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Ring-Opening of Vinylcyclopropane-1,1-dicarboxylates by Boronic Acids under Ligandless Palladium Catalysis in Neat Water

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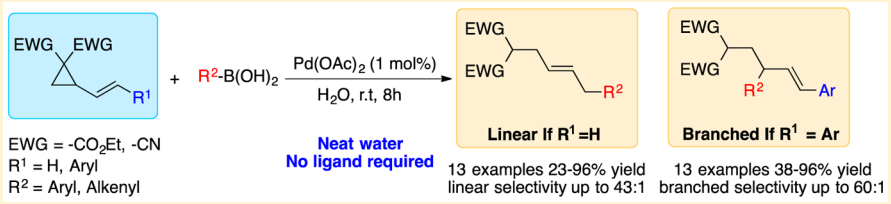
Supporting Information



ABSTRACT: We report a highly efficient ring-opening reaction of vinylcyclopropanes by boronic acids in water, using palladium nanoparticles formed from $Pd(OAc)_2$ under ligandless conditions. Unsubstituted vinylcyclopropanes provide linear addition products with high selectivity, while a switch in regioselectivity to branched products is observed for aryl-substituted vinylcyclopropanes.

INTRODUCTION

Vinylcyclopropane-1,1-dicarboxylates are highly versatile synthetic building blocks that can undergo ready C−C bond cleavage in the presence of an activating agent.[1−4] In the presence of Lewis acids, they undergo nucleophilic attack to form an acyclic product or cycloaddition to give a cyclic structure. Due to the presence of the double bond in these systems, additional reactivity is revealed through ring-opening with low-valent transition metals to give electrophilic π-allyl complexes (Scheme 1a). These complexes can undergo cycloaddition with alkenes,[5−7] aldehydes,[8,9] or imines.[10] Polarity inversion of these systems to form nucleophilic allyl complexes has also recently been demonstrated with iridium catalysts.[11] Most investigations into the reactivity of electrophilic π-allyl complexes derived from vinylcyclopropanes have centered on cycloaddition chemistry, while nucleophilic attack to give acyclic products is less developed. Nucleophilic attack is of interest because of the possibility of obtaining linear or branched ring-opened products from S_N2'- or S_N2-type ring opening, respectively. A rare example of nucleophilic attack has recently been reported by Plietker and co-workers, where they show that nucleophilic ferrate $Bu_4N[Fe^-(CO)_3(NO)]$ (TBAFe) is a catalyst for the generation of an allyl-Fe intermediate from vinylcyclopropanes, which is then subject to attack by soft carbonucleophiles, such as malonates (Scheme 1b).[12] Fürstner reported an Fe-catalyzed addition of Grignard reagents to vinylcyclopropanes to give the linear ring-opened products with moderate to good selectivity over the branched product (Scheme 1b).[13] Both of these examples provide linear structures as the major product; however, Szabó and co-workers had reported an alternative, and elegant, strategy that involved palladium-catalyzed ring-opening of vinylcyclopropane dicarboxylates to produce allylboronates which can subsequently react with iodobenzenes to give branched products (Scheme 1b).[14]

The synthetic versatility of vinylcyclopropane-1,1-dicarboxylate nucleophilic ring opening would be significantly increased if the range of nucleophiles could be increased to include nonstabilized, bench-stable nucleophiles, such as boronic acids, and if both branched and linear products could be obtained in a single step. An attractive feature of vinylcyclopropane-1,1-dicarboxylate nucleophilic ring-opening is the traceless nature of the process, which is highly atom-economical. To further enhance the credentials of reactions involving vinylcyclopropanes, we sought out a catalyst system that was free of ligands and could operate in an aqueous system. This would allow potential application to bioorthogonal reactivity for protein labeling.[15] The use of an amphiphilic palladium(II) pincer complex in water has been reported to form vesicles that catalyze the addition of boronic acids to vinyl epoxide but display poor regioselectivity and utilize a complex catalyst.[16] On the other hand, it has been shown that palladium nanoparticles can form in neat water from $Pd(OAc)_2$ under ligandless conditions and catalyze allyl−aryl coupling.[17]

Herein, we report the efficient and regioselective addition of boronic acids to vinylcyclopropanes, using a ligandless $Pd(OAc)_2$ precatalyst system in neat water, giving a highly efficient and selective arylation of vinylcyclopropanes to linear or branched systems depending upon the substitution pattern on the alkene (Scheme 1c).

RESULTS AND DISCUSSION

Studies commenced with diethyl 2-vinylcyclopropane-1,1-dicarboxylate (**1**), which is easily prepared from (*E*)-1,4-

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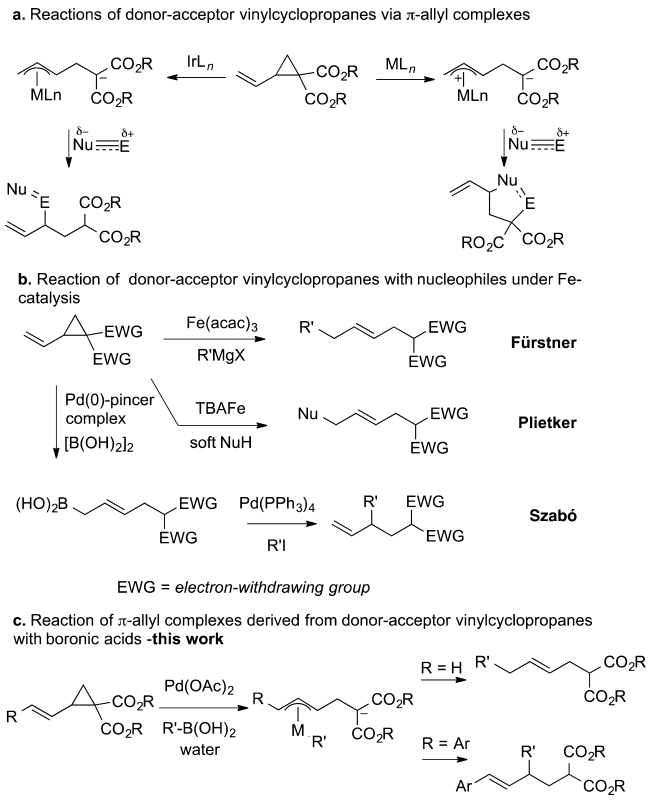
Scheme 1. Examples of Reactions of Donor–Acceptor Vinylcyclopropanes and Proposed Reaction

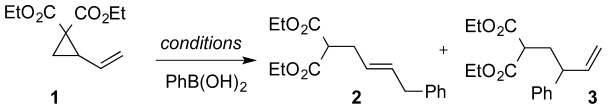


dibromobut-2-ene and diethyl malonate as the starting vinylcyclopropane in conjunction with phenylboronic acid. Conditions that we had previously reported for the ring-opening of vinylaziridines utilizing a Pd(II) catalyst system led to ring opening (Table 1, entry 3), but the product could only be isolated in 48% with low *E*/Z selectivity and accompanied by a significant amount of an inseparable impurity.[18] We then turned our attention to a Pd(0) catalyst system (entry 2) that had been reported for the Suzuki–Miyaura coupling of allylic carbonates with arylboronic acids.[19] These conditions returned the desired product with a good linear/branched and *trans*/*cis* ratio but in moderate conversion and yield. In an attempt to identify a simple catalyst system without ligands, we turned our attention to the use of $Pd(OAc)_2$ in water, a system which has been reported to produce Pd(0) nanoparticles in the presence of boronic acids.[17] Under these conditions, vinylcyclopropane **1** reacted smoothly with phenylboronic acid to provide the linear *trans* ring-opened product in high yield and selectivity (entry 1). Importantly, these conditions negated the use of additional ligands or organic solvents, rendering the process operationally simple; the reaction could also be carried out in air. The importance of the catalyst was highlighted by the observation that under aqueous conditions in the absence of any catalyst a low conversion to a roughly equal amount of branched/linear product was observed (entry 4). Low conversion was also observed when the reaction was carried out in wet THF (entry 5), and only trace product was observed in anhydrous THF (entry 6). Using $Pd(PPh_3)_4$ as an alternative source of Pd(0) proved ineffective with no product being observed (entry 7).

Using the optimized conditions, a range of boronic acids were added to vinylcyclopropane **1** in generally high yield and linear selectivity (Table 2). A range of aryl- and alkenylboronic acids proved effective, giving generally excellent yields and linear *trans* selectivity. Electron-deficient arylboronic acids generally gave the desired product in excellent yield (entries 2–5, 7, 9, and 10). Ortho substitution was also tolerated (entry 5). The yield was lower for more electron-rich systems and naphthyl-derived boronic acids (entry 6, 8, and 11). A cyano group could also be tolerated as the electron-withdrawing group on the vinylcyclopropane (entry 13). Alkenylboronic acids could also be coupled in moderate yield and with complete linear selectivity. (entry 12).

In order to see if branched ring-opened products could be obtained, attention was turned to vinycyclopropanes **4** that are substituted with an aryl group on the olefin unit (Table 3). These vinylcyclopropanes can be simply prepared by cross-metathesis between **1** and the corresponding commercially available styrene. Gratifyingly, using the previously optimized reaction conditions, branched alkene **5** was obtained as the major product over the linear product **6**. The branched products **5** were also obtained solely as *E*-isomers. The scope of this ring-opening was explored with a range of arylboronic acids and proved to be general, providing high or exclusive selectivity for the branched product in each case. A range of functional groups, including halides (entries 2, 4, and 5), esters (entry 6), and ketones (entry 3), were tolerated. Both electron-rich (entry 8) and highly electron-deficient boronic acids could be used (entry 7). Ortho-substituted boronic acids could also be used, but a drop in yield was observed (entry 5); in addition, pent-1-en-1-ylboronic acid, which gave a moderate yield in Table 2,

Table 1. Selected Optimization Conditions



1 2 3

entry	conditions	yield (%)	selectivity **2**:**3**[a]
1	$Pd(OAc)_2$ (1 mol %), H_2O	84	**11.5**:1 (*E*/Z = 98:2)
2	$Pd(OAc)_2$ (2 mol %), PPh_3 (4 mol %), THF/H_2O	51	**8.7**:1 (*E*/Z = 95:5)
3	$Pd(OAc)_2$ (10 mol %), Phen (15 mol %), $AgSbF_6$ (10 mol %), DCE	48[b]	only **2** (*E*/Z = 67:33)
4	no catalyst, H_2O	29[c]	**1.2**:1 (only *E* observed)
5	$Pd(OAc)_2$, THF/H_2O[d]	26[c]	only linear *E* observed
6	$Pd(OAc)_2$, THF	trace	only linear *E* observed
7	$Pd(PPh_3)_4$, H_2O[e]	NR	N/A

[a]Ratios measured from the ^1H NMR of the crude reaction mixture. [b]Inseparable impurity also formed. [c]Conversion, product not isolated. [d]5 equiv of distilled water used. [e]The reaction was carried out under nitrogen.

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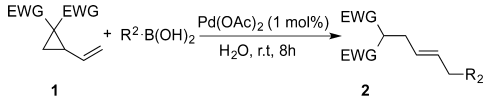
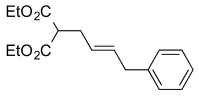
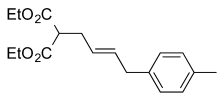
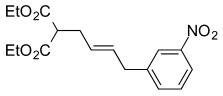
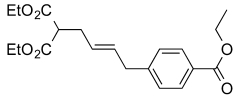
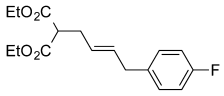
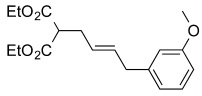
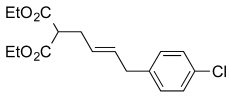
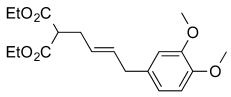
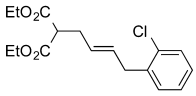
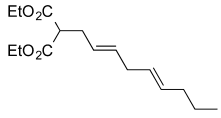
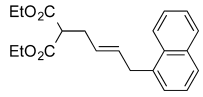
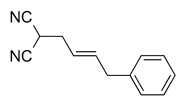
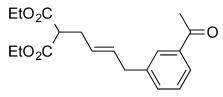
Table 2. Reaction Scope for Linear Product with Respect to Boronic Acid

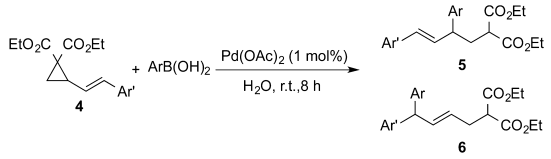


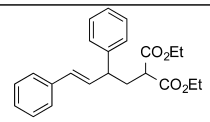
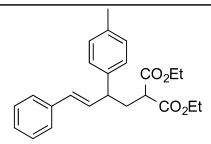
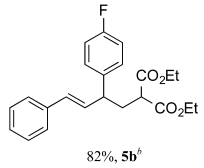
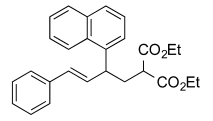
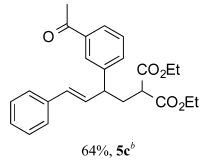
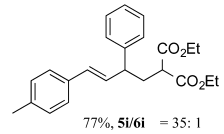
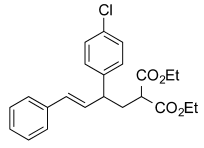
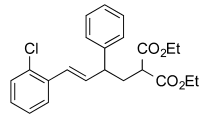
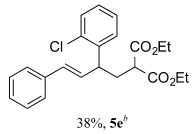
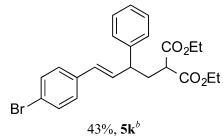
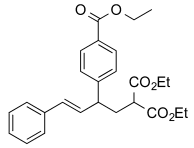
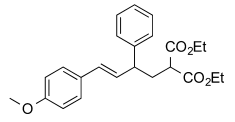
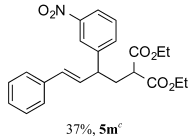
1 2

Entry	Product[a]	Entry	Product[a]
1	 84%, **2a/3a** = 11.5: 1.0 *E*/*Z*= 98: 2	8	 48%, **2h/3h** = 20.4: 1.0 *E*/*Z*= 96: 4
2	 95%, **2b/3b** = 45.9: 1.0 *E*/*Z*= 94: 6	9	 90%, **2i/3i** = 9.7: 1.0 *E*/*Z*= 96: 4
3	 86%, **2c/3c** = 25.0: 1.0 *E*/*Z*= 95:5	10	 72%, **2j/3j** = 9.7: 1.0 *E*/*Z*= 96:4
4	 96%, **2d/3d** = 14.9: 1.0 *E*/*Z*= 94:6	11	 23%, **2k/3k** = 8.3: 1.0 *E*/*Z*= 93:7
5	 65%, **2e/3e** = 7.6: 1.0 *E*/*Z* = 87:13	12	 59%, **2l**[b] *E*/*Z* = 85:15
6	 36%, **2f/3f** = 5.3: 1.0 *E*/*Z*= 91:9	13	 54%, **2m/3m** = 14.8: 1.0 *E*/*Z*= 73:17
7	 61%, **2g/3g** = 18.7: 1.0 *E*/*Z*= 93:7		

[a]Ratios measured from the ^{1}H NMR of the crude reaction mixture. [b]No branched isomer observed.

Table 3. Reaction Scope with Respect to Boronic Acid for Branched Systems



Entry	Product[a]	Entry	Product[a]
1	 84%, **5a/6a** = 25: 1	8	 84%, **5g/6g** = 19:1
2	 82%, **5b**[b]	9	 72%, **5h/6h** = 4: 1
3	 64%, **5c**[b]	10	 77%, **5i/6i** = 35: 1
4	 61%, **5d/6d** = 16: 1	11	 80%, **5j/6j** = 93: 1
5	 38%, **5e**[b]	12	 43%, **5k**[b]
6	 62%, **5f/6f** = 21: 1	13	 64%, **5l/6l** = 59: 1
7	 37%, **5m**[c]		

[a]Ratios measured from the ^{1}H NMR of the crude reaction mixture; only the *E* isomer of the major product was observed. [b]No linear isomer observed.

resulted in a complex mixture of products when reacted with substituted vinylcyclopropane **4a**.

Reaction scope with respect to the Ar′ group on the vinylcyclopropane was also investigated (Table 3, entries 10–13). The high selectivity for the branched products remained for these substrates, and aryl bromides could be tolerated with no Suzuki-type products observed.

We also briefly investigated the decarboxylation of **2a** and showed this to be a facile process under Krapcho conditions to provide ester **7a** (Scheme 2).

The proposed mechanism for the reaction is shown in Scheme 3. As demonstrated by Zhang and co-workers,[17] Pd(0) nanoparticles can be generated by the reaction of palladium acetate and 2 molar equiv of arylboronic acid. In their paper, they used TEM analysis to show that Pd nanoparticles are formed by mixing $Pd(OAc)_2$ and phenylboronic acid. The ^{1}H NMR of the crude reaction mixtures in this present work also showed trace biphenyl, indicating that the $Pd(OAc)_2$ may have been reduced to Pd(0) nanoparticles. Following catalyst activation, oxidative addition to the vinylcyclopropane can occur to give the Pd–allyl complex **A**. Transmetalation likely occurs by assistance of water or alternatively the ester enolate;

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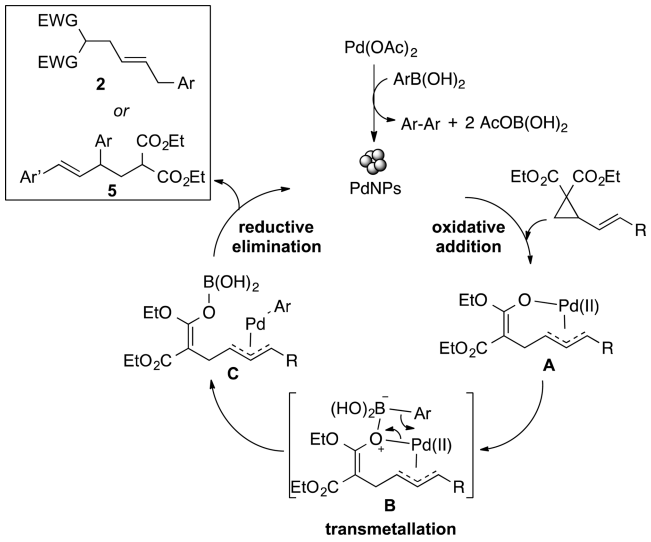
Scheme 2. Decarboxylation Reaction

Scheme 3. Proposed Reaction Mechanism



in the later case, the mechanism would be reminiscent of an intramolecular base-assisted transmetalation (**B**).[20] Furthermore, it has been postulated that facile transmetalation in the coupling of 1,1-diboron compounds is probably assisted by internal coordination between boron and an ester.[21] It is also possible that water plays a role in accelerating transmetalation by forming palladium hydroxide species that have been shown to undergo rapid transmetalation with boronic acids.[22] The resulting complex **C** can then undergo reductive elimination to provide the final ring-opened product, and it is this step that dictates the regiochemical outcome of the reaction.

Reductive elimination when R = H occurs at the least hindered carbon to provide linear products **2**. On the other hand, when R = Ar′ then the reductive elimination occurs to give the branched products **5**. The selective formation of linear product **2** when R = H can be explained by the reductive elimination occurring to place the Ar group on the terminal carbon, yielding the thermodynamically more stable internal alkene rather than the terminal alkene **3**. Furthermore, steric repulsion between Pd−Ar and the vinylcyclopropane substrate is minimized by reductive elimination to the terminal carbon. Conversely, the branched product formation when R = Ar′ can be explained as reductive elimination occurs to give the more stable conjugated system **5** over the internal alkene **6**; for this reason, the transition state for the formation of the conjugated product **5** is also likely to be lower in energy than that for the formation of **6**.

CONCLUSION

In summary, we have developed a new method for the ring-opening of activated vinylcyclopropanes with boronic acids that proceeds under mild conditions using only water as a solvent. The regioselectivity for the process is driven by the reductive elimination step in the catalytic cycle, with branched ring-opened products being obtained for vinylcyclopropane dicarboxylates that have an aryl substituent on the alkene and linear products being obtained for systems with a terminal alkene. The use of a simple Pd(II) precatalyst without the need for ancilliary ligands renders the process practical and economical. Investigation into enantioselective variants of this reaction will be the subject of future work.

EXPERIMENTAL SECTION

General Information. All reactions were performed under atmosphere of nitrogen in oven-dried glassware. Anhydrous solvents were purified by passage through a solvent purification system (purification over activated alumina, copper catalyst, and/or molecular sieves). Flash grade silica gel was used for column chromatography, and thin-layer chromatography was performed on silica gel 60 F254 aluminum-backed sheets. ^{1}H NMR and ^{13}C{^{1}H} NMR were recorded in deuterated chloroform ($CDCl_3$). Coupling constants are recorded in hertz, and chemical shifts are recorded as δ values in ppm, referenced against residual solvent peaks (^{1}H NMR) or to the ^{13}C{^{1}H} resonances of the solvent. The following abbreviations are used in the assignments of ^{1}H NMR signals: s = singlet; d = doublet; td = doublet of triplet; tdd = triplet of doublet of doublet; m = multiplet. Other reagents and starting materials were commercially available and used without further purification.

GP1. Preparation of Diethyl 2-Vinylcyclopropane-1,1-dicarboxylate (1).[23] To a solution of (*E*)-1,4-dibromobut-2-ene (3.0 g, 14.0 mmol, 1.0 equiv) in anhydrous tetrahydrofuran (70 mL) were added diethyl malonate (2.14 mL, 14.0 mmol, 1.0 equiv) and cesium carbonate (11.4 g, 35.1 mmol, 2.5 equiv). The mixture was refluxed at 60 °C. After the reaction proceeded for 16 h, the mixture was extracted with ethyl acetate (50 mL × 3), and the combined organic layer was washed with distilled water and dried over $MgSO_4$. After filtration, the solvent was removed in vacuo. The residue was purified by flash column chromatography (ethyl acetate/hexane, 10:90) to furnish a clear oily liquid in the yield of 87%. The data matched that reported previously.

Preparation of 2-Vinylcyclopropane-1,1-dicarbonitrile ***1m.***[12] This compound was synthesized in 43% yield according to the GP1 using 1,4-dibromobutene (1.0 g, 4.67 mmol, 1.0 equiv), malononitrile (339.7 mg, 5.14 mmol, 1.1 equiv), cesium carbonate (3.81 g, 11.2 mmol, 2.5 equiv), and anhydrous tetrahydrofuran (23.4 mL). Ethyl acetate cannot be completely removed due to volatility of this compound. The data matched that reported previously.

GP2. Preparation of (*E*)-Diethyl 2-styrylcyclopropane-1,1-dicarboxylate (4a).[24,25] To a solution of cinnamaldehyde (3.3 g, 25.0 mmol, 1.0 equiv) in anhydrous dichloromethane (40 mL), which was cooled with −5 °C ice/salt water, was added diethyl malonate (6.4 g, 39.9 mmol, 1.6 equiv) dropwise over 10 min. A few drops of piperidine and sodium sulfate (10 g) were then added at room temperature. The reaction mixture was stirred for 24 h, diluted with ethyl acetate (50 mL), and washed with distilled water (3 × 50 mL), and the organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude product was purified with Kugelrohr distillation to give the intermediate as a dark oil. The data matched that reported previously. To a mixture of sodium hydride (0.535 g, 22.3 mmol, 1.1 equiv, 60% dispersion in mineral oil) and trimethylsulfonium iodide (4.90 g, 22.3 mmol, 1.1 equiv) in anhydrous dimethylformamide (28.5 mL), which has been stirred at room temperature for 30 min, was added a solution of the intermediate in anhydrous dimethylformamide (12.1 mL). The reaction mixture was stirred for overnight, diluted with ethyl acetate (50 mL), washed with distilled water (3 × 50 mL), dried over $MgSO_4$, evaporated under

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reduced pressure, and purified with 15% ethyl acetate in hexane to give a yellow oil (1.00 g) as the product in 14% overall yield. The data matched that reported previously.

GP3. Preparation of Substituted Styrenyl Cyclopropane.[26] *1. Preparation of (E)-Diethyl 2-(4-Methylstyryl)cyclopropane-1,1-dicarboxylate (**4i**).* An oven-dried 10 mL flask was charged with Grubbs' second-generation catalyst (34.5 mg, 0.041 mmol, 5 mol%) under nitrogen atmosphere at room temperature. A solution of **1** (300 mg, 1.41 mmol, 1.0 equiv) and 4-methylstyrene (0.21 mL, 1.63 mmol, 2.0 equiv) in anhydrous dichloromethane (3.2 mL) was added to the flask. Ethyl acetate (50 mL) was added after which the reaction mixture was refluxed at 65 °C overnight, then it was washed with brine (3 × 30 mL), and the organic phase was dried over $MgSO_4$. After filtration, the solvent was removed in vacuo. The resulting crude product was then purified with flash column chromatography (20% ethyl acetate in hexane). The product was isolated as a light green oil (134.1 mg) in 55% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.19 (d, J = 8.1 Hz, 2H), 7.09 (d, J = 7.8 Hz, 2H), 6.60 (d, J = 15.6 Hz, 1H), 5.76 (dd, J = 15.9, 8.7 Hz, 1H), 4.27−4.14 (m, 4H), 2.72 (q, J = 8.7 Hz, 1H), 2.31 (s, 3H), 1.81 (dd, J = 7.2, 5.1 Hz, 1H), 1.64 (dd, J = 7.2, 5.1 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (75Mz, $CDCl_3$): δ 169.9, 167.9, 137.7, 134.2, 133.8, 129.5, 126.3, 123.9, 61.9, 61.8, 36.6, 31.6, 21.5, 21.3, 14.5, 14.4. HRMS (ESI-TOF): m/z 325.1403 $[C_{18}H_{22}O_4 + Na]^+$, calcd 325.1416. IR ν (cm^{-1}): 2926, 2360, 2333, 1734, 1718, 1559, 1502, 1457, 1374, 1319, 1280, 1250, 1201, 1135, 1026, 964.

*2. Preparation of (E)-Diethyl 2-(2-Chlorostyryl)cyclopropane-1,1-dicarboxylate (**4j**).* This compound was synthesized in 96% yield according to the GP3 using **1** (150 mg, 0.707 mmol, 1.0 equiv), 2-chlorostyrene (0.18 mL, 1.41 mmol, 2.0 equiv), and Grubbs' second-generation catalyst (30.0 mg, 0.0350 mmol, 5 mol%) in anhydrous dichloromethane (2.7 mL). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.41−7.38 (m, 1H), 7.34−7.31(m, 1H), 7.20−7.12 (m, 2H), 7.03 (d, J = 15.6 Hz, 1H), 5.82 (dd, J = 15.6, 9.0 Hz, 1H), 4.29−4.16 (m, 4H), 2.79 (q, J = 7.5 Hz, 1H), 1.83 (dd, J = 7.2, 4.8 Hz, 1H), 1.69 (dd, J = J = 7.2, 4.8 Hz, 1H), 1.29 (t, J = 7.2 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (75Mz, $CDCl_3$): δ 169.4, 167.5, 134.8, 132.7, 129.7, 129.7, 128.5, 127.8, 126.8, 126.5, 61.7, 61.6, 36.4, 31.1, 21.1, 14.2, 14.1. HRMS (ESI-TOF): m/z 345.0886 $[C_{17}H_{19}ClO_4 + Na]^+$, calcd 345.0870. IR ν (cm^{-1}): 1730, 1718, 1653, 1559, 1317, 1274, 1199, 1126, 963, 749.

*3. Preparation of (E)-Diethyl 2-(4-Methoxystyryl)cyclopropane-1,1-dicarboxylate (**4l**).* This compound was synthesized in 66% yield according to the GP3 using **1** (120 mg, 0.565 mmol, 1.0 equiv), 4-methoxystyrene (0.15 mL, 1.13 mmol, 2.0 equiv), and Grubbs' second-generation catalyst (24.0 mg, 0.028 mmol, 5 mol%) in anhydrous dichloromethane (2.1 mL). The compound contained 10% of homocoupled styrene which could not be completely removed following multiple attempts at chromatography. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.23 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 6.58 (d, J = 15.5 Hz, 1H), 5.68 (dd, J = 16.0, 8.5 Hz, 1H), 4.26−4.15 (m, 4H), 3.79 (s, 3H), 2.71 (q, J = 8.0 Hz, 1H), 1.80 (dd, J = 7.5, 4.5 Hz, 1H), 1.64 (dd, J = 7.5, 4.5 Hz, 1H), 1.28 (t, J = 7.0 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.7, 167.6, 159.2, 133.1, 129.6, 127.3, 122.4, 114.0, 61.6, 61.5, 55.3, 36.3, 31.4, 21.0, 14.3, 14.1. HRMS (ESI-TOF): m/z 341.1378 $[C_{18}H_{22}O_5 + Na]^+$, calcd 341.1365. IR ν (cm^{-1}): 2166, 2022, 1734, 1719, 1654, 1636, 1578, 1512, 1254, 1201, 1176, 1132, 1032, 964.

*4. Preparation of (E)-Diethyl 2-(4-Bromostyryl)cyclopropane-1,1-dicarboxylate (**4k**).* This compound was synthesized in 13% yield according to the GP3 using **1** (111.5 mg, 0.5250 mmol, 1.0 equiv), 4-bromostyrene (0.14 mL, 1.1 mmol, 2.0 equiv), and Grubbs' second-generation catalyst (22.3 mg, 0.0260 mmol, 5 mol%) in anhydrous dichloromethane (2.1 mL). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40 (d, J = 8.5 Hz, 2H), 7.15 (d, J = 8.5 Hz, 2H), 6.57 (d, J = 15.5 Hz, 1H), 5.82 (dd, J = 16.0, 9.0 Hz, 1H), 4.26−4.15 (m, 4H), 2.71 (q, J = 8.5 Hz, 1H), 1.81 (dd, J = 6.5, 4.5 Hz, 1H), 1.66 (dd, J = 6.5, 4.5 Hz, 1H), 1.29 (t, J = 7.5 Hz, 3H), 1.22 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 169.5, 167.5, 135.7, 132.4, 131.7, 127.6, 125.8, 121.3, 61.7, 61.6, 36.3, 31.0, 21.0, 14.2, 14.1. HRMS (ESI-TOF): m/z 389.0381 $[C_{17}H_{19}BrO_4 + Na]^+$, calcd 389.0364. IR ν (cm^{-1}): 2983, 1721, 1489, 1370, 1318, 1274, 1200, 1131, 1073, 1024, 1009, 964, 813.

GP4: Palladium-Catalyzed Coupling of Vinylcyclopropanes a−h with Boronic Acids in Water. To a 10 mL Schlenck flask equipped with a stir bar was added $Pd(OAc)_2$ (1 mol%), the vinylcyclopropane (1.0 equiv), arylboronic acid (1.5 equiv), and H_2O (0.25 M wrt to the vinylcyclopropane). The mixture was stirred at room temperature, and after 8 h, it was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and evaporated to dryness under reduced pressure. The residue was purified by flash column chromatography (typically ethyl acetate/hexane, 20:80) or straight dichloromethane to furnish the corresponding coupling products. Data for major isomer only reported.

*(E)-Diethyl 2-(4-Phenylbut-2-en-1-yl)malonate (**2a**).* Compound **2a** (147.0 mg) was prepared in 84% yield via the GP4 from **1** (127.7 mg, 0.2230 mmol, 1.0 equiv), phenylboronic acid (110.2 mg, 0.3350 mmol, 1.5 equiv), and palladium acetate (1.35 mg, 0.00223 mmol, 1 mol%).[27] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30−7.25 (m, 2H), 7.20−7.13 (m, 3H), 5.74−5.65 (m, 1H), 5.53−5.43 (m, 1H), 4.19−4.13 (m, 4H), 3.40 (t, J = 7.5 Hz, 1H), 3.32 (d, J = 6.9 Hz, 2H), 2.62 (t, J = 7.2 Hz, 2H), 1.24 (t, J = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 169.0, 140.3, 132.4, 128.5, 128.4, 127.0, 126.0, 61.4, 52.2, 39.0, 31.8, 14.1. HRMS (ESI-TOF): m/z 313.1428 $[C_{17}H_{22}O_4 + Na]^+$, calcd 313.1416. IR ν (cm^{-1}): 1729, 1516, 1262, 1233, 1152, 1140, 1026.

*(E)-Diethyl 2-(4-(3-Nitrophenyl)but-2-en-1-yl)malonate (**2b**).* Compound **2b** (120 mg) was prepared in 95% yield via the GP4 from **1** (80.0 mg, 0.377 mmol, 1.0 equiv), 3-nitrophenylboronic acid (94.5 mg, 0.566 mmol, 1.5 equiv), and palladium acetate (0.85 mg, 0.0038 mmol, 1 mol%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (d, J = 7.5 Hz, 1H), 8.01 (s, 1H), 7.50−7.44 (m, 2H), 5.72−5.66 (m, 1H), 5.59−5.53 (m, 1H), 4.23−4.14 (m, 4H), 3.43 (d, J = 6.5 Hz, 2H), 3.42 (t, J = 8.0 Hz, 1H), 2.65 (t, J = 6.5 Hz, 2H), 1.25 (t, J = 7.5 Hz, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.8, 148.3, 142.3, 134.8, 130.6, 129.2, 128.6, 123.3, 121.3, 61.4, 51.9, 38.4, 31.6, 14.0. HRMS (ESI-TOF): m/z 358.1271 $[C_{17}H_{21}NO_6 + Na]^+$, calcd 358.1267. IR ν (cm^{-1}): 1734, 1730, 1528, 1351, 1153, 1031, 971, 733.

*(E)-Diethyl 2-(4-(4-Fluorophenyl)but-2-en-1-yl)malonate (**2c**).* Compound **2c** (100 mg) was prepared in 86% yield via the GP4 from **1** (80.0 mg, 0.377 mmol, 1.0 equiv), 4-fluorophenylboronic acid (79.2 mg, 0.566 mmol, 1.5 equiv), and palladium acetate (0.85 mg, 0.0038 mmol, 1 mol%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.11−7.07 (m, 2H), 6.95 (t, J = 8.7 Hz, 2H), 5.71−5.61 (m, 1H), 5.51−5.42 (m, 1H), 4.17 (q, J = 7.2 Hz, 4H), 3.40 (t, J = 7.2 Hz, 1H), 3.28 (d. J = 6.0 Hz, 2H), 2.62 (t, J = 6.9 Hz, 2H), 1.24 (t, J = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.0, 161.4 (d, J = 242.2 Hz), 135.9 (d, J = 2.9 Hz), 132.2, 129.8 (d, J = 7.6 Hz), 127.1, 115.1 (d, J = 21 Hz), 61.4, 52.1, 38.1, 31.7, 14.1. HRMS (ESI-TOF): m/z 331.1315 $[C_{17}H_{21}FO_4 + Na]^+$, calcd 331.1322. IR ν (cm^{-1}): 1749, 1734, 1507, 1369, 1221, 1156, 1032, 971, 734.

*(E)-Diethyl 2-(4-(4-Chlorophenyl)but-2-en-1-yl)malonate (**2d**).* Compound **2d** (118 mg) was prepared in 96% yield via the GP4 from **1** (80.0 mg, 0.377 mmol, 1.0 equiv), 4-chlorophenylboronic acid (88.5 mg, 0.566 mmol, 1.5 equiv), and palladium acetate (0.85 mg, 0.0038 mmol, 1 mol%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 7.5 Hz, 2H), 5.67−5.60 (m, 1H), 5.52−5.45 (m, 1H), 4.17 (q, J = 7.2 Hz, 4H), 3.40 (t, J = 7.5 Hz, 1H), 3.27 (d, J = 6.3 Hz, 2H), 2.62 (t, J = 7.2 Hz, 2H), 1.24 (t, J = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.9, 138.7, 131.8, 129.8, 128.8, 128.4,127.4, 61.4, 52.0, 38.2, 31.7, 14.1. HRMS (ESI-TOF): m/z 347.1017 $[C_{17}H_{21}ClO_4 + Na]^+$, calcd 347.1026. IR ν (cm^{-1}): 1744, 1729, 1491, 1370, 1266, 1231, 1176, 1154, 1091, 1029, 1015, 970, 855, 810, 735, 703.

*(E)-Diethyl 2-(4-(2-Chlorophenyl)but-2-en-1-yl)malonate **2e**.* Compound **2e** (79.8 mg) was prepared in 65% yield (some starting material was inseparable) via the GP4 from **1** (80.0 mg, 0.377 mmol, 1.0 equiv), 2-chlorophenylboronic acid (88.5 mg, 0.566 mmol, 1.5 equiv), and palladium acetate (0.85 mg, 0.0038 mmol, 1 mol%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (d, J = 9.0 Hz, 1H), 7.26−7.10 (m, 3H), 5.73−5.63 (m, 1H), 5.51−5.42 (m, 1H), 4.15 (q, J = 6.9 Hz,

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4H), 3.42 (d, J = 6.6 Hz, 2H), 3.39 (t, J = 7.8 Hz, 2H), 2.61 (t, J = 7.8 Hz, 2H), 1.23 (t, J = 6.9 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.0, 138.0, 130.4, 130.3, 129.4, 127.7, 127.5, 126.8, 61.4, 52.1, 36.4, 31.8, 14.1. HRMS (ESI-TOF): m/z 347.1031 $[C_{17}H_{21}ClO_4 + Na]^+$, calcd 347.1026. IR ν (cm^{-1}): 1749, 1734, 1369, 1266, 1151, 1034, 736.

*(E)-Diethyl 2-(4-(Naphthalen-1-yl)but-2-en-1-yl)malonate (**2f**).* Compound **2f** (79.8 mg) was prepared in 36% yield via the GP4 from **1** (80.0 mg, 0.377 mmol, 1.0 equiv), 1-naphthalenephenylboronic acid (97.4 mg, 0.566 mmol, 1.5 equiv), and palladium acetate (0.85 mg, 0.0038 mmol, 1 mol%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.51−7.45 (m, 2H), 7.41 (t, J = 7.0 Hz, 1H), 7.29 (d, J = 7.0 Hz, 1H), 5.85−5.81 (m, 1H), 5.54−5.49 (m, 1H), 4.18−4.07 (m, 4H), 3.77 (d, J = 6.0 Hz, 2H), 3.37 (t, J = 7.0 Hz, 1H), 2.61 (t, J = 7.0 Hz, 2H), 1.19 (t, J = 6.5 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.9, 136.4, 133.9, 131.9, 131.9, 128.7, 127.3, 126.9, 126.1, 125.8, 125.6, 125.5, 124.0, 61.3, 52.1, 36.0, 31.8, 14.1. HRMS (ESI-TOF): m/z 363.1576 $[C_{21}H_{24}O_4 + Na]^+$, calcd 363.1572. IR ν (cm^{-1}): 1744, 1734, 1506, 1369, 1150, 1030, 970, 859, 777.

*(E)-Diethyl 2-(4-(3-Acetylphenyl)but-2-en-1-yl)malonate (**2g**).* Compound **2g** (78.7 mg) was prepared in 61% yield via the GP4 from **1** (80.0 mg, 0.377 mmol, 1.0 equiv), 3-acetylphenylboronic acid (92.8 mg, 0.566 mmol, 1.5 equiv), and palladium acetate (0.85 mg, 0.0038 mmol, 1 mol%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, J = 7.0 Hz, 1H), 7.73 (s, 1H), 7.38−7.33 (m, 2H), 5.70−5.65 (m, 1H), 5.53−5.49 (m, 1H), 4.20−4.12 (m, 4H), 3.39 (d, J = 7.5 Hz, 1H), 3.37 (d, J = 7.0 Hz, 2H), 2.62 (t, J = 7.0 Hz, 2H), 2.59 (s, 3H), 1.22 (t, J = 7.5 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 198.3, 168.9, 140.8, 137.3, 133.3, 131.6, 128.6, 128.3, 127.6, 126.2, 61.4, 52.0, 38.7, 31.7, 26.7, 14.1. HRMS (ESI-TOF): m/z 355.1518 $[C_{19}H_{24}O_5 + Na]^+$, calcd 355.1521. IR ν (cm^{-1}): 1734, 1727, 1684, 1269, 1175, 1155, 969, 859, 797.

*(E)-Diethyl 2-(4-(p-Tolyl)but-2-en-1-yl)malonate (**2h**).* Compound **2h** (54.6 mg) was prepared in 48% yield via the GP4 from **1** (80.0 mg, 0.377 mmol, 1.0 equiv), 4-methylphenylboronic acid (76.9 mg, 0.566 mmol, 1.5 equiv), and palladium acetate (0.85 mg, 0.0038 mmol, 1 mol%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.08 (d, J = 8.0 Hz, 2H), 7.03 (d, J = 8.0 Hz, 2H), 5.69−5.66 (m, 1H), 5.49−5.43 (m, 1H), 4.21−4.12 (m, 4H), 3.39 (t, J = 7.5 Hz, 1H), 3.28 (d, J = 7.5 Hz, 2H), 2.61 (t, J = 7.5 Hz, 2H), 2.31 (s, 3H), 1.24 (t, J = 7.5 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.9, 137.2, 135.5, 132.6, 129.1, 128.4, 126.7, 61.4, 52.2, 38.5, 31.8, 21.0, 14.1. HRMS (ESI-TOF): m/z 327.1577 $[C_{18}H_{24}O_4 + Na]^+$, calcd 327.1572. IR ν (cm^{-1}): 1743, 1734, 1559, 1507, 1369, 1153, 1030, 970, 805.

*(E)-Diethyl 2-(4-(4-(Ethoxycarbonyl)phenyl)but-2-en-1-yl)-malonate (**2i**).* Compound **2i** (90.1 mg) was prepared in 90% yield via the GP4 from **1** (58.4 mg, 0.275 mmol, 1.0 equiv), 4-ethoxycarbonylphenylboronic acid (80.1 mg, 0.413 mmol, 1.5 equiv), and palladium acetate (0.62 mg, 0.0028 mmol, 1 mol%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 8.5 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 5.71−5.65 (m, 1H), 5.53−5.48 (m, 1H), 4.36 (q, J = 7.5 Hz, 2H), 4.22−4.12 (m, 4H), 3.40 (t, J = 8.0 Hz, 1H), 3.37 (d, J = 6.5 Hz, 2H), 2.63 (t, J = 7.0 Hz, 2H), 1.39 (t, J = 7.5 Hz, 3H), 1.24 (t, J = 7.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.9, 166.6, 145.7, 131.4, 130.0, 129.7, 128.5, 127.8, 61.4, 60.8, 52.1, 38.9, 31.7, 14.4, 14.1. HRMS (ESI-TOF): m/z 385.1622 $[C_{20}H_{26}O_6 + Na]^+$, calcd 385.1627. IR ν (cm^{-1}): 1749, 1723, 1715, 1507, 1559, 1272, 1177, 1102, 1020, 857, 761, 703.

*(E)-Diethyl 2-(4-(3-Methoxyphenyl)but-2-en-1-yl)malonate (**2j**).* Compound **2j** (51.0 mg) was prepared in 72% yield via the GP4 from **1** (49.4 mg, 0.220 mmol, 1.0 equiv), 3-methoxyphenylboronic acid (50.1 mg, 0.330 mmol, 1.5 equiv), and palladium acetate (0.50 mg, 0.0022 mmol, 1 mol%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.19 (t, J = 8.0 Hz, 1H), 6.74−6.73 (m, 2H), 6.69 (s, 1H), 5.71−5.65 (m, 1H), 5.51−5.46 (m, 1H), 4.22−4.14 (m, 4H), 3.79 (s, 3H), 3.40 (t, J = 7.5 Hz, 1H), 3.29 (d, J = 6.5 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 1.24 (t, J = 7.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.0, 159.7, 141.9, 132.1, 129.3, 127.0, 120.8, 114.1, 111.3, 61.3, 55.1, 52.1, 38.9, 31.7, 14.0. HRMS (ESI-TOF): m/z 343.1519 $[C_{18}H_{24}O_5 + Na]^+$, calcd 343.1521. IR ν (cm^{-1}): 1734, 1730, 1260, 1151, 1034, 970, 858, 779.

*(E)-Diethyl 2-(4-(3,4-Dimethoxyphenyl)but-2-en-1-yl)malonate (**2k**).* Compound **2k** (18.5 mg) was prepared in 23% yield via the GP4 from **1** (48.1 mg, 0.227 mmol, 1.0 equiv), 3,4-dimethoxyphenylboronic acid (62.3 mg, 0.341 mmol, 1.5 equiv), and palladium acetate (0.510 mg, 0.00227 mmol, 1 mol%). ^1H NMR (500 MHz, $CDCl_3$): δ 6.81−6.78 (m, 1H), 6.70−6.67 (m, 2H), 5.70−5.63 (m, 1H), 5.51−5.45 (m, 1H), 4.21−4.14 (m, 4H), 3.87 (s, 3H), 3.85 (s, 3H), 3.40 (t, J = 7.5 Hz, 1H), 3.26 (d, J = 6.5 Hz, 2H), 2.62 (t, J = 7.0 Hz, 2H), 1.24 (t, J = 7.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.0, 148.9, 147.4, 133.0, 132.6, 126.7, 120.3, 111.9, 111.3, 61.4, 56.0, 55.9, 52.2, 38.5, 31.7, 14.1. HRMS (ESI-TOF): m/z 373.1618 $[C_{19}H_{26}O_6 + Na]^+$, calcd 373.1627. IR ν (cm^{-1}): 1729, 1727, 1515, 1262, 1233, 1153, 1140, 1025.

*Diethyl 2-((2E,5E)-Nona-2,5-dien-1-yl)malonate (**2l**).* Compound **2l** (64.1 mg) was prepared in 59% yield via the GP4 from **1** (82.4 mg, 0.388 mmol, 1.0 equiv), 1-pentenylphenylboronic acid (66.4 mg, 0.582 mmol, 1.5 equiv), and palladium acetate (0.870 mg, 0.00388 mmol, 1 mol %). ^1H NMR (300 MHz, $CDCl_3$): δ 5.75−5.63 (m, 1H, branched), 5.58−5.45 (m, 1H, linear *trans*), 5.38−5.21 (m, 3H, linear *trans*), 5.05−4.99 (m, 2H, branched), 4.19 (q, J = 6.9 Hz, 4H, branched + linear *trans*), 3.38 (t, J = 7.5 Hz, 1H, branched + linear *trans*), 2.68−2.65 (m, 2H, branched + linear *trans*), 2.59 (t, J = 6.9 Hz, 2H, branched + linear *trans*), 2.02−1.93 (m, 2H, branched + linear *trans*), 1.39 (m, 2H, branched + linear *trans*), 1.26 (t, J = 7.2 Hz, 6H, branched + linear *trans*), 0.88 (t, J = 7.2 Hz, 3H, branched + linear *trans*). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.0, 132.3, 131.3, 128.0, 125.8, 61.3, 52.2, 35.5, 34.7, 31.8, 22.6, 14.1, 13.7. HRMS (ESI-TOF): m/z 305.1716 $[C_{16}H_{26}O_4 + Na]^+$, calcd 305.1729. IR ν (cm^{-1}): 1751, 1734, 1559, 1457, 1228, 1151, 1096, 1033, 968, 858. Proton signals for branched isomer are reported where clearly distinguished; this was not the case for the $^{13}C\{^1H\}$, and hence, only the major linear *trans* product is reported.

*(E)-2-(4-Phenylbut-2-en-1-yl)malononitrile (**2m**).* Compound **2m** (210 mg) was prepared in a yield of 54% via the GP4 from **b** (237 mg, 2.01 mmol, 1.0 equiv), phenylboronic acid (368 mg, 3.01 mmol, 1.5 equiv), and palladium acetate (4.50 mg, 0.0201 mmol, 1 mol%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.30 (t, J = 7.0 Hz, 2H, *cis* + *trans*), 7.24−7.16 (m, 3H, *cis* + *trans*), 6.00−5.94 (m, 1H, *cis* + *trans*), 5.58−5.49 (m, 1H, *cis* + *trans*), 3.69 (t, J = 6.0 Hz, 1H, *cis* + *trans*), 3.48 (d, J = 7.0 Hz, 2H, *cis*), 3.38 (d, J = 6.5 Hz, 2H, *trans*), 2.86 (t, J = 7.5 Hz, 2H, *cis*), 2.70 (t, J = 7.0 Hz, 2H, *trans*). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.1, 137.7, 136.0 (*cis*), 128.8 (*cis*), 128.7, 128.6, 128.4 (*cis*), 126.6 (*cis*), 126.5, 122.1, 121.1 (*cis*), 112.3, 38.8, 33.8, 33.7 (*cis*), 28.7 (*cis*), 23.4, 22.9 (*cis*). HRMS (ESI-TOF): m/z 195.0914 $[C_{13}H_{12}N_2 - H]^-$, calcd 195.0922. IR ν (cm^{-1}): 2258, 1768, 1653, 1559, 1266, 1174, 1037, 971, 735, 699. N.B.: Only visible *cis* signals are highlighted in the $^{13}C\{^1H\}$ NMR.

*(E)-Diethyl 2-(2,4-Diphenylbut-3-en-1-yl)malonate (**5a**).* Compound **5a** (64.8 mg) was prepared in 82% yield via the GP4 from **4a** (64.3 mg, 0.223 mmol, 1.0 equiv), phenylboronic acid (40.8 mg, 0.335 mmol, 1.5 equiv), and palladium(II) acetate (0.500 mg, 0.002 mmol, 1 mol%). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.36−7.20 (m, 10H), 6.44 (d, J = 15.9 Hz, 1H), 6.29 (dd, J = 15.9, 8.1 Hz, 1H), 4.17 (q, J = 7.2 Hz, 4H), 3.48 (app q, J = 8.1 Hz, 1H), 3.36 (t, J = 7.5 Hz, 1H), 2.46−2.37 (m, 2H), 1.25 (app q, J = 6.9 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 169.5, 169.4, 142.8, 137.1, 132.2, 130.6, 128.7, 128.5, 127.6, 127.4, 126.8, 126.2, 61.4, 50.2, 47.0, 34.6, 14.1, 14.0. HRMS (ESI-TOF): m/z 389.1745 $[C_{23}H_{26}O_4 + Na]^+$, calcd 389.1729. IR ν (cm^{-1}): 1744, 1734, 1369, 1150, 1028, 966, 859, 746, 693.

*(E)-Diethyl 2-(2-(3-Nitrophenyl)-4-phenylbut-3-en-1-yl)malonate (**5m**).* Compound **5m** (30.1 mg) was prepared in 23% yield via the GP4 from **4a** (94.0 mg, 0.326 mmol, 1.0 equiv), 3-nitrophenylboronic acid (81.7 mg, 0.488 mmol, 1.5 equiv), and palladium acetate (0.730 mg, 0.00326 mmol, 1 mol%). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.14 (s, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.35 (d, J = 7.5 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.26−7.22 (m, 1H), 6.48 (d, J = 16.0 Hz, 1H), 6.23 (dd, J = 15.5, 8.5 Hz, 1H), 4.21−4.11 (m, 4H), 3.62 (app q J = 8.0 Hz, 1H), 3.35 (t, J = 7.5 Hz, 1H), 2.47−2.42(m, 2H), 1.28−1.22 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 169.1, 169.0, 148.5, 145.2, 136.4, 133.8, 132.0, 130.3,

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129.7, 128.6, 127.8, 126.3, 122.5, 122.0, 61.7, 61.6, 50.0, 46.8, 34.3, 14.0, 14.0. HRMS (ESI): m/z 434.1601 $[C_{23}H_{25}NO_6 + Na]^+$, calcd 434.1580. IR ν (cm^{-1}): 1744, 1734, 1719, 1528, 1349, 1152, 1027, 968, 736, 694, 690.

*(E)-Diethyl 2-(2-(4-Fluorophenyl)-4-phenylbut-3-en-1-yl)-malonate (**5b**).* Compound **5b** (69.7 mg) was prepared in 82% yield via the GP4 from **4a** (64.2 mg, 0.223 mmol, 1.0 equiv), 4-fluorophenylboronic acid (46.8 mg, 0.334 mmol, 1.5 equiv), and palladium acetate (0.50 mg, 0.00223 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.33 (d, J = 7.5 Hz, 2H), 7.30−7.27 (m, 3H), 7.26−7.20 (m, 2H), 7.01 (t, J = 8.5 Hz, 2H), 6.41 (d, J = 16.0 Hz, 1H), 6.24 (dd, J = 15.5, 7.5 Hz, 1H), 4.19−4.11 (m, 4H), 3.47 (app q, J = 7.5 Hz, 1H), 3.33 (t, J = 7.0 Hz, 1H), 2.43−2.34 (m, 2H), 1.25−1.21 (m, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 169.4, 169.3, 161.7 (d, J = 244 Hz), 138.6, 137.0, 132.0, 130.8, 129.1 (d J = 8 Hz), 128.6, 127.5, 126.3, 115.5 (d, J = 30 Hz), 61.5, 50.2, 46.3, 34.7, 14.1, 14.1. HRMS (ESI-TOF): m/z 407.1642 $[C_{23}H_{25}FO_4 + Na]^+$, calcd 407.1635. IR ν (cm^{-1}): 1750, 1729, 1507, 1221, 1158, 1027, 967, 832, 744, 693.

*(E)-Diethyl 2-(2-(4-Chlorophenyl)-4-phenylbut-3-en-1-yl)-malonate (**5d**).* Compound **5d** (65.2 mg) was prepared in 61% yield via the GP4 from **4a** (63.9 mg, 0.222 mmol, 1.0 equiv), 4-chlorophenylboronic acid (52.1 mg, 0.333 mmol, 1.5 equiv), and palladium acetate (0.500 mg, 0.00222 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.36−7.29 (m, 5H), 7.23−7.18 (m, 4H), 6.42 (d, J = 15.9 Hz, 1H), 6.23 (dd, J = 15.6, 7.8 Hz, 1H), 4.21−4.10 (m, 4H), 3.47 (app q, J = 7.8 Hz, 1H), 3.33 (t, J = 7.2 Hz, 1H), 2.45−2.33 (m, 2H), 1.24 (app q, J = 7.5 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 169.3, 169.2, 141.4, 136.9, 132.5, 131.6, 131.0, 129.0, 128.9, 128.6, 127.5, 126.3, 61.5, 50.2, 46.4, 34.5, 14.1, 14.0. HRMS (ESI-TOF): m/z 423.1347 $[C_{23}H_{25}ClO_4 + Na]^+$, calcd 423.1339. IR ν (cm^{-1}): 1750, 1729, 1490, 1369, 695.

*(E)-Diethyl 2-(2-(2-Chlorophenyl)-4-phenylbut-3-en-1-yl)-malonate (**5e**).* Compound **5e** (25.3 mg) was prepared in 38% yield via the GP4 from **4a** (47.8 mg, 0.166 mmol, 1.0 equiv), 2-chlorophenylboronic acid (38.9 mg, 0.249 mmol, 1.5 equiv), and palladium acetate (0.370 mg, 0.00166 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37−7.33 (m, 3H), 7.29−7.26 (m, 4H), 7.22−7.15 (m, 2H), 6.47 (d, J = 15.5 Hz, 1H), 6.23 (dd, J = 15.5, 8.0 Hz, 1H), 4.17 (app q, J = 7.0 Hz, 4H), 4.11−4.06 (m, 1H), 3.37 (t, J = 7.0 Hz, 1H), 2.49−2.38 (m, 2H), 1.26 (t, J = 7.0 Hz, 3H), 1.22 (t, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 169.3, 169.3, 140.2, 137.0, 134.0, 131.5, 130.6, 130.0, 128.5, 128.2, 127.8, 127.5, 127.3, 126.3, 61.5, 50.2, 42.7, 33.8, 14.1, 14.0. HRMS (ESI-TOF): m/z 423.1357 $[C_{23}H_{25}ClO_4 + Na]^+$, calcd 423.1339. IR ν (cm^{-1}): 1750, 1734, 1369, 1153, 1034, 966, 749, 697.

*(E)-Diethyl 2-(2-(Naphthalen-1-yl)-4-phenylbut-3-en-1-yl)-malonate (**5h**).* Compound **5h** (94.4 mg) was prepared in 72% yield via the GP4 from **4a** (97.8 mg, 0.340 mmol, 1.0 equiv), 1-naphthalenephenylboronic acid (87.6 mg, 0.509 mmol, 1.5 equiv), and palladium acetate (0.760 mg, 0.00340 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.20 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 7.2 Hz, 1H), 7.55−7.14 (m, 9H), 6.53 (d, J = 15.9 Hz, 1H), 6.46 (dd, J = 15.9, 7.2 Hz, 1H), 4.36 (app q, J = 6.9 Hz, 1H), 4.20 (q, J = 6.9 Hz, 2H), 4.17−4.07 (m, 2H), 3.49 (t, J = 7.2 Hz, 1H), 2.61−2.54 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H), 1.16 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 169.5, 169.5, 139.1, 137.0, 134.1, 131.8, 131.5, 131.3, 129.0, 128.5, 128.4, 127.4, 127.4, 126.3, 126.1, 125.6, 124.1, 123.2, 61.5, 50.3, 41.6, 34.5, 14.1, 14.0. HRMS (ESI-TOF): m/z 439.1882 $[C_{27}H_{28}O_4 + Na]^+$, calcd 439.1885. IR ν (cm^{-1}): 1749, 1729, 1369, 1151, 1027, 969, 778, 697.

*(E)-Diethyl 2-(2-(3-Acetylphenyl)-4-phenylbut-3-en-1-yl)-malonate (**5c**).* Compound **5c** (46.1 mg) was prepared in 60% yield via the GP4 from **4a** (54.9 mg, 0.191 mmol, 1.0 equiv), 3-acetylphenylboronic acid (46.9 mg, 0.286 mmol, 1.5 equiv), and palladium acetate (0.430 mg, 0.00191 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.85 (s, 1H), 7.81 (d, J = 7.5 Hz, 1H), 7.47 (d, J = 7.5 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.33 (d, J = 7.5 Hz, 2H), 7.28 (t, J = 7.5 Hz, 2H), 7.22−7.19 (m, 1H), 6.45 (d, J = 16.0 Hz, 1H), 6.26 (dd, J = 16.0, 8.5 Hz, 1H), 4.19−4.12 (m, 4H), 3.56 (app q, J = 8.0 Hz, 1H), 3.34 (t, J = 7.0 Hz, 1H), 2.60 (s, 3H), 2.47−2.39 (m, 2H), 1.26−1.21 (m, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 198.3, 169.5, 169.4, 143.9, 137.8, 137.0, 132.3, 131.7, 131.5, 129.2, 128.8, 127.8, 127.5, 127.2, 126.5, 61.8, 61.7, 50.4, 47.3, 34.7, 27.0, 14.3, 14.2. HRMS (ESI-MS): m/z 431.1834 $[C_{25}H_{28}O_5 + Na]^+$, calcd 431.1834. IR ν (cm^{-1}): 1749, 1734, 1727, 1684, 1559, 1507, 1369, 1267, 1151, 1027, 967, 693.

*(E)-Diethyl 2-(4-Phenyl-2-p-tolylbut-3-en-1-yl)malonate (**5g**).* Compound **5g** (61.1 mg) was prepared in 84% yield via the GP4 from **4a** (55.3 mg, 0.192 mmol, 1.0 equiv), 4-methylphenylboronic acid (39.2 mg, 0.288 mmol, 1.5 equiv), and palladium acetate (0.440 mg, 0.00192 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31 (d, J = 8.5 Hz, 2H), 7.25 (t, J = 7.5 Hz, 2H), 7.19 (t, J = 8.0 Hz, 1H), 7.12 (s, 4H), 6.42 (d, J = 16.0 Hz, 1H), 6.27 (dd, J = 16.0, 8.5 Hz, 1H), 4.22−4.10 (m, 4H), 3.44 (app q, J = 8.0 Hz, 1H), 3.34 (t, J = 8.0 Hz, 1H), 2.45−2.34 (m, 2H), 2.32 (s, 3H), 1.28−1.20 (m, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 169.5, 169.4, 139.8, 137.2, 136.3, 132.6, 130.4, 129.4, 128.5, 127.5, 127.3, 126.3, 61.4, 50.3, 46.6, 34.7, 21.1, 14.1. HRMS (ESI-TOF): m/z 403.1871 $[C_{24}H_{28}O_4 + Na]^+$, calcd 403.1885. IR ν (cm^{-1}): 1749, 1734, 1265, 1152, 1028, 967, 734, 703.

*(E)-Diethyl 2-(2-(4-(Ethoxycarbonyl)phenyl)-4-phenylbut-3-en-1-yl)malonate (**5f**).* Compound **5f** (84.2 mg) was prepared in 62% yield via the GP4 from **4a** (89.3 mg, 0.310 mmol, 1.0 equiv), 4-(ethoxycarbonyl)phenylboronic acid (90.2 mg, 0.465 mmol, 1.5 equiv), and palladium acetate (0.790 mg, 0.00310 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.00 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.0 Hz, 4H), 7.29−7.25 (m, 2H), 7.22−7.19 (m, 1H), 6.43 (d, J = 15.5 Hz, 1H), 6.25 (dd, J = 15.5, 8.5 Hz, 1H), 4.36 (q, J = 7.5 Hz, 2H), 4.19−4.10 (m, 4H), 3.55 (app q, J = 7.5 Hz, 1H), 3.31 (t, J = 7.5 Hz, 1H), 2.46−2.38 (m, 2H), 1.38 (t, J = 7.5 Hz, 3H), 1.26−1.20 (m, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ169.5, 169.4, 166.6, 148.3, 137.0, 131.5, 131.5, 130.2, 129.3, 128.8, 127.8, 127.8, 126.5, 61.7, 61.1, 50.3, 47.3, 34.6, 14.6, 14.3, 14.2. HRMS (ESI-MS): m/z 461.1942 $[C_{26}H_{30}O_6 + Na]^+$, calcd 461.1940. IR ν (cm^{-1}): 1750, 1729, 1718. 1273, 1104, 1020, 968, 855, 694.

*(E)-Diethyl 2-(2-Phenyl-4-p-tolylbut-3-en-1-yl)malonate (**5i**).* Compound **5i** (128.7 mg) was prepared in 77% yield via the GP4 from **4i** (134.1 mg, 0.4440 mmol, 1.0 equiv), phenylboronic acid (81.2 mg, 0.666 mmol, 1.5 equiv) and palladium acetate (0.994 mg, 0.000444 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31 (t, J = 7.0 Hz, 2H), 7.27−7.14 (m, 5H), 7.08 (d, J = 8.0 Hz, 2H), 6.40 (d, J = 16.0 Hz, 1H), 6.22 (dd, J = 15.5, 8.5 Hz, 1H), 4.18−4.11 (m, 4H), 3.46 (app q, J = 8.5 Hz, 1H), 3.35 (t, J = 7.5 Hz, 1H), 2.44−2.35 (m, 2H), 2.31 (s, 3H), 1.23 (app q, J = 9.0 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 169.5, 169.4, 143.1, 137.1, 134.3, 131.2, 130.5, 129.2, 128.7, 127.6, 126.7, 126.1, 61.4, 50.3, 47.0, 34.7, 21.1, 14.1, 14.0. HRMS (ESI-TOF): m/z 403.1903 $[C_{24}H_{28}O_4 + Na]^+$, calcd 403.1885. IR ν (cm^{-1}): 1749, 1730, 1653, 1507, 1457, 1369, 1150, 1097, 1030, 969, 853, 807, 761, 700.

*(E)-Diethyl 2-(4-(2-Chlorophenyl)-2-phenylbut-3-en-1-yl)-malonate (**5j**).* Compound **5j** (177.1 mg) was prepared in 80% yield via the GP4 from **4j** (218.1 mg, 0.6760 mmol, 1.0 equiv), phenylboronic acid (123.6 mg, 1.014 mmol, 1.5 equiv), and palladium acetate (1.501 mg, 0.006760 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48 (d, J = 5.5 Hz, 1H), 7.35−7.32 (m, 2H), 7.27−7.22 (m, 3H), 7.19−7.13 (m, 3H), 6.83 (d, J = 16.0 Hz, 1H), 6.26 (dd, J = 15.5, 8.5 Hz, 1H), 4.20−4.12 (m, 4H), 3.54 (app q, J = 8.5 Hz, 1H), 3.37 (t, J = 8.0 Hz, 1H), 2.47−2.40 (m, 2H), 1.23 (app q, J = 6.5 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 169.4, 169.3, 142.6, 135.2, 135.1, 132.9, 129.6, 128.8, 128.4, 127.6, 126.9, 126.9, 126.8, 126.8, 61.5, 50.2, 47.3, 34.5, 14.1, 14.1. HRMS (ESI-MS): m/z 423.1348 $[C_{23}H_{25}ClO_4 + Na]^+$, calcd 423.1339. IR ν (cm^{-1}): 1748, 1727, 1472, 1437, 1369, 1264, 1150, 1031, 966, 856, 750, 699.

*(E)-Diethyl 2-(4-(4-Methoxyphenyl)-2-phenylbut-3-en-1-yl)-malonate (**5l**).* Compound **5l** (78.8 mg) was prepared in 64% yield via the GP4 from **4l** (99.6 mg, 0.313 mmol, 1.0 equiv), phenylboronic acid (57.2 mg, 0.470 mmol, 1.5 equiv), and palladium acetate (0.700 mg, 0.000313 mmol, 1 mol%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31 (t, J = 8.0 Hz, 2H), 7.26 (t, J = 8.0 Hz, 4H), 7.21 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 8.0 Hz, 2H), 6.37 (d, J = 16.0 Hz, 1H), 6.13 (dd, J = 16.0,

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8.0 Hz, 1H), 4.18−4.10 (m, 4H), 3.77 (s, 3H), 3.45 (app q, J = 8.0 Hz, 1H), 3.35 (t, J = 7.5 Hz, 1H), 2.42−2.37 (m, 2H), 1.28−1.21 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 169.5, 169.4, 159.0, 143.1, 130.1, 130.0, 129.9, 128.7, 127.6, 127.4, 126.7, 113.9, 61.4, 55.3, 50.3, 47.1, 34.7, 14.1. HRMS (ESI-MS): m/z 419.1832 $[C_{24}H_{28}O_5 + Na]^+$, calcd 419.1834. IR ν (cm^{-1}): 1748, 1727, 1608, 1511, 1457, 1369, 1248, 1150, 1030, 967, 760, 700.

*(E)-Diethyl 2-(4-(4-Bromophenyl)-2-phenylbut-3-en-1-yl)-malonate (**5k**).* Compound **5k** (13.5 mg) was prepared in 43% yield via the GP4 from **4k** (25.6 mg, 0.0715 mmol, 1.0 equiv), phenylboronic acid (13.1 mg, 0.107 mmol, 1.5 equiv), and palladium acetate (0.160 mg, 0.0000715 mmol, 1 mol%). ^1H NMR ($CDCl_3$, 500 MHz): δ 7.40 (d, J = 8.5 Hz, 2H), 7.33 (t, J = 8.0 Hz, 2H), 7.26−7.22 (m, 3H), 7.19 (d, J = 8.5 Hz, 2H), 6.36 (d, J = 16.0 Hz, 1H), 6.27 (dd, J = 16.0, 7.5 Hz, 1H), 4.19−4.11 (m, 4H), 3.47 (app q, J = 8.0 Hz, 1H), 3.31 (t, J = 7.0 Hz, 1H), 2.45−2.36 (m, 2H), 1.22 (app q, J = 6.5 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 169.4, 169.3, 142.5, 136.0, 133.2, 131.6, 129.4, 128.8, 127.8, 127.6, 126.9, 121.1, 61.5, 50.2, 47.1, 34.5, 14.1. HRMS (ESI-MS): m/z 467.0856 $[C_{23}H_{25}BrO_4 + Na]^+$, calcd 467.0834. IR ν (cm^{-1}): 1734, 1694, 1646, 1551, 1515, 1462, 1370, 1223, 1154, 1034, 972, 858, 804, 695.

Procedure for Decarboxylation of Targeted Product 2a.[27] A solution of **2a** (108.6 mg, 0.374 mmol, 1.0 equiv) and NaCl (30.0 mg, 0.512 mmol, 1.37 equiv) in DMSO (0.62 mL) and distilled water (25.4 μL) was heated at 170 °C for 1 h in a microwave. Distilled water (20 mL) was added, and the mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified with column chromatography (15% ethyl acetate in hexane) to afford **7a** (49 mg, 60%) as a brown oily liquid. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.30−7.26 (m, 2H), 7.20−7.16 (m, 3H), 5.66−5.57 (m, 1H), 5.55−5.46 (m, 1H), 4.12 (t, J = 6.5 Hz, 2H), 3.33 (d, J = 6.5 Hz, 2H), 2.40−2.36 (m, 4H), 1.25 (q, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 173.2, 140.7, 130.2, 129.7, 128.5, 128.4, 126.0, 60.3, 49.2, 39.0, 34.3, 27.8, 14.3. HRMS (ESI-TOF): m/z 241.1208 $[C_{14}H_{18}O_2 + Na]^+$, calcd 241.1204. IR ν (cm^{-1}): 1734, 1495, 1452, 1373, 1248, 1178, 1156, 1030, 968, 745, 698.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H NMR and $^{13}C\{^1H\}$ NMR spectra of compound **4**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00672.

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Notes

The authors declare no competing financial interest.

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