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Communications

Study on Transmetalation of a Nickelacycle with Organometallic Reagents

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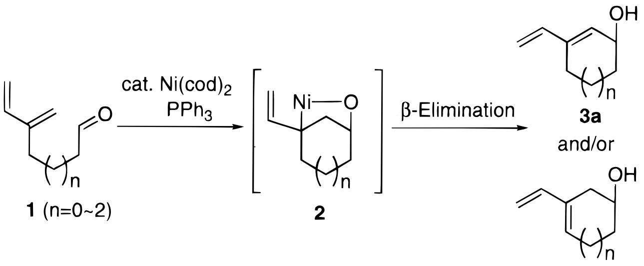
*Summary: A transmetalation of the oxanickelacycle **7**, generated from the 1,3-diene and tethered aldehyde in **6** via oxidative cycloaddition to a zerovalent nickel complex, with various organometallic reagents was investigated. It was found that the tandem reaction, i.e., cyclization of **6** followed by transmetalation of the resulting oxanickelacycle **7**, proceeded smoothly using a catalytic amount of zerovalent nickel complex.*

A nickel-promoted or -catalyzed intramolecular oligomerization of 1,3-dienes and tethered multiple bonds is a quite useful process for regio- and stereoselective construction of various cyclic compounds.[1,2] During the course of our continuing investigations on nickel-catalyzed cyclization of 1,3-diene and tethered aldehyde,[3] we recently found that the cyclizations of substrates **1** using Ni(cod)$_2$ proceeded via oxanickelacycle intermediates **2** and that the cyclized products **3a** and **3b** were produced via β-elimination from **2** in good yields (Scheme 1).[4]

Scheme 1



The process for the formation of **2**, having a unique structure, in this cyclization prompted us to investigate its reactivity. We planned the transmetalation of **2** with various organometallic reagents as shown in Scheme 2.[5]

The oxanickelacycle **2** would be in equilibration with the (π-allyl)nickel intermediate **2′**. If the nickelacycle **2**

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(1) For reviews of transition-metal-catalyzed cycloadditions, see: (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) (a) For [4 + 4] cycloadditions, see: Wender, P. A.; Tebbe, M. J. *Synthesis* **1991**, 1089 and references therein. (b) For [4 + 2] cycloadditions, see: Wender, P. A.; Smith, T. E. *Tetrahedron* **1998**, *54*, 1255 and references therein. (c) For a cyclization of 1,3-diene and allene, see: Wender, P. A.; Jenkins, T. E.; Suzuki, S. *J. Am. Chem. Soc.* **1995**, *117*, 1843. (d) Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539. Tamao, K.; Kobayashi, K.; Ito, Y. *J. Synth. Org. Chem. Jpn.* **1990**, *48*, 381. (e) 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.

(3) (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. (c) Sato, Y.; Takimoto, M.; Mori, M. *Synlett* **1997**, 734. (d) Sato, Y.; Saito, N.; Mori, M. *Tetrahedron Lett.* **1997**, *38*, 3931. (e) Sato, Y.; Saito, N.; Mori, M. *Tetrahedron* **1998**, *54*, 1153.

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

(5) The transmetalation of oxanickelacycles and organometallic reagents has recently been reported by Montgomery in the Ni(0)-catalyzed cyclization of alkyne and tethered aldehyde and by Tamaru in the Ni(0)-catalyzed coupling of 1,3-dienes and aldehydes; see: (a) Oblinger, E.; Montgomery, J. *J. Am. Chem. Soc.* **1997**, *119*, 9065. Tang, X.-Q.; Montgomery, J. *J. Am. Chem. Soc.* **1999**, *121*, 6098. (b) Kimura, M.; Fujimatsu, H.; Ezoe, A.; Shibata, K.; Shimizu, M.; Matsumoto, S.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 397.

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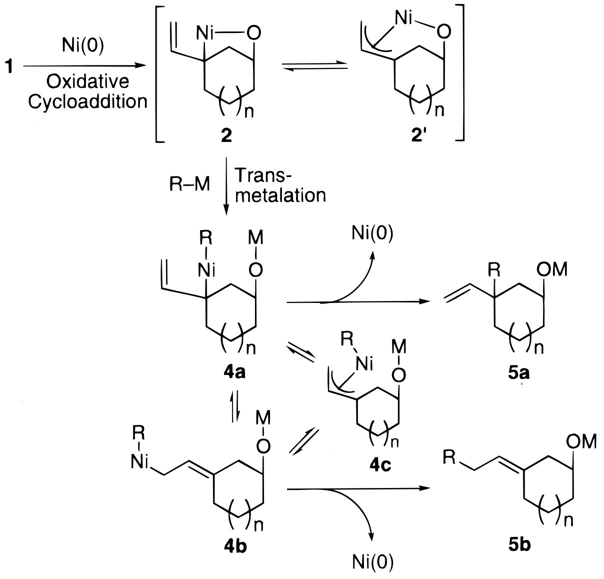
Scheme 2

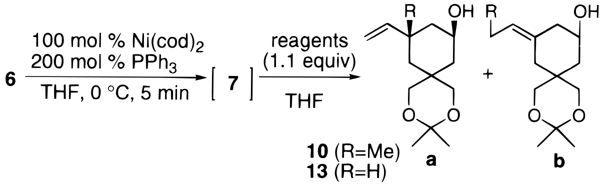


can react with another organometallic reagent through transmetalation, the intermediate **4a** should be formed from **2** and the organometallic reagent (R−M). The intermediate **4a** would be in equilibration with **4b** and **4c**, and reductive elimination from these intermediates would afford the products **5a** and/or **5b**.

First, we tried to investigate a transmetalation of **7** with various Grignard reagents (Scheme 3). To a solution of Ni(cod)$_2$ (100 mol %) and PPh$_3$ (200 mol %) in THF was added a solution of substrate **6** in THF at 0 °C, and the solution was stirred at 0 °C for 5 min. To the solution was added a THF solution of Grignard reagent **8** (1.1 equiv), generated from (trimethylsilyl)acetylene and EtMgBr in THF, and the mixture was stirred at 0 °C for 5 h. After hydrolysis of the reaction mixture, we obtained the products **9a**[6] and **9b**[7] (ratio of 1/2.4) in a total yield of 58%.

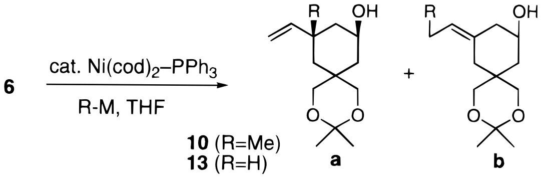
On the other hand, the reaction with MeMgBr, allylmagnesium bromide, or PhMgBr under similar conditions gave **10b**, **11**, or **12** in 64%, 75%, or 80% yield as a single isomer, respectively.[7] It was thought that **9b**, **10b**, **11**, or **12** would be produced via the intermediate **4b**, while **9a** would be produced via **4a** in Scheme 2.[8]

Table 1. Reaction of 7 with Various Organometallic Reagents



run	reagents	temp (°C)	time (h)	product (R)	yield (%) a	yield (%) b
1	MeLi	50	5	**10** (Me)		23
2	Me$_3$Al	23	5	**10** (Me)		53
3	Me$_2$Al(acac)	23	5	**10** (Me)		51
4	Me$_2$Zn	0	5	**10** (Me)		49
5	DIBAL-H	0	1	**13** (H)	79	13
6	*i*-Bu$_2$Al(acac)	0	1	**13** (H)	62	
7	*t*-BuMgCl	room temp	14	**13** (H)	13	50

Table 2. Catalytic Reaction of 6 via the Cyclization−Transmetalation Process



run	reagent (R−M)	Ni(cod)$_2$ (mol %)	temp (°C)	time (h)	product (R)	yield (%) a	yield (%) b	*E*/*Z*
1	*i*-Bu$_2$Al(acac)[a]	20	23	7.5	**13** (H)	53	16	1/0
2	Me$_2$Al(acac)[b]	30	50	48	**10** (Me)		43	1/4.7
3	Me$_2$Zn[a]	20	50	68	**10** (Me)		57	1/1.1

[a] 2 equiv of R−M was used. [b] 3 equiv of R−M was used.

Next, transmetalation of the oxanickelacycle **7** with various organometallic reagents was examined. The results are shown in Table 1. Treatment of nickelacycle **7**, generated from **6** and a stoichiometric amount of Ni(cod)$_2$−PPh$_3$ as mentioned above, with MeLi (run 1) at 50 °C gave the product **10b** in 23% yield as a single isomer. The reaction of **7** with an aluminum reagent, Me$_3$Al or Me$_2$Al(acac),[9] or Me$_2$Zn also afforded only the product **10b** in 53%, 51%, or 49% yield, respectively. It was interesting that the reaction of **7** with DIBAL-H (run 5) gave the hydrogenated product **13a**[6] in 79% yield in preference to **13b**[7] in 13% yield. A similar tendency was observed in the reaction of **7** with *i*-Bu$_2$Al(acac),[9] and the hydrogenated product **13a** was obtained as the sole product in 62% yield. On the other hand, the reaction of **7** with *tert*-butylmagnesium chloride preferentially gave **13b** in 50% yield along with **13a** in 13% yield.

A possible mechanism for producing the hydrogenated products **13a** and **13b** is shown in Scheme 4. In the case of runs 5 and 6, the intermediate **14-*i*-Bu** (i.e., R = *i*-Bu in **14a**) would be formed by transmetalation of **7** with DIBAL-H[10] or *i*-Bu$_2$Al(acac), and β-elimination from **14-*i*-Bu** would occur to produce the nickel hydride complex **15a**. Reductive elimination from **15a** would afford the hydrogenated product **13a**. On the other hand, the intermediate **14-*t*-Bu** (i.e. R = *t*-Bu in **14a**) would be formed in the case of run 7. It was thought that isomerization from **14-*t*-Bu** to **14b** would spontaneously occur because of the bulkiness of the *tert*-butyl group, and β-elimination from **14b** would produce **15b**. The hydrogenated product **13b** was obtained through reductive elimination from **15b**. These results suggested that reductive elimination of **15a** to **13a** or of **15b** to **13b** would occur immediately, giving only **13a** or preferentially **13b**, respectively.

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(6) The stereochemistry of **9a** and **13a** was determined by NOE experiments.

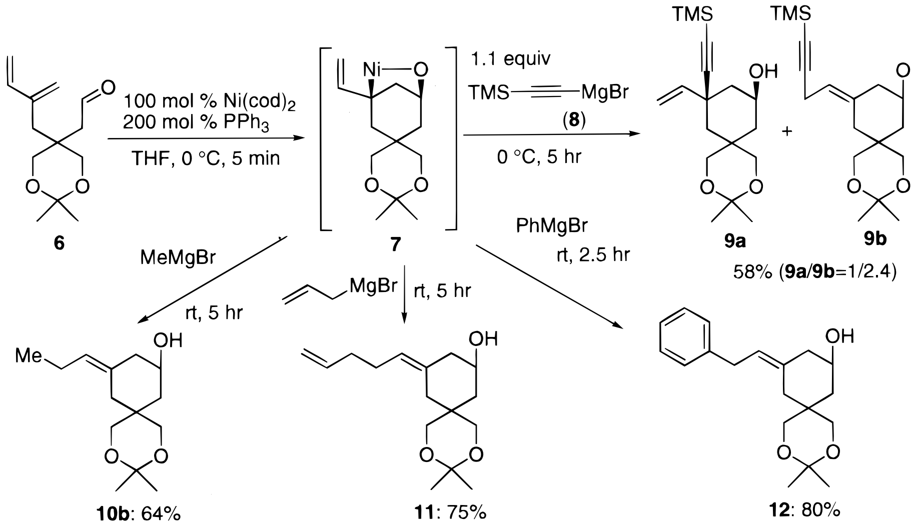
(7) The geometry of the olefin in **9b**, **10b**, **11**, **12**, and **13b** was assigned to be *E* on the basis of the NOE experiments.

(8) One of the reviews pointed out the possibility that the nickel complex **4a** or **4b** in Scheme 2 would remain associated with the alkoxide to form a nickelate species and the reductive elimination would derive from the nickelate intermediate. This possibility cannot be ruled out by our present results.

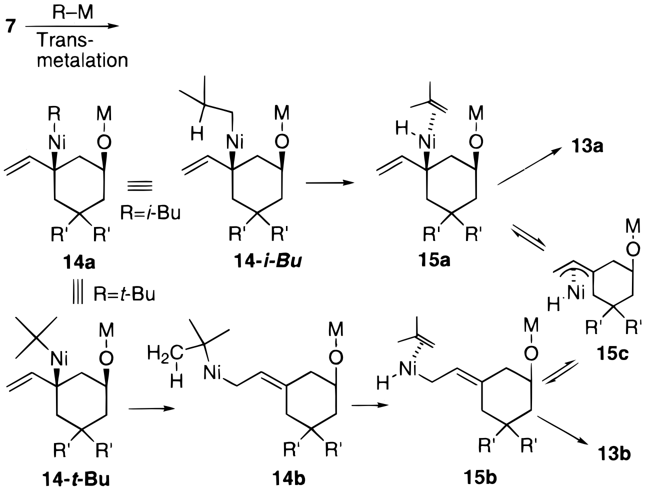
(9) Kroll, W. R.; Naegele, W. *J. Organomet. Chem.* **1969**, *19*, 439.

(10) In the case of DIBAL-H (run 5), it is possible that the intermediate **14a** (R = H) instead of **14-*i*-Bu** was formed by transmetalation of **7** using hydride on the Al atom. It was thought that **14a** (R = H) would show almost the same reactivity as that of **15a**, producing **13a** in preference to **13b**.

Scheme 3



Scheme 4



As shown in Scheme 2, zerovalent nickel species would be regenerated in this reaction. To establish the catalytic cycle in this reaction, the organometallic reagents should be intact or less reactive to the substrate until the nickelacycle has formed. The reaction of **6** with 20 mol % of Ni(cod)$_2$ and 40 mol % of PPh$_3$ in the presence of *i*-Bu$_2$Al(acac) (2 equiv) was examined, and we succeeded in obtaining **13a** in 53% yield and **13b** in 16% yield (Table 2). The reaction using Me$_2$Al(acac) or Me$_2$Zn under similar conditions also proceeded to give only **10b** in 43% (*E*/*Z* = 1/4.7) or 57% (*E*/*Z* = 1/1.1) yield, respectively.[11] Thus, the catalytic cycle in this reaction was established.

In conclusion, transmetalation of oxanickelacycle **7**, generated from the 1,3-diene and tethered aldehyde in **6** via oxidative cycloaddition to a zerovalent nickel complex, with various organometallic reagents was investigated. It was found that the tandem reaction, i.e., cyclization of **6** followed by transmetalation of the resulting oxanickelacycle **7**, proceeded smoothly. In addition, the catalytic cycle in this reaction was also established. Further studies along this line are now in progress.

Supporting Information Available: Text giving the typical procedure for transmetalation of a stoichiometric amount of **7** with PhMgBr, typical procedure for the Ni(0)-catalyzed tandem reaction (cyclization–transmetalation) of **6** with *i*-Bu$_2$Al(acac), and spectral data for **6**, **9a**, **9b**, **10b**, **11**, **12**, **13a**, and **13b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] Although the reason is not clear yet, the product **13b** was afforded as a mixture of *E* and *Z* isomers in these catalytic reactions, while only the *E* isomer of **13b** was obtained as the sole product in the reaction of nickelacycle **7** with Me$_2$Al(acac) (Table 1, run 3) or Me$_2$Zn (Table 1, run 4).