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# Novel Stereoselective Cyclization *via* $\pi$-Allylnickel Complex Generated from 1,3-Diene and Hydride Nickel Complex

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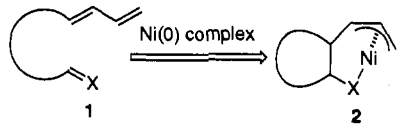
In spite of the many reports about the nickel(0)-catalyzed oligomerization of 1,3-dienes,[1] synthetic utilization of these processes has been restricted to intramolecular [4 + 4] and [4 + 2] cycloadditions of bis-dienes and dienynes[2] and the cocyclization of bis-dienes and dienynes with isocyanides and hydrosilanes.[3] The utility of these processes prompted us to develop the cyclization of 1,3-dienes and other multiple bond-containing heteroatoms. During the course of our investigation, we found a novel stereoselective cyclization of 1,3-diene and the carbonyl group in a chain *via* a $\pi$-allylnickel complex (Scheme 1).

We first examined the intramolecular cyclization of diene aldehyde **4a** (Scheme 2). To a toluene solution containing a stoichiometric amount of the nickel complex **3**, prepared in situ from Ni(acac)$_2$ (100 mol %) and 2 equiv of DIBAL-H in the presence of PPh$_3$ (200 mol %),[4] was added a solution of **4a** 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 alcohol **7c** in 69% yield.[5] The reaction of **4a** using a catalytic amount of **3** (10 mol %) afforded **7c** in only 10% yield. This indicates that a stoichiometric amount of **3** is required for this reaction.

**Scheme 1**



**Scheme 2**

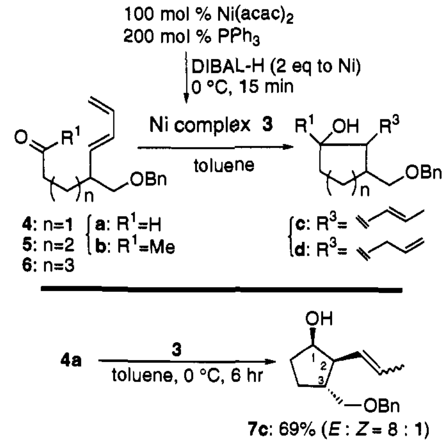
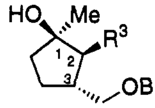
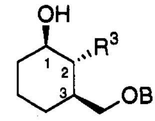
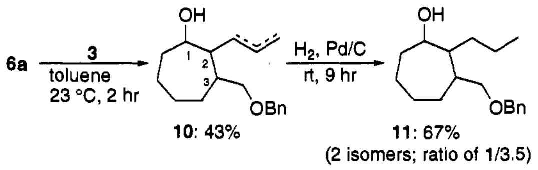


**Table 1.** Cyclization of **4b** and **5a** Using Ni Complex **3** Generated from Ni(acac)$_2$ and DIBAL-H in the Presence of PPh$_3$

| substrate | temp (°C) | time (hr) | yield (**c**+**d**) (%) | cyclized products[a] |
|---|---|---|---|---|
| **4b** | 23 | 7 | 56 | <br>**8c/8d** = 1.8/1 |
| **5a** | 0 | 2 | 82 | <br>**9c/9d** = 1.9/1 |

[a] The ratio was determined from the NMR spectrum.

**Scheme 3**



Encouraged by these results, we investigated the cyclization of various substrates. The reaction of **4b**, having a ketone moiety as a carbonyl group, proceeded smoothly giving an inseparable mixture of cyclopentanols **8c** and **8d** (ratio of 1.8:1) in 56% yield (Table 1).[6] The cyclization of **5a** afforded cyclohexanols **9c** and **9d** (ratio of 1.9:1) in 82% yield.[7] These results indicate that three stereocenters, at C1, C2, and C3 of each cycloalkane ring in **7**, **8**, and **9**, are produced in a stereoselective manner in these cyclizations.

Further, it is noteworthy that the reaction of **6a** using **3** proceeded to give **10**, having a seven-membered ring, in 43% yield (Scheme 3). The NMR spectrum of **11** indicates that cycloheptanol **10** was obtained as two isomers (ratio of 3.5:1). The cycloheptanol **11** was converted into the corresponding cycloheptanone as the sole product by PCC oxidation.

Next, we turned our attention to the mechanism of this cyclization. We initially considered that this cyclization proceeded *via* nickel complexes **13** and **14** (Scheme 4, path A).[8] However,

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(1) 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. 2, p 371. (e) Heimback, P. *Angew. Chem.* **1973,** *85,* 1035; *Angew. Chem., Int. Ed. Engl.* **1973,** *12,* 975. (f) Wilke, G. *Angew. Chem.* **1988,** *100,* 189; *Angew. Chem., Int. Ed. Engl.* **1988,** *27,* 185.

(2) (a) For [4 + 4] cycloadditions, see: Wender, P. A.; Tebbe, M. J. *Synthesis* **1991,** 1089. Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988,** *110,* 5904. Wender, P. A.; Ihle, N. C. *Tetrahedron Lett.* **1987,** *28,* 2451. Wender, P. A.; Snapper, M. L. *Tetrahedron Lett.* **1987,** *28,* 2221. Wender, P. A.; Ihle, N. C. *J. Am. Chem. Soc.* **1986,** *108,* 4678. (b) For [4 + 2] cycloadditions, see: Wender, P. A.; Jenkins, T. E. *J. Am. Chem. Soc.* **1989,** *111,* 6432.

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

(4) It has been reported that the zerovalent nickel complex was formed by the reduction of Ni(acac)$_2$ with DIBAL-H, see: Krysan, D. J.; Mackenzie, P. B. *J. Org. Chem.* **1990,** *55,* 4229. Also see ref 3.

(5) Hydrogenation of **7c** with 10% Pd/C gave corresponding cyclopentanol in 87% yield as the sole product. The three stereocenters in **7c**, at C1, C2, and C3 of the cyclopentane ring, were determined by the X-ray structural analysis of *p*-bromobenzoate of (*E*)-**7c**.

(6) Hydrogenation of **8c** and **8d** with 10% Pd/C gave the corresponding cyclopentanol in 85% yield as the sole product. For the determination of the stereochemistry of **8**, see the supplementary material.

(7) Hydrogenation of **9c** and **9d** with 10% Pd/C gave the corresponding cyclohexanol in 92% yield as the sole product. For the determination of the stereochemistry of **9**, see the supplementary material.

(8) The mechanism shown in path A (Scheme 4) is proposed for the [4 + 4] cycloaddition of bis-diene and the [4 + 2] cycloaddition of dienyne. Also, see ref 2.

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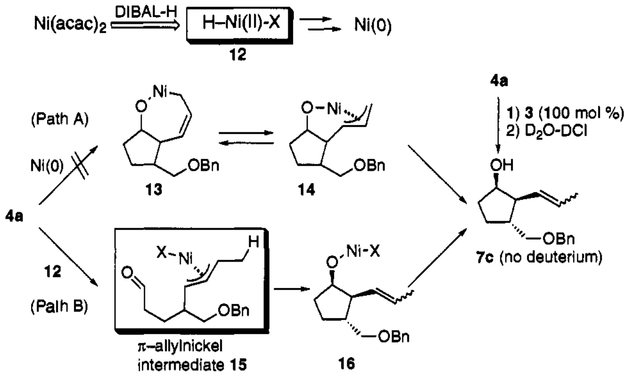
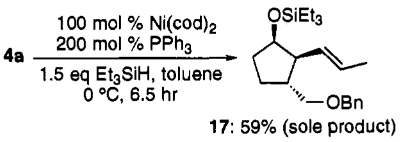
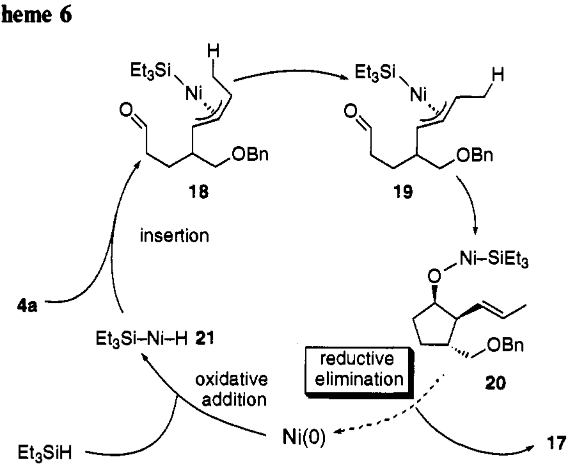
**Scheme 4**



**Scheme 5**



**Scheme 6**

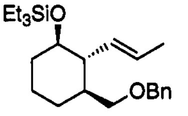
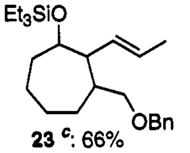


treatment of the reaction mixture of **4a** and **3** with DCl–$D_2O$ provided no product containing deuterium. On the other hand, only a trace amount of **7c** was obtained in the cyclization of **4a** using other zerovalent nickel complexes, generated from $Ni(cod)_2$ and $PPh_3$ or from $NiCl_2(PPh_3)_2$ and *n*-BuLi. These results suggest that the cyclization of **4a** would proceed as shown in path B (Scheme 4), in which the hydride nickel(II) complex **12**, formed by the reduction of $Ni(acac)_2$ with DIBAL-H, plays an important role.

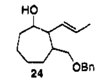
With the aim of confirming the mechanism, we decided to use trialkylsilane as the hydride source.[9] When a toluene solution of **4a**, $Ni(cod)_2$ (100 mol %), $PPh_3$ (200 mol %), and $Et_3SiH$ (1.5 equiv) was stirred at 0 °C for 6.5 h, we were pleased to find that the highly regio- and stereocontrolled cyclized product **17** was obtained as the sole product in 59% yield (Scheme 5). Moreover, the fact that **17** was afforded as the silyl ether indicates the regeneration of zerovalent nickel complex from **20** (Scheme 6).

On the basis of these mechanistic aspects, the reaction 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), and we succeeded in obtaining **17** in 70% yield (Table 2). Similarly, the reaction of **5a** afforded the desired cyclohexanol derivative **22** as the sole product in 71% yield. It was surprising to know that cycloheptanol derivative **23** was also obtained as the sole product in 66% yield in the reaction of **6a**.[10]

**Table 2.** Cyclization of **4a**, **5a**, and **6a** Using a Catalytic Amount of $Ni(cod)_2$ and $PPh_3$ in the Presence of $Et_3SiH$

| substrate | $Ni(cod)_2$ [a] (mol %) | temp (°C) | time (hr) | cyclized product [b] (%) |
|---|---|---|---|---|
| **4a** | 10 | 23 | 21 | **17**: 70% |
| **5a** | 20 | 23 | 1.5 |  **22**: 71% |
| **6a** | 20 | 30 | 12 |  **23** [c]: 66% |

[a] All reactions were carried out in toluene in the presence of $PPh_3$ (2 eq to $Ni(cod)_2$). [b] All cyclized products were obtained as the sole product. [c] Stereochemistry was not yet determined.



Though the reaction of the π-allylnickel complex with the carbonyl compounds could not establish the catalytic cycle,[11] we could overcome this difficulty by preparing π-allylnickel X (X = $SiEt_3$) formed from the 1,3-diene and the zerovalent nickel complex in the presence of $Et_3SiH$.[12]

In conclusion, we have succeeded in developing a novel stereoselective cyclization of the 1,3-diene and the carbonyl group in a chain. This cyclization proceeds by the hydride nickel(II) complex generated from $Ni(acac)_2$ and DIBAL-H. The catalytic cycle was established using $Et_3SiH$ as the hydride source. This cyclization is applicable to the construction of five- to seven-membered rings. The scopes and limitations of this cyclization are currently under investigation.

**Supplementary Material Available:** General procedure for the cyclization using nickel complex generated from $Ni(acac)_2$–DIBAL-H; typical procedure for the catalytic cyclization of **4a** using $Ni(cod)_2$ in the presence of $Et_3SiH$; procedures for determination of the stereochemistry of cyclized products **8** and **9**; characterization data for **4a**, **4b**, **5a**, **6a**, (*E*)-**7c**, **17**, **22**, **23**, **24**; and $^{13}C$-NMR spectrum of **24** (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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

(10) The structure of **23** was confirmed by $^1H$-NMR, $^{13}C$-NMR, and other spectral data of cycloheptanol **24** obtained by desilylation of **23**. The $^{13}C$-NMR spectrum of **24** strongly supported that **23** was produced as a single isomer (see supplementary material). However, the stereochemistry of **23** has not been determined yet.

(11) (a) Billington, D. C. *Chem. Soc. Rev.* **1985**, *14*, 93 and references cited 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. *Ibid.* **1978**, *100*, 5565. (g) Semmelhack, M. F.; Wu, E. C. S. *Ibid.* **1976**, *98*, 3384. (h) Semmelhack, M. F. *Org. React.* **1972**, *19*, 115.

(12) The hydride nickel complex, generated from $Ni(cod)_2$ and $PPh_3$ in the presence of $Et_3SiH$, does not react with a carbonyl group, e.g., when the reaction of 3-phenylpropanal with the nickel complex, generated under the same conditions, was carried out, the unchanged starting material was completely recovered. This result indicates that the first step of this cyclization is the reaction of the hydride nickel complex with the diene moiety furnishing the π-allylnickel X (X = $Et_3Si$).