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Formation of Nickeladihydropyran by Oxidative Addition of Cyclopropyl Ketone. Key Intermediate in Nickel-Catalyzed Cycloaddition

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The oxidative addition of cyclopropanes to a transition metal has been reported; however, its application to a catalytic reaction has been limited due to the poor coordination ability of the cyclopropanes.1 In the case of the cyclopropyl compounds having an unsaturated bond, such as methylenecyclopropane and vinylcyclopropane, the transition metal-catalyzed ring opening reaction is a very powerful method to construct cyclic compounds.² The key to the success of the ring opening reaction might be the η^2 -coordination of an unsaturated bond to locate the cyclopropyl ring on a transition metal, which was suggested by a computational study on a rhodium complex.2f According to this, cyclopropyl ketones are another candidate for the ring opening reaction.2g Although the coordination of an aldehyde or ketone in the η^2 -mode is very rare for the late transition metals, the synthesis and reactivity of several η^2 -aldehyde and η^2 -ketone complexes of nickel have been reported.^{3,4} Thus it seems very promising to attain a nickeladihydropyran complex by the oxidative addition of cyclopropyl ketones to nickel(0) (Scheme 1). Moreover, a nickeladihydropyran might be a transient key intermediate in the reaction of cyclopropyl ketone with AlMe3 in the presence of a catalytic amount of Ni(acac)₂.⁵ Here, we report the formation of a nickeladihydropyran by the oxidative addition of cyclopropyl ketones to nickel(0). Furthermore, catalytic cycloaddition of cyclopropyl ketones to give cyclopentane derivatives proceeding through the nickeladihydropyran is also discussed.

The reaction of cyclopropyl ketone with Ni(cod)₂ and PBu₃ at 100 °C in toluene- d_8 gave an η^2 -enonenickel complex (1a, 1b) quantitatively (Scheme 2). The treatment of 1a and 1b with carbon monoxide (5 atm) led to the dissociation of the coordinated enones, (*E*)-3-penten-2-one and (*E*)-1-phenyl-2-buten-1-one, respectively. In the presence of PCy₃, the ring opening reaction of cyclopropyl methyl ketone also occurred to give μ - η^2 : η^1 -enonenickel dimer complex (2a) quantitatively (Scheme 3). 2a was generated quantitatively as well even in the presence of 2 equiv of PCy₃. The molecular structure of 2a was confirmed by the X-ray structure analysis. The reaction of cyclopropyl phenyl ketone under the same condition gave not only the corresponding μ - η^2 : η^1 -enonenickel complex (2b) but also a mixture of cycloprent products (3b, 3b').⁶

The cycloaddition of cyclopropyl phenyl ketone proceeded catalytically (Scheme 4) to give a mixture of **3b** and **3b'** in 93% yield. At the end of the reaction, the formation of **2b** (76% based on Ni(cod)₂) was observed. Formally, **3b** and **3b'** can be formed by the [3 + 2] cycloaddition of cyclopropyl phenyl ketone with (*E*)-1-phenyl-2-buten-1-one. Somewhat surprisingly, addition of 1 equiv of (*E*)-1-phenyl-2-buten-1-one to the above catalysis mixture gave only a trace amount of a mixture of **3b** and **3b'**, due to the rapid formation of **2b** at the initial stage.⁷ Although cyclopropyl methyl ketone did not undergo the cycloaddition reaction at all under the reaction condition in Scheme 4, the cross cycloaddition of cyclopropyl phenyl ketone to give a mixture of **3b**, **3b'**, **4b**, and **4b'** (Scheme 5).

The reaction of cyclopropyl phenyl ketone (2 equiv) with Ni-(cod)₂ (1 equiv) and PCy₃ (1 equiv) in C_6D_6 was followed at the Scheme 1. Oxidative Addition of Cyclopropyl Ketone



Scheme 2. Reaction of Cyclopropyl Ketone with Ni(0)







Scheme 4

$$\begin{array}{c} Ph \\ = 0 \\ \hline \end{array} \begin{array}{c} 10 \text{ mol}\% \text{ Ni}(\text{cod})_2 \\ \hline 10 \text{ mol}\% \text{ PCy}_3 \\ \hline \text{Toluene-}d_8 \\ 100 \ ^\circ\text{C}, 1.5 \text{ h} \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} 0 \\ \hline \end{array} \begin{array}{c} Ph \\ \hline \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} Ph \\ \end{array} \begin{array}{c} 0 \end{array} \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \end{array} \begin{array}{c} 0 \end{array} \begin{array}{c} 0 \end{array} \end{array} \end{array} \begin{array}{c} 0 \end{array} \end{array} \end{array} \begin{array}{c} 0 \end{array} \end{array} \end{array} \end{array} \begin{array}{c} 0 \end{array} \end{array} \end{array} \end{array} \begin{array}{c} 0 \end{array} \end{array} \end{array} \end{array} \end{array} \end{array} \begin{array}{c} 0 \end{array} \end{array} \end{array} \end{array} \end{array} \end{array}$$

Scheme 5

$$Ph = 0 + e^{0} = 0 \xrightarrow{10 \text{ mol}\% \text{ Ni(cod)}_2}_{100 \text{ °C}, 3 \text{ h}} \xrightarrow{Ph} + e^{0} \xrightarrow{Ph} + e^{0}$$

lower temperature (40 °C) by ¹H and ³¹P NMR. The rapid formation of the η^2 -ketonenickel complex (5, 32% based on Ni) was observed in 5 min.⁸ Then, 5 decreased gradually, and a new complex (6)having a resonance at δ 5.2 in the $^1\mathrm{H}\,\mathrm{NMR}$ spectrum was generated (40%). After 48 h, 6 disappeared, and 2b (60%) and a mixture of **3b** and **3b'** (40% as a mixture) were generated with cyclopropyl phenyl ketone (1 equiv) and 40% of Ni(cod)₂ and PCy₃ remaining intact. To confirm if 6 is the expected nickeladihydropyran intermediate, the isolation of 6 was attempted. At room temperature for 5 h in THF, the reaction of cyclopropyl phenyl ketone with Ni(cod)₂ and PCy₃ generated **6** in 60% yield as confirmed by ${}^{31}P$ NMR. THF and COD were removed completely under reduced pressure. The residue was dissolved in a minimum amount of toluene, and the precipitation gave 6 as pale orange solids in 25% isolated yield. Elemental analysis is consistent with the expected composition.9 The 13C NMR resonance of the methylene carbon attached to Ni is coupled with phosphorus. The ¹H and ¹³C chemical shifts of the nickel enolate moiety (-NiOC(Ph)=CH-) are in the range of those for reported nickel enolates.^{10,11} The treatment of 6

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Scheme 6



Scheme 7



with carbon monoxide (5 atm) led to the formation of the expected lactone (7) quantitatively,¹² which is also consistent with the structure of **6** depicted in Scheme 6.

The isomerization of **6** to **2b** in C₆D₆ proceeded slowly at room temperature. The insertion of (*E*)-3-pentene-2-one proceeded smoothly to give $\eta^{3:}\eta^{1}$ -enolatoalkylnickel complex **8** quantitatively.¹³ In the ¹³C NMR spectrum of **8**, the methylene carbon attached to Ni is found upfield and coupled with phosphorus. Both ¹H and ¹³C resonances of the CH group α to acetyl group ($-CHC(O)CH_3$) are coupled with phosphorus, which indicates that nickel is bound to the α carbon. Furthermore, their chemical shifts (δ 4.96 for H, δ 78.14 for C) are too low for an η^{1} -bound C–enolate structure, and we assume an η^{3} -enolate structure for **8**. The chemical shift of the central carbon (δ 159.5) is also consistent with this structure. Under a carbon monoxide pressure (5 atm), **8** underwent the reductive elimination to give a mixture of **4b** and **4b'**. These observations suggest the occurrence of the isomerization of **8** prior to the reductive elimination.

The cycloaddition reaction might proceed as follows (Scheme 7). The cyclopropyl ketone coordinates to Ni(0) to form η^2 -ketone complex A followed by the oxidative addition to give a nickeladihydropyran **B**. The β -elimination and reductive elimination followed by the tautomerization might generate η^2 -enonenickel C.¹⁴ In the catalytic reaction, the concentration of free enone, which is expected to react with **B** to give **E** (see Scheme 6), is supposed to be low since enones may coordinate to Ni(0) so strongly that cyclopropyl ketones are unable to replace the enone ligand in C. Thus, we assume that the second oxidative addition of cyclopropyl phenyl ketone takes place at C, leading to the formation of D followed by the insertion of an enone to generate E. The coordination ability of cyclopropyl phenyl ketone is much higher than that of cyclopropyl methyl ketone,¹⁵ which might be one reason only cyclopropyl phenyl ketone undergoes the second oxidative addition to C. The generation of the mixture of isomers could be rationalized by the rapid isomerization between E and F prior to the reductive elimination.

In conclusion, we demonstrated that a carbonyl group adjacent to cyclopropyl group is a nice direction group to locate the cyclopropane ring on the Ni(0) center, and the oxidative addition proceeds easily to generate a nickeladihydropyran. Moreover, this complex underwent the insertion of (E)-3-penten-2-one. Both oxidative addition and insertion are important key steps in the catalytic cycloaddition of cyclopropyl phenyl ketone reported for the first time in this paper. Further studies on the reactivity of nickeladihydropyran as well as applications to cross cycloaddition reactions are in progress in our group.

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Supporting Information Available: Experimental procedures (PDF) and crystallographic information (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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- Chem. Lett. **1997**, 1149–1150. (6) Selected spectral data for **2b**: ¹H NMR (C₆D₆): δ 1.13 (d, J = 6.2 Hz, 3H, $-CH=CHCH_3$), 1.84 (m, 1H, $-CH=CHCH_3$), 5.77 (dd, J = 11.1, 3.8 Hz, 1H, $-CH=CHCH_3$). ³¹P NMR (C₆D₆): δ 41.1 (s). ¹³C NMR (C₆D₆): δ 20.39 (s, $-CH=CHCH_3$), 32.99 (s, $-CH=CHCH_3$), 34.30 (d, $J_{CP} = 15.2$ Hz, Cy), 78.79 (d, $J_{CP} = 3.8$ Hz, $-CH=CHCH_3$), 166.17 (s, -C(O)Ph). Anal. Calcd for C₅dH₈oNi₂O₂P₂: C, 69.30; H, 8.93. Found: C, 69.23; H, 8.10. Stereochemistry of **3b** and **3b'** was determined by NOE measurements.
- (7) By the use of 10 mol % of 2b as a catalyst, cyclopropyl phenyl ketone underwent the cycloaddition only slowly to give a mixture of 3b and 3b' at 100 °C (1.5 h 7%, 16 h 91% as a mixture).
- (a) 100 °C (1.5 H 7/6, 10 H 7/6 as a Hinduc).
 (a) Selected spectral data for 5: ³¹P NMR (toluene-d₈, -20 °C): δ 33.17 (d, J = 47.6 Hz), 40.91 (d, J = 47.6 Hz). ¹³C NMR (toluene-d₈, -20 °C): δ 82.72 (dd, J_{CP} = 20.9, 1.9 Hz, -C(O)Ph). Anal. Calcd for C₄₆H₇₆-NiOP₂: C, 72.15; H, 10.00. Found: C, 71.57; H, 9.79.
- (9) Selected spectral data for 6: ¹H NMR (C₆D₆): δ 0.80 (m, 1H, -NiCH₂-CH₂-), 0.99 (m, 1H, -NiCH₂CH₂-), 5.29 (t, J = 4.4 Hz, 1H, -CH=CO-). ³¹P NMR (C₆D₆): δ 31.3(s). ¹³C NMR (C₆D₆): δ 4.94 (d, $J_{CP} = 30.8$ Hz, -NiCH₂CH₂-), 104.70 (s, -CH=CO-), 157.11 (s, -CH=CO). Anal. Calcd for C₅₆H₈₆Ni₂O₂P₂: C, 69.30; H, 8.93. Found: C, 69.31; H, 9.00.
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- (13) Selected spectral data for 8: ¹H NMR (C₆D₆): δ 0.43 (m, 2H, −NiCH₂-CH₂−), 2.00 (s, 3H, −CH=C(CH₃)ONi−), 4.96 (dd, J_{HH} = 10.0 Hz, J_{HP} = 2.7 Hz, 1H, −CH=C(CH₃)ONi−). ³¹P NMR (C₆D₆): δ 35.1 (s). ¹³C NMR (C₆D₆): δ 0.01 (d, J_{CP} = 12.9 Hz, −NiCH₂CH₂−), 22.18 (s, −CH=C(CH₃)ONi−), 78.14 (d, J_{CP} = 16.0 Hz, −CH=C(CH₃)ONi−), 159.54 (s, −CH=C(CH₃)ONi−), 78.14 (s, −CH(COPh)CH(CH₃)−). Anal. Calcd for C₃₃H₅₁NiO₂P: C, 69.61; H, 9.03. Found: C, 68.61; H, 8.91. 8 is depicted tentatively as a complex having the stereochemistry corresponding to the major product 4b.
- (14) The intermediate C may dimerize to the catalytically much less active 2 if the rate of conversion of C to D becomes comparably small.
- (15) No ketone substitution was observed by the addition of cyclopropyl methyl ketone to a solution of 5 in C_6D_6 .

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