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Nickel-Catalyzed Regioselective Synthesis of Tetrasubstituted Alkene Using Alkylative Carboxylation of Disubstituted Alkyne

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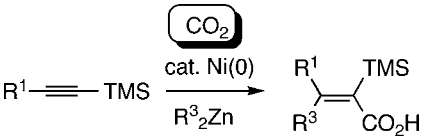
ABSTRACT



Syntheses of α-silyl-*β*,*β*′-dialkyl α,*β*-unsaturated carboxylic acids were achieved from silylated alkyne, carbon dioxide, and a zinc reagent using *a catalytic amount of nickel complex in the presence of an excess amount of DBU.* The regioselectivity of the introduction of CO_2 into disubstituted alkyne is dependent on the electronic property of the substituent R on the alkyne because the thermodynamic stability of oxanickelacycle IV or V should be affected by conjugation of the substituent R with the carboxyl group in IV or V.

Oxidative cyclization of carbon dioxide and multiple bonds using a transition metal gives an oxametallacycle, which should be a useful intermediate for synthesis of various functionalized carboxylic acids.[1,2] On the basis of the results of these studies, the synthesis of α,*β*-unsaturated carboxylic acids from terminal alkynes[2b,c] using a stoichiometric amount of $Ni(cod)_2$ and DBU and an alkylative carboxylation of diene,[3a] allene,[3b,c] or alkyne[3d,e] using $Ni(cod)_2$, DBU, and a zinc reagent has recently been reported. The synthesis of *γ*-pyrone using $Ni(cod)_2$ and phosphine[4] or N-heterocyclic carbene[5] ligand and the cyclization of bisdiene using $Ni(acac)_2$ and a phosphine ligand[6] have been reported as catalytic carboxylation reactions. Other nickel-catalyzed carboxylations of alkyne[7] and other related unsaturated hydrocarbons[8] involve the use of electrochemical methods. Here we report the synthesis of tetrasubstituted alkenes from disubstituted alkynes, carbon dioxide, and a zinc reagent using *a catalytic amount of nickel complex.*

If disubstituted alkyne **I** is treated with Ni(0) under carbon dioxide and then a zinc reagent is added, two carboxylic acids

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[7] (a) Dérien, S.; Duñach, E.; Périchon, J. *J. Am. Chem. Soc.* **1991**, *113*, 8447. (b) Duñach, E.; Périchon, J. *J. Organomet. Chem.* **1988**, *352*, 239. (c) Labbé, E.; Duñach, E.; Périchon, J. *J. Organomet. Chem.* **1988**, *353*, C51. (d) Duñach, E.; Dérien, S.; Périchon, J. *J. Organomet. Chem.* **1989**, *363*, C33. (e) Duñach, E.; Périchon, J. *Synlett* **1990**, 143.

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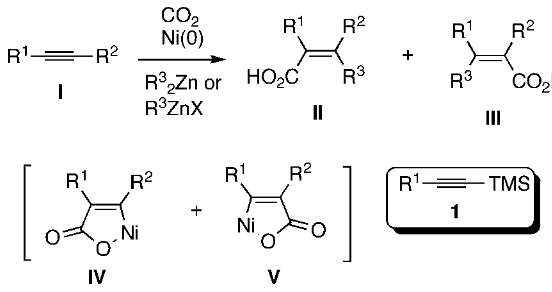
II and **III** should be formed after hydrolysis.[3d] Thus, to realize the formation of tetrasubstituted alkene from disubstituted alkyne **I** and carbon dioxide regioselectively, we planned to use silylated alkyne **1** because a nickel metal would be placed at the carbon connected to the silyl group[9] to give **IV** (R^2 = TMS) (Scheme 1).

Scheme 1. Plan for Synthesis of Tetrasubstituted Alkene Using Alkylative Carboxylation



In this reaction, oxanickelacycle **IVa** is transmetalated with a zinc reagent to give alkylnickel complex **VIa** via transmetalation with $R^3{}_2Zn$, and reductive elimination affords zinc carboxylate **VIIa** and Ni(0). Thus, the reaction should proceed with a catalytic amount of Ni(0) in a similar manner as it has previously been reported[7a] (Figure 1).

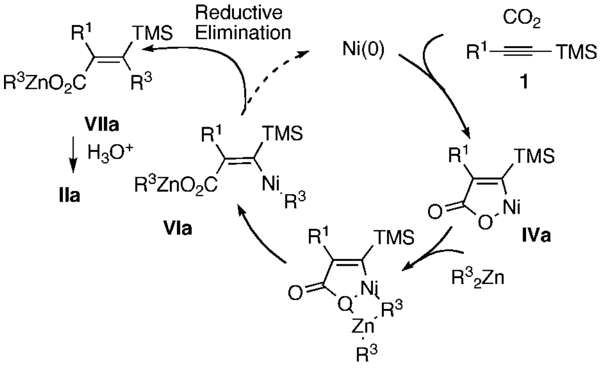
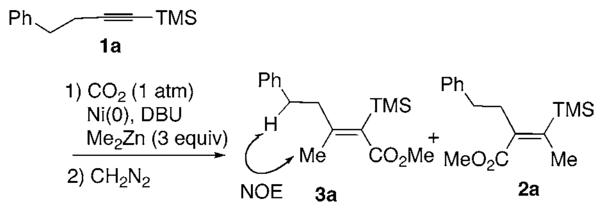


Figure 1. Possible Reaction Course

When a THF solution of **1a** (1 equiv), 20 mol % Ni(cod)$_2$, and 40 mol % diazabicycloundecene (DBU) was stirred under carbon dioxide (1 atm) in the presence of Me$_2$Zn (3 equiv) at 0 °C overnight, none of the product was obtained and **1a** was recovered in 96% yield (Table 1, entry 1).

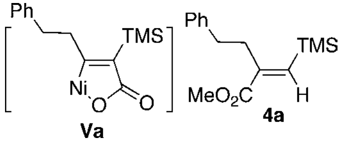
Thus, a stoichiometric reaction was examined, but the unexpected tetrasubstituted alkene **3a** was obtained in 55% yield along with trisubstituted alkene **4a** in 14% yield (entry 2). An NOE experiment with **3a** clearly indicates that CO$_2$ is introduced onto the alkyne carbon having a TMS group. Thus, compound **3a** should be formed from oxanickelacycle **Va** by transmetalation with Me$_2$Zn. The latter compound **4a** should be formed from **IVa**, but transmetalation did not proceed in this case.[10] Although the reason for the predominant formation of oxanickelacycle **Va** is not clear, the fact that tetrasubstituted alkene **3a** was obtained as a major product is interesting. In the catalytic reaction conditions (entry 1), Me$_2$Zn (3 equiv) was added along with Ni(cod)$_2$ and DBU at the same time. It was thought that Me$_2$Zn should be coordinated by DBU (eq 1).[11]

Table 1. Nickel-Mediated and -Catalyzed Carboxylation



entry	Ni (mol %)	DBU (equiv)	solvent	temp (°C)	time (h)	yield (%) 3	yield (%) 2
1	Ni(cod)$_2$ (20)	0.4	THF	0	24	0	0
2	Ni(cod)$_2$ (120)	2.4	THF	0	24	55	0[a]
3	Ni(cod)$_2$ (20)	6.5	THF	0	29	33	8[b]
4	Ni(cod)$_2$ (20)	10	THF	rt	20	68	23
5	Ni(cod)$_2$ (20)	10	toluene	40	18	64	21
6	Ni(cod)$_2$ (10)	10	THF	40	19	64	22
7	Ni(acac)$_2$ (20)	10	THF	40	21	59	20

[a] **4a** was obtained in 14% yield. [b] **1a** was recovered in 35% yield.



$$\mathrm{Me_2Zn + DBU \rightarrow Me_2Zn(DBU)_2} \qquad (1)$$

Thus, to achieve a catalytic reaction, an excess amount of DBU is required. When a THF solution of **1a**, Ni(cod)$_2$ (20 mol %), DBU (6.5 equiv), and Me$_2$Zn (3 equiv) was stirred at 0 °C under carbon dioxide (1 atm) for 29 h, we were very pleased to find that **3a** was obtained in 33% yield along with **2a** in 8% yield (entry 3). To improve the yield of **3a**, reactions were carried out under various conditions.

The use of an excess amount of DBU improved the yield of the desired product **3a** (entry 4). Toluene could be used as a solvent (entry 5), and even 10 mol % Ni(cod)$_2$ gave a good result (entry 6). The use of Ni(acac)$_2$ instead of Ni(cod)$_2$ gave a similar result (entry 7).

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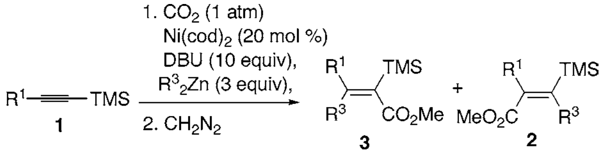
(8) (a) Dérien, S.; Duñach, E.; Périchon, J. *J. Organomet. Chem.* **1990**, *385*, C43. (b) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *Synlett* **1990**, 361. (c) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *J. Chem. Soc., Chem. Commun.* **1991**, 549. (d) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *J. Organomet. Chem.* **1992**, *424*, 213. (e) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *Tetrahedron* **1992**, *48*, 361. (f) Dérien, S.; Clinet, J.-C.; Duñach, E.; Périchon, J. *J. Org. Chem.* **1993**, *58*, 361.

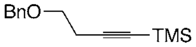
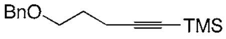
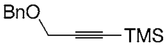
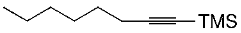
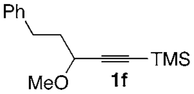
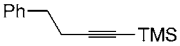
(9) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1989**, *111*, 2870.

(10) Compound **4a** should be obtained from oxanickelacycle **IV** by hydrolysis with a small amount of water in the reaction solution.

(11) Sakai, S.; Suzuki, M.; Aono, T.; Hasebe, K.; Kanbe, H.; Hiroe, M.; Kakei, T.; Fujinami, T.; Takemura, H. *Kobunshi Ronbunshu* **1984**, *41*, 151.

Table 2. Nickel-Catalyzed Alkylative Carboxylation



entry	substrate	R^3_2Zn	yield (%)[a] of	
			3	2
1	 **1b**	Me$_2$Zn	76	0
2	 **1c**	Me$_2$Zn	67	18
3	 **1d**	Me$_2$Zn	56	14
4	 **1e**	Me$_2$Zn	68	10
5[b]	 **1f**	Me$_2$Zn	71	11
7	 **1a**	Bu$_2$Zn	49	9

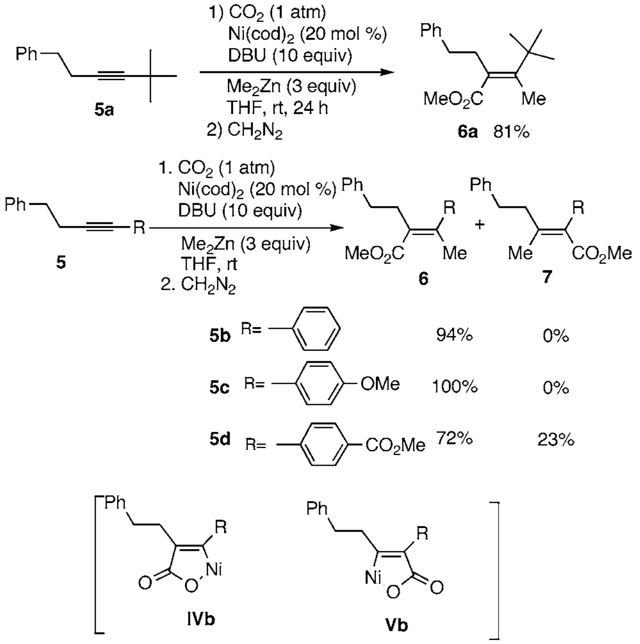
[a] All reactions were carried out using Ni(cod)$_2$ (20 mol %), DBU (10 equiv), and R^3_2Zn (3 equiv) in THF under carbon dioxide at room-temperature overnight. [b] Reaction conditions: 40 °C, 5 h.

Various alkynes **1** were used for this reaction, and the results are shown in Table 2. In each case, tetrasubstituted alkene **3** was formed predominantly in good yield. The use of Bu$_2$Zn as the zinc reagent afforded **3** (R^2 = Bu) in moderate yield (entry 7).

On the other hand, when alkyne **5a** bearing a ^{t}butyl group on the alkyne was treated in a similar manner, only tetrasustituted alkene **6a**, which should be derived from the oxanickelacycle **IVb**, not **Vb**, was obtained in 81% yield. Furthermore, in the case of **5b** bearing a phenyl group, alkene **6b** (R = Ph) was obtained predominantly. These results indicated that the alkyne bearing a ^{t}butyl or phenyl group gave only oxanickelacycle **IVb** (Scheme 2).

To clarify the regioselectivity of introduction of CO$_2$, effects of the substituent on the alkyne were further examined. When alkyne **5c** bearing a 4-methoxyphenyl group on the alkyne was treated in a similar manner, **6c** was obtained in quantitative yield, while **5d**, which has a 4-carbomethoxyphenyl group on the alkyne, gave **6d** and **7d** in 72 and 23% yields, respectively. These results suggested that in the selective formation of oxanickelacycles **IVb**, an electronic effect of the substituent R on oxanickelacycle **IVb** or **Vb** is important because the thermodynamic stability of oxanickelacycle **IVb** or **Vb** should be affected by conjugation of the substituent R with the carboxyl group. Thus, carbon dioxide should be introduced on the alkyne carbon distant from the substituent R, giving thermodynamically more stable oxanickelacycle **IVb**.[12]

Scheme 2. Effects of Substituent on the Alkyne



The remarkable features of this reaction are as follows. The reaction proceeds with a catalytic amount of Ni(0) under mild conditions, and the procedure is simple,[13] that is, a solution of an alkyne, a catalytic amount of Ni(cod)$_2$ or Ni(acac)$_2$, a zinc reagent, and an excess amount of DBU is stirred at 0−40 °C under an atmosphere of carbon dioxide. α-Silyl-β,β'-dialkyl α,β-unsaturated carboxylic acid is obtained from the trimethylsilylalkyne **1** and is a useful precursor in synthetic organic chemistry.

Further studies are in progress.

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Supporting Information Available: Information on experimental procedures and spectral data of **1b**, **1d**, **1f**, **2a**, **2c**−**f**, **3a**−**f**, **4a**, **5a**, **5c**−**d**, and **6a**−**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) In the case of trimethylsilylalkyne **1**, **Va** should be thermodynamically more stable than **IVa** because of the conjugation of the carboxyl group with the alkyl group (R^1) in **Va**, although we first thought that the silyl substitution next to the metal (as in **IV**) is thermodynamically favored.

(13) **General Procedure for Synthesis of Tetrasubstituted Alkyne Using Nickel-Catalyzed Alkylative Carboxylation.** To a stirred suspension of Ni(cod)$_2$ (10∼20 mol %) in degassed THF was added DBU (10 equiv) at 0 °C under an argon atmosphere. A balloon filled with CO$_2$ was attached to the reaction vessel. To the suspension was added a solution of the substrate (1 equiv) in degassed THF and Me$_2$Zn (1.1 equiv) at 0 °C, and the solution was stirred at room temperature for 24 h. To this solution was added 10% HCl (aq) at 0 °C. The aqueous layer was extracted with EtOAc, and the organic layer was washed with brine, dried over Na$_2$SO$_4$, and concentrated. The residue was purified using an appropriate procedure.