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# Ni(0)-Promoted Hydroxycarboxylation of 1,2-Dienes by Reaction with $CO_2$ and $O_2$

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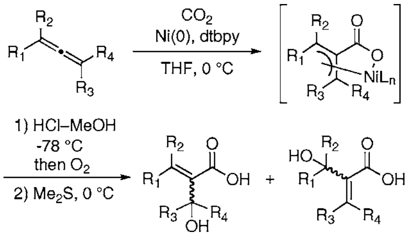
## ABSTRACT



**A novel method for the preparation of hydroxy carboxylic acid derivatives has been developed by $O_2$-oxidation of $\pi$-allylnickel intermediates generated by Ni(0)-mediated coupling of 1,2-dienes with $CO_2$.**

$\pi$-Allylnickel complexes have been recognized as a useful reagent for the carbon−carbon bond formation due to their unique reactivities,[1] and there have been extensive studies on their reaction with various organic halides, carbonyl compounds, alkynes, organometallics, etc.[2] However, only a few examples have been reported so far concerning the reaction of $\pi$-allylnickel complexes with molecular oxygen,[3,4] and no synthetically useful transformation has been realized utilizing such oxidation of $\pi$-allylnickel intermediates.

In this paper, we report that oxidation of $\pi$-allylnickel intermediates, generated by oxidative coupling of 1,2-dienes and carbon dioxide, with molecular oxygen proceeds smoothly and cleanly to afford synthetically useful hydroxy carboxylic acid derivatives in good yield.

During the study on the use of bis(amidine) ligand for the Ni(0)-mediated oxidative coupling of unsaturated molecules such as alkynes and 1,2-dienes with $CO_2$,[5,6] we happened to examine the reaction of cyclic 1,2-diene, cyclonona-1,2-diene **1**, for this reaction. Thus, cyclonona-1,2-diene **1** was added dropwise over 1 h to a THF solution of $Ni(cod)_2$ and a bis(amidine) **7** under a $CO_2$ atmosphere at 0 °C. After 2 h, the

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(1) (a) Heimbach, P.; Jolly, P. W.; Wilke, G. *Adv. Organomet. Chem.* **1970**, *8*, 29. (b) Baker, R. *Chem. Rev.* **1973**, *73*, 487. (c) Billington, D. C. *Chem. Soc. Rev.* **1985**, *14*, 93. (d) 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 959. (e) *Modern Organonickel Chemistry*; Tamaru, Y., Ed.; Wiley-VCH: Weinheim, Germany, 2005. (f) Billington, D. C. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, p 423.

(2) (a) Reference 1c and references cited therein. (b) Hegedus, L. S.; Thompson, D. H. P. *J. Am. Chem. Soc.* **1985**, *107*, 5663. (c) Johnson, J. R.; Tully, P. S.; Mackenzie, P. B.; Sabat, M. *J. Am. Chem. Soc.* **1991**, *113*, 6172. (d) Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 5160. (e) Kobayashi, Y.; Takahisa, E.; Usmani, S. B. *Tetrahedron Lett.* **1998**, *39*, 597. (f) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38. (g) Llebaria, A.; Moréto, J. M. *J. Organomet. Chem.* **1993**, *451*, 1. (h) García-Gómez, G.; Moréto, J. M. *J. Am. Chem. Soc.* **1999**, *121*, 878. (i) Nadal, M. L.; Bosch, J.; Vila, J. M.; Klein, G.; Ricart, S.; Moréto, J. M. *J. Am. Chem. Soc.* **2005**, *127*, 10476. (j) Ikeda, S. *Acc. Chem. Res.* **2000**, *33*, 511.

(3) For reactions of $\sigma$- or $\pi$-allyl complexes with molecular oxygen, see; (a) Julia, M.; Lauron, H.; Verpeaux, J.-N. *J. Organomet. Chem.* **1990**, *387*, 365. (b) Dible, B. R.; Sigman, M. S. *J. Am. Chem. Soc.* **2003**, *125*, 872. (c) Dible, B. R.; Sigman, M. S. *Inorg. Chem* **2006**, *45*, 8430.

(4) For formation of oxygenated compounds as side products, see: Sato, Y.; Takanashi, T.; Hoshiba, M.; Mori, M. *Tetrahedron Lett.* **1998**, *39*, 5579.

(5) Aoki, M.; Kaneko, M.; Izumi, S.; Ukai, K.; Iwasawa, N. *Chem. Commun.* **2004**, 2568.

(6) For examples of Ni(0)-promoted reaction of 1,2-dienes with $CO_2$, see: (a) Hoberg, H.; Oster, B. W. *J. Organomet. Chem.* **1984**, *266*, 321. (b) Sasaki, Y. *J. Mol. Catal.* **1989**, *54*, L9. (c) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *Synlett* **1990**, 361. (d) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *Tetrahedron* **1992**, *48*, 5235. (e) Takimoto, M.; Kawamura, M.; Mori, M. *Org. Lett.* **2003**, *5*, 2599. (f) Takimoto, M.; Kawamura, M.; Mori, M. *Synthesis* **2004**, 791. (g) Takimoto, M.; Kawamura, M.; Mori, M.; Sato, Y. *Synlett* **2005**, 2019.

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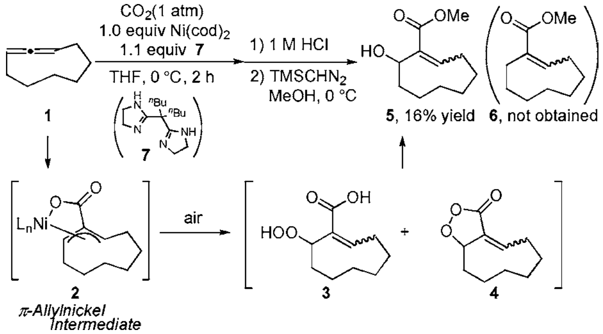
reaction was quenched with 1 M HCl for protonolysis of $\pi$-allylnickel intermediate **2**,[7] and the crude product was treated with trimethylsilyldiazomethane to convert carboxylic acids to the corresponding methyl esters. Purification of the crude product revealed that the desired $\alpha,\beta$-unsaturated carboxylic ester **6** was not produced at all, but that an unexpected $\beta$-hydroxy carboxylic acid methyl ester **5** was obtained as a single isomer albeit in low yield (Scheme 1).

**Scheme 1.** Reaction of $\pi$-Allylnickel Intermediate with Molecular Oxygen

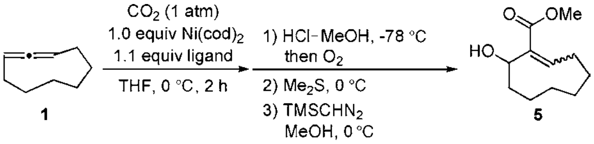


This compound was the oxygenated product of the $\pi$-allylnickel intermediate **2** produced by the oxidative coupling of the 1,2-diene **1** and $CO_2$, and the oxygenation seemed to be caused by molecular oxygen in the air during acidic workup.[8] As the reaction enables introduction of both carboxy and hydroxy groups onto allenic compounds, we decided to examine this novel oxygenation reaction in more detail.

Careful analysis of the reaction revealed that the initial product formed after acidic workup was peroxide **3**, and then it was converted to peroxy lactone **4** slowly. As these intermediates appeared to be unstable and needed to be reduced for producing $\beta$-hydroxycarboxylic acid, we first examined the procedure for the reductive workup. Consequently, it was found that the use of dimethyl sulfide or triphenylphosphine as a reductant gave good results. Due to the ease of removal of excess reagent and its oxidized product, we decided to employ dimethyl sulfide as a reductant for further examination.

Screening of solvents, ligands, temperature, oxidants, etc. revealed that a dramatic effect of ligand on the yield of the product was observed in this reaction (Table 1). Thus, when TMEDA or DBU, a good ligand for Ni(0)-mediated coupling of $CO_2$ with unsaturated compounds,[9] was employed as ligand, the yield of the hydroxylated methyl ester was rather low. On the contrary, use of bipy,[10] dtbpy(4,4′-di-*tert*-butyl-2,2′-bipyridine), or bis(amidine) **7** gave good results. In particular, the reaction with dtbpy proceeded smoothly without the necessity of adding the 1,2-diene **1** slowly.

**Table 1.** Effect of Ligand

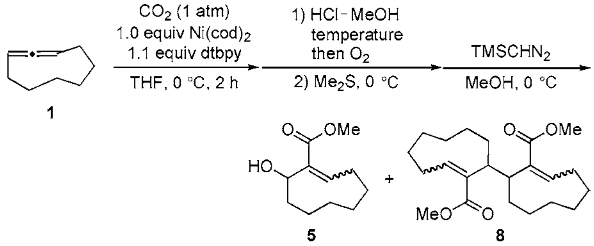


| entry | ligand | yield (%) |
|---|---|---|
| 1[a] | DBU[b] | 7 |
| 2[a] | TMEDA | 14 |
| 3[a] | bis(amidine) **7** | 63[c] |
| 4[a] | bipy | 61 |
| 5 | dtbpy | 68 |

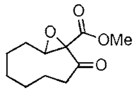
[a] Cyclonona-1,2-diene **1** was added dropwise over 1 h. [b] 2.1 equiv of DBU was used. [c] Yield of the hydroxy carboxylic acid corresponding to **5**.

Furthermore, it was found that the temperature of the oxidation step had a profound effect on this reaction. Thus, when the oxygenation reaction was carried out at room temperature, the yield of the desired hydroxy methyl ester was low, and instead a dimer product **8** was obtained as a major product (Table 2, entry 1). On the contrary, when the temperature of the oxidation step was lowered to −78 °C, the formation of the dimer product **8** was suppressed. Although the mechanism of the dimer formation has not been made clear, dimerization occurred competitively with the oxygenation reaction and was suppressed at lower temperature. Furthermore, when the oxygenation reaction was done

**Table 2.** Effect of Temperature



| entry | temperature | yield (%) | |
|---|---|---|---|
| | | **5** | **8** |
| 1 | -78 °C | 68 | trace |
| 2 | -40 °C | 46 | 23 |
| 3 | 0 °C | 30 | 31 |
| 4 | rt | 19 | 42 |



**9**

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[7] We are not certain whether this intermediate takes the form of the $\pi$-allyl or $\sigma$-allyl complex; however, we just refer to $\pi$-allyl in the text for the simplicity.

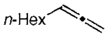
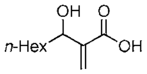
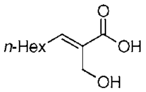
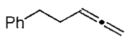
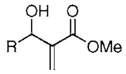
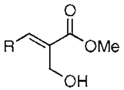
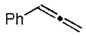
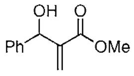
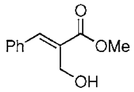
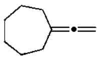
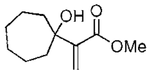
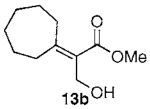
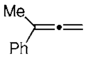
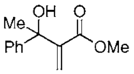
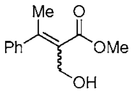
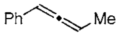
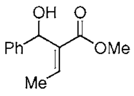
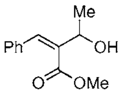
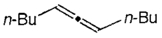
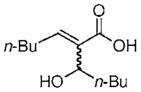
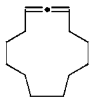
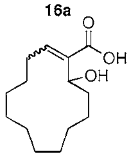
[8] In our previous work (ref 5), $\pi$-allylnickel intermediates formed by oxidative coupling of monosubstituted 1,2-dienes and $CO_2$ easily underwent protonolysis by 1 M aq HCl at rt. The reactivity of $\pi$-allylnickel intermediates appears to be dependent on the substitution pattern of 1,2-dienes.

[9] (a) Burkhart, G.; Hoberg, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 76. (b) Hoberg, H.; Peres, Y.; Milchereit, A. *J. Organomet. Chem.* **1986**, *307*, C38. (c) Saito, S.; Nakagawa, S.; Koizumi, T.; Hirayama, K.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 3975. (d) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895.

[10] (a) Hoberg, H.; Schaefer, D. *J. Organomet. Chem.* **1982**, *236*, C28. (b) Papai, I.; Schubert, G.; Mayer, I.; Besenyei, G.; Aresta, M. *Organometallics* **2004**, *23*, 5252. (c) Geyer, C.; Schindler, S. *Organometallics* **1998**, *17*, 4400.

**Table 3.** Generality of Oxidative Reaction with Various 1,2-Dienes[a]

$$\text{1,2-dienes} \xrightarrow[\text{THF, 0 °C, 2 h}]{\substack{\text{CO}_2\text{(1 atm)} \\ \text{1.0 equiv Ni(cod)}_2 \\ \text{1.1 equiv dtbpy}}} \xrightarrow[\substack{\text{2) Me}_2\text{S, 0 °C} \\ \text{3) TMSCHN}_2 \\ \text{MeOH, 0 °C}}]{\substack{\text{1) HCl-MeOH, -78 °C} \\ \text{then O}_2}} \text{products}$$

| entry | 1,2-diene | products | yield |
|---|---|---|---|
| 1 | <br>**10** | <br>**10a**<br><br>**10b** | 82% (55 : 45) |
| 2[a] | <br>**11** | <br>**11a**<br><br>**11b** (R=$CH_2CH_2Ph$) | 63% (57 : 43) |
| 3[a] | <br>**12** | <br>**12a**<br><br>**12b** | 44% (57 : 43) |
| 4 | <br>**13** | <br>**13a**<br><br>**13b** | 58% (86 : 14) |
| 5[a] | <br>**14** | <br>**14a**<br><br>**14b**<br>(*E* : *Z* = 49 : 51) | 63% (89 : 11) |
| 6[a] | <br>**15** | <br>**15a**<br>(*E* : *Z* = >95 : 5)<br><br>**15b**<br>(*E* : *Z* = 8 : 92) | 61% (41 : 59) |
| 7 | <br>**16** | <br>**16a** | 74%<br>(*E* : *Z* = 47 : 53) |
| 8 | <br>**17** | <br>**17a** | 74%<br>(*E* : *Z* = 58 : 42) |

[a] 1,2-Dienes **11**, **12**, **14**, and **15** were added dropwise over 1 h.

without adding HCl−MeOH at −78 °C, an epoxide **9** was obtained along with the desired hydroxy methyl ester. Thus, it is important for this reaction to do the oxygenation reaction after the treatment with acid at low temperature. It should be noted that protonolysis of the π-allyl intermediate is very slow even at room temperature.[11]

The following procedure was found to be optimal. The 1,2-diene **1** was treated with $CO_2$ in the presence of $Ni(cod)_2$ and dtbpy at 0 °C for 2 h, and then excess HCl−MeOH was added to the mixture at −78 °C under an Ar atmosphere. The reaction mixture was exposed to an $O_2$ atmosphere for 2 h at this temperature, followed by reduction with dimethyl sulfide. Finally, the crude hydroxy carboxylic acid was esterified with trimethylsilyldiazomethane for the purpose of facile purification to give the corresponding hydroxy methyl ester.

The generality of the oxidation of π-allylnickel intermediates was examined with several substituted 1,2-dienes using dtbpy as a ligand. As summarized in Table 3, this reaction could be applied to monoalkyl- or aryl-substituted 1,2-dienes **10**−**12** to give a mixture of regioisomeric products. In both cases, only the *E*-isomer was produced for the *endo* olefins **10b**−**12b**. 1,1-Disubstituted 1,2-dienes **13** and **14** also afforded the desired hydroxy carboxylic acid or its methyl ester in moderate to good yield. In these cases, *exo* olefins **13a** and **14a** were obtained as a major regioisomer. Furthermore, acyclic 1,3-disubstituted 1,2-dienes **15** and **16** as well as 13-membered cyclic 1,2-diene **17** were applicable to this reaction. Although regiochemical and, in some cases, geometrical control of the oxygenation reaction is not necessarily good, this method enables introduction of two functional groups onto 1,2-dienes under mild reaction conditions simply by using $CO_2$ and $O_2$ and would afford a concise method for the preparation of hydroxy carboxylic acid derivatives.

In conclusion, preparation of hydroxy carboxylic acid derivatives utilizing novel oxidation with molecular oxygen of the π-allylnickel intermediates generated by Ni(0)-mediated coupling of 1,2-dienes with $CO_2$ was achieved. Synthetically useful hydroxy carboxylic acid derivatives were obtained in good yield starting from 1,2-dienes, $CO_2$, and $O_2$. Further investigation on the mechanism of this reaction is in progress.

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**Supporting Information Available:** Preparative methods and spectral and analytical data of compounds **10a**,**b**, **11b**, **13**, **13a**,**b**, **14a**,**b**, **15a**,**b**, **16a**, and **17a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] It is necessary to heat the π-allylnickel intermediate **2** in refluxing HCl−MeOH to cause the protonolysis of this intermediate.