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Ytterbium-Catalyzed Conjugate Allylation of Alkylidene Malonates

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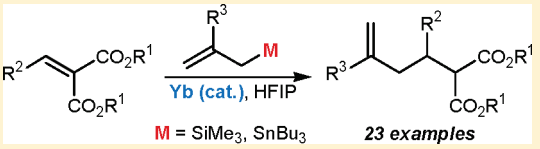
Supporting Information

ABSTRACT: Alkylidene malonates undergo efficient conjugate allylation upon treatment with allylstannanes or allylsilanes under the action of ytterbium catalysis.



Although catalytic conjugate additions of organometallics to electron-deficient alkenes are fundamentally important transformations,[1] such reactions with allylmetal reagents remain relatively underdeveloped.[2−7] However, encouraging progress in this area has been reported recently. For example, Jarvo and co-workers have described palladium-catalyzed conjugate allylation of α,β-unsaturated *N*-acylpyrroles[8a] and alkylidene malononitriles[8b] with allylboronic acid pinacol ester, while the Fillion group has reported scandium-catalyzed conjugate allylation of alkylidene Meldrum's acids with allylstannanes.[9] Enantioselective catalytic conjugate allylations have also been documented recently.[10,11] Morken and co-workers have described enantioselective allylation of alkylidene-activated enones using palladium or nickel catalysis,[10] while the Snapper group has developed asymmetric copper-catalyzed allylation of cyclic unsaturated ketoesters.[11]

Despite these advances, the development of catalytic conjugate allylations with a greater variety of substrates would be beneficial in order to increase the range of products that may be accessed. Herein, we report ytterbium-catalyzed conjugate allylation of alkylidene malonates using allylstannanes or allylsilanes.[12]

In consideration of potential substrates for conjugate allylation, we were drawn to alkylidene malonates for a number of reasons. First, with two activating groups present, alkylidene malonates exhibit high reactivity in conjugate addition reactions, including enantioselective variants.[13] Second, the ability of alkylidene malonates to engage in two-point binding with a Lewis acid catalyst[14] was anticipated to be favorable for promoting reaction with allylmetal reagents that are convenient to handle, but which exhibit low-to-moderate reactivity, such as allylsilanes and allylstannanes. Third, the malonate functionality in the products may potentially be exploited in a range of useful transformations.

Figure 1 depicts the alkylidene malonates employed in this investigation, which were prepared by Knoevenagel condensations under standard conditions,[15] except for **1k**, which is commercially available.

Attempted 1,4-addition of a simple allyl group to substrate **1a** revealed that allytributylstannane (**2**) provided encouraging

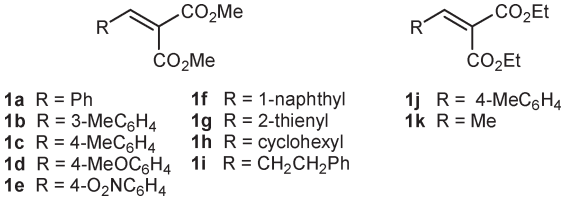


Figure 1. Alkylidene malonates employed in this study.

results in the presence of substoichiometric quantities of certain Lewis acids. Table 1 presents the results obtained in CH_2Cl_2 at room temperature for 24 h. None of the intended product **3a** was obtained with use of 10 mol % of $Cu(OTf)_2$, $Zn(OTf)_2$, or $Al(OTf)_3$ (entries 1, 2, and 5, respectively), while $Mg(OTf)_2$ provided a trace of **3a** (entry 3). Markedly improved results were obtained with catalytic $Yb(OTf)_3 \cdot 2H_2O$[16] (entry 7). To ascertain whether water was playing an important role in this process, the reactions with $Mg(OTf)_2$ and $Al(OTf)_3$ were repeated with the addition of 0.2 equiv of water (entries 4 and 6, respectively). However, water was not beneficial in the case of $Al(OTf)_3$ (entry 6), and had a negative effect in the case of $Mg(OTf)_2$ (entry 4, compare with entry 3). With $Yb(OTf)_3 \cdot 2H_2O$ as the precatalyst, the addition of hexafluoroisopropanol (HFIP)[17] resulted in virtually complete conversion of the starting material into **3a** (entry 8).[18] Surprisingly, attempts to reduce the loading of $Yb(OTf)_3 \cdot 2H_2O$ to 5 mol % were unsuccessful, with minimal conversion into **3a** being observed (entry 9). It should be noted that while the use of anhydrous $Yb(OTf)_3$ in place of $Yb(OTf)_3 \cdot 2H_2O$ led to a similarly high conversion (entry 10), $Yb(OTf)_3 \cdot 2H_2O$ was preferred on the basis of its lower cost and greater ease of handling.

The optimized conditions with $Yb(OTf)_3 \cdot 2H_2O$ (Table 1, entry 8) were then applied to allylation of alkylidene malonates

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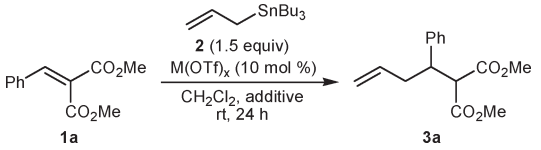
Table 1. Evaluation of Conditions for Allylation of 1a[a]

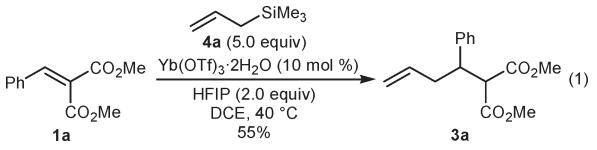


entry	$M(OTf)_x$	additive	conversion (%)[b]
1	$Cu(OTf)_2$		<5
2	$Zn(OTf)_2$		<5
3	$Mg(OTf)_2$		13
4	$Mg(OTf)_2$	H_2O (0.2 equiv)	<5
5	$Al(OTf)_3$		<5
6	$Al(OTf)_3$	H_2O (0.2 equiv)	<5
7	$Yb(OTf)_3 \cdot 2H_2O$		72
8	$Yb(OTf)_3 \cdot 2H_2O$	HFIP (2.0 equiv)	>95
9	$Yb(OTf)_3 \cdot 2H_2O$[c]	HFIP (2.0 equiv)	<10
10	$Yb(OTf)_3$	HFIP (2.0 equiv)	>95

[a] Reactions were conducted with 0.20 mmol of **1a** in 1 mL of CH_2Cl_2. [b] Conversion was measured by ^1H NMR spectroscopy after filtration of the reaction mixtures through a short plug of silica gel. No byproducts were detected in these reactions. [c] Using 5 mol % of $Yb(OTf)_3 \cdot 2H_2O$.

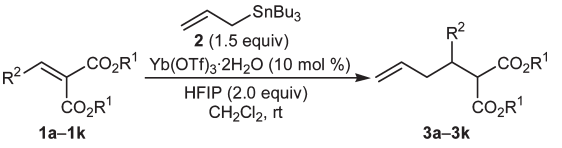
1a−**k** to examine the scope of the process, and gratifyingly, all of these substrates proved to be competent (Table 2). Substrates containing aromatic substituents of electron-neutral (entries 1 and 6), electron-rich (entries 2−4), or electron-poor (entry 5) character were tolerated. With the sterically demanding substrate **1f** containing a 1-naphthyl group, the yield was only 30% and significant starting material remained (entry 6). Furthermore, substrates containing a heteroaryl (entry 7) or a cycloalkyl group (entry 8) underwent conjugate allylation successfully. With alkylidene malonate **1i**, the allylation product **3i** was isolated in a modest 47% yield due to the presence of minor, unidentified side reactions. In addition to substrates prepared from dimethyl malonate, diethyl malonate-derived acceptors were tolerated (entries 10 and 11), and in the case of substrate **1j**, a larger scale reaction (4.00 mmol) proceeded successfully to provide **3j** in 91% yield (entry 10).

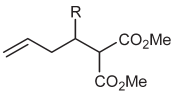
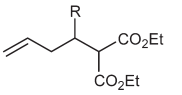
As expected, the less nucleophilic allyltrimethylsilane (**4a**)[19] proved to be an inferior allylating reagent under these conditions, with generally only low conversions into the products **3** observed. However, use of an excess of allyltrimethylsilane (5.0 equiv) at 40 °C under more dilute conditions (0.125 M) in dichloroethane allowed product **3a** to be isolated in 55% yield (eq 1). With more concentrated conditions, products resulting from competitive oligomerization were detected.



Current catalytic conjugate allylations are restricted in that with few exceptions,[5a] only the additions of simple allyl groups are described. We were therefore keen to explore whether the conditions employed in Table 2 could also be applied to the conjugate addition of more highly substituted allyl nucleophiles,

Table 2. Yb-Catalyzed Allylation of Alkylidene Malonates with Allyltributylstannane[a]

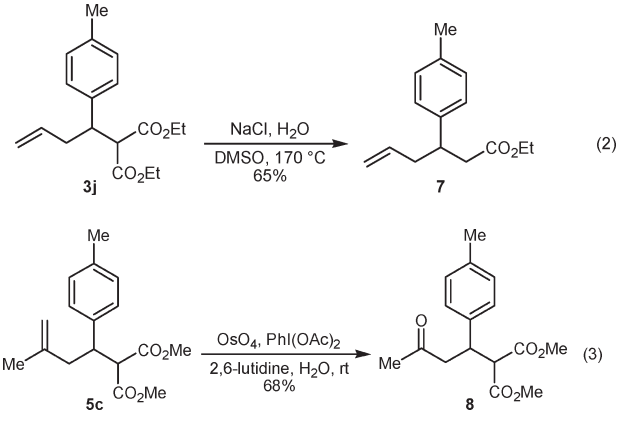


entry	product			yield (%)[b]
1		R = Ph	**3a**	73
2		R = 3-MeC_6H_4	**3b**	61
3		R = 4-MeC_6H_4	**3c**	95
4		R = 4-$MeOC_6H_4$	**3d**	60
5		R = 4-$O_2NC_6H_4$	**3e**	96
6		R = 1-naphthyl	**3f**	30
7		R = 2-thienyl	**3g**	88
8		R = cyclohexyl	**3h**	75
9		R = CH_2CH_2Ph	**3i**	47
10		R = 4-MeC_6H_4	**3j**	91[c]
11		R = Me	**3k**	75

[a] Reactions were conducted with 0.50 mmol of **1a**−**i** in 2 mL of CH_2Cl_2. [b] Isolated yield. [c] Conducted with 4.00 mmol of **1c** in 10 mL of CH_2Cl_2.

and we were pleased to discover that commercially available methallyltrimethylsilane (**4b**) provided good results. Reactions with this reagent again tolerated a wide range of alkylidene malonate substrates, providing methallylated products **5a**−**i** in 65−95% yield (Table 3, entries 1−9). In similar fashion, trimethyl(2-phenylallyl)silane proved to be a competent nucleophile, providing conjugate allylation products **6a**−**c** with representative alkylidene malonates **1d**, **1f**, and **1i** (entries 10−12).

To demonstrate the utility of the products, further manipulation reactions were conducted. For example, Krapcho decarboxylation[20] of **3j** proceeded smoothly to provide **7** in 65% yield (eq 2), while oxidative cleavage of the methallyl group of **5c** was accomplished in 68% yield with $OsO_4/PhI(OAc)_2$/2,6-lutidine[21] (eq 3).



In conclusion, ytterbium-catalyzed conjugate allylations of alkylidene malonates with allylsilanes and allyltributylstannane

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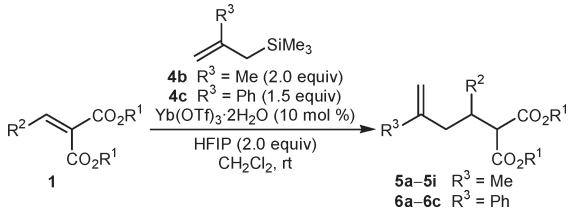
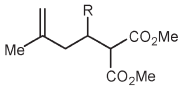
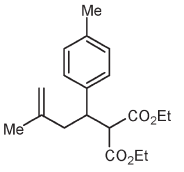
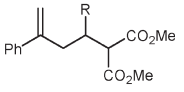
Table 3. Yb-Catalyzed Allylation of Alkylidene Malonates with Allylsilanes.[a]



entry	product			yield (%)[b]
1		R = Ph	**5a**	85
2		R = 3-MeC$_6$H$_4$	**5b**	79
3		R = 4-MeC$_6$H$_4$	**5c**	65
4		R = 4-MeOC$_6$H$_4$	**5d**	65
5		R = 4-O$_2$NC$_6$H$_4$	**5e**	82
6		R = 2-thienyl	**5f**	95
7		R = cyclohexyl	**5g**	89
8		R = CH$_2$CH$_2$Ph	**5h**	84
9			**5i**	71
10		R = 4-MeOC$_6$H$_4$	**6a**	95
11		R = 2-thienyl	**6b**	65
12		R = CH$_2$CH$_2$Ph	**6c**	49

[a] Reactions were conducted with 0.50 mmol of **1** in 2 mL of CH_2Cl_2. [b] Isolated yield.

have been developed. A range of β-substituents on the alkylidene malonate are tolerated, and compared with existing catalytic conjugate allylation reactions,[2−7] this work extends the scope of the nucleophile to substituted allylating reagents. Future work will focus on the development of enantioselective variants of these reactions.

EXPERIMENTAL SECTION[22]

Alkylidene malonates **1a**−**1e**,[23] **1f**,[13a] **1g**,[23] **1h**,[23] **1i**,[24] and **1j**[25] are known, and were prepared by the reaction of the appropriate dialkyl malonate with the appropriate aldehyde in the presence of piperidine and acetic acid in toluene under Dean−Stark conditions.[15] Alkylidene malonate **1k** is commercially available.

Dimethyl 2-(3-methylbenzylidene)malonate (1b): A solution of dimethyl malonate (3.96 g, 30.0 mmol), 3-methylbenzaldehyde (3.00 g, 25.0 mmol), AcOH (0.25 mL, 0.40 mmol), and piperidine (0.38 mL, 0.40 mmol) in toluene (25 mL) was heated to 120 °C for 18 h in a round-bottomed flask fitted with a Dean−Stark apparatus. The reaction was cooled to room temperature, diluted with Et_2O, and washed with 1 M HCl and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification of the residue by column chromatography (5% EtOAc/hexane) gave the alkylidene malonate **1b** (2.38 g, 41%) as a white solid. Mp 40−41 °C; IR ($CHCl_3$) 3020, 2953, 2925, 1735 (C═O), 1629, 1438, 1375, 1217 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (1H, s), 7.29−7.22 (4H, m), 3.85 (6H, s), 2.36 (3H, s); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 167.2, 164.5, 143.1, 138.5, 132.7, 131.5, 130.2, 128.8, 126.4, 125.2, 52.6, 21.3; HRMS (ES) exact mass calcd for $C_{13}H_{15}O_4$ $[M + H]^+$ 235.0965, found 235.0962.

General Procedure A: Allylation with Allyltributylstannane. A solution of alkylidene malonate (0.50 mmol), $Yb(OTf)_3 \cdot 2H_2O$ (33 mg, 0.05 mmol), and hexafluoroisopropanol (105 μL, 1.00 mmol) was stirred in CH_2Cl_2 (2 mL) at room temperature for 10 min. Allyltributylstannane (232 μL, 0.75 mmol) was added dropwise over 1 min and the mixture was stirred at room temperature for 18 h. The reaction was filtered through a short plug of silica gel with EtOAc as eluent, and the filtrate was concentrated in vacuo. Purification of the residue by column chromatography (10% EtOAc/hexane) afforded the allylated product.

Dimethyl 2-(1-phenylbut-3-enyl)malonate (3a):[12] The title compound was prepared following General Procedure A from **1a** (110 mg, 0.50 mmol) to give a colorless oil (95 mg, 73%). IR (film) 3031, 2954, 2254, 1752 (C═O), 1734 (C═O), 1640, 1435, 1255, 1165 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.31−7.27 (2H, m), 7.23−7.17 (3H, m), 5.55 (1H, tdd, J = 17.1, 10.1, 7.0 Hz), 4.97−4.89 (2H, m), 3.78 (3H, s), 3.73 (1H, d, J = 10.6 Hz), 3.54−3.45 (1H, m), 3.45 (3H, s), 2.54−2.38 (2H, m); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.7, 168.1, 140.3, 135.1, 128.3, 128.2, 127.0, 117.1, 57.7, 52.6, 52.2, 45.3, 38.2; HRMS (ES) exact mass calcd for $C_{15}H_{22}NO_4$ $[M + NH_4]^+$ 280.1543, found 280.1548.

Allylation of 1a with allyltrimethylsilane: A solution of **1a** (110 mg, 0.50 mmol), $Yb(OTf)_3 \cdot 2H_2O$ (33 mg, 0.05 mmol), and hexafluoroisopropanol (262 μL, 2.50 mmol) was stirred in DCE (4 mL) at room temperature for 10 min. Allyltrimethylsilane (**4a**) (400 μL, 2.50 mmol) was added dropwise over 1 min and the mixture was then stirred at 40 °C for 18 h. The reaction was filtered through a short plug of silica gel with EtOAc as eluent, and the filtrate was concentrated in vacuo. Purification of the residue by column chromatography (5% EtOAc/hexane) gave **3a** (72 mg, 55%) as a colorless oil.

Dimethyl 2-[1-(3-methylphenyl)but-3-enyl]malonate (3b): The title compound was prepared following General Procedure A from **1b** (117 mg, 0.50 mmol) to give a colorless oil (83 mg, 61%). IR (film) 3079, 2954, 1751 (C═O), 1735 (C═O), 1641, 1436, 1216, 1167 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (1H, t, J = 7.5 Hz), 7.03−6.97 (3H, m), 5.55 (1H, tdd, J = 17.1, 10.1, 7.0 Hz), 4.97−4.90 (2H, m), 3.77 (3H, s), 3.71 (1H, d, J = 10.5 Hz), 3.50−3.44 (1H, m), 3.46 (3H, s), 2.49−2.39 (2H, m), 2.32 (3H, s); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 168.8, 168.1, 140.2, 137.8, 135.2, 128.9, 128.1, 127.7, 125.1, 116.9, 57.7, 52.5, 52.2, 45.2, 38.2, 21.4; HRMS (ES) exact mass calcd for $C_{16}H_{24}NO_4$ $[M + NH_4]^+$ 294.1700, found 294.1696.

Dimethyl 2-[1-(4-methylphenyl)but-3-enyl]malonate (3c):[12] The title compound was prepared following General Procedure A from **1c** (117 mg, 0.50 mmol) to give a colorless oil (129 mg, 95%). IR (film) 3006, 2953, 2253, 1752 (C═O), 1734 (C═O), 1515, 1436, 1256, 1164 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.08 (4H, br s), 5.55 (1H, tdd, J = 17.1, 10.1, 7.0, Hz), 4.97−4.89 (2H, m), 3.77 (3H, s), 3.70 (1H, d, J = 10.5 Hz), 3.46 (3H, s), 3.50−3.40 (1H, m), 2.50−2.34 (2H, m), 2.30 (3H, s); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.8, 168.2, 137.2 (C), 136.5, 135.3, 129.0, 128.0, 117.0, 57.8, 52.5, 52.2, 44.9, 38.2, 21.0; HRMS (ES) exact mass calcd for $C_{16}H_{21}O_4$ $[M + H]^+$ 277.1434, found 277.1430.

Dimethyl 2-[1-(4-methoxyphenyl)but-3-enyl]malonate (3d):[12] The title compound was prepared following General Procedure A from **1d** (125 mg, 0.50 mmol) to give a colorless oil (88 mg, 60%). IR (film) 2954, 2253, 1732 (C═O), 1514, 1467, 1179 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.11 (2H, dm, J = 8.7 Hz), 6.82 (2H, dm, J = 8.7 Hz), 5.55 (1H, tdd, J = 17.1, 10.1, 7.0 Hz), 4.97−4.85 (2H, m), 3.78 (3H, s), 3.77 (3H, s), 3.67 (1H, d, J = 10.5 Hz), 3.46 (3H, s), 3.49−3.42 (1H, m), 2.50−2.34 (2H, m); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.8, 168.2, 158.4, 135.3, 132.2, 129.2, 117.0, 113.7, 57.9, 55.1, 52.5, 52.3, 44.6, 38.3; HRMS (ES) exact mass calcd for $C_{16}H_{24}NO_5$ $[M + NH_4]^+$ 310.1649, found 310.1653.

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Dimethyl 2-[1-(4-nitrophenyl)but-3-enyl]malonate (3e):[12] The title compound was prepared following General Procedure A from **1e** (132 mg, 0.50 mmol) to give a colorless oil (131 mg, 86%). IR (film) 2954, 2253, 1734 (C═O), 1522, 1436, 1348, 1258 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 8.16 (2H, d, J = 8.8 Hz), 7.37 (2H, d, J = 8.8 Hz), 5.51 (1H, tdd, J = 17.1, 10.4, 7.1 Hz), 4.96−4.90 (2H, m), 3.80 (3H, s), 3.77 (1H, d, J = 4.6 Hz), 3.65 (1H, ddd, J = 10.2, 9.9, 4.6 Hz), 3.50 (3H, s), 2.58−2.51 (1H, m), 2.45−2.36 (1H, m); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.1, 167.6, 148.2, 146.9, 133.9, 129.2, 123.5, 118.1, 56.8, 52.8, 52.5, 44.9, 37.9; HRMS (ES) exact mass calcd for $C_{15}H_{21}N_2O_6$ $[M + NH_4]^+$ 325.1394, found 325.1398.

Dimethyl 2-[1-(3-naphthyl)but-3-enyl]malonate (3f): The title compound was prepared following General Procedure A from **1f** (135 mg, 0.50 mmol) to give a colorless oil (47 mg, 30%). IR (film) 2952, 2920, 1754 (C═O), 1736 (C═O), 1434, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (1H, d, J = 8.5 Hz), 7.85 (1H, d, J = 8.1 Hz), 7.74 (1H, d, J = 8.1 Hz), 7.55 (1H, ddd, J = 8.5, 6.8, 1.5 Hz), 7.49 (1H, ddd, J = 8.0, 6.8, 1.1 Hz), 7.44 (1H, t, J = 7.7 Hz), 7.36 (1H, dd, J = 7.2, 1.1 Hz), 5.53 (1H, tdd, J = 17.1, 10.1, 7.1 Hz), 4.94 (1H, br d, J = 17.1 Hz), 4.86 (1H, br d, J = 10.1 Hz), 4.55−4.53 (1H, br s), 3.99−3.96 (1H, m), 3.79 (3H, s), 3.33 (3H, s), 2.67−2.63 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 168.8, 168.2, 136.8, 134.8, 133.9, 131.9, 128.8, 127.5, 126.1, 125.5, 125.1, 124.0, 123.2, 117.3, 57.2, 52.6, 52.2, 38.3, 38.2; HRMS (ES) exact mass calcd for $C_{19}H_{24}NO_4$ $[M + NH_4]^+$ 330.1700, found 330.1703.

Dimethyl 2-(1-thiophen-2-ylbut-3-enyl)malonate (3g): The title compound was prepared following General Procedure A from **1g** (113 mg, 0.50 mmol) to give a colorless oil (118 mg, 88%). IR (film) 3077, 2953, 2253, 1734 (C═O), 1640, 1436, 1262, 1161 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.17 (1H, d, J = 5.1 Hz), 6.92−6.89 (1H, m), 6.85 (1H, d, J = 3.4 Hz), 5.65 (1H, tdd, J = 17.1, 10.1, 7.0 Hz), 5.04−4.97 (2H, m), 3.84 (1H, dt, J = 9.4, 4.9 Hz), 3.76 (3H, s), 3.70 (1H, d, J = 9.8 Hz), 3.55 (3H, s), 2.58−2.41 (2H, m); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.3, 167.9, 143.5, 134.7, 126.4, 125.6, 124.1, 117.6, 58.3, 52.6, 52.4, 40.6, 39.1; HRMS (ES) exact mass calcd for $C_{13}H_{20}NO_4S$ $[M + NH_4]^+$ 286.1108, found 286.1112.

Dimethyl 2-(1-cyclohexylbut-3-enyl)malonate (3h): The title compound was prepared following General Procedure A (0.50 mmol) from **1h** (113 mg) to give a colorless oil (101 mg, 75%). IR (film) 2929, 2853, 2253, 1729 (C═O), 1639, 1435, 1242, 1162 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.78−5.68 (1H, m), 5.03−4.95 (2H, m), 3.72 (3H, s), 3.69 (3H, s), 3.50 (1H, d, J = 7.5 Hz_2), 2.31−2.05 (3H, m), 1.75−1.72 (2H, m), 1.66−1.61 (3H, m), 1.45−1.35 (1H, m), 1.28−0.94 (5H, m); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.8, 168.5, 137.7, 116.0, 53.7, 52.3, 52.1, 43.6, 40.3, 33.5, 30.8, 29.1, 26.8, 26.7, 26.5; HRMS (ES) exact mass calcd for $C_{15}H_{25}O_4$ $[M + H]^+$ 269.1747, found 269.1749.

Dimethyl 2-(1-phenethylbut-3-enyl)malonate (3i): The title compound was prepared following General Procedure A from **1i** (124 mg, 0.50 mmol) to give a colorless oil (68 mg, 47%). IR (film) 3028, 2952, 2256, 1734 (C═O), 1436, 1254, 1195 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) zδ 7.30−7.26 (2H, m), 7.21−7.16 (3H, m), 5.80−5.72 (1H, m), 4.97−4.90 (2H, m), 3.73 (3H, s), 3.73 (3H, s), 3.52 (1H, d, J = 7.2 Hz), 2.72−2.66 (1H, m), 2.64−2.58 (1H, m), 2.36−2.29 (1H, m), 2.27−2.19 (2H, m), 1.77−1.64 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.3, 169.2, 141.9, 135.4, 128.4, 128.3, 125.9, 117.5, 54.5, 52.3, 37.7, 35.4, 33.1, 32.8; HRMS (ES) exact mass calcd for $C_{17}H_{26}NO_4$ $[M + NH_4]^+$ 308.1856, found 308.1859.

Diethyl 2-[1-(4-methylphenyl)but-3-enyl]malonate (3j):[12] A solution of **1j** (1.05 g 4.00 mmol), $Yb(OTf)_3 \cdot 2H_2O$ (248 mg, 0.40 mmol), and hexafluoroisopropanol (0.84 mL, 8.00 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 10 min. Allyltributylstannane (1.8 mL, 6.0 mmol) was added over 1 min and the mixture was stirred at room temperature for 18 h. The reaction was filtered through a short plug of silica gel with EtOAc as eluent, and the filtrate was concentrated in vacuo. Purification of the residue by column chromatography (10% EtOAc/hexane) gave the allylation product **3j** (1.10 g, 91%) as a colorless oil. IR (film) 3078, 2982, 2936, 2253, 1751 (C═O), 1718 (C═O), 1514, 1444, 1252, 1177 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.08 (4H, br, s), 5.56 (1H, tdd, J = 17.1, 10.1, 7.0 Hz), 4.97−4.88 (2H, m), 4.24 (2H, q, J = 7.1 Hz), 3.91 (2H, q, J = 7.1 Hz), 3.66 (1H, d, J = 10.7 Hz), 3.46 (1H, ddd, J = 10.7, 9.6, 4.6 Hz), 2.52−2.35 (2H, m), 2.30 (3H, s), 1.29 (3H, t, J = 7.1 Hz), 0.98 (3H, t, J = 7.1 Hz); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.4, 167.8, 137.3, 136.4, 135.3, 128.9, 128.2, 116.9, 61.5, 61.1, 58.0, 44.9, 38.4, 21.0, 14.1, 13.7; HRMS (ES) exact mass calcd for $C_{18}H_{25}O_4$ $[M + H]^+$ 305.1747, found 305.1750.

Dimethyl 2-(1-methylbut-3-enyl)malonate (3k):[26] The title compound was prepared following General Procedure A from **1k** (86 mg, 0.50 mmol) to give a colorless oil (86 mg, 75%). IR (film) 2982, 2937, 2358, 2254, 1724 (C═O), 1640, 1370, 1265, 1178 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.82−5.71 (1H, m), 5.07−5.02 (2H, m), 4.20 (4H, q, J = 7.1 Hz), 3.27 (1H, d, J = 8.0 Hz), 2.41−2.30 (1H, m), 2.26−2.19 (1H, m), 2.04−1.97 (1H, m), 1.27 (6H, t, J = 7.1 Hz), 1.00 (3H, d, J = 6.8 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.9, 168.7, 135.8, 117.1, 61.2, 61.1, 56.8, 38.7, 33.1, 16.8, 14.1; HRMS (ES) exact mass calcd for $C_{12}H_{21}O_4$ $[M + H]^+$ 229.1434, found 229.1434.

General Procedure B: Allylation with 2-Methallyltrimethylsilane. A solution of alkylidene malonate (0.50 mmol), $Yb(OTf)_3 \cdot 2H_2O$ (33 mg, 0.05 mmol), and hexafluoroisopropanol (105 μL, 1.00 mmol) was stirred in CH_2Cl_2 (2 mL) at room temperature for 10 min. 2-Methallyltrimethylsilane (175 μL, 1.00 mmol) was added dropwise over 1 min and the mixture was stirred at room temperature for 1 h. The reaction was filtered through a short plug of silica gel with EtOAc as eluent, and the filtrate was concentrated in vacuo. Purification of the residue by column chromatography (10% EtOAc/hexane, unless otherwise specified) afforded the allylated product.

Dimethyl 2-(3-methyl-1-phenylbut-3-enyl)malonate (5a): The title compound was prepared following General Procedure B from **1a** (110 mg, 0.50 mmol) to give a colorless oil (117 mg, 85%). IR (film) 2954, 2253, 1754 (C═O), 1734 (C═O), 1454, 1456, 1256, 1160 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.28−7.24 (2H, m), 7.20−7.17 (3H, m), 4.61 (1H, br s, 1H), 4.50 (1H, br s), 3.75 (3H, s), 3.69 (1H, d, J = 10.2 Hz), 3.61 (1H, td, J = 10.2, 4.7 Hz), 3.42 (3H, s), 2.45 (1H, dd, J = 13.6, 4.7 Hz), 2.37 (1H, dd, J = 13.6, 9.5 Hz), 1.62 (3H, s); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.7, 168.1, 142.3, 140.3, 128.2, 126.9, 113.2, 58.3, 52.5, 52.2, 43.9, 42.3, 22.0; HRMS (ES) exact mass calcd for $C_{16}H_{24}NO_4$ $[M + NH_4]^+$ 294.1700, found 294.1703.

Dimethyl 2-[3-methyl-1-(3-methylphenyl)but-3-enyl]-malonate (5b): The title compound was prepared following General Procedure B from **1b** (117 mg, 0.50 mmol) and purified by column chromatography (5% EtOAc/hexane) to give a colorless oil (115 mg, 79%). IR (film) 3020, 2925, 1757 (C═O), 1735 (C═O), 1436, 1310, 1216, 1161 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17−7.14 (1H, m), 7.01−6.98 (3H, m), 4.63 (1H, s), 4.53 (1H, s), 3.76 (3H, s), 3.67 (1H, d, J = 10.2 Hz), 3.59 (1H, app td, J = 10.2, 5.0 Hz), 3.45 (3H, s), 2.45 (1H, dd, J = 13.7, 5.0 Hz), 2.38 (1H, ddd, J = 13.7, 9.8, 0.5 Hz), 2.32 (3H, s), 1.64 (3H, s); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 168.8, 168.2, 142.4, 140.3, 137.6, 129.0, 128.0, 127.7, 125.2, 113.1, 58.4, 52.5, 52.2, 43.7, 42.3, 22.1, 21.4; HRMS (ES) exact mass calcd for $C_{17}H_{26}NO_4$ $[M + NH_4]^+$ 308.1856, found 308.1858.

Dimethyl 2-[3-methyl-1-(4-methylphenyl)but-3-enyl]-malonate (5c): The title compound was prepared following General Procedure B from **1c** (117 mg, 0.50 mmol) to give a colorless oil (94 mg, 65%). IR (film) 2953, 2254, 1752 (C═O), 1734 (C═O), 1514, 1436, 1256, 1160 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.07 (4H, br s), 4.62 (1H, br s), 4.52 (1H, br s), 3.76 (3H, s), 3.66 (1H, d, J = 10.2 Hz), 3.59 (1H, ddd, J = 10.2, 9.8, 4.7 Hz), 3.45 (3H, s), 2.45 (1H, dd, J = 13.6, 4.7 Hz), 2.37 (1H, dd, J = 13.6, 9.8 Hz), 2.29 (3H, s), 1.63 (3H, s); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.8, 168.2, 142.4, 137.2, 136.4, 128.9, 128.0, 113.1, 58.4, 52.5, 52.2, 43.4, 42.2, 22.0,

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21.0; HRMS (ES) exact mass calcd for $C_{17}H_{26}NO_4$ $[M + NH_4]^+$ 308.1856, found 308.1854.

Dimethyl 2-[1-(4-methoxyphenyl)-3-methylbut-3-enyl]-malonate (5d): The title compound was prepared following General Procedure B from **1d** (125 mg, 0.50 mmol) to give a colorless oil (94 mg, 65%). IR (film) 2954, 2253, 1754 (C═O), 1733 (C═O), 1513, 1435, 1249, 1179 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.11 (2H, dm, J = 8.8 Hz), 6.81 (2H, dm, J = 8.8 Hz), 4.64−4.62 (1H, m), 4.52 (1H, br s), 3.78 (3H, s), 3.76 (3H, s), 3.64 (1H, d, J = 10.3 Hz_2), 3.62−3.53 (1H, m), 3.46 (3H, s), 2.44 (1H, dd, J = 13.7, 4.4 Hz), 2.34 (1H, dd, J = 13.7, 8.9 Hz), 1.63 (3H, s); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.8, 168.2, 158.3, 142.4, 132.2, 129.2, 113.5, 113.1, 58.5, 55.0, 52.5, 52.2, 43.1, 42.3, 22.0; HRMS (ES) exact mass calcd for $C_{17}H_{26}NO_5$ $[M + NH_4]^+$ 324.1805, found 324.1808.

Dimethyl 2-[3-methyl-1-(4-nitrophenyl)but-3-enyl]malonate (5e): The title compound was prepared following General Procedure B from **1e** (132 mg, 0.50 mmol) to give a colorless oil (131 mg, 82%). IR (film) 2954, 2253, 1754 (C═O), 1735 (C═O), 1523, 1436, 1348, 1258 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.15 (2H, dm, J = 8.8 Hz), 7.38 (2H, dm, J = 8.8 Hz), 4.63 (1H, br s), 4.47 (1H, br s), 3.79 (3H, s), 3.77−3.69 (2H, m), 3.48 (3H, s), 2.51 (1H, dd, J = 13.9, 3.6 Hz), 2.41−2.32 (1H, m), 1.64 (3H, s); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.1, 167.6, 148.2, 146.9, 141.2, 129.2, 123.5, 114.0, 57.5, 52.8, 52.5, 43.4, 42.1, 21.9; HRMS (ES) exact mass calcd for $C_{16}H_{23}N_2O_6$ $[M + NH_4]^+$ 339.1551, found 339.1550.

Dimethyl 2-(3-methyl-1-thiophen-2-ylbut-3-enyl)malonate (5f): The title compound was prepared following General Procedure B from **1g** (113 mg, 0.50 mmol) to give a colorless oil (135 mg, 95%). IR (film) 3076, 2953, 2253, 1752, 1734 (C═O), 1649, 1436, 1262, 1161 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.15 (1H, dd, J = 5.0, 1.2 Hz), 6.90−6.85 (2H, m), 4.71 (1H, s), 4.63 (1H, s), 3.96 (1H, dt, J = 9.6, 5.0 Hz), 3.75 (3H, s), 3.67 (1H, d, J = 9.4 Hz), 3.54 (3H, s), 2.52 (1H, dd, J = 13.8, 5.0 Hz), 2.40 (1H, ddd, J = 13.8, 9.9, 0.6 Hz), 1.68 (3H, s); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.4, 167.9, 143.6, 141.9, 126.3, 125.6, 124.0, 113.5, 58.7, 52.5, 52.4, 43.3, 39.1, 21.8; HRMS (ES) exact mass calcd for $C_{14}H_{22}NO_4S$ $[M + NH_4]^+$ 300.1264, found 300.1266.

Dimethyl 2-(1-cyclohexyl-3-methylbut-3-enyl)malonate (5g): The title compound was prepared following General Procedure B from **1h** (125 mg, 0.50 mmol) to give a colorless oil (125 mg, 89%). IR (film) 2929, 2253, 1730 (C═O), 1449, 1435, 1261, 1160 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.74 (1H, br s), 4.70 (1H, br s), 3.71 (3H, s), 3.66 (3H, s), 3.48 (1H, d, J = 7.4 Hz_2), 2.39−2.30 (1H, m), 2.21 (1H, dd, J = 14.3, 5.7 Hz), 2.03 (1H, dd, J = 14.3, 7.8 Hz), 1.80−1.54 (5H, m), 1.70 (3H, s), 1.47−1.35 (1H, m), 1.25−0.95 (5H, m); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.8, 169.6, 144.0, 112.3, 53.8, 52.2, 52.0, 41.0, 40.0, 37.6, 30.5, 29.0, 26.8, 26.7, 26.5, 21.7; HRMS (ES) exact mass calcd for $C_{16}H_{30}NO_4$ $[M + NH_4]^+$ 300.2169, found 300.2166.

Dimethyl 2-(1-phenethyl-but-3-enyl)malonate (5h): The title compound was prepared following General Procedure B from **1i** (124 mg, 0.50 mmol) and purified by column chromatography (50% CH_2Cl_2/hexane) to give a colorless oil (128 mg, 84%). IR (film) 3028, 2952, 2254, 1734 (C═O), 1436, 1377, 1234, 1158 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30−7.27 (2H, m), 7.20−7.16 (3H, m), 4.83 (1H, s), 4.75 (1H, s), 3.75 (3H, s), 3.72 (3H, s), 3.57 (1H, d, J = 5.9 Hz), 2.65 (2H, t, J = 8.2 Hz), 2.41−2.37 (1H, m), 2.22−2.14 (2H, m), 1.82−1.66 (2H, m), 1.62 (3H, s); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.5, 169.2, 143.1, 141.9, 128.4, 128.3, 125.8, 113.1, 54.0, 52.3, 52.2, 40.2, 35.7, 32.9, 21.9; HRMS (ES) exact mass calcd for $C_{18}H_{28}NO_4$ $[M + NH_4]^+$ 322.2013, found 322.2015.

Diethyl 2-[3-methyl-1-(4-methylphenyl)but-3-enyl]malonate (5i): The title compound was prepared following General Procedure B (131 mg, 0.50 mmol) from **1j** to give a colorless oil (113 mg, 71%). IR (film) 2982, 2937, 2254, 1751 (C═O), 1719 (C═O), 1513, 1444, 1254, 1156 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.07 (4H, br s), 4.61−4.50 (1H, m), 4.51−4.50 (1H, m), 4.22 (2H, q, J = 7.1 Hz), 3.89 (2H, q, J = 7.1 Hz), 3.64−3.52 (m, 2H), 2.49−2.33 (2H, m), 2.28 (3H, s), 1.62 (3H, s), 1.28 (3H, t, J = 7.1 Hz), 0.96 (3H, t, J = 7.1 Hz); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.4, 167.8, 142.5, 137.2, 136.2, 128.7, 128.1, 113.0, 61.4, 61.0, 58.7, 43.4, 42.4, 22.1, 21.0, 14.0, 13.6; HRMS (ES) exact mass calcd for $C_{19}H_{30}NO_4$ $[M + NH_4]^+$ 336.2169, found 336.2170.

General Procedure C: Allylation with Trimethyl-(2-phenylallyl)silane. A solution of alkylidene malonate (0.50 mmol), $Yb(OTf)_3 \cdot 2H_2O$ (33 mg, 0.05 mmol), and hexafluoroisopropanol (105 μL, 1.00 mmol) was stirred in CH_2Cl_2 (2 mL) at room temperature for 10 min. Trimethyl-(2-phenylallyl)silane[27] (160 μL, 0.75 mmol) was added dropwise over 1 min and the mixture was stirred at room temperature for 1 h. The reaction was filtered through a short silica plug eluted with EtOAc as eluent, and the filtrate was concentrated in vacuo. Purification of the residue by column chromatography (10% EtOAc/hexane, unless otherwise specified) afforded the allylated product.

Dimethyl 2-[1-(4-methoxyphenyl)-3-phenylbut-3-enyl]-malonate (6a): The title compound was prepared following General Procedure C from **1d** (125 mg, 0.50 mmol) to give a yellow oil (176 mg, 95%). IR (film) 2954, 2253, 1753 (C═O), 1734 (C═O), 1514, 1250, 1179 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.34−7.24 (5H, m), 6.93 (2H, d, J = 8.7 Hz), 6.75 (2H, d, J = 8.7 Hz), 5.07 (1H, s), 4.76 (1H, s), 3.78 (3H, s), 3.76 (3H, s), 3.70 (1H, d, J = 10.4 Hz), 3.50 (1H, dt, J = 10.7, 4.3 Hz), 3.42 (3H, s), 3.12 (1H, dd, J = 13.9, 4.1 Hz), 2.66 (1H, dd, J = 13.9, 10.9 Hz); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.8, 168.1, 158.3, 145.4, 140.3, 131.8, 129.3, 128.2, 127.4, 126.4, 115.4, 113.4, 58.1, 55.1, 52.5, 52.2, 43.1, 40.0; HRMS (ES) exact mass calcd for $C_{22}H_{28}NO_5$ $[M + NH_4]^+$ 386.1962, found 386.1968.

Dimethyl 2-(3-phenyl-1-thiophen-2-yl-but-3-enyl)malonate (6b): The title compound was prepared following General Procedure C from **1g** (113 mg, 0.50 mmol) to give a yellow oil (112 mg, 65%). IR (film) 3154, 3003, 2954, 2253, 1733 (C═O), 1448, 1377, 1261, 1197 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.26−7.18 (5H, m), 7.05 (1H, d, J = 5.1 Hz), 6.77 (1H, dd, J = 5.1, 3.3 Hz), 6.60 (1H, d, J = 3.3 Hz), 5.09 (1H, s), 4.84 (1H, s), 3.78 (1H, dt, J = 10.0, 4.5 Hz), 3.69 (3H, s), 3.65 (1H, d, J = 9.4 Hz), 3.44 (3H, s), 3.10 (1H, dd, J = 14.0, 4.2 Hz), 2.68 (1H, dd, J = 14.0, 10.4 Hz); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 168.4, 167.9, 145.0, 143.1, 139.9, 128.3, 127.6, 126.4, 126.3, 125.9, 124.0, 115.7, 58.4, 52.6, 52.4, 40.8, 39.3; HRMS (ES) exact mass calcd for $C_{19}H_{24}NO_4S$ $[M + NH_4]^+$ 362.1421, found 362.1429.

Dimethyl 2-(3-phenyl-1-phenethylbut-3-enyl)malonate (6c): The title compound was prepared following General Procedure C from **1i** (124 mg, 0.50 mmol) and purified by column chromatography (50% CH_2Cl_2/hexane) to give a colorless oil (89 mg, 49%). IR (film) 3029, 2927, 2253, 1738 (C═O), 1732 (C═O), 1455, 1378, 1254, 1198 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41−7.39 (2H, m), 7.35 (2H, t, J = 7.4 Hz), 7.31−7.23 (3H, m), 7.17 (1H, t, J = 7.3 Hz), 7.08 (2H, d, J = 7.4 Hz), 5.35 (1H, s), 5.13 (1H, s), 3.73 (3H, s), 3.71 (3H, s), 3.52 (1H, d, J = 6.0 Hz), 2.79 (1H, dd, J = 14.3, 6.5 Hz), 2.66 (1H, dd, J = 14.3, 8.3 Hz), 2.59 (2H, t, J = 8.2 Hz), 2.34−2.27 (1H, m), 1.76−1.68 (2H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.3, 169.2, 146.3, 141.9, 140.3, 128.4, 128.3, 127.6, 126.4, 125.8, 115.3, 53.9, 52.3, 52.2, 37.3, 36.1, 32.7, 32.6; HRMS (ES) exact mass calcd for $C_{23}H_{30}NO_4$ $[M + NH_4]^+$ 384.2169, found 384.2170.

Ethyl 3-(4-methylphenyl)hex-5-enoate (7): A solution of **3j** (80 mg, 0.26 mmol), NaCl (20 mg, 0.34 mmol), and H_2O (25 μL, 1.39 mmol) in DMSO (0.5 mL) was heated at 170 °C for 30 min in a microwave synthesizer. After the solution was cooled to room temperature, H_2O was added and the mixture was extracted with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification of the residue by column chromatography (5% EtOAc/hexane) gave the monoester **7** (39 mg, 65%) as a colorless oil. IR (film) 3019, 2925, 1730 (C═O), 1640, 1515, 1373, 1260, 1216 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.11 (2H, J = 8.4 Hz),

7.09 (2H, J = 8.4 Hz), 5.68 (1H, tdd, J = 17.1, 10.1, 7.0 Hz), 5.03−4.97 (2H, m), 4.09−4.00 (2H, m), 3.19 (1H, app quin, J = 7.5 Hz), 2.67 (1H, dd, J = 15.3, 6.8 Hz), 2.55 (1H, dd, J = 15.3, 8.4 Hz), 2.41−2.37 (2H, m), 2.32 (3H, s), 1.16 (3H, t, J = 7.1 Hz); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 172.4, 140.5, 136.1, 135.9, 129.0, 127.3, 116.7, 60.2, 41.4, 40.73, 40.65, 21.0, 14.1; HRMS (ES) exact mass calcd for $C_{15}H_{21}O_2$ $[M + H]^+$ 233.1536, found 233.1539.

Dimethyl 2-[3-oxo-1-(4-methylphenyl)butyl]malonate (8): To a solution of **5c** (100 mg, 0.35 mmol) and $PhI(OAc)_2$ (259 mg, 0.80 mmol) in THF (1 mL) at room temperature were added H_2O (0.1 mL), 2,6-lutidine (0.1 mL, 0.86 mmol), and OsO_4 (4% soln in H_2O, 50 μL, 0.008 mmol), then the mixture was stirred at room temperature for 18 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ solution and extracted with EtOAc. The combined organic layers were washed with saturated aqueous $CuSO_4$ solution, dried ($NaSO_4$), filtered, and concentrated in vacuo. Purification of the residue by column chromatography (5% EtOAc/hexane→20% EtOAc/hexane) gave the ketone **8** (70 mg, 68%) as a colorless oil. IR (film) 3053, 3020, 2985, 1751 (C═O), 1735 (C═O), 1437, 1378, 1265, 1216 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (2H, d, J = 8.2 Hz), 7.07 (2H, d, J = 8.0 Hz), 3.94 (1H, dt, J = 9.1, 5.3 Hz), 3.72 (3H, s), 3.71 (1H, d, J = 10.8 Hz), 3.51 (3H, s), 2.92 (2H, dq, J = 16.7, 7.0 Hz), 2.29 (3H, s), 2.03 (3H, s); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 206.1, 168.6, 168.1, 137.2, 136.8, 129.2, 127.8, 57.2, 52.6, 52.3, 47.2, 40.1, 30.2, 21.0; HRMS (ES) exact mass calcd for $C_{16}H_{21}O_5$ $[M + H]^+$ 293.1384, found 293.1385.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Copies of NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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