

Lewis Base-Catalyzed Reductive Aldol Reaction to Access Quaternary Carbons

Yvonne C. DePorre[†], James R. Annand[†], Sukanta Bar, and Corinna S. Schindler*

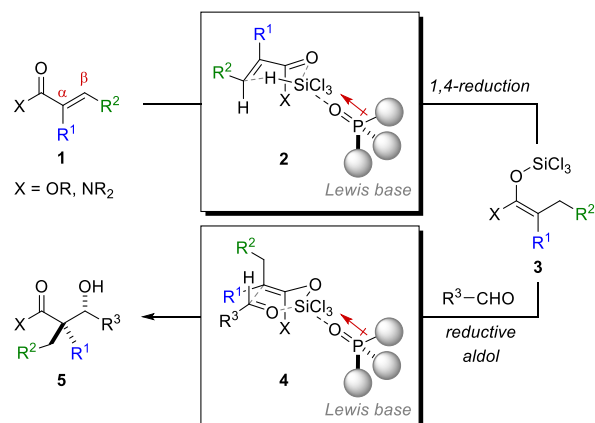
Department of Chemistry, Willard Henry Dow Laboratory, University of Michigan, 930 North University Ave., Ann Arbor, MI 48109, US

Abstract: A synthetic method for the efficient construction of β -hydroxy lactones and lactams bearing α -quaternary carbon centers is described. This transformation relies on an electronically differentiated Lewis base catalyst, which is uniquely capable of promoting a reductive aldol reaction of α,α -disubstituted and α,α,β -trisubstituted enones. This approach provides a valuable synthetic alternative for carbon-carbon bond formation in complex molecular settings due to its orthogonal reactivity compared to traditional aldol reactions. Based on this method described herein, lactones, lactams and morpholine amides bearing α -quaternary carbon centers are accessible in yields up to 85% and 50:1 d.r.

Toxicity is known to be the leading cause for drug candidates failing clinical trials.¹ Recent studies suggest that compounds of higher complexity, as measured by the saturation and presence of sp^3 -hybridized quaternary carbon centers, have fewer off-target effects, show less toxicity, and have a greater success rate in the clinic.² However, synthetic access to molecules with increased complexity requires successful methods for the construction of quaternary carbon centers.³ Despite recent advances, synthetic challenges in the formation of quaternary carbon centers still exist, and prove even more difficult when the desired quaternary carbons are chiral.^{3a} Additionally, quaternary carbon centers in acyclic molecules and molecular fragments remain challenging to access.^{3b,c, 4} Furthermore, most of the methods currently available for the construction of quaternary carbons rely on metal-based catalysts, and the development of alternative catalytic systems was recently described as a future challenge.^{3b} Here we describe a method for the diastereoselective construction of β -hydroxyl lactones and lactams bearing α -quaternary carbon centers that relies on simple, electronically differentiated phosphine oxides as Lewis base catalysts. The reported strategy enables access to structural motifs prevalent in many biologically relevant target structures.^{5, 6}

A synthesis project in our laboratory recently required operational access to complex lactones and lactams **5** bearing quaternary carbons from α,α,β -trisubstituted enones **1** (Figure 1A). A reductive aldol approach seemed particularly desirable, as it would permit a select Michael acceptor such as **1** to react in the presence of enolizable functional groups. Several successful protocols for transition metal-catalyzed reductive aldol reactions for α,β -unsaturated carbonyl compounds **6** have been described that rely on Rh,⁷ Ir,⁸ Cu,⁹ Co,¹⁰ Ru,¹¹ or Pd¹² in combination with boranes, silanes or hydrogen gas as suitable reductants.

A This work: Metal-free Reductive Aldol Reaction for α,α,β -Trisubstituted Enones.



reaction design: electronically differentiated Lewis base catalyzes 1,4-reduction and aldol reaction

B Literature precedent: Enones for intermolecular reductive aldol reactions.

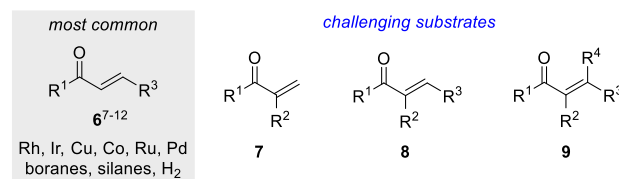


Figure 1. Lewis base catalyzed reductive aldol reaction.

Unfortunately, methods for converting α,α -disubstituted (**7**),¹³ or α,α,β -tri- (**8**)¹⁴ and tetra- (**9**) substituted enones to the reductive aldol products bearing α -quaternary carbons are less common (Figure 1B).¹⁵ An inherent challenge to enones **7-9** relates to the identification of potent catalyst systems that 1) exhibit high levels of chemoselectivity for 1,4-reduction, 2) activate both the resulting enolate nucleophile and aldehyde electrophile for aldol addition while 3) minimizing competing

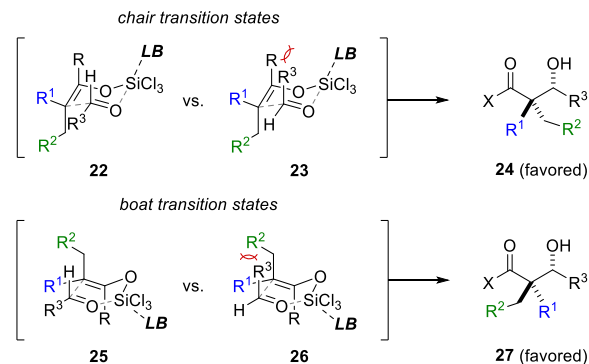
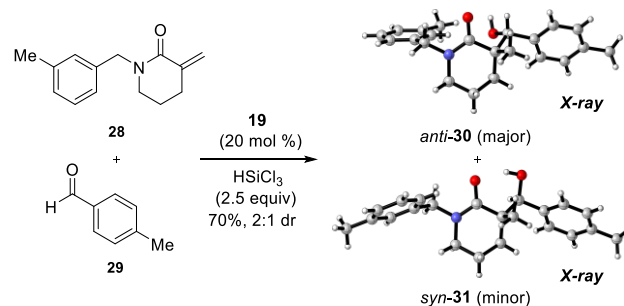
Table 1. Catalyst evaluation for the synthesis of 11.

entry	R	yield (%)	entry	R	yield (%)
1		43	6		39
2		45	7		37
3		0	8		71
4		49	9		20: R = H 18
5		23	10		21: R = OMe 9

Conditions: Reactions were ran in 0.25 M DCM at 30 °C for 48 hours with 1.2 equivalents of benzaldehyde.

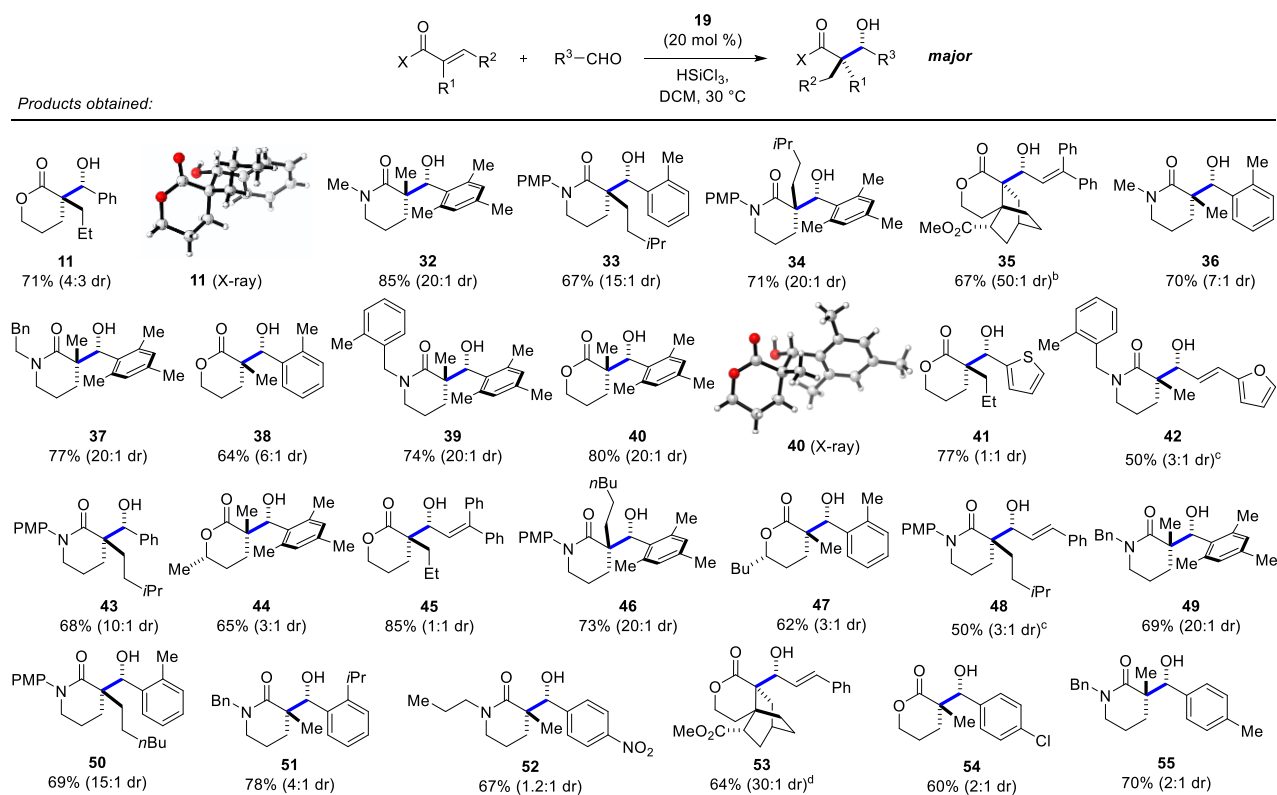
reduction of the aldehyde electrophile. Denmark's pioneering work has established Lewis bases as a powerful class of catalysts capable of enhancing enolate nucleophilicity in asymmetric aldol reactions.¹⁶ Recently, Nakajima has shown that Lewis bases, such as triphenyl phosphine oxide (TPPO) (**12**) and hexamethyl phosphoramide (HMPA) (**13**), are able to promote reductive aldol reactions of α,β -disubstituted enones **6**, though α,α -disubstituted (**7**) and α,α,β -trisubstituted (**8**) enones still remain elusive as substrates.¹⁷ We postulated that the reactivity of these Lewis base catalysts can be tuned to the specific electronic and steric requirements inherent to highly functionalized enones **7-9**, to enable both *in situ* conjugate reduction and activation of the resulting enolate for a subsequent aldol reaction. Aryl phosphine oxide derivatives seemed particularly desirable Lewis bases, as they allow for facile electronic differentiation of the aryl substituents to probe our hypothesis. Our initial studies with lactone **10**, bearing an exocyclic Michael acceptor, benzaldehyde as an electrophile and TPPO (**12**) or HMPA (**13**) as Lewis base catalyst with HSiCl_3 as the reductant, proved promising and resulted in the formation of the reductive aldol product **11** in 43% and 45% yield, respectively (entries 1 and 2, Table 1). Although both catalysts produced **11** in similar yields, the reaction profiles differed. Unreacted starting material (**10**) was recovered when employing TPPO (**12**), but **10** was consumed with HMPA (**13**), forming both 1,4-reduced lactone and benzyl alcohol as side products. These results suggest that HMPA is a potent catalyst for initial conjugate reduction but is too sterically encumbering to fully promote subsequent aldol addition. In comparison, TPPO is not Lewis basic enough to complete the initial conjugate reduction reaction thus resulting in the reisolation of starting material **10**. Attempts to use the HMPA analogs **14** and **15** to decrease steric bulk in the aldol addition resulted in either no reaction or no improved yield of the desired reductive aldol product **11** (entries 3 and 4, Table 1). As a result, subsequent catalyst optimization centered on electronic differentiation of triaryl phosphine oxides to increase their reactivity in the initial 1,4-reduction. Lewis bases **16**, **20** and **21**, bearing electron-donating substituents in the *ortho*-position, formed lactone **11** in low yields most likely due to

the increased steric bulk compared to TPPO (**12**) (entries 5, 9-10, Table 1). *Para*-methyl triarylphosphine oxide **17** showed a reaction profile similar to Lewis base **12** and resulted in the formation of **11** in 39% yield together with reisolated starting material (entry 6, Table 1). In comparison, the corresponding Lewis base **18** bearing a dimethylamine moiety in the *para*-position showed low solubility in dichloromethane and resulted in diminished yields of **11** (entry 7, Table 1). However, *para*-methoxy triarylphosphine **19** led to formation of product **11** in 71% yield with minor competing reduction (entry 8, Table 1) and was identified as the optimal Lewis base catalyst. Subsequent reaction optimization focused on the silane reductant. It was found that 2.5 equivalents of trichlorosilane were optimal, while increased amounts resulted in diminished yields of the desired reductive aldol products due to competing reduction side-products. Additionally, 20 mol% catalyst loadings proved superior with minimal reduction of the aldehyde electrophile (<10%), while stoichiometric quantities of Lewis base **19** resulted in diminished yields of **11** in 28%. Notably, the diastereomeric ratio of aldol product **11** remained constant despite changes in catalyst loading.¹⁸

A Possible chair and boat transition states in the reductive aldol reaction**B** Major and minor diastereomer obtained in the reductive aldol reaction**Figure 2.** Transition state models for aldol addition of enolate **3**.

Transition state models similar to those proposed by Denmark for phosphoramidate-catalyzed aldol reactions of pre-formed trichlorosilyl enolates can justify the stereochemical outcome observed in the reductive aldol reaction.¹⁹ Stereochemical models are consistent with a boat transition state **25** resulting in the major diastereomer **27** with both CH_2R^2 and hydroxyl substituent being *anti* to one another. The minor diastereomer with CH_2R^2 and hydroxyl group being *syn* to one another could be formed via the less favorable boat transition state **26** or by a chair transition state **22** (Figure 2A). The relative configuration of both diastereomeric products of lactam **28** and toluanal **29** was confirmed using x-ray analysis to result in the formation of lactam *anti*-**30** as the major

Scheme 1. Substrate scope for lactones and lactams.^a

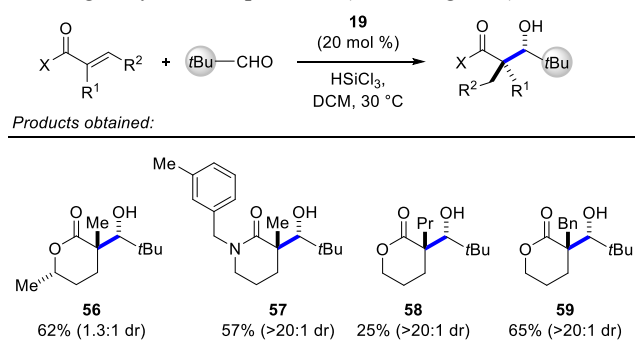


^aStandard Conditions: Michael acceptor (1 mmol), aldehyde (1.5 mmol), pOMe-TPPO (**19**, 20 mol %), HSiCl₃ (2.5 equiv), in dichloromethane (0.25 M) at 30 °C for 48 h. ^breaction is complete in 12 h. ^cin toluene (0.25 M). ^daldehyde is added after 8 h. Reaction is quenched 12 h after addition of the aldehyde.

diastereomer and *syn*-**31** as the minor diastereomer in combined 70% yield (Figure 2B)

The conditions developed proved efficient for construction of a variety of α,α -disubstituted and α,α,β -trisubstituted lactones and lactams, (Scheme 1) affording yields and diastereomeric ratios up to 85% and 50:1, respectively. For 6-membered monocyclic lactones and lactams, the *anti*-product was favored with diastereomeric ratios up to 20:1 d.r., increasing with both aldehyde and alkene bulk (**11**, **32-34**, **36-52**, **54-55**, Scheme 1). Importantly, sterically encumbered tricyclic lactones resulted in the formation of the corresponding β -hydroxylactones **35** and **53** in up to 67% yield and 50:1 d.r. (Scheme 1). *N*-alkyl- or *N*-aryl-substituted lactams proved efficient under the optimized reaction conditions and resulted in up to 85% yield and 20:1 d.r. of the desired reductive aldol products (e.g. **32**, Scheme 1). Notably, lactams bearing removable para-methoxyphenyl (PMP) or benzyl protecting groups afforded high yields and good to excellent diastereomeric ratios of the desired β -hydroxylactams (**34**, **48-51**, Scheme 1). Aryl aldehydes with varying substitution are viable electrophiles, and increased hindrance on the aromatic moieties lead to higher diastereomeric ratios (e.g. **32**, **34**, Scheme 1). Aldehydes conjugated to heterocycles including furan and thiophene were tolerated well as electrophiles rendering yields up to 77% (**41**, **42**, Scheme 1). Initial efforts to extend the substrate scope to unsaturated aldehydes, such as cinnamaldehyde, proved challenging due to the formation of competing aldol condensation products. However, conducting the reaction in toluene under otherwise identical conditions attenuated this competing self-condensation and resulted in good yields of the respective β -hydroxylactone and -lactam adducts (**42**, **45**, **48**, Scheme 1). Aliphatic aldehydes lacking

acidic α -protons, such as pivaldehyde, proved viable under the conditions developed for reductive aldol reactions of α,α,β -trisubstituted enones and lactams resulting in the desired products in good yields in up to 65% (**56-59**, Figure 3).²⁰



Conditions: Michael acceptor (1 mmol), aldehyde (1.5 mmol), pOMe-TPPO (**19**, 20 mol %), HSiCl₃ (2.0 equiv), in dichloromethane (0.2 M) at 30 °C for 48 h.

Figure 3. Reductive aldol reactions using pivaldehyde.

Furthermore, morpholine amides **60** and **61** proved viable substrates for the Lewis base-catalyzed reductive aldol reaction. Morpholine amides are important synthetic alternatives to Weinreb amides characterized by their ease of use.²¹ Upon conversion of **60** with a variety of aldehydes under the optimized conditions, the corresponding aldol products were obtained bearing a methyl group *syn* and an ethyl group *anti* to the β -hydroxyl group (**61**, **64**, **65**, Figure 4).

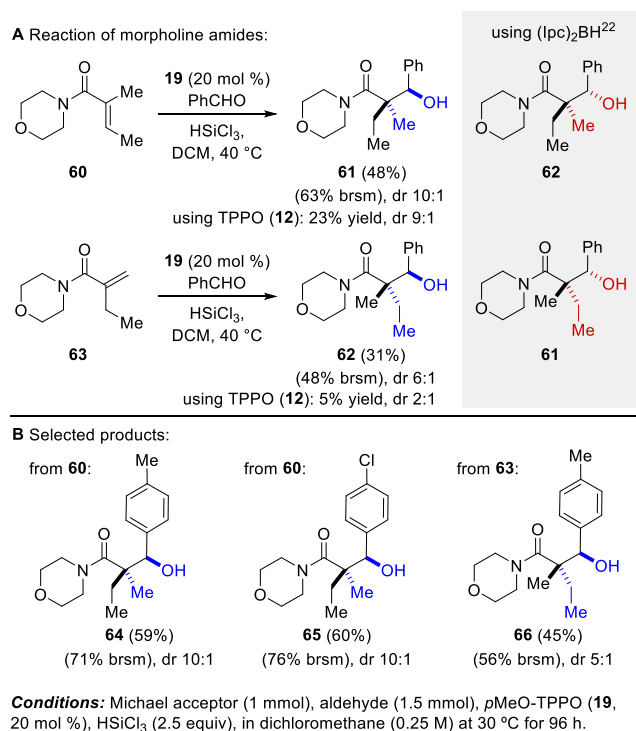


Figure 4. Reductive aldol reactions of morpholine amides.

Notably, the products of this reductive aldol approach are formed in up to 60% yield and 10:1 d.r. while the use of TPPO (**12**) as catalyst resulted in overall diminished yields. Importantly, the products are diastereomeric to those obtained via an alternate approach relying on (Ipc)₂BH, thus providing a valuable complementary synthetic alternative (**62**, Figure 5).²¹ The same observation was made for the conversion of **63** under the optimized reaction conditions, resulting in the formation of **62** and **66**, albeit in lower yields (Figure 4). The reductive aldol products are easily converted to versatile building blocks bearing quaternary carbons (Figure 5). β -Hydroxylactam **49** was reduced to its piperidine analog **67** in 96% yield in a two-step sequence. Also, β -hydroxylactone product **11** was converted upon treatment with LiAlH₄ to the corresponding triol **68** incorporating an α -quaternary carbon center in 72% yield.

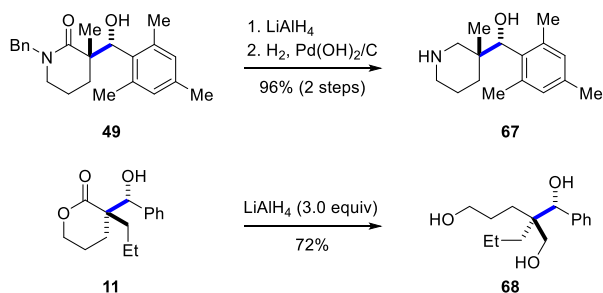


Figure 5. Transformations of reductive aldol products **11** and **49**.

In summary, a synthetic method for the efficient construction of β -hydroxylactones, -lactams and morpholine amides bearing α -quaternary carbon centers is described. The simple *para*-methoxy triarylphosphine oxide **19** was identified as a Lewis base catalyst uniquely effective in promoting the reductive aldol reaction of α,α -disubstituted and α,α,β -

trisubstituted enones to form the desired products in up to 85% yield and 50:1 d.r. Importantly, this reaction complements existing protocols for the conversion of morpholine amides relying on (Ipc)₂BH as reagent, resulting in the formation of diastereomeric products.

ASSOCIATED CONTENT

Supporting Information.

Experimental procedures and compound characterization data, including the ¹H/¹³C NMR spectra, as well as data concerning deuterium labeling studies

This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

* E-mail: corinnas@umich.edu.

Author Contributions

† Y.C.D. and J.R.A. contributed equally.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We thank the Petroleum Research Fund (PRF#54688-DNI1), the University of Michigan Office of Research and the NSF/National Science Foundation (CHE-1654223) for financial support. Y.C.D. thanks the National Science Foundation for a predoctoral fellowship. We thank Dr. Jeff W. Kampf (Department of Chemistry, Willard Henry Dow Laboratory, University of Michigan) for X-ray crystallographic studies.

REFERENCES

- (1) Kramer, J. A.; Sagartz, J. E.; Morris, D. L. *Nat. Rev. Drug Discovery* **2007**, *6*, 636-649.
- (2) Lovering, F. *Med. Chem. Comm.* **2013**, *4*, 515-519.
- (3) (a) Liu, Y.; Han, S.-J.; Liu, W.-B.; Stoltz, B. M. *Acc. Chem. Res.* **2015**, *48*, 740-751. (b) Quasdorf, K. W.; Overman, L. E. *Nature* **2014**, *516*, 181-191. (c) Prakash, J.; Marek, I. *Chem. Commun.* **2011**, *47*, 4593-4623. (d) Murphy, J. J.; Bastida, D.; Paria, S.; Fagnoni, M.; Melchiorre, P. *Nature* **2016**, *532*, 218-222.
- (4) For a recent example, see: Minko, Y.; Pasco, M.; Lercher, L.; Botoshansky, M.; Marek, I. *Nature* **2012**, *490*, 522-526.
- (5) For selected examples, see: (a) *acochlearine*: Meriçi, A. H.; Süzgeç, S.; Bitiş, L.; Meriçi, F.; Özçelik, H.; Zapp, J.; Becker, H. *Pharmazie* **2006**, *61*, 483-485. (b) *pseudolaric acid B*: Zhou, B. N.; Ying, B. P.; Song, G. Q.; Chen, Z. X.; Han, J.; Yan, Y. F. *Planta Med* **1983**, *47*, 35-38. (c) *scholarisine A*: Cai, X.-H.; Tan, Q.-G.; Liu, Y.-P.; Feng, T.; Du, Z.-Z.; Li, W.-Q.; Luo, X.-D. *Org. Lett.* **2008**, *10*, 577-580.
- (6) For additional recent examples, see: (a) Holmbo, S. D.; Godfrey, N. A.; Hirner, J. J.; Pronin, S. V. *J. Am. Chem. Soc.* **2016**, *138*, 12316-12319. (b) Huang, C.-Y.; Doyle, A. G. *J. Am. Chem. Soc.* **2015**, *137*, 5638-5641. (c) Pratsch, G.; Lackner, G. L.; Overman, L. E. *J. Org. Chem.* **2015**, *80*, 6025-6036.
- (7) For examples using Rh, see: (a) Taylor, S. J.; Duffey, M. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528-4529. (b) Russell, A. E.; Fuller, N. O.; Taylor, S. J.; Aurisset, P.; Morken, J. P. *Org. Lett.* **2004**, *6*, 2309-2312. (c) Bocknack, B. M.; Wang, L.-C.; Krische, M. J. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5421-5424. (d) Fuller, N. O.; Morken, J. P. *Synlett* **2005**, *9*, 1459-1461. (e) Nishiyama, H.; Shiomi, T.; Tsuchiya, Y.; Matsuda, I. *J. Am. Chem. Soc.* **2005**, *127*, 6972-6973. (f) Jung, C.-K.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 17051-17056. (g) Han, S. B.; Krische, M. J. *Org. Lett.* **2006**, *8*,

- 5657-5660. (h) Ito, J.; Shiomi, T.; Nishiyama, H. *Adv. Synth. Catal.* **2006**, *348*, 1235-1240. (i) Shiomi, T.; Ito, J.; Yamamoto, Y.; Nishiyama, H. *Eur. J. Org. Chem.* **2006**, *24*, 5594-5600. (j) Shiomi, T.; Nishiyama, H. *Org. Lett.* **2007**, *9*, 1651-1654. (k) Hashimoto, T.; Shiomi, T.; Ito, J.; Nishiyama, H. *Tetrahedron* **2007**, *63*, 12883-12887. (l) Hashimoto, T.; Ito, J.; Nishiyama, H. *Org. Lett.* **2007**, *9*, 1651-1654. (m) Bee, C.; Han, S. B.; Hassan, A.; Iida, H.; Krische, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 2746-2747. (n) Shiomi, T.; Adachi, T.; Ito, J.; Nishiyama, H. *Org. Lett.* **2009**, *11*, 1011-1014.
- (8) For an example using Ir, see: Zhao, C.-X.; Duffey, M. O.; Taylor, S. J.; Morken, J. P. *Org. Lett.* **2001**, *3*, 1829-1831.
- (9) For examples using Cu, see: (a) Lam, H. W.; Murray, G. J.; Firth, J. D. *Org. Lett.* **2005**, *7*, 5743-5746. (b) Lam, H. W.; Joensuu, P. M. *Org. Lett.* **2005**, *7*, 4225-4228. (c) Chuzel, O.; Deschamps, J.; Chausteur, C.; Riant, O. *Org. Lett.* **2006**, *8*, 5943-5946. (d) Deschamps, J.; Chuzel, O.; Hannedouche, J.; Riant, O. *Angew. Chem. Int. Ed.* **2006**, *45*, 1292-1297. (e) Zhao, D.; Oisaki, K.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2006**, *47*, 1403-1407. (f) Zhao, D.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 14440-14441. (g) Lipshutz, B. H.; Amorelli, B.; Unger, J. B. *J. Am. Chem. Soc.* **2008**, *130*, 14378-14379. (h) Deschamps, J.; Riant, O. *Org. Lett.* **2009**, *11*, 1217-1220. (i) Kato, M.; Oki, H.; Ogata, K.; Fukuzawa, S. *Synlett* **2009**, *8*, 1299-1302. (j) Ou, J.; Wong, W.-T.; Chiu, P. *Tetrahedron* **2012**, *68*, 3450-3456.
- (10) For an example using Co, see: Lumby, R. J.; Joensuu, P. M.; Lam, H. W. *Tetrahedron* **2008**, *64*, 7729-7740.
- (11) For an example using Ru, see: Doi, T.; Fukuyama, T.; Minamoto, S.; Ryu, I. *Synlett* **2006**, *18*, 3013-3016.
- (12) For an example using Pd, see: Kiyooka, S.; Shimizu, A.; Torii, S. *Tetrahedron Lett.* **1998**, *39*, 5237-5238.
- (13) For intermolecular reductive aldol reactions converting α,α -disubstituted enones, see: (a) Revis, A.; Hilty, T. K. *Tetrahedron Lett.* **1987**, *28*, 4809-4812. (b) Ghosh, A. K.; Kass, J.; Anderson, D. D.; Xu, X.; Marian, C. *Org. Lett.* **2008**, *10*, 4811-4814.
- (14) For intermolecular reductive aldol reactions converting examples of α,β -disubstituted enones, see: (a) Lipshutz, B. H.; Chrisman, W.; Noson, K.; Papa, P.; Sclafani, J. A.; Vivian, R. W.; Keith, J. M. *Tetrahedron* **2000**, *56*, 2779-2788. (b) Matsuda, I.; Takahashi, K.; Sato, S. *Tetrahedron Lett.* **1990**, *31*, 5331-5334. (c) Lipshutz, B. H.; Papa, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 4580-4582.
- (15) For selected intramolecular examples, see: (a) Joensuu, P. M.; Murray, G. J.; Fordyce, E. A. F.; Luebbbers, T.; Lam, H. W. *J. Am. Chem. Soc.* **2008**, *130*, 7328-7338. (b) Sloan, L. A.; Baker, T. M.; Macdonald, S. J. F.; Procter, D. J. *Synlett* **2007**, *20*, 3155-3159. (c) Chiu, P.; Szeto, C.-P.; Geng, Z.; Cheng, K.-F. *Org. Lett.* **2001**, *3*, 1901-1903. (d) Lipshutz, B. H.; Amorelli, B.; Unger, J. B. *J. Am. Chem. Soc.* **2008**, *130*, 14378-14379.
- (16) Denmark, S. E.; Beutner, G. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 1560-1638.
- (17) (a) Sugiura, M.; Sato, N.; Kotani, S.; Nakajima, M. *Chem. Commun.* **2008**, *29*, 4309-4311. (b) Sugiura, M.; Sato, N.; Sonoda, Y.; Kotani, S.; Nakajima, M. *Chem. Asian J.* **2010**, *5*, 478-481.
- (18) (a) Denmark, S. E.; Su, X.; Nishigaichi, Y. *J. Am. Chem. Soc.* **1998**, *120*, 12990-12991. (b) Denmark, S. E.; Pham, S. M. *Helv. Chim. Acta* **2000**, *83*, 1846-1853. (c) Denmark, S. E.; Pham, S. M.; Stavenger, R. A.; Su, X.; Wong, K.-T.; Nishigaichi, Y. *J. Org. Chem.* **2006**, *71*, 3904-3922.
- (19) For a recent example of tandem SiCl_3H reactivity, see: Chen, L.; Du, Y.; Zeng, X.-P.; Shi, T.-D.; Zhou, F.; Zhou, J. *Org. Lett.* **2015**, *17*, 1557-1560.
- (20) See Supporting Information for details.
- (21) (a) Martín, R.; Romea, P.; Tey, C.; Urpi, F.; Vilarrasa, J. *Synlett* **1997**, *12*, 1414-1416. (b) Concellón, J. M.; Rodríguez-Solla, H.; Méjica, C.; Blanco, E. G. *Org. Lett.* **2007**, *9*, 2981-2984. (c) Dhoro, F.; Kristensen, T. E.; Stockmann, V.; Yap, G. P. A.; Tius, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 7256-7257. (d) Concellón, J. M.; Rodríguez-Solla, H.; Díaz, P. *J. Org. Chem.* **2007**, *72*, 7974-7979. (e) Lin, K.-W.; Tsai, C.-H.; Hsieh, I.-L.; Yan, T.-H. *Org. Lett.* **2008**, *10*, 1927-1930. (f) Concellón, J. M.; Rodríguez-Solla, H.; del Amo, V.; Díaz, P. *Synthesis* **2009**, *15*, 2634-2645. (g) Rye, C.; Barker, D. *Synlett* **2009**, *20*, 3315-3319.
- (22) (a) Nuhant, P.; Allais, C.; Roush, W. R. *Angew. Chem. Int. Ed.* **2013**, *52*, 8703-8707. (b) Allais, C.; Tsai, A. S.; Nuhant, P.; Roush, W. R. *Angew. Chem. Int. Ed.* **2013**, *52*, 12888-12891.

SYNOPSIS TOC

