8248 *J. Org. Chem.* **1996,** *61,* 8248−8255

Nickel-Catalyzed Tandem Coupling of α,*β*-Enones, Alkynes, and Alkynyltins for the Regio- and Stereoselective Synthesis of Conjugated Enynes

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Received July 1, 1996[⊗]

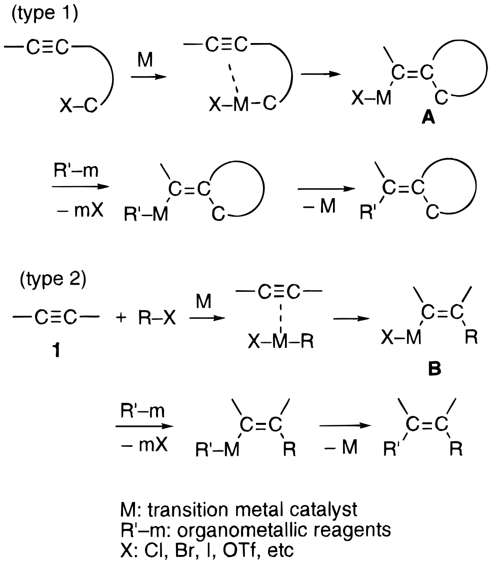
The nickel-catalyzed reaction of α,*β*-enones **2** with alkynes **1**, alkynyltins **6**, and Me_3SiCl was carried out by the successive construction of two carbon−carbon bonds to give enol silyl ethers **5**, which were then hydrolyzed to conjugated enynes **7**, with high regio- and stereoselectivities (isomeric purities: 92−98%).

Introduction

Tandem (or one-pot) reactions are an important topic in organic synthesis.[1,2] Such reactions permit complex molecules to be reasonably well constructed in a few steps. We investigated the successive introduction of carbon moieties into alkyne units based on a transition-metal-catalyzed coupling reaction with organometallic reagents, which is one of the most powerful tools in carbon−carbon bond formation.[3] As a method for catalytic tandem coupling,[4] the intramolecular cyclization and coupling of *ω*-alkynyl electrophiles in the presence of a palladium catalyst (M = Pd(0)) has been the subject of recent research (type 1 in Scheme 1).[5] The reaction proceeds via the oxidative addition of a C−X bond to the Pd(0) catalyst and the intramolecular addition of the generated C−Pd−X species to a carbon−carbon triple bond (i.e., carbopalladation), which leads to an organopalladium(II) intermediate **A**, followed by coupling with organometallic reagents (R′−m). On the other hand, little is known about the regio- and stereocontrolled intermolecular coupling of alkynes **1**, organic electrophiles (R−X), and R′−m (type 2).[6,7] In intermolecular tandem coupling, the R−M−X species may react with R′−m to give an undesired cross-coupling product (R−R′), rather than add to **1** to produce intermediate **B**.[8]

To achieve type 2 tandem coupling, we focused on an (η^3-siloxyallyl)nickel species, such as **3**, which can be generated by reacting α,*β*-enone **2** coordinated to a nickel complex with chlorotrialkylsilane (R_3SiCl) (Scheme 2) *in situ*.[9] The insertion of alkyne **1** into the (η^3-allyl)nickel unit of intermediate **3** may produce an alkenylnickel species **4**,[10] which is a key intermediate for transmetalation with organometallics, followed by reductive elimination to give coupling product **5**. In addition, we expected that organotin compounds could be used as organometallics in the tandem coupling. Organotins are

Scheme 1. Examples of Tandem Reaction Involving the Transition-Metal-Catalyzed Coupling



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[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1996.

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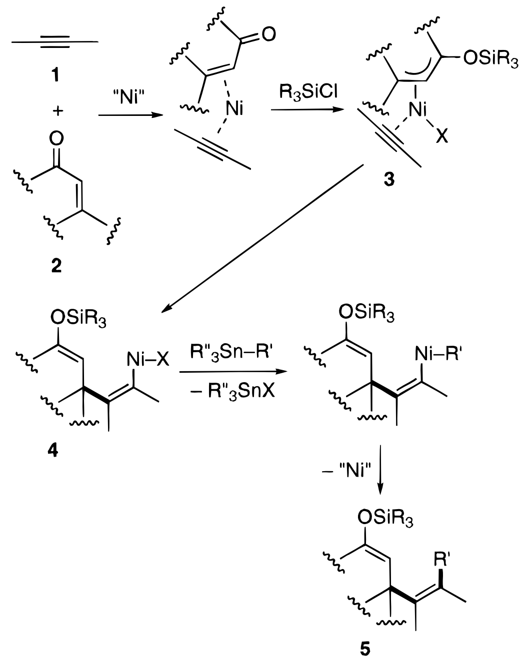
S0022-3263(96)01236-4 CCC: $12.00

Table 1. Results of the Nickel-Catalyzed Reaction of 1a with 2a and 6a in the Presence of R_3SiCl[a]

run	catalyst	R_3SiX	solvent	yield of **7a**, %[b]
1	none	Me_3SiCl	THF	0
2	$Ni(acac)_2$	Me_3SiCl	THF	14
3	$Ni(acac)_2$/DIBALH (1:1)	Me_3SiCl	THF	80
4	$Ni(acac)_2$/DIBALH (1:1)	no	THF	0
5	$Ni(acac)_2$/DIBALH (1:1)	Me_3SiBr	THF	trace
6	$Ni(acac)_2$/DIBALH (1:1)	Me_3SiOTf	THF	0
7	$Ni(acac)_2$/DIBALH (1:1)	$^tBuMe_2SiCl$	THF	trace
8	$Ni(acac)_2$/DIBALH (1:1)	Me_3SiCl	DMF	trace
9	$Ni(acac)_2$/DIBALH (1:1)	Me_3SiCl	toluene	trace
10	$Ni(acac)_2$/DIBALH/PPh_3 (1:1:4)	Me_3SiCl	THF	47
11	$Pd_2(dba)_3$[c]	Me_3SiCl	THF	0
12	$Pd(PPh_3)_4$	Me_3SiCl	THF	0

[a] Reaction conditions: catalyst (0.1 mmol), **6a** (1.1 mmol), **1a** (1.2 mmol), **2a** (1.0 mmol), and R_3SiX (1.2 mmol) in solvent (5 mL) at room temperature for 2 h and then hydrolysis by aqueous acid at room temperature for 20 min. [b] Isolated yield. [c] 0.05 mmol.

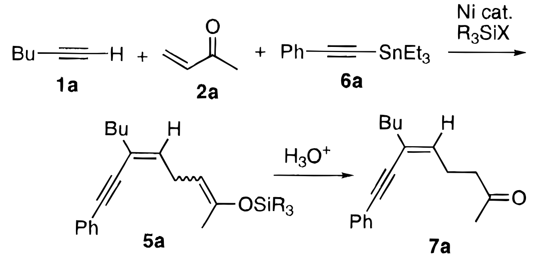
Scheme 2



easier to prepare and handle than other organometallics. While the palladium-catalyzed reaction with organotins has presented a versatile method for constructing carbon–carbon bonds,[11] it seems that the catalytic activities of other transition metal complexes have not been fully investigated.[7a,12] Therefore, we examined the tandem coupling of alkynes **1**, enones **2**, and organotins in the presence of a nickel catalyst.

Results and Discussion

The first attempts at the coupling of 1-hexyne (**1a**), 3-butene-1-one (**2a**), and vinyl- or allyl(tributyl)tin using a variety of nickel catalysts and chlorotrialkylsilanes were not successful. However, we then found that the desired tandem coupling proceeded efficiently when alkynyltin **6** was used as the organotin (eq 1).[13] Thus,



(1)

the reaction of **2a** (1 equiv) with **1a** (1.2 equiv), (phenylethynyl)triethyltin (**6a**, 1.1 equiv), and chlorotrimethylsilane (Me_3SiCl, 1.2 equiv) in THF (5 mL) in the presence of $Ni(acac)_2$ (10 mol %) at room temperature for 2 h gave the conjugated enyne **5a**. Product **5a**, which has an enol silyl ether function, was hydrolyzed quantitatively by aqueous acid to give the corresponding carbonyl compound **7a** in 14% yield (run 2 in Table 1). The yield of **7a** increased to 80% when the reaction was carried out in the presence of the nickel catalyst that was generated from an equimolar amount of $Ni(acac)_2$ and diisobutylaluminum hydride (DIBALH) *in situ* (run 3). The direct coupling product of **2a** with **6a** was not observed.[14] The reaction did not proceed in the absence of Me_3SiCl (run 4). The use of Me_3SiBr, Me_3SiOTf, or $^tBuMe_2SiCl$ instead of Me_3SiCl also gave unsatisfactory results (runs 5–7). DMF and toluene were less efficient solvents than THF

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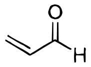
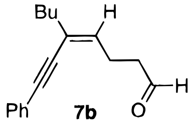
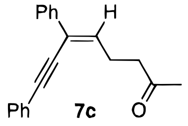
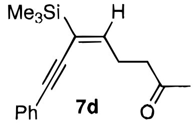
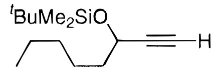
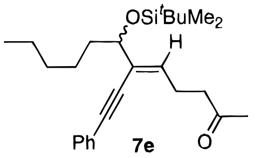
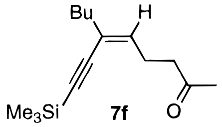
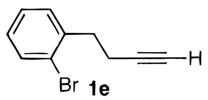
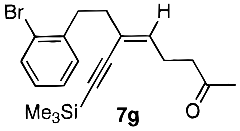
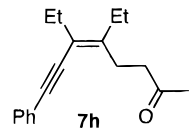
(12) Ni: (a) Tanaka, M. *Synthesis* **1981**, 47. (b) Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am.Chem. Soc.* **1992**, *114*, 5160. (c) Cui, D.-M.; Hashimoto, N.; Ikeda, S.; Sato, Y. *J. Org. Chem.* **1995**, *60*, 5752. Recently, the examples of Cu-mediated cross coupling with organotins were reported. See: (d) Piers, E.; Wong, T. *J. Org. Chem.* **1993**, *58*, 3609. (e) Falck, J. R.; Bhatt, R. K.; Ye, J. *J. Am. Chem. Soc.* **1995**, *117*, 5973. (f) Allred, G. D.; Liebeskind, L. S. *J. Am.Chem. Soc.* **1996**, *118*, 2748. Also see: (g) Behling, J.; Babiak, K.; Ng, J.; Campbell, A.; Moretti, R.; Koerner, M.; Lipshutz, B. *J. Am. Chem. Soc.* **1988**, *110*, 2641. (h) Behling, J.; Ng, J.; Bagbiak, K.; Campbell, A.; Elsworth, E.; Koerner, M.; Lipshutz, B. *Tetrahedron Lett.* **1989**, *30*, 27.

(13) A portion of this work has been previously communicated. See: Ikeda, S.; Sato, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5975.

(14) The reaction of **2a** with **6a** and Me_3SiCl in the absence of **1a** gave **5c** (**7c**, 26% yield based on **1a** after hydrolysis), along with a trace amount of **1b**.

Table 2. Nickel-Catalyzed Coupling Reaction of 1 with 2 and 6 in the Presence of Me_3SiCl[a]

entry	alkyne **1**	enone **2**	alkynyltin **6**	product **7**[b,c]	yield, %[d]
1	**1a**	**2a**	**6a**	**7a**	80 (95)
2	**1a**	**2a**	$Ph-C\equiv C-SnBu_3$ **6b**	**7a**	64 (95)
3	**1a**	 **2b**	**6a**	 **7b**	74 (95)
4[e]	**1a**	**2b**	**6b**	**7b**	57 (95)
5	$Ph-C\equiv C-H$ **1b**	**2a**	**6a**	 **7c**	52 (>98)
6	$Me_3Si-C\equiv C-H$ **1c**	**2a**	**6a**	 **7d**	71 (>98)
7	 **1d**	**2a**	**6b**	 **7e**	31 (>98)
8	**1a**	**2a**	$Me_3Si-C\equiv C-SnBu_3$ **6c**	 **7f**	74 (97)
9	 **1e**	**2a**	**6c**	 **7g**	63 (92)
10	$Et-C\equiv C-Et$ **1f**	**2a**	**6b**	 **7h**	58 (>98)

[a] Reaction conditions: $Ni(acac)_2$ (0.1 mmol), DIBALH (1.0 M hexane, 0.1 mL), **1** (1.2 mmol), **2** (1.0 mmol), **6** (1.1 mmol), and Me_3SiCl (1.2 mmol) in THF (5 mL) at room temperature for 2 h. [b] Hydrolyzed product by aqueous acid. [c] The spectral and analytical data have already been reported in our preliminary communication. See ref 13. [d] Isolated yield. Isomeric purity is based on the ^1H NMR spectra and GC results and is in parentheses. [e] $Ni(cod)_2$ (0.1 mmol) was used in place of $Ni(acac)_2$ and DIBALH.

was (runs 8 and 9). The addition of PPh_3 (40 mol %) to the nickel catalyst led to a lower yield of **7a** (run 10). Interestingly, the reaction did not occur when $Pd_2(dba)_3$ or $Pd(PPh_3)_4$ was used (runs 11 and 12).

The results of the reaction in the presence of the nickel catalyst and subsequent hydrolysis are summarized in Table 2. Most importantly, the coupling reaction with a variety of terminal alkynes, **1a**–**e**, regio- and stereoselectively gave the corresponding compounds, **7a**–**g** (entries 1–9). For example, the sole product **7d** (entry 6) was assigned to 8-phenyl-6-(trimethylsilyl)-5-octen-7-yn-2-one and not to a regioisomer, i.e., 8-phenyl-5-(trimethylsilyl)-5-octen-7-yn-2-one (**8**), by ^1H NMR spectral data. The double bond in **7d** was assigned an *E* geometry by the NOE experiments (Figure 1). In all of the cases, an enone unit was selectively added to the terminal carbon of **1** and an alkynyl group of **6** was introduced to the internal carbon of **1**. The enone unit and the alkynyl unit were added to **1** in a syn manner. The regio- and stereoselectivities of **7** are shown in Table 2 in terms of

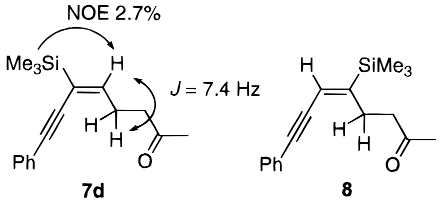


Figure 1.

Table 3. The Results of the Nickel-Catalyzed Reaction of 1a with 2c and 6b in the Presence of Me_3SiCl[a]

run	additive	temp.	time, h	yield of **7i**, %[b]
1	no	rt	4	0
2	no	reflux	4	0
3	PPh_3	rt	4	0
4	PPh_3	reflux	4	0
5	Et_3N	reflux	4	0
6	pyridine	rt	4	0
7	pyridine	reflux	2	71
8	2,2′-bipyridine[c]	reflux	2	14

[a] Reaction conditions: $Ni(acac)_2$ (0.1 mmol), DIBALH (1.0 M hexane, 0.1 mL), additive (0.2 mmol), **6b** (1.1 mmol), **1a** (1.2 mmol), **2c** (1.0 mmol), and Me_3SiCl (1.2 mmol) in THF (5 mL), and then hydrolysis by aqueous acid at room temperature for 20 min. [b] Isolated yield. [c] 0.1 mmol.

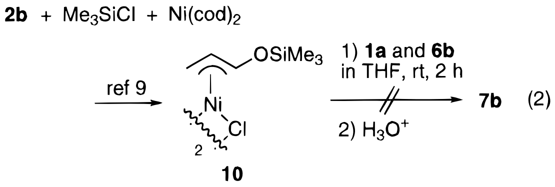
the isomeric purity. Acrolein (**2b**) also reacted smoothly to give **7b** in a good yield (entry 3). The coupling reaction also proceeded efficiently in the presence of $Ni(cod)_2$ catalyst (entry 4) and with **6c** instead of **6a** and **6b** (entry 8). A siloxy group at the propargylic position of **1d** (entry 7) and an arene–bromine bond in **1e** (entry 9) remained intact under these reaction conditions. An internal alkyne such as 3-hexyne (**1f**) was used in the coupling reaction to give **7h** as a sole product (entry 10).

Next we attempted to add cyclic enones such as 2-cyclopenten-1-one (**2c**) and the alkynyl unit of **6** to **1** by nickel-catalyzed tandem coupling. These results are summarized in Table 3. The coupling of **2c** with **1a** and **6b** did not proceed in the presence of catalyst prepared from $Ni(acac)_2$ and DIBALH (run 1). Even under reflux conditions the reaction did not give the desired product, **7i** (run 2). A similar result was observed with β-substituted acyclic enones, such as 4-hexen-3-one (**2g**). These results show that the intermediate **4** was not produced from the reaction of a β-substituted enone such as **2c** or **2g** with a "naked" nickel catalyst generated from $Ni(acac)_2$ and DIBALH. The enones may tightly coordinate to the more electron-rich nickel complex[15] and accelerate *O*-silylation of the coordinated enone.[9] We examined the addition of various donating ligands to the nickel catalyst. Even though the addition of PPh_3 or Et_3N was ineffective (runs 3–5), pyridine (20 mol %) was an efficient additive under THF reflux conditions (**7i**: 71% yield, run 7). 2,2′-Bipyridine was less efficient than pyridine (run 8).

The results of the tandem coupling of a variety of cyclic enones **2c**–**f** in the presence of nickel–pyridine catalyst are shown in Table 4. Interestingly, the reaction of **2c** with some terminal alkynes **1a** and **1c**–**e** (entries 1–4) gave the corresponding products **7i**–**l**, respectively, with complete regio- and stereoselectivity (i.e., isomeric purities >98%), although the regioselectivity in the reaction of **2a** was dependent on the alkynes **1a**–**e** used (isomeric purities: 92–98%, see Table 2). Unfortunately, similar reactions with alkynes such as methyl propionate (**1g**, entry 5), propargyl bromide (**1h**, entry 6), and propargyl benzoate (**1i**, entry 7) did not give the corresponding products. The six- and seven-membered cyclic enones **2d** and **2e** (entries 9 and 10) and 2-pentylcyclopentenone (**2f**, entry 11) could be used in the selective coupling to give **7n**–**p**, respectively. This catalytic system was also effective in the coupling of acyclic enones **2g**–**i** to obtain **7q**–**s** as the sole isomers, respectively (entries 12–14). However, there was hardly any reaction with chalcone (**2j**, entry 15) or mesityl oxide (**2k**, entry 16).

It was also interesting to stereoselectively introduce the conjugated enynyl unit to a tricyclic dienone, such as tricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-one (**2l**), since the stereoselective functionalization of enantiomeric tricyclic dienone derivatives, which leads to the enantiocontrolled synthesis of a variety of natural products, is well known.[16] We examined the tandem coupling of **2l**, **1c**, **6b**, and Me_3SiCl in the presence of nickel–pyridine catalyst in THF at reflux for 2 h and obtained the corresponding product **7t** in 63% yield as the sole product (Scheme 3). The stereochemistry of **7t** was assigned as depicted in Scheme 3 by the ^1H NMR spectral data and NOE experiments. The reaction may proceed via the coordination of the *exo*-site of the cyclopentenone unit of **2l** to the nickel–pyridine catalyst, leading to an intermediate, **9**, stereoselectively.

To clarify the reaction pathway depicted in Scheme 2, we prepared an η^3-(siloxyallyl)nickel complex **10** *in situ* and investigated the reaction of **10** with **1a** and **6b**.[17] However, complex **10** did not react to give the corresponding product **7b** (eq 2). Thus, **1a** was not inserted into the η^3-(allyl)nickel unit of **10** in the stoichiometric reaction. On the other hand, the $Ni(cod)_2$-catalyzed coupling of **2b**, **1a**, **6b**, and Me_3SiCl gave **7b** in 54% yield, even with an excess amount of 1,5-cyclooctadiene (cod, eq 3). These results suggest that the tandem coupling does not proceed via the insertion of alkyne **1** into the η^3-(allyl)nickel unit of **3** to produce intermediate **4** (path A in Scheme 4). The possibility of another pathway via the conjugate addition of an alkenyltin to **2** was also negligible.[12b,18] Thus, **6b** did not react with **1a** to give an alkenyltin such as [(2-butyl-4-phenyl-1-buten-3-yn)-yl]tributyltin (**11**, eq 4). As a plausible route which leads to intermediate **4**, path B via the reaction of intermediate **12** with Me_3SiCl seems more appropriate (Scheme 4). Highly regioselective coupling may result from the steric



$$\mathbf{2b} + \mathbf{1a} + \mathbf{6b} + Me_3SiCl \xrightarrow[2)\ H_3O^+]{1)\ \text{cat. } Ni(cod)_2 + \text{COD (2 equiv vs. } \mathbf{2b})} \mathbf{7b} \quad (3)$$

54% yield

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(15) Yamamoto, T.; Yamamoto, A.; Ikeda. S. *J. Am. Chem. Soc.* **1971**, *93*, 3360.

(16) Ogasawara, K. *Pure Appl. Chem.* **1994**, *66*, 2119. Ogasawara, K. *J. Synth. Org. Chem. Jpn.* **1996**, *54*, 29.

(17) Mackenzie's group reported that the η^3-(siloxy)allyl nickel complexes such as **10** were generated *in situ* and used without purification (contaminated with COD) in the stoichiometric reaction with halocarbon. See ref 9.

(18) Perlmutter, P. *Conjugate Addition Reaction in Organic Synthesis*; Pergamon Press: London, 1992.

Table 4. Nickel-Catalyzed Coupling Reaction of β-Substituted 2c−k with 1 and 6 in the Presence of Me_3SiCl[a]

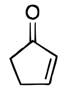
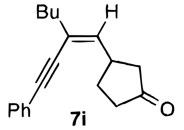
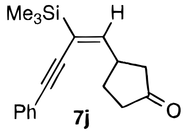
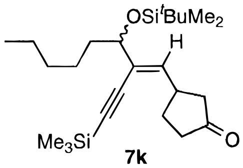
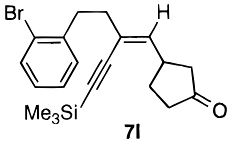
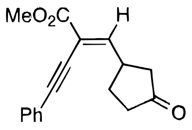
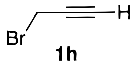
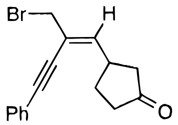
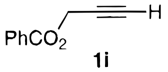
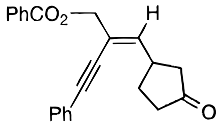
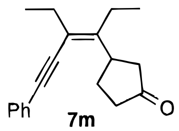
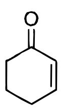
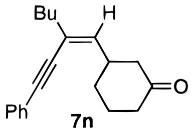
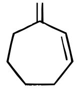
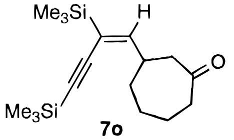
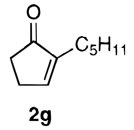
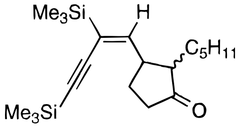
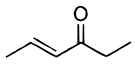
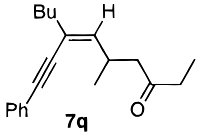
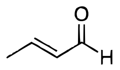
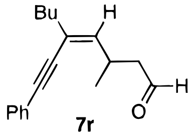
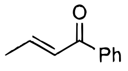
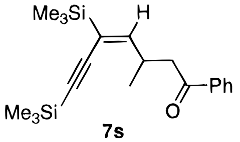
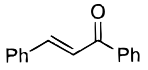
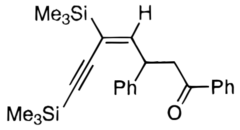
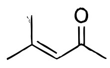
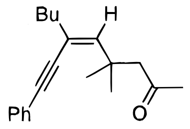
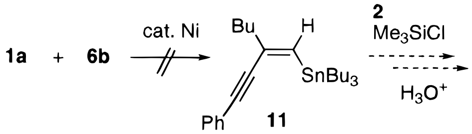
entry	alkyne **1**	enone **2**	alkynyltin **6**	product **7**[b]	yield, %[c]
1	**1a**	 **3c**	**6b**	 **7i**	71 (>98)
2	**1c**	**3c**	**6b**	 **7j**	65 (>98)
3	**1d**	**3c**	**6c**	 **7k**	40 (>98)
4	**1e**	**3c**	**6c**	 **7l**	47 (>98)
5	$MeO_2C-\equiv-H$ **1g**	**3c**	**6b**		0
6	 **1h**	**3c**	**6b**		0
7	 **1i**	**3c**	**6b**		0
8	**1f**	**3c**	**6b**	 **7m**	39 (>98)
9	**1a**	 **2e**	**6b**	 **7n**	43 (>98)
10	**1c**	 **2f**	**6c**	 **7o**	60 (>98)
11	**1c**	 **2g**	**6c**	 **7p**	46 (>98)[d]

Table 4 (Continued)

entry	alkyne **1**	enone **2**	alkynyltin **6**	product **7**[b]	yield, %[c]
12	**1a**	 **2d**	**6b**	 **7q**	49 (>98)
13	**1a**	 **2h**	**6b**	 **7r**	69 (>98)
14	**1c**	 **2i**	**6c**	 **7s**	72 (>98)
15	**1c**	 **2j**	**6c**		trace
16	**1a**	 **2k**	**6b**		0

[a] Reaction conditions: Ni(acac)$_2$ (0.1 mmol), DIBALH (1.0 M hexane, 0.1 mL), pyridine (0.2 mmol), **6** (1.1 mmol), **1** (1.2 mmol), **2** (1.0 mmol), and Me$_3$SiCl (1.2 mmol) in THF (5 mL) at reflux for 2 h. [b] Hydrolyzed product by aqueous acid. [c] Isolated yield. Isomeric purity is in parentheses. [d] Diastereoselectivity after treatment of 0.2 N NaOH in MeOH (3 mL) overnight: 92/8.



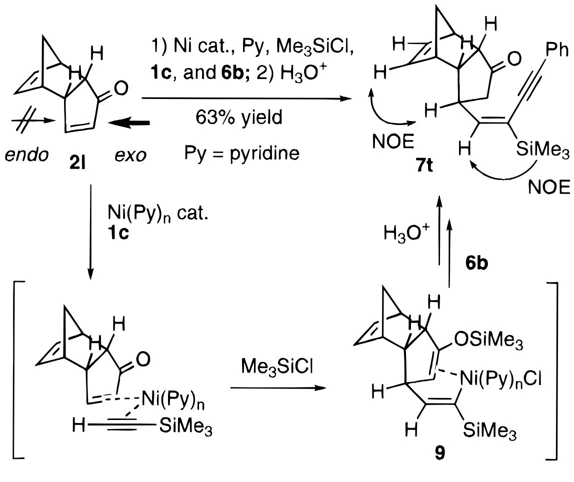
(4)

crowding between R of the alkyne and the substitution group at the β-position of the enone in **12b** being greater than that in **12a** (Scheme 5). The equilibrium between **12a** and **12b** lies in the direction of **12a**, which leads to **4a**. Recently, our group[19] and Montgomery's[20] group reported that the reaction of enones with alkynes and organozincs took place via a pathway closely related to the present reaction.

Conclusion

We described here a new nickel-catalyzed tandem coupling reaction of enones **2**, alkynes **1**, alkynyltins **6**, and Me$_3$SiCl. This reaction was carried out by the successive construction of two carbon–carbon bonds to give conjugated enynes **7**, after hydrolysis of the enol silyl ethers **5**. Most importantly, the coupling reaction with a variety of terminal alkynes **1a**–**e** regio- and stereoselectively gave the corresponding compounds, **7**. In all of the cases, an enone unit was selectively added to the terminal carbon of **1** and an alkynyl group of **6** was introduced to the internal carbon of **1**. The enone and alkynyl units were added to **1** in a syn manner. The present reaction provides a new synthetic method for the selective construction of conjugated enynes, which are important in the synthesis of a wide range of natural products, using tandem coupling.[21]

Scheme 3



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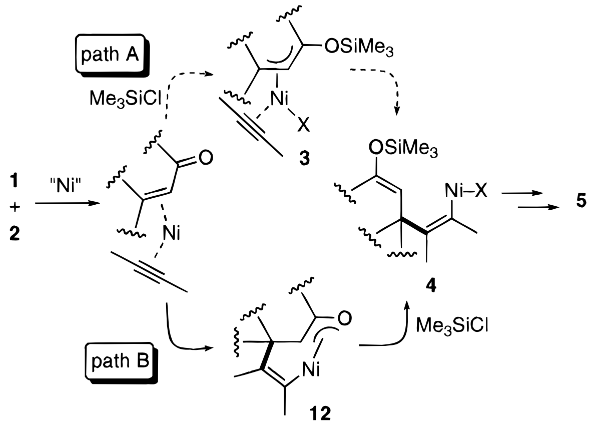
(19) Ikeda, S.; Yamamoto, H.; Kondo, K.; Sato, Y. *Organometallics* **1995**, *14*, 5015.

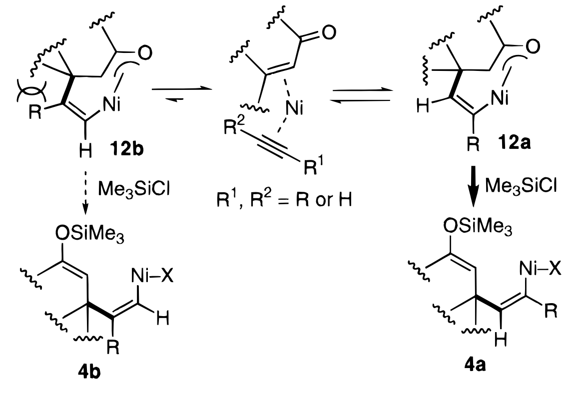
(20) Montgomery, J.; Savchenko, A. V. *J. Am. Chem. Soc.* **1996**, *118*, 2099.

(21) For recent papers on the synthesis of conjugated enynes, see: Okuro, K.; Furuune, M.; Miura, M.; Nomura, M. *Tetrahedron Lett.* **1992**, *33*, 5363. Luo, F.-T.; Fwu, S.-L.; Huang, W.-S. *Tetrahedron Lett.* **1992**, *33*, 6839. Torii, S.; Okumoto, H.; Tadokoro, T.; Nishimura, A.; Rashid, M. A. *Tetrahedron Lett.* **1993**, *34*, 2139. Nuss, J. M.; Rennels, R. A.; Levine, B. H. *J. Am. Chem. Soc.* **1993**, *115*, 6991.

Scheme 4



Scheme 5



Experimental Section

General Comments. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. THF was distilled from sodium benzophenone ketyl under N_2. Toluene, Me_3SiCl, Me_3SiBr, Me_3SiOTf, pyridine, and Et_3N were distilled from CaH_2 under N_2. DMF was distilled from BaO under N_2. $Pd_2(dba)_3$,[22] $Pd(PPh_3)_4$,[23] (phenylethynyl)triethyltin (**6a**),[24] (phenylethynyl)tributyltin (**6b**),[24] [(trimethylsilyl)ethynyl]tributyltin (**6c**),[24] and tricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-one (**2l**)[25] were prepared by literature procedures. 3-[(*tert*-Butyldimethylsilyl)oxy]-1-octyne (**1d**) was prepared by the reaction of 1-octyn-3-ol with ^{t}BuMe$_2$SiCl.[26] 1-(3-Butynyl)-2-bromobenzene (**1e**) was prepared by the reaction of 1-bromobenzyl bromide with allenylmagnesium bromide.[27] Propargyl benzoate (**1i**) was prepared from the reaction of propargyl bromide with benzoyl chloride in the presence of pyridine.

General Procedure for the Coupling Reaction in the Presence of Nickel–Pyridine Catalyst. To a solution of $Ni(acac)_2$ (0.1 mmol) in THF (5 mL) were added DIBALH in a 1.0 M toluene solution (0.1 mL) and pyridine (0.2 mmol) at 0 °C under N_2, and the mixture was stirred for 5 min. To this black solution were then added **6** (1.1 mmol), **1** (1.2 mmol), **2** (1.0 mmol), and Me_3SiCl (1.2 mmol) at 0 °C, and then the mixture was stirred at reflux for 2 h. To this was added aqueous acid (2 mL, acetone/HCl(aq) = 5:1), and it was again stirred at room temperature for 15 min; then aqueous NH_4F (30 mL) was added, and stirring continued for 30 min to remove the trialkyltin chloride. After filtration by Celite, the aqueous layer was extracted with Et_2O (30 mL × 3). The combined organic layers were washed with aqueous $NaHCO_3$ (50 mL) and then with brine (50 mL), dried over $MgSO_4$ for 30 min, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel) to yield **7**. The isomeric purity of the product obtained was determined by ^{1}H NMR spectroscopy and GC. An analytical sample was obtained by bulb-to-bulb distillation.

3-[(*Z*)-[1-(2-Butyl-4-phenyl-1-buten-3-yn)yl]]cyclopentanone (7i, entry 1 in Table 4): isomeric purity >98%; a pale yellow oil; bp 165 °C (3 mmHg); $R_f = 0.25$ (hexane/AcOEt = 4:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (t, $J = 7.3$ Hz, 3 H), 1.36 (tq, $J = 7.4$, 7.3 Hz, 2 H), 1.53–1.60 (m, 2 H), 1.65–2.54 (c, 8 H), 3.40–3.46 (m, 1 H), 5.65 (d, $J = 9.1$ Hz, 1 H), 7.30–7.45 (m, 5 H); IR (neat) 2957, 2931, 1744, 1157, 1103, 756, 693 cm^{-1}; MS (DIEI, 70 eV) *m/z* (relative intensity) 266 (M^+, 100). Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.74; H, 8.54.

3-[(*E*)-[1-[4-Phenyl-2-(trimethylsilyl)-1-buten-3-yn]yl]]cyclopentanone (7j, entry 2 in Table 4): isomeric purity >98%; a pale yellow oil; bp 165 °C (3 mmHg); $R_f = 0.23$ (hexane/AcOEt = 6:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.21 (s, 9 H), 1.65–2.59 (c, 6 H), 3.50–3.66 (m, 1 H), 6.03 (d, $J = 8.6$ Hz, 1 H), 7.28–7.44 (m, 5 H); NOE (270 MHz) irradiated at 0.21 ppm, observed 6.03 ppm, 1.9%; IR (neat) 2959, 1746, 1489, 1404, 1248, 1154, 841, 756, 693 cm^{-1}; GC/MS (EI, 70 eV) *m/z* (relative intensity) 283 ($M^+ + 1$, 21), 282 (M^+, 85), 73 (100). Anal. Calcd for $C_{18}H_{22}OSi$: C, 76.54; H, 7.85. Found: C, 76.41; H, 7.86.

3-[(*E*)-[1-[2-[1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]hexyl]-4-(trimethylsilyl)-1-buten-3-yn]yl]]cyclopentanone (7k, entry 3 in Table 4): regioselectivity >98%, diastereomers mixture; a colorless oil; bp 170 °C (3.5 mmHg); $R_f = 0.20$ (hexane/AcOEt = 9:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.03 (s, 3 H), 0.04 (s, 3 H), 0.19 (s, 9 H), 0.88 (t, $J = 7.4$ Hz, 3 H), 0.89 (s, 9 H), 1.24–1.39 (m, 6 H), 1.59–2.54 (c, 8 H), 3.25–3.43 (m, 1 H), 4.05 (t, $J = 5.9$ Hz, 1 H), 5.95 (dt, $J = 9.2$, 1.6 Hz, 1 H); IR (neat) 2957, 2932, 2859, 2145, 1748, 1464, 1252, 1090, 841, 775 cm^{-1}; GC/MS (EI, 70 eV) *m/z* (relative intensity) 420 (M^+, 0), 363 ($M^+ - {}^t$Bu, 100). Anal. Calcd for $C_{24}H_{44}O_2Si_2$: C, 68.51; H, 10.54. Found: C, 68.48; H, 10.73.

3-[(*Z*)-[1-[2-(2-Bromophenyl)ethyl-4-(trimethylsilyl)-1-buten-3-yn]yl]]cyclopentanone (7l, entry 4 in Table 4): isomeric purity >98%; a pale yellow oil; bp 170 °C (0.7 mmHg); $R_f = 0.20$ (hexane/AcOEt = 6:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.22 (s, 9 H), 1.51–2.33 (c, 6 H), 2.41 (t, $J = 7.5$ Hz, 2 H), 2.97 (t, $J = 7.5$ H, 2 H), 3.31 (m, 1 H), 5.50 (d, $J = 9.0$ Hz, 1 H), 7.05–7.54 (m, 4 H); IR (neat) 2959, 2141, 1743, 1471, 1249, 842, 754 cm^{-1}; GC/MS (EI, 70 eV) *m/z* (relative intensity) 390 ($M^+ + 2$, 12), 388 (M^+, 12), 73 (100). Anal. Calcd for $C_{20}H_{25}OSiBr$: C, 61.69; H, 6.47. Found: C, 61.45; H, 6.68.

3-[(*Z*)-[1-(1,2-Diethyl-4-phenyl-1-buten-3-yn)yl]]cyclopentanone (7m, entry 8 in Table 4) isomeric purity: >98%; a pale yellow oil; bp 160 °C (1 mmHg); $R_f = 0.34$ (hexane/AcOEt = 5:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.03 (t, $J = 7.6$ Hz, 3 H), 1.18 (t, $J = 7.6$ Hz, 3 H), 1.63–2.43 (c, 10 H), 3.70–3.84 (m, 1 H), 7.26–7.41 (m, 5 H); IR (neat) 2968, 2934, 2876, 1743, 1489, 756, 692 cm^{-1}; GC/MS (EI, 70 eV) *m/z* (relative intensity) 267 ($M^+ + 1$, 54), 266 (M^+, 98), 195 (100). Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.49; H, 8.24.

3-[(*Z*)-[1-(2-Butyl-4-phenyl-1-buten-3-yn)yl]]cyclohexanone (7n, entry 9 in Table 4): isomeric purity >98%; a pale yellow oil; bp 175 °C (3.5 mmHg); $R_f = 0.33$ (hexane/AcOEt = 4:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (t, $J = 7.3$ Hz, 3 H), 1.34 (tq, $J = 7.0$, 7.3 Hz, 2 H), 1.45–1.62 (m, 2 H), 1.68–2.55 (m, 8 H), 3.04–3.18 (m, 1 H), 5.71 (dt, $J = 7.1$, 1.3 Hz, 1 H), 7.28–7.46 (m, 5 H); IR (neat) 2957, 2932, 2861, 1713, 1491, 1445, 1223, 756, 691 cm^{-1}; MS (DIEI, 70 eV) *m/z* (relative intensity) 280 (M^+, 100). Anal. Calcd for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.55; H, 8.77.

3-[(*E*)-[1-[2,4-Bis(trimethylsilyl)-1-buten-3-yn]yl]]cycloheptenone (7o, entry 10 in Table 4): isomeric purity >98%; a pale yellow oil; bp 150 °C (3.5 mmHg); $R_f = 0.26$ (hexane/AcOEt = 4:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.12 (s, 9

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H), 0.19 (s, 9 H), 1.39−2.60 (m, 10 H), 3.00−3.19 (m, 1 H), 5.94 (d, *J* = 8.6 Hz, 1 H); IR (neat) 2959, 2930, 2854, 2126, 1703, 1250, 841, 758, 631 cm^{-1}; GC/MS (EI, 70 eV) *m*/*z* (relative intensity) 306 (M$^+$, 19), 73 (100). Anal. Calcd for $C_{17}H_{30}OSi_2$: C, 66.60; H, 9.86. Found: C, 66.33; H, 10.01.

3-[(*E*)-[1-[2,4-Bis(trimethylsilyl)-1-buten-3-yn]yl]]-2-pentylcyclopentanone (**7p, entry 11 in Table 4**): regioselectivity >98%, stereoselectivity 92%; a pale yellow oil; bp 140 °C (3.5 mmHg); R_f = 0.42 (hexane/AcOEt = 5:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.15 (s, 9 H), 0.17 (s, 9 H), 0.86 (t, *J* = 6.8 Hz, 3 H), 1.11−2.43 (c, 13 H), 3.00−3.31 (m, 1 H), 5.85 (d, *J* = 10.2 Hz, 0.08 H), 5.97 (d, *J* = 7.9 Hz, 0.92 H); IR (neat) 2959, 2930, 2123, 1744, 1460, 1250, 843, 758 cm^{-1}; GC/MS (EI, 70 eV) *m*/*z* (relative intensity) 348 (M$^+$, 16), 73 (100). Anal. Calcd for $C_{20}H_{36}OSi_2$: C, 68.90; H, 10.41. Found: C, 68.64; H, 10.41.

(*Z*)-7-Butyl-5-methyl-9-phenyl-6-nonen-8-yn-3-one (**7q, entry 12 in Table 4**): isomeric purity >98%; a pale yellow oil; bp 160 °C (3 mmHg); R_f = 0.37 (hexane/AcOEt = 4:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.3 Hz, 3 H), 1.03 (t, *J* = 7.3 Hz, 3 H), 1.06 (d, J = 6.6 H, 3 H), 1.33 (qt, *J* = 7.3, 7.2 Hz, 2 H), 1.49−1.58 (m, 2 H), 2.14 (t, *J* = 7.2 Hz, 2 H), 2.37−2.51 (m, 2 H), 3.27−3.37 (m, 1 H), 5.54 (d, *J* = 8.8 Hz, 1 H), 7.27−7.48 (m, 5 H); IR (neat) 2959, 2932, 2872, 1713, 1491, 1458, 1377, 756, 693 cm^{-1}; MS (DIEI, 70 eV) *m*/*z* (relative intensity) 282 (M$^+$, 23), 225 (100). Anal. Calcd for $C_{20}H_{26}O$: C, 85.06; H, 9.28. Found: C, 84.83; H, 9.11.

(*Z*)-5-Butyl-3-methyl-7-phenyl-4-hepten-6-ynal (**7r, entry 13 in Table 4**): isomeric purity >98%; a pale yellow oil; bp 130 °C (2.8 mmHg); R_f = 0.37 (hexane/AcOEt = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.3 Hz, 3 H), 1.13 (d, *J* = 6.9 Hz, 3 H), 1.29−1.38 (m, 2 H), 1.51−1.58 (m, 2 H), 2.18 (td, *J* = 7.4, 1.1 Hz, 2 H), 2.42−2.45 (m, 2 H), 3.35−3.42 (m, 1 H), 5.55 (dt, *J* = 9.5, 1.1 Hz, 1 H), 7.29−7.46 (m, 5 H), 9.75 (t, *J* = 2.5 Hz, 1 H); IR (neat) 2959, 2930, 1726, 1491, 1460, 756, 690 cm^{-1}; GC/MS (EI, 70 eV) *m*/*z* (relative intensity) 254 (M$^+$, 41), 225 (100); HRMS for $C_{18}H_{22}O$ (M$^+$), calcd 254.1671, found 254.1650.

(*E*)-5,7-Bis(trimethylsilyl)-3-methyl-1-phenyl-4-nonen-6-yn-1-one (**7s, entry 14 in Table 4**): isomeric purity >98%; a yellow oil; bp 145 °C (3 mmHg); R_f = 0.42 (hexane/AcOEt = 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (s, 9 H), 0.15 (s, 9 H), 1.09 (d, *J* = 6.8 Hz, 3 H), 2.87 (dd, *J* = 15.0, 8.6 Hz, 1 H), 3.13 (dd, *J* = 15.0, 5.3 Hz, 1 H), 3.41−3.53 (m, 1 H), 5.97 (d, *J* = 8.8 Hz, 1 H), 7.45−7.98 (m, 5 H); IR (neat) 2959, 2899, 2129, 1685, 1450 cm^{-1}; GC/MS (EI, 70 eV) *m*/*z* (relative intensity) 343 (M$^+$ + 1, 6), 342 (M$^+$, 19), 73 (100). Anal. Calcd for $C_{20}H_{30}OSi_2$: C, 70.11; H, 8.83. Found: C, 69.93; H, 8.73.

5-[(*E*)-[1-[4-Phenyl-2-(trimethylsilyl)-1-buten-3-yn]yl]]-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (**7t in Scheme 3**): isomeric purity >98%; a pale yellow crystal; mp 73.5−74 °C; R_f = 0.34 (hexane/AcOEt = 4:1); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.21 (s, 9 H), 1.43 (d, *J* = 7.4 Hz, 1 H), 1.58 (d, *J* = 7.4 Hz, 1 H), 2.18 (ddd, *J* = 18.5, 7.9, 2.0 Hz, 1 H), 2.38 (dd, *J* = 18.3, 9.1 Hz, 1 H), 2.77−2.85 (m, 1 H), 2.96−3.06 (m, 1 H), 3.09−3.18 (m, 1 H), 3.21 (br s, 2 H), 6.12 (d, *J* = 8.8 Hz, 1 H), 6.19 (dd, *J* = 5.7, 3.1 Hz, 1 H), 6.29 (dd, *J* = 5.7, 3.1 Hz, 1 H), 7.26−7.44 (m, 5 H); NOE (270 MHz) irradiated at 0.21 ppm, observed 6.12 ppm, 7.2%; irradiated at 3.09−3.18 ppm, observed 6.29 ppm, 11.7%; irradiated at 6.29 ppm, observed 3.09−3.18 ppm, 6.1%; IR (neat) 2959, 1734, 1248, 839, 756 cm^{-1}; GC/MS (EI, 70 eV) *m*/*z* (relative intensity) 346 (M$^+$, 49), 73 (100). Anal. Calcd for $C_{23}H_{26}OSi$: C, 79.72; H, 7.56. Found: C, 79.51; H, 7.61.

JO961236H