since they were both dried rigorously. In fact, the addition of 1 equiv of water only moderately affected the yield and enantioselectivity of the reaction.

Enantioselective Addition-Alkylation Using Alkynylsilanes and Alkoxylsilanes. With the success of reduction-

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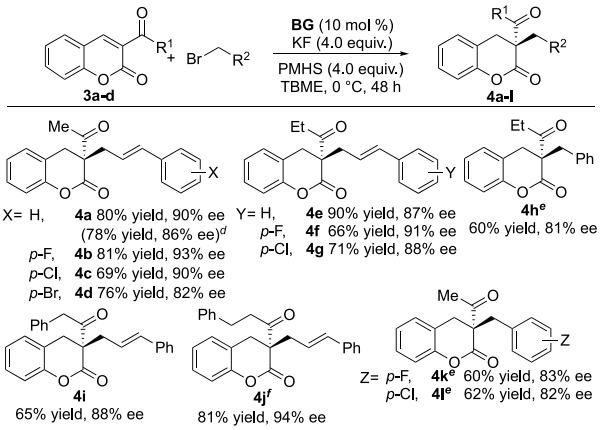
Scheme 2. Reduction-Alkylation of Coumarins[a,b,c]

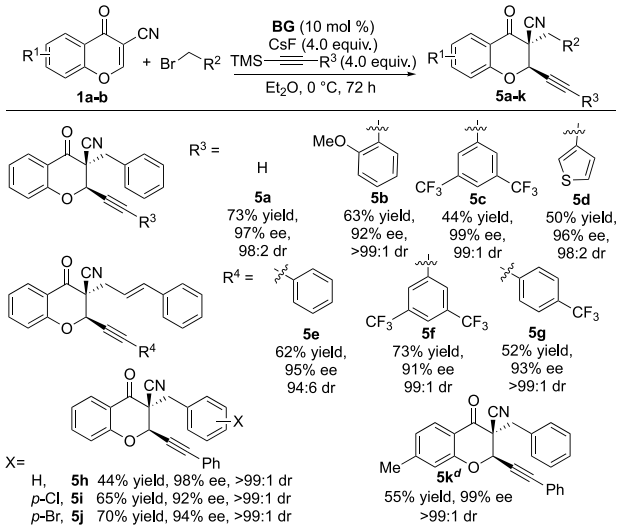


[a]Reaction was carried out with **3a−3d** (0.1 mmol), electrophile (0.4 mmol), PMHS (0.4 mmol), KF (0.40 mmol), and catalyst **BG** (10 mol %) in 0.5 mL of TBME at 0 °C for 48 h. [b]Unless otherwise noted, yields are isolated yields. [c]ee was determined by HPLC analysis on a chiral stationary phase. [d]Using CsF as the fluoride source. [e]Reaction was carried out with **3** (0.1 mmol), electrophile (0.3 mmol), PMHS (0.3 mmol), KF (0.3 mmol), and catalyst **BG** (10 mol %) in 0.5 mL of iPr$_2$O at 0 °C for 48 h. [f]Absolute configuration was determined by X-ray analysis.

alkylation, we then investigated if other functional groups can be added in place of hydride.[10a,b] We tested alkynylsilanes and found that the addition-alkylation proceeded well for chromones **1a** and **1b**, and following alkylation, two vicinal chiral carbon centers were constructed with excellent enantioselectivities and diastereoselectivities (Scheme 3).

However, because of the lower reactivity of alkynylsilanes, only moderate yields were obtained. Terminal alkynylsilane

Scheme 3. Addition-Alkylation of Chromones Using Alkynylsilanes[a,b,c]

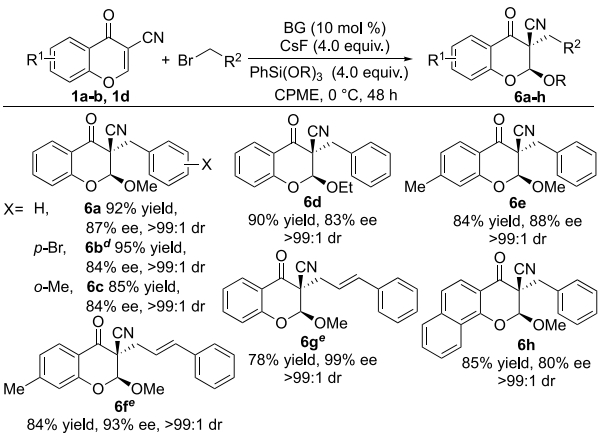


[a]The reaction was carried out with **1a** and **1b** (0.1 mmol), electrophile (0.4 mmol), (trimethylsilyl)ethynyl compound (0.4 mmol), CsF (0.4 mol), and catalyst **BG** (10 mol %) in 0.5 mL of Et$_2$O at 0 °C for 72 h. [b]Unless otherwise noted, yields are isolated total yields. [c]ee was determined by HPLC analysis on a chiral stationary phase. [d]Absolute configuration was determined by X-ray analysis.

also worked well with decent results for alkynylchromone **5a** (73% yield, 97% ee, >99:1 dr). Cinnamyl bromide was also able to furnish alkynylchromones (**5e−5g**) with good results.

Alkyoxylsilanes, on the other hand, reacted smoothly with high reactivities and high yields were achieved (Scheme 4).

Scheme 4. Addition-Alkylation of Chromones Using Alkoxylsilanes[a,b,c]

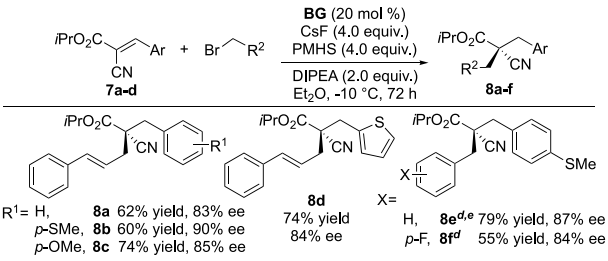


[a]Reaction was carried out with **1a** and **1b** or **1d** (0.1 mmol), electrophile (0.4 mmol), trialkyloxy(phenyl)silane (0.4 mmol), CsF (0.4 mol), and catalyst **BG** (10 mol %) in 0.5 mL of CPME at 0 °C for 48 h. [b]Unless otherwise noted, yields are isolated total yields. [c]ee was determined by HPLC analysis on a chiral stationary phase. [d]Absolute configuration was determined by X-ray analysis. [e]Using iPr$_2$O as solvent.

The transfer of the alkyoxyl group from alkoxylsilanes[11a−c] also resulted in the construction of two vicinal chiral carbon centers with high yields, good enantioselectivities, and excellent diastereoselectivities for chromones **6a−6h**. Changing trimethoxylsilane to triethoxylsilane did not affect the profile of the alkoxylated chromones **6a** and **6d** significantly.

Enantioselective Reduction-Alkylation of α-Cyanocinnamic Esters. The scope of our reduction-alkylation reaction was further extended to include linear substrate such as α-cyanocinnamic esters (Scheme 5).[12a,b] These esters, **7a−7d**, furnished enantioenriched reduction-alkylation adducts

Scheme 5. Reduction-Alkylation of α-Cyanocinnamic Esters[a,b,c]



[a]Reaction was carried out with **7a−7d** (0.05 mmol), electrophile (0.2 mmol), PMHS (0.2 mmol), CsF (0.2 mol), *N*,*N*-diisopropylethylamine (DIPEA) (0.1 mmol), and catalyst **BG** (20 mol %) in 1.0 mL of Et$_2$O at −10 °C for 72 h. [b]Unless otherwise noted, yields are isolated total yields. [c]ee was determined by HPLC analysis on a chiral stationary phase. [d]Using nBu$_2$O as solvent. [e]Absolute configuration determination was determined using free acid of **8e** (Supporting Information, p S37).

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8a−8f containing a highly functionalized quaternary carbon center, which is important for the preparation of biologically active compounds.[13] Remarkably, a thiophene-containing acrylate was able to add to cinnamyl bromide without affecting both the yield and the enantioselectivity (**8d** 74% yield, 84% ee). The addition of amine such as DIPEA accelerated the reaction, allowing the reaction temperature to be lowered without impacting the enantioselectivity of the adducts (see the Supporting Information, pp S6−S8, for more information). At this moment, we are unsure of the role played by these additives.

Identification of Reaction Intermediates. In 2007, McGrady and Steed reported the hypervalent silicate complexes of $[K([18]crown\text{-}6)]^+$ salt with $[Ph_3SiF_2]^-$ and $[(p\text{-}FC_6H_4)_3Si(F)H]^-$, which were characterized by NMR spectroscopy and X-ray diffraction.[14] We attempted but were unable to obtain any suitable crystals for X-ray studies. We thus decided to study the hypervalent silicate species using ^{19}F NMR. According to known data (see the Supporting Information, p S6, for more details), changing the counterion does not influence the ^{19}F NMR chemical shifts of the hypervalent silicates significantly. Hence, the ^{19}F NMR chemical shifts of ammonium silicates can be used to predict the chemical shifts of the bisguanidinium silicate intermediates.

We first use ^{19}F NMR to study the hypervalent silicates generated using tetrabutylammonium fluoride (TBAF) (see the Supporting Information, pp S9−S14, for more details). Density functional theory calculations using the gauge independent atomic orbital method were performed to predict the ^{19}F NMR shifts of possible intermediates produced for comparison with the experimental data (see the Supporting Information, pp S17−S31, for more details). We started with a training set consisting of ten fluorinated molecules and improved it by subsequent addition of experimental results. The geometries of the electronic structures for configurational isomers of each compound were also taken into consideration. The ^{19}F NMR spectrum of a mixture of TBAF and Ph_3SiH showed one new peak at δ −98.3 ppm (Table 2), which is fairly consistent with our calculated NMR shift for $TBA^+[Ph_3SiFH]^-$ (δ −95.5 ppm). The mixture of TBAF and alkynylsilanes showed messy signals in the ^{19}F NMR spectrum; hence, calculations were not done. The mixture of TBAF and $PhSi(OMe)_3$ showed one new peak at δ −115.7 ppm, which is consistent with our calculated NMR shift for $TBA^+[PhSi(OMe)_3F]^-$ (δ −113.1 ppm). In addition, the ^1H NMR spectrum of the mixture of TBAF and Ph_3SiH in deuterated chloroform showed a peak at δ 5.57 ppm, which is consistent with our calculated NMR shift for Si−H in $TBA^+[Ph_3SiFH]^-$ (δ 5.90 ppm). Using these data, we were able to propose that the crucial intermediates observed in the experiments using bisguanidinium **BG** are pentacoordinated hypervalent silicate ion pairs.

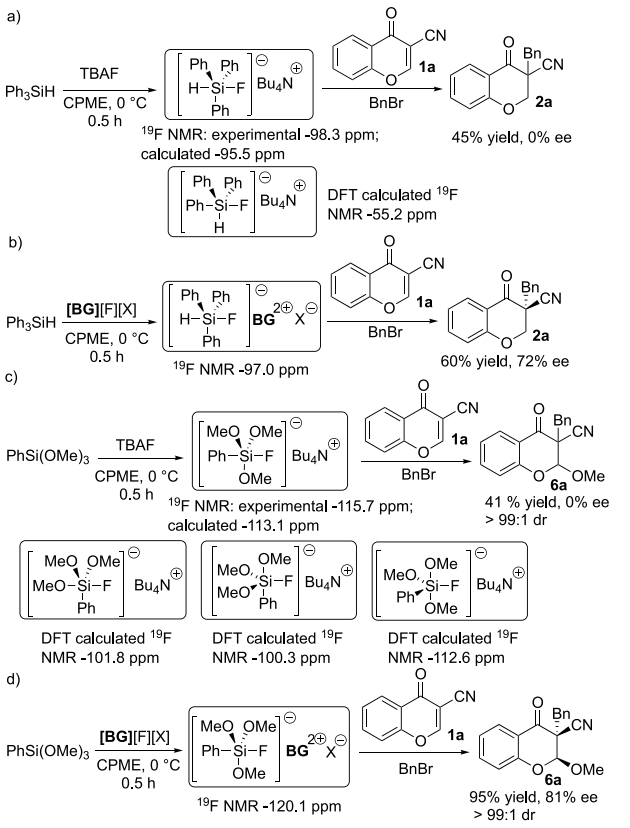
Table 2. Experimental and DFT Predicted ^{19}F NMR of Hypervalent Silicates[a]

hypervalent silicates	experimental ^{19}F NMR (ppm)	DFT predicted ^{19}F NMR (ppm)
TBA^+ $[Ph_3SiFH]^-$	−98.3	−95.5
$\mathbf{BG}^{2+}$ $[Ph_3SiFH]^-[X]^-$	−97.0	
$TBA^+[PhSi(OMe)_3F]^-$	−115.7	−113.1
$\mathbf{BG}^{2+}[PhSi(OMe)_3F]^-[X]^-$	−120.1	

[a]X = F, Cl, or hypervalent silicate.

We wanted to "catch" the bisguanidinium hypervalent silicate intermediates "in the act". First, we changed the sequence of the addition of reagents (cf. Table 1); we generate the hypervalent silicate through the addition of the fluoride source to Ph_3SiH or $PhSi(OMe)_3$ at the onset of the experiments (Scheme 6); this is followed by chromone **1a**

Scheme 6. Identification of Hypervalent Silicate Intermediates



and, last, benzyl bromide. Following the addition of the fluoride source to Ph_3SiH, the experiments can be interrupted and ^{19}F NMR measured (Scheme 6a,b). In both experiments, using TBAF and [**BG**][F][X], ^{19}F NMR observed the pentacoordinated hypervalent silicate described above (Table 2). When the experiments were resumed, reduced chromone **3a** was obtained in moderate yields with good enantioselectivity observed only in the experiment using [**BG**][F][X] (see the Supporting Information, p S6, for the preparation method). Similarly, when the fluoride source was added to $PhSi(OMe)_3$, the experiments can be interrupted and ^{19}F NMR measured (Scheme 6c,d). As before, only in the experiment using [**BG**][F][X] gave chromone **6a** with enantioselectivity. Using a combination of DFT calculation and experimental results, we also proposed that the apical positions in $\mathbf{BG}^+[PhSi(OMe)_3F]^-[X]^-$ are occupied by the Ph and F groups (Scheme 6d).

CONCLUSIONS

We have developed bisguanidinium **BG**-catalyzed enantioselective reduction-alkylation and addition-alkylation reactions. Silicon hydrides, alkynylsilanes, and alkoxylsilanes were

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activated with fluoride in the presence of bisguanidinium **BG** catalyst to form hypervalent silicate ion pairs. These activated silicates then underwent 1,4-additions to chromones, coumarins, and α-cyanocinnamic esters, generating enolsilicate intermediates, followed by stereoselective alkylation. The reductive-alkylation reaction proceeded under mild conditions with polymethylhydrosiloxane, a cheap and environmentally friendly hydride source. The addition-alkylation reactions with alkynylsilanes and alkoxylsilanes resulted in the construction of two vicinal chiral carbon centers with excellent enantioselectivities and diasteroselectivities. DFT calculations and experimental NMR studies revealed that pentacoordinated silicates are crucial intermediates.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.0c00183.

Experimental details and characterization data (PDF)
Compound **2b** (CIF)
Compound **2d** (CIF)
Compound **2r** (CIF)
Compound **4f** (CIF)
Compound **5k** (CIF)
Compound **6b** (CIF)
Free acid of compound **8e** (CIF)

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#W.C. and E.C.X.A. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. Reactivity of Penta- and Hexacoordinate Silicon Compounds and Their Role as Reaction Intermediates. *Chem. Rev.* **1993**, *93*, 1371−1448. (b) Benaglia, M.; Guizzetti, S.; Pignataro, L. Stereoselective Reactions Involving Hypervalent Silicate Complexes. *Coord. Chem. Rev.* **2008**, *252*, 492−512. (c) Furin, G. G.; Vyazankina, O. A.; Gostevsky, B. A.; Vyazankin, N. S. Synthetic Aspects of the Use of Organosilicon Compounds Under Nucleophilic Catalysis Conditions. *Tetrahedron* **1988**, *44*, 2675−2749.

(2) (a) Boyer, J.; Corriu, R. J. P.; Perz, R.; Reye, C. Reduction Selective De Composes Carbonyles Par Catalyse Heterogene a La Surface Des Sels. *Tetrahedron* **1981**, *37*, 2165−2171. (b) Corriu, R. J. P.; Perz, R.; Reye, C. Activation of Silicon-Hydrogen, Silicon-Oxygen, Silicon-Nitrogen Bonds in Heterogeneous Phase. *Tetrahedron* **1983**, *39*, 999−1009. (c) Kobayashi, Y.; Takahisa, E.; Nakano, M.; Watatani, K. Reduction of Carbonyl Compounds by Using Polymethylhydrosiloxane: Reactivity and Selectivity. *Tetrahedron* **1997**, *53*, 1627−1634. (d) Schiffers, R.; Kagan, H. B. *Synlett* Asymmetric Catalytic Reduction of Ketones with Hypervalent Trialkoxysilanes. *Synlett* **1997**, *1997*, 1175−1178. (e) Iwasaki, F.; Onomura, O.; Mishima, K.; Maki, T.; Matsumura, Y. Catalytic Activation of Trichlorosilane for Efficient and Stereoselective Reduction of Ketones. *Tetrahedron Lett.* **1999**, *40*, 7507−7511. (f) LaRonde, F. J.; Brook, M. A. Stereoselective Reduction of Ketones by Histidine-Alkoxysilane Complexes: The Role of Imidazole in Nucleophilic Substitution at Silicon. *Tetrahedron Lett.* **1999**, *40*, 3507−3510. (g) Nishikori, H.; Yoshihara, R.; Hosomi, A. Optically Active Lithium-Alkoxide Catalyzed Asymmetric Reduction of Imines with Trimethoxyhydrosilane. *Synlett* **2003**, *4*, 0561−0563. (h) Malkov, A. V.; Mariani, A.; MacDougall, K. N.; Kocovsky, P. Role of Noncovalent Interactions in the Enantioselective Reduction of Aromatic Ketimines with Trichlorosilane. *Org. Lett.* **2004**, *6*, 2253−2256.

(3) (a) Han, Z. S.; Zhang, L.; Xu, Y.; Sieber, J. D.; Marsini, M. A.; Li, Z.; Reeves, J. T.; Fandrick, K. R.; Patel, N. D.; Desrosiers, J. N.; Qu, B.; Chen, A.; Rudzinski, D. M.; Samankumara, L. P.; Ma, S.; Grinberg, N.; Roschangar, F.; Yee, N. K.; Wang, G.; Song, J. J.; Senanayake, C. H. Efficient Asymmetric Synthesis of Structurally Diverse P-Stereogenic Phosphinamides for Catalyst Design. *Angew. Chem., Int. Ed.* **2015**, *54*, 5474−5477. (b) Yang, H.; Weng, G.; Fang, D.; Peng, C.; Zhang, Y.; Zhang, X.; Wang, Z. Enantioselective Conjugate Hydrosilylation of α,β-unsaturated Ketones. *RSC Adv.* **2019**, *9*, 11627−11633. (c) Sugiura, M.; Sato, N.; Kotani, S.; Nakajima, M. Lewis Base-Catalyzed Conjugate Reduction and Reductive Aldol Reaction of α,β-Unsaturated Ketones Using Trichlorosilane. *Chem. Commun.* **2008**, 4309−4311. (d) Sugiura, M.; Ashikari, Y.; Takahashi, Y.; Yamaguchi, K.; Kotani, S.; Nakajima, M. Lewis Base-Catalyzed Enantioselective Conjugate Reduction of β,β-Disubstituted α,β-Unsaturated Ketones with Trichlorosilane: E/Z-Isomerization,

Regioselectivity, and Synthetic Applications. *J. Org. Chem.* **2019**, *84*, 11458−11473. (e) Jiang, Y.; Chen, X.; Zheng, Y.; Xue, Z.; Shu, C.; Yuan, W.; Zhang, X. Highly Diastereoselective and Enantioselective Synthesis of α-Hydroxy β-Amino Acid Derivatives: Lewis Base Catalyzed Hydrosilylation of α-Acetoxy β-Enamino Esters. *Angew. Chem., Int. Ed.* **2011**, *50*, 7304−7307. (f) Ye, J.; Wang, C.; Chen, L.; Wu, X.; Zhou, L.; Sun, J. Chiral Lewis Base-Catalyzed, Enantioselective Reduction of Unprotected β-Enamino Esters with Trichlorosilane. *Adv. Synth. Catal.* **2016**, *358*, 1042−1047.

(4) (a) Sugiura, M.; Sato, N.; Sonoda, Y.; Kotani, S.; Nakajima, M. Diastereo- and Enantioselective Reductive Aldol Reaction with Trichlorosilane Using Chiral Lewis Bases as Organocatalysts. *Chem. - Asian J.* **2010**, *5*, 478−481. (b) DePorre, Y. C.; Annand, J. R.; Bar, S.; Schindler, C. S. Lewis-Base-Catalyzed Reductive Aldol Reaction to Access Quaternary Carbons. *Org. Lett.* **2018**, *20*, 2580−2584.

(5) (a) Hashimoto, T.; Maruoka, K. Recent Development and Application of Chiral Phase-Transfer Catalysts. *Chem. Rev.* **2007**, *107*, 5656−5682. (b) Mahlau, M.; List, B. Asymmetric Counteranion-Directed Catalysis: Concept, Definition, and Applications. *Angew. Chem., Int. Ed.* **2013**, *52*, 518−533. (c) Brak, K.; Jacobsen, E. N. Asymmetric Ion-Pairing Catalysis. *Angew. Chem., Int. Ed.* **2013**, *52*, 534−561. (d) Shirakawa, S.; Maruoka, K. Recent Developments in Asymmetric Phase-Transfer Reactions. *Angew. Chem., Int. Ed.* **2013**, *52*, 4312−4348.

(6) (a) Wang, C.; Zong, L.; Tan, C.-H. Enantioselective Oxidation of Alkenes with Potassium Permanganate Catalyzed by Chiral Dicationic Bisguanidinium. *J. Am. Chem. Soc.* **2015**, *137*, 10677−10682. (b) Ye, X.; Moeljadi, A. M. P.; Chin, K. F.; Hirao, H.; Zong, L.; Tan, C.-H. Enantioselective Sulfoxidation Catalyzed by a Bisguanidinium Diphosphatobisperoxotungstate Ion Pair. *Angew. Chem., Int. Ed.* **2016**, *55*, 7101−7105. (c) Zong, L.; Wang, C.; Moeljadi, A. M. P.; Ye, X.; Ganguly, R.; Li, Y.; Hirao, H.; Tan, C.-H. Bisguanidinium Dinuclear Oxodiperoxomolybdosulfate Ion Pair-Catalyzed Enantioselective Sulfoxidation. *Nat. Commun.* **2016**, *7*, 13455. (d) Teng, B.; Chen, W.; Dong, S.; Kee, C. W.; Gandamana, D. A.; Zong, L.; Tan, C.-H. Pentanidium- and Bisguanidinium-Catalyzed Enantioselective Alkylations Using Silylamide as Brønsted Probase. *J. Am. Chem. Soc.* **2016**, *138*, 9935−9940. (e) Cao, W.; Tan, D.; Lee, R.; Tan, C.-H. Enantioselective 1,2-Anionotropic Rearrangement of Acylsilane through a Bisguanidinium Silicate Ion Pair. *J. Am. Chem. Soc.* **2018**, *140* (5), 1952−1955. (f) Zong, L.; Tan, C.-H. Phase-Transfer and Ion-Pairing Catalysis of Pentanidiums and Bisguanidiniums. *Acc. Chem. Res.* **2017**, *50*, 842−856.

(7) Park, E. J.; Kim, M. H.; Kim, D. Y. J. Enantioselective Alkylation of α-Keto Esters by Phase-Transfer Catalysis Using Chiral Quaternary Ammonium Salts. *J. Org. Chem.* **2004**, *69*, 6897−6899.

(8) (a) Xiang, S.; Zhang, B.; Zhang, Li; Cui, Y.; Jiao, N. The Versatile Roles of Ammonium Salt Catalysts in Enantioselective Reduction and Alkylation of α,β-Unsaturated Aldehydes: Iminium Catalysis, Enamine Catalysis and Acid Catalysis. *Chem. Commun.* **2011**, *47*, 5007−5009. (b) Chae, J.; Yun, J.; Buchwald, S. L. One-Pot Sequential Cu-Catalyzed Reduction and Pd-Catalyzed Arylation of Silyl Enol Ethers. *Org. Lett.* **2004**, *6* (26), 4809−4812.

(9) (a) Alexakis, A.; Bäckvall, J.; Krause, N.; Pàmies, O.; Diéguez, M. Enantioselective Copper-Catalyzed Conjugate Addition and Allylic Substitution Reactions. *Chem. Rev.* **2008**, *108*, 2796−2823. (b) Murakata, M.; Jono, T.; Mizuno, Y.; Hoshino, O. Construction of Chiral Quaternary Carbon Centers by Catalytic Enantioselective Radical-Mediated Allylation of α-Iodolactones Using Allyltributyltin in the Presence of a Chiral Lewis Acid. *J. Am. Chem. Soc.* **1997**, *119*, 11713−11714. (c) Hardman-Baldwin, A.; Visco, M.; Wieting, J.; Stern, C.; Kondo, S.; Mattson, A. Silanediol-Catalyzed Chromonenone Functionalization. *Org. Lett.* **2016**, *18*, 3766−3769. (d) Kitanosono, T.; Zhu, L.; Liu, C.; Xu, P.; Kobayashi, S. An Insoluble Copper(II) Acetylacetonate−Chiral Bipyridine Complex that Catalyzes Asymmetric Silyl Conjugate Addition in Water. *J. Am. Chem. Soc.* **2015**, *137*, 15422−15425.

(10) (a) DeRatt, L.; Pappoppula, M.; Aponick, A. A Facile Enantioselective Alkynylation of Chromones. *Angew. Chem., Int. Ed.* **2019**, *58*, 8416−8420. (b) Guan, Y.; Attard, J.; Mattson, A. Copper Bis(Oxazoline)-Catalyzed Enantioselective Alkynylation of Benzopyrylium Ions. *Chem. - Eur. J.* **2020**, *26*, 1742−1747.

(11) (a) Nakamura, H.; Sekido, M.; Ito, M.; Yamamoto, Y. Palladium-Catalyzed Alkoxyllylation of Activated Olefins. *J. Am. Chem. Soc.* **1998**, *120*, 6838−6839. (b) Patil, N.; Huo, Z.; Yamamoto, Y. Palladium Catalyzed Three Component Coupling Reaction Between Chromones, Alcohols, and Allylic Acetates: Diversity-Oriented Synthesis of Highly Substituted Chromones. *Tetrahedron* **2007**, *63*, 5954−5961. (c) Dieskau, A.; Holzwarth, M.; Plietker, B. Fe-Catalyzed Multicomponent Reactions: The Regioselective Alkoxy Allylation of Activated Olefins and its Application in Sequential Fe Catalysis. *Chem. - Eur. J.* **2012**, *18*, 2423−2429.

(12) (a) Nagata, K.; Sano, D.; Itoh, T. Catalytic Asymmetric Alkylation of α-Cyanocarboxylates Using a Phase-Transfer Catalyst. *Synlett* **2007**, *2007*, 0547−0550. (b) Nagata, K.; Sano, D.; Shimizu, Y.; Miyazaki, M.; Kanemitsu, T.; Itoh, T. Catalytic Asymmetric Alkylation of α-Cyanocarboxylates and Acetoacetates Using a Phase-Transfer Catalyst. *Tetrahedron: Asymmetry* **2009**, *20*, 2530−2536.

(13) Christoffers, J.; Baro, A. Stereoselective Construction of Quaternary Stereocenters. *Adv. Synth. Catal.* **2005**, *347*, 1473−1482.

(14) Prince, P. D.; Bearpark, M. J.; McGrady, G. S.; Steed, J. W. Hypervalent Hydridosilicates: Synthesis, Structure and Hydride Bridging. *Dalton Trans.* **2008**, *2*, 271−282.

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