Synthetic Methods

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Efficient and Selective Formation of Unsaturated Carboxylic and Phenylacetic Acids from Diketene**

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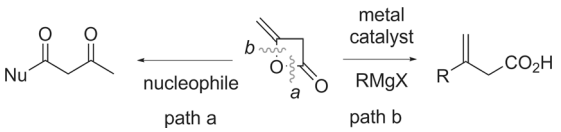
Abstract: *A nickel catalyst promotes the multicomponent coupling reaction of diketene, an alkyne, and Me_2Zn to provide 3-methylene-4-hexenoic acids in excellent yields. Under similar conditions, the combination of the nickel catalyst and $Et_2Al(OEt)$ promotes a cycloaddition reaction involving dimerization of an alkyne to furnish phenylacetic acids. In the presence of PPh_3, a formal [2+2+1+1] cycloaddition reaction proceeds to afford regioisomeric phenylacetic acids via cleavage of the C=C bond.*

Diketene is a unique and important key intermediate formed by dimerization of ketene,[1] and is often used as an acetoacetylation reagent for versatile nucleophiles, such as alcohols, amines, thiols, and carbanions, in organic synthesis (Scheme 1, path a).[2] In the presence of transition-metal catalysts, diketene smoothly reacts with organometallic compounds, such as Grignard reagents and organozinc reagents, to cleave the vinyl–oxygen bond to construct 3-substituted 3-butenoic acids (Scheme 1, path b).[3] The 3-butenoic acid skeleton serves as a synthon for the preparation of physiologically active molecules and fine chemicals.[4]

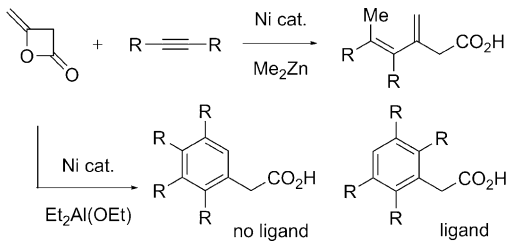


Scheme 1. Reactivity of diketene with nucleophiles.

Phenylacetic acid (α-toluic acid) acts as an active auxin and is a critical constituent of many physiologically active molecules, such as tetraline-based natural products, analgesics, and nonsteroidal anti-inflammatory drugs (NSAIDs).[5] Although efficient preparations of phenylacetic acid and its analogues are widely demanded for use in medicinal chemistry, most involve limitations such as handling and harsh reaction conditions.[6] Therefore, straightforward and selective formations of unsaturated carboxylic acids and phenylacetic acids from the commercially available diketene, promoted by transition-metal catalysts with organometallic reagents, will be beneficial.

Nickel-catalyzed coupling reactions are an attractive synthetic method for the construction of useful and complex molecules in modern organic chemistry.[7] We have previously demonstrated the nickel(0)-catalyzed multicomponent coupling reaction of an alkyne, dimethylzinc, and unsaturated hydrocarbons (such as conjugated dienes and vinylcyclopropanes) to accomplish C–C bond formations with high regio- and stereoselectivities.[8] All of these coupling reactions proceeded via nickelacyle intermediates by oxidative cyclization of unsaturated hydrocarbons and a nickel(0) catalyst.

Herein, we disclose the nickel-catalyzed multicomponent coupling reaction of an alkyne, dimethylzinc, and diketene (as a butenoic acid equivalent) to provide 3-methylene-4-hexenoic acids in a single manipulation (Scheme 2). Under similar catalytic conditions, $Et_2Al(OEt)$ accelerates a formal [2+2+2] cycloaddition reaction with diketene and two equivalents of an alkyne to produce phenylacetic acid derivatives. Furthermore, in the presence of a ligand, symmetrically substituted phenylacetic acids are produced with accompanying cleavage of the C=C bond of diketene. Although nickel-catalyzed cycloaddition reactions with alkynes have been developed,[9] efficient syntheses of phenylacetic acids by a cycloaddition reaction between an alkyne and diketene have not been reported to date.



Scheme 2. Nickel-catalyzed multicoupling reaction of diketene with organometals.

The three-component coupling reaction with alkyne, diketene, and dimethylzinc was conducted in the presence of a $[Ni(acac)_2]$ catalyst (1 mol%) in THF under a nitrogen atmosphere. Table 1 summarizes the results obtained from using a wide variety of alkynes, including symmetrical and

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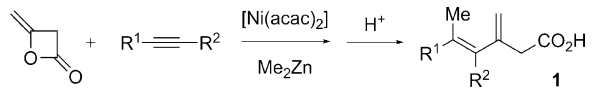
Table 1: Three-component coupling reaction of a diketene, alkyne, and dimethylzinc.[a]

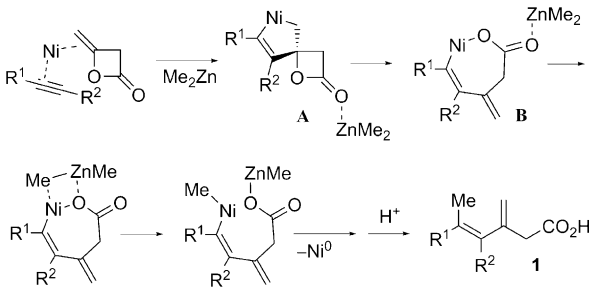


Entry	Alkyne		t [h]	Yield [%][b] [ratio]
	R^1	R^2		
1	Me	Me	1	**1a**: 91
2	Et	Et	3	**1b**: 95
3	*n*Pr	*n*Pr	3	**1c**: 90
4	TMS	TMS	6	**1d**: 81
5	Ph	Ph	24	**1e**: 29
6	TMS	Me	3	**1f**: 91 [single]
7	TMS	Ph	24	**1g**: 87 [3:1][c]
8	Ph	Et	24	**1h**: 50 [10:1][c]

[a] The reaction was undertaken in the presence of $[Ni(acac)_2]$ (0.01 mmol), alkyne (1.0 mmol), diketene (1.5 mmol), and Me_2Zn (1.2 mmol) in THF at 50 °C under nitrogen atmosphere. Yields were calculated based on alkyne. [b] Yield of isolated product. [c] The ratio shows the regioisomeric ratio with respect to olefin geometry. Major isomer is depicted as the structure of compound **1**. The substituents of R^1 and R^2 on major isomer are opposite each other on minor isomer. acac = acetylacetonate, THF = tetrahydrofuran, TMS = trimethylsilyl.

unsymmetrical substituted alkynes. Symmetrical substituted alkynes, such as 2-butyne, 3-hexyne, and 4-octyne reacted with diketene and dimethylzinc smoothly to give the three-component coupling products **1** in excellent yields as a single isomer (entries 1–3). Bis(trimethylsilyl)acetylene also participated in a similar coupling reaction to afford **1d** in reasonable yield (entry 4). Diphenylacetylene provided the expected coupling product **1e** in modest yield (entry 5), but an electron-deficient alkyne such as dimethyl acetylenedicarboxylate did not take part in the reaction. The regioselectivity of the unsymmetrical alkynes depended on the type of substituents. 1-Trimethylsilyl-1-propyne coupled with dimethylzinc at the trimethylsilyl-substituted carbon atom and diketene at the methyl-substituted carbon atom to provide **1f**, through *syn* addition, as a single stereoisomer (entry 6). 1-Trimethylsilyl-2-phenylethyne and 1-phenyl-1-butyne provided the expected unsaturated carboxylic acids as a mixture of regioisomers of **1g** and **1h**, respectively (entries 7 and 8).

A plausible mechanism for the coupling reaction of an alkyne, diketene, and dimethylzinc is illustrated in Scheme 3.

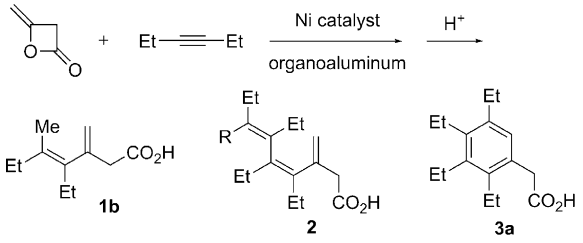


Scheme 3. A plausible reaction mechanism for nickel-catalyzed multi-coupling reaction of diketene and alkyne with Me_2Zn.

Nickel-catalyzed oxidative cyclization of alkyne and diketene in the presence of dimethylzinc proceeds to form the nickel-acyclopentene intermediate **A**, with subsequent C–O bond cleavage to provide the seven-membered oxanickelacycle **B**. The methyl group transfer from dimethylzinc to nickel provides unsaturated carboxylic acids (**1**) by reductive elimination and regeneration of the active nickel(0) catalyst.

The features of the coupling reaction of diketene and alkyne, promoted by a nickel catalyst, changed dramatically when organoaluminum reagents were used in place of dimethylzinc (Table 2). For example, in the presence of

Table 2: Three-component coupling reaction of a diketene, alkyne, and organoaluminum.[a]



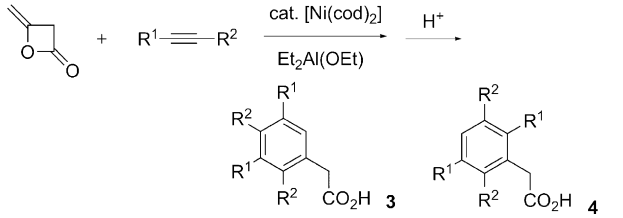
Entry	Organoaluminum	Solvent	Yield [%][b]
1	Me_3Al	THF	**1b**: 50
2	Et_3Al	THF	complex mixture
3	Et_2AlCl	THF	complex mixture
4	$Et_2Al(OEt)$	THF	complex mixture
5	Me_3Al	toluene	**2a**: 24 (R = Me), **3a**: 34
6	Et_3Al	toluene	**2b**: 34 (R = Et), **3a**: 10
7	Et_2AlCl	toluene	complex mixture
8	$Et_2Al(OEt)$	toluene	**3a**: 98

[a] The reaction was undertaken in the presence of $[Ni(cod)_2]$ (0.1 mmol), alkyne (1.0 mmol), diketene (3.0 mmol), and organoaluminum (1.2 mmol) at RT under nitrogen atmosphere for 72 h. [b] Yield of isolated product. cod = 1,5-cyclooctadiene.

$[Ni(cod)_2]$ in THF solvent, Me_3Al, diketene, and 3-hexyne combined in a 1:1:1 ratio to form the three-component coupling product **1b** (Table 2; entry 1), as well as the products shown in Table 1. Under similar reaction conditions, complex mixtures were produced using Et_3Al, Et_2AlCl, and $Et_2Al(OEt)$ (Table 2, entries 2–4). Among these investigations using various kinds of solvents, toluene was most effective for the coupling reaction and provided unsaturated carboxylic acids and phenylacetic acid by the insertion of two equivalents of an alkyne. In the presence of a nickel catalyst and Me_3Al, diketene underwent a [2+2+2] cycloaddition with two equivalents of 3-hexyne to afford the phenylacetic acid **3a** in 34% yield, along with the linear coupling product,the trienyl carboxylic acid **2a**, in 24% yield as a byproduct (entry 5). Use of Et_3Al also produced a similar result to give a mixture of **2b** and **3a** in modest yields (entry 6). Although Et_2AlCl resulted in the formation of a complex mixture, $Et_2Al(OEt)$ effectively promoted the [2+2+2] cycloaddition reaction to provide **3a** in 98% as a single product (entries 7 and 8).

As shown in Table 3, the cycloaddition reaction of diketene with alkynes in the presence of a nickel catalyst and $Et_2Al(OEt)$ was applied to a wide variety of alkynes.

Table 3: Three-component coupling reaction of a diketene, alkyne, and organoaluminum.[a]

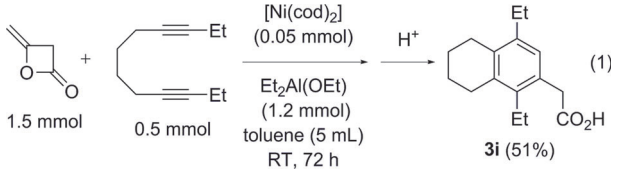


Entry	R^1	R^2	Ligand	Yield [%][b]
1	Et	Et	none	**3a**: 98
2	Me	Me	none	**3b**: 80
3	*n*Pr	*n*Pr	none	**3c**: 76
4	*n*Bu	*n*Bu	none	**3d**: 65
5	Ph	Ph	none	**3e**: 24
6	TMS	Me	none	**3f**: 77[c]
7	*t*Bu	H	none	**3g**: 65
8	TMS	H	none	**3h**: 40
9	Et	Et	PPh_3	**4a**: 73
10	Et	Et	$P(c\text{-Hex})_3$	**4a**: 20
11	Et	Et	$P(n\text{Bu})_3$	complex mixture
12	Et	Et	Xantphos	**4a**: 22
13	Me	Me	PPh_3	**4b**: 60
14	*n*Pr	*n*Pr	PPh_3	**4c**: 80
15	*n*Bu	*n*Bu	PPh_3	**4d**: 71
16	Ph	Ph	PPh_3	**4e**: 50
17	TMS	Me	PPh_3	**4f**: 45
18	*t*Bu	H	PPh_3	**4g**: 34
19	TMS	H	PPh_3	**4h**: 60

[a] The reaction was undertaken in the presence of $[Ni(cod)_2]$ (0.1 mmol), ligand (0.2 mmol), alkyne (1.0 mmol), diketene (3.0 mmol), and $Et_2Al(OEt)$ (1.2 mmol) in toluene (5 mL) at RT under nitrogen atmosphere for 72 h. [b] Yield of isolated product. [c] In entry 6, **3f** was obtained as a desilylation product **3f′** ($R^1 = H$) in 77%. Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene.

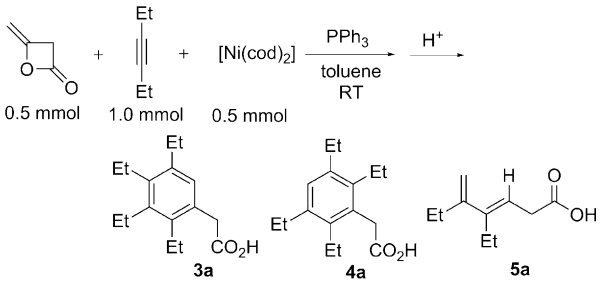
Surprisingly, use of phosphine ligands under similar catalytic conditions changed the outcome to provide the regioisomeric phenylacetic acid **4** exclusively. Among the results of utilizing monodentate and bidentate phosphine ligands, PPh_3 was the most efficient ligand for furnishing the phenylacetic acids **4** as the sole products (entries 9–12). Symmetrical dialkyl-substituted alkynes underwent the cycloaddition reaction with diketene to provide unsymmetrical phenylacetic acids (**3**) by means of the nickel catalyst and $Et_2Al(OEt)$ system in the absence of PPh_3 (entries 1–4), whereas the formal [2+2+1+1] cycloaddition reaction product, the symmetrically substituted phenylacetic acids **4**, were selectively produced in the presence of the PPh_3 ligand (entries 9, and 13–15). The structures of both the unsymmetrical and symmetrical phenylacetic acids **3a** and **4a**, respectively, were determined unequivocally by X-ray crystallographic analysis.[10] Although cycloaddition reactions involving unsymmetrical disubstituted alkynes often exhibit complicated regioselectivities,[11] the desired coupling products **3f** and **4f** were produced single isomers when using 1-trimethylsilyl-1-propyne, regardless of the presence or absence of phosphine ligand (entries 6 and 17). Terminal alkynes possessing *t*Bu and TMS groups participated in the coupling reaction and the distinct regioselective formation of phenylacetic acids **3** and **4** were accomplished (entries 7 and 8, 18 and 19).

The cycloaddition reaction was applied to the construction of a benzobicyclic ring through a coupling reaction of a diyne moiety with diketene. 3,9-Dodecadiyne underwent the cycloaddition reaction with diketene and provided tetrahydronaphthylacetic acid **3i** under the nickel catalyst and $Et_2Al(OEt)$ system [Eq. (1)]. Unfortunately, in the



presence of PPh_3, an intractable mixture was obtained from 3,9-dodecadiyne under similar reaction conditions.

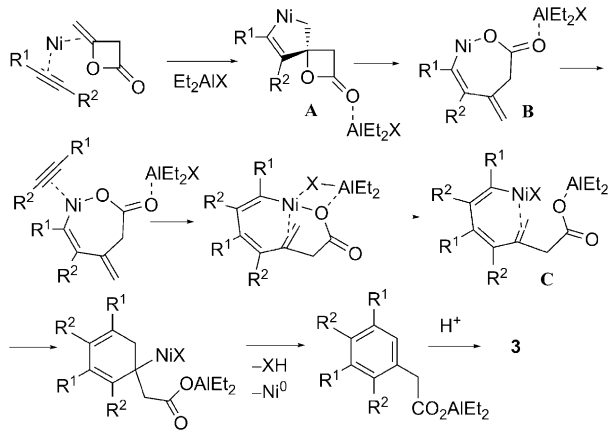
The reactions of a stoichiometric amount of $[Ni(cod)_2]$, alkyne, and diketene without $Et_2Al(OEt)$ were conducted (Scheme 4). In the absence of a phosphine ligand, the mixture



PPh_3 (mmol)	*T* [h]	Product
0	72	complex mixture
1	72	**4a** (54%)
1	1	**5a** (80%)

Scheme 4. C–C bond-cleavage reaction of diketene promoted by stoichiometric amount of $[Ni(cod)_2]$ in the presence or in the absence of phosphine ligand.

of $[Ni(cod)_2]$ (0.5 mmol), 3-hexyne (1 mmol), and diketene (0.5 mmol) did not provide the expected phenylacetic acid **3a**. Instead an intractable mixture was obtained. In contrast, in the presence of two equivalents of PPh_3, based on the nickel(0) complex, the reaction mixture of $[Ni(cod)_2]$ (0.5 mmol), PPh_3 (1.0 mmol), 3-hexyne (1.0 mmol), and diketene (0.5 mmol) was stirred for 72 h followed by protonolysis with aqueous HCl and provided the symmetrical phenylacetic acid **4a** in 54%.[12] Protonolysis of the reaction mixture at one hour afforded (3*E*)-4-ethyl-5-methylene-3-heptenoic acid (**5a**) as the sole product in 80% yield with high *E* stereoselectivity and resulted from the C=C bond-cleavage reaction of diketene.[13] These results suggest that scission of the C=C bond is triggered by synergistic effects of both nickel(0) and PPh_3, and $Et_2Al(OEt)$ seems to serve as a promoter to regenerate the active nickel(0) species for the catalytic reaction system through an important key intermediate.[14]



Scheme 5. A plausible reaction mechanism for the formation of phenylacetic acids in the absence of PPh_3.

Although it is premature to provide a complete explanation of the reactivities described here, a plausible mechanism for the cycloaddition reactions of diketene and alkyne promoted by a nickel catalyst and Et_2AlX are proposed in Scheme 5. In the absence of a phosphine ligand, oxidative cyclization of alkyne and diketene with the nickel(0) catalyst provides the nickelacycle **A**, which then undergoes the ring expansion reaction to form the oxanickelacycle **B**. Insertion of an additional alkyne, promoted by Et_2AlX, affords the vinylnickel intermediate **C** by transmetalation with Et_2AlX. Intramolecular carbonickelation through *6-endo-trig* cyclization of **C** (X = OEt), and subsequent β-hydride elimination occurs to afford **3** with liberation of a nickel(0) species.[15] A more straightforward mechanism involving [2+2+2] cycloaddition reaction with two equivalents of alkyne and diketene followed by E2 elimination of spirofused cyclohexadiene cannot be ruled out. However, the formation of **2**, depending on the organoaluminum and solvent, would suggest the intramolecular carbonickelation through **C** as a crucial key intermediate as shown in Scheme 5. For Me_3Al and Et_3Al, reductive elimination might proceed through **C** (X = Me or Et) rather than carbonickelation to afford the linear unsaturated carboxylic acids **2a** and **2b** as major products.[16]

In the presence of PPh_3, the unusual observation of the product **4**, while confirmed by X-ray analysis, cannot be justified through well-established mechanistic pathways. A complete scission of the diketene skeleton is apparently seen, with a single methine CH derived from diketene inserting between the two alkyne units. A mechanism involving complex rearrangements of nickela-2-cyclopentene to nickela-3-cyclopentene involving nickel carbene formation is mostly likely to rationalize the C–C bond cleavage reaction of diketene skeleton,[17] but the precise details of this unusual transformation await further study.[18]

In conclusion, the multicomponent coupling reaction of diketene, and alkyne, and Me_2Zn has been demonstrated to give 3-methylene-4-hexenoic acids in excellent yields. Under similar reaction conditions, the combination of a nickel catalyst and $Et_2Al(OEt)$ accelerates the dimerization of the alkyne followed by a [2+2+2] cycloaddition reaction to furnish phenylacetic acid derivatives. In the presence of PPh_3, a formal [2+2+1+1] cycloaddition reaction proceeds to afford the alternative regioisomeric phenylacetic acid derivatives from an accompanying the C=C bond-cleavage reaction of diketene. Synthetic applications involving the cleavage reaction of various C=C bonds are currently under investigation.

Experimental Section

General procedure for the formation of unsaturated carboxylic acids (entry 2, Table 1): Diketene (126.1 mg, 1.5 mmol), 3-hexyne (82.1 mg, 1 mmol), and dimethylzinc (1.2 mmol, 1.0 M hexane solution) were added via syringe under a nitrogen atmosphere to a solution of $[Ni(acac)_2]$ (2.6 mg, 0.01 mmol) in dry THF (5 mL). The mixture was stirred at 50 °C for 3 h. The mixture was diluted with 30 mL of EtOAc, and washed with 2 N HCl and then brine. The extract was dried ($MgSO_4$) and concentrated in vacuo and the residual oil was subjected to column chromatography over silica gel (*n*-hexane/EtOAc = 4:1 v/v) to give **1b** (173.2 mg, 95 %, $R_f = 0.33$; *n*-hexane/EtOAc = 8:1 v/v).)

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[1] a) A. Wahhab, J. Leba, *Tetrahedron Lett.* **2000**, *41*, 1487–1490; b) D. A. Ketcha, L. J. Wilson, D. E. Portlock, *Tetrahedron Lett.* **2000**, *41*, 6253–6257; c) C. Spanka, B. Clapham, K. D. Janda, *J. Org. Chem.* **2002**, *67*, 3045–3050.

[2] a) S. O. Lawesson, S. Gronwall, R. Sandberg, *Org. Synth.* **1962**, *42*, 28–29; b) A. Nudelman, R. Kelner, N. Broida, H. E. S. Gottlieb, *Synthesis* **1989**, 387–388.

[3] a) K. Itoh, M. Fukui, Y. Kurachi, *J. Chem. Soc. Chem. Commun.* **1977**, 500–501; b) K. Itoh, T. Yogo, Y. Ishii, *Chem. Lett.* **1977**, 103–106; c) K. Itoh, T. Harada, H. Nagashima, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3746–3748; d) P. S. Arora, Q. N. Van, M. Famulok, A. J. Shaka, J. S. Nowick, *Bioorg. Med. Chem.* **1998**, *6*, 1421–1428.

[4] a) Y. Tezuka, T. Ogura, S. Kawaguchi, *Bull. Chem. Soc. Jpn.* **1969**, *42*, 443–446; b) T. Yamamoto, J. Ishizu, A. Yamamoto, *Bull. Chem. Soc. Jpn.* **1982**, *55*, 623–624; c) T. Fujisawa, T. Sato, Y. Gotoh, M. Kawashima, T. Kawara, *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3555–3559; d) Y. Abe, M. Sato, H. Goto, R. Sugawara, E. Takahashi, T. Kato, *Chem. Pharm. Bull.* **1983**, *31*, 4346–4354; e) A. Duchêne, M. Abarbri, J.-L. Parrain, M. Kitamura, R. Noyori, *Synlett* **1994**, 524–526; f) M. Abarbri, J.-L. Parrain, M. Kitamura, R. Noyori, A. Duchêne, *J. Org. Chem.* **2000**, *65*, 7475–7478.

[5] a) K. M. Engle, D.-H. Wang, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 14137–14151; b) D.-H. Wang, K. M. Engle, B.-F. Shi, J.-Q. Yu, *Science* **2010**, *327*, 315–319.

[6] a) T. León, A. Correa, R. Martin, *J. Am. Chem. Soc.* **2013**, *135*, 1221–1224; b) X.-F. Cheng, Y. Li, Y.-M. Su, F. Yin, J.-Y. Wang, J. Sheng, H. U. Vora, X.-S. Wang, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 1236–1239.

[7] a) J. Montgomery, *Acc. Chem. Res.* **2000**, *33*, 467–473; b) S.-I. Ikeda, *Acc. Chem. Res.* **2000**, *33*, 511–519; c) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901–2916; d) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127–2198; e) J. Montgomery, *Angew. Chem.* **2004**, *116*, 3980–3998; *Angew. Chem. Int. Ed.* **2004**, *43*, 3890–3908; f) Y. Tamaru, *Modern Organonickel Chemistry*, Wiley-VCH, Weinheim, **2005**; g) R. M. Moslin, K. M.

Moslin, T. F. Jamison, *Chem. Commun.* **2007**, 4441 – 4449; h) F.-S. Han, *Chem. Soc. Rev.* **2013**, *42*, 5270 – 5298.

[8] a) M. Kimura, A. Ezoe, M. Mori, Y. Tamaru, *J. Am. Chem. Soc.* **2005**, *127*, 201 – 209; b) K. Kojima, M. Kimura, Y. Tamaru, *Chem. Commun.* **2005**, 4717 – 4719; c) M. Kimura, K. Kojima, Y. Tatsuyama, Y. Tamaru, *J. Am. Chem. Soc.* **2006**, *128*, 6332 – 6333; d) M. Kimura, M. Mori, R. Mukai, K. Kojima, Y. Tamaru, *Chem. Commun.* **2006**, 2813 – 2815; e) K. Kojima, M. Kimura, S. Ueda, Y. Tamaru, *Tetrahedron* **2006**, *62*, 7512 – 7520; f) M. Kimura, Y. Tatsuyama, K. Kojima, Y. Tamaru, *Org. Lett.* **2007**, *9*, 1871 – 1873; g) M. Kimura, M. Togawa, Y. Tatsuyama, K. Matsufuji, *Tetrahedron Lett.* **2009**, *50*, 3982 – 3984; h) T. Mori, T. Nakamura, M. Kimura, *Org. Lett.* **2011**, *13*, 2266 – 2269.

[9] For nickel-catalyzed [2+2] cycloaddition reaction of alkyne with alkenes, see: a) P. Binger, A. Brinkman, P. Wedemann, *Chem. Ber.* **1983**, *116*, 2920 – 2930; b) D.-J. Huang, D. K. Rayabarapu, L. P. Li, T. Sambaiash, C.-H. Cheng, *Chem. Eur. J.* **2000**, *6*, 3706 – 3713; c) A. Nishimura, M. Ohashi, S. Ogoshi, *J. Am. Chem. Soc.* **2012**, *134*, 15692 – 15695; d) A. Nishimura, M. Ohashi, S. Ogoshi, *Chem. Lett.* **2013**, *42*, 904 – 905.

[10] CCDC 832667 (**3a**) and 828924 (**4a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[11] a) P. Chini, A. Santambrogio, N. Palladino, *J. Chem. Soc. C* **1967**, 830 – 835; b) M. V. Russo, A. Furlani, *Tetrahedron Lett.* **1976**, *17*, 2655 – 2656; c) P. Mauret, P. Alphonse, *J. Organomet. Chem.* **1984**, *276*, 249 – 256; d) C. Ester, A. Maderna, H. Prizkow, W. Siebelt, *Eur. J. Inorg. Chem.* **2000**, 1177 – 1184; e) C. Müller, R. J. Lachicotte, W. D. Jones, *Organometallics* **2002**, *21*, 1975 – 1981.

[12] As for the stoichiometric reaction of a mixture of $[Ni(cod)_2]$ (0.5 mmol), PPh_3 (1 mmol), 3-hexyne (0.5 mmol), and diketene (0.5 mmol) in Scheme 4, addition of PhMgBr to the reaction mixture provided (3*Z*)-4-ethyl-5-methylene-3-phenyl-3-heptenoic acid in 26% along with (3*Z*)-4-ethyl-5-methylene-3-[(3*Z*)-4-phenyl-3-hexenyl]-3-heptenoic acid in 39%. See the Supporting Information for details.

[13] Reaction of **5a** with 3-hexyne under the reaction conditions failed to produce significant quantities of **4a**. See the Supporting Information for details.

[14] $Et_2Al(OEt)$ promotes transmetalation with palladium carboxylate to generate catalytically active Pd^0 species. See: J. Takaya, K. Sasano, N. Iwasawa, *Org. Lett.* **2011**, *13*, 1698 – 1701.

[15] Intramolecular carbonickelations of alkenylnickel species on sp^2 framework by 6-*endo-trig* cyclization have been reported: a) S. Ikeda, H. Miyashita, M. Taniguchi, H. Kondo, M. Okano, Y. Sato, K. Odashima, *J. Am. Chem. Soc.* **2002**, *124*, 12060 – 12061; b) S. Ikeda, R. Sanuki, H. Miyachi, H. Miyashita, M. Taniguchi, K. Odashima, *J. Am. Chem. Soc.* **2004**, *126*, 10331 – 10338.

[16] Y. Nakao, K. S. Kanyiva, T. Hiyama, *J. Am. Chem. Soc.* **2008**, *130*, 2448 – 2449.

[17] Palladacyclopentene rearrangements from 2-cyclopentene to 3-cyclopentene via a palladium carbene complex have been reported by B. M. Trost et al.: a) B. M. Trost, G. J. Tanoury, *J. Am. Chem. Soc.* **1988**, *110*, 1636 – 1638; b) B. M. Trost, M. Yanai, K. Hoogsteen, *J. Am. Chem. Soc.* **1993**, *115*, 5294 – 5295; c) B. M. Trost, A. S. K. Hashmi, *J. Am. Chem. Soc.* **1994**, *116*, 2183 – 2184. A possible reaction mechanism involving nickelacyclopentene rearrangement to form **4a** was proposed in Scheme S1 of the Supporting Information.

[18] For nickel-catalyzed β-carbon elimination, see: a) Y. Ni, J. Montgomery, *J. Am. Chem. Soc.* **2006**, *128*, 2609 – 2614; b) S. Ikeda, H. Obara, E. Tsuchida, N. Shirai, K. Odashima, *Organometallics* **2008**, *27*, 1645 – 1648; c) P. Kumar, J. Louie, *Org. Lett.* **2012**, *14*, 2026 – 2029; d) Y. Li, Z. Lin, *Organometallics* **2013**, *32*, 3003 – 3011.

