Palladium(0)-Catalyzed Coupling Reaction of Lithium (α-Carbalkoxyvinyl)cuprates with Organic Halides

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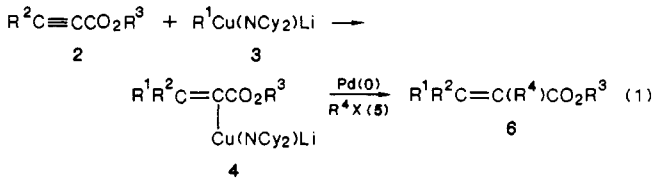
The palladium(0)-catalyzed coupling reaction of lithium (α-carbalkoxyvinyl)(dicyclohexylamido)cuprates and organic halides such as aryl, vinyl, and benzyl halides was investigated. The lithium (α-carbalkoxyvinyl)(dicyclohexylamido)cuprates were generated by conjugate addition of organo(dicyclohexylamido)cuprates to α,β-acetylenic esters. The coupling reaction using a $Pd(PPh_3)_4$ catalyst proceeded at room temperature to give synthetically useful α,β-substituted acrylates in good yields. The coupling reaction of the (α-carbalkoxyvinyl)(dicyclohexylamido)cuprate derived from a β-unsubstituted α,β-acetylenic ester took place stereoselectively to give an (*E*)-α,β-substituted acrylate derivative. In the vinyl halide reaction, the stereochemistry of the vinyl halide component is retained in the coupling product. The use of the dicyclohexylamido group as a nontransferable ligand is important. Thus, in the reaction using an (α-carbalkoxyvinyl)(1-hexynyl)cuprate complex, a nonselective coupling involving the 1-hexynyl group took place.

Because α-substituted acrylate units and related groups are found as structural features of a variety of natural products, various methods have been developed for the synthesis of acrylate derivatives.[1,2] The synthetic method using (α-carbalkoxyvinyl)metals is direct and attractive.[2] Lithium (α-carbalkoxyvinyl)cuprates ($R^1R^2C{=}C(CO_2R^3)CuYLi$, **1**),[2a-c,3] which are readily generated by conjugate addition of lithium organocuprates to α,β-acetylenic esters **2**, are well-known. Very recently we have reported (α-carbalkoxyvinyl)aluminums[4] generated by hydroalumination of α,β-acetylenic esters with diisobutylaluminum hydride–hexamethylphosphoric triamide. It is important to expand the scope of the reactions of these (α-carbalkoxyvinyl)metals and to develop a novel synthetic method of the acrylate derivatives. Here we have studied an unprecedented palladium(0)-catalyzed coupling reaction of (α-carbalkoxyvinyl)(dicyclohexylamido)cuprates **4** with aryl, vinyl, and benzyl halides **5** (eq 1).[5] Palladium(0)-



catalyzed carbon–carbon bond forming reactions using organometallic compounds containing metal atoms such as Li, Mg, Zn, B, Al, and Sn have been extensively utilized in organic synthesis.[6] On the other hand, few examples of those employing organocopper compounds have been known.[7] One feature of the organocoppers is their relatively high tolerability to functional groups.

Table I. Conjugate Addition Reaction of Organo(dicyclohexylamido)cuprates 3 to α,β-Acetylenic Esters 2[a]

$R^2C{\equiv}CCO_2R^3$ (2)	$R^1Cu(NCy_2)Li$ (3)	temp, °C (time, h)	$R^1R^2C{=}CHCO_2R^3$: %[b] (*Z*:*E*)[c]
MeC≡CCO₂Et (**2b**)	$PhCu(NCy_2)Li$	−50 (1)	62 (18:82)
		−50 (1)–room temp (1)	80 (31:69)
PhC≡CCO₂Me (**2c**)	$MeCu(NCy_2)Li$	−50 (1)	80 (24:76)
		−50 (1)–room temp (1)	76 (26:74)

[a] Compound **2**, 0.500 mmol; **2**:**3** = 1:1; solvent, Et_2O, 5 mL. [b] Yield was determined by GC. [c] *E*/*Z* ratio was determined by GC.

For the generation and the reaction of **1**, a nontransferable ligand Y plays an important role. A 1-hexynyl group has been reported to be a suitable nontransferable ligand in comparison with cyano and methyl ligands.[2c] Thus it has been known that lithium (α-carbethoxyvinyl)(1-hexynyl)cuprate (**1a**, $R^1 = R^2 = Me$, $R^3 = Et$, Y = C≡CBu) is thermally stable at 0 °C–room temperature and it transfers the α-carbethoxyvinyl group selectively to electrophiles such as aldehydes and ketones.[2c] The palladium(0)-catalyzed coupling reaction of **1a** and iodobenzene was first examined. When **1a** generated from lithium methyl(1-hexynyl)cuprate and ethyl 2-butynoate (**2b**) was reacted with iodobenzene in the presence of 5 mol % $Pd(PPh_3)_4$ at room temperature for 2 h, a nonselective coupling reaction involving the 1-hexynyl group took place to give ethyl 2-phenyl-3-methyl-2-butenoate (**6d**) and an undesirable product of 1-phenyl-1-hexyne in 44% and 38% yields, respectively.[8]

The recent report on a dicyclohexylamido group as a useful nontransferable ligand in the conjugate addition of organocuprates to α,β-enones[9] prompted us to examine its

(1) (a) Hoffmann, H. M. R.; Rabe, J. *J. Org. Chem.* **1985**, *50*, 3849 and references therein. (b) Baraldi, P. G.; Guarneri, M.; Pollini, G. P.; Simoni, D.; Barco, A.; Benetti, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2501 and references therein. (c) Perlmutter, P.; Teo, C. C. *Tetrahedron Lett.* **1984**, *25*, 5951.

(2) For Cu reagents, see: (a) Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851. (b) Klein, J.; Levene, R. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1971 and references therein. (c) Marino, J. P.; Linderman, R. J. *J. Org. Chem.* **1983**, *48*, 4621 and references therein. For Li reagents, see: (d) Feit, B. A.; Melamed, U.; Schmidt, R. R.; Speer, H. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1329. (e) Boykin, D. A.; Parham, W. E. *J. Org. Chem.* **1979**, *44*, 424.

(3) Copper(I) allenolate ($R^1R^2C{=}C{=}C(OR^3)OCuYLi$) may be another possible structure for the organocuprate generated by the conjugate addition of lithium organocuprate to α,β-acetylenic ester. To our knowledge, however, no decisive conclusion about its structure has been obtained. Thoughout the paper, the expression of lithium (α-carbalkoxyvinyl)-cuprate was adopted.

(4) Tsuda, T.; Yoshida, T.; Kawamoto, T.; Saegusa, T. *J. Org. Chem.* **1987**, *52*, 1624.

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(6) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: New York, 1982; Vol. 8, pp 910–926.

(7) (a) Jabri, N.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1982**, *23*, 1589. (b) Ruitenberg, K.; Kleijn, H.; Westmijze, H.; Meijer, J.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 405.

(8) Results of the coupling reactions using other catalytic systems were as follows. $PdCl_2(PPh_3)_2$–DIBAH (**6d** 39%, 1-phenyl-1-hexyne 29%, unreacted PhI 32%) and bis(cyclooctadiene)nickel–$2PPh_3$ (**6d** 7%, 1-phenyl-1-hexyne 8%, unreacted PhI 82%).

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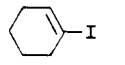
Table II. Palladium(0)-Catalyzed Reaction of (α-Carbalkoxyvinyl)cuprates ($R^1R^2C{=}C(CO_2R^3)Cu(NCy_2)Li$, 4) and Organic Halides (R^4X, 5)[a]

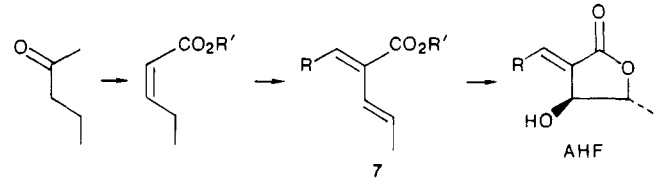
entry	$R^2C{\equiv}CCO_2R^3$ (2)	$R^1Cu(NCy_2)Li$ (3)	R^4X (5)	$R^1R^2C{=}C(R^4)CO_2R^3$ (6) % [b] [isolated yield][c] (Z:E)[d]
1	$HC{\equiv}CCO_2Me$ (**2a**)	$MeCu(NCy_2)Li$	PhI	$MeCH{=}C(Ph)CO_2Me$ (**6a**) 73 [63] (14:86)
2			(*E*)-BuCH=CHI	$MeCH{=}C(CH{=}CHBu)CO_2Me$ (**6b**) [57] (10:90)[e]
3			(*Z*)-BuCH=CHI	**6b** [47] (8:92)[f]
4		$BuCu(NCy_2)Li$	(*E*)-BuCH=CHI	$BuCH{=}C(CH{=}CHBu)CO_2Me$ (**6c**) [60] (8:92)[e]
5			(*Z*)-BuCH=CHI	**6c** [50] (7:93)[f]
6	$MeC{\equiv}CCO_2Et$ (**2b**)	$MeCu(NCy_2)Li$	PhI	$Me_2C{=}C(Ph)CO_2Et$ (**6d**) 91 [89]
7			PhBr	**6d** 60[h]
8			(*E*)-BuCH=CHI[g]	$Me_2C{=}C(CH{=}CHBu)CO_2Et$[e] (**6e**) 73 [62]
9			(*E*)-PhCH=CHBr	$Me_2C{=}C(CH{=}CHPh)CO_2Et$[e] (**6f**) 75 [59]
10				$Me_2C{=}C($$)CO_2Et$ (**6g**) 87 [70]
11			$PhCH_2Br$	$Me_2C{=}C(CH_2Ph)CO_2Et$ (**6h**) 65
12			$PhCH_2I$	**6h** 64 [53]
13		$BuCu(NCy_2)Li$	PhI	$BuC(Me){=}C(Ph)CO_2Et$ (**6i**) 66 [61] (40:60)
14		$PhCu(NCy_2)Li$	PhI	$PhC(Me){=}C(Ph)CO_2Et$ (**6j**) [77][i] (44:56)
15	$PhC{\equiv}CCO_2Me$ (**2c**)	$MeCu(NCy_2)Li$	PhI	$PhC(Me){=}C(Ph)CO_2Me$ (**6k**) [52] (38:62)

[a] Compound **2**, 1.00 mmol; **2**:**3**:5:$Pd(PPh_3)_4$ = 1:1:1:0.05; solvent, Et_2O (10 mL)–THF (3 mL); time, 1 h. Conjugate addition of **3** to **2** was done at −70 °C. [b] Yield was determined by GC. [c] The values in brackets are isolated yields obtained by PLC. [d] Z:E ratio was determined by ^1H NMR. [e] E stereochemistry of the 1-hexenyl group was demonstrated by ^1H NMR. [f] Z stereochemistry of the 1-hexenyl group was demonstrated by ^1H NMR. [g] R^4X:**2b** = 1.5. [h] Reaction time, 48 h. [i] Conjugate addition of **3** to **2** was done at −50 °C.

effectiveness for the generation and the reaction of lithium (α-carbalkoxyvinyl)cuprates. The dicyclohexylamido ligand was found to be effective for the generation of thermally stable lithium (α-carbalkoxyvinyl)cuprates. Thus the conjugate addition of organo(dicyclohexylamido)cuprates **3** to **2b** and **2c** at −50 °C–room temperature produces methyl and ethyl 3-phenyl-2-butenoates, respectively, in good yields with E:Z ratios[10] of 8:2–7:3 (Table I). The product from the conjugate addition of the dicyclohexylamido ligand to **2b** and **2c** was not detected by GC analysis.

The dicyclohexylamido ligand acts as an excellent nontransferable ligand in the palladium(0)-catalyzed coupling reaction of (α-carbalkoxyvinyl)cuprates with iodobenzene. The organo(dicyclohexylamido)cuprate **4** ($R^1 = R^2 = Me$, $R^3 = Et$), which was generated by the conjugate addition of methyl(dicyclohexylamido)cuprate (**3**, $R^1 = Me$) to **2b**, transfers selectively the α-carbethoxyvinyl group to iodobenzene to produce **6d** in 89% isolated yield (Table II, entry 6). No formation of *N*,*N*-dicyclohexylaniline was observed in GC analysis. Results of the reactions using other organo(dicyclohexylamido)cuprates and α,β-acetylenic esters are summarized in Table II. The (α-carbalkoxyvinyl)cuprates generated from butyl- and phenyl(dicyclohexylamido)cuprates (**3**, R^1 = Bu and Ph) and **2b** also react with iodobenzene in the presence of $Pd(PPh_3)_4$ catalyst to give α-phenyl-β-disubstituted acrylates in moderate to good yields (entries 13 and 14). Unsubstituted and phenyl-substituted α,β-acetylenic esters **2a** and **2c** react similarly (entries 1 and 15). The E/Z stereoselectivity of the coupling reaction of iodobenzene and the (α-carbalkoxyvinyl)cuprates generated from β-substituted α,β-acetylenic esters **2b** and **2c** is low, while the reaction of the (α-carbalkoxyvinyl)cuprate generated from the unsubstituted α,β-acetylenic ester **2a** proceeds stereoselectively to produce (*E*)-α-phenylcrotonate predominantly (entry 1).[11] Bromobenzene and benzyl halides can be used as an organic halide in place of iodobenzene.

Scheme I



7 AHF

Vinyl halides also couple with (α-carbalkoxyvinyl)cuprates to give α-alkenylacrylate derivatives, in which the stereochemistry of the vinyl halide components is retained and the stereochemical consequence of the α,β-acetylenic moieties is similar to that in the iodobenzene reaction. The reactions of (*E*)- and (*Z*)-1-iodohexenes with (α-carbomethoxyvinyl)cuprate (**4**, $R^1 = Me$, $R^2 = H$, $R^3 = Me$) from methyl(dicyclohexylamido)cuprate (**3**, $R^1 = Me$) and the unsubstituted acetylenic ester **2a** produce stereoselectively methyl (*E*)-(α-(*E*)-1-hexenyl)- and methyl (*E*)-(α-(*Z*)-1-hexenyl)crotonates, respectively (entries 2 and 3). (α-Carbomethoxyvinyl)cuprate (**4**, R^1 = Bu, $R^2 = H$, $R^3 = Me$) gave similar results (entries 4 and 5). Thus the reaction of vinyl halides and the (α-carbalkoxyvinyl)cuprates generated from the unsubstituted α,β-acetylenic ester provides

(9) Bertz, S. H.; Dabbagh, G.; Villacorta, G. M. *J. Am. Chem. Soc.* **1982**, *104*, 5824.

(10) Explanation of the E/Z stereochemistry of the conjugate addition product should await the structural information on the organocopper intermediate, i.e., a copper(I) allenolate or an (α-carbalkoxyvinyl)cuprate intermediate.[3]

(11) Discussion of the E/Z stereochemistry of the coupling product necessitates a further study on the structure of the organopalladium(II) intermediate leading to the coupling product, i.e., organopalladium(II) allenolate or organo(α-carbalkoxyvinyl)palladium(II).

a method of the stereoselective synthesis of α-alkenyl-β-alkylacrylates. A general synthesis of the naturally occurring 3-alkylidene-4-hydroxy-2(3*H*)-furanone (AHF) system has been recently developed,[12] which utilizes the stereochemically defined α-alkenyl-β-alkylacrylate **7** as a key intermediate (Scheme I). This procedure for **7**, however, needs multistep manipulation.

In summary, we have shown that the palladium(0)-catalyzed reaction of lithium (α-carbalkoxyvinyl)cuprates with organic halides offers a convenient preparative method of the α,β-substituted acrylate derivatives including the stereochemically defined α-alkenyl-β-alkylacrylates.

Experimental Section

IR spectra were determined on a Hitachi 260-50 grating spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Hitachi R-20B (60 MHz) instrument unless otherwise stated. ^{1}H NMR spectra (400 MHz) were recorded in $CDCl_3$ on a JEOL JNM-JX-400 instrument. All chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Coupling constants (*J*) are reported in hertz. Mass spectra were obtained on a JEOL DX-300 instrument. Elemental analyses were performed by the Microanalytical Center of Kyoto University. Gas chromatographic analyses (GC) were made on a Shimadzu 4CPT instrument. GC quantitative analyses of reaction products were made with internal standards with calibration based upon authentic samples employing a 20% silicone DC 550 on Celite 545 column.

Reactions were carried out under an atmosphere of nitrogen. Cuprous iodide was obtained from Wako Pure Chemical Industries, LTD, and used without further purification. Methyllithium in ether, *n*-butyllithium in hexane, and phenyllithium in cyclohexane–ether were obtained from Aldrich Chemical Co. Tetrakis(triphenylphosphine)palladium was prepared by the reported procedure.[13] Tetrahydrofuran (THF) and diethyl ether were distilled from lithium aluminum hydride under nitrogen. Methyl 2-propynoate (**2a**) and ethyl 2-butynoate (**2b**) were commercial reagents and were distilled under nitrogen after drying over anhydrous calcium sulfate (Drierite). Methyl 3-phenyl-2-propynoate (**2c**) was prepared by the reaction of commercially available 3-phenyl-2-propynoic acid and diazomethane.[14] Iodobenzene, bromobenzene, and benzyl bromide were commercial reagents and were distilled under nitrogen after drying over Drierite. (*E*)-β-Bromostyrene was obtained from the commercially available mixture of (*E*)- and (*Z*)-β-bromostyrenes according to the reported procedure.[15] (*E*)- and (*Z*)-1-Iodohexene,[16] 1-iodocyclohexene,[17] and benzyl iodide[18] were prepared by the reported procedures. Dicyclohexylamine was a commercial reagent and was distilled from potassium hydroxide under nitrogen.

General Procedure for the Palladium(0)-Catalyzed Coupling Reaction of Lithium (α-Carbalkoxyvinyl)cuprates and Organic Halides. We used two 50-mL flasks connected with a glass tube as a reaction apparatus. In one flask, dicyclohexylamine (0.219 mL, 1.10 mmol) was dissolved in 5 mL of ether and the solution was cooled to −30 °C. A 1.90 M ether solution of methyllithium (0.553 mL, 1.05 mmol) was added, and the mixture was stirred for 30 min at −30 °C to produce lithium dicyclohexylamide. In another flask, CuI (0.209 g, 1.10 mmol) was suspended in 5 mL of ether, to which the solution of lithium dicyclohexylamide was transferred by decantation through the connecting glass tube. The resulting white slurry was stirred for 1 h at −30 °C. A 1.90 M solution of methyllithium (0.526 mL, 1.00 mmol) was added, and the mixture was cooled to −70 °C after being stirred for 40 min. α,β-Acetylenic ester (1.00 mmol) was added, and the mixture was stirred for 40 min. Organic halide (1.00 mmol) and 3 mL of THF solution containing $Pd(PPh_3)_4$ (0.0578 g, 0.0500 mmol) were added. The mixture was allowed to react at room temperature for 2 h. Addition of a GC internal standard and subsequent GC analysis of the mixture gave a GC yield of a coupling product. The mixture was treated with 10 mL of 3 N HCl solution followed by addition of 100 mL of ether. The separated ether solution was washed twice with 10 mL of 3 N HCl solution and 10 mL of saturated $NaHCO_3$ solution. The ether solution was dried over anhydrous magnesium sulfate, filtered, and concentrated under vacuum. The residue was purified by preparative layer chromatography (PLC) on a silica gel plate (20 × 20 × 0.2 cm) with a mixture of EtOAc and hexane as eluent to give the coupling product.

The coupling products (**6a–k**) were identified as follows. The spectral data of (*E*)- and (*Z*)-**6a**, **6d**, **6h**, (*E*)- and (*Z*)-**6j**, (*E*)- and (*Z*)-**6k**, and (*E*)- and (*Z*)-ethyl β-methylcinnamates are compatible with those of the literature. (*E*)-**6a**[19] (PLC, EtOAc:hexane = 1:10 v/v): IR (neat, cm^{-1}) 1720, 1645, 1605, 1500; ^{1}H NMR 1.73 (d, *J* = 7.2, 3 H), 3.72 (s, 3 H), 7.2–7.8 (m, 6 H); MS, *m/e* (relative intensity) 176 (M^+, 100), 144 (87), 117 (93), 116 (60), 115 (64). (*Z*)-**6a**[19] (PLC, EtOAc:hexane = 1:10 v/v): IR (neat, cm^{-1}) 1725, 1635, 1600, 1495; ^{1}H NMR 2.05 (d, *J* = 7.2, 3 H), 3.81 (s, 3 H), 6.27 (q, *J* = 7.2, 1 H), 7.2–7.6 (m, 5 H). The mixture of (*E,E*)-**6b** and (*Z,E*)-**6b** was isolated by PLC (EtOAc:hexane = 1:10 v/v). Analysis of ^{1}H NMR spectra of the mixture gave the following ^{1}H NMR data of (*E,E*)-**6b** and (*Z,E*)-**6b**. They were not separable by PLC (EtOAc:hexane = 1:10 v/v), but were separated by GC (a 20% silicone DC 550 column). GC–mass spectroscopy of the mixture gave the following mass spectral data. (*E,E*)-**6b**: IR (neat, cm^{-1}) 1720, 1620, 965, 815; ^{1}H NMR (400 MHz) 0.91 (t, *J* = 7.3, 3 H), 1.23–1.47 (m, 4 H), 1.89 (d, *J* = 7.3, 3 H), 2.17 (q, *J* = 7.0, 2 H), 3.75 (s, 3 H), 6.01 (dt, *J* = 16.0, 6.6, 1 H), 6.11 (d, *J* = 16.0, 1 H), 6.72 (q, *J* = 7.3, 1 H); MS, *m/e* (relative intensity) 182 (M^+, 94), 139 (100), 126 (86), 79 (91); HRMS, *m/e* 182.1299, calcd for $C_{11}H_{18}O_2$ 182.1307. (*Z,E*)-**6b**: ^{1}H NMR (400 MHz) 0.89 (t, *J* = 7.3), 1.23–1.47 (m), 1.86 (d, *J* = 6.8), 2.08 (q, *J* = 6.7), 3.84 (s), 5.67 (dt, *J* = 15.8, 7.0), 5.90 (q, *J* = 7.3), 6.02 (d, *J* = 15.8); MS, *m/e* (relative intensity) 182 (M^+, 100), 139 (79), 126 (66), 79 (66). The mixture of (*E,Z*)-**6b** and (*Z,Z*)-**6b** was isolated by PLC (EtOAc:hexane = 1:7 v/v). Analysis of ^{1}H NMR spectra of the mixture gave the following ^{1}H NMR data of (*E,Z*)-**6b** and (*Z,Z*)-**6b**. They were not separable by PLC (EtOAc:hexane = 1:7 v/v), but were separated by GC (a 20% silicone DC 550 column). GC–mass spectroscopy of the mixture gave the following mass spectral data. (*E,Z*)-**6b**: IR (neat, cm^{-1}) 1720, 1630, 690; ^{1}H NMR (400 MHz) 0.86 (t, *J* = 7.1, 3 H), 1.23–1.38 (m, 4 H), 1.75 (d, *J* = 7.1, 3 H), 1.87 (q, *J* = 7.3, 2 H), 3.74 (s, 3 H), 5.68 (dt, *J* = 11.3, 7.3, 1 H), 5.92 (d, *J* = 11.3, 1 H), 6.92 (q, *J* = 7.2, 1 H); MS, *m/e* (relative intensity) 182 (M^+, 54), 139 (100), 126 (86), 79 (83); HRMS, *m/e* 182.1310, calcd for $C_{11}H_{18}O_2$ 182.1307. (*Z,Z*)-**6b**: ^{1}H NMR (400 MHz) 0.89 (t, *J* = 7.0), 1.23–1.38 (m), 2.00 (d, *J* = 7.4), 2.07 (q, *J* = 7.2), 3.76 (s), 5.49 (dt, *J* = 11.4, 7.5), 5.99 (d, *J* = 11.5), 6.03 (q, *J* = 7.2). The mixture of (*E,E*)-**6c** and (*Z,E*)-**6c** was isolated by PLC (EtOAc:hexane = 1:6 v/v). In the ^{1}H NMR (400 MHz) spectra of the mixture, the following absorptions of (*E,E*)-**6c** appeared in addition to the minor absorptions assignable to (*Z,E*)-**6c**. They were not separable by PLC (EtOAc:hexane = 1:6 v/v), but were separated by GC (a 20% silicone DC 550 column). GC–mass spectroscopy of the mixture gave the following mass spectral data. (*E,E*)-**6c**: IR (neat, cm^{-1}) 1725, 1630, 970; ^{1}H NMR (400 MHz) 0.91 (t, *J* = 7.2, 6 H), 1.3–1.5 (m, 8 H), 2.16 (q, *J* = 6.8, 2 H), 2.29 (q, *J* = 7.4, 2 H), 3.75 (s, 3 H), 6.00 (dt, *J* = 15.9, 6.7, 1 H), 6.11 (d, *J* = 16, 1 H), 6.61 (t, *J* = 7.6, 1 H); MS, *m/e* (relative intensity) 224 (M^+, 100), 195 (26), 181 (60), 125 (88); HRMS, *m/e* 224.1753, calcd for $C_{14}H_{24}O_2$ 224.1777. (*Z,E*)-**6c**: ^{1}H NMR (400 MHz) 2.08 (q, *J* = 6.8), 2.22 (q, *J* = 7.4), 3.80 (s), 5.56 (d, *J* = 15.8), 5.67 (dt, *J* = 16.4, 7.6), 5.79 (t, *J* = 7.6); MS, *m/e* (relative intensity) 224 (M^+, 100), 195 (19), 181 (44), 125 (50). The mixture of (*E,Z*)-**6c** and (*Z,Z*)-**6c** was isolated by PLC (EtOAc:hexane = 1:6 v/v). In the ^{1}H NMR (400 MHz) spectra of the mixture, the following absorptions of (*E,Z*)-**6c** appeared in addition to the minor absorptions assignable to (*Z,Z*)-**6c**. They

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were not separable by PLC (EtOAc:hexane = 1:6 v/v), but were separated by GC (a 20% silicone DC 550 column). GC–mass spectroscopy of the mixture gave the following mass spectral data. (*E,Z*)-**6c**: IR (neat, cm^{-1}) 1720, 1660, 735; ^1H NMR (400 MHz) 0.86 (t, J = 7.2, 3 H), 0.89 (t, J = 7.2, 3 H), 1.2–1.5 (m, 8 H), 1.88 (q, J = 7.3, 2 H), 2.11 (q, J = 7.4, 2 H), 3.74 (s, 3 H), 5.67 (dt, J = 11.4, 7.2, 1 H), 5.92 (d, J = 11.4, 1 H), 6.81 (t, J = 7.2, 1 H); MS, m/e (relative intensity) 224 (M^+, 66), 195 (22), 181 (59), 125 (100); HRMS, m/e 224.1781, calcd for $C_{14}H_{24}O_2$ 224.1777. (*Z,Z*)-**6c**: ^1H NMR (400 MHz) 2.08 (q, J = 7.5), 3.75 (s), 5.50 (dt, J = 11.5, 7.4), 5.99 (d, J = 11.5); MS, m/e (relative intensity) 224 (M^+, 100), 195 (25), 181 (51), 125 (67). **6d**[20] (PLC, EtOAc:hexane = 1:20 v/v): IR (neat, cm^{-1}) 1710, 1630, 1595, 1490; ^1H NMR 1.21 (t, J = 7.1, 3 H), 1.69 (s, 3 H), 2.11 (s, 3 H), 4.17 (q, J = 7.1, 2 H), 7.26 (s, 5 H); MS, m/e (relative intensity) 204 (M^+, 100), 158 (84), 131 (81), 130 (43), 129 (43). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.55; H, 7.62. **6e** (PLC, EtOAc:hexane = 1:10 v/v): IR (neat, cm^{-1}) 1730, 1650, 960; ^1H NMR 0.7–1.1 (m, 3 H), 1.1–1.6 (m, 4 H), 1.33 (t, J = 7.2, 3 H), 1.81 (s, 6 H), 2.0–2.3 (m, 2 H), 4.33 (q, J = 7.2, 2 H), 5.52 (dt, J = 16.2, 6.6, 1 H), 6.26 (d, J = 16.2, 1 H); MS, m/e (relative intensity) 210 (M^+, 94), 95 (100), 93 (74), 81 (77). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.20; H, 10.71. **6f** (PLC, EtOAc:hexane = 1:5 v/v): mp 71–73 °C (hexane); IR (KBr, cm^{-1}) 1720, 1630, 1600, 1490, 945, 765; ^1H NMR 1.37 (t, J = 7.2, 3 H), 1.90 (s, 3 H), 1.95 (s, 3 H), 4.35 (q, J = 7.2, 2 H), 6.41 (d, J = 16.2, 1 H), 7.02 (d, J = 16.2, 1 H), 7.1–7.5 (m, 5 H); MS, m/e (relative intensity) 230 (M^+, 100), 183 (47), 157 (86), 143 (49). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.31; H, 7.93. **6g** (PLC, EtOAc:hexane = 1:10 v/v): IR (neat, cm^{-1}) 1710, 1620; ^1H NMR 1.27 (t, J = 7.2, 3 H), 1.3–1.9 (m, 4 H), 1.79 (s, 3 H), 1.97 (s, 3 H) 1.9–2.2 (m, 4 H), 4.18 (q, J = 7.2, 2 H), 5.3–5.6 (m, 1 H); MS, m/e (relative intensity) 208 (M^+, 40), 135 (48), 134 (35), 43 (100). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.17; H, 9.95. **6h**[21] (PLC, EtOAc:hexane = 1:10 v/v): IR (neat, cm^{-1}) 1710, 1640, 1605, 1500; ^1H NMR 1.17 (t, J = 7.2, 3 H), 1.88 (s, 3 H), 2.08 (s, 3 H), 3.71 (s, 2 H), 4.11 (q, J = 7.2, 2 H), 7.20 (s, 5 H); MS, m/e (relative intensity) 218 (M^+, 22), 172 (100), 144 (80), 126 (51). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.05; H, 8.48. (*E*)-**6i** (PLC, EtOAc:hexane = 1:20 v/v): IR (neat, cm^{-1}) 1715; ^1H NMR (400 MHz) 0.77 (t, J = 7.3, 3 H), 1.20 (t, J = 7.1, 3 H), 1.10–1.45 (m, 4 H), 1.96 (t, J = 7.9, 2 H), 2.08 (s, 3 H), 4.14 (q, J = 7.1, 2 H), 7.15–7.35 (m, 5 H); MS, m/e (relative intensity) 246 (M^+, 100), 200 (46), 171 (81); HRMS, m/e 246.1639, calcd for $C_{16}H_{22}O_2$ 246.1620. (*Z*)-**6i** (PLC, EtOAc:hexane = 1:20 v/v): IR (neat, cm^{-1}) 1720; ^1H NMR (400 MHz) 0.95 (t, J = 7.3, 3 H), 1.22 (t, J = 6.9, 3 H), 1.30–1.60 (m, 4 H), 1.67 (s, 3 H), 2.41 (t, J = 7.8, 2 H), 4.15 (q, J = 7.1, 2 H), 7.15–7.35 (m, 5 H); MS, m/e (relative intensity) 246 (M^+, 73), 200 (50), 171 (100); HRMS, m/e 246.1618, calcd for $C_{16}H_{22}O_2$ 246.1620. The mixture of (*E*)- and (*Z*)-**6j** was isolated by PLC (EtOAc:hexane = 1:20 v/v). Analysis of ^1H NMR spectra of the mixture gave the following ^1H NMR data of (*E*)- and (*Z*)-**6j**. They were not separable by PLC (EtOAc:hexane = 1:20 v/v), but were separated by GC (a 20% silicone DC 550 column). GC–mass spectroscopy of the mixture gave the following mass spectral data. (*E*)-**6j**:[22] ^1H NMR 1.28 (t, J = 6.9, 3 H), 2.35 (s, 3 H), 4.27 (q, J = 7.0, 2 H), 7.07 (s, 5 H), 7.09 (s, 5 H); MS, m/e (relative intensity) 266 (M^+, 100), 220 (50), 193 (28), 192 (36). (*Z*)-**6j**:[23] ^1H NMR 0.85 (t, J = 6.9, 3 H), 2.05 (s, 3 H), 3.89 (q, J = 7.0, 2 H), 7.33 (s, 5 H), 7.37 (s, 5 H); MS, m/e (relative intensity) 266 (M^+, 100), 220 (59), 193 (44), 192 (53). IR spectra of the mixture of (*E*)-**6j** and (*Z*)-**6j** showed absorptions at 1715, 1600, and 1490 cm^{-1}. (*E*)-**6k**[24] (PLC, EtOAc:hexane = 1:20 v/v): IR (neat, cm^{-1}) 1725, 1625, 1605, 1495; ^1H NMR 2.36 (s, 3 H), 3.76 (s, 3 H), 7.06 (s, 10 H); MS, m/e (relative intensity) 252 (M^+, 100), 220 (43), 192 (52), 135 (53). (*Z*)-**6k**[24] (PLC, EtOAc:hexane = 1:20 v/v): IR (neat, cm^{-1}) 1730, 1605, 1500; ^1H NMR 2.03 (s, 3 H), 3.42 (s, 3 H), 7.33 (s, 5 H), 7.37 (s, 5 H); MS, m/e (relative intensity) 252 (M^+, 100), 220 (43), 192 (50), 135 (54).

General Procedure for the Conjugate Addition of Lithium Organo(dicyclohexylamido)cuprates to α,β-Acetylenic Esters. Generation of lithium organo(dicyclohexylamido)cuprates and their conjugate addition to α,β-acetylenic esters were done under the conditions shown in Table I according to the previously described general procedure for the palladium(0)-catalyzed coupling reaction. The conjugate addition reaction was quenched with 2.5 mL of 1 N HCl solution followed by addition of a GC internal standard. GC analysis of the organic layer gave a GC yield of the conjugate addition product which was isolated by GC and was identified as follows. (*E*)-Ethyl β-methylcinnamate:[25] IR (neat, cm^{-1}) 1710, 1630, 1580, 1495; ^1H NMR 1.32 (t, J = 7.2, 3 H), 2.58 (d, J = 1.2, 3 H), 4.23 (q, J = 7.2, 2 H), 6.14 (q, J = 1,2, 1 H), 7.1–7.5 (m, 5 H); MS, m/e (relative intensity) 190 (M^+, 84), 161 (34), 145 (100), 144 (48), 117 (31). (*Z*)-Ethyl β-methylcinnamate:[25] IR (neat, cm^{-1}) 1725, 1635, 1600, 1490; ^1H NMR 1.07 (t, J = 7.2, 3 H), 2.18 (d, J = 1.8, 3 H), 4.00 (q, J = 7.2, 2 H), 5.92 (q, J = 1.8, 1 H), 7.0–7.4 (m, 5 H); MS, m/e (relative intensity) 190 (M^+, 91), 161 (36), 145 (100), 144 (51), 117 (36). (*E*)-Methyl β-methylcinnamate: IR (neat, cm^{-1}) 1725, 1635, 1600, 1495; ^1H NMR 2.58 (d, J = 1.2, 3 H), 3.76 (s, 3 H), 6.0–6.2 (m, 1 H), 7.2–7.5 (m, 5 H); MS, m/e (relative intensity) 176 (M^+, 91), 175 (37), 145 (100), 144 (43), 117 (39); HRMS, m/e 176.0848, calcd for $C_{11}H_{12}O_2$ 176.0837. (*Z*)-Methyl β-methylcinnamate: IR (neat, cm^{-1}) 1730, 1640, 1600, 1490; ^1H NMR 2.18 (d, J = 1.2, 3 H), 3.55 (s, 3 H), 5.92 (q, J = 1.2, 1 H), 7.1–7.5 (m, 5 H); MS, m/e (relative intensity) 176 (M^+, 100), 175 (37), 145 (79), 144 (39), 117 (33); HRMS, m/e 176.0823, calcd for $C_{11}H_{12}O_2$ 176.0837.

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