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Nickel(0)-Mediated Sequential Addition of Carbon Dioxide and Aryl Aldehydes into Terminal Allenes

Masanori Takimoto, Mitsunobu Kawamura, and Miwako Mori*

Graduate School of Pharmaceutical Sciences, Hokkaido University,
Sapporo 060-0812, Japan

mori@pharm.hokudai.ac.jp

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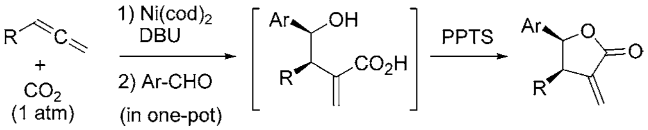
ABSTRACT

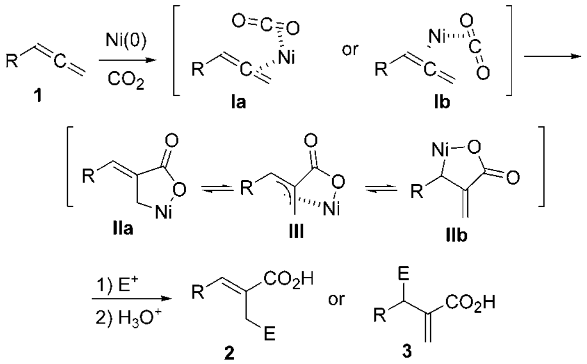


Nickel-mediated sequential addition of carbon dioxide and aryl aldehydes into terminal allenes is reported. The reaction proceeded in a diastereoselective manner to afford α-methylene-γ-hydroxy carboxylic acids, which allowed stereoselective preparation of cis-β,γ-disubstituted α-methylene-γ-lactones.

Carbon dioxide (CO_2) is regarded as an important natural carbon resource because of its abundant reserve and low degree of toxicity. However, the low reactivity of CO_2 has restricted the range of utility in synthetic organic chemistry. One of the potential methods for overcoming such difficulties in using CO_2 for organic synthesis may be employment of nickel complexes because they exhibit high levels of activity for coupling of CO_2 and various unsaturated hydrocarbons.[1,2] In the course of our study,[3] we found that various allenes reacted with CO_2 and a zerovalent nickel complex to form a nucleophilic nickel complex that could react with aryl aldehydes in a highly stereoselective manner. We report here this nickel-mediated sequential coupling reaction and its application to stereoselective synthesis of β,γ-disubstituted α-methylene-γ-lactones.

Our initial idea is presented in Scheme 1. According to the previous reports,[4] terminal allene **1** is expected to provide oxanickelacycle **IIa** and/or **IIb** by oxidative cycloaddition of **1** and CO_2 to a zerovalent nickel complex. It was thought that nickelacycles **IIa** and **IIb** might be in equilibrium with

Scheme 1. Nickel-Mediated Sequential Addition of CO_2 and Electrophile into Allene



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(1) Reviews: (a) Behr, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 661. (b) Braunstein, P.; Matt, D.; Nobel, D. *Chem. Rev.* **1988**, *88*, 747. (c) Leitner, W. *Coord. Chem. Rev.* **1996**, *153*, 257. (d) Yin, X.; Moss, J. R. *Coord. Chem. Rev.* **1999**, *181*, 27. (e) Walther, D.; Ruben, M.; Rau, S. *Coord. Chem. Rev.* **1999**, *182*, 67.

(2) Recent reports: (a) Saito, S.; Nakagawa, S.; Koizumi, T.; Hirayama, K.; Yamamoto, Y. *J. Org. Chem.* **1998**, *64*, 3975. (b) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188. See also ref 4 and references therein.

(3) (a) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895. (b) Takimoto, M.; Shimizu, K.; Mori, M. *Org. Lett.* **2001**, *3*, 3345. (c) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2002**, *124*, 10008.

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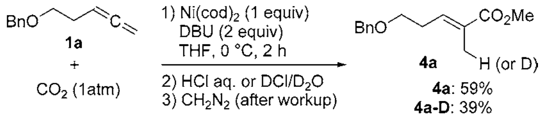
π-allylnickel complex **III**. Generally, π-allylnickel complexes have a nucleophilic nature.[6] Thus, it appears that oxanickelacycles **II** could react with electrophiles (E^+) to afford carboxylic acid **2** and/or **3**.

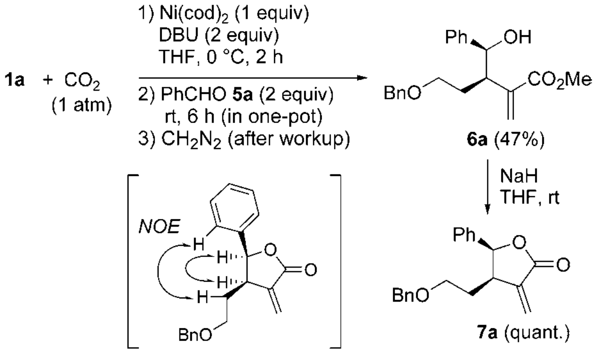
Our investigation started with screening of ligands that could mediate the oxidative cycloaddition under mild conditions in a short reaction time. Various ligands (amines and phosphines) were examined, and it was found that only 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) could mediate the desired process effectively.[2a,3a−b,7] In the presence of DBU (2 equiv with respect to nickel), terminal allene **1a** (1 equiv) easily reacted with CO_2 (1 atm) and $Ni(cod)_2$ (1 equiv) in THF under mild conditions (0 °C, 2 h) to afford carboxylic acid **4a** in 59% yield after hydrolysis (Scheme 2). Treatment of the above-mentioned reaction mixture with DCl/D_2O afforded **4a-D**. These results suggested that the expected nickelacycle intermediates should be formed.

Scheme 2. Nickel-Mediated Addition of CO_2 into **1a**



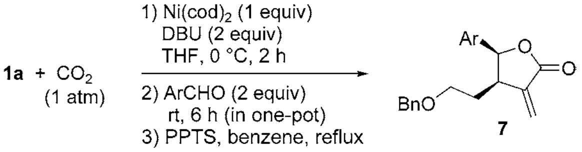
Reactivity of the generated oxanickelacycle was first examined by choosing benzaldehyde **5a** as an electrophile. After a reaction of **1a** with CO_2 was carried out under similar conditions, **5a** was added to the resulting solution and the mixture was stirred at room temperature for 6 h. Hydrolysis of the reaction mixture followed by treatment of the crude product with diazomethane afforded γ-hydroxy carboxylic acid methyl ester **6a** in 47% yield from **1a** (Scheme 3). Ester **6a** was readily converted to α-methylene-γ-lactone **7a** in quantitative yield by treatment with NaH. From the results of NOE experiments for **7a**, the stereochemistries of **7a** and **6a** were determined as shown in Scheme 3.

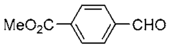
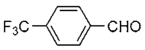
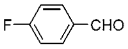
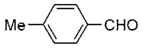
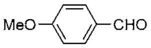
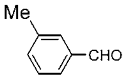
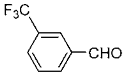
Scheme 3. Sequential Addition of CO_2 and **5a** into **1a**



The overall yield of **7a** was improved when acid-catalyzed lactonization was carried out without isolation of **6a**; after the sequential reaction of **1a** with CO_2 and **5a**, the crude carboxylic acid was heated in benzene in the presence of a catalytic amount of PPTS with azeotropic removal of water to provide **7a** in 60% yield from **1a** (Table 1, entry 1).

Table 1. Addition of CO_2 and Various Aldehydes into **1a**



entry	ArCHO	Product	yield
1	**5a**	**7a**	60%
2	 **5b**	**7b**	66%
3	 **5c**	**7c**	62%
4	 **5d**	**7d**	57%
5	 **5e**	**7e**	56%
6	 **5f**	**7f**	46%
7	 **5g**	**7g**	63%
8	 **5h**	**7h**	61%

Various aryl aldehydes were examined for lactone synthesis from **1a** using this procedure. The results were summarized in Table 1 (entries 2−8). In each case, the desired lactone was obtained as a single diastereomer.[8] The yields were generally good except in the case of aldehyde **5f**, having an electron-donating substituent at the para position (entry 6).

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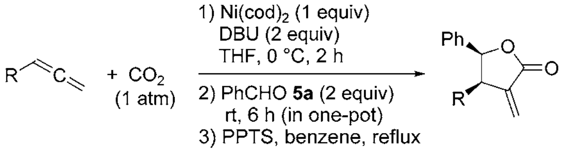
(4) (a) Hoberg, H.; Oster, B. W. *J. Organomet. Chem.* **1984**, *266*, 321. (b) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *Synlett* **1990**, 361. For metal-catalyzed cooligomerization of allenes with CO_2, see ref 5.

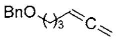
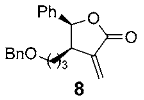
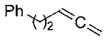
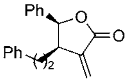
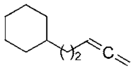
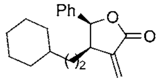
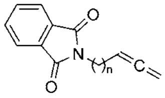
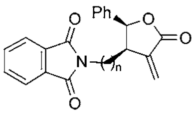
(5) (a) Döhring, A.; Jolly, P. W. *Tetrahedron Lett.* **1980**, *21*, 3021. (b) Aresta, M.; Quaranta, E. *C_1 Mol. Chem.* **1985**, *1*, 283. (c) Sasaki, Y. *J. Mol. Catal.* **1989**, *54*, L9. (d) Tsuda, T.; Yamamoto, T.; Saegusa, T. *J. Organomet. Chem.* **1992**, *429*, C46.

(6) Reviews: (a) Semmelhack, M. F. *Org. React.* **1972**, *19*, 115. (b) Billington, D. C. *Chem. Soc. Rev.* **1985**, *14*, 93. (c) Krysan, D. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier Science, Ltd.: Oxford, UK, 1995; Vol. 12, p 978.

(7) (a) Hoberg, H.; Peres, Y.; Milchereit, A. *J. Organomet. Chem.* **1986**, *307*, C38. (b) Hoberg, H.; Peres, Y.; Milchereit, A. *J. Organomet. Chem.* **1986**, *307*, C41. (c) Hoberg, H.; Peres, Y.; Krüger, C.: Tsay, Y.-H. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 771.

Table 2. Addition of CO_2 and **5a** into Various Allenes



entry	allene	product	yield
1	 **1b**	 **8**	58%
2	 **1c**	 **9**	57%
3	 **1d**	 **10**	73%
4	 **1e** (n=2)	 **11** (n=2)	67%
5	**1f** (n=3)	**12** (n=3)	63%

A variety of terminal allenes were next examined for lactone synthesis using aldehyde **5a** (Table 2). Elongation of a tether of allene **1a** did not affect the yield (entry 1), and the reaction of **1b** provided lactone **8** in 58% yield. Simple terminal allenes **1c** and **1d**, which had no heteroatom in the tethers, afforded the desired products in good yields (entries 2 and 3). Terminal allenes that had nitrogen substituents were also applicable. The use of allene **1e** and **1f** for the reaction gave lactones **11** and **12**, respectively, in good yields (entry 4).

In summary, nickel-mediated sequential addition of CO_2 and aryl aldehydes into terminal allenes was developed. The reaction proceeds under mild conditions in a highly regio- and stereoselective manner and provides a novel method for synthesis of α-methylene-γ-lactones. Further studies on expansion of the scope of this process and on the reaction mechanism are now in progress.

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Supporting Information Available: Information on experimental procedures and compound characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Use of aliphatic aldehydes did not afford good results. When 1-butanal was used in the reaction of **1a**, the desired α-methylene-γ-lactones were obtained in 35% yield as a mixture of stereoisomers at the γ-position of the lactone ring along with the carboxylic acid corresponding to ester **4a** in 45% yield.