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Decarboxylative Allylic Alkylation of Phthalides: Stabilized Benzylic Nucleophiles for sp^3–sp^3 Coupling

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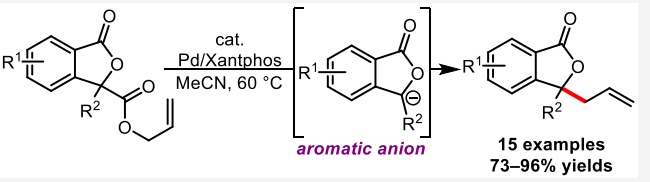
ABSTRACT: A new family of stabilized benzylic nucleophiles for the palladium-catalyzed decarboxylative allylic alkylation reaction has been developed. Allyl esters derived from 3-carboxyphthalides were found to undergo palladium-catalyzed deallylation and decarboxylation under mild reaction conditions, a process facilitated by the formation of a stabilized aromatic anion. The regioselective allylic coupling of this intermediate afforded a variety of functionalized phthalides in 73–96% yields.



Metal-catalyzed decarboxylative coupling reactions present an attractive alternative to traditional couplings, obviating the need for stoichiometric reagents typically required for transmetalation and generating CO_2 as the sole byproduct.[1] Among these transformations, the palladium-catalyzed decarboxylative allylic alkylation (DAA) reaction has emerged as a powerful tool for the construction of sp^3–sp^3 carbon–carbon bonds.[2] Enolate derivatives and related "soft" nucleophiles, whose conjugate acid has a pK_a of <25, have proven to be successful Pd-catalyzed DAA substrates and have served as a robust platform for complex molecule synthesis.[3] On the contrary, adaptation of this chemistry to "hard" nucleophiles (those with conjugate acid pK_a values of >25) remains a significant challenge.[4] Indeed, the more reactive nature of such nucleophiles often requires the use of harsher conditions to promote decarboxylation[5] and can preclude the incorporation of electrophilic functional groups into the substrate. Consequently, a need to develop new solutions to engage a broader range of DAA nucleophiles remains.

One strategy for engaging recalcitrant DAA substrates relies on the incorporation of functional groups or reagents that "soften" or stabilize an otherwise hard nucleophile.[6] Within this realm, benzylic nucleophiles have proven to be the most successful.[7] Tunge[8] and Chruma[9] independently reported that glycinate imines readily undergo Pd-catalyzed allylic alkylation to afford homoallylic amines in good yields, presumably via the formation of a stabilized α-imino benzylic anion (Scheme 1A). Alternatively, the introduction of *o*- or *p*-nitro groups to arylacetic ester derivatives was found to enable their Pd-catalyzed decarboxylative allylation in excellent yield (Scheme 1B).[10] More recently, Lundgren and co-workers demonstrated that a variety of electron-deficient arylacetic acids are excellent substrates for Ir- or Pd-catalyzed asymmetric DAA in which coupling precedes decarboxylation (Scheme 1C).[11]

We saw an opportunity to expand the current repertoire of DAA nucleophiles by using aromaticity as the primary means by which to soften a benzylic nucleophile. Specifically, we hypothesized that C3-allyl ester-substituted phthalides could undergo a palladium-mediated deallylation and decarboxylation, a process facilitated in part by the stability of the resulting aromatic anion (Scheme 1D). This intermediate could then undergo regioselective alkylation to deliver an allylated phthalide product. Notably, the resulting phthalide comprises the core of several natural products and bioactive synthetic phthalides (Figure 1), making this an attractive method for the construction of medicinally relevant compounds.[12] Herein, we report the realization of our synthetic plan, which we anticipate will serve as a novel platform for broadening the scope of DAA substrates.

We began our studies by treating 3-carboxyphthalide derivative **1a** with 10 mol % $Pd(PPh_3)_4$ in THF. Although little reactivity was observed at room temperature, we were pleased to obtain allyl lactone **2a** in 42% yield when the reaction mixture was heated to 60 °C (Table 1, entries 1 and 2). Analysis of the crude reaction mixture by ^1H NMR revealed that decomposition was a competitive reaction pathway under these conditions. Additionally, attempts to isolate analytically pure **2a** by column chromatography were complicated by the co-elution of an unknown product. To our surprise, further purification and characterization of this minor product revealed it to be cyclopropane **3**,[13] presumably the result of addition of the intermediate benzylic anion to the central carbon of the π-allyl intermediate (Scheme 2). The resulting palladocyclobutane can then undergo reductive elimination to afford **3**.[14]

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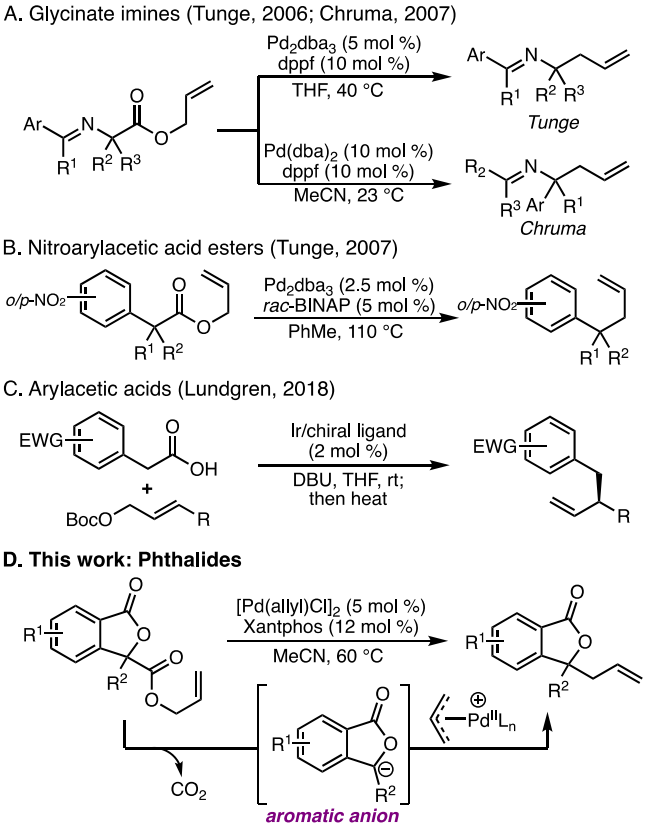
Scheme 1. Decarboxylative Allylic Alkylations of Stabilized Benzylic Nucleophiles



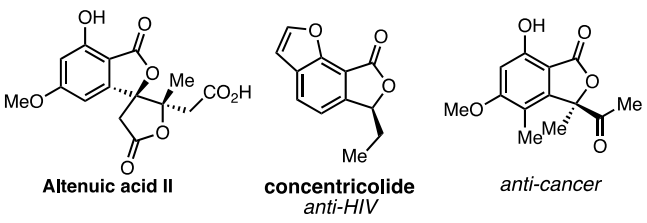
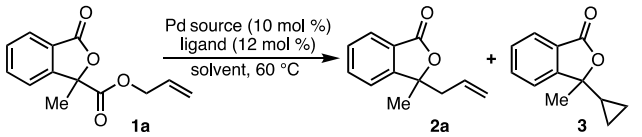


Figure 1. Representative biologically relevant phthalides.

While this type of reactivity was unexpected, there have been some reports of intermolecular cyclopropanation of enolates mediated by palladium π-allyl species,[15−18] and only a single report of an intramolecular variant has been published.[19] This mode of reactivity proved to be persistent in our hands, making chromatographic separation of **2a** from **3** particularly challenging.

To circumvent these issues, we set out to improve the yield and regioselectivity by screening several bidentate phosphine ligands. Interestingly, exposure of **1a** to 5 mol % $Pd_2(dba)_3$ and 12 mol % dppe at 60 °C skewed the product ratio toward the cyclopropane adduct (entry 3). Changing the ligand to dppf or *rac*-BINAP under otherwise identical conditions provided a modest improvement in the regioisomeric ratio (entries 4 and 5). Fortunately, a more dramatic improvement was observed when Xantphos was used, affording **2a** in 58% yield and in >20:1 rr (entry 6).[20] Of the solvents evaluated, acetonitrile provided the most significant boost in yield without compromising the regioselectivity for **2a** (entries 7−9). A brief screen of palladium sources revealed $[Pd(allyl)Cl]_2$ to be optimal, affording the desired lactone in 92% yield after 48 h.

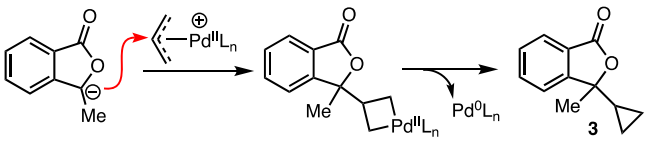
Table 1. Optimization of the DAA Reaction[a]



entry	Pd source	ligand	solvent	time (h)	2a:3[b]	yield (%)[c]
1[d]	$Pd(PPh_3)_4$	–	THF	24	–	<5
2	$Pd(PPh_3)_4$	–	THF	2	8:1	42
3	$Pd_2(dba)_3$	dppe	THF	3	3:1	58
4	$Pd_2(dba)_3$	dppf	THF	3	6:1	76
5	$Pd_2(dba)_3$	(±)-BINAP	THF	3	6:1	82
6	$Pd_2(dba)_3$	Xantphos	THF	6	>20:1	58
7	$Pd_2(dba)_3$	Xantphos	PhMe	8	16:1	75
8	$Pd_2(dba)_3$	Xantphos	DME	12	>20:1	70
9	$Pd_2(dba)_3$	Xantphos	MeCN	16	>20:1	82
10	$Pd(OAc)_2$	Xantphos	MeCN	24	>20:1	76
11	$[Pd(allyl)Cl]_2$	Xantphos	MeCN	48	>20:1	92

[a]Reactions were conducted on a 0.1 mmol scale using 10 mol % Pd source, 12 mol % ligand, and 1 mL of solvent at 60 °C for the indicated time. [b]Determined by ^{1}H NMR analysis of the crude reaction. [c]Determined by ^{1}H NMR spectroscopy using *p*-nitroanisole as an internal standard. [d]Reaction conducted at room temperature.

Scheme 2. Proposed Mechanism for Decarboxylative Cyclopropanation



Despite the longer reaction times required for $[Pd(allyl)Cl]_2$ relative to $Pd_2(dba)_3$ (entry 9 vs entry 11), the significant improvement in yield prompted us to move forward with the Pd(II) conditions.

With optimized conditions in hand, we next evaluated the scope of the reaction by varying the substituent at position C3 of the phthalide (Scheme 3). We found that the C3 substituent had a dramatic effect on the reaction rate: reactions required anywhere between 6 and 96 h to completely consume the starting material. Despite this variability in reaction times, all C3 substituents evaluated underwent decarboxylative coupling in excellent yields (**1a−1k**). Simple alkyl, benzyl, and silyl ether-bearing substrates **1a−1e** performed well under our reaction conditions, affording their corresponding product in nearly quantitative yield. Using substrate **1d**, the reaction was performed on a 1 mmol scale without a significant change in the yield. Aryl bromide and vinyl chloride substrates **1f** and **1g**, respectively, were well tolerated, which presented an exciting opportunity to explore tandem DAA/cross-coupling chemistry (*vide infra*). Of particular note were the high yields observed with substrates bearing acidic functional groups, including a terminal alkyne (**1h**) and enolizable ketone, nitrile, and ester moieties (**1i−1k**, respectively), groups that are typically incompatible with strongly basic conditions.

Substrates bearing substituents on the aromatic backbone or the allyl ester fragment of the phthalide were also examined. Both electron rich (**1l**) and electron poor (**1m** and **1n**) arenes delivered the corresponding coupling products in excellent yields. On the contrary, the DAA reaction proved to be

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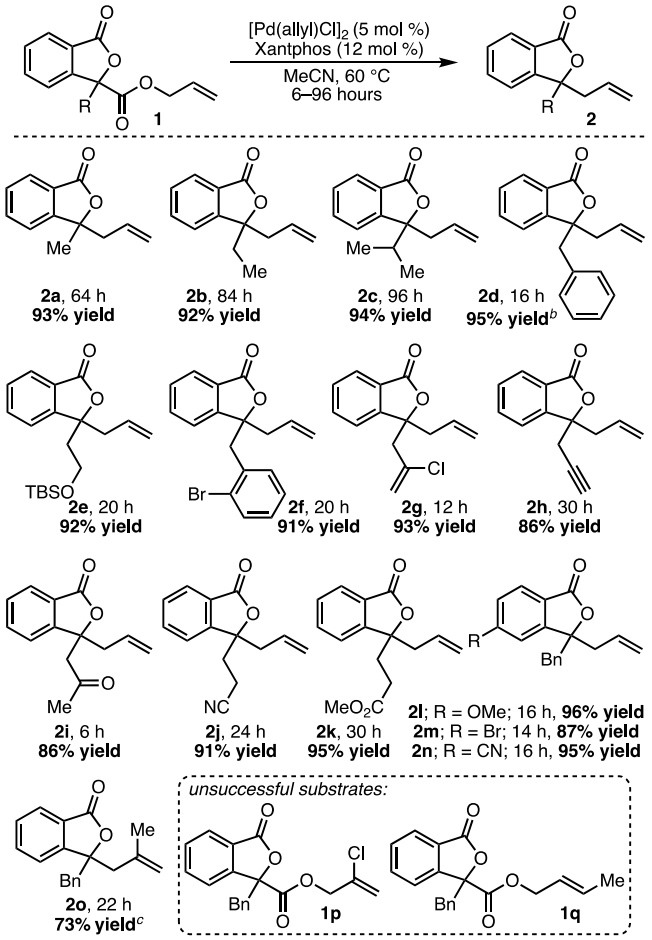
Scheme 3. Scope of Decarboxylative Allylic Alkylation of Phthalides[a]

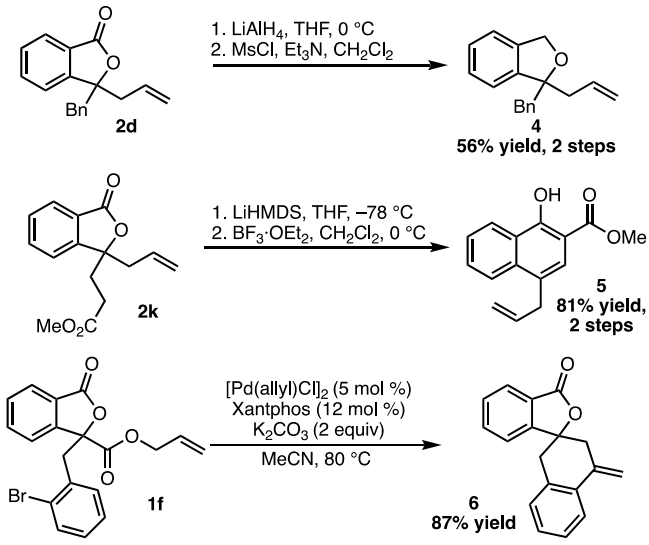


[a]Reactions were conducted on a 0.3 mmol scale using 5 mol % $[Pd(allyl)Cl]_2$, 12 mol % Xantphos, and 3 mL of MeCN at 60 °C for 6–96 h. [b]On a 1.0 mmol scale; 94% yield. [c]$Pd_2(dba)_3$ was used instead of $[Pd(allyl)Cl]_2$.

particularly sensitive to the substitution pattern about the allyl ester. For example, 2-methallyl ester **1o** proved to be an excellent DAA substrate; however, its 2-chloro congener **1p** was unreactive, delivering only trace amounts of its corresponding product. Exposure of crotyl ester **1q** to the optimized conditions did not afford any allylation products; instead, only protonation product **S2** was observed.[21] Nevertheless, the formation of such products is suggestive of a DAA mechanism in which the phthalide anion intermediate is formed.[22]

The 3,3-disubstituted phthalide products generated using our methodology can be readily converted to a variety of functionalized structural motifs. For example, lactone **2d** was readily converted to phthalan derivative **4** in 56% yield using a two-step reduction/intramolecular displacement[23] protocol (Scheme 4). Alternatively, exposure of **2k** to LiHMDS at −78 °C followed by Lewis acid-mediated dehydration[24] provided access to regiodefined naphthol derivative **5** in good yield. Finally, we capitalized on our reaction's tolerance of aryl bromide functionalities to explore a tandem DAA/intramolecular Heck reaction of bromobenzyl substrate **1f**. In the event, exposure of **1f** to our optimal catalyst, K_2CO_3, and

Scheme 4. Derivatization Studies



MeCN at 80 °C promoted facile formation of spirocyclic phthalide **6** in 87% yield.

In summary, we have developed a mild decarboxylative allylic alkylation reaction of a new family of benzylic nucleophiles. We found that 3,3-disubstituted phthalides are a successful platform by which to "soften" an otherwise hard nucleophile and allow for their regioselective allylic alkylation in excellent yields and with a broad functional group tolerance. The expansion of this methodology to related aromatic anions, as well as an exploration of the mechanism of the reaction, is ongoing in our laboratory.

EXPERIMENTAL SECTION

Materials and Methods. Unless otherwise stated, reactions were performed under an argon atmosphere using anhydrous solvents. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), and acetonitrile (MeCN) were dried by being passed through activated alumina columns. Anhydrous toluene (PhMe), benzene, dimethylformamide (DMF), 1,2-dimethoxyethane (DME), and 1,4-dioxane were obtained from various commercial sources and used as received. For palladium-catalyzed decarboxylative allylation reactions, all solvents were degassed by bubbling argon through the solvent prior to use. All other commercially obtained reagents were used as received unless specifically indicated. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 precoated plates (0.25 mm). Flash column chromatography was performed using silica gel (particle sizes of 0.032–0.063 mm) purchased from Silicycle. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance (at 300 and 75 MHz, respectively) or a Bruker Avance Neo (at 400 and 101 MHz, respectively) instrument and are reported relative to internal chloroform (^1H, δ 7.26, ^{13}C, δ 77.0). Data for ^1H NMR spectra are reported as follows: chemical shifts (δ ppm) (multiplicity, coupling constants (hertz), integration). Multiplicity and qualifier abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; app, apparent. Analytical chiral HPLC was performed with an Agilent chromatography system (1260 Infinity Series) with a Chiracel OD-H column or Chiralpak AD-H and AS-H columns. IR spectra were recorded on a Shimadzu Prestige-21 spectrometer and are reported in frequency of absorption (inverse centimeters). High-resolution mass spectra were recorded using an Agilent 6230 LC/TOF system in electrospray ionization (ESI) mode or at the Caltech Mass Spectral Facility using fast-atom bombardment (FAB) or field ionization (FI).

General Screening Procedure for Pd-Catalyzed Decarboxylative Allylic Alkylation (Table 1). In the glovebox, a 1-dram vial

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was charged with the Pd source (0.1 equiv), a ligand (0.12 equiv), and the indicated solvent (0.5 mL), and the reaction mixture was allowed to stir for 10 min. Then, a solution of **1a** (24 mg, 0.1 mmol, 1.0 equiv) in the same or indicated solvent (0.5 mL) was added. The vial was sealed and placed in a 60 °C heating block, and its contents were allowed to stir for the indicated time. The reaction mixture was cooled to room temperature; 4-nitroanisole (7.9 mg, 0.052 mmol, 0.5 equiv) was added, and the resulting solution was filtered through a short plug of silica, eluted with ethyl acetate, and concentrated under reduced pressure. Product ratios and yields were determined by ^{1}H NMR analysis of the crude reaction.

General Procedure for Pd-Catalyzed Decarboxylative Allylic Alkylation (Scheme 3). On the benchtop, an oven-dried 1-dram vial was charged with **1a** (72 mg, 0.31 mmol), and then the vial was cycled into the glovebox (three evacuation/backfill cycles). Once inside the glovebox, a separate 2-dram vial containing a stir bar was charged with $[Pd(allyl)Cl]_2$ (5.7 mg, 0.016 mmol) and Xantphos (22 mg, 0.037 mmol). The substrate was then added to the 2-dram vial as a solution in MeCN (3 × 1 mL rinses, 3 mL total). The vial was sealed and placed in a 60 °C heating block, and its contents were allowed to stir until TLC analysis revealed the starting material had been completely consumed (64 h). The reaction mixture was cooled to room temperature, filtered through a short plug of silica, eluted with ethyl acetate, and concentrated under reduced pressure. The crude product was purified by column chromatography (15−20% Et_2O/pentane) to give **2a** (55 mg, 93% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 7.6 Hz, 1H), 7.65 (td, J = 7.5, 1.1 Hz, 1H), 7.50 (td, J = 7.5, 1.0 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 5.67−5.48 (m, 1H), 5.12−4.98 (m, 2H), 2.77−2.56 (m, 2H), 1.64 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 169.8, 153.4, 134.0, 131.0, 129.0, 126.0, 125.7, 121.1, 120.2, 86.7, 44.3, 25.4; FTIR (thin film, cm^{-1}) 3079, 2981, 2933, 1761, 1653, 1614, 1467; HRMS (FI) m/z calcd for $C_{12}H_{12}O_2$ $[M]^+$ 188.0832, found 188.0830.

Preparation of 3-Allyl-3-ethylphthalide ***2b****.* The title compound was prepared from 0.30 mmol of **1b** following the general procedure described above and allowed to stir for 84 h. The crude product was purified by flash chromatography (10% Et_2O in pentane) to give **2b** (56 mg, 92% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 7.6 Hz, 1H), 7.65 (td, J = 7.5, 1.2 Hz, 1H), 7.50 (td, J = 7.5, 1.0 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H), 5.62−5.44 (m, 1H), 5.10−4.97 (m, 2H), 2.80−2.59 (m, 2H), 2.12 (dq, J = 14.7, 7.4 Hz, 1H), 1.93 (dq, J = 14.7, 7.4 Hz, 1H), 0.72 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.1, 151.8, 133.9, 130.9, 128.9, 127.1, 125.6, 121.3, 120.0, 89.5, 43.0, 31.1, 7.4; FTIR (thin film, cm^{-1}) 3079, 2973, 2940, 1761, 1640, 1613, 1466; HRMS (FI) m/z calcd for $C_{13}H_{15}O_2$ $[M + H]^+$ 203.1067, found 203.1064.

Preparation of 3-Allyl-3-isopropylphthalide ***2c****.* The title compound was prepared from 0.30 mmol of **1c** following the general procedure described above and allowed to stir for 96 h. The crude product was purified by flash chromatography (10% Et_2O in pentane) to give **2c** (62 mg, 94% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 7.6 Hz, 1H), 7.64 (td, J = 7.5, 1.2 Hz, 1H), 7.49 (td, J = 7.5, 1.0 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 5.54−5.35 (m, 1H), 5.08−4.92 (m, 2H), 2.81 (ddt, J = 14.2, 7.5, 1.1 Hz, 1H), 2.69 (ddt, J = 14.2, 6.9, 1.2 Hz, 1H), 2.28 (hept, J = 6.8 Hz, 1H), 0.98 (d, J = 6.8 Hz, 3H), 0.81 (d, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.3, 151.4, 133.6, 130.9, 128.9, 127.3, 125.6, 121.8, 119.9, 91.6, 40.8, 35. 0, 16.9, 16.7; FTIR (thin film, cm^{-1}) 3079, 2972, 2881, 1759, 1642, 1614, 1465; HRMS (FI) m/z calcd for $C_{14}H_{17}O_2$ $[M + H]^+$ 217.1223, found 217.1222.

Preparation of 3-Allyl-3-benzylphthalide ***2d****.* The title compound was prepared from 0.30 mmol of **1d** following the general procedure described above and allowed to stir for 16 h. The crude product was purified by flash chromatography (15−20% Et_2O in pentane) to give **2d** (76 mg, 95% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73−7.56 (m, 2H), 7.47−7.30 (m, 2H), 7.17−7.07 (m, 3H), 7.05−6.93 (m, 2H), 5.66−5.43 (m, 1H), 5.15−4.97 (m, 2H), 3.33 (d, J = 13.9 Hz, 1H), 3.19 (d, J = 14.0 Hz, 1H), 2.88−2.65 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 169.6, 151.1, 134.1, 133.5, 130.7, 130.5, 128.9, 128.0, 127.0, 126.9, 125.5, 121.8, 120.3, 88.6, 44.7, 42.8; FTIR (thin film, cm^{-1}) 3063, 3031, 2920, 1762, 1612, 1496, 1466; HRMS (FI) m/z calcd for $C_{18}H_{16}O_2$ $[M + \bullet]^+$ 264.1145, found 264.1145.

Preparation of 3-Allyl-3-(2-siloxyethyl)phthalide ***2e****.* The title compound was prepared from 0.30 mmol of **1e** following the general procedure described above and allowed to stir for 20 h. The crude product was purified by flash chromatography (10% Et_2O in pentane) to give **2e** (92 mg, 92% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dt, J = 7.6, 1.0 Hz, 1H), 7.64 (td, J = 7.5, 1.1 Hz, 1H), 7.49 (td, J = 7.5, 0.9 Hz, 1H), 7.39 (dt, J = 7.7, 0.9 Hz, 1H), 5.58−5.44 (m, 1H), 5.07−4.99 (m, 2H), 3.67 (ddd, J = 10.4, 7.1, 5.8 Hz, 1H), 3.46 (dt, J = 10.4, 6.7 Hz, 1H), 2.79−2.63 (m, 2H), 2.32 (ddd, J = 14.5, 7.0, 5.8 Hz, 1H), 2.16 (ddd, J = 14.4, 7.1, 6.6 Hz, 1H), 0.78 (s, 9H), −0.07 (s, 3H), −0.12 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.9, 152.1, 133.8, 130.7, 128.9, 126.5, 125.6, 121.8, 120.3, 87.9, 58.2, 43.8, 40.7, 25.8, 18.1, −5.61, −5.62; FTIR (thin film, cm^{-1}) 2954, 2929, 2857, 1767, 1614, 1466; HRMS (FI) m/z calcd for $C_{19}H_{29}O_3Si$ $[M + H]^+$ 333.1881, found 333.1874.

Preparation of 3-Allyl-3-(2-bromobenzyl)phthalide ***2f****.* The title compound was prepared from 0.30 mmol of **1f** following the general procedure described above and allowed to stir for 20 h. The crude product was purified by flash chromatography (15% Et_2O in pentane) to give **2f** (95 mg, 91% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 1H), 7.63 (td, J = 7.5, 1.1 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.47−7.38 (m, 2H), 7.29 (dd, J = 7.7, 1.8 Hz, 1H), 7.15 (td, J = 7.5, 1.4 Hz, 1H), 7.01 (td, J = 7.7, 1.8 Hz, 1H), 5.59−5.36 (m, 1H), 5.11−4.94 (m, 2H), 3.61 (d, J = 14.4 Hz, 1H), 3.43 (d, J = 14.4 Hz, 1H), 2.85−2.75 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 169.6, 150.9, 134.3, 133.6, 132.9, 132.2, 130.5, 129.1, 128.7, 127.3, 126.8, 125.7, 125.3, 122.2, 120.4, 88.8, 43.3, 42.4; FTIR (thin film, cm^{-1}) 3058, 2924, 1765, 1613, 1466; HRMS (FI) m/z calcd for $C_{18}H_{15}BrO_2$ $[M]^+$ 342.0250, found 342.0244.

Preparation of 3-Allyl-3-(2-chloroallyl)phthalide ***2g****.* The title compound was prepared from 0.30 mmol of **1g** following the general procedure described above and allowed to stir for 12 h. The crude product was purified by flash chromatography (15% Et_2O in pentane) to give phthalide **2g** (71 mg, 93% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 7.6 Hz, 1H), 7.66 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.44 (d, J = 7.6 Hz, 1H), 5.64−5.45 (m, 1H), 5.26−5.14 (m, 2H), 5.14−5.00 (m, 2H), 3.15 (d, J = 14.8 Hz, 1H), 2.93 (d, J = 14.8 Hz, 1H), 2.89−2.65 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 169.8, 150.5, 135.0, 133.9, 130.5, 129.6, 127.2, 125.9, 122.5, 121.0, 118.7, 87.2, 47.4, 43.4; FTIR (thin film, cm^{-1}) 3080, 2918, 1761, 1631, 1467; HRMS (FI) m/z calcd for $C_{14}H_{13}ClO_2$ $[M]^+$ 248.0599, found 248.0596.

Preparation of 3-Allyl-3-propargylphthalide ***2h****.* The title compound was prepared from 0.30 mmol of **1h** following the general procedure described above and allowed to stir for 30 h. The crude product was purified by flash chromatography (15−20% Et_2O in pentane) to give **2h** (55 mg, 86% yield) as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 1H), 7.74−7.63 (m, 1H), 7.63−7.51 (m, 2H), 5.59 (dddd, J = 16.9, 10.1, 7.8, 6.6 Hz, 1H), 5.21−5.05 (m, 2H), 2.94−2.72 (m, 2H), 2.93 (dd, J = 16.7, 2.7 Hz, 1H), 2.74 (dd, J = 16.8, 2.6 Hz, 1H), 2.05 (t, J = 2.7 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 169.3, 151.0, 134.0, 130.3, 129.5, 126.5, 125.7, 121.9, 120.77, 86.2, 77.9, 72.3, 41.7, 29.2; FTIR (thin film, cm^{-1}) 3297, 3081, 2914, 1762, 1613, 1467; HRMS (FI) m/z calcd for $C_{14}H_{12}O_2$ $[M]^+$ 212.0832, found 212.0831.

Preparation of 3-Allyl-3-(2-oxopropyl)phthalide ***2i****.* The title compound was prepared from 0.30 mmol of **1i** following the general procedure described above and allowed to stir for 6 h. The crude product was purified by flash chromatography (40−50% Et_2O in pentane) to give **2i** (59 mg, 86% yield) as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 1H), 7.71−7.60 (m, 1H), 7.60−7.47 (m, 2H), 5.68−5.48 (m, 1H), 5.15−5.02 (m, 2H), 3.16 (d, J = 16.6 Hz, 1H), 3.03 (d, J = 16.5 Hz, 1H), 2.88 (ddt, J = 14.2, 8.2, 0.9 Hz, 1H), 2.72 (ddt, J = 14.2, 6.4, 1.3 Hz, 1H), 2.13 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 204.2, 169.4, 151.5, 134.1, 130.6, 129.4, 126.3, 125.7, 122.4, 120.7, 86.4, 50.3, 42.7, 31.4; FTIR (thin

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film, cm^{-1}) 3080, 2916, 1762, 1725, 1613, 1467; HRMS (FI) m/z calcd for $C_{14}H_{14}O_3$ $[M]^+$ 230.09375, found 230.09378.

Preparation of 3-Allyl-3-(2-cyanoethyl)phthalide ***2j.*** The title compound was prepared from 0.30 mmol of **1j** following the general procedure described above and allowed to stir for 24 h. The crude product was purified by flash chromatography (60% Et_2O in pentane) to give **2j** (63 mg, 91% yield) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 5.62−5.42 (m, 1H), 5.16−5.03 (m, 2H), 2.80−2.60 (m, 2H), 2.60−2.47 (m, 1H), 2.41−2.20 (m, 2H), 2.03−1.85 (m, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 169.0, 149.7, 134.6, 130.0, 129.7, 126.6, 126.2, 121.4, 121.3, 118.3, 86.9, 43.3, 33.6, 11.6; FTIR (thin film, cm^{-1}) 3080, 2934, 2250, 1765, 1613, 1467; HRMS (FI) m/z calcd for $C_{14}H_{13}NO_2$ $[M]^+$ 227.0941, found 227.0939.

Preparation of 3-Allyl-3-(3-methoxy-3-oxopropyl)phthalide ***2k.*** The title compound was prepared from 0.30 mmol of **1k** following the general procedure described above and allowed to stir for 30 h. The crude product was purified by flash chromatography (40% Et_2O in pentane) to give **2k** (75 mg, 95% yield) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (dt, J = 7.6, 1.0 Hz, 1H), 7.67 (td, J = 7.5, 1.1 Hz, 1H), 7.52 (td, J = 7.5, 0.9 Hz, 1H), 7.36 (dt, J = 7.7, 0.9 Hz, 1H), 5.58−5.45 (m, 1H), 5.10−5.02 (m, 2H), 3.57 (s, 3H), 2.78−2.62 (m, 2H), 2.54−2.42 (m, 1H), 2.34−2.20 (m, 2H), 1.99−1.87 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 172.9, 169.5, 150.8, 134.1, 130.3, 129.3, 126.9, 125.8, 121.5, 120.6, 88.0, 51.7, 43.5, 33.0, 28.1; FTIR (thin film, cm^{-1}) 3079, 2953, 1766, 1738, 1642, 1613, 1466; HRMS (FI) m/z calcd for $C_{15}H_{17}O_4$ $[M + H]^+$ 261.1121, found 261.1124.

Preparation of 3-Allyl-3-benzyl-5-methoxyphthalide ***2l.*** The title compound was prepared from 0.30 mmol of **1l** following the general procedure described above and allowed to stir for 16 h. The crude product was purified by flash chromatography (30−40% Et_2O in pentane) to give **2l** (85 mg, 96% yield) as a pale yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 8.5, 0.5 Hz, 1H), 7.19−7.12 (m, 3H), 7.08−7.01 (m, 2H), 6.92 (dd, J = 8.5, 2.2 Hz, 1H), 6.72 (dd, J = 2.2, 0.5 Hz, 1H), 5.57 (dddd, J = 17.0, 10.1, 7.6, 6.7 Hz, 1H), 5.12−5.02 (m, 2H), 3.88 (s, 3H), 3.27 (d, J = 14.0 Hz, 1H), 3.17 (d, J = 13.9 Hz, 1H), 2.78 (ddt, J = 14.3, 7.6, 1.1 Hz, 1H), 2.69 (ddt, J = 14.2, 6.8, 1.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.3, 164.2, 153.9, 134.2, 130.8, 130.5, 128.0, 127.0, 126.9, 120.2, 119.4, 115.8, 106.2, 87.8, 55.8, 44.8, 42.7; FTIR (thin film, cm^{-1}) 3031, 2918, 1756, 1607, 1492, 1454; HRMS (FI) m/z calcd for $C_{19}H_{18}O_3$ $[M]^+$ 294.1251, found 294.1248.

Preparation of 3-Allyl-3-benzyl-5-bromophthalide ***2m.*** The title compound was prepared from 0.30 mmol of **1m** following the general procedure described above and allowed to stir for 14 h. The crude product was purified by flash chromatography (10% Et_2O in pentane) to give **2m** (89 mg, 87% yield) as a white solid: ^1H NMR (300 MHz, $CDCl_3$) δ 7.60−7.48 (m, 2H), 7.23−7.11 (m, 3H), 7.07−6.96 (m, 2H), 5.55 (ddt, J = 17.2, 9.8, 7.2 Hz, 1H), 5.16−5.03 (m, 2H), 3.32 (d, J = 14.0 Hz, 1H), 3.16 (d, J = 14.0 Hz, 1H), 2.87−2.64 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 168.5, 152.9, 133.7, 132.5, 130.5, 130.3, 128.8, 128.1, 127.1, 126.8, 126.0, 125.2, 120.9, 88.2, 44.7, 42.6; FTIR (thin film, cm^{-1}) 3063, 3031, 2918, 1761, 1607, 1590, 1454; HRMS (FI) m/z calcd for $C_{18}H_{15}BrO_2$ $[M]^+$ 342.0250, found 342.0247.

Preparation of 3-Allyl-3-benzyl-5-cyanophthalide ***2n.*** The title compound was prepared from 0.30 mmol of **1n** following the general procedure described above and allowed to stir for 16 h. The crude product was purified by flash chromatography (25% Et_2O in pentane) to give **2n** (83 mg, 95% yield) as a white solid: ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (dd, J = 7.9, 0.9 Hz, 1H), 7.69 (dd, J = 7.9, 1.2 Hz, 1H), 7.68−7.61 (m, 1H), 7.20−7.11 (m, 3H), 7.01−6.92 (m, 2H), 5.65−5.45 (m, 1H), 5.16−5.03 (m, 2H), 3.38 (d, J = 14.1 Hz, 1H), 3.20 (d, J = 14.1 Hz, 1H), 2.93−2.70 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 167.5, 151.4, 133.2, 132.7, 130.7, 130.4, 129.8, 128.3, 127.3, 126.4, 125.8, 121.4, 117.6, 117.0, 89.0, 44.5, 42.6; FTIR (thin film, cm^{-1}) 3065, 3031, 2921, 2233, 1771, 1617, 1496; HRMS (FI) m/z calcd for $C_{19}H_{15}NO_2$ $[M]^+$ 289.1097, found 289.1096.

Preparation of 3-Benzyl-3-(2-methallyl)phthalide ***2o.*** The title compound was prepared from 0.30 mmol of **1o** following the general procedure described above using $Pd_2(dba)_3$ instead of $[Pd(allyl)Cl]_2$, and allowed to stir for 22 h. The crude product was purified by flash chromatography (20% Et_2O in pentane) to give **2o** (61 mg, 73% yield) as a white solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.57 (m, 2H), 7.46−7.35 (m, 2H), 7.14−7.05 (m, 3H), 7.01−6.93 (m, 2H), 4.82−4.75 (m, 1H), 4.64 (d, J = 1.0 Hz, 1H), 3.37 (d, J = 14.0 Hz, 1H), 3.17 (d, J = 14.0 Hz, 1H), 2.89 (d, J = 14.0 Hz, 1H), 1.58 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 151.2, 139.3, 134.1, 133.2, 130.5, 128.8, 127.9, 127.1, 126.8, 125.3, 122.0, 116.8, 89.0, 46.3, 45.2, 24.1; FTIR (thin film, cm^{-1}) 3031, 2921, 1761, 1613, 1496, 1467; HRMS (FI) m/z calcd for $C_{19}H_{18}O_2$ $[M]^+$ 278.1301, found 278.1302.

Scale-up Procedure for Decarboxylative Allylic Alkylation of 1d. On the benchtop, an oven-dried 2-dram vial was charged with **1d** (309 mg, 1.00 mmol), and then the vial was cycled into the glovebox (three evacuation/backfill cycles). Once inside the glovebox, a separate scintillation vial containing a stir bar was charged with $[Pd(allyl)Cl]_2$ (18 mg, 0.05 mmol) and Xantphos (70 mg, 0.12 mmol). The substrate was then added to the scintillation vial as a solution in MeCN (3 × 3.33 mL rinses, 10 mL total). The vial was sealed and placed in a 60 °C heating block, and its contents were allowed to stir for 20 h. The reaction mixture was cooled to room temperature, filtered through a short plug of silica, eluted with ethyl acetate, and concentrated under reduced pressure. The crude product was purified by column chromatography (15% Et_2O/pentane) to give **2d** (250 mg, 94% yield) as an off-white solid.

Attempted Decarboxylative Allylic Alkylation of Crotyl Ester 1q. On the benchtop, an oven-dried 1-dram vial was charged with **1q** (97 mg, 0.30 mmol), and then the vial was cycled into the glovebox (three evacuation/backfill cycles). Once inside the glovebox, a separate 2-dram vial containing a stir bar was charged with $[Pd(allyl)Cl]_2$ (5.5 mg, 0.015 mmol) and Xantphos (21 mg, 0.036 mmol). The substrate was then added to the 2-dram vial as a solution in MeCN (3 × 1 mL rinses, 3 mL total). The vial was sealed and placed in a 60 °C heating block, and its contents were allowed to stir at 60 °C for 24 h. The reaction mixture was cooled to room temperature, filtered through a short plug of silica, eluted with ethyl acetate, and concentrated under reduced pressure. The crude product was purified by column chromatography (20% EtOAc in hexanes) to give protonation product **S2** (21 mg, 31% yield) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.7 Hz, 1H), 7.60 (td, J = 7.5, 1.1 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.33−7.24 (m, 3H), 7.25−7.18 (m, 2H), 7.17 (dd, J = 7.6, 0.9 Hz, 1H), 5.69 (t, J = 6.4 Hz, 1H), 3.29 (dd, J = 14.1, 6.6 Hz, 1H), 3.16 (dd, J = 14.1, 6.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.2, 149.1, 135.0, 133.7, 129.7, 129.2, 128.5, 127.2, 126.3, 125.7, 122.3, 81.2, 40.9; FTIR (thin film, cm^{-1}) 3030, 2920, 1761, 1601, 1496, 1467; HRMS (FI) m/z calcd for $C_{15}H_{12}O_2$ $[M]^+$ 224.0832, found 224.0834.

General Cyclopropanation/Dihydroxylation Procedure for the Isolation of Cyclopropane Products. *Preparation of 3-Methyl-3-cyclopropylphthalide* ***3.*** On the benchtop, an oven-dried 2-dram vial was charged with **1a** (200 mg, 0.86 mmol), and then the vial was cycled into the glovebox (three evacuation/backfill cycles). Once inside the glovebox, a separate scintillation vial containing a stir bar was charged with $Pd_2(dba)_3$ (39 mg, 0.043 mmol) and dppe (22 mg, 0.037 mmol). The substrate was then added to the scintillation vial as a solution in MeCN (3 × 2.9 mL rinses, 8.7 mL total). The vial was sealed and placed in a 60 °C heating block, and its contents were allowed to stir for 3 h. The reaction mixture was cooled to room temperature, filtered through a short plug of silica, eluted with ethyl acetate, and concentrated under reduced pressure. The crude product was purified by column chromatography (15% Et_2O in pentane) to give an inseparable ∼3:1 **2a**/**3** mixture (141 mg, 87% combined yield) as a colorless oil. The purified product mixture (141 mg, 0.74 mmol) was dissolved in acetone (12 mL), and then H_2O (3 mL) was added, followed by NMO (261 mg, 2.23 mmol) and $K_2OsO_4{\cdot}2H_2O$ (27 mg, 0.074 mmol). The resulting suspension was allowed to stir at room temperature for 20 h, the reaction quenched with saturated aqueous

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$Na_2S_2O_3$, and the mixture stirred vigorously for 20 min. The reaction mixture was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (10% EtOAc in hexanes) to give **3** (26 mg, 18% yield) as a colorless oil. The structure of **3** was corroborated by its independent synthesis using the procedure described below: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, J = 7.6 Hz, 1H), 7.65 (td, J = 7.5, 1.2 Hz, 1H), 7.50 (td, J = 7.5, 1.0 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 1.65 (s, 3H), 1.40−1.27 (m, 1H), 0.61−0.49 (m, 1H), 0.48−0.27 (m, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.0, 153.7, 133.9, 128.9, 125.7, 125.6, 121.1, 86.5, 24.9, 19.7, 1.7, 1.0; FTIR (thin film, cm^{-1}) 3088, 3010, 2980, 2929, 1762, 1615, 1465; HRMS (FAB) m/z calcd for $C_{12}H_{13}O_2$ $[M + H]^+$ 189.0916, found 189.0900.

Preparation of 3-Benzyl-3-cyclopropylphthalide ***S1***. The title compound was prepared from 0.34 mmol of **1d** following the general cyclopropanation/dihydroxylation procedure described above. The crude product was purified by flash chromatography (10% EtOAc in hexanes) to give **S1** (10 mg, 11% yield over two steps) as a colorless oil. The structure of **S1** was assigned by analogy to cyclopropane **3**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dt, J = 7.6, 1.0 Hz, 1H), 7.61 (td, J = 7.5, 1.1 Hz, 1H), 7.42 (td, J = 7.5, 0.9 Hz, 1H), 7.33 (dt, J = 7.7, 0.9 Hz, 1H), 7.17−7.10 (m, 3H), 7.06−7.00 (m, 2H), 3.37 (d, J = 13.8 Hz, 1H), 3.30 (d, J = 13.8 Hz, 1H), 1.53−1.41 (m, 1H), 0.64−0.53 (m, 1H), 0.51−0.37 (m, 2H), 0.36−0.28 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.7, 151.4, 134.4, 133.4, 130.6, 128.9, 127.89, 126.8, 126.6, 125.5, 121.8, 88.1, 45.3, 18.8, 2.0, 1.0; FTIR (thin film, cm^{-1}) 3058, 3031, 2924, 1759, 1599, 1496, 1465; HRMS (ESI) m/z calcd for $C_{18}H_{17}O_2$ $[M + H]^+$ 265.1223, found 265.1223.

Independent Synthesis of Cyclopropane 3 from 2-Acetylbenzoic Acid. To a solution of cyclopropylmagnesium bromide[25] (4.8 mmol) in THF (8 mL) at room temperature was added a solution of 2-acetylbenzoic acid (328 mg, 2.0 mmol) in THF (2 mL), dropwise via cannula transfer. The reaction mixture was allowed to stir at room temperature for 2 h, heated to 40 °C, and stirred for an additional 90 min. The reaction mixture was cooled to room temperature, the reaction quenched with H_2O, and THF removed under reduced pressure. The suspension was diluted with aqueous NaOH (5 wt %, 10 mL), diluted with H_2O (10 mL), and then washed with Et_2O (2 × 20 mL). The aqueous layer was cooled to 0 °C, acidified to pH <2 with concentrated HCl, and then extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (10% EtOAc in hexanes) to give **3** (146 mg, 39% yield) as a pale yellow oil. Spectroscopic data for **3** obtained via this pathway were identical to those obtained via decarboxylative allylation of **1a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 7.6 Hz, 1H), 7.66 (td, J = 7.5, 1.1 Hz, 1H), 7.50 (td, J = 7.5, 1.0 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 1.66 (s, 3H), 1.40−1.27 (m, 1H), 0.61−0.49 (m, 1H), 0.48−0.27 (m, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.0, 153.7, 133.9, 128.9, 125.8, 125.7, 121.1, 86.5, 25.0, 19.8, 1.8, 1.1.

Preparation of Phthalan 4. A flame-dried 25 mL flask was charged with lithium aluminum hydride (24 mg, 0.61 mmol), and then THF (3 mL) was added. The suspension was cooled to 0 °C and stirred for 10 min before **2d** (80 mg, 0.30 mmol) was added in a single portion. The reaction mixture was allowed to stir for 5 min at 0 °C before being warmed to room temperature and stirred for an additional 1 h. The reaction mixture was diluted with Et_2O (3 mL) and cooled to 0 °C, and then the reaction carefully quenched by the sequential addition of H_2O (30 mL), aqueous NaOH (15 wt %, 30 mL), and H_2O (90 mL). The slurry was warmed to room temperature and stirred for 15 min, and $MgSO_4$ was added. The mixture was stirred for an additional 15 min, filtered, and concentrated under reduced pressure to give a crude diol product, which was used immediately in the subsequent step without further purification. The crude diol was dissolved in CH_2Cl_2 (1.5 mL) and then cooled to 0 °C. After the mixture had been stirred at 0 °C for 10 min, triethylamine (160 mL, 1.12 mmol) and MsCl (32 mL, 0.42 mmol) were sequentially added, and the reaction mixture was allowed to stir at 0 °C for 30 min, warmed to room temperature, and stirred for 1 h. The reaction was quenched with H_2O (10 mL), and the mixture diluted with CH_2Cl_2 (10 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography (5% EtOAc in Hexanes) to deliver phthalan **4** (39 mg, 56% yield, two steps) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.16 (m, 2H), 7.16−7.07 (m, 4H), 7.07−6.97 (m, 3H), 5.70 (ddt, J = 17.2, 10.1, 7.1 Hz, 1H), 5.09−4.96 (m, 2H), 4.93 (d, J = 12.2 Hz, 1H), 4.62 (d, J = 12.2 Hz, 1H), 3.11 (d, J = 13.5 Hz, 1H), 3.02 (d, J = 13.5 Hz, 1H), 2.73−2.54 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.8, 139.8, 137.0, 133.6, 130.6, 127.5, 127.4, 126.9, 126.0, 121.7, 120.7, 118.0, 90.8, 72.5, 46.8, 45.0; FTIR (thin film, cm^{-1}) 3075, 3029, 2912, 2856, 1640, 1603, 1495; HRMS (FI) m/z calcd for $C_{18}H_{18}O$ $[M]^+$ 250.1352, found 250.1336.

Preparation of Naphthol 5. An oven-dried 10 mL flask was charged with **2k** (52 mg, 0.20 mmol) followed by THF (2 mL). The colorless solution was cooled to 0 °C and stirred for 10 min at that temperature before LiHMDS (400 mL of a 1 M solution in THF, 0.40 mmol) was added dropwise. After the mixture had been stirred at 0 °C for 30 min, the reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the mixture was warmed to room temperature and extracted with EtOAc (20 mL). The organic layer was washed with brine (2 × 15 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a crude alcohol product that was used immediately in the subsequent step without further purification. The crude alcohol was dissolved in CH_2Cl_2 (2 mL), and the resulting solution was cooled to 0 °C. After the mixture had been stirred at that temperature for 10 min, $BF_3{\cdot}OEt_2$ (50 mL, 0.20 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 30 min. The reaction mixture was quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (2 × 20 mL), and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (2% EtOAc in hexanes) to afford **5** (39 mg, 81% yield) as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.87 (s, 1H), 8.46 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 8.7 Hz, 1H), 7.69−7.59 (m, 2H), 7.54 (ddd, J = 8.2, 6.8, 1.2 Hz, 1H), 6.09 (ddt, J = 16.6, 10.2, 6.2 Hz, 1H), 5.17−5.01 (m, 2H), 4.00 (s, 3H), 3.72 (d, J = 6.2 Hz, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.4, 160.0, 136.9, 135.8, 129.3, 126.5, 125.5, 125.2, 124.5, 124.0, 123.9, 116.3, 105.1, 52.2, 36.7; FTIR (thin film, cm^{-1}) 3056, 2955, 1667, 1634, 1510, 1452; HRMS (FI) m/z calcd for $C_{15}H_{14}O_3$ $[M]^+$ 242.0938, found 242.0933.

Preparation of Spirocycle 6. On the benchtop, an oven-dried 1-dram vial was charged with **1f** (78 mg, 0.20 mmol), and then the vial was cycled into the glovebox (three evacuation/backfill cycles). Once the vial had been placed inside the glovebox, a separate 2-dram vial containing a stir bar was sequentially charged with $[Pd(allyl)Cl]_2$ (3.7 mg, 0.01 mmol), Xantphos (14 mg, 0.024 mmol), and K_2CO_3 (56 mg, 0.40 mmol). The substrate was then added to the 2-dram vial as a solution in MeCN (3 × 0.67 mL rinses, 2 mL total). The vial was sealed and placed in a 80 °C heating block, and its contents were allowed to stir at that temperature for 26 h. The reaction mixture was cooled to room temperature, the reaction quenched with water (15 mL), and then the mixture extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by column chromatography (20% Et_2O in pentane) to give **6** (46 mg, 87% yield) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.87 (m, 1H), 7.79 (dd, J = 7.7, 1.7 Hz, 1H), 7.59−7.48 (m, 2H), 7.34−7.22 (m, 2H), 7.16−7.07 (m, 2H), 5.78 (s, 1H), 5.06 (t, J = 1.3 Hz, 1H), 3.42 (d, J = 16.6 Hz, 1H), 3.24 (d, J = 16.6 Hz, 1H), 3.07 (dd, J = 14.3, 1.2 Hz, 1H), 2.89 (dd, J = 14.3, 1.3 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.5, 152.5, 138.8, 134.0, 133.3, 132.7, 129.6, 129.4, 128.6, 127.1, 125.81, 125.77, 124.0, 121.9, 112.5, 85.0, 42.9, 40.8; FTIR (thin film, cm^{-1}) 3061, 2927, 1760, 1613, 1465; HRMS (FI) m/z calcd for $C_{18}H_{14}O_2$ $[M]^+$ 262.0988, found 262.0989.

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■ ASSOCIATED CONTENT

Supporting Information

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Evaluation of chiral ligands for enantioselective DAA, experimental procedures, characterization data for the preparation of compounds **1a−1q** and **S4−S7**, and ^{1}H and ^{13}C NMR spectra for all synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

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