Synthesis of Cyclohexenols and Cycloheptenols via the Regioselective Reductive Ring Opening of Oxabicyclic Compounds

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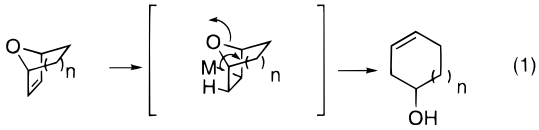
Received December 19, 1996[⊗]

Abstract: The reductive ring opening of oxabicyclic compounds has been achieved. While $RMgBr/MgBr_2$ works in a few limited substrates, diisobutylaluminum hydride reacts with oxabicyclic[3.2.1]- and -[2.2.1]alkenes to provide cycloheptenols and cyclohexenols in good yield and in some cases in good regioselectivity. With some substrates further reduction of the alkene was observed which led us to examine transition metals such as nickel which are known to accelerate the hydroalumination reaction. The reaction with $Ni(COD)_2$ (COD = cyclooctadiene) gave the best reactivity−selectivity profile, and significantly higher yields were obtained with minimal overreduction of the alkene. Phosphine ligands were shown to dramatically improve the regioselectivity of ring opening of bridgehead-substituted oxabicyclic compounds. The best ligand was 1,4-bis(diphenylphosphino)butane which gave up to 380:1 selectivity. A series of deuterium quenching experiments showed that the selectivity of the hydroalumination varies according to the reaction protocol and ligand-metal ratio.

Transition metal catalyzed hydrometalations play an important role in organic synthesis due to the utility of the resulting organometallic compounds.[1] The combination of the metal catalyst and its accompanying ligands offers the opportunity to tune the reactivity and prepare enantiomerically enriched products. This strategy is amply illustrated by rhodium- and ruthenium-catalyzed hydroborations, palladium- and rhodium-catalyzed hydrosilations, and palladium-, rhodium-, and molybdenum-catalyzed hydrostannations.[2−4]

Nickel-catalyzed hydroaluminations of unsaturated hydrocarbons have been known for many years, particularly the hydroalumination of alkynes to yield vinylic alanes. However, the utility of the hydroalumination of alkenes has been limited due to the low reactivity of the alkylalane and the propensity of the carbon aluminum bond to undergo racemization.[5]

Oxabicyclo[3.2.1]octenes and oxabicyclo[2.2.1]heptenes have been used as templates to control the regio- and stereoselectivity in the synthesis of polyfunctionalized 7- and 6-membered rings. A variety of ring opening strategies have been reported providing novel routes to natural products with diverse stereochemical motifs.[6] While carbon nucleophiles were found to efficiently react in an S_N2' fashion, there existed no efficient source of hydride to efficiently react with these systems.[7−9a] We therefore investigated the possibility of using a hydrometalation−elimination sequence to achieve this goal. We envisaged that the initially produced organometallic species would undergo β-elimination to form the ring-opened compound (eq 1).[9,10] We now describe our successful development of an efficient reducing system including a determination of the reactivity and regioselectivity of the reaction and present our preliminary studies relating to the mechanism.



n = 1,2 (1)

Results and Discussions

Identifying Diisobutylaluminum Hydride (DIBAL-H) as a Good Reducing Reagent. The first system we identified for the reductive ring opening was the combination of an organomagnesium or organolithium reagent bearing β-hydrogens and excess $MgBr_2$.[9b] In general, these reactions are sluggish, proceed in moderate to good yield, and are mainly limited to

[⊗] Abstract published in *Advance ACS Abstracts,* June 1, 1997.

(1) *The Chemistry of the Metal Bonds*; Hartley, F. R., Ed.; John Wiley and Sons: New York, 1987; Vol. 4.

(2) Metal-catalyzed hydroboration: Mannig, D.; Noth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878. For a review, see: Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179. For discussions on the mechanism, see: Evans, D. A.; Fu, G. C.; Anderson, B. A. *J. Am. Chem. Soc.* **1992,** *114*, 6679 and references therein.

(3) For recent reviews of metal-catalyzed hydrosilation, see: (a) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 8, p 763. (b) Mikolajczyk, M.; Drabowicz, J.; Kielbasinski, P. *Stereoselective Synthesis*; Houben-Weyl, 4th ed.; E21e, p 5733.

(4) Metal-catalyzed hydrostannation: (a) Ichinose, Y.; Oda, H.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3468. (b) Kikukawa, K.; Umekawa, H.; Wada, F.; Matsuda, T. *Chem. Lett.* **1988**, 881. (c) Zhang, H. X.; Guibe, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857. (d) Miyake, H.; Yamamuram, K. *Chem. Lett.* **1991**, 1099. (e) Koerber, K.; Gore, J.; Vatele, J.-M. *Tetrahedron Lett.* **1991**, *32*, 1187. (f) Casson, S.; Kocienski, P. *Synthesis* **1993**, 1133. (g) Lautens, M.; Kumanovic, S.; Meyer, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1329 and references therein.

(5) For a recent review of alkene and alkyne hydroalumination, see: Eisch, J. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 8, p 733.

(6) For reviews describing the synthesis, reactions, and utility of oxabicyclic compounds, see: (a) Chiu, P.; Lautens, M. *Top. Curr. Chem.* **1997**, *190*, 3. (b) Keay, B. A.; Woo, S. *Synthesis* **1996**, 669. (c) Shipman, M. *Contemp. Org. Synth.* **1995**, *2* (1), 1. (d) Lautens, M. *Synlett* **1993**, 177. (e) Ager, D. J.; East, M. B. *Tetrahedron* **1993**, *49*, 5683. (f) Lautens, M. *Pure Appl. Chem.* **1992**, *64*, 1873 and references therein. (g) Vogel, P.; Fattori, D.; Gasparini, F.; Le Drian, C. *Synlett* **1990**, 173. (h) Harmata, M. In *Advances in Cycloadditions*; Lautens, M., Ed.; JAI Press: Greenwich, CT; Vol. 4, p 41. (i) West, F. G. *Ibid*; p 1.

(7) Lautens, M.; Ma, S.; Yee, A. *Tetrahedron Lett.* **1995**, *36*, 4185.

(8) Lautens, M.; Belter, R. K. *Tetrahedron Lett.* **1992**, *33*, 2617.

(9) (a) Lautens, M.; Chiu, P.; Colucci, J. T. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 281. (b) Lautens, M.; Chiu, P. *Tetrahedron Lett.* **1991**, *32*, 4827.

(10) Lautens, M.; Chiu, P.; Ma, S.; Rovis, T. *J. Am. Chem. Soc.* **1995**, *117*, 532.

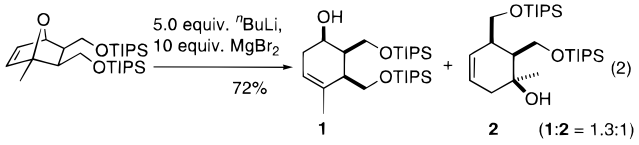
S0002-7863(96)04361-2 CCC: $14.00

Table 1. Reductive Ring-Opening Reactions Using DIBAL-H

Entry	Substrate	Reaction time (h)	Product	Yield[c] (%)
1	**6**, X=Y=H	36[a]	**7**	64[d]
2	**8**, X=Me, Y=H	12[a]	**9**	83[e]
3	**10**, X=H, Y=Me	12[a]	**11**	89
4	**12**	16[b]	**13**	80

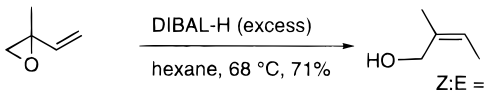
[a] DIBAL-H (6 equiv) in refluxing hexanes. [b] DIBAL-H (6 equiv) in refluxing ether. [c] Yields of isolated and analytically pure material. [d] Could not be separated from 16% of overreduced product, yield estimated from the ^{1}H NMR spectrum of the mixture. [e] 10% of overreduced product.

oxabicyclic[2.2.1] compounds. Furthermore, low regioselectivity is observed for unsymmetrical substrates (eq 2).



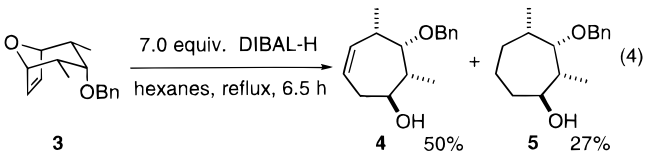
(2)

The limitations of the RM−$MgBr_2$ system as a general method to achieve the reductive ring opening led us to seek a more efficient and versatile reducing agent. Inspired by Katzenellenbogen's report of the reduction of vinyl epoxides using DIBAL-H (eq 3), we examined these conditions with the oxabicyclic substrates.[10,11]



(3)

We showed that treatment of **3** with 7.0 equiv of DIBAL-H in hexanes at reflux afforded the ring-opened product **4** in 50% yield along with the overreduction product **5** in 27% yield (eq 4).[6b,9a,10,12] Decreasing the amount of DIBAL-H to 1.5 equiv



(4)

avoided the formation of **5** and gave **4** in 65% yield along with 25% recovered starting material. A number of oxabicyclo[2.2.1] and -[3.2.1] compounds were shown to undergo ring opening (Table 1). The amount of overreduced product varied as a function of the substrate. For example, **6** which lacked substituents gave a 64% yield of ring opening product and 16% of overreduced product (entry 1). Compound **10** with bridgehead substituents gave exclusively the cycloheptenol **11** in 89% yield without any overreduction product (entry 3). For compound **12**, the additional reactivity of the bicyclic[2.2.1] structure allowed the reductive ring opening to occur under milder conditions (entry 4).

Table 2. Regioselectivity of DIBAL-H Reductive Ring Opening

Entry	Substrate	Product (**a**:**b**)			Yield[f] (%)
1[a]	**14**, R=TBS	**15a**	(1:6.4)[d]	**15b**	72
2[a]	**16**, R=Bn	**17a**	(1:5.6)[d]	**17b**	42[g]
3[b]	**18**, R=H	**19a**	(1:1.3)[e]	**19b**	75
4[c]	**18**, R=H	**19a**	(9.5:1)[e]	**19b**	85

[a] DIBAL-H (5 equiv) in refluxing hexanes. [b] DIBAL-H (6 equiv) in refluxing hexanes. [c] MeLi (1.2 equiv) then 5 equiv of DIBAL-H in refluxing hexanes. [d] Ratio was determined by ^{1}H NMR. [e] Ratio was determined by GC. [f] Yield of both regioisomers. [g] Isolated yield of product obtained along with 53% recovered starting material.

Regioselectivity of DIBAL-H-Promoted Ring Opening. We also examined the regioselectivity of reductive ring opening of unsymmetrical [3.2.1] substrates. As shown in Table 2, the trisubstituted cycloheptenol **a** will be obtained if the hydride adds distal to the bridgehead substituent, whereas the disubstituted cycloheptenol **b** will be produced if the hydride attacks the position of the double bond proximal to the substituent. When the hydroxyl group in the substrate was protected, the reaction favored the formation of regioisomer **b** which resulted from the delivery of the bulky alkylaluminum to the less-hindered reaction site distal to the bridgehead substituent in accord with the regioselectivity anticipated for hydroalumination (entries 1 and 2). In contrast, treatment of **18** with DIBAL-H alone resulted in virtually no selectivity (entry 3). However, when **18** was deprotonated with MeLi prior to hydroalumination, the major product was the regioisomer **19a** (entry 4). This reversal of regioselectivity demonstrated that the remote *endo* alkoxide group exerts a directing effect on the mode of the hydroalumination reaction. It is worth noting that the double bonds in oxabicyclic compounds with an *endo* alkoxide function at C_3 are more reactive toward organolithium reagents providing further support of an *endo* alkoxide activation.[8]

The high regioselectivity of the ring opening of unsymmetrical substrates required an *endo* hydroxyl group at C_3. Moreover, the overreduction following the ring opening observed in some of the symmetrical substrates and the potential of an enantioselective ring opening prompted us to investigate transition metal catalyzed hydroalumination processes.

Ni(COD)$_2$-Catalyzed Reductive Ring Opening (COD = cyclooctadiene). An early study of hydroalumination of alkenes by triisobutylaluminum reported that the most active catalysts are Ti(IV), Zr(IV), and Ni(0), and to a lesser extent, Co(II), Fe(III), and Rh(III).[13] Hydroalumination of olefins by lithium aluminum hydride has traditionally been catalyzed by $TiCl_4$ and $ZrCl_4$.[14] It was also reported that dialkylaluminum hydride addition to olefins are catalyzed by titanium and nickel.[15]

Several metals including nickel, titanium, and zirconium were examined for their ability to catalyze the hydroalumination. A D_2O quenching experiment was performed after treating sub-

(11) Lenox, R. S.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1973**, *95*, 957.

(12) Keay also showed that excess DIBAL-H in CH_2Cl_2 leads to the regioselective ring opening of an oxabicyclic substrate to give a ring-opened product in 28% yield, see: Woo, S.; Keay, B. A. *Tetrahedron Lett.* **1992**, *33*, 2661.

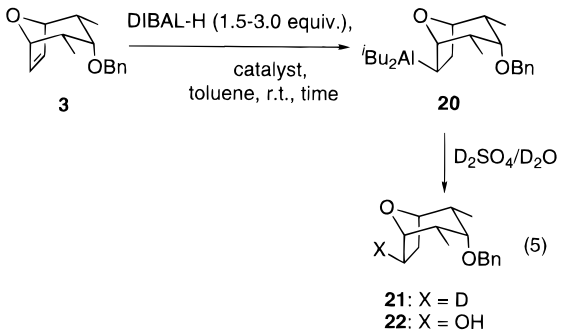
(13) Asinger, F.; Fell, B.; Janssen, R. *Chem. Ber.* **1964**, *97*, 2515.

Table 3. Survey of Metals for Catalysis of Hydroalumination

entry	catalyst (mol %)	reaction time[a]	yield (%)	D (%)[b]
1	Cp_2ZrCl_2 (5)	12 h	0	
2	Cp_2TiCl_2 (10)	1 h	57	65
3	Cp_2TiCl_2 (60)	45 min	70	45
4	$Ni(acac)_2$ (10)	15 min	77	74
5	$Ni(acac)_2$ (60)	7 min	88	20
6	$Ni(COD)_2$ (10)	30 min	67	83
7	$Ni(COD)_2$ (60)	7 min	75	83

[a] Reaction time of the metal-catalyzed hydroalumination before workup. [b] Deuterium incorporation in the product as analyzed by ^{1}H NMR.

strate **3** with DIBAL-H and a fixed amount of catalyst in toluene at room temperature (eq 5). The deuterium incorporation in



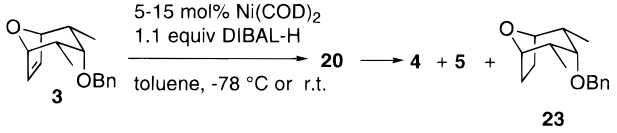
(5)

the product **21** was determined by ^{1}H NMR and was used as a measure of the efficiency of the catalyst and the integrity of the C−Al bond (Table 3). Exposure of the organoalane **20** to oxygen gave the *exo* alcohol **22** in 42% yield, and this was assumed to correlate to the stereochemistry of the hydroalumination step.[16]

Hydroalumination of **3** using a zirconium complex failed which was consistent with Negishi's observation that catalytic Cp_2ZrCl_2 does not accelerate hydroalumination.[17] Cp_2TiCl_2 and $Ni(acac)_2$ both gave moderate levels of **21** using 10 mol % of catalyst (entries 2 and 4), and increasing the amount of Cp_2TiCl_2 or $Ni(acac)_2$ led to lower deuterium incorporation (entries 3 and 5). These experiments indicated that the hydroaluminated intermediate was protonated under the reaction conditions before the D_2O quench, and the extent of this internal protonation depended on the amount of catalyst used. By whatever pathway quenching occurs, it decreases the amount of hydroaluminated substrate available to undergo ring opening to the desired product. In contrast, high levels of deuterium incorporation were consistently obtained with either high or low levels of $Ni(COD)_2$ (entries 6 and 7). $Ni(COD)_2$ was identified as the catalyst of choice for effecting the hydroalumination step in the overall reductive ring opening.

Hydroalumination of oxabicyclic alkenes occurs at temperatures as low as −78 °C in the presence of $Ni(COD)_2$ (Scheme 1). Reaction of **3** with 1.1 equiv of DIBAL-H in the presence of 5−15 mol % of $Ni(COD)_2$ is complete within a few minutes at room temperature, whereas reaction of **3** with 5 equiv of DIBAL-H in the absence of nickel required extended heating at 50−70 °C. The organoalane **20** was converted to the ring-opened product **4** in one of two ways. Simply heating a solution of **20** at 70 °C for 12−16 h led to a mixture of **4**, **5**, and **23**. Much better results were obtained when **20** was heated in the presence of a Lewis acid. Diisobutylaluminum chloride (DIBAL-Cl, 5 equiv) was the most efficient and gave **4** in 76% yield, with minimal formation of **5** (<5%) arising from hydroalumination of **4**.

Scheme 1



An example of the dramatic improvement in the efficiency of the nickel catalyzed hydroalumination is illustrated in the reaction of an unsubstituted oxabicyclic compound **24** (Scheme 2).[7] Using 5 equiv of DIBAL-H in the absence of catalyst, a 1:1 mixture of the cycloheptene diol **25** and cycloheptane diol **26** was obtained. Addition of nickel avoided the formation of the alkane **26** but the ring opening was inefficient and an equimolar amount of **27** was isolated. However, the combination of a nickel catalyst and DIBAL-H then DIBAL-Cl gave **25** in 85% yield with only a trace of **27** which was easily separated.

Effect of Phosphine Ligands on the Ring Opening of Unsymmetrical Oxabicyclic Substrates. We had demonstrated that nickel(0)-catalyzed hydroalumination of oxabicycles clearly offered advantages over the noncatalyzed reaction, but several issues needed to be probed, including the regioselectivity of the ring opening in the case of unsymmetrical oxabicyclic compounds. We found that with substrates lacking a bridgehead substituent the hydroalumination of the alkene occurred readily but the subsequent ring-opening step had to be carried out in the presence of a Lewis acid and heat as mentioned above. Conversely, ring opening occurred spontaneously for the unsymmetrical substrates bearing a substituent on the bridgehead position even though the initial rate of the hydroalumination was reduced compared to that of the unsubstituted substrate (Table 4). We observed that unsymmetrical oxabicycles **14** and **18** afforded two regioisomers in good yields under noncatalyzed hydroalumination conditions with a preference for the tertiary alcohols (entries 1 and 3). A greater proportion of product "**a**" was isolated in the presence of 10 mol % of $Ni(COD)_2$, but the yield was unacceptably low and a product analogous to a "hydrogenation" of the starting material was obtained (entries 2 and 4). (note in entry 2 the reaction still favors "**b**").

The effect of adding ligands to the nickel-catalyzed reductive ring opening was examined next. Eisch noted that the addition of phosphines to the nickel-catalyzed hydroalumination of a substituted indene significantly enhances the regioselectivity of the reaction (Scheme 3).[15c] Presumably, the reaction proceeds *via* initial hydronickelation in which the hydride is delivered to the more hindered site, and the more sterically encumbered metal species resides in the more accessible position. However, electronic effects also favor this regioisomer since formation of a benzylnickel species should be preferred over an alkylnickel compound.

Of the monodentate ligands examined (Ph_3P, Cy_3P (Cy = cyclohexyl), $(o\text{-tolyl})_3P$ and $(i\text{-PrO})_3P$), Ph_3P was found to give the highest regioselectivity for isomer **a**. However, the presence of the ligand was detrimental to the reaction rate, and a higher ratio of nickel catalyst (31 mol %) to substrate was required (Table 4, entry 5). We wondered if the excess DIBAL-H which was present in the reaction mixture reacted with the catalyst slowly to terminate the catalytic cycle.[15d] Thus, if we could

(14) (a) Sato, F.; Sato, S.; Kodama, H.; Sato, M. *J. Organomet. Chem.* **1977**, *142*, 71. (b) Isagawa, K.; Tatsumi, K.; Otsuji, Y. *Chem. Lett.* **1976**, 1145.

(15) (a) Asinger, F.; Fell, B.; Theissen, F. *Chem. Ber.* **1967**, *100*, 937. (b) Fischer, K.; Jonas, K.; Misbach, P.; Stabba, R.; Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 943. (c) Eisch, J. J.; Fichter, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 6815. (d) Eisch, J. J.; Sexsmith, S. R.; Fichter, K. C. *J. Organomet. Chem.* **1990**, *382*, 273.

(16) The catalyst used in this experiment was $Ni(acac)_2$.

(17) Negishi, E.; Yoshida, T. *Tetrahedron Lett.* **1980**, *21*, 1501.

Scheme 2

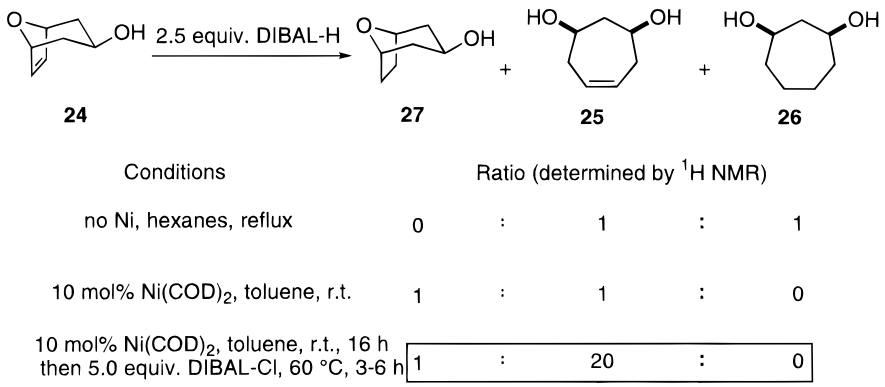
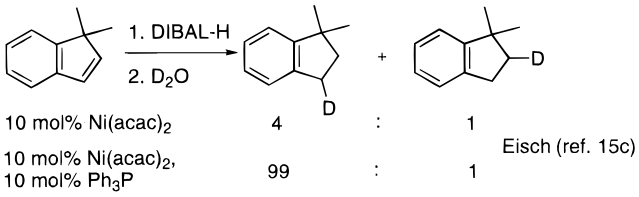


Table 4. Reductive Ring Opening of **14** and **18** Under Catalyzed and Noncatalyzed Conditions

entry	substrate	reaction conditions[a]	ratio **a**/**b**[b]	yield (%)[c]
1	**14**	*d*	**15a/15b** 1:6.4	72
2	**14**	10 mol % Ni(COD)$_2$	**15a/15b** 1:2.0	24
3	**18**	*d*	**19a/19b** 1:1.3	75
4	**18**	10 mol % Ni(COD)$_2$	**19a/19b** 4.8:1	38
5	**18**	31 mol % Ni(COD)$_2$, 62 mol % Ph$_3$P	**19a/19b** 7.0:1	58
6	**18**	10 mol % Ni(COD)$_2$,[e] 20 mol % Ph$_3$P	**19a/19b** 19:1	71

[a] DIBAL-H (1.2 equiv) used for **14**, 2.5 equiv of DIBAL-H used for **18**, toluene, otherwise specified. [b] Determined by GC or 400 MHz ^{1}H NMR. [c] Isolated yield. [d] DIBAL-H (5.5 equiv) hexanes. [e] DIBAL-H was added over 3 h.

Scheme 3



decrease the amount of DIBAL-H relative to the catalyst in the reaction, then the catalyst should be active until the starting material was fully consumed. Indeed, when the DIBAL-H was added to the mixture slowly *via* a syringe pump, 10 mol % of Ni(COD)$_2$ and 20 mol % of phosphine was sufficient and the product was isolated in 71% yield with even higher regioselectivity (Table 4, entry 6). A most remarkable observation was that the intermediate from hydroalumination was not detected under the slow addition conditions. We have previously noted a similar relationship between the rate of addition of DIBAL-H and the enantiomeric excess in a study on enantioselective ring opening reactions.[10]

Tolman and co-workers have shown that Ni(Ph$_3$P)$_4$ dissociates in solution and the equilibrium existing between Ni(Ph$_3$P)$_4$ and Ni(Ph$_3$P)$_3$/Ph$_3$P lies entirely on the side of the tricoordinate nickel species.[18] We varied the ligand/nickel ratio in order to explore the effect on the regioselectivity of the reaction. The alcohol **18** was chosen as the model compound and a set of typical reaction conditions was established (Table 5). Different amounts of triphenylphosphine were transferred to 10 mol % of Ni(COD)$_2$ in toluene (0.1 M) and the mixture was stirred for 1 h at room temperature. The oxabicyclic alcohol **18** was premixed with 1.2 equiv of DIBAL-H and the resulting alkoxyalane was transferred to the Ni(COD)$_2$/Ph$_3$P solution. Another 1.3 equiv of DIBAL-H was then added over 1−3 h *via* a syringe pump, and the reaction was worked up after 16 h at room temperature. The regioselectivity increased when the

(18) Tolman, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 2956.

Table 5. The Effect of the Ph$_3$P/Ni Ratio on the Regioselectivity of Reductive Ring Opening of **18**

entry	equiv of Ph$_3$P (based on Ni(COD)$_2$)	ratio **19a/19b**[a]	yield (%)
1	0	83:17	38[b]
2	1	88:12	66[c]
3	2	95:5	71[b]
4	3	96.6:3.4	74[b]
5	4	98:2	75[b]
6	5	98:2	50[c]

[a] Ratio was determined by GC (carbowax column). [b] Isolated yield. [c] GC yield.

triphenylphosphine/nickel ratio increased, and the optimum yield and regioselectivity was reached when 4 equiv of triphenylphosphine per nickel were used (entries 2−5). Additional triphenylphosphine did not affect the regioselectivity, although the yield was sharply decreased (entry 6). Surprisingly, commercially available Ni(Ph$_3$P)$_4$ under the same reaction conditions was less regioselective (**19a**/**19b** 45:55) and gave a lower yield (37%) along with a major byproduct arising from hydrogenation of the starting material.

Given that different phosphines have different steric and electronic properties, the nature of the phosphine was expected to play a crucial role in the selectivity of the reaction.[19] We briefly looked at bidentate phosphines. When 2.0 equiv of dppe (dppe = 1,2-bis(diphenylphosphino)ethane) were added to the reaction, no reaction occurred. In contrast, 2.0 equiv of dppb (dppb = 1,4-bis(diphenylphosphino)butane) gave even higher regioselectivity (**19a**/**19b** 99.6:0.4) and yield (82%) than Ph$_3$P.[20] To date, dppb is the most effective ligand in regioselective ring opening of oxabicyclic compounds we have found.

Scope and Limitations of the Nickel Catalyzed Regioselective Ring Opening. A series of oxabicylic substrates were examined, and the results are summarized in Table 6. The methyl and TBDMS (TBDMS = *tert*-butyldimethylsilyl) ethers, **28** and **14**, respectively, underwent ring opening, demonstrating that the presence of the free hydroxyl group is not a requirement for high selectivity (entries 1 and 2). For some substrates we found that the time of addition of DIBAL-H to the reaction with **28** could be shortened to 10 min without significant deterioration in the regioselectivity. However, a longer addition time (2 h) was necessary to ensure high regioselectivity in the opening of substrate **14**.

The reaction is also sensitive to the nature of the bridgehead substituent. The methyl- and phenyl-substituted compounds

(19) Tolman, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 2953.

(20) We found that the bidentate chiral ligand BINAP, which also has four carbons between the two phosphine atoms, gave the best ee in the asymmetric ring opening of oxabicyclic[2.2.1] substrates. See: ref 10.

(21) Lautens, M.; Klute, W. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 442.

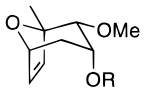
Table 6. Nickel-Catalyzed Reductive Ring-Opening Reactions

Entry	Substrate	Products[a]		Yield[b] (ratio **a**:**b**)
1	**28**, X=Y=R=Me	**29a**	**29b**	80%(380:1[c])
2	**14**, X=Y=Me, R=TBS	**15a**	**15b**	76%(>49:1[d])
3	**30**, X=R=H, Y=Me	**31a**	**31b**	72%(167:1[c])
4	**32**, X=Me, Y=Ph, R=H	**33a**	**33b**	93%(>49:1[d])
5	**34**, X=Me, Y=TMS, R=H	**35a**	**35b**	No reaction
6	**36**, X=Me, Y=^{t}Bu, R=H			No reaction
7	**37**	**38a**	**38b**	82%(19:1[d])
8	**39**	**40a**	**40b**	78%(39:1[c])
9	**41**	**42a**	**42b**	88%(>49:1[d])

[a] Typical conditions: 10 mol % $Ni(COD)_2$, 20 mol % dppb, 1.2−3.0 equiv of DIBAL-H, toluene. [b] Isolated yield of the major regioisomer. [c] Ratio determined by GC. [d] Ratio determined by ^{1}H NMR.

undergo highly regioselective ring opening in excellent yield (entries 1, 2, and 4), whereas the trimethylsilyl-substituted **34** was much less reactive under the standard $Ni(COD)_2$/dppb reaction conditions (entry 5). Only when 100 mol % of $Ni(COD)_2$ and 5.0 equiv of DIBAL-H were employed did **34** react to give **35a** and **35b** in a 1.3:1 ratio and in 82% yield. It is interesting to note that in the absence of ligand the two regioisomers were still formed in an approximately 1:1 ratio but the conversion was low. When the bridgehead group was increased in size to *tert*-butyl (entry 6), no ring opening was observed regardless of the amount of $Ni(COD)_2$, of the Ni/P ratio, or when a smaller hydrometalation agent such as Et_2AlH was used. Clearly there is a maximum size of the substituent which can be accommodated at the bridgehead.

Under the reaction conditions, the tricyclic compound **37** (entry 7) gave the bicyclic diol **38a** as the major product (19:1) in high yield. Oxabicyclic[2.2.1] substrates with *exo* or *endo* substituents (**39** and **41**) undergo the ring opening and the trisubstituted cyclohexenols are obtained in good yields with excellent regioselectivities (entries 8, 9). Reactions with oxabicyclic[3.2.1] systems normally required several hours to go to completion, but the reaction of oxabicyclo[2.2.1] compounds was complete as soon as the final portion of DIBAL-H was added. When the oxygenated substrate **43** and the corresponding silyl ether **44** were subjected to the reaction conditions, complex mixtures were obtained (eq 6). The isolated product was less polar than the starting material and lacked a methoxy group which was somehow eliminated during the reaction conditions.



(6)

43 R = H
44 R = TBDMS

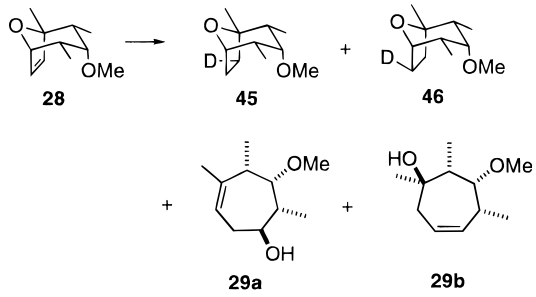
In order to shed light on the reaction pathway, we conducted several deuterium quenching experiments with substrate **28** (Table 7). When DIBAL-H was added to **28** in the presence of $Ni(COD)_2$ in the absence of a phosphine ligand (entries 1 and 2), **45** and **46** were obtained in a combined 76% yield, and the ring-opened products were obtained in 18% combined yield after 5 min (entry 1). Under these conditions, isomer **29a** was the major ring-opened product. Deuterium incorporation in the oxabicyclic alkanes was 94%, and the major regioisomer was **46** (**46**/**45** = 6.8:1). If the reaction was stirred for 3 days prior to the deuterium quench, the ring-opened products were obtained in 39% yield in a ratio of 2.7:1 favoring **29b** (entry 2). When the reaction was conducted in the presence of dppb (with fast addition of DIBAL-H), a low yield of **45** + **46** was obtained (i.e., less than the mole percent of the catalyst used) (entries 3 and 4). In comparison with the ligand-free experiment, the presence of the ligand significantly decreased the rate of hydrometalation (<5% starting material remaining *vs* 73%, entries 1 and 3) but the ratio of ring-opened product to hydrometalated product increased (18:76 *vs* 20:5). The regioselectivity of the ring-opened products was much higher in the presence of the ligand (68:1 *vs* 6.5:1) but still lower than that obtained when the reaction was run under the "optimized" conditions (entry 4). More surprisingly, the regioselectivity of the deuterated products was modest and opposite to that expected based on the final product (1:2.9 and 1:6.8 for **45**/**46** *vs* 6.5:1 and 68:1 for **29a**/**29b**)! In all cases the amount of **45** isolated was relatively small, implying that the organoalane that leads to **45** undergoes fast opening once it is formed.

Among the issues these experiments were designed to address were the following: Does the major reaction pathway occur by a net hydrometalation−elimination sequence, and if so, is the reaction a hydronickelation-reductive elimination or an aluminonickelation−reductive elimination? Is the reaction pathway the same for all substrates? Is the mechanism the same when a ligand is present? Why are the major products from the regioselective ring opening those containing a more substituted olefin which implies that the hydride added to the carbon which is adjacent to a more substituted carbon?

The mechanistic pathways we considered are illustrated Scheme 4: (1) a Lewis acid induced weakening or cleavage of the bridging C−O bond to give **47** (X = Ni−H or H) followed by inter- or intramolecular hydride delivery, (2) hydronickelation to form **48** followed by β-elimination of the bridging oxygen or reductive elimination of nickel(0) from a C−Ni−Al species, (3) aluminonickelation to form **49** followed by reductive elimination of nickel(0) from a C−Ni−H species. Complicating this discussion is the uncertainty surrounding the intermediacy of aluminonickel hydrides and the possibility that nickel does not insert into the Al−H bond.[22] We are currently unable to resolve this latter issue, and the discussion which follows will assume that a nickel hydride species of some type is formed during the reaction.

(22) Pörschke, K.-R.; Kleimann, W.; Tsay, Y.-H.; Krüger, C.; Wilke, G. *Chem. Ber.* **1990**, *123*, 1267.

Table 7. Trapping Experiments for Substrate **28**

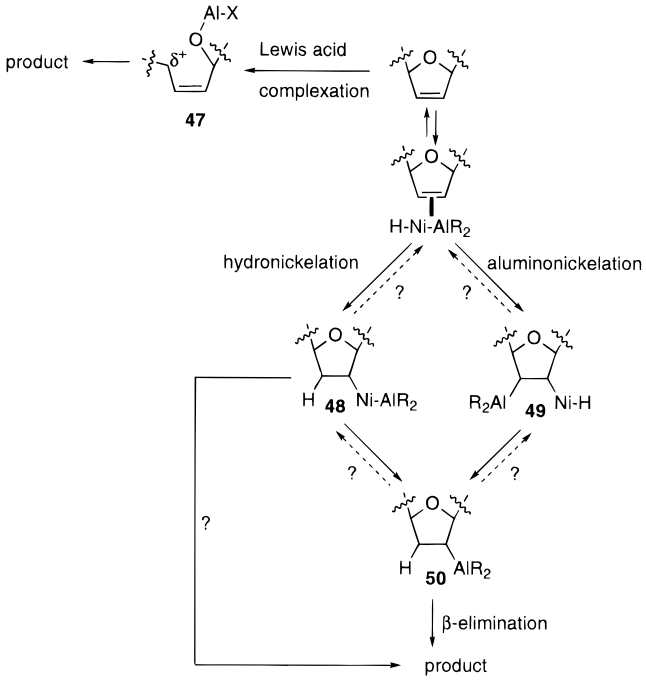


28 **45** **46** **29a** **29b**

Entry	Conditions[a]	**28**[b]	Ratio[c] **45** : **46** (Yield[b])	% D[d]	Ratio[b] **29a** : **29b** (Yield[b])
1	no phosphine 5 min	0	1 : 6.8 (76%)	94	6.5 : 1 (18%)
2	no phosphine 3 d	0	-- (38%)	0	1 : 2.7 (39%)
3	20 mol% dppb 5 min	73	1 : 2.9 (5%)	86	68 : 1 (20%)
4	20 mol% dpp[e]	0	--	--	380 : 1 (80%)

[a] Conditions: 10 mol % $Ni(COD)_2$ with or without dppb, 1.1 equiv of DIBAL-H added over 10 min, toluene. After the time indicated, the reaction was quenched with 10% D_2SO_4/D_2O. [b] GC yield. [c] Ratio determined by ^2H NMR after isolation of **45** and **46**. [d] Percentage of deuterium incorporation in **45** and **46** was determined by ^1H NMR. [e] The reaction was stirred for 16 h after the addition was complete.

Scheme 4



The isolation of **45**/**46** and **29a**/**29b** and the increase in the yield of **29a**/**29b** over time (Table 7, entries 1 and 2) suggest that a two-step process involving formation of **50** is one pathway that can occur and is certainly the major pathway when DIBAL-H is added quickly. However, the rate at which the β-elimination of the aluminum alkoxide occurs is clearly influenced by the substrate, the position of the aluminum relative to the bridgehead, and the reaction conditions. Ring opening of the hydroaluminated product can be slow, and Lewis acid is then required for substrates which lack bridgehead substituents. When a substituent is placed at the bridgehead position and a phosphine ligand is present, it is often difficult to observe the hydrometalated species which suggests that either the β-elimination is now much faster or that the reaction takes a different course (i.e., *via* **47** or from **48** directly to the product). The ratio of regioisomeric products is significantly altered by the combination of the nickel catalyst and phosphine ligand, clearly demonstrating that the metal, ligand, and substrate are all present at the regioselectivity-determining step. The most perplexing result is the preference for **46** at the hydrometalation stage but the preference for **29a** at the ring-opening stage. One possibility is that the organoalane which when quenched gives **45**, eliminates very rapidly compared to the regioisomer alane. It is also possible that the metalation is reversible.

The selective formation of regioisomers of type "**a**" in Table 6 in the presence of the ligand can be explained by an aluminonickelation, which would position the less bulky dialkylaluminum proximal to the bridgehead and the bulky hydridophosphinonickel distal to the bridgehead, or an electron deficient aluminum species which complexes to the bridging oxygen and weakens the C−O bond to form the more-stabilized allylic cation. The change in regioselectivity as a function of phosphine implies the former scenario is occuring, since it is difficult to explain why the regioselectivity would improve in the presence of increasing amounts of phosphine if the triggering event is cleavage of the bridging C−O bond prior to delivery of the hydride moiety. The question of reversibility has not been proven but a reversible hydronickelation and preferential elimination of the minor regioisomer would also explain the results we have observed.

In conclusion, we have demonstrated that DIBAL-H in the presence of nickel catalyst is effective in the reductive ring opening of oxabicyclic compounds and the use of phosphine ligands significantly enhances the regioselectivity in the reaction of unsymmetrical substrates. This methodology, combined with the oxidative cleavage reactions of the cycloheptene or cyclohexene, provides a route to acyclic compounds with synthetically useful arrays.

Experimental Section

(1*S,5*S**,6*S**,7*R**)-6-(Benzyloxy)-5,7-dimethylcyclohept-3-en-1-ol (4) and (1*S**,2*R**,3*S**,4*S**)-3-(Benzyloxy)-2,4-dimethylcycloheptan-1-ol (5). (A) Excess DIBAL-H.** DIBAL-H (neat, 0.23 mL, 1.3 mmol) was added dropwise at 0 °C to a solution of **3** (47.8 mg, 0.19 mmol) in hexanes (1.4 mL). The clear solution was heated at reflux for 6.5 h, and the reaction was quenched. Workup yielded a yellow oil which was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to afford **4** (24.1 mg, 50%) and **5** (12.9 mg, 27%). For **4**: white crystals; mp 53−54 °C; IR (CCl_4) 3634, 3027, 2965, 2935, 2877, 1455, 1344, 1155, 1108, 1099, 1066, 1027, 944 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31 (5H, m), 5.71 (1H, dddd, J = 10.4, 6.1, 5.4, 2.3 Hz), 5.43 (1H, dd, J = 10.5, 4.4, 1.2 Hz), 4.66 (2H, s), 3.57 (1H, td, J = 9.2, 4.8 Hz, 1H), 3.48 (1H, d, J = 2.5 Hz), 2.60 (1H, m), 2.39 (1H, ddd, J = 14.3, 13.0, 3.7 Hz), 2.31 (1H, dddd, J = 14.3, 6.6, 1.9, 1.4 Hz), 1.81 (1H, dqd, J = 9.5, 6.8, 2.6 Hz), 1.48 (1H, exchanges with D_2O, s), 1.20 (3H, d, J = 6.9 Hz), 1.18 (3H, d, J = 7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.3, 136.1, 128.1, 127.2, 127.1, 125.4, 86.2, 75.4, 70.2, 49.6, 38.9, 37.4, 20.8, 17.5.; HRMS calcd for $C_{16}H_{22}O_2$ 246.1620, found 246.1627. Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.98; H, 9.28. For **5**: colorless oil; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31 (5H, m), 4.66 (2H, s), 3.63 (1H, m), 3.43 (1H, s), 2.00 (1H, m), 1.60 (7H, m), 1.29 (1H, s), 1.22 (3H, d, J = 6.9 Hz), 1.03 (3H, d, J = 6.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.8, 128.2, 127.1, 126.8, 88.6, 75.9, 75.7, 46.6, 40.0, 36.7, 32.7, 22.2, 21.3, 19.8.

(B) One Equivalent of DIBAL-H. DIBAL-H (0.52 mL, 2.97 mmol) was added dropwise at 0 °C to a solution of **3** (724 mg, 2.97 mmol) in hexanes (29.7 mL). The clear solution was heated at reflux for 3.5 h, and the reaction was quenched. Workup yielded a yellow

oil which was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to afford cycloheptenol **4** (470.2 mg, 65%) and 180.1 mg of starting material.

(C) Nickel-Catalyzed DIBAL-H Addition. To $Ni(COD)_2$ (2.6 mg, 0.0095 mmol) was added **3** (23.0 mg, 0.094 mmol) in toluene (0.9 mL), and then DIBAL-H (0.14 mL, 0.78 mmol) was added dropwise. The progress of the reaction was followed by TLC. The starting material was consumed after 30 min. To the reaction mixture was added 2.0 mL of dry hexanes, followed by DIBAL-Cl (0.1 mL, 0.51 mmol). The reaction mixture was heated at reflux for 2 h. The reaction was quenched by the addition of saturated NH_4Cl aqueous solution, and then enough 10% H_2SO_4 was added to make the aqueous layer transparent. The organic layer was separated, and the aqueous layer was extracted three times with ether and two times with ethyl acetate. The combined organics were dried over $MgSO_4$. Removal of the solvent *in vacuo* yielded a product mixture that was purified by chromatography with 10% EtOAc in hexanes to afford **4** (18.3 mg, 76%).

General Procedure for the Reductive Opening of Oxabicyclic Substrates Using DIBAL-H. The substrate was dissolved in hexane (0.1 M solution), and the solution was cooled to 0 °C prior to addition of 6.0 equiv of neat DIBAL-H. The ice bath was then removed, and the reaction mixture was heated to reflux. When the reaction was complete, the reaction mixture was diluted with ether and cooled to 0 °C and the reaction was quenched with a saturated solution of NH_4Cl. Fifteen minutes of stirring at room temperature produced a white gel which was dissolved by the dropwise addition of 10% H_2SO_4. The organic layer was separated, and the aqueous layer was extracted three to five times with ethyl acetate. The combined organics were dried over $MgSO_4$, and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography on silica gel.

(1*S,3*S**)-Cyclohept-5-ene-1,3-diol (7).** Alcohol **6** (31.1 mg, 0.25 mmol) was suspended in dry hexanes (2.2 mL) (**6** was not completely soluble in hexanes). DIBAL-H (neat, 0.26 mL, 1.5 mmol) was added dropwise at 0 °C. The cloudy mixture was heated to reflux. After warming, the reaction mixture became a colorless solution. The reaction was heated at reflux overnight. The crude oil obtained upon workup was purified by chromatography with 80% EtOAc/hexanes to give an inseparable 4:1 mixture of **7** and the corresponding overreduced product totaling 25.3 mg. The yield of **7** was calculated to be 64%. Spectral data for the mixture: white solid; IR (nujol) 3295, 3019, 2930, 2908, 1376, 1363, 1336, 1296, 1249, 1052, 1031 cm^{-1}. For **7**: ^1H NMR (200 MHz, $CDCl_3$) δ 5.77 (2H, m), 4.00 (2H, m), 2.39 (4H, m), 2.06 (2H, t, $J = 5.5$ Hz), 1.62 (2H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 128.6, 65.6, 47.8, 36.1; HRMS calcd for $C_7H_{10}O$ $(M - H_2O)^+$ 110.0732, found 110.0732.

(1*S,2*R**,3*S**,4*S**)-2,4-Dimethylcyclohept-5-ene-1,3-diol (9).** To **8** (46.8 mg, 0.304 mmol) in dry hexanes (2.7 mL) was added DIBAL-H (neat, 0.32 mL, 1.8 mmol) at 0 °C. The reaction mixture was heated at reflux for 12 h. The crude oil obtained upon workup was separated with 20% EtOAc/hexanes to afford **9** (39.5 mg, 83%) and 5.0 mg of the corresponding overreduced product (10%). For **9**: white crystalline solid; mp 64−65 °C; IR (CCl_4) 3634, 3607, 3581, 2967, 2934, 2899, 2880, 1459, 1444, 1375, 1194, 1156, 1070, 1027, 968, 960, 939 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.88 (1H, dddd, $J = 10.3$, 8.3, 5.4, 2.6 Hz), 5.32 (1H, dddd, $J = 10.3$, 4.1, 2.4, 1.0 Hz), 3.46 (1H, d, $J = 7.0$ Hz), 3.36 (1H, ddd, $J = 9.3$, 9.3, 3.2 Hz), 2.62 (1H, qm, $J = 7.2$ Hz), 2.38 (1H, ddd, $J = 14.1$, 8.4, 3.2 Hz), 2.32 (1H, ddddd, $J = 14.1$, 9.3, 5.4, 2.3, 1.1 Hz), 1.67 (1H, br, exchanges with D_2O), 1.66 (1H, dqd, $J = 9.3$, 6.9, 2.4 Hz), 1.30 (1H, br d, $J = 9.8$ Hz, exchanges with D_2O), 1.18 (3H, d, $J = 7.3$ Hz), 1.16 (3H, d, $J = 6.8$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 135.4, 128.7, 78.3, 68.8, 49.8, 38.4, 37.6, 20.4, 17.6; HRMS calcd for $C_9H_{14}O$ $(M - H_2O)^+$ 138.1045, found 138.1041. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.81; H, 10.18.

(1*S,3*S**)-1,5-Dimethylcyclohept-5-ene-1,3-diol (11).** To **10** (46.0 mg, 0.299 mmol) in dry hexanes (2.6 mL) was added DIBAL-H (neat, 0.32 mL, 1.8 mmol) at 0 °C. The colorless and transparent solution was allowed to reflux overnight. The crude product obtained upon workup was separated with 20−30% EtOAc/hexanes to afford **11** (41.7 mg, 89%). For **11**: colorless oil; IR (neat) 3400−3200, 2964, 2925, 2880, 2845, 1452, 1434, 1376, 1328, 1261, 1239, 1113, 1084, 1031, 1003, 910, 867 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.41 (1H, m), 3.76 (1H, ddddd, $J = 10.7$, 10.5, 4.4, 3.3, 2.6 Hz), 2.45 (1H, ddm, $J = 13.7$, 10.5 Hz), 2.21 (4H, m), 1.81 (3H, dd, $J = 1.6$, 1.5 Hz), 1.66 (1H, dd, $J = 13.1$, 10.7 Hz), 1.24 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.2, 121.0, 70.7, 65.3, 54.4, 43.3, 39.9, 31.7, 26.3; HRMS calcd for $C_8H_{13}O_2$ $(M - CH_3)^+$ 141.0916, found 141.0925.

(1*R,5*S**,6*R**)-5,6-Bis(benzyloxymethyl)cyclohex-3-enol (13).** To **12** (43.3 mg, 0.129 mmol) in freshly distilled ether (1.2 mL) was added DIBAL-H (neat, 0.07 mL, 0.39 mmol) at 0 °C. The reaction mixture was heated at reflux overnight. The reaction was not complete; therefore, another 0.07 mL (0.39 mmol) of DIBAL-H was added at 0 °C. It was heated at reflux for 4 h. The crude product obtained upon workup was purified by chromatography with 10−20% EtOAc/hexanes to give **13** (34.8 mg, 80%). For **13**: colorless oil; IR (neat) 3419, 3026, 2908, 2875, 2865, 1496, 1454, 1363, 1214, 1095, 1075, 1028, 736, 697 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.30 (10H, m), 5.68 (1H, ddd, $J = 9.9$, 6.2, 3.4 Hz), 5.52 (1H, dm, $J = 9.9$ Hz), 4.49 (1H, d, $J = 12.1$ Hz), 4.44 (1H, d, $J = 11.8$), 4.42 (1H, d, $J = 12.1$ Hz), 4.36 (1H, d, $J = 11.8$ Hz), 4.27 (1H, d, $J = 10.0$ Hz, exchanges with D_2O), 3.91 (1H, dtd, $J = 10.0$, 5.2, 2.7 Hz), 3.63 (1H, dd, $J = 9.3$, 7.8 Hz), 3.53 (1H, dd, $J = 9.3$, 7.5 Hz), 3.42 (1H, dd, $J = 9.5$, 4.6 Hz), 3.35 (1H, dd, $J = 9.4$, 4.9 Hz), 2.65 (1H, m), 2.46 (1H, dddd, $J = 7.8$, 7.5, 7.1, 2.7 Hz), 2.31 (1H, dm, $J = 17.9$ Hz), 2.14 (1H, dm, $J = 18.0$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 138.0, 137.5, 128.4, 128.4, 128.0, 127.8, 127.8, 127.7, 127.6, 127.6, 127.0, 125.8, 73.5, 73.3, 69.7, 69.5, 66.8, 39.9, 37.4, 33.6; HRMS calcd for $C_{22}H_{26}O_3$ 338.1882, found 338.1867.

(1*S,5*S**,6*S**,7*R**)-6-(*tert*-Butyldimethylsiloxy)-4,5,7-trimethylcyclohept-3-en-1-ol (15a) and (1*R**,5*R**,6*R**,7*R**)-6-(*tert*-butyldimethylsiloxy)-1,5,7-trimethylcyclohept-3-en-1-ol (15b).** To **14** (23.3 mg, 0.0826 mmol) in hexanes (0.80 mL) was added DIBAL-H (0.08 mL, 0.45 mmol) dropwise at room temperature. The reaction mixture was heated at reflux for 2.5 h, after which the reaction was quenched. The crude oil obtained upon workup was purified by flash chromatography using 5% EtOAc/hexanes to give **15a** (2.3 mg, 10%) and **15b** (14.7 mg, 62%). For **15a**: crystalline solid; mp 44−45 °C; IR (CCl_4) 3629, 2956, 2931, 2857, 2886, 1471, 1462, 1442, 1381, 1257, 1154, 1091, 1073, 1061, 1023, 968, 939, 880, 861, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.42 (1H, tm, $J = 6.0$ Hz), 3.88 (1H, dd, $J = 4.2$, 2.2 Hz), 3.56 (1H, m), 2.42 (1H, qm, $J = 7.1$ Hz), 2.32 (2H, t, $J = 6.1$ Hz), 1.83 (1H, dqd, $J = 8.1$, 7.1, 4.2 Hz), 1.68 (3H, d, $J = 1.1$ Hz), 1.58 (1H, br s), 1.12 (3H, d, $J = 7.3$ Hz), 0.91 (3H, d, $J = 7.2$ Hz), 0.89 (9H, s), 0.06 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 119.6, 75.3, 72.3, 49.2, 44.9, 35.5, 26.0, 23.9, 18.3, 16.3, 16.0, −3.8, −4.4; HRMS calcd for $C_{12}H_{23}O_2Si$ $(M - Bu)^+$ 227.1467, found 227.1469. For **15b**: crystalline solid; mp 81−82 °C; IR (CCl_4) 3617, 3478, 3028, 2931, 2857, 1471, 1462, 1388, 1371, 1253, 1161, 1110, 1051, 1030, 1009, 944, 869, 842 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.71 (1H, dddd, $J = 10.3$, 7.9, 5.9, 2.0 Hz), 5.44 (1H, ddd, $J = 10.3$, 5.2, 1.8 Hz), 3.70 (1H, m), 2.58 (1H, m), 2.43 (1H, ddm, $J = 13.8$, 5.7 Hz), 2.24 (1H, dd, $J = 13.8$, 7.9 Hz), 1.80 (1H, qd, $J = 7.2$, 2,6 Hz), 1.65 (1H, br s), 1.18 (3H, s), 1.13 (3H, d, $J = 7.4$ Hz), 1.07 (3H, d, $J = 7.2$ Hz), 0.89 (9H, s), 0.06 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 125.9, 78.8, 72.7, 52.7, 42.9, 39.4, 26.2, 24.4, 20.0, 18.6, 15.4, −3.3, −4.4; HRMS calcd for $C_{16}H_{31}O_2Si$ $(M - H)^+$ 283.2093, found 283.2113.

(1*S,5S*,6*S**,7R*)-6-(Benzyloxy)-4,5,7-trimethylcyclohept-3-en-1-ol (17a) and (1*R**,5*R**,6*R**,7*R**)-6-(Benzyloxy)-1,5,7-trimethylcyclohept-3-en-1-ol (17b).** To **16** (49.1 mg, 0.19 mmol) in hexanes (1.7 mL) was added DIBAL-H (0.17 mL, 0.95 mmol) dropwise at 0 °C. The reaction mixture was allowed to warm up and then heated to reflux. After 6.5 h, the reaction was quenched. The crude oil obtained upon workup was assessed by GC as a 5.6:1 mixture of **17b** to **17a**. The oil was purified by flash chromatography using 10% ether/hexanes to give 20.9 mg of **17b** and **17a** as a 6:1 mixture (GC analysis) along with 26.1 mg of starting material. This represents a 90% yield of product based on recovered starting material. For **17a**: ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.4, 139.2, 128.2, 127.4, 127.3, 126.9, 120.1, 83.9, 74.1, 72.0, 48.0, 42.2, 36.0, 23.2, 17.2, 16.2. For **17b**: ^1H NMR (200 MHz, $CDCl_3$) δ 7.31 (5H, m), 5.74 (1H, dddd, $J = 10.3$, 8.0, 5.9, 2.2 Hz), 5.49 (1H, ddd, $J = 10.2$, 4.9, 1.8 Hz), 4.66 (2H, s), 3.47 (1H, s), 2.66 (1H, m), 2.38 (1H, ddm, $J = 13.8$, 5.9 Hz), 2.26 (1H, dd, $J = 13.9$, 8.1 Hz), 1.90 (1H, qd, $J = 7.1$, 2.6 Hz), 1.55 (1H, exchanges with

D_2O, br s), 1.20 (3H, s), 1.19 (3H, d, $J = 7.4$ Hz), 1.15 (3H, d, $J = 7.1$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.5, 136.7, 128.2, 127.1, 126.8, 126.3, 86.5, 76.1, 72.6, 52.2, 43.1, 38.6, 23.9, 20.5, 15.0; HR GC/MS of the mixture, major component (**17b**) calcd for $C_{17}H_{24}O_2$ 260.1776, found 260.1765, minor component (**17a**) calcd for $C_{17}H_{24}O_2$ 260.1776, found 260.1774.

(1*S,2*R**,3*S**,4*S**)-2,4,5-Trimethylcyclohept-5-ene-1,3-diol (19a) and (1*R**,2*R**,3*R**,4*R**)-1,2,4-Trimethylcyclohept-5-ene-1,3-diol (19b).** To **18** (42.7 mg, 0.254 mmol) in hexanes (2.0 mL) was added DIBAL-H (0.25 mL, 1.4 mmol) at 0 °C. There was a rapid evolution of gas. The reaction mixture was allowed to reflux overnight. The reaction was worked up, and the crude oil thus obtained was separated with 10% EtOAc/hexanes to give **19a** (14.2 mg, 33%) and **19b** (18.1 mg, 42%). For **19a**: white crystalline solid; mp 68−69 °C; IR (CCl_4) 3645, 3632, 2968, 2944, 2904, 2883, 2879, 1462, 1444, 1380, 1181, 1157, 1088, 1025, 964 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.71 (1H, dddq, $J =$ 8.2, 5.8, 2.0, 1.4 Hz), 3.44 (1H, br d, $J = 5.0$ Hz), 3.28 (1H, br td, $J = 9.7$, 3.7 Hz), 2.79 (1H, qd, $J = 6.6$, 1.8 Hz), 2.36 (1H, dm, $J = 13.8$ Hz), 2.25 (1H, ddd, $J = 13.8$, 8.5, 3.7 Hz), 1.71 (3H, d, $J = 1.0$ Hz), 1.65 (2H, 1H exchanges with D_2O, dqd, $J = 9.6$, 6.8, 2.7 Hz), 1.17 (4H, 1H exchanges with D_2O, d, $J = 6.9$ Hz), 1.13 (3H, d, $J = 6.6$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 122.7, 79.4, 69.6, 50.2, 40.5, 36.9, 22.4, 17.5, 17.3; HRMS calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1307. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.33; H, 10.53. For **19b**: white crystalline solid; mp 68−69 °C; IR (CCl_4) 3646, 2967, 2927, 2880, 2868, 1452, 1375, 1320, 1162, 1142, 1103, 963, 941 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.87 (1H, dddd, $J = 10.4$, 8.2, 5.6, 2.5 Hz), 5.40 (1H, ddd, $J = 10.3$, 4.7, 2.3 Hz), 3.50 (1H, dd, $J = 8.4$, 2.6 Hz), 2.67 (1H, m), 2.43 (1H, ddd, $J = 13.5$, 5.6, 2.2 Hz), 2.23 (1H, dd, $J = 13.6$, 8.6 Hz), 1.77 (1H, qd, $J = 7.1$, 2.5 Hz), 1.33 (1H, exchanges with D_2O, br s), 1.21 (3H, s), 1.15 (3H, d, $J = 6.6$ Hz), 1.13 (4H, 1H exchanges with D_2O, d, $J = 7.0$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 135.4, 129.2, 78.3, 71.8, 51.9, 43.5, 38.1, 23.7, 20.1, 14.6; HRMS calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1300.

To **18** (43.4 mg, 0.26 mmol) in dry hexanes (1.3 mL) was added MeLi (low halide, 1.4 M in Et_2O, 0.29 mL, 0.406 mmol) at 0 °C. There was effervescence, and the formation of a white precipitate was observed. The reaction mixture was warmed with a hot water bath for about 10 min to ensure complete deprotonation. The reaction mixture was then cooled to 0 °C, and DIBAL-H (0.23 mL, 1.3 mmol) was added. No effervescence was observed, but the reaction mixture became slightly cloudy. After the mixture was heated to reflux overnight, another 0.12 mL (0.67 mmol) of DIBAL-H was added, and the reaction mixture was heated to reflux for another night. The crude oil obtained upon workup showed a 9.5:1 selectivity for **19a** to **19b** as assessed by GC. The oil was purified using 10−20% EtOAc/hexanes to give **19a** (32.6 mg, 73%) and **19b** (2.1 mg, 5%).

(1*R,2*S**,3*S**,4*R**,5*S**,6*S**)-3-(Benzyloxy)-2,4-dimethyl-8-oxabicyclo[3.2.1]octane-6-*d*$_1$ (21) and (1*R**,2*S**,3*S**,4*S**,5*R**,6*S**)-3-(Benzyloxy)-2,4-dimethyl-8-oxabicyclo[3.2.1]octan-6-ol (22).** To **3** (51.5 mg, 0.211 mmol) and $Ni(acac)_2$ (4.3 mg, 0.024 mmol) in toluene (1.0 mL) was added DIBAL-H (0.26 mL, 1.0 M in toluene, 0.26 mmol) at room temperature. After 15 min, the starting material was consumed. O_2 was bubbled through the dark brown solution for 25 min. Then, the reaction was worked up by the addition of D_2SO_4/D_2O. The aqueous layer was extracted three times with ether, and the combined organics were dried over $MgSO_4$. The volatiles were removed, and the residue was purified by chromatography with 5% EtOAc/hexanes to afford **21** with **23** (14.6 mg, 29%), **22** (23.3 mg, 42%). For **21** (as a mixture with **23**): oil; IR (CCl_4) 3031, 2953, 2931, 2875, 1496, 1453, 1372, 1359, 1341, 1315, 1193, 1168, 1095, 1068, 1036, 973, 947, 919, 734, 695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.33 (5H, m), 4.50 (2H, s), 4.01 (2H, m), 3.44 (1H, t, $J = 4.0$ Hz), 2.27 (1H, d, $J = 9.8$ Hz), 2.21 (1H, s), 2.09 (2H, m), 1.68 (1H, m), 0.96 (6H, d, $J = 7.2$ Hz); ^2H NMR (60 MHz, $CHCl_3$) d 1.65; ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.2, 128.2, 127.1, 126.8, 80.8, 78.5, 77.2, 75.8, 39.8, 24.5, 24.2 (t), 13.4. For **22**: oil; IR (CCl_4) 3415, 2956, 2935, 2876, 1452, 1372, 1343, 1089, 1066, 1053, 1028, 980, 961, 942, 905, 734, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31 (5H, m), 4.68 (1H, dd, $J = 7.1$, 2.1 Hz), 4.48 (2H, s), 4.15 (1H, dd, $J = 7.8$, 3.4 Hz), 3.85 (1H, d, $J = 3.7$ Hz), 3.41 (1H, t, $J = 4.0$ Hz), 2.89 (1H, dd, $J = 13.2$, 7.0 Hz), 2.04 (2H, m), 1.89 (1H, br d, $J = 6.2$ Hz), 1.52 (1H, ddm, $J = 13.3$, 7.9 Hz), 1.03 (3H, d, $J = 7.3$ Hz), 0.91 (3H, d, $J = 7.2$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 138.7, 128.3, 127.3, 126.9, 87.0, 80.3, 79.1, 75.9, 72.6, 39.0, 38.5, 38.2, 13.2, 13.1.

General Procedure for Survey of Transition Metal Catalysts. A solution of the substrate **3** in toluene was added to the catalyst followed by dropwise addition of DIBAL-H. When the starting material was consumed, the reaction was quenched with D_2SO_4/D_2O. The organic layer was separated from the aqueous layer, which was then extracted three times with ether. The combined organics were dried over $MgSO_4$. Removal of the solvent *in vacuo* yielded a product mixture that was analyzed for deuterium incorporation by ^1H NMR. Integration of the peak at 1.65 ppm was used to assess the deuterium incorporation.

Ni(COD)$_2$ (10 mol %). Following the general procedure, to $Ni(COD)_2$ (4.7 mg, 0.017 mmol) were added **3** (37.4 mg, 0.153 mmol) in 1.0 mL of toluene and then DIBAL-H (neat, 0.04 mL, 0.224 mmol) at −20 °C. After 30 min, the reaction was complete and was quenched with 10% D_2SO_4/D_2O. After workup, extraction, and drying over K_2CO_3, removal of solvent yielded a residue that was separated with 10% Et_2O/hexanes to give **21** and **23** (25.0 mg, 67%). Integration of the ^1H NMR spectrum showed an 83% deuterium incorporation.

***cis*-Cyclohept-5-ene-1,3-diol (25).** DIBAL-H (1.0 M in toluene, 18.23 mL, 18.23 mmol) was added to a solution of **24** (1.0 g, 7.93 mmol) in toluene (12 mL) at 0 °C which led to the rapid evolution of H_2 gas. The resulting pale yellow solution was warmed to room temperature and transferred *via* a cannula to a flask containing $Ni(COD)_2$ (230 mg, 0.84 mmol). The reaction mixture was stirred for 16 h at room temperature. DIBAL-Cl (7.7 mL, 39.44 mmol) was added to the reaction mixture, and the temperature was raised to 60 °C and stirred for an additional 6.5 h. The reaction mixture was cooled to 0 °C, and the reaction was quenched with saturated aqueous NH_4Cl. The aqueous layer was acidified with 10% HCl to pH 3 and saturated with NaCl, and the mixture was extracted with EtOAc 10 times. The combined organic solutions were dried over Na_2SO_4 and concentrated, and the residue was purified by flash chromatography on silica gel (Et_2O to EtOAc) to give **25** (865 mg, 85%) as a white solid: mp 106−107 °C (Et_2O); IR (nujol) 3218, 2907, 1455, 1363, 1005, 955 cm^{-1}; ^1H NMR (200 MHz, CD_3CN) d 5.70 (2H, m), 3.46 (2H, m), 2.51 (2H, br s), 2.21 (5H, m), 1.61 (1H, dd, $J = 20.9$, 10.4 Hz); ^{13}C NMR (50 MHz, CD_3CN) d 129.1, 67.6, 51.6, 37.9; HRMS calcd for $C_7H_{13}O_2$ $(M + H)^+$ 129.0916, found 129.0923. Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.83; H, 9.43.

General Procedure for the Reductive Ring Opening Using Ni(COD)$_2$/dppb. The reaction scale was typically 0.3−0.5 mmol. $Ni(COD)_2$ (0.1 equiv) in toluene (1.0 mL) was added to dppb (0.2 equiv), and the resulting light brown solution was stirred at room temperature for 1 h. Substrates bearing a free hydroxyl moiety were premixed with DIBAL-H (1.0 M in hexanes, 1.1 equiv) in toluene (1.0 mL) to form the aluminum alkoxide. Protected alcohols were dissolved in toluene (1.0 mL) and added directly to the flask containing $Ni(COD)_2$/dppb. DIBAL-H (1.1−1.9 equiv) was added *via* a syringe pump over the indicated time. The reaction mixture was stirred at room temperature overnight and cooled to 0 °C. The reaction was quenched by the addition of saturated aqueous NH_4Cl, and sufficient 10% HCl was added to make the aqueous layer transparent. The organic layer was separated, and the aqueous layer was extracted three times with Et_2O. The combined organics were dried over $MgSO_4$. Removal of the solvent *in vacuo* yielded a product mixture that was purified by chromatography. If the reaction product was a diol, the reaction was quenched by 1.0 mL of 1.1 M Rochelle salt solution. The resulting suspension was stirred at room temperature for 4 h and filtered, and the white gel was washed with hot EtOAc several times. The combined filtrate was dried over Na_2SO_4. Removal of the solvent *in vacuo* yielded a product mixture that was purified by chromatography.

(1*S,2*R**,3*S**,4*S**)-2,4,5-Trimethylcyclohept-5-ene-1,3-diol (19a).** The reaction was carried out as in the general procedure using dppb (23.6 mg, 0.055 mmol) and $Ni(COD)_2$ (7.6 mg, 0.028 mmol). Substrate **18** (46.4 mg, 0.28 mmol) had been premixed with DIBAL-H (1.0 M in hexanes, 0.33 mL, 0.33 mmol). Additional DIBAL-H (0.36 mL, 0.36 mmol) was added *via* a syringe pump over 4 h. The crude product was purified by chromatography on silica gel (6% 2-propanol/CH_2Cl_2) to give a mixture of **19a** and **19b** (38.3 mg, 82%). The ratio of

products was determined by GC (carbowax column, 140 °C, retention time for **19a** 37.25 min, for **19b** 20.65 min) to be a 300:1 mixture of **19a**/**19b**.

(1*S,5*S**,6*S**,7*R**)-6-Methoxy-4,5,7-trimethylcyclohept-3-en-1-ol (29a).** The reaction was carried out as in the general procedure using dppb (45.9 mg, 0.108 mmol), $Ni(COD)_2$ (14.8 mg, 0.054 mmol), and substrate **28** (97.9 mg, 0.54 mmol). DIBAL-H (1.0 M in hexanes, 0.60 mL, 0.60 mmol) was added dropwise over 15 min. The crude product was purified by chromatography on silica gel (50% Et_2O/hexanes) to give **29a** and **29b** (79.6 mg, 80%). The ratio of products was determined by GC (chiral γ-TA column, 135 °C, retention time for **29a** 21.41 min, for **29b** 14.54 and 15.14 min) to be a 380:1 mixture of **29a**/**29b**. An authentic sample of minor regioisomer was prepared by another method.[21] For **29a**: colorless liquid; IR (neat) 3380, 2927, 1445, 1373, 1188, 1097, 1025, 972, 956 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.50 (1H, m), 3.47 (3H, s), 3.43 (1H, m), 3.27 (1H, dd, J = 4.0, 1.5 Hz), 2.64 (1H, dd, J = 15.0, 7.4 Hz), 2.31 (1H, m), 2.23 (1H, ddd, J = 14.6, 8.4, 2.9 Hz), 1.88 (1H, m), 1.72 (3H, s), 1.19 (1H, m), 1.18 (3H, d, J = 7.3 Hz), 1.14 (3H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 120.0, 87.3, 71.4, 61.3, 48.4, 41.4, 36.2, 23.0, 17.5, 16.2; HRMS calcd for $C_{11}H_{20}O_2$ 184.1463, found 184.1458.

(1*S,5*S**,6*S**,7*R**)-6-(*tert*-Butyldimethylsiloxy)-4,5,7-trimethylcyclohept-3-en-1-ol (15a).** The reaction was carried out as in the general procedure using dppb (10.5 mg, 0.025 mmol), $Ni(COD)_2$ (3.4 mg, 0.012 mmol), and substrate **14** (34.9 mg, 0.12 mmol). DIBAL-H (1.0 M in hexanes, 0.15 mL, 0.15 mmol) was added *via* a syringe pump over 2 h. The crude product was purified by chromatography on silica gel (6% EtOAc in hexanes) to give **15a** (26.7 mg, 76%). The reaction product was analyzed by 400 MHz ^1H NMR, and the minor regioisomer **15b** was not detected.

(1*S,3*S**)-5-Methylcyclohept-5-ene-1,3-diol (31a).** The reaction was carried out as in the general procedure using dppb (35.4 mg, 0.083 mmol) and $Ni(COD)_2$ (11.4 mg, 0.041 mmol). Substrate **30** (58.0 mg, 0.41 mmol) was premixed with DIBAL-H (1.0 M in hexanes, 0.45 mL, 0.45 mmol). Additional DIBAL-H (0.58 mL, 0.58 mmol) was added *via* a syringe pump over 1 h. The crude product was purified by chromatography on silica gel (Et_2O) to give a mixture of **31a** and **31b** (42.2 mg, 72%). The ratio of product was determined by GC (carbowax column, 140 °C, retention time for **31a** 36.62 min, for **31b** 20.23 min) to be a 167:1 mixture of **31a**/**31b**. An authentic sample of the minor regioisomer was prepared by a less-selective reaction without dppb. For **31a**: white crystalline solid; mp 77−78 °C (Et_2O); IR (KBr) 3299, 2930, 2896, 1447, 1344, 1297, 1190, 1077, 1045, 1018, 903, 866, 831 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.48 (1H, tm, J = 6.6 Hz), 3.95 (2H, m), 2.34 (2H, m), 2.02 (2H, t, J = 5.7 Hz), 1.96 (2H, br s), 1.77 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 137.7, 120.9, 66.0, 65.5, 48.2, 41.7, 35.6, 26.8; HRMS calcd for $C_8H_{14}O_2$ 142.0994, found 142.0994. Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.74; H, 10.16.

(1*S,2*R**,3*S**,4*S**)-2,4-Dimethyl-5-phenylcyclohept-5-ene-1,3-diol (33a).** The reaction was carried out as in the general procedure using dppb (21.7 mg, 0.051 mmol) and $Ni(COD)_2$ (7.0 mg, 0.025 mmol). Substrate **32** (58.5 mg, 0.26 mmol) was premixed with DIBAL-H (1.0 M in hexanes, 0.26 mL, 0.26 mmol). DIBAL-H (0.51 mL, 0.51 mmol) was added *via* a syringe pump over 6 h. The crude product was purified by chromatography on silica gel (40% hexanes/Et_2O) to give **33a** (55.0 mg, 93%). The ratio of products was >49:1 as determined by integration of the peaks corresponding to the vinylic protons. The minor compound was assumed to be the regioisomer but an authentic sample was not prepared. For **33a**: white solid; mp 98−99 °C (Et_2O); IR (neat) 3408, 2930, 1448, 1383, 1117, 1019, 969, 845, 765, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (5H, m), 5.84 (1H, tm, J = 7.2 Hz), 3.71 (1H, dd, J = 8.4, 2.6 Hz), 3.49 (1H, m), 3.13 (1H, dd, J = 15.0, 7.4 Hz), 2.54 (1H, dd, J = 8.1, 2.2 Hz), 2.53 (1H, d, J = 7.0 Hz), 1.87 (1H, m), 1.72 (1H, br s), 1.62 (1H, br s), 1.24 (3H, d, J = 6.9 Hz), 1.01 (3H, d, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 142.4, 128.3, 127.6, 126.54, 126.49, 77.7, 69.8, 49.4, 41.6, 37.0, 18.7, 17.0; HRMS calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1468.

(1*S,2*R**,3*R**,4*R**)-2,4-Dimethyl-5-(trimethylsilyl)cyclohept-5-ene-1,3-diol (35a) and (1*S**,2*R**,3*R**,4*R**)-2,4-Dimethyl-1-(trimethylsilyl)cyclohept-5-ene-1,3-diol (35b).** To $Ni(COD)_2$ (64.5 mg, 0.23 mmol) was added **34** (53.0 mg, 0.23 mmol) and DIBAL (1.0 M in hexanes, 0.23 mL, 0.23 mmol) in 1.0 mL of toluene. A second portion of DIBAL-H (0.94 mL, 0.94 mmol) was added *via* a syringe pump over 45 min. The reaction mixture was stirred at room temperature for 2 h, and the reaction was quenched by Rochelle salt solution (1.1 M, 3.0 mL). The resulting suspension was stirred at room temperature for 4 h, the organic layer was separated, and the aqueous layer was extracted three times with ethyl acetate. The combined organics were dried over Na_2SO_4. Removal of the solvent *in vacuo* yielded a product mixture that was purified by chromatography on silica gel (50% EtOAc/hexanes) to give a 1.3:1 mixture of **35a** and **35b** (43.8 mg, 82%) as determined by integration of the peaks corresponding to vinylic protons. For **35a**: mp 116−117 °C (50% Et_2O in pentane); IR (CCl_4) 3636, 3578, 2965, 2900, 2882, 1552, 1539, 1460, 1250, 1157, 1034, 1008, 968, 951, 909 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.30 (1H, m), 3.54 (1H, dd, J = 8.8, 2.2 Hz), 3.34 (1H, m), 2.91 (1H, m), 2.47 (1H, d, J = 7.0 Hz), 2.45 (1H, m), 1.75 (1H, qm, J = 7.0 Hz), 1.48 (1H, br s), 1.32 (3H, d, J = 7.3 Hz), 1.15 (3H, d, J = 7.0 Hz), 1.08 (1H, d, J = 9.5 Hz), 0.12 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 139.3, 78.2, 69.4, 49.7, 42.1, 38.4, 19.6, 16.7, 0.7; HRMS calcd for $C_{12}H_{23}O_2Si$ $(M - H)^+$ 227.1467, found 227.1461. Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59. Found: C, 63.32; H, 10.69. For **35b**: mp 73−74 °C (20% Et_2O/pentane); IR (CCl_4) 3592, 2965, 2935, 2899, 1550, 1456, 1374, 1249, 1214, 1165, 1139, 1072, 959 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.67 (1H, m), 5.49 (1H, dm, J = 11.0 Hz), 3.58 (1H, dm, J = 9.0 Hz), 2.89 (1H, br m), 2.56 (1H, dddd, J = 15.4, 5.5, 1.8, 1.1 Hz), 2.34 (1H, dd, J = 15.4, 6.9 Hz), 1.97 (1H, qd, J = 7.3, 3.6 Hz), 1.58 (1H, s), 1.35 (3H, d, J = 9.2 Hz), 1.17 (3H, d, J = 7.7 Hz), 1.12 (1H, d, J = 7.3 Hz), 0.10 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.0, 127.0, 78.7, 70.7, 52.4, 38.7, 36.5, 20.0, 16.8, −1.6; HRMS calcd for $C_{11}H_{21}O_2Si$ $(M - CH_3)^+$ 213.1311, found 213.1319. Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59. Found: C, 63.20; H, 10.54.

(1*S,2*S**,6*R**,9*S**)-5-Methylbicyclo[4.2.1]non-4-ene-2,9-diol (38a).** The reaction was carried out as in the general procedure using dppb (15.2 mg, 0.036 mmol) and $Ni(COD)_2$ (4.9 mg, 0.018 mmol). Substrate **37** (29.6 mg, 0.18 mmol) was premixed with DIBAL-H (1.0 M in hexanes, 0.20 mL, 0.20 mmol). A second portion of DIBAL-H (0.25 mL, 0.25 mmol) was added *via* a syringe pump over 3 h. The crude product was purified by chromatography on silica gel (50% EtOAc/hexanes) to give **38a** and **38b** (24.4 mg, 82%). The ratio of products was determined to be a 19:1 mixture of **38a** to **38b** by integration of the peaks corresponding to vinylic protons. An authentic sample of the minor regioisomer was prepared by a less-selective reaction without dppb. For **38a**: white crystalline needle; mp 134.5−135.5 °C (EtOAc); IR (KBr) 3384, 3302, 2920, 2848, 1446, 1370, 1328, 1300, 1274, 1095, 1075, 1017, 898, 883 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.50 (1H, dm, J = 8.8 Hz), 4.17 (1H, dt, J = 10.6, 7.2 Hz), 4.02 (1H, dm, J = 11.0 Hz), 2.56 (1H, m), 2.44 (1H, t, J = 6.6 Hz), 2.35 (1H, m), 2.20 (1H, dddd, J = 15.0, 9.1, 4.8, 1.2 Hz), 2.02 (1H, m), 1.90 (1H, ddd, J = 13.4, 10.2, 3.3 Hz), 1.80 (1H, d, J = 11.0 Hz), 1.78−1.52 (2H, m), 1.73 (3H, dd, J = 2.5, 1.4 Hz), 1.31 (1H, d, J = 4.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 142.3, 119.7, 76.1, 65.1, 50.2, 45.8, 32.6, 28.1, 27.6, 21.0; HRMS Calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1147. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.82.

(1*R,5*R**,6*R**)-5,6-Bis(methoxymethyl)-4-methylcyclohex-3-en-1-ol (40a).** The reaction was carried out as in the general procedure using dppb (22.0 mg, 0.052 mmol), $Ni(COD)_2$ (7.1 mg, 0.026 mmol), and substrate **39** (51.1 mg, 0.26 mmol). DIBAL-H (1.0 M in hexanes, 0.31 mL, 0.31 mmol) was added dropwise over 15 min. The crude product was purified by flash chromatography on silica gel (75% Et_2O/hexanes) to give a mixture of **40a** and **40b** (40.0 mg, 78%). The ratio of products was determined to be 39:1 mixture of **40a** to **40b** by GC (chiral Supelco column, 155 °C, retention time for **40a** 21.83 min, for **40b** 15.64 and 15.85 min). An authentic sample of the minor regioisomer was prepared by another method.[21] For **40a**: colorless oil; IR (neat) 3429, 2890, 1450, 1190, 1107 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.69 (1H, m), 5.52 (1H, m), 4.25 (1H, d, J = 9.9 Hz), 3.89 (1H, m), 1.57 (1H, dd, J = 9.2, 8.1 Hz), 3.51 (1H, dd, J = 9.2, 7.5 Hz), 3.35 (3H, s), 3.34 (2H, m), 3.33 (3H, s), 2.59 (1H, m), 2.32 (2H, m), 2.15(1H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 126.9, 125.8, 72.1,

66.5, 58.9, 58.8, 39.8, 37.3, 33.6. HRMS calcd for $C_{11}H_{21}O_3$ $(M + H)^+$ 201.1491, found 201.1482.

(1*R,5*S**)-5-(Hydroxymethyl)-4-methylcyclohex-3-en-1-ol (42a).** The reaction was carried out as in the general procedure using dppb (36.6 mg, 0.086 mmol) and $Ni(COD)_2$ (11.8 mg, 0.043 mmol). Substrate **41** (60.0 mg, 0.43 mmol) was premixed with DIBAL-H (1.0 M in hexanes, 0.47 mL, 0.47 mmol). Additional DIBAL-H (0.60 mL, 0.60 mmol) was added dropwise *via* a syringe pump over 30 min. The crude product was purified by flash chromatography on silica gel (Et_2O) to give a mixture of **42a** and **42b** (53.5 mg, 88%). The ratio of products was determined to be >49:1 mixture of **42a** to **42b** using 400 MHz ^1H NMR by integration of the peaks corresponding to the vinylic protons. The minor compound was tentatively assigned to be **42b**, although an authentic sample was not prepared. For **42a**: white solid; mp 58−59 °C (Et_2O); IR (KBr) 3265, 2901, 1495, 1445, 1371, 1343, 1058, 1037, 1017, 982, 951, 862, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.44 (1H, m), 4.10 (1H, m), 3.69 (2H, m), 2.35 (1H, m), 1.96 (1H, m), 1.74 (1H, m), 1.71 (3H, s), 1.55 (1H, br s), 1.35 (1H, br s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 133.0, 122.0, 64.4, 64.0, 41.3, 34.4, 33.9, 21.6.

(1*R,2*R**,3*R**,4*R**,5*S**)-3-Methoxy-1,2,4-trimethyl-8-oxabicyclo-[3.2.1]octane.** To dppb (47.1 mg, 0.111 mmol) was added a solution of $Ni(COD)_2$ (15.2 mg, 0.055 mmol) in 2.0 mL toluene. The resulting light brown solution was stirred at room temperature for 1 h. Substrate **28** (100.6 mg, 0.55 mmol) was added to the flask containing $Ni(COD)_2$/dppb. DIBAL-H (1.0 M in hexanes, 0.61 mL, 0.61 mmol) was added dropwise over 10 min. The reaction mixture was stirred at room temperature for an additional 5 minutes and cooled to 0 °C, and the reaction was quenched by addition of 2.0 mL of 20% D_2SO_4/D_2O. The resulting suspension was stirred at room temperature for 16 h, the organic layer was separated, and the aqueous layer was extracted with Et_2O three times. The combined organic layers were dried over $MgSO_4$, and the volatiles were removed *in vacuo*. The crude mixture was analyzed by GC (γ-TA column): 26% ring opening products and major to minor regioisomer is 68:1, 4.8% hydrogenation product. The hydrogenation product was isolated after the crude mixture was ozonolyzed. The ratio of **45** to **46** was 1:2.9 which was determined by ^2H NMR (1.23 and 1.73 ppm respectively); 86% deuterium incorporation was determined by integration of the corresponding peaks in the ^1H NMR. The spectra of hydrogenation product: colorless oil; IR (neat) 2927, 2825, 1464, 1375, 1342, 1301, 1257, 1216, 1175, 1102, 1077, 1032, 991, 926, 890, 829 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.93 (1H, dd, J = 7.7, 3.3 Hz), 3.32 (3H, s), 3.06 (1H, t, J = 3.7 Hz), 2.20 (1H, ddd, J = 11.7, 9.9, 4.4 Hz), 2.07 (1H, m), 1.99 (1H, qt, J = 7.3, 3.3 Hz), 1.73 (2H, m), 1.23 (1H, ddm, J = 11.7, 4.4 Hz), 1.20 (3H, s), 0.92 (3H, d, J = 7.3 Hz), 0.89 (3H, d, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 83.7, 82.0, 79.4, 62.3, 44.9, 40.2, 30.5, 25.8, 25.0, 13.13, 13.09.

Acknowledgment. The E. W. R. Steacie Memorial Fund, Natural Science and Engineering Research Council (NSERC) of Canada, Bio-Mega/Boehringer Ingelheim Inc., Eli Lilly Grantee Program, and the Petroleum Research Fund, administered by the ACS, are thanked for financial support.

JA964361J