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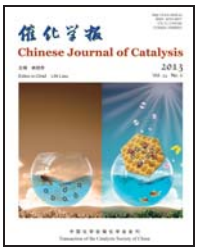

Article

Sequential Ag-catalyzed carboxylative coupling/Ru-catalyzed cross-metathesis reactions for the synthesis of functionalized 2-alkynoates

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ABSTRACT

Sequential reactions can provide efficient access to a variety of important organic compounds that would be otherwise difficult to obtain using conventional methods and readily available starting materials. Based on the importance of 2-alkynoates in organic synthesis, the current research aimed to develop a method for the convenient synthesis of functionalized 2-alkynoates from terminal alkynes, CO_2, terminal alkene-derived bromides, and methyl acrylate using a combination of the carboxylative coupling and cross-metathesis reactions. The initial ligand-free silver-catalyzed carboxylative coupling reactions of a variety of different aryl-substituted terminal alkynes and CO_2 with 5-bromopentene and 6-bromohexene provided a series of 4-pentenyl 2-alkynoates and 5-hexenyl 2-alkynoates, respectively, in good yield. These resulting 2-alkynoates were further transformed into methyl (*E*)-6-acetylenecarboxy-2-hexenoates and (*E*)-7-acetylenecarboxy-2-heptenoates in moderate to good yields by their cross-metathesis reactions with methyl acrylate in the presence of the Grubbs-Hoveyda catalyst. All of the new products characterized spectroscopically.

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1. Introduction

Methods for the synthesis of high value-added fine chemicals using carbon dioxide as a raw material have been the subject of increasing levels of attention during the course of the last two decades, because carbon dioxide is an abundant, inexpensive, and nontoxic renewable C_1 feedstock [1–7]. In the presence of suitable homogeneous transition-metal catalysts, carbon dioxide can be efficiently transformed into a variety of different functionalized carboxylic acids and related derivatives [8–22]. The copper- and silver-catalyzed direct carboxylation reactions of terminal alkynes using CO_2 as the carboxylative agent have recently been established as efficient and straightforward methods for the synthesis of functionalized propiolic acids and 2-alkynoates [23,34]. In 2010, we reported the highly selective synthesis of allylic 2-alkynoates according to the carboxylative coupling reaction of terminal alkynes, CO_2, and allylic chlorides using a 10 mol% loading of (IPr)CuCl (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) as the catalyst [28]. In a later publication, we also disclosed a convenient method for the selective synthesis of functionalized propiolic acids via the direct carboxylation of terminal alkynes with CO_2 under ligand-free conditions using only a 1 mol% loading of AgI as the catalyst [30]. More recently, this simple silver-based catalytic system has also been used as a catalyst for the highly efficient and selective carboxylative coupling reaction of a vari-

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ety of different terminal alkynes, CO_2, and chloride compounds to yield 2-alkynoates exclusively. Furthermore, the ligand-free silver catalyst system showed significantly enhanced levels of activity and selectivity at much lower catalyst loadings than the corresponding copper catalyst system [34].

Over the past two decades, olefin metathesis has become one of the most powerful and broadly applicable tools for the construction of carbon-carbon double bonds in organic synthesis [35–39]. In contrast, the cross-metathesis reaction has not been developed to the same extent because of the lack of efficient catalysts capable of controlling the chemoselectivity and stereoselectivity of the reaction [40–44]. Interestingly, however, as a convenient method to gain functionalized and higher olefins from simple alkene precursors, cross-metathesis has emerged as a powerful synthetic strategy and played a crucial role in the total syntheses of many natural products and biologically active compounds, with the utility of technique being significantly enhanced by the development of highly active and selective catalysts [45–50].

Based on the importance of 2-alkynoates in organic synthesis [51–55] and the success of olefin metathesis in a recent study [56], our attentions became focused on the development of a sequential carboxylative coupling/cross-metathesis reaction sequence for the synthesis of functionalized 2-alkynoates from CO_2, and other simple and readily available starting materials. With this goal in mind, it was envisaged that the carboxylative coupling of terminal alkynes, CO_2, and terminal alkene-derived halides would provide access to terminal alkene-derived 2-alkynoates that could then be subjected to the conditions of the cross-metathesis reactions with an olefin of lower reactivity to give functionalized 2-alkynoates, which would be otherwise difficult to obtain using conventional methods (Scheme 1). Herein, we present an efficient and convenient synthetic protocol for the selective synthesis of functionalized 2-alkynoates in good yields from terminal alkynes, CO_2, terminal alkene-derived bromides, and methyl acrylate. The two-steps of this synthetic procedure involved the silver-catalyzed carboxylative coupling and ruthenium-catalyzed cross-metathesis reactions.

2. Experimental

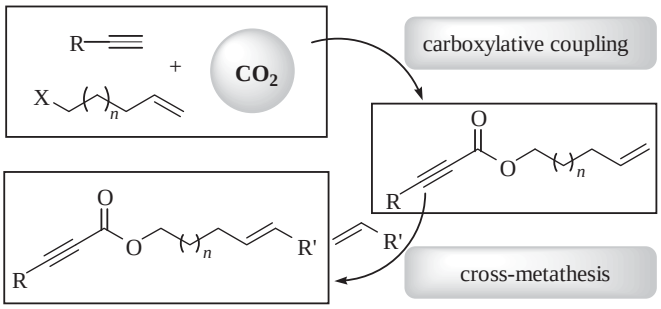
Unless otherwise statement, all manipulations were performed using standard Schlenk techniques under a dry argon or CO_2 atmosphere. *N,N*-Dimethylformamide (DMF) was distilled from CaH_2 at 60 °C under reduced pressure and stored over 4A molecular sieves. NMR spectra (^{1}H NMR, 400 MHz; ^{13}C NMR, 100 MHz) were recorded on a Bruker AvanceII 400M type spectrometer (Bruker). Multiplicity abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High resolution mass spectra (HRMS) were recorded on a Q-TOF mass spectrometer (Micromass, Wythenshawe, UK) equipped with Z-spray ionization source. Infrared (IR) spectra were measured using a Nicolet NEXUS FT-IR spectrophotometer. The second-generation Grubbs catalyst **5** [57,58] and Grubbs-Hoveyda catalyst **6** [59] were synthesized according to the reported procedures. Carbon dioxide (99.999%), commercially available terminal alkynes, bromide compounds, silver(I) salt, methyl acrylate, and other all of the other reagents were used without further purification.

2.1. General procedure for the Ag-catalyzed carboxylative coupling of terminal alkynes, CO_2, and bromides

A 70 ml oven dried autoclave containing a stirrer bar was charged the AgI (0.5 mg, 0.002 mmol) and Cs_2CO_3 (978 mg, 3.0 mmol). The autoclave was purged three time with CO_2 and the terminal alkynes **1** (2.0 mmol), bromides **2** (3.0 mmol), and dry DMF (20 ml) were then added sequentially via a syringe. The autoclave was then sealed and pressurized to the appropriate pressure with CO_2. The reaction mixture was then stirred at 60 °C for 24 h and the autoclave was cooled to room temperature and the remaining CO_2 slowly vented from the system. The reaction mixture was diluted with water (30 ml) and extracted with ethyl acetate (30 ml × 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and filtered. The solvent was removed under vacuum. The product was isolated by column chromatography on silica gel.

All new products prepared by the above procedure were characterized spectroscopically as shown below.

4-Pentenyl phenylpropiolate (**3a**). 69% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.36 (m, 5H, 5C*H*), 5.82 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH$_2$), 5.08 (d, *J* = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 5.02 (d, *J* = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.25 (t, *J* = 6.7 Hz, 2H, OC*H*$_2$), 2.21–2.16 (m, 2H, CHC*H*$_2$), 1.86–1.79 (m, 2H, CH$_2$C*H*$_2$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.10 (*C*-O), 137.16 (vinyl *C*), 132.97 (aromatic *C*), 130.62 (aromatic *C*), 128.57 (aromatic *C*), 119.64 (aromatic *C*), 115.56 (vinyl *C*), 86.16 (alkynyl *C*), 80.68 (alkynyl *C*), 65.42 (O*C*H$_2$), 29.89 (*C*H$_2$), 27.60 (*C*H$_2$). IR (neat, cm^{-1}): 2959, 2223, 1709, 1640, 1490, 1285,



Scheme 1. Synthesis of functionalized 2-alkynoates via the sequential carboxylative coupling/cross-metathesis reactions.

758, 689. HRMS (ESI, *m*/*z*) calcd. for $C_{14}H_{14}O_2Na$ $[M+Na]^+$: 237.0891; found: 237.0892.

4-Pentenyl 4-methylphenylpropiolate (**3b**). 87% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 8.0 Hz, 2H, 2C*H*), 7.18 (d, J = 8.0 Hz, 2H, 2C*H*), 5.82 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.07 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 5.02 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.24 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 2.38 (s, 2H, C*H*$_3$), 2.21–2.16 (m, 2H, CHC*H*$_2$), 1.86–1.79 (m, 2H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.25 (*C*-O), 141.27 (aromatic *C*), 137.19 (vinyl *C*), 132.98 (aromatic *C*), 129.36 (aromatic *C*), 116.51 (aromatic *C*), 115.53 (vinyl *C*), 86.72 (alkynyl *C*), 80.33 (alkynyl *C*), 65.35 (O*C*H$_2$), 29.90 (*C*H$_2$), 27.62 (*C*H$_2$), 21.69 (*C*H$_3$). IR (neat, cm^{-1}): 2957, 2217, 1708, 1641, 1508, 1290, 817, 748. HRMS (ESI, *m*/*z*) calcd. for $C_{15}H_{16}O_2Na$ $[M+Na]^+$: 251.1048; found: 251.1046.

4-Pentenyl 4-methoxylphenylpropiolate (**3c**). 91% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8.7 Hz, 2H, 2C*H*), 6.88 (d, J = 8.7 Hz, 2H, 2C*H*), 5.82 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.07 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 5.02 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.23 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 3.82 (s, 2H, C*H*$_3$), 2.20–2.15 (m, 2H, CHC*H*$_2$), 1.85–1.78 (m, 2H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.50 (aromatic *C*), 154.37 (*C*-O), 137.22 (vinyl *C*), 134.92 (aromatic *C*), 115.52 (vinyl *C*), 114.28 (aromatic *C*), 111.36 (aromatic *C*), 87.02 (alkynyl *C*), 80.10 (alkynyl *C*), 65.27 (O*C*H$_2$), 55.37 (O*C*H$_3$), 29.91 (*C*H$_2$), 27.62 (*C*H$_2$). IR (neat, cm^{-1}): 2959, 2210, 1705, 1605, 1510, 1286, 834, 747. HRMS (ESI, *m*/*z*) calcd. for $C_{15}H_{16}O_3Na$ $[M+Na]^+$: 267.0997; found: 267.0993.

4-Pentenyl 4-tert-butylphenylpropiolate (**3d**). 87% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8.2 Hz, 2H, 2C*H*), 7.40 (d, J = 8.2 Hz, 2H, 2C*H*), 5.82 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.08 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 5.02 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.25 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 2.21–2.16 (m, 2H, CHC*H*$_2$), 1.85–1.79 (m, 2H, $CH_2CH_2CH_2$), 1.32 (s, 9H, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.26 (aromatic *C*), 154.23 (*C*-O), 137.18 (vinyl *C*), 132.89 (aromatic *C*), 125.64 (aromatic *C*), 116.53 (aromatic *C*), 115.55 (vinyl *C*), 86.65 (alkynyl *C*), 80.35 (alkynyl *C*), 65.32 (O*C*H$_2$), 35.01 (*C*(CH$_3$)$_3$), 31.04 (*C*H$_3$), 29.92 (*C*H$_2$), 27.61 (*C*H$_2$). IR (neat, cm^{-1}): 2964, 2220, 1709, 1290, 1200, 1117, 837, 748. HRMS (ESI, *m*/*z*) calcd. for $C_{18}H_{22}O_2Na$ $[M+Na]^+$: 293.1517; found: 293.1519.

4-Pentenyl 4-trifluoromethylphenylpropiolate (**3e**). 85% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.1 Hz, 2H, 2C*H*), 7.64 (d, J = 8.1 Hz, 2H, 2C*H*), 5.82 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.08 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 5.02 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.27 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 2.21–2.16 (m, 2H, CHC*H*$_2$), 1.87–1.80 (m, 2H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.78 (*C*-O), 137.19 (vinyl *C*), 133.29 (aromatic *C*), 132.49 (aromatic *C*), 132.14 (aromatic *C*), 125.67 (aromatic *C*), 123.63 (*C*F$_3$), 115.78 (vinyl *C*), 84.06 (alkynyl *C*), 82.40 (alkynyl *C*), 65.87 (O*C*H$_2$), 30.01 (*C*H$_2$), 27.70 (*C*H$_2$). IR (neat, cm^{-1}): 2960, 2232, 1715, 1324, 1288, 1197, 1178, 1132, 1067, 844, 748. HRMS (ESI, *m*/*z*) calcd. for $C_{15}H_{13}O_2F_3Na$ $[M+Na]^+$: 305.0765; found: 305.0774.

4-Pentenyl 5-phenyl-2-pentynoate (**3f**). 65% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (m, 5H, 5C*H*), 5.80 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.05 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 5.00 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.16 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 2.90 (t, J = 7.6 Hz, 2H, C*H*$_2$), 2.62 (t, J = 7.6 Hz, 2H, C*H*$_2$), 2.17–2.12 (m, 2H, CHC*H*$_2$), 1.81–1.74 (m, 2H, $CH_2CH_2CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.76 (*C*-O), 139.63 (aromatic *C*), 137.21 (vinyl *C*), 128.59 (aromatic *C*), 128.38 (aromatic *C*), 126.67 (aromatic *C*), 115.53 (vinyl *C*), 88.40 (alkynyl *C*), 73.74 (alkynyl *C*), 65.16 (O*C*H$_2$), 33.85 (*C*H$_2$), 29.91 (*C*H$_2$), 27.56 (*C*H$_2$), 20.88 (*C*H$_2$). IR (neat, cm^{-1}): 2954, 2237, 1709, 1258, 1070, 750, 699. HRMS (ESI, *m*/*z*) calcd. for $C_{16}H_{18}O_2Na$ $[M+Na]^+$: 265.1204; found: 265.1211.

4-Pentenyl 2-nonynoate (**3g**). 64% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 5.80 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.04 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 5.00 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.17 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 2.33 (t, J = 7.2 Hz, 2H, C*H*$_2$), 2.17–2.12 (m, 2H, CHC*H*$_2$), 1.81–1.74 (m, 2H, $CH_2CH_2CH_2$), 1.61–1.29 (m, 8H, 4C*H*$_2$), 0.89 (t, J = 6.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.93 (*C*-O), 137.17 (vinyl *C*), 115.43 (vinyl *C*), 89.60 (alkynyl *C*), 73.07 (alkynyl *C*), 65.09 (O*C*H$_2$), 31.17 (*C*H$_2$), 29.86 (*C*H$_2$), 28.48 (*C*H$_2$), 27.53 (*C*H$_2$), 27.47 (*C*H$_2$), 22.42 (*C*H$_2$), 18.65 (*C*H$_2$), 13.96 (*C*H$_3$). IR (neat, cm^{-1}): 2959, 2236, 1713, 1642, 1258, 1083. HRMS (ESI, *m*/*z*) calcd. for $C_{14}H_{22}O_2Na$ $[M+Na]^+$: 245.1517; found: 245.1521.

5-Hexenyl phenylpropiolate (**4a**). 75% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.60–7.36 (m, 5H, 5C*H*), 5.80 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.04 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 4.98 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.25 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 2.14–2.11 (m, 2H, CHC*H*$_2$), 1.76–1.72 (m, 2H, $CH_2CH_2CH_2$), 1.54–1.50 (m, 2H, C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.17 (*C*-O), 138.19 (vinyl *C*), 132.98 (aromatic *C*), 130.63 (aromatic *C*), 128.58 (aromatic *C*), 119.63 (aromatic *C*), 115.00 (vinyl *C*), 86.12 (alkynyl *C*), 80.70 (alkynyl *C*), 65.99 (O*C*H$_2$), 33.24 (*C*H$_2$), 27.88 (*C*H$_2$), 25.07 (*C*H$_2$). IR (neat, cm^{-1}): 2936, 2221, 1709, 1640, 1490, 1286, 758, 689. HRMS (ESI, *m*/*z*) calcd. for $C_{15}H_{16}O_2Na$ $[M+Na]^+$: 251.1048; found: 251.1045.

5-Hexenyl 4-methylphenylpropiolate (**4b**). 76% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 8.0 Hz, 2H, 2C*H*), 7.19 (d, J = 8.0 Hz, 2H, 2C*H*), 5.82 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 5.04 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 4.99 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.24 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 2.39 (s, 2H, C*H*$_3$), 2.15–2.09 (m, 2H, CHC*H*$_2$), 1.76–1.71 (m, 2H, $CH_2CH_2CH_2$), 1.56–1.50 (m, 2H, C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.25 (*C*-O), 141.23 (aromatic *C*), 138.17 (vinyl *C*), 132.95 (aromatic *C*), 129.35 (aromatic *C*), 116.52 (aromatic *C*), 114.95 (vinyl *C*), 86.62 (alkynyl *C*), 80.38 (alkynyl *C*), 65.85 (O*C*H$_2$), 33.23 (*C*H$_2$), 27.90 (*C*H$_2$), 25.08 (*C*H$_2$), 21.66 (*C*H$_3$). IR (neat, cm^{-1}): 2937, 2218, 1709, 1641, 1509, 1290, 817, 748. HRMS (ESI, *m*/*z*) calcd. for $C_{16}H_{18}O_2Na$ $[M+Na]^+$: 265.1204; found: 265.1211.

5-Hexenyl 4-methoxylphenylpropiolate (**4c**). 86% isolated yield. Oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 8.7 Hz, 2H, 2C*H*), 6.79 (d, J = 8.7 Hz, 2H, 2C*H*), 5.72 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH_2), 4.95 (d, J = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 4.89 (d, J = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.14 (t, J = 6.7 Hz, 2H, OC*H*$_2$), 3.74 (s, 2H, C*H*$_3$), 2.05–1.99 (m, 2H, CHC*H*$_2$), 1.67–1.60 (m, 2H, $CH_2CH_2CH_2$), 1.46–1.38 (m, 2H, C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.49 (aromatic *C*), 154.39 (*C*-O), 138.20 (vinyl *C*),

134.90 (aromatic *C*), 114.94 (vinyl *C*), 114.27 (aromatic *C*), 111.37 (aromatic *C*), 86.94 (alkynyl *C*), 80.14 (alkynyl *C*), 65.78 (O*C*H$_2$), 55.35 (O*C*H$_3$), 33.23 (*C*H$_2$), 27.91 (*C*H$_2$), 25.08 (*C*H$_2$). IR (neat, cm^{-1}): 2937, 2214, 1705, 1604, 1510, 1288, 834, 747. HRMS (ESI, *m*/*z*) calcd. for $C_{16}H_{18}O_3Na$ [M+Na]$^+$: 281.1154; found: 281.1162.

5-Hexenyl 4-tert-butylphenylpropiolate (**4d**). 88% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.5 Hz, 2H, 2C*H*), 7.39 (d, *J* = 8.5 Hz, 2H, 2C*H*), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH$_2$), 5.04 (d, *J* = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 4.98 (d, *J* = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.24 (t, *J* = 6.6 Hz, 2H, OC*H*$_2$), 2.14–2.09 (m, 2H, CHC*H*$_2$), 1.77–1.70 (m, 2H, CH$_2$C*H*$_2$CH$_2$), 1.56–1.48 (m, 2H, C*H*$_2$), 1.32 (s, 9H, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.18 (aromatic *C*), 154.16 (*C*-O), 138.11 (vinyl *C*), 132.85 (aromatic *C*), 125.60 (aromatic *C*), 116.58 (aromatic *C*), 114.97 (vinyl *C*), 86.49 (alkynyl *C*), 80.43 (alkynyl *C*), 65.78 (O*C*H$_2$), 34.96 (*C*(CH$_3$)$_3$), 33.24 (*C*H$_3$), 31.01 (*C*H$_2$), 27.91 (*C*H$_2$), 25.08 (*C*H$_2$). IR (neat, cm^{-1}): 2964, 2220, 1709, 1290, 1201, 1175, 837, 748. HRMS (ESI, *m*/*z*) calcd. for $C_{19}H_{24}O_2Na$ [M+Na]$^+$: 307.1674; found: 307.1678.

5-Hexenyl 4-trifluoromethylphenylpropiolate (**4e**). 83% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.1 Hz, 2H, 2C*H*), 7.64 (d, *J* = 8.1 Hz, 2H, 2C*H*), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH$_2$), 5.03 (d, *J* = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 4.99 (d, *J* = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.26 (t, *J* = 6.7 Hz, 2H, OC*H*$_2$), 2.14–2.09 (m, 2H, CHC*H*$_2$), 1.78–1.71 (m, 2H, CH$_2$C*H*$_2$CH$_2$), 1.56–1.48 (m, 2H, C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.68 (*C*-O), 138.11 (vinyl *C*), 133.14 (aromatic *C*), 132.33 (aromatic *C*), 132.00 (aromatic *C*), 125.51 (aromatic *C*), 123.50 (*C*F$_3$), 115.02 (vinyl *C*), 83.87 (alkynyl *C*), 82.29 (alkynyl *C*), 66.27 (O*C*H$_2$), 33.21 (*C*H$_2$), 27.85 (*C*H$_2$), 25.06 (*C*H$_2$). IR (neat, cm^{-1}): 2938, 2228, 1716, 1324, 1289, 1197, 1177, 1133, 1068, 844, 748. HRMS (ESI, *m*/*z*) calcd. for $C_{16}H_{15}O_2F_3Na$ [M+Na]$^+$: 319.0922; found: 319.0926.

5-Hexenyl 5-phenyl-2-pentynoate (**4f**). 66% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (m, 5H, 5C*H*), 5.80 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH$_2$), 5.03 (d, *J* = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 4.98 (d, *J* = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.16 (t, *J* = 6.6 Hz, 2H, OC*H*$_2$), 2.90 (t, *J* = 7.6 Hz, 2H, C*H*$_2$), 2.63 (t, *J* = 7.7 Hz, 2H, C*H*$_2$), 2.12–2.06 (m, 2H, CHC*H*$_2$), 1.72–1.65 (m, 2H, CH$_2$C*H*$_2$CH$_2$), 1.51–1.44 (m, 2H, C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.80 (*C*-O), 139.64 (aromatic *C*), 138.21 (vinyl *C*), 128.58 (aromatic *C*), 128.37 (aromatic *C*), 126.66 (aromatic *C*), 114.97 (vinyl *C*), 88.34 (alkynyl *C*), 73.77 (alkynyl *C*), 65.71 (O*C*H$_2$), 33.86 (*C*H$_2$), 33.24 (*C*H$_2$), 27.85 (*C*H$_2$), 25.08 (*C*H$_2$), 20.88 (*C*H$_2$). IR (neat, cm^{-1}): 2934, 2236, 1709, 1252, 1070, 750, 699. HRMS (ESI, *m*/*z*) calcd. for $C_{17}H_{20}O_2Na$ [M+Na]$^+$: 279.1361; found: 279.1372.

5-Hexenyl 2-nonynoate (**4g**). 59% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH$_2$), 5.02 (d, *J* = 16.9 Hz, 1H, *trans* CH=C*H*$_2$), 4.97 (d, *J* = 10.2 Hz, 1H, *cis* CH=C*H*$_2$), 4.16 (t, *J* = 6.7 Hz, 2H, OC*H*$_2$), 2.33 (t, *J* = 7.1 Hz, 2H, C*H*$_2$), 2.11–2.06 (m, 2H, CHC*H*$_2$), 1.72–1.30 (m, 12H, 6C*H*$_2$), 0.89 (t, *J* = 6.5 Hz, 3H, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.95 (*C*-O), 138.15 (vinyl *C*), 114.87 (vinyl *C*), 89.50 (alkynyl *C*), 73.09 (alkynyl *C*), 65.61 (O*C*H$_2$), 33.20 (*C*H$_2$), 31.17 (*C*H$_2$), 28.48 (*C*H$_2$), 27.80 (*C*H$_2$), 27.47 (*C*H$_2$), 25.02 (*C*H$_2$), 22.42 (*C*H$_2$), 18.63 (*C*H$_2$), 13.96 (*C*H$_3$). IR (neat, cm^{-1}): 2954, 2236, 1713, 1641, 1250, 1083. HRMS (ESI, *m*/*z*) calcd. for $C_{15}H_{24}O_2Na$ [M+Na]$^+$: 259.1674; found: 259.1683.

2.2. General procedure for the cross-metathesis reaction of the terminal alkene-derived 2-alkynoates with methyl acrylate

To a solution of the terminal alkene-derived 2-alkynoates **3** or **4** (0.2 mmol) in toluene (0.1 mol/L) in a Schlenk tube containing a stirrer bar were added methyl acrylates (50 equiv) and the Grubbs-Hoveyda catalyst (5 mol%). The resulting reaction mixtures were heated under an argon atmosphere at 60 °C for 12 h. The mixtures were then quickly filtered through silica and the solvent removed under reduced pressure to give the crude residues, which were purified by flash column chromatography on silica gel to provide the cross-metathesis products **8** or **9**.

All new products prepared by the above procedure were characterized spectroscopically as shown below.

Methyl (*E*)-6-phenylacetylenecarboxy-2-hexenoate (**8a**). 31% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.36 (m, 5H, 5C*H*), 6.97 (dt, *J* = 15.6, 6.9 Hz, 1H, C*H*CH$_2$), 5.89 (d, *J* = 15.6, 1H, C*H*CO), 4.26 (t, *J* = 6.9 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.38–2.32 (m, 2H, CHC*H*$_2$), 1.93–1.86 (m, 2H, CH$_2$C*H*$_2$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.84 (*C*-O), 154.00 (*C*-O), 147.51 (alkenyl *C*), 133.01 (aromatic *C*), 130.69 (aromatic *C*), 128.58 (aromatic *C*), 121.89 (alkenyl *C*), 119.55 (aromatic *C*), 86.54 (alkynyl *C*), 80.47 (alkynyl *C*), 64.98 (O*C*H$_2$), 51.47 (O*C*H$_3$), 28.52 (*C*H$_2$), 26.91 (*C*H$_2$). IR (neat, cm^{-1}): 2956, 2924, 2219, 1716, 1660, 1463, 1278, 1261, 1024, 757, 689. HRMS (ESI, *m*/*z*) calcd. for $C_{16}H_{16}O_4Na$ [M+Na]$^+$: 295.0946; found: 295.0935.

Methyl (*E*)-6-(4-methylphenyl)acetylenecarboxy-2-hexenoate (**8b**). 63% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.0 Hz, 2H, 2C*H*), 7.19 (d, *J* = 8.0 Hz, 2H, 2C*H*), 6.98 (dt, *J* = 15.7, 6.4 Hz, 1H, C*H*CH$_2$), 5.89 (d, *J* = 15.7, 1H, C*H*CO), 4.25 (t, *J* = 6.4 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.39 (s, 3H, C*H*$_3$), 2.39–2.33 (m, 2H, CHC*H*$_2$), 1.93–1.86 (m, 2H, CH$_2$C*H*$_2$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.01 (*C*-O), 154.30 (*C*-O), 147.74 (alkenyl *C*), 141.54 (aromatic *C*), 133.18 (aromatic *C*), 129.53 (aromatic *C*), 122.01 (alkenyl *C*), 116.54 (aromatic *C*), 87.26 (alkynyl *C*), 80.29 (alkynyl *C*), 65.07 (O*C*H$_2$), 51.68 (O*C*H$_3$), 29.87 (*C*H$_2$), 28.70 (*C*H$_2$), 27.07 (*C*H$_3$). IR (neat, cm^{-1}): 2950, 2924, 2214, 1709, 1659, 1436, 1382, 1289, 1168, 1034, 817, 747. HRMS (ESI, *m*/*z*) calcd. for $C_{17}H_{18}O_4Na$ [M+Na]$^+$: 309.1103; found: 309.1102.

Methyl (*E*)-6-(4-methoxylphenyl)acetylenecarboxy-2-hexenoate (**8c**). 68% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.9 Hz, 2H, 2C*H*), 6.97 (dt, *J* = 15.6, 6.9 Hz, 1H, C*H*CH$_2$), 6.89 (d, *J* = 8.9 Hz, 2H, 2C*H*), 5.88 (d, *J* = 15.6, 1H, C*H*CO), 4.24 (t, *J* = 6.9 Hz, 2H, OC*H*$_2$), 3.84 (s, 3H, OC*H*$_3$), 3.73 (s, 3H, OC*H*$_3$), 2.38–2.32 (m, 2H, CHC*H*$_2$), 1.92–1.85 (m, 2H, CH$_2$C*H*$_2$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.00 (*C*-O), 161.72 (aromatic *C*), 154.41 (*C*-O), 147.76 (alkenyl *C*), 135.13 (aromatic *C*), 121.98 (alkenyl *C*), 114.45 (aromatic *C*), 111.43 (aromatic *C*), 87.55 (alkynyl *C*), 80.09 (alkynyl *C*), 64.98 (O*C*H$_2$), 55.56 (O*C*H$_3$), 51.64 (O*C*H$_3$), 28.70 (*C*H$_2$), 27.08 (*C*H$_2$). IR (neat,

cm^{-1}) : 2955, 2922, 2212, 1708, 1658, 1604, 1462, 1288, 1165, 1026, 835, 746. HRMS (ESI, *m/z*) calcd. for $C_{17}H_{18}O_5Na$ [M+Na]$^+$: 325.1052; found: 325.1058.

Methyl (*E*)-6-(4-tert-butylphenyl)acetylenecarboxy-2-hexenoate (**8d**). 89% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.2 Hz, 2H, 2C*H*), 7.40 (d, *J* = 8.2 Hz, 2H, 2C*H*), 6.97 (dt, *J* = 15.7, 6.4 Hz, 1H, C*H*CH$_2$), 5.89 (d, *J* = 15.7, 1H, C*H*CO), 4.25 (t, *J* = 6.4 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.38–2.33 (m, 2H, CHC*H*$_2$), 1.93–1.86 (m, 2H, CH$_2$C*H*$_2$CH$_2$), 1.32 (s, 9H, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.97 (*C*-O), 154.54 (*C*-O), 154.29 (aromatic *C*), 147.70 (alkenyl *C*), 133.04 (aromatic *C*), 125.77 (aromatic *C*), 121.98 (alkenyl *C*), 116.52 (aromatic *C*), 87.21 (alkynyl *C*), 80.23 (alkynyl *C*), 65.03 (O*C*H$_2$), 51.59 (O*C*H$_3$), 35.19 (*C*(CH$_3$)$_3$), 31.17 (*C*H$_3$), 28.67 (*C*H$_2$), 27.04 (*C*H$_2$). IR (neat, cm^{-1}): 2960, 2219, 1716, 1658, 1436, 1290, 1201, 1171, 1040, 838, 748. HRMS (ESI, *m/z*) calcd. for $C_{20}H_{24}O_4Na$ [M+Na]$^+$: 351.1572; found: 351.1581.

Methyl (*E*)-6-(4-trifluoromethyl)acetylenecarboxy-2-hexenoate (**8e**). 49% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.7 Hz, 2H, 2C*H*), 7.65 (d, *J* = 7.7 Hz, 2H, 2C*H*), 6.97 (dt, *J* = 15.5, 6.9 Hz, 1H, C*H*CH$_2$), 5.89 (d, *J* = 15.5, 1H, C*H*CO), 4.27 (t, *J* = 6.9 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.38–2.32 (m, 2H, CHC*H*$_2$), 1.93–1.88 (m, 2H, CH$_2$C*H*$_2$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.98 (*C*-O), 153.67 (*C*-O), 147.56 (alkenyl *C*), 133.34 (aromatic *C*), 132.59 (aromatic *C*), 132.26 (aromatic *C*), 125.70 (aromatic *C*), 123.52 (*C*F$_3$), 122.10 (alkenyl *C*), 84.42 (alkynyl *C*), 82.19 (alkynyl *C*), 65.43 (O*C*H$_2$), 51.67 (O*C*H$_3$), 28.66 (*C*H$_2$), 27.01 (*C*H$_2$). IR (neat, cm^{-1}): 2953, 2927, 2230, 1716, 1660, 1324, 1287, 1172, 1067, 845, 747. HRMS (ESI, *m/z*) calcd. for $C_{17}H_{15}O_4NaF_3$ [M+Na]$^+$: 363.0820; found: 363.0814.

Methyl (*E*)-7-phenylacetylenecarboxy-2-heptenoate (**9a**). 30% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.36 (m, 5H, 5C*H*), 6.97 (dt, *J* = 15.6, 7.0 Hz, 1H, C*H*CH$_2$), 5.86 (d, *J* = 15.6, 1H, C*H*CO), 4.24 (t, *J* = 6.9 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.30–2.24 (m, 2H, CHC*H*$_2$), 1.79–1.56 (m, 4H, 2C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.98 (*C*-O), 154.10 (*C*-O), 148.53 (alkenyl *C*), 133.00 (aromatic *C*), 130.65 (aromatic *C*), 128.57 (aromatic *C*), 121.51 (alkenyl *C*), 119.61 (aromatic *C*), 86.36 (alkynyl *C*), 80.57 (alkynyl *C*), 65.59 (O*C*H$_2$), 51.43 (O*C*H$_3$), 31.63 (*C*H$_2$), 27.92 (*C*H$_2$), 24.37 (*C*H$_2$). IR (neat, cm^{-1}): 2958, 2924, 2201, 1722, 1701, 1660, 1460, 1259, 1024, 800, 745. HRMS (ESI, *m/z*) calcd. for $C_{17}H_{18}O_4Na$ [M+Na]$^+$: 309.1103; found: 309.1091.

Methyl (*E*)-7-(4-methylphenyl)acetylenecarboxy-2-heptenoate (**9b**). 49% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.9 Hz, 2H, 2C*H*), 7.18 (d, *J* = 7.9 Hz, 2H, 2C*H*), 6.97 (dt, *J* = 15.7, 6.4 Hz, 1H, C*H*CH$_2$), 5.86 (d, *J* = 15.7, 1H, C*H*CO), 4.24 (t, *J* = 6.4 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.38 (s, 3H, C*H*$_3$), 2.30–2.24 (m, 2H, CHC*H*$_2$), 1.78–1.56 (m, 4H, 2C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.15 (*C*-O), 154.40 (*C*-O), 148.76 (alkenyl *C*), 141.48 (aromatic *C*), 133.16 (aromatic *C*), 129.51 (aromatic *C*), 121.61 (alkenyl *C*), 116.58 (aromatic *C*), 87.07 (alkynyl *C*), 80.38 (alkynyl *C*), 65.68 (O*C*H$_2$), 51.63 (O*C*H$_3$), 31.81 (*C*H$_2$), 29.86 (*C*H$_2$), 28.08 (*C*H$_2$), 24.52 (*C*H$_3$). IR (neat, cm^{-1}): 2957, 2925, 2217, 1708, 1658, 1435, 1382, 1290, 1169, 1038, 817, 747. HRMS (ESI, *m/z*) calcd. for $C_{18}H_{20}O_4Na$ [M+Na]$^+$: 323.1259; found: 323.1247.

Methyl (*E*)-7-(4-methoxylphenyl)acetylenecarboxy-2-heptenoate (**9c**). 56% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.8 Hz, 2H, 2C*H*), 6.97 (dt, *J* = 15.6, 7.0 Hz, 1H, C*H*CH$_2$), 6.89 (d, *J* = 8.8 Hz, 2H, 2C*H*), 5.86 (d, *J* = 15.6, 1H, C*H*CO), 4.23 (t, *J* = 7.0 Hz, 2H, OC*H*$_2$), 3.84 (s, 3H, OC*H*$_3$), 3.73 (s, 3H, OC*H*$_3$), 2.30–2.25 (m, 2H, CHC*H*$_2$), 1.78–1.56 (m, 4H, C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.16 (*C*-O), 161.68 (aromatic *C*), 154.53 (*C*-O), 148.78 (alkenyl *C*), 135.12 (aromatic *C*), 121.61 (alkenyl *C*), 114.44 (aromatic *C*), 111.49 (aromatic *C*), 87.38 (alkynyl *C*), 80.17 (alkynyl *C*), 65.60 (O*C*H$_2$), 55.56 (O*C*H$_3$), 51.62 (O*C*H$_3$), 31.82 (*C*H$_2$), 28.10 (*C*H$_2$), 24.53 (*C*H$_2$). IR (neat, cm^{-1}): 2924, 2850, 2212, 1705, 1657, 1604, 1510, 1460, 1286, 1163, 1029, 835, 747. HRMS (ESI, *m/z*) calcd. for $C_{18}H_{20}O_5Na$ [M+Na]$^+$: 339.1208; found: 339.1216.

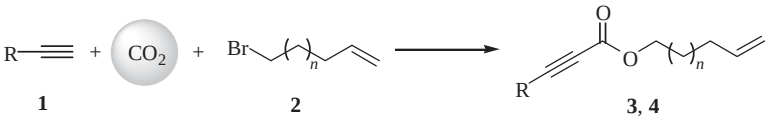
Methyl (*E*)-7-(4-tert-butylphenyl)acetylenecarboxy-2-heptenoate (**9d**). 77% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.7 Hz, 2H, 2C*H*), 7.39 (d, *J* = 8.7 Hz, 2H, 2C*H*), 6.97 (dt, *J* = 15.6, 6.4 Hz, 1H, C*H*CH$_2$), 5.86 (d, *J* = 15.6, 1H, C*H*CO), 4.24 (t, *J* = 6.4 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.30–2.24 (m, 2H, CHC*H*$_2$), 1.77–1.72 (m, 2H, CH$_2$C*H*$_2$CH$_2$), 1.63–1.56 (m, 2H, C*H*$_2$) 1.32 (s, 9H, C*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.08 (*C*-O), 154.47 (*C*-O), 154.37 (aromatic *C*), 148.70 (alkenyl *C*), 133.02 (aromatic *C*), 125.75 (aromatic *C*), 121.60 (alkenyl *C*), 116.58 (aromatic *C*), 87.02 (alkynyl *C*), 80.33 (alkynyl *C*), 65.64 (O*C*H$_2$), 51.55 (O*C*H$_3$), 35.17 (*C*(CH$_3$)$_3$), 31.77 (*C*H$_2$), 31.16 (*C*H$_3$), 28.05 (*C*H$_2$), 24.50 (*C*H$_2$). IR (neat, cm^{-1}): 2962, 2216, 1716, 1660, 1436, 1290, 1201, 1170, 1034, 838, 747. HRMS (ESI, *m/z*) calcd. for $C_{21}H_{26}O_4Na$ [M+Na]$^+$: 365.1729; found: 365.1717.

Methyl (*E*)-7-(4-trifluoromethyl)acetylenecarboxy-2-heptenoate (**9e**). 44% isolated yield. Oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.2 Hz, 2H, 2C*H*), 7.65 (d, *J* = 8.2 Hz, 2H, 2C*H*), 6.97 (dt, *J* = 15.5, 7.0 Hz, 1H, C*H*CH$_2$), 5.86 (d, *J* = 15.5, 1H, C*H*CO), 4.26 (t, *J* = 7.0 Hz, 2H, OC*H*$_2$), 3.73 (s, 3H, OC*H*$_3$), 2.31–2.25 (m, 2H, CHC*H*$_2$), 1.78–1.59 (m, 2H, 2C*H*$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.98 (*C*-O), 153.62 (*C*-O), 148.49 (alkenyl *C*), 133.17 (aromatic *C*), 132.38 (aromatic *C*), 132.06 (aromatic *C*), 125.53 (aromatic *C*), 123.43 (*C*F$_3$), 121.54 (alkenyl *C*), 84.10 (alkynyl *C*), 82.15 (alkynyl *C*), 65.90 (O*C*H$_2$), 51.47 (O*C*H$_3$), 31.62 (*C*H$_2$). 29.71 (*C*H$_2$), 27.88 (*C*H$_2$). IR (neat, cm^{-1}): 2951, 2228, 1717, 1658, 1324, 1288, 1174, 1067, 845, 748. HRMS (ESI, *m/z*) calcd. for $C_{18}H_{17}O_4NaF_3$ [M+Na]$^+$: 377.0977; found: 377.0972.

3. Results and discussion

Sequential reactions can offer efficient methods for the synthesis of a variety of different important organic compounds that would be otherwise difficult to prepare using conventional methods. Our recent studies on the carboxylative coupling [34] and olefin metathesis [56] reactions provided a platform for the synthesis of functionalized 2-alkynoates from CO_2, and other simple and readily available starting materials via the combination of these two reactions. Considering the high reaction efficiency of the carboxylative coupling reaction and the use of the relatively costly Grubbs-Hoveyda catalyst in the cross-metathesis reaction, the carboxylative coupling reaction was conducted prior to the cross-metathesis reaction.

Table 1
Ag-catalyzed carboxylative coupling of terminal alkynes, CO_2, and bromides.



1 **2** **3**, **4**

Entry	R	*n*	Product	Isolated yield (%)
1	Ph	1	**3a**	69
2	4-MeC_6H_4	1	**3b**	87
3	4-$MeOC_6H_4$	1	**3c**	91
4	4-^{t}BuC_6H_4	1	**3d**	87
5	4-$CF_3C_6H_4$	1	**3e**	85
6	$PhCH_2CH_2$	1	**3f**	65
7	*n*-hexyl	1	**3g**	64
8	Ph	2	**4a**	75
9	4-MeC_6H_4	2	**4b**	76
10	4-$MeOC_6H_4$	2	**4c**	86
11	4-^{t}BuC_6H_4	2	**4d**	88
12	4-$CF_3C_6H_4$	2	**4e**	83
13	$PhCH_2CH_2$	2	**4f**	66
14	*n*-hexyl	2	**4g**	59

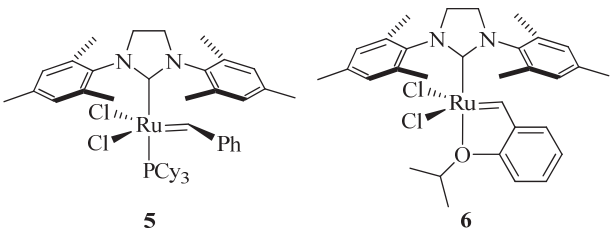
Reaction conditions: 2.0 mmol terminal alkyne **1**, 3.0 mmol bromide **2**, 3.0 mmol Cs_2CO_3, 0.002 mmol AgI, 2.0 MPa CO_2, 20 ml DMF, 60 °C, 24 h.

3.1. Ag-catalyzed carboxylative coupling of terminal alkynes, CO_2, and bromides

In the present study, the silver(I) catalytic system consisted of 0.1 mol% of AgI and 1.5 equivalents of Cs_2CO_3, which was used as base. This catalytic system was used for the carboxylative coupling of terminal alkynes, CO_2 and terminal alkene-derived bromides (5-bromopentene or 6-bromohexene) under 2.0 MPa CO_2 pressure at 60 °C in DMF over a period of 24 h. As shown in Table 1, a series of 4-pentenyl 2-alkynoates (**3**) and 5-hexenyl 2-alkynoates (**4**) were obtained in moderate to good yields via the carboxylative coupling reaction of various terminal alkynes and CO_2 with 5-bromopentene or 6-bromohexene, respectively. Similarly, the carboxylative reaction proceeded in a highly selective manner and no direct coupling by-products were detected even in the cases of complete conversion. Phenylacetylenes bearing both electron-donating and electron-withdrawing substituents on the ring were successfully converted to the corresponding carboxylative products in good yields (Table 1, entries 1–5 and 8–12). Compared with the aryl-substituted terminal alkynes, the alkyl-substituted terminal alkynes gave relatively low yields (Table 1, entries 6, 7, 13, and 14). This difference was attributed to the higher stability of the aryl-substituted silver(I) acetylide relative to the alkyl-substituted silver(I) acetylide intermediate which is generally thought to be initially formed according to the possible mechanism of the carboxylative coupling of the terminal alkyne, CO_2, and halide [34].

3.2. Cross-metathesis reactions of the terminal alkene-derived 2-alkynoates with methyl acrylate

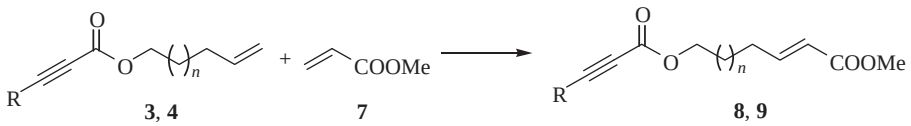
With a variety of different alkene-derived 2-alkynoates in hand, we proceeded to investigate our interest in the synthesis of functionalized 2-alkynoates via the cross-metathesis reaction of the alkene-derived 2-alkynoates with an olefin of lower reactivity. Generally, the Grubbs-Hoveyda catalyst **6** [59] shows higher catalytic activity towards cross-metathesis reactions than the second-generation Grubbs catalyst **5** [57,58] (Scheme 2). With this in mind, catalyst **6** was used in our experimental investigations. As shown in Table 2, in the presence of a 5 mol% loading of catalyst **6**, the aryl-substituted 4-pentenyl (**3a**–**3e**) and 5-hexenyl (**4a**–**4e**) propiolates underwent cross-metathesis reactions with an excess of methyl acrylate in toluene at 60 °C to give the desired aryl-substituted methyl (*E*)-6-acetylenecarboxy-2-hexenoates (**8a**–**8e**) and (*E*)-7-acetylenecarboxy-2-heptenoates (**9a**–**9e**), respectively, in moderate to good yields (Table 2, entries 1–4, 6, and 9–13). No intermolecular or intramolecular enyne metathesis products were detected, because the electron-deficient internal alkyne moiety in the alkene-derived 2-alkynoates cannot undergo the enyne metathesis reaction with the electron-deficient olefin substrate methyl acrylate in the presence of a Grubbs-type catalyst. The second-generation Grubbs catalyst **5** showed no catalytic activity towards the cross-metathesis reaction between the alkene-derived 2-alkynoates and methyl acrylate (Table 2, entry 5). Compared with aryl-substituted 4-pentenyl propiolates **3a**–**3e**, the aryl-substituted 5-hexenyl propiolates **4a**–**4e** gave relatively low yields of the cross-metathesis products. According to the well-defined olefin metathesis mechanism, the Grubbs-Hoveyda catalyst **6** initially reacted with the alkene-derived 2-alkynoates to form a new ruthenium alkyli-



5 **6**

Scheme 2. The second-generation Grubbs catalyst **5** and Grubbs-Hoveyda catalyst **6**.

Table 2
Cross-metathesis reaction of terminal alkene-derived 2-alkynoates with methyl acrylate.



3, **4** **7** **8**, **9**

Entry	3 or 4			Product	Isolated yield (%)
	R	*n*			
1	Ph	1	**3a**	**8a**	31
2	4-MeC_6H_4	1	**3b**	**8b**	63
3	4-$MeOC_6H_4$	1	**3c**	**8c**	68
4	4-^{t}BuC_6H_4	1	**3d**	**8d**	89
5[a]	4-^{t}BuC_6H_4	1	**3d**	**8d**	<1[c]
6	4-$CF_3C_6H_4$	1	**3e**	**8e**	49
7	$PhCH_2CH_2$	1	**3f**	**8f**	<1[c]
8	*n*-hexyl	1	**3g**	**8g**	<1[c]
9	Ph	2	**4a**	**9a**	30
10	4-MeC_6H_4	2	**4b**	**9b**	49
11	4-$MeOC_6H_4$	2	**4c**	**9c**	56
12	4-^{t}BuC_6H_4	2	**4d**	**9d**	77
13	4-$CF_3C_6H_4$	2	**4e**	**9e**	44
14	$PhCH_2CH_2$	2	**4f**	**9f**	<1[b]
15	*n*-hexyl	2	**4g**	**9g**	<1[b]

Reaction conditions: 0.2 mmol 2-alkynoates **3** or **4**, 10 mmol methyl acrylate **7**, 0.01 mmol Grubbs-Hoveyda catalyst **6**, 2 ml toluene, 60 °C, 12 h. [a] 0.01 mmol **5** as catalyst. [b] Yield was determined by ^{1}H NMR.

dene complex as a catalytically active intermediate. The occurrence of chelate coordination would become possible in this newly formed complex because of the existence of carbonyl and alkyne group in 2-alkynoates substrate. Aryl-substituted 2-alkynoate substrates with longer chains gave lower yields likely because their chelate intermediates showed higher levels of stability and their catalytic activities were inhibited. Alkyl-substituted 4-pentenyl (**3f** and **3g**) and 5-hexenyl (**4f** and **4g**) propiolates failed to undergo the cross-metathesis reactions with methyl acrylate even at elevated temperatures, with higher catalyst loadings and with prolonged reaction times, which might be attributed to the preponderantly competitive coordination of the alkyne moiety in alkyl-substituted propiolate substrates to the ruthenium center (Table 2, entries 7, 8, 14, and 15). Other cross-metathesis partners such as acrolein, acrylonitrile and *t*-butyl acrylate gave the corresponding cross-metathesis products in very low yields (< 5%).

4. Conclusions

A silver-catalyzed carboxylative coupling reaction was successfully developed for the coupling of a variety of different aryl-substituted terminal alkynes and CO_2 with 5-bromopentene or 6-bromohexene to give a series of 4-pentenyl 2-alkynoates or 5-hexenyl 2-alkynoates in good yields. The resulting 2-alkynoates were further transformed into methyl (*E*)-6-acetylenecarboxy-2-hexenoates or (*E*)-7-acetylenecarboxy-2-heptenoates in moderate to good yields via their cross-metathesis reaction with methyl acrylate in the presence of the Grubbs-Hoveyda catalyst. This carboxylative coupling/cross-metathesis reaction sequence offers an efficient and convenient method for the synthesis of functionalized 2-alkynoates from CO_2, and other simple and readily available starting materials.

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Graphical Abstract

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Sequential Ag-catalyzed carboxylative coupling/Ru-catalyzed cross-metathesis reactions for the synthesis of functionalized 2-alkynoates

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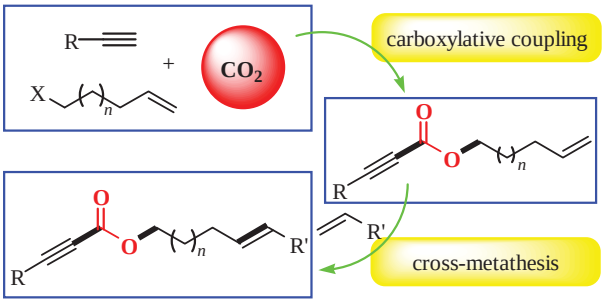
An efficient and convenient method has been developed for the synthesis of functionalized 2-alkynoates in good yield from terminal alkynes, CO_2, terminal alkene-derived bromides, and methyl acrylate via the combination of silver-catalyzed carboxylative coupling and ruthenium-catalyzed cross-metathesis reactions.



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银催化羧化偶联反应及钌催化交叉复分解反应串联合成官能团炔酸酯

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摘要：通过将Ag催化的羧化偶联反应与Ru催化的交叉复分解反应串联，用端炔、二氧化碳、端烯基取代的溴代物和甲基丙烯酸甲酯高效高产率地合成了一系列官能团化的炔酸酯.

关键词：二氧化碳；羧化偶联反应；银催化剂；交叉复分解反应; Grubbs-Hoveyda催化剂；均相催化

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