Further Studies on Nickel-Promoted or -Catalyzed Cyclization of 1,3-Diene and a Tethered Carbonyl Group

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Abstract: A nickel-promoted intramolecular cyclization of 1,3-diene with the tethered carbonyl group was developed using the catalyst generated by reduction of $Ni(acac)_2$ with DIBAL-H in the presence of PPh_3. It was found that the addition of 1,3-CHD to the reaction mixture affected the regiochemistry of olefin on the side chain of the cyclized product. The reaction course of this cyclization can be accounted for by two possible mechanisms. In one mechanism, a nickel hydride complex plays a key role and the cyclization proceeds via π-allylnickel intermediate. In the other mechanism, a zero-valent nickel complex is the active species and the cyclization proceeds via nickelacycle intermediates. These mechanistic considerations led to finding two nickel-(0)-catalyzed cyclizations of 1,3-diene and the tethered aldehyde, in which the five- to seven-membered ring products were produced in a regio- and stereoselective manner via π-allylnickel intermediate or via a transmetalation process of nickelacycle intermediates with $^{i}Bu_2$-ALAC.

Introduction

Transition metal-catalyzed cycloaddition is a useful and promising strategy for the stereoselective construction of various cyclic compounds.[1] The co-oligomerization of 1,3-dienes is one of the most important processes in cycloaddition, and the pioneering work of nickel-promoted co-oligomerization of 1,3-dienes, in which 1,5-cyclooctadiene was produced by the reaction of two molecules of butadiene with $Ni(CO)_4$ in the presence of $P(OPh)_3$, was reported by Reed in 1954.[2] Since then, although there have been many efforts to investigate the nickel-promoted or -catalyzed oligomerization of 1,3-dienes and multiple bonds, synthetic utilization of these processes has been restricted due to competition with linear polymerization as well as the difficulty in controlling regio- and stereoselectivity.[3] On the other hand, the intramolecular versions of this process are useful for regio- and stereoselective ring construction, and a few excellent reactions have been reported. For example, Wender reported a nickel-catalyzed [4+4] cycloaddition of bis-1,3-dienes, in which eight-membered-ring compounds were produced stereoselectively by a zero-valent nickel catalyst under mild conditions.[4] A [4+2] cycloaddition of 1,3-diene and tethered alkyne or allene was also reported by the same group.[5] A cocyclization of bis-1,3-dienes in the presence of hydrosilane and a cyclization of 1,3-diene and tethered alkyne with isocyanide were reported by Tamao and Ito.[6] The utility of these processes prompted us to investigate the cyclization of 1,3-dienes and other multiple bonds containing a heteroatom, and we achieved a nickel-promoted or -catalyzed cyclization of 1,3-dienes and tethered carbonyl groups to give five- to seven-membered ring compounds in a stereoselective manner.[7] We describe herein our full results as well as new findings that have arisen from our continuing studies on nickel-promoted or -catalyzed stereoselective cyclization of 1,3-dienes and the tethered carbonyl groups.[8]

Results and Discussion

Cyclization of 1,3-Diene with Tethered Aldehyde Using the Catalyst Generated from $Ni(acac)_2$ and DIBAL-H in the Presence of PPh_3. At first, we investigated the cyclization of diene aldehydes **10**−**12**, and these substrates were synthesized as shown in Scheme 1. The reaction of the dianion, generated from sorbic acid (**1**) and LDA,[9] with the iodide **2** or **3** followed

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(1) (a) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92. (b) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635−662.

(2) Reed, H. W. B. *J. Chem. Soc.* **1954**, 1931.

(3) For reviews, see: (a) Heimback, P.; Jolly, P. W.; Wilke, G. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic: New York, 1970; Vol. 8, p 29. (b) Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic: New York, 1975; Vol. 2. (c) Jolly, P. W. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: New York, 1982; Vol. 8, p 613. (d) Keim, W.; Behr, A.; Roper, M. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: New York, 1982; Vol. 8, p 371. (e) Fischer, K.; Jonas, K.; Misbach, P.; Stabba, R.; Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 943. (f) Heimback, P. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 975. (g) Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 185.

(4) For [4+4] cycloadditions, see: (a) Wender, P. A.; Tebbe, M. J. *Synthesis* **1991**, 1089. (b) Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988**, *110*, 5904. (c) Wender, P. A.; Ihle, N. C. *Tetrahedron Lett.* **1987**, *28*, 2451. (d) Wender, P. A.; Snapper, M. L. *Tetrahedron Lett.* **1987**, *28*, 2221. (e) Wender, P. A.; Ihle, N. C. *J. Am. Chem. Soc.* **1986**, *108*, 4678.

(5) For [4+2] cycloadditions, see: (a) Wender, P. A.; Smith, T. E. *Tetrahedron* **1998**, *54*, 1255. (b) Wender, P. A.; Smith, T. E. *J. Org. Chem.* **1996**, *61*, 824. (c) Wender, P. A.; Smith, T. E. *J. Org. Chem.* **1995**, *60*, 2962. (d) Wender, P. A.; Jenkins, T. E. *J. Am. Chem. Soc.* **1989**, *111*, 6432. For a cyclization of 1,3-diene and allene, see: (e) Wender, P. A.; Jenkins, T. E.; Suzuki, S. *J. Am. Chem. Soc.* **1995**, *117*, 1843.

(6) (a) Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett.* **1992**, 539. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 381.

(7) Portions of this work have previously been communicated; see: (a) Sato, Y.; Takimoto, M.; Hayashi, K.; Katsuhara, T.; Takagi, K.; Mori, M. *J. Am. Chem. Soc.* **1994**, *116*, 9771. (b) Sato, Y.; Takimoto, M.; Mori, M. *Tetrahedron Lett.* **1996**, *37*, 887. For extensions to a nitrogen-containing system, see: (c) Sato, Y.; Saito, N.; Mori, M. *Tetrahedron Lett.* **1997**, *38*, 3931. (d) Sato, Y.; Saito, N.; Mori, M. *Tetrahedron* **1998**, *54*, 1153.

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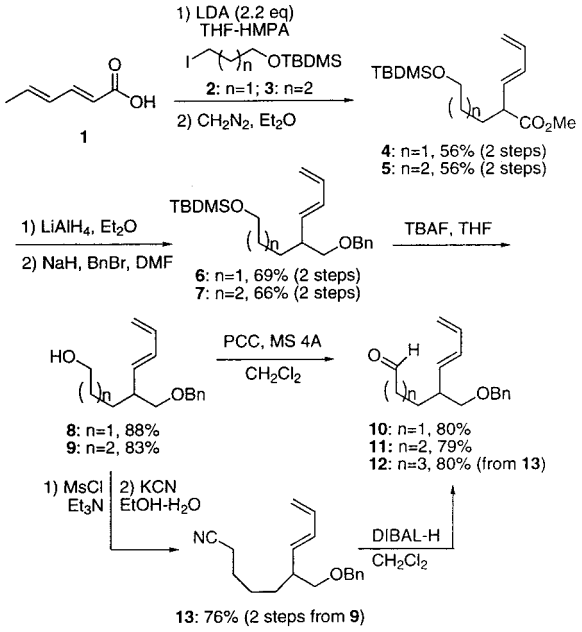
Scheme 1



by treatment with diazomethane afforded the ester **4** or **5** in good yield, respectively. After reduction of ester **4** or **5**, the resulting alcohol was treated with benzyl bromide to give **6** or **7**, and deprotection of the TBDMS group in **6** or **7** followed by oxidation of the alcohol produced substrate **10** or **11**, respectively. On the other hand, substrate **12** was obtained from **9** via **13** in three steps.

To a toluene solution containing a stoichiometric amount of the nickel complex **14**, prepared in situ from $Ni(acac)_2$ (100 mol %) and 2 equiv of DIBAL-H in the presence of PPh_3 (200 mol %),[6,10] was added a solution of **10** in toluene. The resulting solution was stirred at 0 °C for 6 h. Hydrolysis of the reaction mixture with 10% HCl at 0 °C afforded an alcohol **15-I** in 69% yield. Hydrogenation of **15-I** with Pd/C gave the cyclopentanol **16** in 87% yield as a sole product, which indicates that three stereocenters at C1, C2, and C3 on the cyclopentane ring in **15-I** were produced in a stereoselective manner during the cyclization. The stereochemistry of **15-I** was unequivocally determined by X-ray structural analysis of *p*-bromobenzoate **17** derived from (*E*)-**15-I** (Scheme 2). Cyclization of **10** using various amounts of the nickel complex **14** was carried out, and the results are summarized in Table 1. Although the yields in cyclization using 50 and 30 mol % of **14** (runs 2 and 3) exceeded the amounts of **14**, reducing the amount of the catalyst tended to decrease the yield of the cyclized product **15**. It is interesting that the cyclized product **15-T**, having a terminal olefin on the side chain, was produced in preference to **15-I**, having an internal olefin on the side chain, in cyclization using a catalytic amount of **14** (runs 2−4). This phenomenon will be discussed in a later section.

Scheme 2

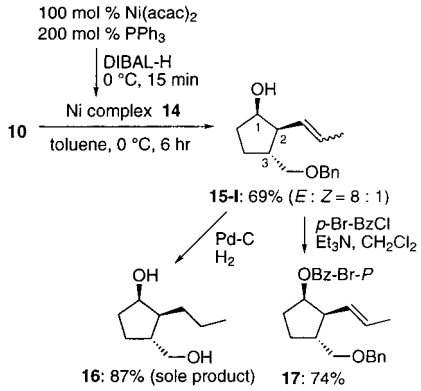
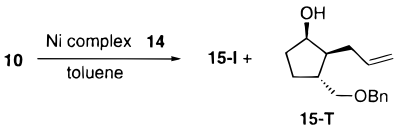


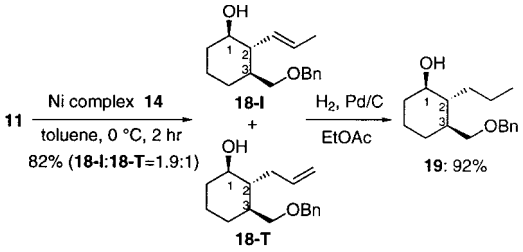
Table 1. Cyclization Using Various Amounts of Ni Complex **14**



				yield (%)		
run	Ni (mol %)	temp (°C)	time (hr)	**15-I** + **15-T**	**15-I**	**15-T**
1	100	0	6	69	69[a]	
2	50	0	6	65	6[b]	59
3	30	0	20	36		36
4	10	rt	20	10		10

[a] *E*:*Z* = 8:1. [b] The ratio was not determined.

Scheme 3



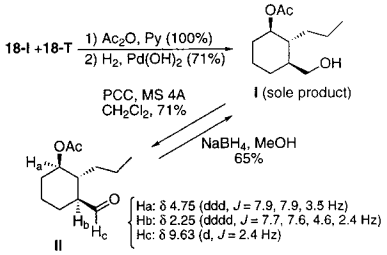
Encouraged by these results, the cyclization of various substrates was investigated. When substrate **11** was treated with a stoichiometric amount of **14**, prepared by the above-mentioned method, in toluene at 0 °C, cyclohexanols **18-I** and **18-T** (ratio of 1.9:1) were obtained in 82% yield. Hydrogenation of a mixture of **18-I** and **18-T** with 10% Pd/C gave cyclohexanol **19** in 92% yield as a sole product (Scheme 3), which indicates that the three stereocenters at C1, C2, and C3 on the cyclohexane ring in **18-I** and **18-T** were formed stereoselectively during cyclization.[11] It is noteworthy that the cyclization is applicable

(8) A nickel-promoted or -catalyzed intermolecular coupling of 1,3-diene and a carbonyl compound has been reported by Baker; see: (a) Baker, R.; Cook, A. H.; Crimmin, M. J. *J. Chem. Soc., Chem. Commun.* **1975**, 727. (b) Baker, R.; Crimmin, M. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1264. For recent reports on nickel-catalyzed intermolecular coupling of 1,3-diene and a carbonyl compound, see: (c) Kimura, M.; Ezoe, A.; Shibata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4033. (d) Takimoto, M.; Hiraga, Y.; Sato, Y.; Mori, M. *Tetrahedron Lett.* **1998**, *39*, 4543. For a cyclization of 1,3-diene and a tethered α,β-unsaturated carbonyl group, see: Montgomery, J.; Oblinger, E.; Savchenko, A. V. *J. Am. Chem. Soc.* **1997**, *119*, 4911.

(9) Ballester, P.; Costa, A.; Garcia-Raso, A.; Gomez-Solivellas, A.; Mestres, R. *Tetrahedron Lett.* **1985**, *26*, 3625.

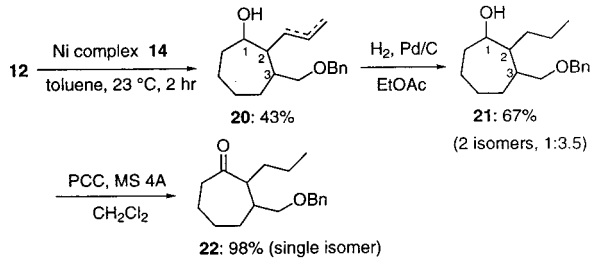
(10) Krysan, D. J.; Mackenzie, P. B. *J. Org. Chem.* **1990**, *55*, 4229.

(11) The stereochemistry of **18** (a mixture of **18-I** and **18-T**) was determined by the coupling constants of H_a and H_b from the NMR spectrum of **II**, which was obtained by acetylation of **18** followed by hydrogenation with $Pd(OH)_2$ and then PCC oxidation. Reduction of **II** afforded the same alcohol **I** again, which indicates that no epimerization at the C3 position occurred during conversion of **I** into **II**.



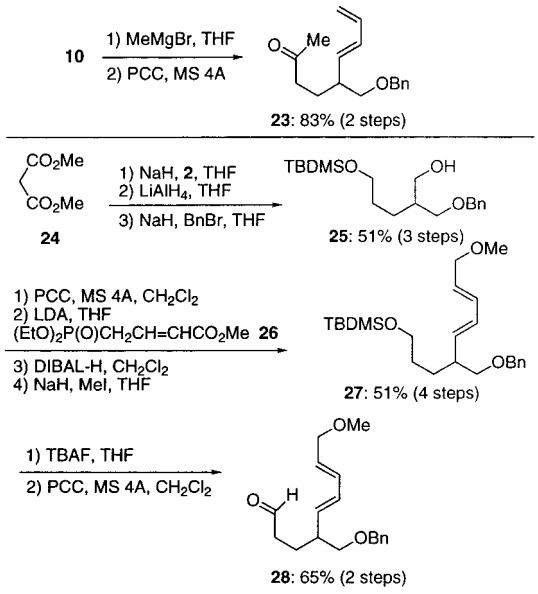
to the construction of a seven-membered ring. The reaction of **12** with a stoichiometric amount of **14** proceeded to give a mixture of cycloheptanols **20**, having a seven-membered ring, in 43% yield. Hydrogenation of **20** with 10% Pd/C gave **21** as two isomers (ratio of 3.5:1). To confirm that the cyclized product had a seven-membered-ring framework, **21** was finally converted into cycloheptanone **22** as a sole product by PCC oxidation (Scheme 4). To examine the applicability of this

Scheme 4



reaction to other carbonyl groups or internal dienes, the cyclizations of **23** and **28** were planned, and these substrates were prepared as shown in Scheme 5. Substrate **23**, having a

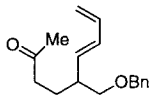
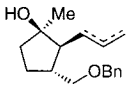
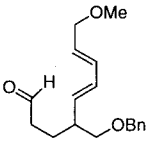
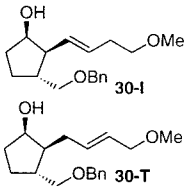
Scheme 5



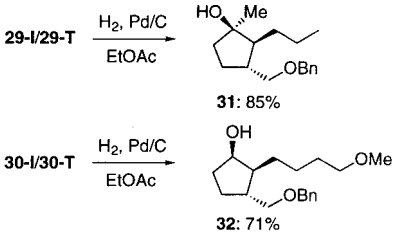
ketone moiety as a carbonyl group, was easily synthesized by the nucleophilic addition of methylmagnesium bromide to aldehyde **10** followed by oxidation of the resulting alcohol. For the synthesis of **28**, a coupling reaction of dimethyl malonate (**24**) with iodide **2** followed by reduction of the ester group and partial protection of the alcohol afforded **25** in good yield. Oxidation of alcohol **25** followed by the Wadsworth−Horner−Emmons reaction with **26** gave the corresponding dienoate, which was converted to **27** by reduction with DIBAL-H followed by methylation. Deprotection followed by oxidation gave substrate **28**, having an internal diene moiety.

The cyclization of ketone **23** proceeded smoothly to give a mixture of cyclopentanols **29-I** and **29-T** (ratio of 1.8:1) in 56% yield (Table 2). Hydrogenation of a mixture of **29-I** and **29-T** with Pd/C gave the cyclopentanol **31** as a sole product.[12] On the other hand, cyclization of **28** afforded a mixture of cyclopentanols **30-I** and **30-T** (ratio of 2.0:1) in 61% yield, and cyclopentanol **32** was also obtained as a sole product from a

Table 2. Cyclizations of **23** and **28** Using Ni Complex **14**

substrate	temp (°C)	time (hr)	products
 **23**	23	7	 **29**: 56% (**29-I**:**29-T**=1.8:1)
 **28**	0	2	 **30-I** **30-T** 61% (**30-I**:**30-T**=2.0:1)

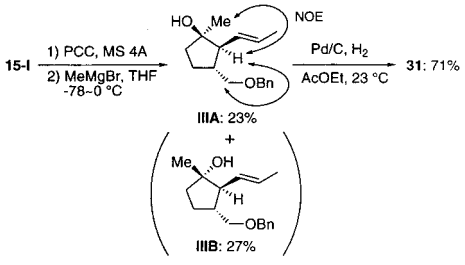
Scheme 6



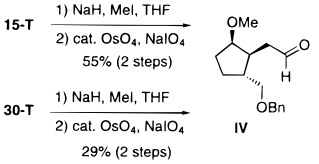
mixture of **30-I** and **30-T** by hydrogenation (Scheme 6).[13] These results indicate that three stereocenters at C1, C2, and C3 of each cyclopentane ring in **29** and **30** are produced in a stereoselective manner in these cyclizations.

Regiocontrolled Effect of 1,3-Dienes as an Additive on Nickel-Promoted Cyclization. As shown in Table 1, we found that cyclized product **15-T** having a terminal olefin on the side chain was obtained in preference to **15-I** having an internal one when a catalytic amount of nickel complex **14** was used. Although the reason is still not clear, it was speculated that an excess of the diene part on substrate **10** coordinated to nickel complex **14** acting as a ligand and affected the regiochemistry of the cyclized product. That is, nickel complex **14′** coordinated by 1,3-diene might possess a reactivity different from that of

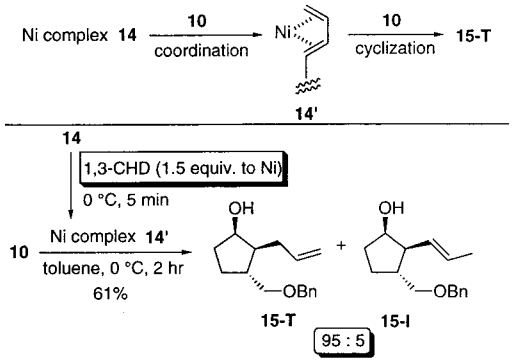
(12) The stereochemistry of **29** was determined as follows; PCC oxidation of **15-I** followed by treatment with MeMgBr afforded a separable mixture of cycloheptanols **IIIA** and **IIIB**. The stereochemistry of **IIIA** was determined from NMR (COSY, NOESY) spectra. Hydrogenation of **IIIA** afforded **31**, whose spectral data were completely identical with that obtained from a mixture of **29** by hydrogenation.



(13) The stereochemistry of **30** was determined by conversion of **30-T** into the aldehyde **IV**, which was obtained from **15-T** as follows:



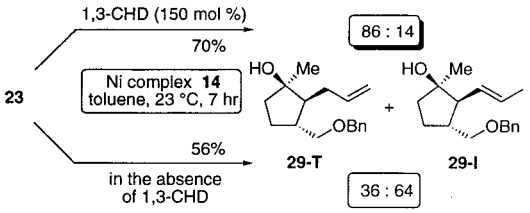
Scheme 7



14 (Scheme 7). On the basis of this assumption, we examined the effect of 1,3-diene on the cyclization of **10** using nickel complex **14**. To a stirred toluene solution of **14**, generated in situ by treatment of $Ni(acac)_2$ (100 mol %) and PPh_3 (200 mol %) with DIBAL-H (200 mol %), was added 150 mol % of 1,3-cyclohexadiene (1,3-CHD) at 0 °C, and the solution was stirred for a few minutes. A toluene solution of substrate **10** was then added to the resultant mixture, and the solution was stirred at 0 °C for 2 h. It was very surprising to find that hydrolysis of the reaction mixture with 10% HCl at 0 °C preferentially produced the cyclopentane derivative **15-T**, having a *terminal olefin* on the side chain, along with a small amount of **15-I** (ratio of 95:5) in 61% yield. As described above, under similar conditions in the absence of 1,3-CHD, only **15-I** was obtained in 69% yield. This result prompted us to try cyclization of various substrates under similar conditions in the presence of 1,3-CHD.

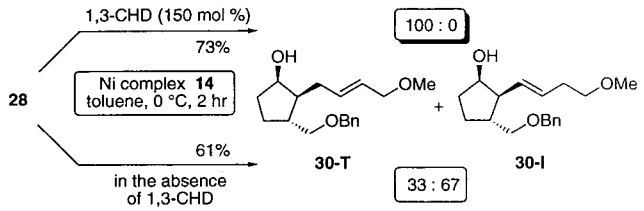
The reaction of **23** proceeded smoothly at 25 °C, preferentially giving **29-T** along with **29-I** in 70% yield (ratio of 86:14), while the ratio of **29-T** to **29-I** was 36:64 in the above-mentioned cyclization in the absence 1,3-CHD (Scheme 8). A remarkable

Scheme 8



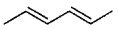
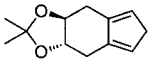
effect of the addition of 1,3-CHD was also observed in the cyclization of **28**, having an internal 1,3-diene moiety, and the cyclized product **30-T** was obtained in 73% yield as a sole product (Scheme 9). In the cyclization of **11** in the presence of

Scheme 9



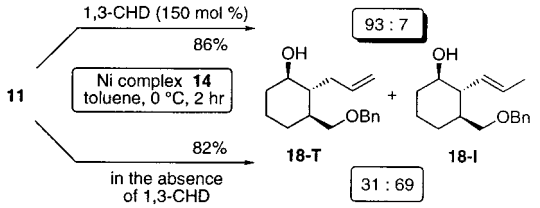
1,3-CHD, the cyclohexane derivative **18-T** was obtained, in preference to **18-I**, in 86% yield in the ratio of 93:7, while the above-mentioned cyclization in the absence of 1,3-CHD gave preferentially **18-I** (ratio of 31:69) in 82% yield (Scheme 10). The reaction of **12** in the presence of 1,3-CHD produced the cycloheptane derivatives **20-T** as a mixture of two isomers with

Table 3. Cyclization of **10** in the Presence of Various Alkenes

run [a]	alkene [b]	yield 15-T+15-I (%)	ratio [c] 15-T/15-I
1	none	69	0/100
2		61	95/5
3	 **33**	57	80/20
4	 **34**	80	58/42
5	 **35**	72	46/54
6	 **36**	71	25/75
7	 **37**	70	98/2

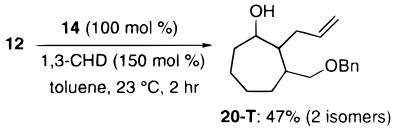
[a] All reactions were carried out in toluene at 0 °C. [b] A total of 150 mol % alkenes (runs 2−7) was used. [c] The ratio was determined by ^1H NMR.

Scheme 10



respect to the C1, C2, or C3 position of the cycloheptane ring in 47% yield. It is notable that both cyclized products in a mixture of **20-T** had only terminal olefins on the side chain, and no cyclized products having an internal olefin on the side chain were formed (Scheme 11).

Scheme 11



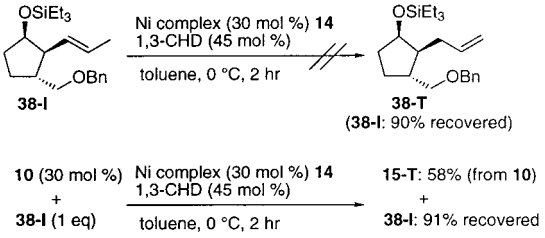
To find the best additive to control the regioselectivity of olefin on the side chain, reactions of **10** with nickel complex **14** in the presence of various alkenes were carried out. The results are summarized in Table 3. A 1,4-diene (run 5) and a monoolefin (run 6) were less effective for the formation of **15-T** than 1,3-dienes (runs 2, 3, 4, and 7), and 1,3-CHD (run 2) showed higher selectivity than a linear 1,3-diene **33** or *s-trans*-1,3-diene **34**. These results indicated that a s-cis conformation of 1,3-diene would be necessary for coordination to nickel complex **14** in order to change the reactivity of the catalyst. It was very interesting that **15-T** was obtained in 70% yield with the highest selectivity (**15-T**:**15-I** = 98:2) when cyclopentadiene **37**[14] was used as an additive.[15]

(14) Halterman, R. L.; Vollhardt, K. P. C. *Tetrahedron Lett.* **1986**, *27*, 1461.

(15) In this reaction, unchanged **37** was recovered in 69% yield, which suggests that **37** would not react with the complex **14** under the conditions of this cyclization.

It is possible that the formation of the cyclized product having a terminal olefin was caused by the isomerization of that having an internal olefin during the cyclization. To investigate this possibility, silyl ether **38-I** was treated with nickel catalyst **14**, generated from $Ni(acac)_2$ (30 mol %), PPh_3 (60 mol %), and DIBAL-H (60 mol %), in the presence of 1,3-CHD (45 mol %) in toluene at 0 °C for 2 h. As a result, unchanged **38-I** was recovered in 90%. Furthermore, when **38-I** (1 equiv) was added to the reaction solution of the cyclization of **10** (0.3 equiv) with **14** (0.3 equiv) in the presence of 1,3-CHD (0.45 equiv) in toluene at 0 °C, unchanged **38-I** was recovered again in 91% along with the usual cyclized product **15-T** in 58% yield based on **10** (Scheme 12). These results suggest that the cyclized

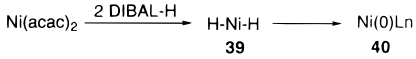
Scheme 12



product having a terminal olefin was not produced from that having an internal one via olefin isomerization during the cyclization, although the role of 1,3-diene in regioselectivity of the cyclized product remains unclear.

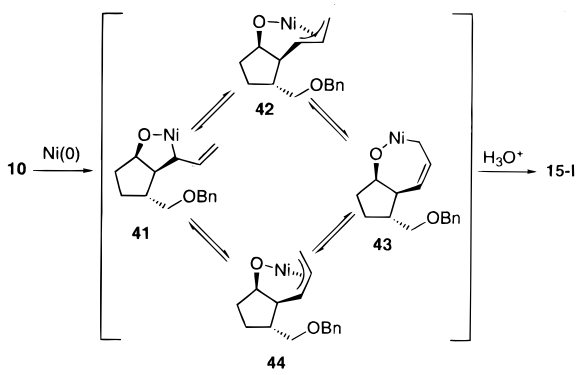
Possible Mechanism for Cyclization Using the Catalyst Generated from $Ni(acac)_2$-PPh_3 and DIBAL-H. Having established the nickel-promoted stereoselective cyclization of 1,3-dienes and the tethered carbonyl groups, we turned our attention to the investigation of the mechanism of this reaction. In this cyclization, a catalyst generated in situ by reduction of $Ni(acac)_2$ with DIBAL-H (2 equiv to $Ni(acac)_2$) in the presence of PPh_3 was used. However, the structure of this catalyst was not clear, although this catalytic system had been used in various reactions.[6,10,16] Among them, a modified method for preparation of zero-valent nickel complex, $Ni(cod)_2$, from $Ni(acac)_2$ and DIBAL-H in the presence of 1,5-cyclooctadiene (1,5-COD), was reported by Krysan and Mackenzie.[10] They assumed that zero-valent nickel complex **40** was formed by the reduction of $Ni(acac)_2$ with DIBAL-H (2 equiv to $Ni(acac)_2$) followed by reductive elimination from bis(hydride)nickel(II) intermediate **39** (Scheme 13). If the active species in our cyclization is a

Scheme 13



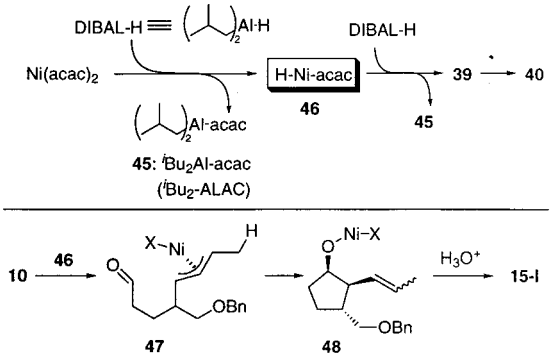
zero-valent nickel complex such as **40**, the reaction mechanism could assumed to be that shown in Scheme 14. In the cyclization of **10**, the substrate would oxidatively add to the zero-valent nickel complex producing nickelacycle **41**, which might be in equilibration with π-allylnickel intermediates **42** and **44** and another nickelacycle **43**. Hydrolysis of nickel complexes **42**, **43**, and **44** by acidic workup would produce the cyclized product **15-I**. It is also possible that the cyclized product having a terminal olefin (i.e., **15-T**, **18-T**, **29-T**, and **30-T**) was produced from a nickelacycle such as **41**. The possibility of an alternative

Scheme 14. Possible Mechanisms for Cyclization Promoted by a Ni(0) Complex



mechanism, however, arose from further consideration of the process of generation of zero-valent nickel complex **40** from $Ni(acac)_2$ (Scheme 15). Namely, nickel(II) hydride complex **46**

Scheme 15



would be formed along with diisobutylaluminum acetylacetonate (^{i}Bu$_2$-ALAC, **45**) by reduction of $Ni(acac)_2$ with DIBAL-H during the generation of zero-valent nickel complex **40** via **39**.[17] Since complex **46** might be reactive to olefins, the reaction of **46** with the 1,3-diene moiety in **10** could produce π-allylnickel intermediate **47**.[18] The π-allylnickel part in **47** could react with tethered aldehyde giving **48**, which is hydrolyzed with acidic workup to afford cyclized product **15-I**. However, the formation of cyclized products having a terminal olefin cannot be explained by this mechanism, because the isomerization of an internal olefin into a terminal one in the cyclized products did not occur during the cyclization, as described in the previous section. Various experiments were carried out to investigate which of the mechanisms, that shown in Scheme 14 or that shown in Scheme 15, is more reasonable, and the results are described in the following sections.

Cyclization Using Zero-Valent Nickel Complexes. At first, the reaction mixture of **10** with a stoichiometric amount of nickel complex **14** was hydrolyzed with $DCl-D_2O$, since it was thought that a product containing deuterium on the carbon framework should be obtained if this cyclization proceeded via nickel complexes **41**−**44** in Scheme 14. As a result, treatment of the reaction mixture with $DCl-D_2O$ provided no deuterated product, only giving **15-I** (not containing deuterium) in 69% yield (E:Z = 8:1). To examine the possibility that complexes

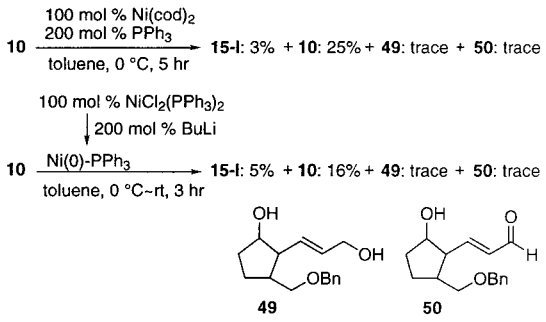
(16) (a) Cuvigny, T.; Julia, M. *J. Organomet. Chem.* **1986**, *317*, 383. (b) Hansen, R. T.; Carr, D. B.; Schwartz, J. *J. Am. Chem. Soc.* **1978**, *100*, 2244. (c) Sato, Y.; Nishimata, T.; Mori, M. *J. Org. Chem.* **1994**, *59*, 6133. (d) Sato, Y.; Nishimata, T.; Mori, M. *Heterocycles* **1997**, *44*, 443. (e) Suginome, M.; Matsuda, T.; Ito, Y. *Organometallics* **1998**, *17*, 5233.

(17) Formation of the nickel hydride complex **46** by the reaction of $Ni(acac)_2$ with ^{i}Bu$_3$Al was reported by Wilke.[3e] In this paper, it was proposed that ^{i}Bu-Ni-acac complex was initially formed and successive β-elimination from this complex produced **46**.

(18) Wilke also reported that an olefin insertion into the hydrogen−metal bond of complex **46** proceeded to give the corresponding alkyl-Ni-acac complex.[3e]

41−**44** were decomposed in situ with a trace amount of H_2O contained in the reaction mixture or by a hydrogen abstraction reaction from the solvent before acidic workup, the cyclization of **10** was carried out in toluene containing D_2O (10 equiv to nickel complex **14**) or in toluene-d_8, and **15-I** (not containing deuterium) was obtained in 65 or 62% yield, respectively. Next, we tried the cyclization of **10** using the zero-valent nickel complex, $Ni(cod)_2$, or the catalyst generated from $NiCl_2(PPh_3)_2$ and *n*-BuLi.[19] In both cyclizations, only a trace amount of **15-I** was obtained along with trace amounts of **49** and **50**, and the starting material **10** was recovered in both cases (Scheme 16).

Scheme 16

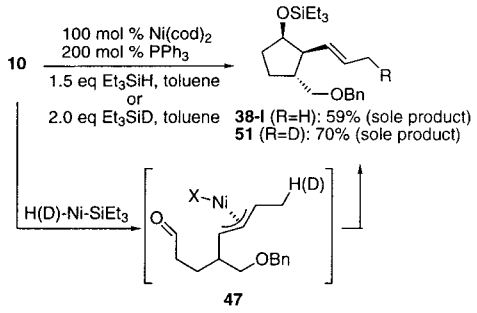


These results lead us to study the alternative mechanism depicted in Scheme 15, in which the cyclization would proceed via π-nickelacycle intermediate **47** generated from the 1,3-diene moiety in **10** and a nickel(II) hydride complex such as **46**.

Cyclization Using the Nickel(II) Hydride Complex Generated from a Zero-Valent Nickel Complex and Trialkylsilane

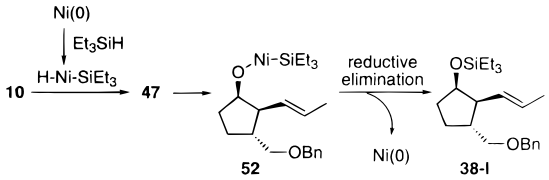
It was known that trialkylsilane oxidatively adds to a low-valent transition metal complex to form a metal hydride complex such as **46**.[20] In addition, it was also reported that a π-allylnickel intermediate was formed by the reaction of 1,3-diene and the nickel hydride complex generated from a zero-valent nickel complex and trialkyl- or trialkoxysilane.[21] To investigate the mechanism concerned with nickel hydride complex **46**, we tried the cyclization of **10** using the nickel hydride complex generated from $Ni(cod)_2$ and PPh_3 in the presence of triethylsilane (Et_3SiH). When a toluene solution of **10**, $Ni(cod)_2$ (100 mol %), PPh_3 (200 mol %), and Et_3SiH (1.5 equiv) was stirred at 0 °C for 6.5 h, we were pleased to find that the highly regio- and stereo-controlled cyclized product **38-I** was obtained as the sole product in 59% yield, in which three stereocenters at the C1, C2, and C3 positions on the cyclopentane were produced with the same selectivity as that of the cyclized product **15-I**. The reaction of **10** with $Ni(cod)_2$ (100 mol %) and PPh_3 (200 mol %) in the presence of triethylsilyl deuteride (Et_3SiD) instead of Et_3SiH also stereoselectively produced deuterated product **51** in 70% yield (D content >95%) (Scheme 17). These results are consistent with the mechanism shown in Scheme 15, although the formation of nickel hydride complex **46** from $Ni(acac)_2$ and DIBAL-H was not directly proved. Thus, we ultimately adopted the mechanism shown in Scheme 15 in preliminary communications.[7] It was interesting that the reaction of **10** using a stoichiometric amount of the nickel hydride complex formed from $Ni(cod)_2$ and Et_3SiH in the presence of 1,3-CHD (150 mol %) gave the cyclized product **38-I** in 66% yield as the sole product. It indicates that the nickel hydride complex is more reactive to the 1,3-diene moiety of the substrate than 1,3-CHD and that the effect of 1,3-CHD on the regioselectivity of the olefin in the cyclized product could not be reproduced in this reaction system.

Scheme 17



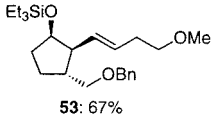
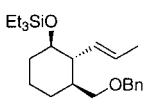
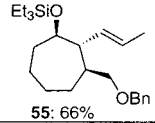
Ni(0)-Catalyzed Cyclization Using a Zero-Valent Nickel Complex in the Presence of Trialkylsilane. As shown in Scheme 17, the cyclization of **10** using $Ni(cod)_2$ and PPh_3 in the presence of Et_3SiH produced the cyclized product **38-I** as a silyl ether. It indicates that reductive elimination of **38-I** from **52** accompanying regeneration of the zero-valent nickel complex occurred in this cyclization and that this cyclization would proceed with a catalytic amount of Ni(0) complex (Scheme 18).

Scheme 18



On the basis of this assumption, the reaction of **10** was carried out with a catalytic amount of $Ni(cod)_2$ (10 mol %) and PPh_3 (20 mol %) in the presence of Et_3SiH (5 equiv). As the result, we succeeded in obtaining **38-I** in 70% yield (Table 4, run 1). Similarly, the cyclization of other substrates using a catalytic amount of zero-valent nickel complex was investigated, and the results are summarized in Table 4. The cyclization of **28**, having an internal diene moiety, also proceeded stereoselectively to

Table 4. Cyclization of Various Substrates Using a Catalytic Amount of $Ni(cod)_2$ and PPh_3 in the Presence of Et_3SiH

run	substrate	$Ni(cod)_2$[a] (mol %)	temp (°C)	time (hr)	cyclized product[b]
1	**10**	10	23	21	**38-I**: 70%
2	**28**	20	30	3.5	 **53**: 67%
3	**11**	20	23	1.5	 **54**: 71%
4	**12**	20	30	12	 **55**: 66%

[a] All reactions were carried out in toluene in the presence of PPh_3 (2 equiv to $Ni(cod)_2$) and Et_3SiH (5 equiv). [b] All cyclized products were obtained as a sole product.

(19) Henningsen, M. C.; Jeropoulos, S.; Smith, E. H. *J. Org. Chem.* **1989**, *54*, 3015.

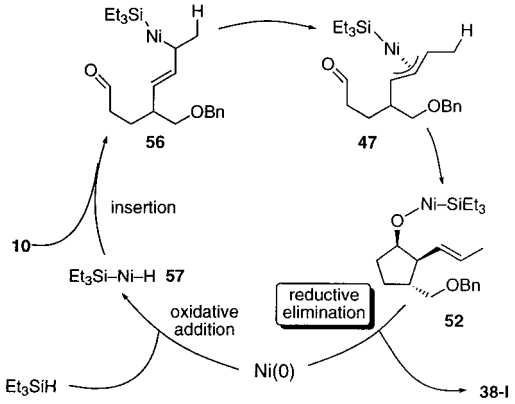
(20) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley: Chichester, U.K., 1989; p 1479 and references therein.

(21) Lappert, M. F.; Nile, T. A.; Takahashi, S. *J. Organomet. Chem.* **1974**, *72*, 425. Also, see: ref 6.

give the cyclized product **53** in 67% yield as the sole product. The cyclohexanol derivative **54** was obtained from **11** in a stereoselective manner. The stereochemistry of these cyclized products **53** and **54** was determined by conversion into **30-I** and **18-I**, respectively. Surprisingly, cycloheptanol derivative **55** was also obtained as the sole product in this reaction system.[22]

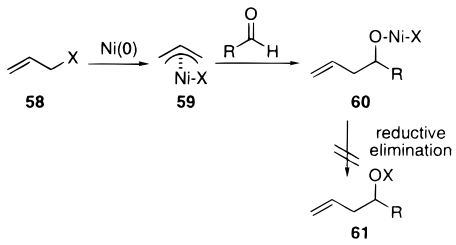
The probable catalytic cycle of this cyclization is shown in Scheme 19. Nickel hydride complex **57** is formed by the oxida-

Scheme 19



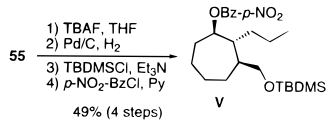
tive addition of Et_3SiH to the zero-valent nickel complex, and the reaction of **10** with **57** produces π-allylnickel intermediate **47** via **56**.[21] The π-allylnickel moiety in **47** reacts with the tethered carbonyl group to give **52**, and the cyclized product **38-I** is afforded by the reductive elimination from **52** accompanying the regeneration of the zero-valent nickel complex. It is known that a π-allylnickel complex can react with a carbonyl group to give a homoallyl alcohol derivative.[23] In general, π-allylnickel species **47** was prepared by the reaction of allyl halide **58** with the zero-valent nickel complex in these studies (Scheme 20). Since the reductive elimination of **61** from **60**

Scheme 20



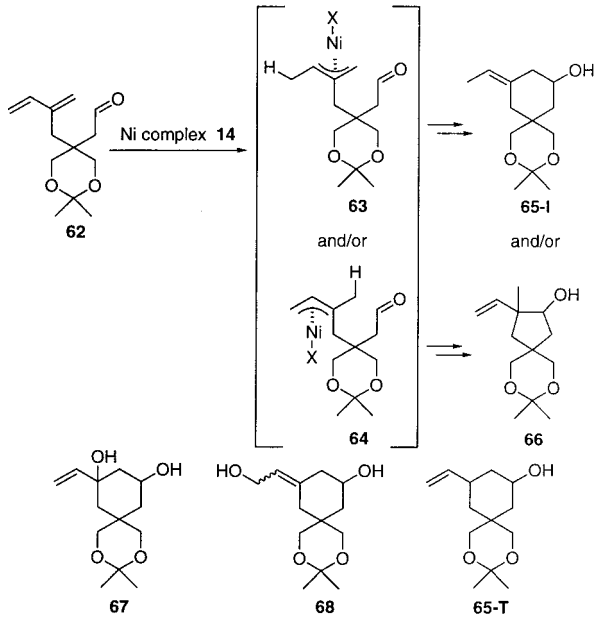
does not proceed, a stoichiometric amount of zero-valent nickel complex is needed in this reaction. On the other hand, the π-allylnickel intermediate in our cyclization was produced by

(22) The stereochemistry of **55** was determined by X-ray analysis of *p*-nitrobenzoate **V** derived from **55**.



(23) (a) Billington, D. C. *Chem. Soc. Rev.* **1985**, *14*, 93 and references therein. (b) Hegedus, L. S.; Varaprath, S. *Organometallics* **1982**, *1*, 259. (c) Hegedus, L. S.; Evans, B. R.; Korte, D. E.; Waterman, E. L.; Sjoberg, K. *J. Am. Chem. Soc.* **1976**, *98*, 3901. (d) Hegedus, L. S.; Wagner, S. D.; Waterman, E. L.; Siirala-Hansen, K. *J. Org. Chem.* **1975**, *40*, 593. (e) Semmelhack, M. F.; Brichner, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3945. (f) Semmelhack, M. F.; Yamashita, A.; Tomesch, J. C.; Hirotsu, K. *J. Am. Chem. Soc.* **1978**, *100*, 5565. (g) Semmelhack, M. F.; Wu, E. C. S. *J. Am. Chem. Soc. J. Am. Chem. Soc.* **1976**, *98*, 3384. (h) Semmelhack, M. F. *Org. React.* **1972**, *19*, 115.

Scheme 21



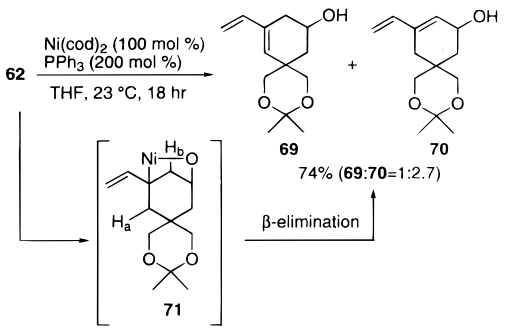
the reaction of 1,3-diene and nickel hydride complex **57**, which made it possible for the reductive elimination of **38-I** from **52** to proceed and for a catalytic cycle of the cyclization to be established.

Reinvestigation of Cyclization Using a Zero-Valent Nickel Complex: Role of ^{i}Bu$_2$-ALAC (45). During the course of our continuing investigations of this cyclization, we have very recently found that a zero-valent nickel complex could promote cyclization in the case of substrate **62**.[24] Namely, nickel complex **14**, generated from $Ni(acac)_2$ and DIBAL-H in the presence of PPh_3, was initially used in the cyclization of **62**, in which it was expected that product **65** or **66** would be obtained via π-allylnickel intermediate **63** or **64** according to the above-mentioned mechanism (Scheme 21). However, the cyclized products **67**, **68**, and **65-T** were obtained in a total 39% yield (ratio of 1.5:1:1.3) along with other undefined products. The formation of **67**, **68**, and **65-T** could not be explained by the mechanism via π-allylnickel intermediate **63** or **64**, and the result was quite similar to that in the cyclization of **10** using the zero-valent nickel complex shown in Scheme 16. In addition, the cyclization of **62** using the nickel hydride complex generated from $Ni(cod)_2$, PPh_3, and Et_3SiH did not give the corresponding cyclized product as a silyl ether but gave complex mixtures. These results suggest that a nickel hydride complex cannot promote the cyclization of **62**. Thus, the cyclization of **62** using zero-valent nickel complex, $Ni(cod)_2$, was investigated. As a result, the cyclized products **69** and **70** were obtained in good yields in this cyclization. It was noteworthy that **69** and **70** could be produced by β-hydride elimination from nickelacycle **71**, which was generated from **62** and a zero-valent nickel complex (Scheme 22).

These results lead us to reconsider the mechanism depicted in Scheme 14, in which the cyclization would proceed via nickelacycle intermediates **41**−**44** generated from substrate **10** and a zero-valent nickel complex. As described in Scheme 16, other zero-valent nickel complexes did not promote the cyclization of **10**, while the catalyst **14** generated from $Ni(acac)_2$ and DIBAL-H could promote the cyclization. If **14** is a zero-valent nickel complex, we wondered what was the difference between **14** and other zero-valent catalysts such as $Ni(cod)_2$ or

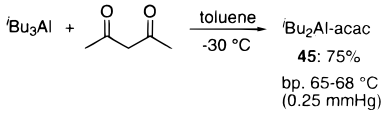
(24) Sato, Y.; Takanashi, T.; Hoshiba, M.; Mori, M. *Tetrahedron Lett.* **1998**, *39*, 5579.

Scheme 22



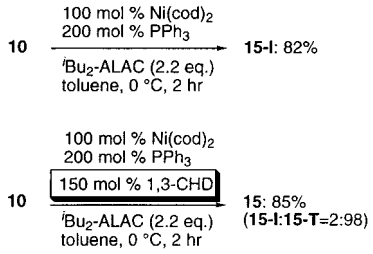
a catalyst generated from $NiCl_2(PPh_3)_2$ and *n*-BuLi. Thus, we directed our attention to **45**, which might be formed during the conversion of $Ni(acac)_2$ to a zero-valent nickel complex by DIBAL-H. Diisobutylaluminum acetylacetonate ($^iBu_2$-ALAC, **45**) was easily prepared from triisobutylaluminum and 2,4-pentanedione according to the literature (Scheme 23).[25] The

Scheme 23



cyclization of **10** using $Ni(cod)_2$ (100 mol %) and PPh_3 (200 mol %) in the presence of $^iBu_2$-ALAC (2.2 equiv) in toluene was carried out, and we were very pleased to find that the cyclized product **15-I** was obtained in 82% yield. In addition,

Scheme 24



the effect of 1,3-CHD on the regioselectivity of the cyclized product was also seen in this cyclization. Thus, the cyclization of **10** under the same conditions in the presence of 1,3-CHD gave **15-T** exclusively in good yield (Scheme 24). These results indicated that $^iBu_2$-ALAC plays an important role in producing the cyclized product from nickelacycle intermediates **41**−**44**, and a possible mechanism is shown in Scheme 25. The nickelacycle intermediates **41**−**44** would be generated by the reaction of **10** and a zero-valent nickel complex.[26] Among these nickelacycles, it was thought that the nickelacycle **41** might be most reactive to $^iBu_2$-ALAC (**45**) in the next transmetalation step, since the nickelacycles **42** and **44** were stabilized by the coordination of the η^3-allyl group, and the abundance of **43** in the equilibrium seemed to be less than that of other nickelacycles. The transmetalation of **41** with aluminum reagent **45** would proceed via **72** to give σ-allylnickel complex **73**. The π-allylnickel hydride complex **76** would be formed from **73** via π-allylnickel intermediate **74** or via σ-allylnickel hydride intermediate **75**. Reductive elimination of **77** from **76** followed by hydrolysis afforded cyclized product **15**. As mentioned above, it was shown that 1,3-CHD controls the regioselectivity of the cyclized product. It was thought that the additive 1,3-CHD might prevent the formation of π-allylnickel complex **74** or **76** by coordination to the η^1-allyl complex **73** or **75**. As a result, spontaneous reductive elimination of **77-T** from σ-allylnickel hydride **75** would be the major pathway in the cyclization in the presence of 1,3-CHD, producing **15-T** predominantly.

Nickel(0)-Catalyzed Cyclization via Transmetalation Using $^iBu_2$-ALAC. As shown in Scheme 25, it was thought that a zero-valent nickel species would be regenerated by reductive elimination of **77-T** or **77** from **75** or **76** and that the cyclization would proceed catalytically with respect to the zero-valent nickel complex. The cyclization of **10** using a catalytic amount of $Ni(cod)_2$ (5 mol %) and PPh_3 (10 mol %) in the presence of $^iBu_2$-ALAC (**45**) (1.5 equiv) was carried out. As a result, we succeeded in obtaining the cyclized product **15-T** as the sole product in 84% yield (Scheme 26). It was very interesting that only **15-T** having a terminal olefin on the side chain was obtained in this catalytic cyclization, while the reaction using a stoichiometric amount of $Ni(cod)_2$ and PPh_3 in the presence of **45** produced only **15-I** having an internal olefin on the side chain as previously shown in Scheme 24. In addition, the effect of 1,3-diene was also observed in the cyclization using a stoichiometric amount of zero-valent nickel complex in the presence of **45**, in which **15-T** was preferentially produced in

Scheme 25. Possible Mechanism for the Cyclization Promoted by a Ni(0) Complex in the Presence of $^iBu_2$ALAC

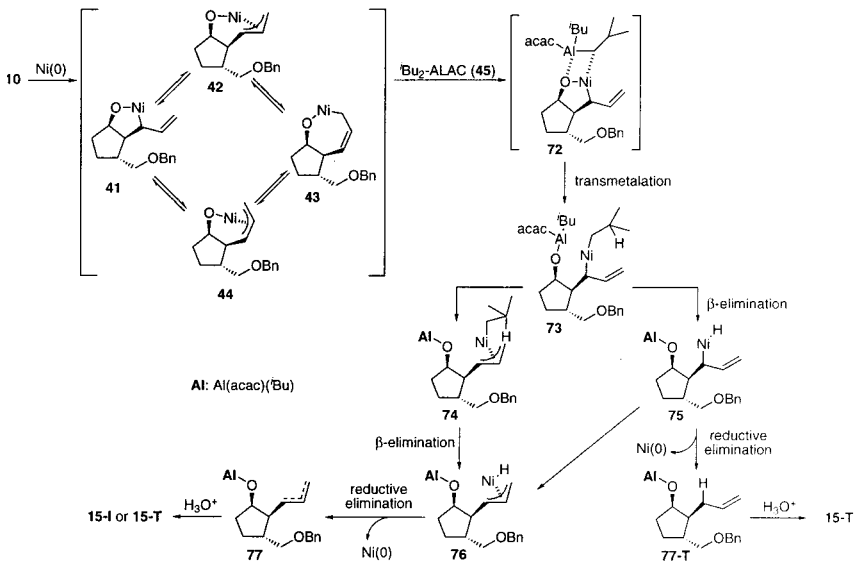
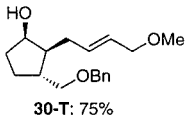
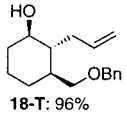
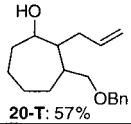


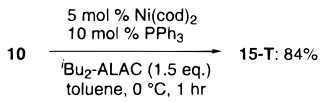
Table 5. Ni(0)-Catalyzed Cyclization of Various Substrates with $^{i}Bu_2$-ALAC

run[a]	substrate	temp (°C)	time (hr)	cyclized product
1[b]	**28**	0	12	 **30-T**: 75%
2[c]	**11**	0	1	 **18-T**: 96%
3[c]	**12**	23	7	 **20-T**: 57%

[a] All reactions were carried out in toluene using $^{i}Bu_2$-ALAC (1.5 equiv). [b] $Ni(cod)_2$ (10 mol %), PPh_3 (20 mol %). [c] $Ni(cod)_2$ (5 mol %), PPh_3 (10 mol %).

the cyclization in the presence of 1,3-CHD. The fact that **15-T** was selectively produced in the catalytic reaction can be

Scheme 26



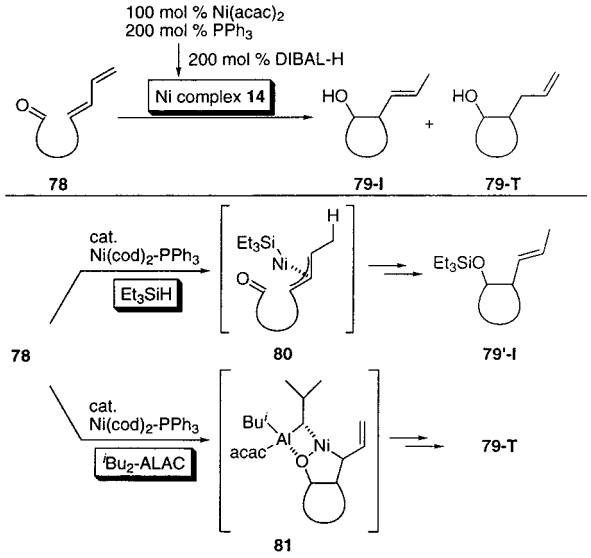
explained by the effect of 1,3-diene on the regiochemistry of the product. Namely, the 1,3-diene moiety in the case of an excess amount of the substrate compared to the Ni(0) complex would coordinate to the nickel complex and affect the regiochemistry of the product, in a manner similar to that shown in Table 1.

Next, nickel(0)-catalyzed cyclization of other substrates was carried out, and the results are summarized in Table 5. The reaction of **28** using $Ni(cod)_2$ (10 mol %), PPh_3 (20 mol %), and $^{i}Bu_2$-ALAC (**45**) (1.5 equiv) afforded the cyclized product **30-T** as the sole product in 75% yield. In the cyclization of **11**, the cyclized product **18-T** was obtained as the sole product in 96% yield. In the case of a seven-membered-ring construction, the cyclization of **12** using $Ni(cod)_2$ (5 mol %), PPh_3 (10 mol %), and $^{i}Bu_2$-ALAC (**45**) (1.5 equiv) produced the cycloheptane derivatives **20-T** in 57% yield as an inseparable mixture of two isomers (ratio of 1:4.2) with respect to the C1, C2, or C3-position on the cycloheptane ring. However, both products in **20-T** have only a terminal olefin at each side chain, indicating that the regiochemistry of olefin on the side chain was completely controlled in this system. Thus, we could extend the zero-valent nickel-promoted cyclization of 1,3-diene and a tethered carbonyl group via transmetalation of nickellacycles and $^{i}Bu_2$-ALAC to a catalytic reaction from which a cyclized product having a terminal olefin on the side chain is obtained in a stereoselective manner.

Conclusions

The main results described in this article are summarized in Scheme 27. A nickel-promoted intramolecular cyclization of

Scheme 27



1,3-diene with the tethered carbonyl group was developed using catalyst **14** generated by reduction of $Ni(acac)_2$ with DIBAL-H in the presence of PPh_3, and the cyclized product **79-I** and **79-T** were obtained in a stereoselective manner with respect to the stereochemistry of the substituents on the cycloalkane ring. It was found that the addition of 1,3-CHD to the reaction mixture under the same conditions affected the regiochemistry of olefin on the side chain, and **79-T** having a terminal olefin on the side chain was exclusively produced. The reaction course of this cyclization can be accounted for by two possible mechanisms. In one mechanism, a nickel hydride complex plays a key role and the cyclization proceeds via a π-allylnickel intermediate. In the other mechanism, a zero-valent nickel complex is the active species and the cyclization proceeds via nickelacycle intermediates. These mechanistic considerations led us to find two nickel(0)-catalyzed cyclizations of 1,3-diene and the tethered aldehyde, in which the cyclized product **79′-I** having an internal olefin or the cyclized product **79-T** having a terminal olefin was produced respectively via π-allylnickel intermediate **80**[27] or via a transmetalation process of nickelacycle intermediates with $^{i}Bu_2$-ALAC (**45**) such as **81**. These cyclizations should be quite interesting and synthetically useful since they are complementary to each other to afford the cyclized product **79′-I** or **79-T** in a stereoselective manner using the same catalyst system, $Ni(cod)_2$-PPh_3, only depending upon the difference of additives, Et_3SiH or $^{i}Bu_2$-ALAC.

Experimental Section

General Information. All manipulations were performed under an argon atmosphere unless otherwise mentioned. All solvents and reagents were purified when necessary using standard procedures. Column chromatography was performed on silica gel 60 (Merck, 70−230 mesh), and flash chromatography was performed on silica gel 60 (Merck, 230−400 mesh) using the indicated solvent. Melting points were determined with a Yanagimoto meilting point microapparatus and are uncorrected. NMR spectra were measured on JEOL GX 270 (^{1}H at 270 MHz), JEOL EX 270 (^{1}H at 270 MHz, ^{13}C at 67.5 MHz), JEOL EX 400 (^{1}H at 400

(25) Kroll, W. R.; Naegele, W. *J. Organomet. Chem.* **1969**, *19*, 439.

(26) A similar mechanism via transmetalation of oxanickelacycles and organometallic reagents was recently proposed by Montgomery in nickel(0)-catalyzed cyclization of alkyne and tethered aldehyde and by Tamaru in nickel(0)-catalyzed coupling of 1,3-dienes and aldehydes; see: (a) Oblinger, E.; Montgomery J. *J. Am. Chem. Soc.* **1997**, *119*, 9065. (b) Kimura, M.; Fujimatsu, H.; Ezoe, A.; Shibata, K.; Shimizu, M.; Matsumoto, S.; Tamaru, Y. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 397.

(27) Very recently, a nickel-catalyzed cyclization of alkyne and tethered aldehyde in the presence of triethylsilane was reported, in which the mechanism of the cyclization was accounted for by σ bond metathesis of triethylsilane and the nickel−oxygen bond of oxanickelacycle; see: Tang, X.-Q.; Montgomery, J. *J. Am. Chem. Soc.* **1999**, *121*, 6098. The mechanism of the cyclization using triethylsilane described in this article could be also accounted for by the same mechanism based on the σ bond methathesis, and its possibility could not be ruled out.

MHz, ^{13}C at 400 MHz), JEOL AL 400 (^1H at 400 MHz, ^{13}C at 100 MHz), or Bruker ARX-500 (^1H at 500 MHz, ^{13}C at 125 MHz) magnetic resonance spectrometer. Infrared spectra were recorded on a Perkin-Elmer FTIR 1605 spectrometer. Mass spectra were measured on JEOL DX-303 and JEOL HX-110 mass spectrometers. Elemental analysis were determined with Yanaco CHN CORDER MT-3.

Typical Procedure for Cyclization Using a Stoichiometric Amount of Nickel Complex 14 Generated from Ni(acac)$_2$, PPh$_3$, and DIBAL-H (Cyclization of 10 in Scheme 2). To a cooled solution of Ni(acac)$_2$ (55 mg, 0.21 mmol) and PPh$_3$ (112 mg, 0.42 mmol) in degassed toluene (5.0 mL) was added dropwise a solution of DIBAL-H (1.02 M in toluene, 0.42 mL, 0.42 mmol) at 0 °C, and the mixture was stirred for 15 min at room temperature. To the mixture was added a solution of **10** (55 mg, 0.21 mmol) in degassed toluene (5.0 mL) at 0 °C, and the mixture was stirred at 0 °C for 6 h. The reaction mixture was hydrolyzed with 10% HCl aqueous solution, and the mixture was extracted with ether. The organic layer was washed with saturated $NaHCO_3$ aqueous solution, and brine and dried over Na_2SO_4. After removal of the solvent, the residue was purified by silica gel column chromatography (hexane/EtOAc 5:1) to afford the cyclized product **15-I** (36 mg, 69%, *E*:*Z* = 8:1). Spectral data for **(*E*)-15-I**: IR (neat) 3422, 3063, 3028, 2956, 2932, 1586, 1495, 1453, 1363 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.42−1.60 (m, 3 H), 1.71 (d, J = 5.5 Hz, 3 H), 1.80−1.96 (m, 1 H), 1.96−2.12 (m, 1 H), 2.17−2.32 (m, 2 H), 3.30 (dd, J = 9.2, 6.7 Hz, 1 H), 3.49 (dd, J = 9.2, 3.7 Hz, 1 H), 4.10−4.17 (m, 1 H), 4.47 (d, J = 12.1 Hz, 1 H), 4.53 (d, J = 12.1 Hz, 1 H), 5.48 (dd, J = 15.4, 5.5 Hz, 1 H), 5.57 (dq, J = 15.4, 5.5 Hz, 1 H), 7.28−7.37 (m, 5 H); MS *m*/*z* 246 (M$^+$), 229, 169, 155, 91 (bp); HRMS *m*/*z* calcd for $C_{16}H_{22}O_2$ 246.1621, found 246.1609. Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.98; H, 9.06.

General Procedure for Cyclization Using a Stoichiometric Amount of Nickel Complex 14 in the Presence of 1,3-Cyclohexadiene. To a cooled suspension of Ni(acac)$_2$ (100 mol % to substrate) and PPh$_3$ (200 mol % to substrate) in degassed toluene (0.04 M) was added dropwise a solution of DIBAL-H (1.02 M in toluene, 200 mol % to substrate) at 0 °C, and the mixture was stirred at room temperature for 15 min. To the mixture was added 1,3-cyclohexadiene (150 mol % to substrate) at 0 °C, and the solution was stirred for ∼3 min. Then a solution of substrate in degassed toluene (0.04 M) was added to the mixture, and the mixture was stirred. The reaction was monitored by TLC. The reaction mixture was hydrolyzed with 10% aqueous HCl, and the aqueous layer was extracted with ether. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography to give the desired cyclized product.

(1*R,2*S**,3*R**)-3-Benzyloxymethyl-2-(2-propenyl)cyclopentan-1-ol (15-T).** Following the general procedure, a crude material, which was obtained from the cyclization of **10** (49 mg, 0.20 mmol) using nickel complex **14** generated from Ni(acac)$_2$ (51 mg, 0.20 mmol), PPh$_3$ (105 mg, 0.40 mmol), and DIBAL-H (0.41 mL, 0.41 mmol) in the presence of 1,3-CHD (0.028 mL, 0.30 mmol) at 0 °C for 2 h, was purified by silica gel column chromatography (hexane/EtOAc 5:1) to afford **15** (30 mg, 61%, **15-T**:**15-I** = 95:5 based on ^1H NMR). Spectral data for **15-T**: IR (neat) 3340, 3070, 3020, 2925, 1640, 1600, 1450, 1360 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.41 (br s, 1 H), 1.43−1.54 (m, 1 H), 1.60−1.72 (m, 2 H), 1.77−1.86 (m, 1 H), 1.98−2.12 (m, 2 H), 2.19−2.32 (m, 2 H), 3.35 (dd, J = 8.8, 6.3 Hz, 1 H), 3.37 (dd, J = 8.8, 4.9 Hz, 1 H), 4.20−4.25 (m, 1 H), 4.50 (d, J = 12.1 Hz, 1 H), 4.52 (d, J = 12.1 Hz, 1 H), 5.00 (br.d, J = 10.3 Hz, 1 H), 5.10 (ddd, J = 17.1, 2.0, 3.4 Hz, 1 H), 5.72 (dddd, J = 17.1, 10.3, 7.8, 6.4 Hz, 1 H), 7.25−7.37 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7 (CH_2), 33.2 (CH_2), 33.5 (CH_2), 42.0 (CH), 47.5 (CH), 73.0 (CH_2), 73.6 (CH_2), 74.8 (CH), 115.4 (=CH_2), 127.5 (Ar), 128.3 (Ar), 138.1 (CH=), 138.7 (Ar); MS *m*/*z* 247 (M$^+$ + 1), 228, 169, 155, 91 (bp). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.10; H, 8.89.

(1*R,2*S**,3*R**)-3-(Benzyloxymethyl)-1-methyl-2-(2-propenyl)cyclopentan-1-ol (29-T).** Following the general procedure, a crude material, which was obtained from the cyclization of **23** (40 mg, 0.16 mmol) using nickel complex **14** generated from Ni(acac)$_2$ (40 mg, 0.16 mmol), PPh$_3$ (81 mg, 0.33 mmol), and DIBAL-H (0.32 mL, 0.32 mmol) in the presence of 1,3-CHD (0.022 mL, 0.24 mmol) at 23 °C for 7 h, was purified by silica gel column chromatography (hexane/EtOAc 5:1) to afford **29** (28 mg, 70%, **29-T**:**29-I** = 86:14 based on ^1H NMR). Spectral data for **29-T**: IR (neat) 3459, 3074, 3031, 2956, 2860, 1716, 1638, 1494, 1455 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.31 (s, 3 H), 1.39−1.59 (m, 2 H), 1.60−1.76 (m, 3 H), 1.86−2.24 (m, 1 H), 2.05−2.25 (m, 2 H), 2.26−2.42 (m, 1 H), 3.33 (dd, J = 9.1, 7.1 Hz, 1 H), 3.50 (dd, J = 9.1, 4.5 Hz, 1 H), 4.49 (d, J = 12.2 Hz, 1 H), 4.53 (d, J = 12.2 Hz, 1 H), 5.06 (br d, J = 10.0 Hz, 1 H), 5.09 (br d, J = 17.2 Hz, 1 H), 5.87 (ddq, J = 17.2, 10.0, 7.2 Hz, 1 H), 7.26−7.42 (m, 5 H); MS *m*/*z* 260 (M$^+$), 242, 169, 152, 91 (bp). Anal. Calcd for $C_{17}H_{24}O_2$: C, 74.42; H, 9.29. Found: C, 74.45; H, 9.36.

(1*R,2*S**,3*R**)-3-(Benzyloxymethyl)-2-[(2*E*)-4-methoxy-2-butenyl]-cyclopentan-1-ol (30-T).** Following the general procedure, a crude material, which was obtained from the cyclization of **28** (55 mg, 0.19 mmol) using nickel complex **14** generated from Ni(acac)$_2$ (49 mg, 0.19 mmol), PPh$_3$ (100 mg, 0.38 mmol), and DIBAL-H (0.37 mL, 0.38 mmol) in the presence of 1,3-CHD (0.027 mL, 0.29 mmol) at 0 °C for 2 h, was purified by silica gel column chromatography (hexane/EtOAc 2:1) to afford **30-T** (41 mg, 73%) as a single isomer: IR (neat) 3445, 3038, 2921, 2851, 1666, 1596, 1498, 1442 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.40−1.87 (m, 5 H), 1.93−2.13 (m, 2 H), 2.25 (dd, J = 7.3, 7.3 Hz, 2 H), 3.30 (s, 3 H), 3.35 (dd, J = 9.1, 6.3 Hz, 1 H), 3.47 (dd, J = 9.1, 6.4 Hz, 1 H), 3.86 (d, J = 6.0 Hz, 2 H), 4.18−4.26 (m, 1 H), 4.48 (d, J = 12.3 Hz, 1 H), 4.53 (d, J = 12.3 Hz, 1 H), 5.62 (dt, J = 15.6, 6.0 Hz, 1 H), 5.75 (dt, J = 15.6, 6.7 Hz, 1 H), 7.23−7.38 (m, 5 H); MS *m*/*z* 272 (M$^+$ − H_2O), 258, 240, 227, 91 (bp); HRMS (EI) calcd for $C_{18}H_{24}O_2$ (M$^+$ − H_2O) 272.1777, found 272.1768. Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.41; H, 9.05.

(1*R,2*S**,3*R**)-3-(Benzyloxymethyl)-2-(2-propenyl)cyclohexan-1-ol (18-T).** Following the general procedure, a crude material, which was obtained from the cyclization of **11** (50 mg, 0.19 mmol) using nickel complex **14** generated from Ni(acac)$_2$ (50 mg, 0.19 mmol), PPh$_3$ (101 mg, 0.39 mmol), and DIBAL-H (0.38 mL, 0.39 mmol) in the presence of 1,3-CHD (0.028 mL, 0.29 mmol) at 0 °C for 2 h, was purified by silica gel column chromatography (hexane/EtOAc 5:1) to afford **18** (43 mg, 86%, **18-T**:**18-I** = 93:7 based on ^1H NMR). Spectral data for **18-T**: IR (neat) 3392, 3056, 2934, 2858, 1641, 1495, 1452 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.15−1.58 (m, 5 H), 1.63−1.87 (m, 3 H), 1.88−2.01 (m, 1 H), 2.15−2.29 (m, 1 H), 2.45−2.59 (m, 1 H), 3.37−3.50 (m, 2 H), 3.54 (dd, J = 9.2, 3.1 Hz, 1 H), 4.47 (d, J = 12.1 Hz, 1 H), 4.52 (d, J = 12.1 Hz, 1 H), 5.00−5.12 (m, 2 H), 5.88 (ddt, J = 17.3, 10.2, 7.4 Hz, 1 H), 7.24−7.43 (m, 5 H); MS *m*/*z* 260 (M$^+$), 242, 169, 91 (bp). Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.23; H, 9.35.

3-(Benzyloxymethyl)-2-(2-propenyl)cycloheptan-1-ol (20-T). Following the general procedure, a crude material, which was obtained from the cyclization of **12** (50 mg, 0.18 mmol) using nickel complex **14** generated from Ni(acac)$_2$ (47 mg, 0.18 mmol), PPh$_3$ (96 mg, 0.37 mmol), and DIBAL-H (0.36 mL, 0.37 mmol) in the presence of 1,3-CHD (0.026 mL, 0.28 mmol) at 23 °C for 2 h, was purified by silica gel column chromatography (hexane/EtOAc 7:1) to afford **20-T** (23 mg, 47% as an inseparable mixture of two isomers (ratio of 5:23 based on ^1H NMR): IR (neat) 3440, 3027, 2925, 2862, 1640, 1495 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.24−1.99 (m, 11 H), 1.93−2.53 (m, 2 H), 3.31−3.50 (m, 2 H), 3.75−3.89 (m, 23/28 H), 3.99−4.08 (m, 5/28 H), 4.45−4.56 (m, 2 H), 5.00−5.12 (m, 2 H), 5.70−5.94 (m, 1 H), 7.24−7.43 (m, 5 H); MS *m*/*z* 274 (M$^+$), 256, 183, 91. Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.68; H, 9.60.

General Procedure for Catalytic Cyclization Using Ni(cod)$_2$ and PPh$_3$ in the Presence of Et$_3$SiH (Table 4). Ni(cod)$_2$ and PPh$_3$ were dissolved in degassed toluene, and the mixture was stirred at 0 °C for 30 min. To the mixture were added Et$_3$SiH (5 equiv) and a solution of substrate in degassed toluene, and the mixture was stirred at the temperature shown in Table 4. After usual workup, the residue was purified by silica gel column chromatography to give the cyclized product.

(1*R,2*S**,3*R**)-1-(Benzyloxymethyl)-2-[(*E*)-1-propenyl]-3-(triethylsilyloxy)cyclopentane (38-I).** Following the general procedure, a crude material, which was obtained from the cyclization of **10** (49 mg, 0.20 mmol) with Ni(cod)$_2$ (5.5 mg, 0.02 mmol), PPh$_3$ (10 mg, 0.04 mmol), and Et$_3$SiH (0.16 mL, 1.0 mmol) at 23 °C for 21 h, was purified

by silica gel column chromatography (hexane/ether 50:1) to afford **38-I** (50 mg, 70%): IR (neat) 3020, 2950, 1580, 1450, 1238 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.55 (q, J = 7.7 Hz, 6 H), 0.94 (t, J = 7.7 Hz, 9 H), 1.40−1.63 (m, 2 H), 1.65 (d, J = 6.2 Hz, 3 H), 1.69−1.84 (m, 1 H), 1.95−2.09 (m, 2 H), 2.13−2.29 (m,1 H), 3.26 (dd, J = 9.2, 7.3 Hz, 1 H), 3.49 (dd, J = 9.2, 4.0 Hz, 1 H), 4.08−4.15 (m 1 H), 4.46 (d, J = 12.4 Hz, 1 H), 4.53 (d, J = 12.4 Hz, 1 H), 5.37 (dq, J = 15.5, 6.2 Hz, 1 H), 5.50 (dd, J = 15.4, 8.8 Hz, 1 H), 7.27−7.33 (m, 5 H); MS m/z 360 (M^+), 331, 269, 87; HRMS calcd for $C_{22}H_{36}O_2Si$ 360.2486, found 360.2463. Anal. Calcd for $C_{22}H_{36}O_2Si$: C, 73.28; H, 10.06. Found: C, 73.27; H, 9.96.

(1*R,2*S**,3*R**)-1-(Benzyloxymethyl)-2-[(*E*)-4-methoxy-1-butenyl]-3-(triethyl-silyloxy)cyclopentane (53).** Following the general procedure, a crude material, which was obtained from the cyclization of **28** (45 mg, 0.16 mmol) with $Ni(cod)_2$ (8.6 mg, 0.031 mmol), PPh_3 (16 mg, 0.062 mmol), and Et_3SiH (0.13 mL, 0.78 mmol) at 30 °C for 3.5 h, was purified by silica gel column chromatography (hexane/EtOAc 15:1) to afford **53** (43 mg, 67%): IR (neat) 3030, 2953, 2563, 2730, 1724, 1604, 1587, 1490, 1450 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.56 (q, J = 7.8 Hz, 6 H), 0.95 (t, J = 7.8 Hz, 9 H), 1.41−1.86 (m, 3 H), 1.94−2.12 (m, 1 H), 2.14−2.32 (m, 2 H), 2.29 (dd, J = 7.0, 7.0 Hz, 2 H), 3.27 (dd, J = 9.1, 7.1 Hz, 1 H), 3.33 (s, 3 H), 3.37 (t, J = 7.0 Hz, 2 H), 3.49 (dd, J = 9.1, 4.9 Hz, 1 H), 4.11−4.17 (m, 1 H), 4.47 (d, J = 12.2 Hz, 1 H), 4.53 (d, J = 12.2 Hz, 1 H), 5.36 (dt, J = 15.6, 6.6 Hz, 1 H), 5.59 (dd, J = 15.5, 8.9 Hz, 1 H), 7.22−7.38 (m, 5 H); MS m/z 404 (M^+), 375, 283, 171, 91; HRMS (EI) calcd for $C_{24}H_{40}O_3Si$ 404.2748, found 404.2762. Anal. Calcd for $C_{24}H_{40}O_3Si$: C, 71.24; H, 9.96. Found: C, 71.31; H, 10.01.

(1*R,2*R**,3*S**)-1-(Benzyloxymethyl)-2-[(*E*)-1-propenyl]-3-(triethylsilyloxy)cyclohexane (54).** Following the general procedure, a crude material, which was obtained from the cyclization of **11** (56 mg, 0.22 mmol) with $Ni(cod)_2$ (12 mg, 0.044 mmol), PPh_3 (23 mg, 0.087 mmol), and Et_3SiH (0.17 mL, 1.1 mmol) at 23 °C for 1.5 h, was purified by silica gel column chromatography (hexane/ether 100:3) to afford **54** (58 mg, 71%): IR (neat) 2937, 2879, 1494, 1455 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.56 (q, J = 7.8 Hz, 6 H), 0.94 (t, J = 7.8 Hz, 9 H), 1.00−1.50 (m, 4 H), 1.64 (dd, J = 6.4, 1.6 Hz, 3 H), 1.69−1.84 (m, 2 H), 1.84−1.98 (m, 2 H), 3.21 (dd, J = 9.1, 7.6 Hz, 1 H), 3.29 (ddd, J = 10.2, 9.5, 4.5 Hz, 1 H), 3.51 (dd, J = 9.1, 3.3 Hz, 1 H), 4.41 (d, J = 12.0 Hz, 1 H), 4.49 (d, J = 12.0 Hz, 1 H), 5.07 (ddq, J = 15.2, 9.2, 1.6 Hz, 1 H), 5.39 (dq, J = 15.2, 6.4 Hz, 1 H), 7.23−7.42 (m, 5 H); MS m/z 374 (M^+), 346, 283, 91. Anal. Calcd for $C_{23}H_{38}O_2Si$: C, 73.34; H, 10.22. Found: C, 73.55; H, 10.38.

(1*R,2*R**,3*S**)-1-(Benzyloxymethyl)-2-[(*E*)-1-propenyl]-3-(triethylsilyloxy)cycloheptane (55).** Following the general procedure, a crude material, which was obtained from the cyclization of **12** (50 mg, 0.18 mmol) with $Ni(cod)_2$ (10 mg, 0.037 mmol), PPh_3 (19 mg, 0.073 mmol), and Et_3SiH (0.15 mL, 0.92 mmol) at 30 °C for 12 h, was purified by silica gel column chromatography (hexane/ether 100:1) to afford **55** (48 mg, 66%): IR (neat) 3027, 2940, 1657, 1499, 1456 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.55 (q, J = 8.0 Hz, 6 H), 0.94 (t, J = 8.0 Hz, 9 H), 1.20−2.00 (m, 10 H), 1.62 (d, J = 5.7 Hz, 3 H). 3.18 (dd, J = 9.1, 8.1 Hz, 1 H), 3.42 (dd, J = 9.1, 3.6 Hz, 1 H), 3.70 (ddd, J = 7.5, 5.5, 2.0 Hz, 1 H), 4.41 (d, J = 12.0 Hz, 1 H), 4.49 (d, J = 12.0 Hz, 1 H), 5.19 (dd, J = 15.1, 8.8 Hz, 1 H), 5.31 (dq, J = 15.1, 5.7 Hz, 1 H), 7.24−7.42 (m, 5 H); MS m/z 388 (M^+), 359, 293, 91. Anal. Calcd for $C_{24}H_{40}O_2Si$: C, 74.17; H, 10.37. Found: C, 74.28; H, 10.45.

Cyclization of 10 Using $Ni(cod)_2$, PPh_3, and $^iBu_2$-ALAC (Scheme 24). $Ni(cod)_2$ (62 mg, 0.23 mmol) and PPh_3 (118 mg, 0.45 mmol) were dissolved in degassed toluene (5.1 mL), and the mixture was stirred at 0 °C for 30 min. To the mixture was added $^iBu_2$-ALAC (0.5 M in toluene, 1.0 mL, 0.5 mmol), and the mixture was stirred at room temperature for 15 min. To the mixture was added a solution of **10** (55 mg, 0.23 mmol) in degassed toluene (5.1 mL) at 0 °C, and the mixture was stirred at the same temperature for 2 h. The reaction mixture was hydrolyzed with 10% aqueous HCl, and the aqueous layer was extracted with ether. After the usual workup, the cyclized product **15-I** was obtained in 82% yield.

Cyclization of 10 Using $Ni(cod)_2$, PPh_3, and $^iBu_2$-ALAC in the Presence of 1,3-CHD (Scheme 24). In a similar manner, **15** was obtained in 85% yield (48 mg, **15-T**:**15-I** = 98:2 based on ^1H NMR) from the reaction of **10** (56 mg, 0.23 mmol) with $Ni(cod)_2$ (63 mg, 0.23 mmol), PPh_3 (120 mg, 0.45 mmol), and $^iBu_2$-ALAC (0.5 M in toluene, 1.0 mL, 0.5 mmol) in the presence of 1,3-CHD (0.033 mL, 0.34 mmol) in toluene at 0 °C for 2 h.

General Procedure for Catalytic Cyclization Using $Ni(cod)_2$, PPh_3, and $^iBu_2$-ALAC. $Ni(cod)_2$ and PPh_3 were dissolved in degassed toluene (0.04 M), and the mixture was stirred at 0 °C for 20 min. To the mixture was added $^iBu_2$-ALAC (1.0 M in toluene, 1.5 equiv to substrate), and the mixture was stirred at room temperature for 15 min. To the mixture was added a solution of substrate in degassed toluene (0.04 M) at 0 °C, and the mixture was stirred at the temperature indicated in Scheme 2 or Table 1. The reaction mixture was hydrolyzed with saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with ether. After the usual workup, the residue was purified by silica gel column chromatography to give the cyclized product.

Cyclization of 10 (Scheme 26). Following the general procedure, a crude material, which was obtained from **10** (57 mg, 0.23 mmol), $Ni(cod)_2$ (3.2 mg, 0.012 mmol), PPh_3 (6.1 mg, 0.023 mmol), and $^iBu_2$-ALAC (0.35 mL, 0.35 mmol), was purified by silica gel column chromatography (hexane/AcOEt 6:1) to afford **15-T** (48 mg, 84%), whose spectral data were completely identical with those noted above.

Cyclization of 28 (Table 5, Run 1). Following the general procedure, a crude material, which was obtained from **28** (61 mg, 0.21 mmol), $Ni(cod)_2$ (5.8 mg, 0.021 mmol), PPh_3 (11 mg, 0.042 mmol), and $^iBu_2$-ALAC (0.32 mL, 0.32 mmol), was purified by silica gel column chromatography (hexane/AcOEt 5:2) to afford **30-T** (46 mg, 75%), whose spectral data were completely identical with those noted above.

Cyclization of 11 (Table 5, Run 2). Following the general procedure, a crude material, which was obtained from **11** (60 mg, 0.23 mmol), $Ni(cod)_2$ (3.2 mg, 0.012 mmol), PPh_3 (6.1 mg, 0.023 mmol), and $^iBu_2$-ALAC (0.35 mL, 0.35 mmol), was purified by silica gel column chromatography (hexane/AcOEt 6:1) to afford **18-T** (58 mg, 96%), whose spectral data were completely identical with those noted above.

Cyclization of 12 (Table 5, Run 3). Following the general procedure, a crude material, which was obtained from **12** (62 mg, 0.23 mmol), $Ni(cod)_2$ (3.1 mg, 0.011 mmol), PPh_3 (6.0 mg, 0.023 mmol), and $^iBu_2$-ALAC (0.34 mL, 0.34 mmol), was purified by silica gel column chromatography (hexane/AcOEt 6:1) to afford **20-T** (36 mg, 57%) as an inseparable mixture of two isomers (ratio of 1/4.2), whose spectral data were completely identical with those noted above.

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Supporting Information Available: Experimental procedures and spectral data for the synthesis of substrates **10**−**12**, **23**, and **28**; spectral data for **16**, **17**, **19**, **31**, **32**, **51**, **I**, **II**, **IIIA**, **IV**, and **V**. This material is available free of charge via the Internet at http://pubs.acs.org.

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