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# Crystal Structure and Solution State Characterization of Lithium (*S*)-(1-(Bis(2-methoxyethyl)amino)-3-methylbutan-2-yl)(methyl)amide

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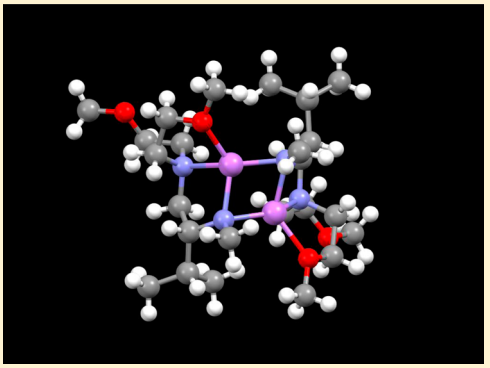
Supporting Information

**ABSTRACT:** The solid state structure of lithiated (*S*)-$N^1$,$N^1$-bis(2-methoxyethyl)-$N^2$,3-dimethylbutane-1,2-diamine, which is a chiral amide base synthesized from (*S*)-valine was determined by single-crystal X-ray diffraction. The complex in solution state is also characterized by a variety of NMR experiments including diffusion-ordered NMR spectroscopy (DOSY) with diffusion coefficient-formula weight correlation analyses and other one- and two-dimensional NMR techniques by dissolving the crystal in toluene-$d_8$. The crystallography and NMR results suggest that the chiral amide is dimeric in both solid and solution states.



Organolithium reagents are among the most widely used reagents in the synthesis of organic compounds.[1] Non-nucleophilic organolithium amide bases such as lithium diisopropylamide and lithium hexamethyldisilazide have long been widely employed in the deprotonation of various organic compounds.[1c,d,2] Chiral lithium amide bases were also developed for asymmetric addition and deprotonation.[3] Moreover, chiral lithium amide bases can also be used in catalytic dynamic resolution in enantioselective synthesis.[4] Owing to the versatility and stereoselectivity of chiral lithium amides, they have been studied by several groups for more than 20 years.[3,5] Many studies revealed that the reactivity and stereoselectivity of lithium amides highly depend on the aggregation state of the amides.[6] Therefore, aggregation state determination of chiral lithium amides is critical in understanding, choosing, and designing chiral amines.

In an attempt to generate an internally solvated chiral lithium amide, (*S*)-$N^1$,$N^1$-bis(2-methoxyethyl)-$N^2$,3-dimethyl-butane-1,2-diamine (**1**) was synthesized from Boc-protected (*S*)-valine in two steps (Scheme 1). Bis(2-methoxyethyl)amine was chosen to be incorporated into the ligand because of its extensive use in internally solvating the lithium atom in several organolithium compounds.[7] Upon reaction of chiral amine **1** with n-BuLi as outlined in Scheme 1, we expected to generate either monomeric lithium amide **2** or dimeric lithium amide **3** with a $Li_2N_2$ core, which is the representative dimer for (*S*)-valine derived chiral lithium amide.[5a,e,8] In lieu of obtaining either **2** or **3**, we crystallized and characterized a dimeric aggregate **4** portrayed in Scheme 1 and Figure 1. The dimer **4** adopts a ladder-type structure, which is similar to the structure of lithiated (*S*)-*N*-isopropyl-*O*-triisopropylsilylvalinol in hydrocarbon solvent that our group characterized two years ago.[5e] Despite the fact that the crystal was grown in a solution containing a significant amount of diethyl ether or THF, there was no ether or even THF coordinating the dimer in the crystal structure. Moreover, only one oxygen from the bis(2-methoxyethyl)amine is chelated to a lithium atom as shown in Figure 1.

Characterization of lithiated amine **1** in the solution state was also conducted through application of various one- and two-dimensional NMR techniques on the solution of the crystal dissolved in toluene-$d_8$. The sample can be prepared either by dissolving dry crystals of lithium amide **4** that had been washed by anhydrous pentane twice in toluene-$d_8$ or by adding a stoichiometric amount of *n*-butyllithium into the solution of chiral amine **1** in toluene-$d_8$. The spectra produced are nearly the same except that there are some large heptane peaks (from the *n*-Bu$^6$Li solution) when the latter method is used.

A series of $^1$H and $^{13}$C NMR experiments including $^1$H NMR, $^{13}$C NMR, COSY, HSQC, and HMBC were carried out in order to assign the $^1$H and $^{13}$C signals. The result is summarized in Table 1.

$^6$Li NMR was then used to determine the number of different lithium atoms present. The fact that there is only one sharp peak at −50 °C indicates that only one kind of lithium exists and is consistent with monomeric amide **2** and dimeric amide **4** but not dimeric amide **3** (Figure 2).

DOSY techniques were then used to determine the formula weight of the lithiated complex and hence the aggregation state. We first applied DOSY NMR with internal references for the

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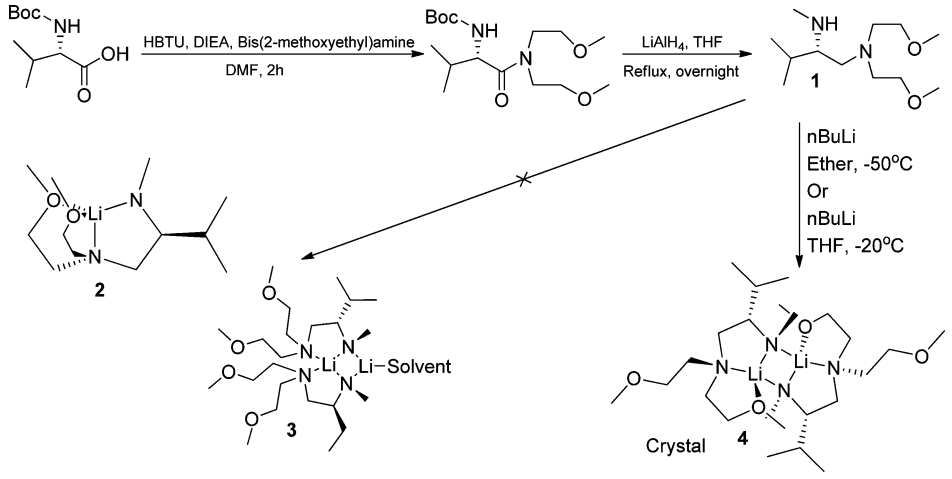
**Scheme 1. Synthesis and Crystallization of Lithium Amide 1**



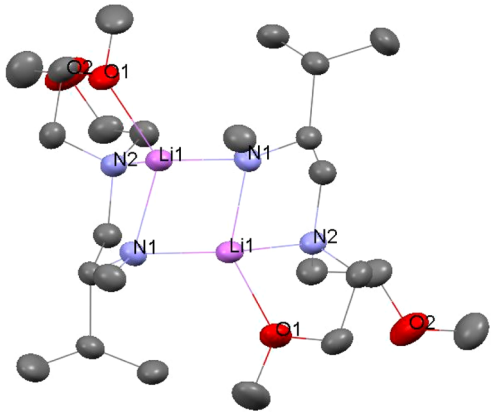
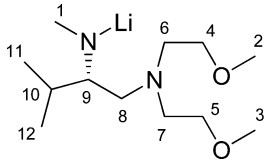




**Figure 1.** Crystal structure of lithiated (*S*)-$N^1$,$N^1$-bis(2-methoxyethyl)-$N^2$,3-dimethylbutane-1,2-diamine, **4**. Thermal ellipsoid plots are at the 50% probability level. Hydrogen atoms have been omitted for clarity.

**Table 1. $^1$H and $^{13}$C Signal Assignments of Lithiated Amine 1**




| carbon atom | $^{13}$C | $^1$H |
|---|---|---|
| 1 | 44.0 | 3.37 |
| 2 | 59.3 | 3.04 |
| 3 | 58.9 | 2.98 |
| 4 | 69.5 | 3.02, 2.63 |
| 5 | 68.9 | 3.31, 3.10 |
| 6 | 57.2 | 2.68, 2.28 |
| 7 | 54.1 | 3.00, 2.73 |
| 8 | 48.1 | 2.92, 2.08 |
| 9 | 70.6 | 2.96 |
| 10 | 26.3 | 2.60 |
| 11 | 16.2 | 0.97 |
| 12 | 15.1 | 1.20 |

determination of formula weights of reactive complexes by *D*–FW correlation analysis. A linear regression plot of the logarithms of NMR determined diffusion coefficients against

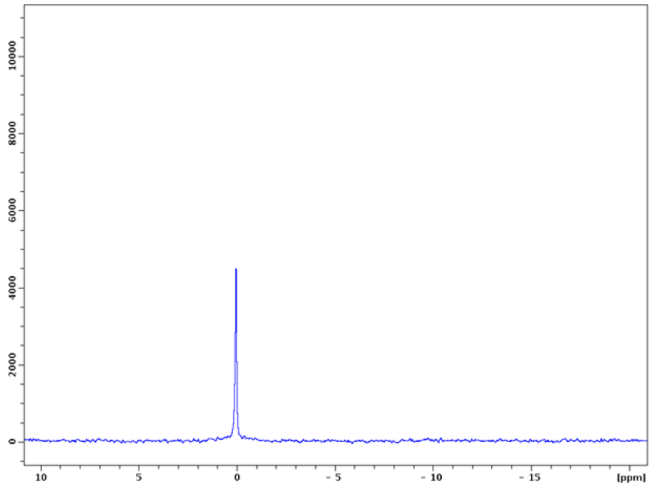



**Figure 2.** $^6$Li NMR of [$^6$Li] Amide **1**.

the known formula weights of the references is used to deduce the formula weight of an unknown complex from its diffusion coefficient.[5e,f,6f,9] In this proton DOSY, benzene (BEN, 78.11 g/mol), cyclooctene (COE, 110.2 g/mol), 1-tetradecene (TDE, 196.4 g/mol), and squalene (SQU, 410.7 g/mol) were added to the sample solution as our internal references.

After the addition of internal references, the signals of lithiated amine **1** from 1.0 to 2.5 ppm were overlapped with the signals from the internal references; thus, distinct peaks from 2.5 to 7.2 ppm were picked for our D-FW analysis. As seen in the DOSY spectrum (Figure 3), distinct peaks from lithiated amine **1** have very similar diffusion coefficients.

The correlation between log FW and log *D* of the linear regression is high ($r^2$ > 0.99), and the average predicted formula weight for the resonances of lithiated amine **1** is 483.8 g/mol, which is very close to unsolvated dimer **4** of 476.6 g/mol (Figure 4, Table 2). Despite the fact that monomer **2** is consistent with our $^6$Li NMR, our DOSY result showed that lithiated amine **1** in the solution state cannot be monomer **2**, which has a formula weight of only 238.3 g/mol and a 103% difference from the result. The possibility of a THF solvated monomer, which has a formula weight of 310.4 g/mol, can also be ruled out because of the 55.9% difference between the predicted and the actual formula weight. Another possible structure that is consistent with the $^6$Li NMR result is the THF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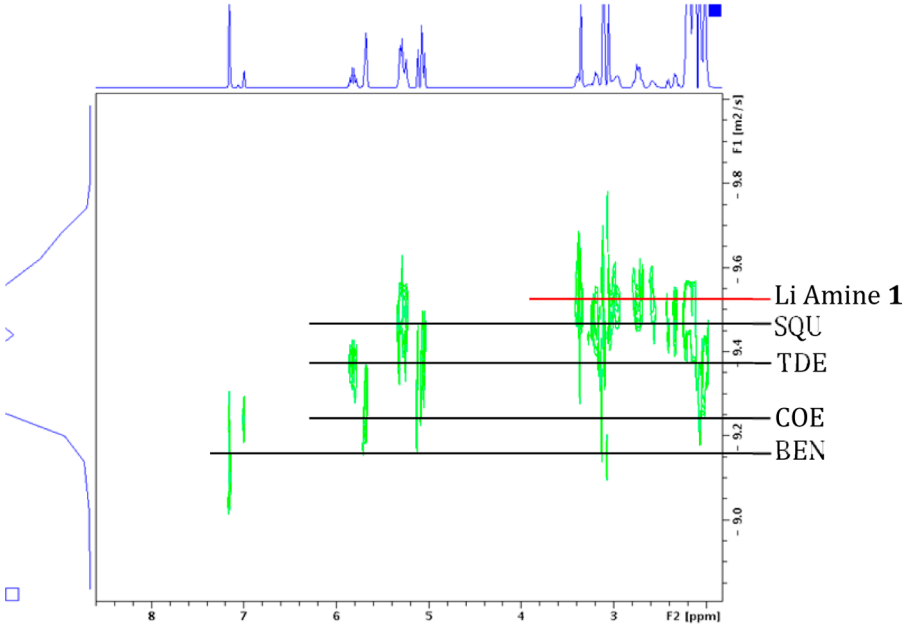


**Figure 3.** $^{1}$H DOSY of lithiated amine **1**.

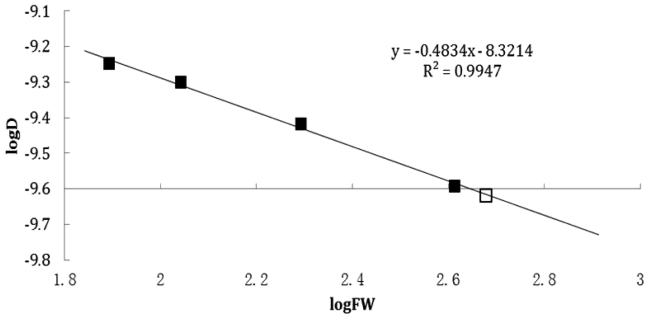


**Figure 4.** *D*−FW analysis of $^{1}$H DOSY data. Internal references are shown as solid squares and lithiated amine **1** is shown as open square.

**Table 2. *D*−FW Analysis of $^{1}$H DOSY Data**

| entry | compd | FW (g/mol) | $10^{-10}D$ ($m^2/s$) | predicted FW (g/mol) | % error |
|---|---|---|---|---|---|
| 1 | BEN | 78.11 | 5.661 | 82.26 | −5.3 |
| 2 | COE | 110.2 | 4.997 | 106.5 | 3.4 |
| 3 | TDE | 196.4 | 3.818 | 185.8 | 5.4 |
| 4 | SQU | 410.7 | 2.555 | 426.6 | −3.9 |
| 5 | Li-**1**[a] | 476.6[b] | 2.370 | 498.3 | −4.6 |
| 6 | Li-**1**[a] | 476.6[b] | 2.378 | 494.9 | −3.8 |
| 7 | Li-**1**[a] | 476.6[b] | 2.451 | 464.9 | 2.5 |
| 8 | Li-**1**[a] | 476.6[b] | 2.418 | 478.1 | −0.3 |
| 9[c] | Li-**1**[a] | 476.6[b] | 2.404 | 483.7 | −1.5 |
| standard dev. of predicted FW of Li-**1** | | | | 15.5 | 3.3 |
| 10 | Li-**1**[a] | 238.3[d] | 2.404 | 483.7 | −103 |
| 11 | Li-**1**[a] | 310.4[e] | 2.404 | 483.7 | −55.9 |
| 12 | Li-**1**[a] | 620.8[f] | 2.404 | 483.7 | 22.0 |

[a]Li-**1** represents lithiated amine **1** in Tol-$d_8$. [b]476.6 g/mol is the formula weight of unsolvated dimer **4**. [c]The average of the above four diffusion coefficients. [d]238.3 g/mol is the formula weight of unsolvated monomer **2**. [e]310.4 g/mol is the formula weight of a THF solvated monomer. [f]620.8 g/mol is the formula weight of a THF solvated dimer with 2 THF.

disolvated dimer; however, the disolvated dimer has a formula weight of 620.8 g/mol, which is a 22.0% difference from our predicted formula weight. Therefore, only a symmetric unsolvated dimer is consistent with our $^{6}$Li and DOSY NMR results.

In summary, a single crystal of lithium (*S*)-(1-(bis(2-methoxyethyl)amino)-3-methylbutan-2-yl)(methyl)amide can be easily grown in both pentane−ether and pentane−THF solution. The crystal structure is a symmetric dimer shown in Figure 1. The solution state study was carried out by various one- and two-dimensional NMR techniques. The $^{6}$Li NMR result revealed that only one kind of lithium exists and ruled out the possibility of dimer **3**. After assigning the $^{1}$H and $^{13}$C signals, $^{1}$H DOSY was run to evaluate the formula weight of the lithiated amine **1** in toluene-$d_8$, and the result of *D*−FW analysis suggested that lithium amine **1** existed as a unsolvated dimer in toluene-$d_8$. With the crystallography and NMR data, we have definitive evidence that dimeric lithium amide **4** exists in both solid and solution states.

## EXPERIMENTAL SECTION

**Synthesis of (*S*)-*N*$^1$,*N*$^1$-Bis(2-methoxyethyl)-*N*$^2$,3-dimethylbutane-1,2-diamine (1).** To a solution of Boc-L-valine (3.00 g, 13.8 mmol) dissolved in 50 mL of anhydrous dimethyl-formamide and *N*,*N*-diisopropylethylamine (3.57 g, 27.6 mmol) under $N_2$ atmosphere was added *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (7.80 g, 20.6 mmol) all at once. After stirring at room temperature for 15 min, bis(2-methoxyethyl)amine (2.02 g, 15.2 mmol) was added dropwise, and the reaction mixture was allowed to stir for 2 h before quenching with 80 mL of 1 N HCl solution. The mixture was extracted with EtOAc (3 × 80 mL) three times, and the combined organic phase was washed with 1 N HCl (3 × 25 mL) three times and 40 mL of brine and dried over $Na_2SO_4$. The solvent was first removed by rotary evaporation and then by oil pump yielding a reddish brown viscous liquid. The liquid was used in the next step without further purification.

To a solution of the previous obtained liquid dissolved in 100 mL of anhydrous THF at 0 °C was slowly added lithium aluminum hydride (3.84 g, 101 mmol). After the addition, the reaction mixture was allowed to reflux overnight under $N_2$ atmosphere. The reaction mixture was then cooled to 0 °C and quenched carefully by adding 0.5


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N NaOH slowly upon stirring until all the salts appeared white. The solution was allowed to stir for 5 min before dying over $Na_2SO_4$. After sitting for 15 min, the reaction mixture was then filtered, and the white solid salts were washed with EtOAc (4 × 50 mL). The solvent of the filtered organic phase was removed by rotary evaporation and purification was performed by vacuum distillation. Purification (bp =116 °C, 3 mmHg) gave a colorless oil (1.71g, 7.36 mmol, 53.3%). $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.42 (dt, 4H, $J$ = 6.2, 2.4 Hz), 3.33 (s, 6H), 2.78−2.59 (m, 4H), 2.49−2.43 (m, 1H), 2.36 (s, 3H), 2.34−2.23 (m, 2H), 2.17−1.92 (br, 1H), 1.92−1.79 (m, 1H), 0.90 (d, 3H, $J$ = 7.0 Hz), 0.84 (d, 3H, $J$ = 7.0 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 71.2, 62.8, 58.7, 55.4, 54.6, 35.2, 27.9, 19.0, 16.9; HRMS-ESI with quadrupole mass analyzer, $m/z$ $[M + H]^+$ calcd for $C_{12}H_{29}N_2O_2$ 233.2229, found 233.2230.

**Synthesis of *n*-Bu$^6$Li.** The n-Bu$^6$Li solution was prepared in heptane according to the method that our group has published previously.[5e]

**Preparation of XRD Quality Crystals of Lithium (*S*)-(1-(Bis(2-methoxyethyl)amino)-3-methylbutan-2-yl)(methyl)-amide (4).** (I) To a solution of chiral amine **1** (0.10 g, 0.43 mmol) in 1 mL of pentane at 0 °C under Ar atmosphere was slowly added 1 equiv of *n*-BuLi. The reaction mixture was allowed to stir at 0 °C until white precipitates formed. Anhydrous diethyl ether was then added to the mixture until all the precipitates dissolved into the solution and the solution became clear. XRD quality crystals were grown when the solution was stored at −50 °C overnight. (II) To a solution of chiral amine **1** (0.10g, 0.43 mmol) in 1 mL of pentane at 0 °C under an Ar atmosphere was slowly added 1 equiv of n-BuLi. The reaction mixture was allowed to stir at 0 °C until white precipitates formed. Anhydrous tetrahydrofuran was then added to the mixture until all the precipitates dissolved into the solution and the solution became clear (the amount of tetrahydrofuran required is much less than that of diethyl ether). XRD quality crystals were grown over a few days when the solution was stored at a −20 °C freezer.

**Procedures for NMR Experiments.** NMR samples were prepared in tubes sealed with rubber septa caps and parafilm. NMR tubes were evacuated in vacuo, flame-dried, and filled with argon before use. NMR experiments were carried out at −40 °C except the characterization of chiral amine **1**, which was done at room temperature and referenced to $CDCl_3$. $^1$H chemical shifts were referenced to toluene-$d_8$ at 7.09 ppm and $^{13}$C chemical shifts were referenced to toluene-$d_8$ at 137.86 ppm. DOSY experiments were performed on a 400 MHz spectrometer equipped with a $z$-axis gradient amplifier and a probe with a $z$-axis gradient coil. Maximum gradient strength was 0.214 T/m. $^1$H DOSY was performed using the dstebpgp3s pulse program, using double stimulated echo and LED, with bipolar gradient pulses and three spoil gradients. Diffusion time was 200 ms, and rectangular gradient pulse duration was 900 $\mu$s. Gradient recovery delays were 900 $\mu$s. Individual rows of the quasi-2-D diffusion databases were phased and baseline corrected. Actual diffusion coefficients used for $D$−FW analysis were obtained using a T1/T2 analysis module.

The lithiated amine **1** samples can be prepared by dissolving dry crystals in toluene-$d_8$ or formed *in situ* by adding *n*-Bu$^6$Li into a toluene-$d_8$ solution of chiral amine **1**. Crystals were first prepared by the method described above except *n*-Bu$^6$Li was used instead. The crystals were kept at −78 °C in a cold bath immediately after removal from a −50 °C freezer, the solvent was removed by syringe, and the crystals were washed twice with anhydrous pentane. After the removal of solution by syringe, the crystals were then kept in a dry ice−acetonitrile bath and evacuated *in vacuo* for 1 h. Toluene-$d_8$ (0.60 mL) was then added to the crystals under an Ar atmosphere. The solution was allowed to stir at −40 °C for 20 min before being transferred into a sealed NMR tube via syringe. Alternatively, about 30 mg of chiral amine **1** was added via syringe into a sealed NMR tube. Toluene-$d_8$ (0.60 mL) was then added via syringe to the NMR tube. The solution was then kept in a −40 °C bath before the addition of 1 equiv of *n*-Bu$^6$Li solution. After the addition, the NMR tube was shaken vigorously and kept at −40 °C for 1 h before the signal acquisition. This latter method was not preferred overall since a significant amount of heptane is retained.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Supplemental NMR and crystallographic information. This material is available free of charge via the Internet at http://pubs.acs.org. CCDC 934643 contains supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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## ■ REFERENCES

(1) (a) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon: Oxford, 2002. (b) Hodgson, D. *Organo-lithiums in Enantionselective Synthesis*; Springer: New York, 2003. (c) Trost, B. M., Fleming, I., Eds. *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991. (d) Wu, G.; Huang, M. *Chem. Rev.* **2006**, *106*, 2596−2616.

(2) (a) Collum, D.; McNeil, A. J.; Ramirez, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3002−3017. (b) Lucht, B.; Collum, D. *Acc. Chem. Res.* **1999**, *32*, 1035−1042. (c) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879−933.

(3) (a) Whitesell, J. K.; Felman, S. W. *J. Org. Chem.* **1980**, *45*, 755−756. (b) Eleveld, M. B.; Hogeveen, H. *Tetrahedron Lett.* **1984**, *45*, 5187−5190. (c) Shirai, R.; Tanaka, M.; Koga, K. *J. Am. Chem. Soc.* **1986**, *108*, 543−545. (d) Cain, C. M.; Cousins, R. P. C.; Coumbarides, G.; Simpkins, N. S. *Tetrahedron* **1990**, *46*, 523−544. (e) Bhuniya, D.; DattaGupta, A.; Singh, V. K. *J. Org. Chem.* **1996**, *61*, 6108−6113. (f) Corruble, A.; Valnot, J.-Y.; Maddaluno, J.; Duhamel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1519−1523. (g) Simpkins, N. S.; Hume, S. C. *J. Org. Chem.* **1998**, *63*, 912−913. (h) Corruble, A.; Valnot, J.-Y.; Maddaluno, J.; Duhamel, P. *J. Org. Chem.* **1998**, *63*, 8266−8275. (i) Matsuo, J.; Odashima, K.; Kobayashi, S. *Org. Lett.* **1999**, *1*, 345−348. (j) Arvidsson, P. I.; Davidsson, O.; Hilmersson, G. *Tetrahedron: Asymmetry* **1999**, *10*, 527−534. (k) De Sousa, S. E.; O'Brien, P.; Pilgram, C. D. *Tetrahedron* **2002**, *58*, 4643−4654. (l) Flinois, K.; Yuan, Y.; Bastide, C.; Harrison-Marchand, A.; Maddaluno, J. *Tetrahedron* **2002**, *58*, 4707−4716. (m) Rodeschini, V.; Simpkins, N. S.; Wilson, C. *J. Org. Chem.* **2007**, *72*, 4265−4267. (n) Stivala, C. E.; Zakarian, A. *J. Am. Chem. Soc.* **2011**, *133*, 11936−11939.

(4) (a) Beng, T. K.; Gawley, R. E. *J. Am. Chem. Soc.* **2010**, *132*, 12216−12217. (b) Beng, T. K.; Tyree, W. S.; Parker, T.; Su, C.; Williard, P. G.; Gawley, R. E. . *J. Am. Chem. Soc.* **2012**, *134*, 16845−16855.

(5) (a) Hilmersson, G.; Davidsson, O. *J. Org. Chem.* **1995**, *60*, 7660−7669. (b) Williard, P. G.; Sun, C. *J. Am. Chem. Soc.* **1997**, *119*, 11693−11694. (c) Sott, R.; Granander, J.; Hilmersson, G. *J. Am. Chem. Soc.* **2004**, *126*, 6798−6805. (d) Li, D.; Sun, C.; Liu, J.; Hopson, R.; Li, W.; Williard, P. G. *J. Org. Chem.* **2008**, *73*, 2373−2381. (e) Kagan, G.; Li, W.; Li, D.; Hopson, R.; Williard, P. G. *J. Am. Chem. Soc.* **2011**, *133*, 6596−6602. (f) Oulyadi, H.; Fressigne, C.; Yuan, Y.; Maddaluno, J.; Harrison-Marchand, A. *Organometallics* **2012**, *31*, 4801−4809.

(6) (a) Sato, D.; Kawasaki, H.; Shimada, I.; Arata, Y.; Okamura, K.; Date, T.; Koga, K. . *J. Am. Chem. Soc.* **1992**, *114*, 761−763. (b) Arvidsson, P. I.; Hilmersson, G.; Ahlberg, P. *J. Am. Chem. Soc.* **1999**, *121*, 1883−1887. (c) Arvidsson, P. I.; Hilmersson, G.; Davidsson, O. *Chem.—Eur. J.* **1999**, *5*, 2348−2355. (d) Sott, R.; Granander, J.; Hilmersson, G. *Chem.—Eur. J.* **2002**, *8*, 2081−2087. (e) Pate, F.; Duguet, N.; Oulyadi, H.; Harrison-Marchand, A.; Fressigne, C.; Valnot, J.; Lasne, M.; Maddaluno, J. *J. Org. Chem.* **2007**,

72, 6982−6991. (f) Liu, J.; Li, D.; Sun, C.; Williard, P. G. *J. Org. Chem.* **2008**, *73*, 4045−4052. (g) Lecachey, B.; Duguet, N.; Oulyadi, H.; Fressigne, C.; Harrison-Marchand, A.; Yamamoto, Y.; Tomioka, K.; Maddaluno, J. *Org. Lett.* **2009**, *11*, 1907−1910.

(7) (a) Fraenkel, G.; Chen, X.; Gallucci, J.; Ren, Y. *J. Am. Chem. Soc.* **2008**, *130*, 4140−4145. (b) Fraenkel, G.; Chen, X.; Chow, A.; Gallucci, J.; Liu, H. *J. Org. Chem.* **2005**, *70*, 9131−9138. (c) Fraenkel, G.; Chow, A.; Fleischer, R.; Liu, H. *J. Am. Chem. Soc.* **2004**, *126*, 3983−3995. (d) Colquhoun, V. P.; Strohmann, C. *J. Chem. Soc., Dalton Trans.* **2012**, *41*, 1897−1902.

(8) (a) Granander, J.; Sott, R.; Hilmersson, G. *Chem.—Eur. J.* **2006**, *12*, 4191−4197. (b) Hilmersson, G.; Arvidsson, P. I.; Davidsson, O. *Organometallics* **1997**, *16*, 3352−3362. (c) Hilmersson, G. *Chem.—Eur. J.* **2000**, *6*, 3069−3075. (d) Sott, R.; Granander, J.; Williamson, C.; Hilmersson, G. *Chem.—Eur. J.* **2005**, *11*, 4785−4792.

(9) (a) Li, D.; Hopson, R.; Li, W.; Liu, J.; Williard, P. G. *Org. Lett.* **2008**, *10*, 909−911. (b) Li, D.; Sun, C.; Williard, P. G. *J. Am. Chem. Soc.* **2008**, *130*, 11726−11736. (c) Kagan, G.; Li, W.; Hopson, R.; Williard, P. G. *Org. Lett.* **2009**, *11*, 4818−4821. (d) Kagan, G.; Li, W.; Hopson, R.; Williard, P. G. *Org. Lett.* **2010**, *12*, 520−523. (e) Li, W.; Kagan, G.; Yang, H.; Cai, C.; Hopson, R.; Sweigart, D. A.; Williard, P. G. *Org. Lett.* **2010**, *12*, 2698−2701. (f) Lecachey, B.; Oulyadi, H.; Lameiras, P.; Harrison-Marchand, A.; Gerard, H.; Maddaluno, J. *J. Org. Chem.* **2010**, *75*, 5976−5983.