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A Method for the Selective Hydrogenation of Alkenyl Halides to Alkyl Halides

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Supporting Information

ABSTRACT: A general method for the selective hydrogenation of alkenyl halides to alkyl halides is described. Fluoro, chloro, bromo, iodo, and *gem*-dihaloalkenes are viable substrates for the transformation. The selectivity of the hydrogenation is consistent with reduction by a hydrogen atom transfer pathway.

The selective hydrogenation of alkenyl halides to alkyl halides is a capricious transformation that is often complicated by the formation of hydrodehalogenation products (Figure 1, top). A literature survey reveals a small number of

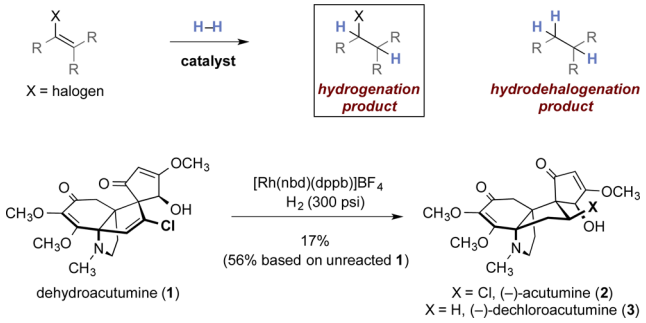

Figure 1. Reduction of alkenyl halides often results in mixtures of hydrogenation and hydrodehalogenation products (top). Reduction of dehydroacutumine (**1**) to form (−)-acutumine (**2**) and (−)-dechloroacutumine (**3**, bottom).[3]

focused studies of this reaction that proceed in variable yields and selectivities.[1] Although other isolated reductions of alkenyl halides have been reported,[2] a general process that is broadly amenable to simple alkenyl halides does not exist, to our knowledge. In a recent synthetic project in our laboratory[3] selective hydrogenation of the complex alkenyl chloride **1** was required to access the natural product (−)-acutumine (**2**, Figure 1, bottom).[4] Among a broad range of catalysts surveyed, $[Rh(nbd)(dppb)]BF_4$[5] was uniquely, although modestly, effective (17%; 56% based on unreacted **1**).[6] Nearly all other catalysts investigated formed the hydrodechlorination product (−)-dechloroacutumine (**3**)[7] exclusively or provided only trace amounts of **2**, in accord with our expectations based on the literature.

These data suggest the challenge of alkenyl halide reduction arises not from poor reactivity but rather in suppression of hydrodehalogenation. One pathway for the latter process may comprise insertion of the π-system into a metal hydride, to place the metal atom distal to the halogen, elimination of the resulting β-haloalkylmetal intermediate (**4**), and reduction (Figure 2, top).[8] Other manifolds, such as C−X oxidative addition, can be envisioned, and the pathway operative is likely to depend on the nature of the substituents (X and R).

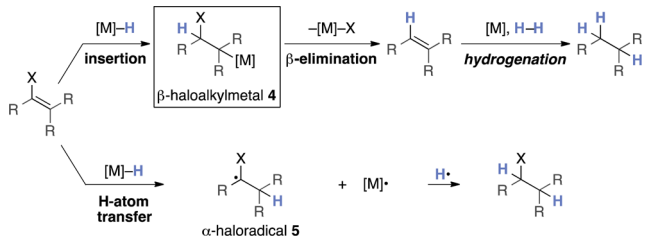

Figure 2. The formation of hydrodehalogenation products in metal-catalyzed hydrogenation of alkenyl halides may arise from generation of unstable β-haloalkylmetal intermediates (e.g., **4**, top). Postulated hydrogen atom addition to an alkenyl halide to provide an α-haloradical **5** (bottom).

We reasoned that metal-mediated hydrogen atom transfer may provide a viable approach to alkenyl halide hydrogenation. Halogen atoms decrease adjacent (α) C−H bond dissociation energies by 3.7, 4.9, 3.0, and 1.5 kcal/mol for F, Cl, Br and I, respectively (for $H-CH_2-X$; compare to 4.5 kcal/mol for a methyl group).[9] Thus, in the absence of substituents that might override the halogen bias, hydrogen atom addition to form a stable α-haloradical intermediate (**5**) should be favored (Figure 2, bottom). Trapping of **5** with a hydrogen atom donor would provide the desired product.

The reduction of alkenes by metal-mediated hydrogen atom transfer has been extensively studied since the 1970s.[10] Many of these investigations employed early metal hydrides and 1,3-dienes or styrenes as substrates.[11] In detailed measurements of hydrogen atom transfer from $(\eta^5\text{-}C_5H_5)Cr(CO)_3H$, Norton has shown that the steric environment of the alkene and the stability of the incipient alkyl radical significantly influence the rate of hydrogen atom transfer.[12] For example, hydrogen atom addition to 1,1-diphenylethylene is ∼780 times faster than addition to 1,1-diphenyl-2-methylethylene and is seven orders of magnitude faster than addition to 1-octene. Hydrogen atom addition to 2-methyloctene was reported to occur ∼50-fold faster than addition to 1-octene, indicating that electronic activation by the internal methyl group overrides the additional

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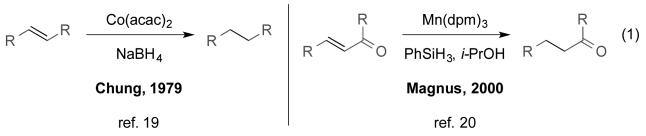
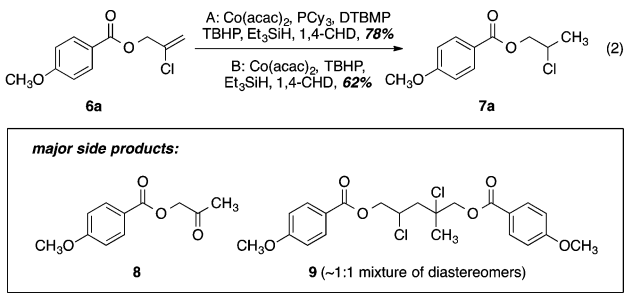
steric encumbrance introduced. This latter determination provides encouraging precedent for the analysis outlined above. Norton and co-workers have applied these fundamental studies to the development of catalytic reductive diene cyclization reactions initiated by hydrogen atom transfer to unsaturated esters.[13] In addition, Nishinaga,[14] Mukaiyama–Isayama,[15] Carreira,[16] Boger,[17] and others[18] have reported efficient cobalt-, manganese-, and iron-catalyzed (or mediated) alkene hydrofunctionalization reactions. Of particular relevance to our work, cobalt and manganese-based catalysts have been employed in the reduction of unactivated alkenes (using sodium borohydride as reductant)[19] and unsaturated ketones (using phenylsilane as reductant, eq 1),[20] and reduction products have been observed in cobalt-mediated hydration reactions.[15b] Evidence suggests these transformations proceed by hydrogen atom transfer,[16d,17,21] although migratory insertion into metal hydroperoxide intermediates has also been proposed.[15e,22] These catalysts are unique in their ability to effect hydrogen atom transfer to unactivated alkenes and provided the starting point for our studies.[23] A recent report from Shenvi and co-workers describing the reduction of unactivated alkenes (including an alkenyl bromide and chloride) by manganese tris(dipivaloylmethane) prompts us to disclose our results.[24]



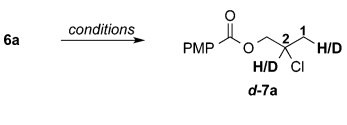
We began by studying the hydrogenation of 2-chloroallyl 4-methoxybenzoate (**6a**) to form 2-chloropropyl 4-methoxybenzoate (**7a**) in the presence of a variety of manganese and cobalt-based catalyst precursors and terminal reductants (eq 2). These optimization experiments revealed production of the ketone **8** and the dimer **9** as competitive with the desired reduction pathway. We speculate that the ketone is produced by oxygenation of a carbon-centered radical intermediate. Ultimately, two experimental protocols were developed. The first, which appears to be effective only for 2,2-disubstituted alkenes, comprises a mixture of cobalt bis(acetylacetonate) (25 mol %), activated by *t*-butylhydroperoxide (TBHP),[15f,16,21] tricyclohexylphosphine, 2,6-di-*t*-butyl-4-methylpyridine (DTBMP), and a combination of 1,4-cyclohexadiene (1,4-CHD) and triethylsilane as reducing agents, under argon. After warming to 50 °C for 10.5 h, the desired reduction product **7a** was obtained in 78% yield.



A comprehensive tabulation of the results obtained with a range of catalyst precursors, hydrogen atom donors, ligands, bases, and solvents are presented in the Tables S1–S5. Several observations are noted herein. Tricyclohexylphosphine was found to accelerate the rate, potentially by preventing formation of stable cobalt–alkyl intermediates,[25] and the yield of product in the absence of DTBMP was diminished slightly (59%, Table S4). Both triethylsilane and 1,4-cyclohexadiene were necessary; in the absence of either, the yield of **7a** was low (<1% in the absence of Et_3SiH, 12% in the absence of 1,4-cyclohexadiene, Table S4). These observations are consistent with deuterium-labeling experiments (vide infra) that indicate each reagent contributes a hydrogen atom. *n*-Propyl 4-methoxybenzoate was not detected in any of the experiments above (^1H NMR analysis). Reduction of **6a** using manganese tris(dipivaloylmethane)[24a] provided **7a** in 45% yield, reduction using cobaloxime complexes under dihydrogen[13c] did not proceed, and reduction with palladium on carbon as catalyst under 1 atm of dihydrogen provided a 4% yield of **7a** and an 87% yield of *n*-propyl 4-methoxybenzoate.

An alternative and simpler procedure we developed, which has proven to be amenable to tri- and tetrasubstituted alkenes, comprises treatment of the substrate with 1 equiv each of cobalt bis(acetylacetonate) and TBHP, in the presence of triethylsilane and 1,4-cyclohexadiene under air at ambient temperature. Under these conditions, the product **7a** was obtained in 62% yield after 40 min (eq 2). Among many catalyst precursors examined, cobalt bis(acetylacetonate) was the only species that mediated high conversion of **6a** (Table S2). The yield of **7a** was only marginally diminished in the absence of TBHP (58%) and decreased significantly in the absence of triethylsilane (<1%) or 1,4-cyclohexadiene (5%, Table S5). As cobalt bis(acetylacetonate) is relatively inexpensive, this procedure may be advantageous for its simplicity and rate.

TBHP and triethylsilane have been shown to react with Co(II) complexes to form Co(III) hydride intermediates,[21] which may effect hydrogen atom transfer to the substrate, and we speculated that 1,4-CHD serves as a trap for the alkyl radical intermediate. Isotopic labeling experiments were conducted to probe these hypotheses (Figure 3). These experiments were



entry	conditions	result
1	Et_3Si–**D**, CH_3OH 1,4-cyclohexadiene	C-1 **64% D** C-2 **0% D**
2	Et_3Si–**D**, CD_3OD 1,4-cyclohexadiene	C-1 **65% D** C-2 **0% D**
3	Et_3Si–**H**, CD_3OD 1,4-cyclohexadiene	C-1 **0% D** C-2 **0% D**

Figure 3. Deuterium labeling experiments.

executed without added TBHP (which has only a marginal effect on efficiency, vide supra) and in methanol (or methanol-d_4). Using triethylsilane-d_1 in methanol, the product ***d*-7a** was formed with 64% deuterium atom incorporation at C-1 (entry 1). Conducting the reduction with triethylsilane-d_1 in methanol-d_4 resulted in 65% deuterium atom incorporation at C-1 (entry 2). When triethylsilane in methanol-d_4 was employed, deuterium was not detected at C-1 (entry 3), and within the limits of detection, deuterium was not incorporated at C-2 in any of these experiments. These data suggest that the internal (C-2) hydrogen atom derives from 1,4-CHD and that the terminal (C-1) hydrogen atom derives primarily from silane. The origin of incomplete C-1 deuteration in entries 1 and 2 is not fully understood but may be due to reaction of the putative cobalt deuteride with 1,4-CHD to form HD, benzene, and a cobalt hydride, or exchange of the deuterium with the acac ligand.

In its present form, the scope of the reaction encompasses fluoro, chloro, bromo, and iodoalkenes, cyclic and acylic alkenyl halides, and *gem*-dihaloalkenes (Table 1). Thus, the fluo-

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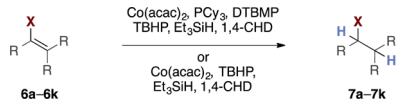
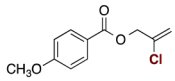
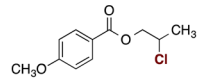
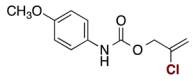
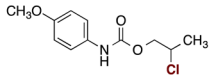
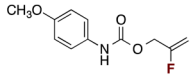
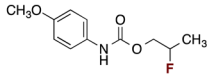
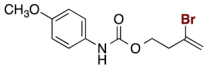
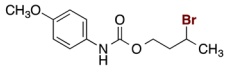
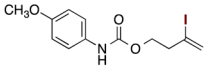
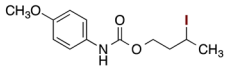
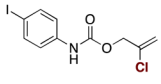
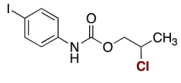
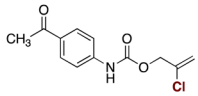
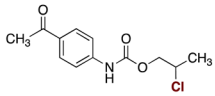
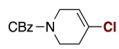
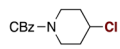
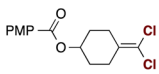
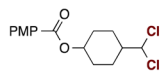
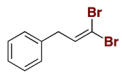
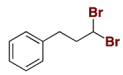
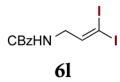
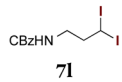
Table 1. Preliminary Scope of the Reduction Reaction



entry	substrate	product	yield[a]
1	 **6a**	 **7a**	78%[b]
2	 **6b**	 **7b**	71%[b]
3	 **6c**	 **7c**	64%[b]
4	 **6d**	 **7d**	78%[b]
5	 **6e**	 **7e**	61%[c]
6	 **6f**	 **7f**	72%[b]
7	 **6g**	 **7g**	74%[b]
8	 **6h**	 **7h**	59%[c]
9	 **6i**	 **7i** (1:1 dr)	81%[c]
10	 **6j**	 **7j** (1.2:1 dr)	72%[c]
11	 **6k**	 **7k**	51%[c]
12	 **6l**	 **7l**	41%[c,d]

[a]Isolated yield after purification by flash-column chromatography. [b]Conditions: $Co(acac)_2$ (25 mol %), PCy_3 (25 mol %), TBHP (25 mol %), DTBMP (50 mol %), 1,4-CHD (5 equiv), Et_3SiH (5 equiv), *n*-PrOH (0.3 M), argon, 50 °C. [c]Conditions: $Co(acac)_2$ (1 equiv), TBHP (1 equiv), 1,4-CHD (5 equiv), Et_3SiH (5 equiv), *n*-PrOH (0.3 M), air, 24 °C. [d]Determined by ^1H NMR analysis against an internal standard.

roalkene **6c** was cleanly reduced to provide the fluoroalkane **7c** (entry 3). The alkenyl bromide **6d** and iodide **6e** were also reduced in good yield (entries 4, 5, respectively). The carbamates **6f** and **6g** (entries 6 and 7) and the piperidine derivative **6h** (entry 8), which contain aryl iodide, aryl ketone, and benzyloxycarbonyl functional groups that would be anticipated to be reactive toward traditional hydrogenation catalysts, were selectively reduced at the alkenyl halide function. Finally, the *gem*-dichloro and *gem*-dibromoalkenes **6j** and **6k**, respectively, were also reduced to provide the *gem*-dihaloalkane products **7j** and **7k** (entries 10 and 11, respectively). The successful reduction of **6j** suggests that the *gem*-dichloro substituent exerts a stronger directing effect than a *gem*-dialkyl substituent, as initial hydrogen atom transfer to the dichloro terminus of the alkene would be expected to produce an unstable β,β-dichloroalkyl radical intermediate. This is consistent with the relative C−H bond dissociation energies of propane (secondary C−H = 98.1 kcal/mol) and dichloromethane (95.7 kcal/mol).[9] Reaction of the *gem*-diiodoalkene **6l** did not proceed to completion (41% product **7l** + 42% **6l** remaining, entry 12). Qualitatively, alkenyl bromides and chlorides appear to react faster than iodides or fluorides. Attempted reduction of 1-phenyl-1-chloropropene led to unidentified decomposition products, while attempted reduction of a trialkylchloroalkene resulted in recovery of starting material. Nitroarenes are incompatible with the reaction conditions.

The work we have reported builds on prior studies of metal-mediated hydrogen atom addition and alkene hydrofunctionalization reactions and constitutes a useful method for the selective hydrogenation of alkenyl halides. The selectivity of the reaction (hydrogenation vs hydrodehalogenation) is thought to arise from the activating effect of the halogen substituent, which biases the direction of hydrogen atom addition. To a first approximation, the feasibility of a given substrate can be assessed by consideration of homolytic C−H BDEs in the product. A large number of natural products contain alkyl halides, and this method may prove useful in their synthesis.[26] Future studies will focus on functionalizing the putative α-haloalkyl radical intermediates.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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ration for Science Advancement, and the Camille and Henry Dreyfus Foundation.

REFERENCES

(1) Chloroalkenes: (a) Ham, G. E.; Coker, W. P. *J. Org. Chem.* **1964**, *29*, 194. Fluoroalkenes: (b) Allmendinger, T.; Dandois, C.; Walliser, B. *Tetrahedron Lett.* **1991**, *32*, 2735. (c) Engman, M.; Diesen, J. S.; Paptchikhine, A.; Andersson, P. G. *J. Am. Chem. Soc.* **2007**, *129*, 4536. (d) Kaukoranta, P.; Engman, M.; Hedberg, C.; Bergquist, J.; Andersson, P. G. *Adv. Synth. Catal.* **2008**, *350*, 1168. Diiodoalkenes: (e) Cloarec, J.-M.; Charette, A. B. *Org. Lett.* **2004**, *6*, 4731. 1-Boryl-1-haloalkenes: (f) Gazić Smilović, I.; Casas-Arce, E.; Roseblade, S. J.; Nettekoven, U.; Zanotti-Gerosa, A.; Kovacevic, M.; Casar, Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 1014. (g) Roseblade, S. J.; Casas-Arcé, E.; Nettekoven, U.; Gazić Smilović, I.; Zanotti-Gerosa, A.; Časar, Z. *Synthesis* **2013**, *45*, 2824. (h) Pieber, B.; Martinez, S. T.; Cantillo, D.; Kappe, C. O. *Angew. Chem., Int. Ed.* **2013**, *52*, 10241. (i) Roseblade, S. J.; Gazić Smilović, I.; Časar, Z. *Tetrahedron* **2014**, *70*, 2654.

(2) Heterogeneous hydrogenation: (a) Stille, J. K.; Sonnenberg, F. M.; Kinstle, T. H. *J. Am. Chem. Soc.* **1966**, *88*, 4922. (b) Chauhan, B. P. S.; Rathore, J. S.; Bandoo, T. *J. Am. Chem. Soc.* **2004**, *126*, 8493. Diimide: (c) Wilt, J. W.; Gutman, G.; Ranus, W. J.; Zigman, A. R. *J. Org. Chem.* **1967**, *32*, 893. (d) Warm, A.; Vogel, P. *J. Org. Chem.* **1986**, *51*, 5348. (e) Chang, K.-H.; Jenkins, M. N.; Wu, H.-R.; Li, W.-S. *Tetrahedron Lett.* **2003**, *44*, 1351. (f) Du, H. C.; Liu, K. C.; Li, W. S. *Synth. Commun.* **2006**, *36*, 621. (g) Kim, H.; Lee, H.; Lee, D.; Kim, S.; Kim, D. *J. Am. Chem. Soc.* **2007**, *129*, 2269. Homogeneous hydrogenation: (h) Wang, C.-J.; Sun, X.; Zhang, X. *Angew. Chem., Int. Ed.* **2005**, *44*, 4933. (i) Sun, X.; Zhou, L.; Li, W.; Zhang, X. *J. Org. Chem.* **2008**, *73*, 1143. (j) Krska, S. W.; Mitten, J. V.; Dormer, P. G.; Mowrey, D.; Machrouhi, F.; Sun, Y.; Nelson, T. D. *Tetrahedron* **2009**, *65*, 8987. (k) Stumpf, A.; Reynolds, M.; Sutherlin, D.; Babu, S.; Bappert, E.; Spindler, F.; Welch, M.; Gaudino, J. *Adv. Synth. Catal.* **2011**, *353*, 3367.

(3) (a) King, S. M.; Calandra, N. A.; Herzon, S. B. *Angew. Chem., Int. Ed.* **2013**, *52*, 3642. (b) Calandra, N. A.; King, S. M.; Herzon, S. B. *J. Org. Chem.* **2013**, *78*, 10031.

(4) Isolation of (−)-acutumine (**2**): (a) Goto, K.; Sudzuki, H. *Bull. Chem. Soc. Jpn.* **1929**, *4*, 220. (b) Tomita, M.; Okamoto, Y.; Kikuchi, T.; Osaki, K.; Nishikawa, M.; Kamiya, K.; Sasaki, Y.; Matoba, K.; Goto, K. *Tetrahedron Lett.* **1967**, *8*, 2421. (c) Sugimoto, Y.; Inanaga, S.; Kato, M.; Shimizu, T.; Hakoshima, T.; Isogai, A. *Phytochemistry* **1998**, *49*, 1293.

(5) (a) Brown, J. M.; Naik, R. G. *J. Chem. Soc., Chem. Commun.* **1982**, 348. (b) Evans, D. A.; Morrissey, M. M. *J. Am. Chem. Soc.* **1984**, *106*, 3866.

(6) Attempts to achieve higher conversions of **1** using [Rh(nbd)(dppb)]BF_4 led to the production of **3** exclusively, indicating the presence of pathways that cleave the C_{sp^3}−Cl bond in **2**.

(7) Isolation of (−)-dechloroacutumine (**3**): (a) Sugimoto, Y.; Inanaga, S.; Kato, M.; Shimizu, T.; Hakoshima, T.; Isogai, A. *Phytochemistry* **1998**, *49*, 1293. (b) Sugimoto, Y.; Matsui, M.; Takikawa, H.; Sasaki, M.; Kato, M. *Phytochemistry* **2005**, *66*, 2627.

(8) Peterson, A. A.; Thoreson, K. A.; McNeill, K. *Organometallics* **2009**, *28*, 5982.

(9) BDEs of C−H bonds. In *Comprehensive Handbook of Chemical Bond Energies*; CRC Press: Boca Raton, 2007; pp 19−145.

(10) For reviews, see: (a) Eisenberg, D. C.; Norton, J. R. *Isr. J. Chem.* **1991**, *31*, 55. (b) Gansäuer, A.; Shi, L.; Otte, M.; Huth, I.; Rosales, A.; Sancho-Sanz, I.; Padial, N.; Oltra, J. E. Hydrogen Atom Donors: Recent Developments. In *Radicals in Synthesis III*; Heinrich, M., Gansäuer, A., Eds.; Springer: Berlin Heidelberg, 2012; Vol. *320*, pp 93−120.

(11) (a) Sweany, R. L.; Halpern, J. *J. Am. Chem. Soc.* **1977**, *99*, 8335. (b) Roth, J. A.; Orchin, M. *J. Organomet. Chem.* **1979**, *182*, 299. (c) Sweany, R. L.; Comberrel, D. S.; Dombourian, M. F.; Peters, N. A. *J. Organomet. Chem.* **1981**, *216*, 37. (d) Nalesnik, T. E.; Freudenberger, J. H.; Orchin, M. *J. Mol. Catal.* **1982**, *16*, 43. (e) Roth, J. A.; Wiseman, P.; Ruszala, L. *J. Organomet. Chem.* **1982**, *240*, 271. (f) Ungvary, F.; Marko, L. *Organometallics* **1982**, *1*, 1120. (g) Connolly, J. W. *Organometallics* **1984**, *3*, 1333. (h) Garst, J. F.; Bockman, T. M.; Batlaw, R. *J. Am. Chem. Soc.* **1986**, *108*, 1689. (i) Thomas, M. J.; Shackleton, T. A.; Wright, S. C.; Gillis, D. J.; Colpa, J. P.; Baird, M. C. *J. Chem. Soc., Chem. Commun.* **1986**, 312. (j) Wassink, B.; Thomas, M. J.; Wright, S. C.; Gillis, D. J.; Baird, M. C. *J. Am. Chem. Soc.* **1987**, *109*, 1995. (k) Choi, J.; Pulling, M. E.; Smith, D. M.; Norton, J. R. *J. Am. Chem. Soc.* **2008**, *130*, 4250.

(12) (a) Tang, L.; Papish, E. T.; Abramo, G. P.; Norton, J. R.; Baik, M.-H.; Friesner, R. A.; Rappé, A. *J. Am. Chem. Soc.* **2003**, *125*, 10093. (b) Choi, J.; Tang, L.; Norton, J. R. *J. Am. Chem. Soc.* **2007**, *129*, 234.

(13) (a) Smith, D. M.; Pulling, M. E.; Norton, J. R. *J. Am. Chem. Soc.* **2007**, *129*, 770. (b) Hartung, J.; Pulling, M. E.; Smith, D. M.; Yang, D. X.; Norton, J. R. *Tetrahedron* **2008**, *64*, 11822. (c) Li, G.; Han, A.; Pulling, M. E.; Estes, D. P.; Norton, J. R. *J. Am. Chem. Soc.* **2012**, *134*, 14662.

(14) Nishinaga, A.; Yamada, T.; Fujisawa, H.; Ishizaki, K.; Ihara, H.; Matsuura, T. *J. Mol. Catal.* **1988**, *48*, 249.

(15) (a) Mukaiyama, T.; Isayama, S.; Inoki, S.; Kato, K.; Yamada, T.; Takai, T. *Chem. Lett.* **1989**, *18*, 449. (b) Inoki, S.; Kato, K.; Takai, T.; Isayama, S.; Yamada, T.; Mukaiyama, T. *Chem. Lett.* **1989**, *18*, 515. (c) Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989**, *18*, 569. (d) Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989**, *18*, 1071. (e) Kato, K.; Yamada, T.; Takai, T.; Inoki, S.; Isayama, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 179. (f) Isayama, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1305.

(16) (a) Waser, J.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4099. (b) Waser, J.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 5676. (c) Waser, J.; Nambu, H.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 8294. (d) Waser, J.; Gaspar, B.; Nambu, H.; Carreira, E. M. *J. Am. Chem. Soc.* **2006**, *128*, 11693. (e) Gaspar, B.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 4519. (f) Gaspar, B.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 5758.

(17) (a) Barker, T. J.; Boger, D. L. *J. Am. Chem. Soc.* **2012**, *134*, 13588. (b) Leggans, E. K.; Barker, T. J.; Duncan, K. K.; Boger, D. L. *Org. Lett.* **2012**, *14*, 1428.

(18) (a) Magnus, P.; Payne, A. H.; Waring, M. J.; Scott, D. A.; Lynch, V. *Tetrahedron Lett.* **2000**, *41*, 9725. (b) Taniguchi, T.; Goto, N.; Nishibata, A.; Ishibashi, H. *Org. Lett.* **2010**, *12*, 112.

(19) Chung, S.-K. *J. Org. Chem.* **1979**, *44*, 1014.

(20) Magnus, P.; Waring, M. J.; Scott, D. A. *Tetrahedron Lett.* **2000**, *41*, 9731.

(21) Tokuyasu, T.; Kunikawa, S.; Masuyama, A.; Nojima, M. *Org. Lett.* **2002**, *4*, 3595.

(22) Hamilton, D. E.; Drago, R. S.; Zombeck, A. *J. Am. Chem. Soc.* **1987**, *109*, 374.

(23) For the reductive opening of epoxides by hydrogen atom transfer from bis(η^5-cyclopentadienyl)titanium hydride, see: (a) Gansäuer, A.; Otte, M.; Piestert, F.; Fan, C.-A. *Tetrahedron* **2009**, *65*, 4984. (b) Gansäuer, A.; Shi, L.; Otte, M. *J. Am. Chem. Soc.* **2010**, *132*, 11858. (c) Gansäuer, A.; Klatte, M.; Brandle, G. M.; Friedrich, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 8891.

(24) (a) Iwasaki, K.; Wan, K. K.; Oppedisano, A.; Crossley, S. W.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 1300. For a related intermolecular reductive coupling of alkenes, see: (b) Lo, J. C.; Yabe, Y.; Baran, P. S. *J. Am. Chem. Soc.* **2014**, *136*, 1304.

(25) Ng, F. T. T.; Rempel, G. L.; Halpern, J. *Inorg. Chim. Acta* **1983**, *77*, L165.

(26) For reviews, see: (a) Gribble, G. W. *Acc. Chem. Res.* **1998**, *31*, 141. (b) Bedke, D. K.; Vanderwal, C. D. *Nat. Prod. Rep.* **2011**, *28*, 15. (c) Wang, B.-G.; Gloer, J. B.; Ji, N.-Y.; Zhao, J.-C. *Chem. Rev.* **2013**, *113*, 3632.