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Ring-Opening of Donor−Acceptor Cyclopropanes by Boronic Acids and Potassium Organotrifluoroborates under Transition-Metal-Free Conditions

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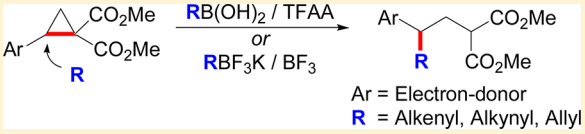
Supporting Information

ABSTRACT: The ring-opening of cyclopropane-1,1-dicarboxylates with vicinal donor aryl groups by boronic acids and potassium organotrifluoroborates under metal-free conditions has been developed. The reaction utilizes trifluoroacetic acid or boron trifluoride as promoters.



Due to their ring strain, cyclopropane rings constitute important starting materials in synthesis by their participation in ring-opening reactions, annulations or rearrangements. When donor and acceptor groups are placed vicinally on the ring, the bond between them becomes especially prone to heterolytic cleavage.[1] These donor−acceptor (D−A) cyclopropanes are useful for the preparation of a variety of open-chain 1,3-bifunctionalized scaffolds by their reaction with nucleophiles at their donor site (Scheme 1a). In particular, cyclopropane-1,1-dicarboxylates have been used as synthetic equivalents of the a^4 synthon enabling the introduction of substituents into the γ-position of carbonyl compounds (homo-Michael addition). Some of the resulting molecules have been used as advanced intermediates in the construction of pharmacologically relevant targets.[1]

Heteroatom-centered nucleophiles have been widely used toward this end.[2] As the formation of C−C bonds is a fundamental reaction in the assembly of the carbon backbone of organic molecules, the addition of carbon-centered nucleophiles such as Friedel−Crafts-reactive electron-rich aromatics[3] or enolates[4] has also drawn intense attention. Most of these reactions have been carried out under Lewis acid activation. Likewise, the direct addition of simple carbon nucleophiles, such as organocuprates[5] or Grignard reagents,[6] although less considered, has also been explored for the installment of carbon sp^3 or sp^2 centers toward the synthesis of natural products. Given the sensitivity of this type or reactions to humidity and temperature, the scope of transformations of this type could be significantly widened with the use of more bench-stable reagents such as boronic acids and their derivatives.

Boronic acids[7] and potassium organotrifluoroborates[8] are attractive reagents for the synthesis of complex molecules due to their low toxicity, thermal stability, and wide functional group tolerance. Due to their relatively low intrinsic nucleophilicity,[9] activation by transition-metal catalysis has been widely used to promote the addition of their carbon backbone to electrophilic centers. Thus, for example, the ring-opening of vinylcyclopane-1,1-dicarboxylates by boronic acids under palladium catalysis for the synthesis of 2-(2,4-diaryl-but-3-enyl)malonates has been recently featured (Scheme 1b).[10] Comparatively, reactions in which boronic acids act as nucleophiles in addition reactions under metal-free conditions remain scarce.[11,12] This is a new rapidly expanding field of organoboron chemistry which has not been yet fully explored.

On the basis of our recently reported ring-opening reaction of epoxides,[13] we envisioned the possibility of carrying out the addition of boronic acids and potassium organotrifluoroborates to cyclopropane-1,1-dicarboxylates under transition-metal-free conditions to give 2-(het)arylsubstituted but-3-enyl-, but-3-ynyl-, or pent-4-enylmalonates (Scheme 1c).

We commenced our studies by exploring the reaction between dimethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate (**1a**), which was readily prepared from dimethyl (*E*)-2-(4-methoxy-benzylidene)malonate and dimethylsulfoxonium ylide,[14] and (*E*)-2-phenylvinylboronic acid (**2a**) or potassium (*E*)-2-phenylvinyltrifluoroborate (**3a**).

Optimization of the reaction conditions using **2a** and TFAA as promoter of the reaction (Table 1, entries 1−3) led to **4a** in 81% yield (Table 1, entry 3). We also explored the possibility of catalyzing the reaction with tartaric acid (Table 1, entry 4), which had proven of use in the conjugate addition reaction of boronic acids to electron-deficient alkenes.[15] However, the yield was much lower than under TFAA catalysis. With the aim of yield optimization and widened scope in the nucleophilic partner, we turned our attention to potassium organotrifluoroborates. We observed that promotion with BF_3OEt_2 was superior to promotion with TFAA (Table 1, entries 5,6). Lower yield was observed when acetonitrile was used as solvent (Table 1, entry 7).

Under the optimized conditions, we first extended the reaction to a variety of D−A cyclopropane-1,1-dicarboxylates (**1**) and (*E*)-2-arylvinylboronic acids (**2a−d**) toward the synthesis of other 2-(2,4-diaryl-but-3-enyl)malonates (**4b−i**) (Scheme 2).

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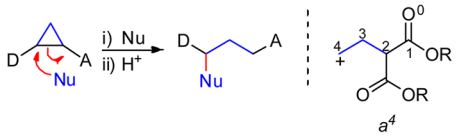
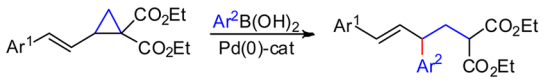
Scheme 1. Ring-Opening Reactions of D−A Cyclopropanes

a) Reactions of D-A cyclopropanes with nucleophiles



b) Pd(0)-catalyzed reaction of D-A vinylcyclopropanes with boronic acids[10]



c) This work: Transition-metal-free reaction of D-A cyclopropanes with boronic acids or potassium organotrifluoroborates.

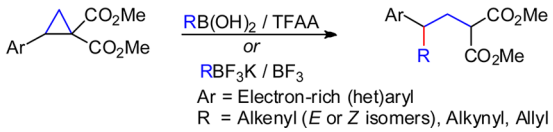
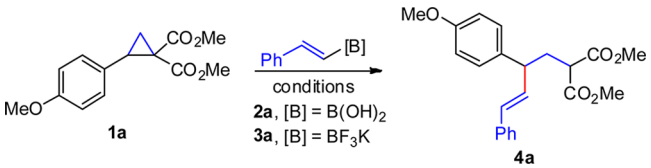


Table 1. Selected Optimization of Reaction Conditions



entry	conditions	4a (yield %)[a]
1	**2a** (1.15 equiv), TFAA (0.1 equiv), DCM, rt, 24 h	12
2	**2a** (1.15 equiv), TFAA (0.5 equiv), DCM, rt, 24 h	45
3	**2a** (1.25 equiv), TFAA (0.5 equiv), DCM, rt, 24 h	89
4	**2a** (1.25 equiv), Tartaric acid (0.5 equiv), DCM, rt, 24 h	53
5	**3a** (3.0 equiv), TFAA (0.5 equiv), DCM, rt, 24 h	37
6	**3a** (2.0 equiv), BF_3OEt_2 (2.0 equiv), DCM, 0 °C - rt, 18 h	91
7	**3a** (2.0 equiv), BF_3OEt_2 (2.0 equiv), CH_3CN, 0 °C - rt, 18 h	63

[a]Yields of isolated products after chromatography.

Treatment of **1a** in DCM solution in the presence of TFAA (General Procedure 1) with differently arylsubstituted (*E*)-2-arylvinylboronic acids led to compounds **4b−d**. Whereas **4b** and **4c** were obtained in excellent yields under these conditions, the yield of **4d**, product of the reaction with (*E*)-(4-methoxyphenyl)vinylboronic acid (**2d**), was low. On the other hand, treatment of **1a** with the corresponding organotrifluoroborate **3d** in the presence of BF_3 (General Procedure 2) permitted the synthesis of **4d** with better yield. Cyclopropanes **1b−d**, with electron-donating substituents on the phenyl ring, and the heteroarylsubstituted compound **1d**, afforded the corresponding products **4e−g** upon reaction with **2a** with good yields in the presence of TFAA (General Procedure 1). However, when the starting cyclopropane was not substituted with electron-donating substituents, the resulting malonates **4i,j** were produced in low yields. The scope of the reaction was then extended to other types of alkenyl substituents different from styryl derivatives to furnish the 2-pent-3-enylmalonates **4k,l**. However, opposite to the 2-arylvinylboronic acids **2a−c**, the reactions with the propenylboronic acids **2e,f** took place in very low yields. Therefore, we shifted to their potassium organotrifluoroborate counterparts **3e,f**. With the use of these organotrifluoroborates under BF_3 promotion (General Procedure 2), the synthesis of compounds **4k,l** took place in good yield. As expected, these results show that the *E* or *Z* geometry of the boronate is conserved throughout the reaction. In addition, we were pleased to find that BF_3-promotion of the ring-opening reactions of compounds **1a,c** could also be extended to alkynyltrifluoroborates (**3g,h**) and to potassium allyltrifluoroborate (**3i**),[16] to give the 2-(het)arylbut-3-ynylmalonates **4m−o** and the 2-het(aryl)pent-4-enylmalonates **4p,q** in good yields. In the allylation reactions, we observed that better yields were obtained when the reaction was promoted by TFAA instead of BF_3 (General Procedure 3).

To establish the stereochemical course of the ring-opening process, we have carried out the reaction of cyclopropane **1h** with **2a** (Scheme 3). The reaction led exclusively to the formation of the *trans* isomer of the ring-opened product **4r**, in agreement with an inversion of the configuration.

A reaction course which explains the formation of compounds **4** is proposed in Scheme 4. Interaction of a boronic acid with TFAA can give a mono- or a diacylboronate, and interaction with tartaric acid can form a dioxaborolanone.[17] Similarly, potassium organotrifluoroborates are known to produce organodifluoroboranes under the influence of Lewis acids.[18] In all these intermediates, the Lewis acidity of the boron atom is enhanced with respect to that of the starting boronic acid, and is able to coordinate Lewis-basic sites on the

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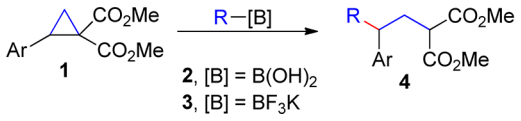
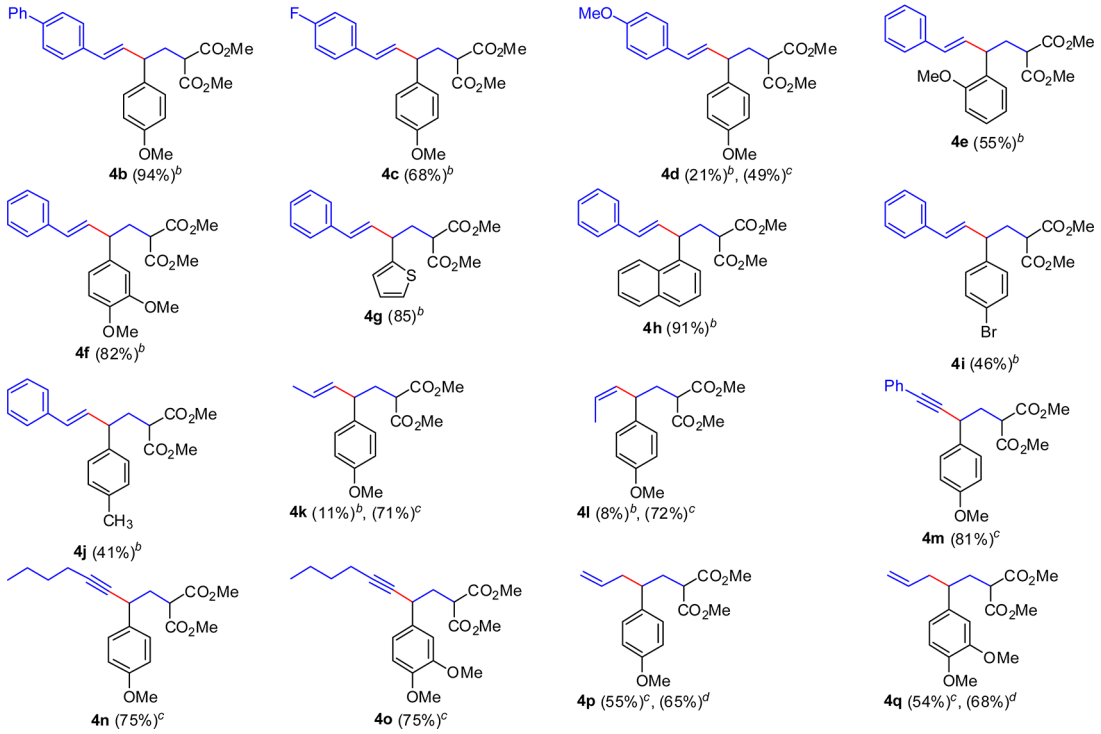
Scheme 2. Reactions of Cyclopropanes 1 with Compounds 2 and 3[a]



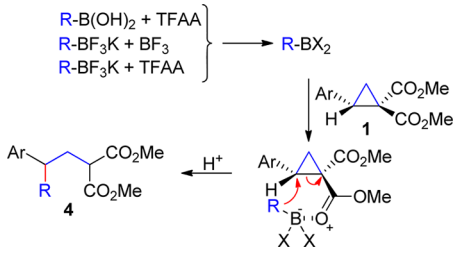
1, Ar = **a**, Ar = *p*MeO-C_6H_4; **b**, *o*-MeO-C_6H_4; **c**, 3,4-$(MeO)_2C_6H_3$; **d**, 2-Thienyl; **e**, 2-Naphthyl; **f**, *p*Br-C_6H_4; **g**, *p*Tolyl
2, **3**, R = **a**, PhCH=CH; **b**, BiphenylCH=CH; **c**, *p*-F-C_6H_4CH=CH; **d**, *p*-MeO-C_6H_4CH=CH; **e**, *trans*-Propenyl; **f**, *cis*-Propenyl; **g**, 2-Phenylethynyl; **h**, 1-Hexynyl; **i**, Allyl



[a]Yields of isolated products after chromatography. [b]General Procedure 1: **2** (1.25 equiv), TFAA (0.5 equiv), DCM, rt, 18 h. [c]General Procedure 2: **3** (2.0 equiv), $BF_3{\cdot}OEt_2$ (2.0 equiv), DCM, 0 °C to rt, 18 h. [d]General Procedure 3: **3** (2.0 equiv), TFAA (0.5 equiv), DCM, rt, 18 h.

Scheme 3. Ring-Opening of Compound 5

Scheme 4. Proposed Reaction Course



substrate. Although direct attack of the boron species under the influence of the Lewis acid cannot be ruled out, we suggest the transient formation of electron-deficient trivalent boron species (RBX_2),[19] which may coordinate with the ester groups of the substrate **1**. Internal nucleophilic attack[20] from the resulting activated complex would account for product formation.

The functionality present in the final products of the cyclopropane ring-opening reaction makes them attractive starting materials for further synthetic manipulation. Thus, for example, we have explored the sequence bishydroxylation–lactonization–decarboxylation of compound **4a** (Scheme 5). Reaction of **4a** with catalytic amounts of OsO_4 in the presence of NMO gave rise to diol **5** as a single racemic diastereomer.[21] After purification, compound **5** was cyclized into **6**, which showed a *cis* relative disposition of the aryl and hydroxybenzyl chains of the cycle, as determined by inspection of the coupling constants of the ring hydrogen atoms. This allowed us to ascertain the stereochemistry of the diastereoselective bishydroxylation step, which could be understood according to Houks model by approach of the electrophile away from the bulky $CH_2(CO_2Me)_2$ substituent.[22]

In conclusion, we have developed an efficient procedure for the ring-opening of the cyclopropane ring of D–A cyclopropanes using bench-stable boronic acids or potassium organotrifluoroborates as synthetic equivalents of alkenyl, alkynyl, and allyl carbon nucleophiles. The reactions are carried out under metal-free conditions.

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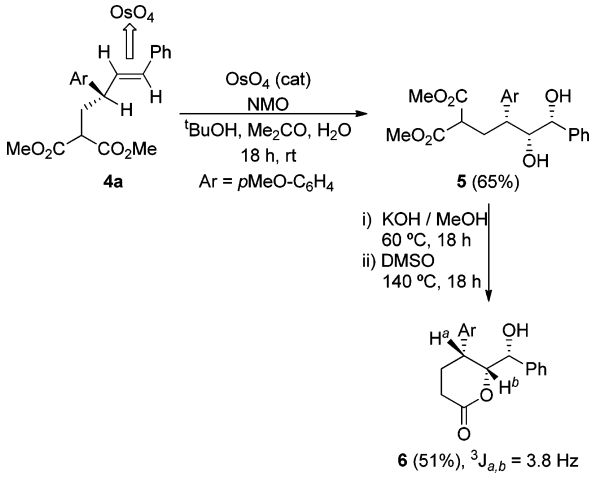
Scheme 5. Bishydroxylation−Lactonization−Decarboxylation of 4a



EXPERIMENTAL SECTION

General Considerations. All commercially available reagents including anhydrous solvents were used without purification. Compounds **1a**,[23] **1b**,[24] **1c**,[25] **1d**,[26] **1e**,[27] **1f**,[28] **1g**,[23] and **1h**[28] were prepared by cyclopropanation of the corresponding malonates following previously reported procedures. Alkenylboronic acids **2** and alkenylorganotrifluoroborates **3** were commercially available with the exception of compounds **3g** and **3h**,[29] which were prepared following previously reported procedures. Analytical thin-layer chromatography (TLC) was performed on commercial silica gel plates (0.25 mm) precoated with a fluorescent indicator. Flash chromatography (FC) was performed on silica gel F-60. Visualization was effected with ultraviolet light and ethanolic vanillin solution. NMR spectra were recorded on a 300 MHz or a 500 MHz spectrometer as specified. Chemical shifts are given in ppm. ^{1}H NMR chemical shifts were referenced to the residual solvent signal. ^{13}C NMR chemical shifts were referenced to the deuterated solvent signal. H-substitution for ^{13}C-signals have been obtained from DEPT-135 spectra. IR spectra were recorded using concentrated solutions in CH_2Cl_2/KBr disc method and reported in terms of frequency absorption (cm^{-1}).

Synthesis of Compounds 4: General Procedure 1. To a stirred solution of cyclopropane **1** (0.09 mmol) and boronic acid **2** (0.112 mmol) in anhydrous CH_2Cl_2 (0.5 mL) was added TFAA (0.045 mmol, 6.2 μL) at rt. After the mixture stirred overnight, a saturated solution of $NaHCO_3$ (0.5 mL) was added. The layers were separated, and the aqueous one was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed in vacuo to give a colorless oil which was purified by chromatography on silica gel column with hexane/ethyl acetate (8:2 v/v) as eluent to afford compounds **4**.

Synthesis of Compounds 4: General Procedure 2. To a stirred solution of cyclopropane **1** (0.09 mmol) and potassium organotrifluoroborate **3** (0.18 mmol) in anhydrous CH_2Cl_2 (0.9 mL) was added BF_3-Et_2O (0.18 mmol, 22 μL) at 0 °C. After the mixture stirred for 1 h, the reaction was allowed to warm to rt and stir overnight. The reaction was quenched with $NaHCO_3$ (0.5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed in vacuo to give a colorless oil which was purified by chromatography on silica gel column with hexane/ethyl acetate (8:2 v/v) as eluent to afford compounds **4**.

Synthesis of Compounds 4: General Procedure 3. To a stirred solution of cyclopropane **1** (0.09 mmol) and potassium organotrifluoroborate **3** (0.18 mmol) in anhydrous CH_2Cl_2 (0.6 mL) was added TFAA (0.045 mmol, 6 μL) at rt. After the mixture stirred overnight, a saturated solution of $NaHCO_3$ (0.5 mL) was added. The layers were separated, and the aqueous one was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed in vacuo to give a colorless oil which was purified by chromatography on silica gel column with hexane/ethyl acetate (8:2 v/v) as eluent to afford compounds **4**.

Thus, were prepared:

*(E)-Dimethyl 2-[2-(4-Methoxyphenyl)-4-phenylbut-3-en-1-yl]-malonate (**4a**).* Following General Procedure 1, reaction of **1a** (25 mg, 0.09 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (17.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4a** as a colorless oil (29.6 mg, 80%). R_f 0.40 (ethyl acetate:hexane = 2:8). IR ν 1751, 1736, 1511 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.35−2.52 (m, 2H), 3.39−3.48 (m, 2H), 3.72 (s, 3H), 3.73 (s, 3H), 3.81 (s, 3H), 6.28 (dd, *J* = 15.9 Hz, *J* = 7.9 Hz, 1H), 6.44 (d, *J* = 15.9 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.28−7.37 (m, 5H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.8 (CH_2), 46.3 (CH), 50.0 (CH), 52.6 (CH_3), 52.7 (CH_3), 55.3 (CH_3), 114.2 (2 × CH), 126.3 (2 × CH), 127.4 (CH), 128.6 (2 × CH), 128.7 (2 × CH), 130.3 (CH), 132.6 (CH), 134.7 (C), 137.2 (C), 158.5 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 71.81, H, 6.49. This reaction was scaled starting with 500 mg of **1a**, affording **4a** in similar yield (620 mg, 89%).

*(E)-Dimethyl 2-{4-([1,1′-Biphenyl]-4-yl)-2-(4-methoxyphenyl)but-3-en-1-yl} Malonate (**4b**).* Following General Procedure 1, reaction of **1a** (25.0 mg, 0.09 mmol) with (*E*)-2-(4-biphenyl)vinylboronic acid **2b** (25.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4b** as a colorless oil (37.4 mg, 94%). R_f 0.40 (ethyl acetate:hexane = 2:8). IR ν 1754, 1735, 1499 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.35−2.51 (m, 2H), 3.37−3.45 (m, 2H), 3.70 (s, 3H), 3.71 (s, 3H), 3.80 (s, 3H), 6.30 (dd, *J* = 15.8 Hz, *J* = 7.8 Hz, 1H), 6.45 (d, *J* = 15.8 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 7.18 (d, *J* = 8.7 Hz, 2H), 7.33−7.45 (m, 5H), 7.51−7.60 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.9 (CH_2), 46.4 (CH), 50.1 (CH), 52.7 (2 × CH_3), 55.4 (CH_3), 114.3 (2 × CH), 126.8 (2 × CH), 127.0 (2 × CH), 127.3 (2 × CH), 127.4 (CH), 128.7 (2 × CH), 128.9 (2 × CH), 129.9 (CH), 132.9 (CH), 134.8 (C), 136.3 (C), 140.2 (C), 140.9 (C), 158.6 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{28}H_{28}O_5$: C, 75.65; H, 6.35. Found: C, 75.73, H, 6.41.

*(E)-Dimethyl 2-[(4-Fluorophenyl)-2-(4-methoxyphenyl)but-3-en-1-yl]malonate (**4c**).* Following General Procedure 1, reaction of **1a** (25.0 mg, 0.09 mmol) with (*E*)-2-(4-fluorophenyl)vinylboronic acid **2c** (18.3 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4c** as a colorless oil (23.1 mg, 68%). R_f 0.40 (ethyl acetate:hexane = 2:8). IR ν 1751, 1733, 1509 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30−2.48 (m, 2H), 3.33−3.43 (m, 2H), 3.69 (s, 3H), 3.70 (s, 3H), 3.79 (s, 3H), 6.16 (dd, *J* = 15.9 Hz, *J* = 7.8 Hz, 1H), 6.36 (d, *J* = 15.9 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.97 (t, *J* = 8.7 Hz, 3H) 7.15 (d, *J* = 8.7 Hz, 2H), 7.28−7.31 (m, 1H) ppm. ^{19}F-NMR (282 MHz, $CDCl_3$) δ −115.2 ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.9 (CH_2), 46.3 (CH), 50.1 (CH), 52.7 (2 × CH_3), 55.4 (CH_3), 114.3 (2 × CH), 115.5 (2 × CH, d, J_{CF} = 21.6 Hz), 127.8 (2 × CH, d, J_{CF} = 7.9 Hz), 128.7 (2 × CH), 129.2 (CH), 132.5 (CH, d, J_{CF} = 2.2 Hz), 133.4 (C, d, *J* = 3.3 Hz), 134.7 (C), 158.6 (C), 162.2 (C, d, J_{CF} = 246.6 Hz), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{22}H_{23}FO_5$: C, 68.38; H, 6.00. Found: C, 68.44, H, 6.09.

*(E)-Dimethyl 2-[2,4-Bis(4-methoxyphenyl)but-3-en-1-yl]-malonate (**4d**).* Following General Procedure 2, reaction of **1a** (25.0 mg, 0.09 mmol) with potassium (*E*)-(4-methoxyphenyl)-vinyltrifluoroborate **3d** (43.2 mg, 0.18 mmol) and BF_3-Et_2O (22 μL, 0.18 mmol) in CH_2Cl_2 (0.9 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4d** as a colorless oil (17.1 mg, 49%). R_f 0.3 (ethyl acetate:hexane = 4:6). IR ν 1751, 1735, 1509 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30−2.47 (m, 2H), 3.34−3.41 (m, 2H), 3.69 (s, 3H), 3.70 (s, 3H), 3.79 (s, 6H), 6.10 (dd, *J* = 15.7 Hz, *J* = 8.0 Hz, 1H), 6.34 (d, *J* = 15.7 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H) ppm. ^{13}C NMR

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(75 MHz, $CDCl_3$) δ 35.0 (CH_2), 46.3 (CH), 50.1 (CH), 52.7 (2 × CH_3), 55.4 (2 × CH_3), 114.0 (2 × CH), 114.2 (2 × CH), 127.5 (2 × CH), 128.7 (2 × CH), 129.8 (CH), 130.1 (C), 130.5 (CH), 135.1 (C), 158.5 (C), 159.1 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.28, H, 6.49.

*(E)-Dimethyl 2-[2-(2-Methoxyphenyl)-4-phenylbut-3-en-1-yl]-malonate (**4e**).* Following General Procedure 1, reaction of **1b** (25.0 mg, 0.09 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (17.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4e** as a colorless oil (18.1 mg, 55%). R_f 0.40 (ethyl acetate:hexane = 2:8). IR ν 1753, 1736, 1493 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.30−2.40 (m, 1H), 2.44−2.54 (m, 1H), 3.37 (dd, *J* = 7.9 Hz, *J* = 6.8 Hz, 1H), 3.68 (s, 6H), 3.82 (s, 3H), 3.92 (q, *J* = 7.6 Hz, 1H), 6.34 (dd, *J* = 15.9 Hz, *J* = 7.5 Hz, 1H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.85−6.95 (m, 2H), 7.18−7.22 (m, 4H), 7.27−7.35 (m, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.0 (CH_2), 40.3 (CH), 50.2 (CH), 52.6 (CH_3), 52.7 (CH_3), 55.5 (CH_3), 110.9 (CH), 121.0 (CH), 126.3 (2 × CH), 127.3 (CH), 127.8 (CH), 128.2 (CH), 128.6 (2 × CH), 130.5 (CH), 131.0 (C), 132.0 (CH), 137.5 (C), 157.1 (C), 170.0 (C), 170.1 (C) ppm. Anal. Calcd for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 71.80, H, 6.63.

*(E)-Dimethyl 2-[2-(3,4-Dimethoxyphenyl)-4-phenyl-but-3-en-1-yl]malonate (**4f**).* Following General Procedure 1, reaction of **1c** (26.5 mg, 0.09 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (17.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4f** as a colorless oil (29.2 mg, 82%). R_f 0.30 (ethyl acetate:hexane = 4:6). IR ν 1752, 1733, 1514 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.31−2.50 (m, 2H), 3.36−3.44 (m, 2H), 3.70 (s, 3H), 3.71 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 6.25 (dd, *J* = 15.7 Hz, *J* = 7.7 Hz, 1H), 6.42 (d, *J* = 15.7 Hz, 1H), 6.75−6.85 (m, 3H), 7.20−7.22 (m, 1H), 7.29−7.35 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.8 (CH_2), 46.7 (CH), 50.0 (CH), 52.7 (CH_3), 52.8 (CH_3), 56.0 (CH_3), 56.1 (CH_3), 110.9 (CH), 111.5 (CH), 119.6 (CH), 126.4 (2 × CH), 127.5 (CH), 128.7 (2 × CH), 130.5 (CH), 132.5 (CH), 135.3 (C), 137.2 (C), 148.0 (C), 149.2 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.28, H, 6.47.

*(E)-Dimethyl 2-(4-Phenyl-2-(thien-2-yl)-but-3-en-1-yl)malonate (**4g**).* Following General Procedure 1, reaction of **1d** (21.6 mg, 0.09 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (17.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4g** as a yellow solid (26.1 mg, 85%). Mp: 36−38 °C. R_f 0.40 (ethyl acetate:hexane = 2:8). IR ν 1751, 1733, 1509 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.36−2.47 (m, 2H), 3.43 (t, *J* = 7.3 Hz, 1H), 3.54−3.62 (m, 1H) 3.68 (s, 3H), 3.72 (s, 3H), 6.20 (dd, *J* = 15.7 Hz, *J* = 7.6 Hz, 1H), 6.43 (d, *J* = 15.7 Hz, 1H), 7.01 (dd, *J* = 5.0 Hz, *J* = 1.2 Hz, 1H), 7.06−7.07 (m, 1H), 7.21−7.36 (m, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.5 (CH_2), 42.8 (CH), 50.0 (CH), 52.7 (CH_3), 52.8 (CH_3), 120.7 (CH), 126.1 (CH), 126.4 (2 × CH), 127.2 (CH), 127.6 (CH), 128.7 (2 × CH), 131.0 (CH), 131.7 (CH), 137.1 (C), 143.5 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{19}H_{20}O_4S$: C, 66.26; H, 5.85. Found: C, 66.34, H, 5.79.

*(E)-Dimethyl 2-[2-(Naphth-1-yl)-4-phenylbut-3-en-1-yl]malonate (**4h**).* Following General Procedure 1, reaction of **1e** (25.5 mg, 0.09 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (17.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4h** as a white solid (31.7 mg, 91%). Mp: 34−37 °C. R_f 0.50 (ethyl acetate:hexane = 2:8). IR ν 1751, 1734, 1497 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.55−2.62 (m, 2H), 3.52 (t, *J* = 7.3 Hz 1H), 3.64 (s, 3H), 3.74 (s, 3H), 4.37 (q, *J* = 7.6 Hz 1H), 6.42 (dd, *J* = 15.9 Hz, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 15.9 Hz, 1H), 7.19−7.36 (m, 5H), 7.46−7.54 (m, 4H), 7.74−7.77 (m, 1H), 7.85−7.88 (m, 1H), 8.18 (d, *J* = 8.3 Hz 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.7 (CH_2), 41.7 (CH), 50.1 (CH), 52.7 (CH_3), 52.8 (CH_3), 123.3 (CH), 124.2 (CH), 125.7 (CH), 125.8 (CH), 126.3 (CH), 126.4 (2 × CH), 127.5 (CH), 127.6 (CH), 128.7 (2 × CH), 129.1 (CH), 131.4 (CH), 131.6 (C), 131.9 (CH), 134.3 (C), 137.2 (C), 139.1 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{25}H_{24}O_4$: C, C, 77.30; H, 6.23. Found: C, 77.39, H, 6.17.

*(E)-Dimethyl 2-[2-(4-Bromophenyl)-4-phenylbut-3-en-1-yl]-malonate (**4i**).* Following General Procedure 1, reaction of **1f** (28.2 mg, 0.09 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (17.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4i** as a colorless oil (17.2 mg, 46%). R_f 0.60 (ethyl acetate:hexane = 2:8). IR ν 1752, 1732, 1497 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.31−2.46 (m, 2H), 3.34−3.44 (m, 2H), 3.69 (s, 3H) 3.71 (s, 3H), 6.21 (dd, *J* = 15.9 Hz, *J* = 7.8 Hz, 1H), 6.41 (d, *J* = 15.9 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.19−7.32 (m, 5H), 7.45 (d, *J* = 8.4 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.6 (CH_2), 46.6 (CH), 49.9 (CH), 52.8 (2 x CH_3), 120.7 (C), 126.4 (2 × CH), 127.7 (CH), 128.7 (2 × CH), 129.5 (2 × CH), 131.2 (CH), 131.6 (CH), 132.0 (2 × CH), 136.9 (C), 141.9 (C), 169.7 (C), 169.8 (C) ppm. Anal. Calcd for $C_{21}H_{21}BrO_4$: C, 60.44; H, 5.07. Found: C, 60.53, H, 4.99.

*(E)-Dimethyl 2-[4-Phenyl-2-(p-tolyl)but-3-en-1-yl]malonate (**4j**).* Following General Procedure 1, reaction of **1g** (22.3 mg, 0.09 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (17.0 mg, 0.11 mmol) and TFAA (6 μL, 0.05 mmol) in CH_2Cl_2 (0.5 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4j** as a colorless oil (12.6 mg, 41%). R_f 0.50 (ethyl acetate:hexane = 2:8). IR ν 1751, 1734, 1502 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.37−2.45 (m, 2H), 3.36−3.46 (m, 2H), 3.69 (s, 3H), 3.70 (s, 3H), 6.25 (dd, *J* = 15.8 Hz, *J* = 7.9 Hz, 1H), 6.42 (d, *J* = 15.8 Hz, 1H), 7.13 (s, 4H), 7.19−7.34 (m, 5H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2 (CH_3), 34.8 (CH_2), 46.8 (CH), 50.1 (CH), 52.7 (2 × CH_3), 126.4 (2 × CH), 127.5 (CH), 127.6 (2 × CH), 128.6 (2 × CH), 129.6 (2 × CH), 130.5 (CH), 132.6 (CH), 136.5 (C), 137.3 (C), 139.8 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 75.05, H, 6.77.

*(E)-Dimethyl 2-[2-(4-Methoxyphenyl)pent-3-en-1-yl]malonate (**4k**).* Following General Procedure 2, reaction of **1a** (25.0 mg, 0.09 mmol) with potassium (*E*)-1-propenyltrifluoroborate **3e** (26.6 mg, 0.18 mmol) and BF_3-Et_2O (22 μL, 0.18 mmol) in CH_2Cl_2 (0.9 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4k** as a colorless oil (19.4 mg, 71%). R_f 0.50 (ethyl acetate:hexane = 2:8). IR ν 1753, 1737, 1509 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.65 (d, *J* = 4.8 Hz, 3H), 2.25 (t, *J* = 7.5 Hz, 2H), 3.13−3.20 (m, 1H), 3.33 (t, *J* = 7.4 Hz, 1H) 3.69 (s, 3H), 3.73 (s, 3H), 3.78 (s, 3H), 5.45−5.55 (m, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 7.09 (d, *J* = 8.8 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.1 (CH_3), 35.1 (CH_2), 46.0 (CH), 50.1 (CH), 52.7 (2 × CH_3), 55.4 (CH_3), 114.1 (2 × CH), 126.1 (CH), 128.5 (2 × CH), 133.8 (CH), 135.7 (C), 158.3 (C), 170.0 (C), 170.1 (C) ppm. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.73, H, 6.98.

*(Z)-Dimethyl 2-[2-(4-Methoxyphenyl)pent-3-en-1-yl]malonate (**4l**).* Following General Procedure 2, reaction of **1a** (25.0 mg, 0.09 mmol) with potassium (*Z*)-1-propenyltrifluoroborate **3f** (26.6 mg, 0.18 mmol) and BF_3-Et_2O (22 μL, 0.18 mmol) in CH_2Cl_2 (0.9 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4l** as a colorless oil (19.7 mg, 72%). R_f 0.50 (ethyl acetate:hexane = 2:8). IR ν 1753, 1737, 1513 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.63 (dd, *J* = 6.4 Hz, *J* = 1.2 Hz, 3H), 2.12−2.22 (m, 1H), 2.26−2.35 (m, 1H), 3.33−3.38 (m, 1H), 3.59−3.64 (m, 1H), 3.71 (s, 3H), 3.73 (s, 3H), 3.78 (s, 3H), 5.43−5.60 (m, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.1 (CH_3), 35.8 (CH_2), 40.0 (CH), 50.0 (CH), 52.7 (2 × CH_3), 54.4 (CH_3), 114.2 (2 × CH), 125.3 (CH), 128.3 (2 × CH), 133.1 (CH), 136.0 (C), 158.2 (C), 169.9 (C), 170.0 (C) ppm. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.59, H, 7.31.

*Dimethyl 2-[2-(4-Methoxyphenyl)-4-phenylbut-3-yn-1-yl]-malonate (**4m**).* Following General Procedure 2, reaction of **1a** (25.0 mg, 0.09 mmol) with potassium phenylethynyltrifluoroborate **3g** (37.4 mg, 0.18 mmol) and BF_3-Et_2O (22 μL, 0.18 mmol) in CH_2Cl_2 (0.9 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4m** as a colorless oil (26.2 mg, 81%). R_f 0.40 (ethyl acetate:hexane = 2:8). IR ν 2249 (w), 1751, 1735, 1511 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.34−2.45 (m, 2H), 3.70−3.77 (m, 7H), 3.81 (s, 3H), 3.88−3.93 (dd, *J* = 9.1 Hz, *J* = 5.9 Hz 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.29−7.31 (m, 3H), 7.35 (d, *J* = 8.8 Hz, 2H), 7.43−7.46 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.7 (CH), 37.4 (CH_2), 50.0 (CH),

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52.8 (2 × CH_3), 55.4 (CH_3), 84.5 (C), 89.9 (C), 114.2 (2 × CH), 123.4 (C), 128.2 (CH), 128.4 (2 × CH), 128.7 (2 × CH), 131.8 (2 × CH), 132.7 (C), 158.9 (C), 169.6 (C), 169.7 (C) ppm. Anal. Calcd for $C_{22}H_{22}O_5$: C, 72.12; H, 6.05. Found: C, 71.95, H, 5.97.

*Dimethyl 2-[2-(4-Methoxyphenyl)oct-3-yn-1-yl]malonate (**4n**).* Following General Procedure 2, reaction of **1a** (25.0 mg, 0.09 mmol) with potassium 1-hexynyltrifluoroborate **3h** (33.8 mg, 0.18 mmol) and BF_3-Et_2O (22 μL, 0.18 mmol) in CH_2Cl_2 (0.9 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4n** as a colorless oil (23.2 mg, 75%). R_f 0.50 (ethyl acetate:hexane = 2:8). IR ν 2258 (w), 1755, 1739, 1513 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, J = 7.1 Hz, 3H), 1.38−1.53 (m, 4H), 2.14−2.25 (m, 3H), 2.27−2.37 (m, 1H), 3.64−3.74 (m, 5H), 3.75 (s, 3H), 3.79 (s, 3H), 6.85 (d, J = 8.7 Hz, 2H), 7.28 (d, J = 8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8 (CH_3), 18.7 (CH_2), 22.1 (CH_2), 31.2 (CH_2), 35.1 (CH), 37.8 (CH_2), 50.0 (CH), 52.7 (2 × CH_3), 55.4 (CH_3), 80.2 (C), 84.8 (C), 114.0 (2 × CH), 128.6 (2 × CH), 133.6 (C), 158.7 (C), 169.7 (C), 169.9 (C) ppm. Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.56. Found: C, 69.44, H, 7.47.

*Dimethyl 2-[2-(3,4-Dimethoxyphenyl)oct-3-yn-1-yl]malonate (**4o**).* Following General Procedure 2, reaction of **1c** (26.5 mg, 0.09 mmol) with potassium 1-hexynyltrifluoroborate **3h** (33.8 mg, 0.18 mmol) and BF_3-Et_2O (22 μL, 0.18 mmol) in CH_2Cl_2 (0.9 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4o** as a colorless oil (25.3 mg, 75%). R_f 0.30 (ethyl acetate:hexane = 2:8). IR ν 2257 (w), 1755, 1739, 1513 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, J = 7.0 Hz, 3H), 1.41−1.53 (m, 4H), 2.13−2.26 (m, 3H), 2.29−2.39 (m, 1H), 3.67−3.79 (m, 8H), 3.86 (s, 3H), 3.89 (s, 3H), 6.80−6.91 (m, 3H), ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8 (CH_3), 18.7 (CH_2), 22.1 (CH_2), 31.2 (CH_2), 35.6 (CH), 37.8 (CH_2), 50.0 (CH), 52.7 (2 × CH_3), 56.0 (CH_3), 56.1 (CH_3), 80.2 (C), 84.9 (C), 110.8 (CH), 111.3 (CH), 119.6 (CH), 134.1 (C), 148.1 (C), 149.1 (C), 169.7 (C), 169.9 (C) ppm. Anal. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 66.95, H, 7.46.

*Dimethyl 2-[2-(4-Methoxyphenyl)pent-4-en-1-yl]malonate (**4p**).* Following General Procedure 3, reaction of **1a** (25.0 mg, 0.09 mmol) with potassium allyltrifluoroborate **3i** (26.6 mg, 0.18 mmol) and TFAA (6 μL, 0.045 mmol) in CH_2Cl_2 (0.6 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4p** as a colorless oil (17.7 mg, 65%). R_f 0.50 (ethyl acetate:hexane = 2:8). IR ν 1754, 1737, 1514 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.00−2.10 (m, 1H), 2.30−2.40 (m, 3H), 2.52−2.61 (m, 1H), 3.15 (dd, J = 10.3 Hz, J = 4.8 Hz, 1H), 3.61 (s, 3H), 3.73 (s, 3H), 3.79 (s, 3H), 4.92−5.00 (m, 2H), 5.56−5.69 (m, 1H), 6.84 (dd, J = 8.7, 2H), 7.04 (d, J = 8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.1 (CH_2), 41.7 (CH_2), 42.9 (CH), 49.9 (CH), 52.5 (CH_3), 52.6 (CH_3), 55.4 (CH_3), 114.1 (2 × CH), 116.6 (CH_2), 128.8 (2 × CH), 135.0 (C), 136.4 (CH), 158.4 (C), 170.0 (C), 170.1 (C) ppm. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.73, H, 7.32.

*Dimethyl 2-(2-(3,4-Dimethoxyphenyl)pent-4-en-1-yl)malonate (**4q**).* Following General Procedure 3, reaction of **1c** (26.5 mg, 0.09 mmol) with potassium allyltrifluoroborate **3i** (26.6 mg, 0.18 mmol) and TFAA (6 μL, 0.045 mmol) in CH_2Cl_2 (0.6 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4q** as a colorless oil (20.4 mg, 68%). R_f 0.30 (ethyl acetate:hexane = 2:8). IR ν 1755, 1737, 1513 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.00−2.09 (m, 1H), 2.30−2.40 (m, 3H), 2.52−2.62 (m, 1H), 3.17 (dd, J = 10.2 Hz, J = 4.7 Hz, 1H), 3.62 (s, 3H), 3.74 (s, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 4.93−5.02 (m, 2H), 5.57−5.71 (m, 1H), 6.63−6.68 (m, 2H), 6.80 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.1 (CH_2), 41.6 (CH_2), 43.4 (CH), 49.9 (CH), 52.5 (CH_3), 52.6 (CH_3), 56.0 (2 x CH_3), 110.9 (CH), 111.03 (CH), 116.6 (CH_2), 120.0 (CH), 135.6 (C), 136.4 (CH), 147.8 (C), 149.1 (C), 170.0 (C), 170.1 (C) ppm. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.37, H, 7.09.

*Dimethyl rac-2-((1S,2R)-1-((E)-Styryl)-2,3-dihydro-1H-inden-2-yl)-malonate (**4r**).* Following General Procedure 1, reaction of **1h** (30 mg, 0.12 mmol) with (*E*)-2-phenylvinylboronic acid **2a** (22.5 mg, 0.15 mmol) and TFAA (9 μL, 0.06 mmol) in CH_2Cl_2 (0.7 mL) yielded after flash chromatography (Hexane/AcOEt 8/2) **4r** as a colorless oil (28.9 mg, 69%). R_f 0.40 (ethyl acetate:hexane = 2:8). IR ν 1750, 1740, 1510 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.83 (dd, J = 15.6 Hz, J = 9.8 Hz, 1H), 2.98 (quint, J = 8.9 Hz, 1H), 3.30 (dd, J = 15.6 Hz, J = 7.6 Hz, 1H), 3.59 (s, 3H), 3.65 (d, J = 8.4 Hz, 1H), 3.75 (s, 3H), 3.81 (t, J = 9.2 Hz, 1H), 6.12 (dd, J = 15.7 Hz, J = 9.1 Hz, 1H), 6.53 (d, J = 15.7 Hz, 1H), 7.11 (d, J = 7.1 Hz, 1H), 7.21 (m, 4H), 7.32 (t, J = 7.4 Hz, 2H), 7.40 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.4 (CH_2), 46.4 (CH), 52.6 (CH_3), 52.7 (CH_3), 53.2 (CH), 54.9 (CH), 124.6 (CH), 124.7 (CH), 126.4 (2 × CH), 126.8 (CH), 127.4 (CH), 127.6 (CH), 128.7 (2 × CH), 131.0 (CH), 132.5 (CH), 137.1 (C), 141.7 (C), 144,3 (C), 169.0 (C), 169.1 (C) ppm. Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.49, H, 6.39.

*Dimethyl rac-2-[(2R,3R,4R)-3,4-Dihydroxy-2-(4-methoxyphenyl)-4-phenylbutyl]malonate (**5**).* To a mixture of NMO (*N*-methylmorpholine *N*-oxide, 0.09 mmol, 10.5 mg) in H_2O (62 μL) and acetone (0.6 mL) under argon atmosphere was added compound **4a** (30 mg, 0.08 mmol). The mixture was cooled to 0 °C and OsO_4 (54 μL, 2.5 wt % in ^tBuOH) was added. The reaction was stirred at rt overnight and quenched with a Na_2SO_3 saturated solution (0.5 mL). Acetone was removed in vacuo, and the resulting residue was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed in vacuo to give a colorless oil which was purified by chromatography on silica gel column with hexane/ethyl acetate (1:1 v/v) as eluent to afford **5** as a colorless oil (19.5 mg, 65%). R_f 0.30 (ethyl acetate:hexane = 4:6). IR ν 3250 (br), 1750, 1510 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.33−2.42 (m, 3H), 2.45−2.49 (m, 1H), 2.53 (br s, 1H), 3.15 (dd, J = 9.2 Hz, J = 5.7 Hz, 1H), 3.58 (s, 3H), 3.63 (s, 3H), 3.81 (s, 3H), 3.96 (dd, J = 6.4 Hz, J = 4.2 Hz, 1H), 4.37 (d, J = 6.4 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H), 7.27−7.37 (m, 5H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.0 (CH_2), 44.4 (CH), 49.8 (CH), 52.5 (CH_3), 52.6 (CH_3), 55.4 (CH_3), 75.3 (CH), 78.1 (CH), 114.1 (2 × CH), 127.3 (2 × CH), 128.4 (CH), 128.7 (2 × CH), 130.7 (2 × CH), 131.0 (C), 140.9 (C), 158.9 (C), 169.8 (C), 169.9 (C) ppm. Anal. Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.76, H, 6.45.

*rac-(5R,6R)-6-[(R)-Hydroxy(phenyl)methyl]-5-(4-methoxyphenyl)-tetrahydro-2H-pyran-2-one (**6**).* To a stirred solution of diol **5** (19.5 mg, 0.05 mmol) in methanol (0.3 mL) was added KOH (7 mg, 0.13 mmol). The mixture was stirred at 60 °C overnight, quenched with 1 M HCl (0.3 mL), and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over $MgSO_4$ and filtered. The solvent was removed in vacuo and DMSO (0.3 mL) was added. The mixture was stirred at 140 °C overnight, quenched with NH_4Cl (0.5 mL), and extracted with Et_2O (3 × 5 mL). The organic layer was washed with NaCl, dried over $MgSO_4$, and filtered. The solvent was removed in vacuo to give white solid which was purified by chromatography on silica gel column with hexane/ethyl acetate (1:1 v/v) as eluent to afford compound **6** as a colorless oil (7.7 mg, 51%). R_f 0.40 (ethyl acetate:hexane = 1:1). IR ν 3240 (br), 1740, 1505 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 2.06−2.10 (m, 1H), 2.21−2.26 (m, 1H), 2.66 (t, J = 7.2 Hz, 2H), 2.83−2.86 (m, 1H), 3.83 (s, 3H), 4.62 (dd, J = 7.5 Hz, J = 3.8 Hz, 1H), 4.69 (d, J = 7.5 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 7.04−7.07 (m, 4H), 7.28−7.29 (m, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.2 (CH_2), 28.1 (CH_2), 38.4 (CH), 55.4 (CH_3), 73.7 (CH), 86.6 (CH), 114.3 (2 × CH), 127.5 (2 × CH), 128.6 (2 × CH), 128.8 (CH), 129.9 (2 × CH), 131.3 (C), 138.7 (C), 158.9 (C), 171.6 (C) ppm. Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.15, H, 6.36.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00320.

^1H, ^{13}C, and ^{19}F NMR spectra of compounds **4**, **5** and **6** (PDF)

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Notes

The authors declare no competing financial interest.

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