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# Recyclable and Reusable $[RuCl_2(p\text{-cymene})]_2/Cu(OAc)_2/PEG\text{-}400/H_2O$ System for Oxidative C−H Bond Alkenylations: Green Synthesis of Phthalides

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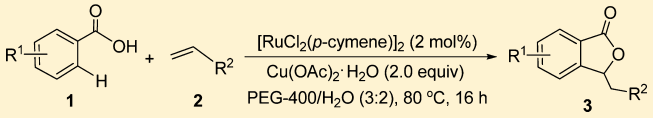
Supporting Information

**ABSTRACT:** $[RuCl_2(p\text{-cymene})]_2$ in a mixture of poly(ethylene glycol) (PEG-400) and water is shown to be an extremely efficient catalyst for the cross-dehydrogenative C−H bond alkenylation reaction between benzoic acids and alkenes. The reaction could be conducted at 80 °C using $Cu(OAc)_2\cdot H_2O$ as oxidant, yielding a variety of phthalide derivatives in good to excellent yields. More importantly, both $[RuCl_2(p\text{-cymene})]_2$ and $Cu(OAc)_2$ in the PEG-400/$H_2O$ system could be easily recycled and reused six times without any loss of catalytic activity.




Phthalides (isobenzofuranone), a family of five-membered lactones in plants, are valuable intermediates in organic synthesis and indispensable structural motifs of a large number of bioactive molecules,[1] and many methods have been developed for their constructions.[2] Benzylic alcohol and 2-halobenzylic alcohol undergo tandem carbonylation/cyclization reaction to give phthalides.[3] Chan and Scheidt reported *N*-heterocyclic carbene-catalyzed intramolecular hydroacylation of 2-benzoylbenzaldehydes to produce phthalides in moderate yields.[4] Lin et al. described the catalytic enantioselective preparation of chiral phthalides by reductive cyclization of 2-acylarylcarboxylates.[5] The iridium-catalyzed dehydrogenative lactonization[6] or organocatalytic domino oxidation[7] of 1,2-benzenedimethanols also gave phthalides in good yields. However, the development of a simple and efficient method to synthesize phthalide derivatives still remains a highly desirable goal in organic synthesis.

The transition-metal-catalyzed functionalizations of a C−H bond have provided a straightforward and atom-economical way to construct complex organic molecules and have received much attention.[8] Onomura et al. described an efficient synthesis of 3-arylphthalides by palladium-catalyzed arylation of methyl 2-formylbenzoate with organoboronic acids.[9] Cheng et al. developed an efficient rhodium-catalyzed cascade aryl addition/intramolecular esterification of phthalaldehyde with arylboronic acids, affording the 3-arylphthalides in moderate to good yields.[1c] The intramolecular ketone hydroacylations of 2-acylbenzaldehyde derivatives promoted by a rhodium−chiral diphosphine complex[10] or a cobalt−chiral diphosphine complex[11] have been reported to afford enantioenriched phthalides. Recently, the cross-dehydrogenative C−H bond alkenylations catalyzed by palladium,[12] rhodium,[13] and ruthenium[14] complexes have also attracted considerable attention because these methods avoid the tedious, multistep synthesis of prefunctionalized starting materials and, thus, enable a streamlining of organic synthesis. However, industrial applications of these homogeneous precious metal catalysts remain a challenge because they are expensive, cannot be recovered and reused, and are difficult to be separated from the product mixture, which is a very serious problem in the pharmaceutical industry.[15] Therefore, from the standpoint of green chemistry, the development of a recyclable and reusable catalyst system that allows for highly efficient cross-dehydrogenative C−H bond alkenylation of a wide range of substrates is worthwhile.

There are very important economical and environmental reasons for developing recyclable catalytic systems for organic transformations from both academic and industrial perspectives. In order to satisfy both recyclability and environmental concerns, a more facile and efficient approach is to immobilize the catalyst in a liquid phase by dissolving it into a nonvolatile and nonmixing liquid, such as ionic liquids[16] and PEG.[17] Although ionic liquids provide some advantages, the tedious preparation of ionic liquids is a main disadvantage and their environmental safety is still debated because the toxicity and environmental burden data are unknown for the most of them. It is well-known that poly(ethylene glycols) (PEGs), having negligible vapor pressure, are commercially available and inexpensive, thermally stable, recoverable, nontoxic compounds which serve as efficient media for environmentally friendly and safe chemical reactions.[18] In recent years, PEGs have been successfully utilized as reaction media for the palladium-catalyzed cross-coupling reactions such as Heck reaction,[17a,b] Suzuki reaction,[17c,d] the homocoupling and cross-coupling of aryl halides,[17e] the direct arylation of 1,2,3-triazoles with aryl bromides,[17f] carbonylative Suzuki coupling,[17g] and carbonylative Sonogashira coupling[17h] with facile recycla-

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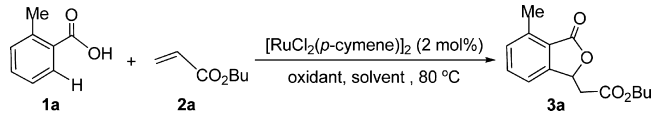
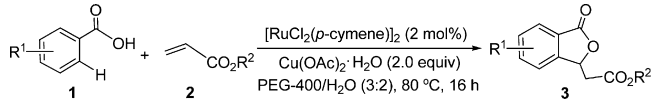
**Table 1. Optimization of Ruthenium-Catalyzed Oxidative Alkenylation of 2-Methylbenzoic Acid with Butyl Acrylate**[a]

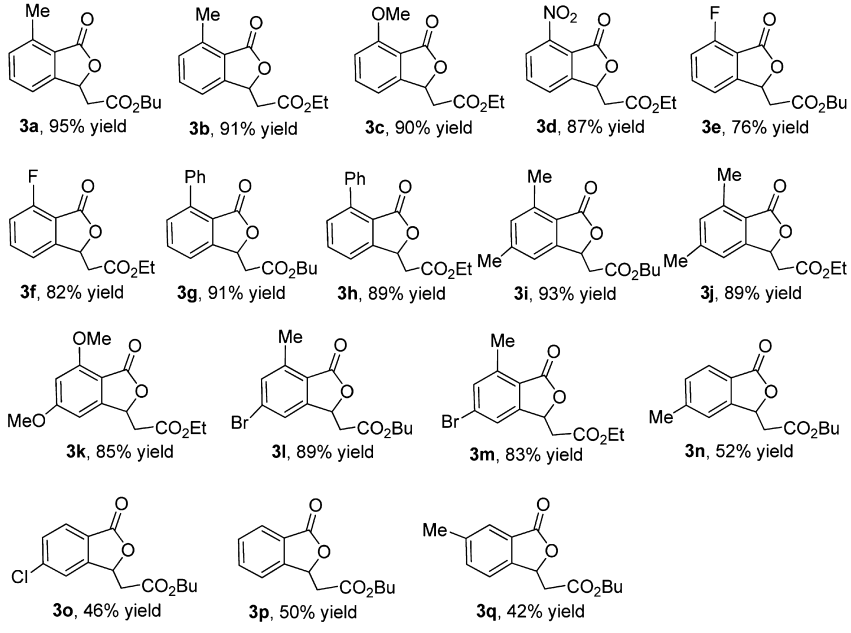



| entry | solvent (*w*/*w*) | oxidant | time (h) | yield (%)[b] |
|---|---|---|---|---|
| 1 | PEG-400 | $Cu(OAc)_2·H_2O$ | 30 | 61 |
| 2 | PEG-400/$H_2O$ (4:1) | $Cu(OAc)_2·H_2O$ | 20 | 78 |
| 3 | PEG-400/$H_2O$ (3:2) | $Cu(OAc)_2·H_2O$ | 16 | 95 |
| 4 | PEG-400/$H_2O$ (1:1) | $Cu(OAc)_2·H_2O$ | 16 | 86 |
| 5 | PEG-400/$H_2O$ (2:3) | $Cu(OAc)_2·H_2O$ | 16 | 90 |
| 6 | PEG-400/$H_2O$ (1:4) | $Cu(OAc)_2·H_2O$ | 16 | 92 |
| 7 | PEG-400/$H_2O$ (3:2) | $PhI(OAc)_2$ | 24 | 0 |
| 8 | PEG-400/$H_2O$ (3:2) | benzoquinone | 24 | 33 |
| 9 | PEG-400/$H_2O$ (3:2) | $AgNO_3$ | 24 | 0 |
| 10 | PEG-400/$H_2O$ (3:2) | AgOAc | 24 | 8 |
| 11 | PEG-400/$H_2O$ (3:2) | $CuBr_2$ | 24 | 0 |
| 12 | PEG-600 | $Cu(OAc)_2·H_2O$ | 30 | 58 |
| 13 | PEG-600/$H_2O$ (3:2) | $Cu(OAc)_2·H_2O$ | 16 | 89 |
| 14 | PEG-1000 | $Cu(OAc)_2·H_2O$ | 30 | 51 |
| 15 | PEG-1000/$H_2O$ (3:2) | $Cu(OAc)_2·H_2O$ | 24 | 76 |
| 16[c] | PEG-400/$H_2O$ (3:2) | $Cu(OAc)_2·H_2O$ | 12 | 90 |
| 17[d] | PEG-400/$H_2O$ (3:2) | $Cu(OAc)_2·H_2O$ | 48 | 49 |

[a]Reaction conditions: **1a** (1.0 mmol), **2a** (2.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.0 mol %), oxidant (2.0 mmol), solvent (5.0 g), 80 °C, under Ar. [b]Isolated yield. [c]At 100 °C. [d]At 60 °C.

**Table 2. Ruthenium-Catalyzed Oxidative Alkenylation of Benzoic Acids with Butyl or Ethyl Acrylates**[a,b]




[a]Reaction conditions: **1** (1.0 mmol), **2** (2.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.0 mol %), $Cu(OAc)_2·H_2O$ (2.0 mmol), PEG-400 (3.0 g), $H_2O$ (2.0 g), 80 °C, 16 h, under Ar. [b]Isolated yield.

bility of solvents and palladium catalysts. However, to the best of our knowledge, the ruthenium-catalyzed carbon−carbon coupling reactions in PEGs have not been reported until now. We herein report the application of the $[RuCl_2(p\text{-cymene})]_2$/$Cu(OAc)_2·H_2O$/PEG-400/$H_2O$ system as an extremely effective and reusable catalytic medium for the tandem intermolecular oxidative alkenylation/oxa-Michael addition reaction of benzoic acids with alkenes.

Initially, the intermolecular oxidative alkenylation of 2-methylbenzoic acid with butyl acrylate was chosen as a model



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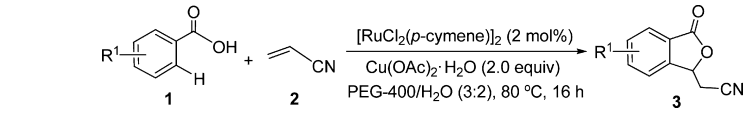
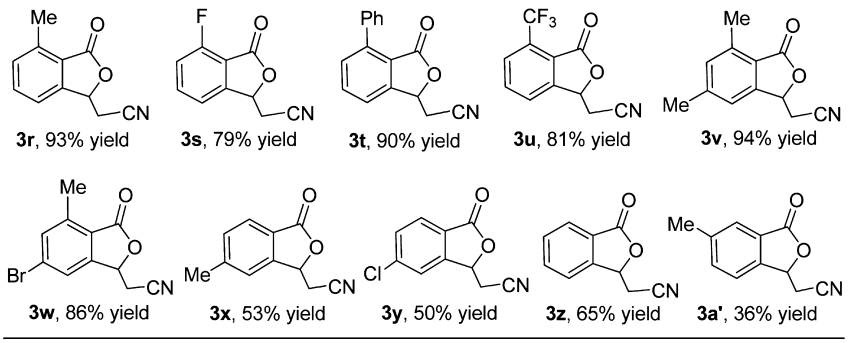
**Table 3. Ruthenium-Catalyzed Oxidative Alkenylation of Benzoic Acids with Acrylonitrile**[a,b]




[a]Reaction conditions: **1** (1.0 mmol), **2** (2.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.0 mol %), $Cu(OAc)_2{\cdot}H_2O$ (2.0 mmol), PEG-400 (3.0 g), $H_2O$ (2.0 g), 80 °C, 16 h, under Ar. [b]Isolated yield.

reaction to determine the optimum conditions, and the results are summarized in Table 1. At first, the solvent effect was examined, and a significant solvent effect was observed. It is evident that the reaction proceeded slowly, and the desired product **3a** was isolated in only 61% yield when PEG-400 alone was used as solvent (Table 1, entry 1). However, a mixture of PEG-400 and $H_2O$ was found to be more effective than PEG-400 (Table 1, entries 2−6). The reaction run in PEG-400/$H_2O$ (3:2) gave **3a** in 95% yield (Table 1, entry 3). Our next studies focused on the effect of oxidant on the model reaction. When $PhI(OAc)_2$, $AgNO_3$, and $CuBr_2$ were used as the oxidant, no reaction was observed, whereas benzoquinone and AgOAc afforded low yields (Table 1, entries 7−11), so $Cu(OAc)_2{\cdot}H_2O$ was finally selected as the oxidant for the reaction. In addition, the efficiency of various chain length PEGs on the reaction was also examined under the same reaction conditions (Table 1, entries 12−15). PEG-400 was superior to PEG-600 and PEG-1000. For the temperatures evaluated (60, 80, and 100 °C), 80 °C gave the best result. It was found that the reaction was accomplished when it was carried out in PEG-400/$H_2O$ (3:2) at 80 °C for 16 h. Reducing the reaction temperature to 60 °C resulted in a significant decrease in yield, and a longer reaction time was needed (Table 1, entry 17). Therefore, the optimal catalytic system involved the use of $[RuCl_2(p\text{-cymene})]_2$ (2 mol %), $Cu(OAc)_2{\cdot}H_2O$ (2.0 equiv) in PEG-400/$H_2O$ (3:2) at 80 °C under Ar for 16 h (Table 1, entry 3).

As a result of these studies, we were encouraged to examine the reaction with a broad range of substrates to determine the specificity and scope of substrates. Thus, a variety of substituted benzoic acids were reacted with butyl or ethyl acrylates under the optimized conditions, and the results are listed in Table 2. As shown in Table 2, it is evident that most of the ruthenium-catalyzed tandem oxidative C−H bond alkenylation/oxa-Michael addition reactions proceeded smoothly under mild conditions in PEG-400/$H_2O$ medium, affording good to excellent yields of phthalide derivatives. For example, the reactions of sterically hindered *ortho*-substituted acids such as 2-methylbenzoic acid, 2-methoxybenzoic acid, 2-nitrobenzoic acid, 2-fluorobenzoic acid, and 2-phenylbenzoic acid with butyl or ethyl acrylates gave the corresponding phthalides **3a**−**3h** in 76−95% yields. The results indicated that the electronic effect of substituents on the benzene ring has limited influence on the reaction, and both electron-donating and electron-withdrawing groups were tolerated well. The reactions of 2,4-disubstituted acids such as 2,4-dimethylbenzoic acid, 2,4-dimethoxybenzoic acid, and 4-bromo-2-methylbenzoic acid with butyl or ethyl acrylates also proceeded effectively under the optimized conditions to afford the desired products **3i**−**3m** in high yields. The $[RuCl_2(p\text{-cymene})]_2/Cu(OAc)_2{\cdot}H_2O$/PEG-400/$H_2O$ catalytic system turned out to be broadly applicable and, hence, also enabled the selective oxidative alkenylation of benzoic acids not carrying an *ortho*-substituent such as 4-methylbenzoic acid, 4-chlorobenzoic acid, and benzoic acid with butyl acrylate, but the corresponding products **3n**−**3p** were isolated in only moderate yields and a byproduct was formed due to the presence of dialkenylation. When 3-methylbenzoic acid was used as the substrate, the desired product **3q** was obtained in only 42% yield and three other byproducts were also detected because of the presence of unsymmetrical monoalkenylation and dialkenylation.

Encouraged by the above results, we next investigated the reaction of benzoic acids with acrylonitrile under the optimized reaction conditions for acrylic acid esters, and the results are listed in Table 3. We were pleased to find that the standard conditions were compatible with a variety of *ortho*-substituted benzoic acids bearing methyl, fluoro, phenyl, and trifluoromethyl groups. It was found that both electron-rich and electron-deficient *ortho*-substituted benzoic acids underwent the tandem oxidative alkenylation/oxa-Michael addition reaction with acrylonitrile efficiently and generated the corresponding phthalide derivatives **3r**−**3u** in good to excellent yields. The reactions of 2,4-disubstituted acids such as 2,4-dimethylbenzoic acid and 4-bromo-2-methylbenzoic acid with acrylonitrile also proceeded smoothly under the standard reaction conditions to afford the corresponding products **3v** and **3w** in 94% and 86% yields, respectively. However, for the benzoic acids not bearing an *ortho*-substituent, the reactions with acrylonitrile afforded the desired products **3x**−**3z** in only moderate yields owing to the presence of dialkenylation. The reaction of 3-methylbenzoic acid with acrylonitrile gave the desired product **3a′** in only 36% yield due to the existence of unsymmetrical monoalkenylation and dialkenylation. We attempted to carry out the tandem oxidative alkenylation/oxa-Michael addition reaction of *ortho*-substituted



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benzoic acids with acrylamide under the same conditions; unfortunately, the reaction did not occur at all.

To check the reusability of the solvent as well as the catalytic system, the tandem oxidative alkenylation/oxa-Michael addition reaction of 2-methylbenzoic acid with butyl acrylate was first evaluated in the presence of $[RuCl_2(p\text{-cymene})]_2$ (2 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (2.0 equiv) in PEG-400/$H_2O$ (3:2, 5 g) at 80 °C. As demonstrated in Table 4, we were gratified to observe that

**Table 4. Recovery and Reuse of $[RuCl_2(p\text{-cymene})]_2$/$Cu(OAc)_2{\cdot}H_2O$/PEG-400/$H_2O$ System for the Tandem Reactions**[a]

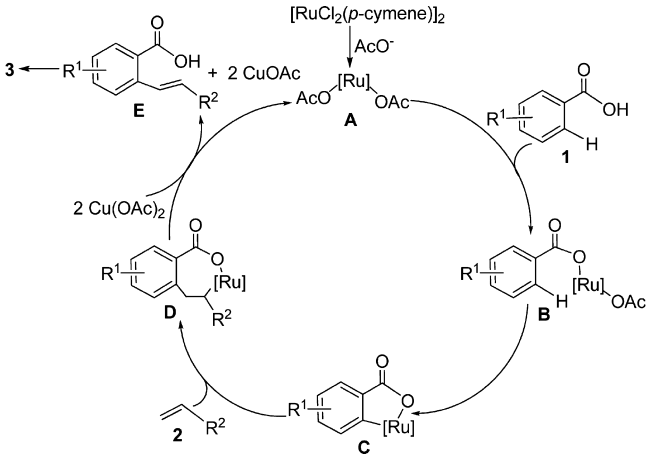
| | | | isolated yield (%) | | | | | |
|---|---|---|---|---|---|---|---|---|
| entry | product | time (h)[b] | 1 | 2 | 3 | 4 | 5 | 6 |
| 1 | **3a** | 18 | 94 | 95 | 93 | 96 | 94 | 95 |
| 2 | **3v** | 19 | 93 | 95 | 94 | 93 | 95 | 93 |

[a]Reaction conditions: **1** (1.0 mmol), **2** (2.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.0 mol %), $Cu(OAc)_2{\cdot}H_2O$ (2.0 mmol), PEG-400 (3.0 g), $H_2O$ (2.0 g), 80 °C, under Ar. [b]Average reaction time of six runs.

the $[RuCl_2(p\text{-cymene})]_2/Cu(OAc)_2{\cdot}H_2O$/PEG-400/$H_2O$ system could be recycled and reused six times without any loss of activity. After initial experimentation, the reaction mixture was extracted with light petroleum ether (3 × 10 mL), and the $[RuCl_2(p\text{-cymene})]_2/Cu(OAc)_2{\cdot}H_2O$/PEG-400/$H_2O$ system was then subjected to a second run of the tandem reaction by charging with the same substrates (2-methylbenzoic acid and butyl acrylate) without addition of $[RuCl_2(p\text{-cymene})]_2$ and $Cu(OAc)_2{\cdot}H_2O$. The results of six runs showed that they were almost consistent in yields and rates (94, 95, 93, 96, 94, and 95%, respectively, for 18 h; entry 1). The reaction of 2,4-dimethylbenzoic acid with acrylonitrile could also be recycled and reused six times without any loss of activity in the presence of $[RuCl_2(p\text{-cymene})]_2$ (2 mol %) and $Cu(OAc)_2{\cdot}H_2O$ (2.0 equiv) in PEG-400/$H_2O$ (3:2, 5 g) at 80 °C (entry 2).

A plausible mechanism for the ruthenium-catalyzed oxidative C−H bond alkenylation reaction of benzoic acids **1** with alkenes **2** is illustrated in Scheme 1. First, the reaction of $[RuCl_2(p\text{-cymene})]$ with acetate generates in situ ruthenium(II) diacetate complex **A**. Coordination of the carboxyl oxygen of **1** to the ruthenium(II) diacetate complex **A** with liberation of AcOH gives a ruthenium(II) benzoate **B**. Subsequent *ortho*-C−H bond ruthenation to form a ruthenacycle intermediate **C**, alkene

**Scheme 1. Proposed Catalytic Cycle**




insertion, and $\beta$-hydride elimination successively occur to produce an olefinated intermediate **E**. The latter undergoes intramolecular oxa-Michael addition reaction to afford the desired phthalide **3**. After the release of intermediate **E**, the resulting [Ru(0)] species may be oxidized in the presence of $Cu(OAc)_2$ to regenerate ruthenium(II) diacetate complex **A**.

In conclusion, a highly efficient and reusable $[RuCl_2(p\text{-cymene})]_2/Cu(OAc)_2{\cdot}H_2O$/PEG-400/$H_2O$ system for the tandem intermolecular oxidative C−H bond alkenylation/oxa-Michael addition reaction of benzoic acids with alkenes has been developed. In the presence of $[RuCl_2(p\text{-cymene})]_2$ (2.0 mol %), the tandem intermolecular oxidative alkenylation/oxa-Michael addition reactions of a variety of substituted benzoic acids with electron-deficient alkenes such as butyl or ethyl acrylates and acrylonitrile proceeded smoothly and efficiently at 80 °C using $Cu(OAc)_2{\cdot}H_2O$ (2.0 equiv) as oxidant in a mixture of PEG-400 and water to afford the desired phthalide derivatives in good to excellent yields. Furthermore, the $[RuCl_2(p\text{-cymene})]_2/Cu(OAc)_2{\cdot}H_2O$/PEG-400/$H_2O$ system could be recycled and reused six times without any loss of catalytic activity. This protocol will serve as an efficient and green way to prepare phthalide derivatives.

## EXPERIMENTAL SECTION

**General Methods.** All chemicals were reagent grade and used as purchased. The products were purified by flash chromatography on silica gel. A mixture of EtOAc and light petroleum ether was generally used as eluent. All products were characterized by comparison of their spectra and physical data with authentic samples. IR spectra were recorded on an FT-IR spectrometer. $^1H$ and $^{13}C$ NMR spectra were recorded at 400 or 100 MHz with $CDCl_3$ or DMSO-$d_6$ as the solvent and TMS as an internal standard. Chemical shifts are reported in $\delta$ (ppm) relative to TMS. HRMS spectra were recorded on a Q-Tof spectrometer with micromass MS software using electrospray ionization (ESI). Melting points are uncorrected.

**General Procedure for the Ruthenium-Catalyzed Oxidative Alkenylation Reaction in PEG-400/$H_2O$.** A mixture of benzoic acid **1** (1.0 mmol), alkene **2** (2.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.02 mmol), $Cu(OAc)_2{\cdot}H_2O$ (2.0 mmol), PEG-400 (3.0 g), and $H_2O$ (2.0 g) was added to a sealed tube under Ar, and then the mixture was stirred at 80 °C for 16 h until complete consumption of starting material as judged by TLC. After being cooled to room temperature, the mixture was extracted three times with light petroleum ether (3 × 10 mL). The combined ether phase was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (light petroleum ether−ethyl acetate = 10:1) to afford the desired products **3**.

The mixture of $[RuCl_2(p\text{-cymene})]_2$, $Cu(OAc)_2{\cdot}H_2O$, PEG-400, and $H_2O$ was then subjected to a second run of the tandem reaction by charging with the same substrates (benzoic acid **1** and alkene **2**) under the same conditions without further addition of $[RuCl_2(p\text{-cymene})]_2$ and $Cu(OAc)_2{\cdot}H_2O$.

*3-[(n-Butoxycarbonyl)methyl]-7-methylphthalide (**3a**).*[19] Colorless oil (248.6 mg, 95%). IR (neat): 2961, 1765, 1734, 1602, 1203, 1175, 1048, 1009, 788, 689 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.56−7.52 (m, 1H), 7.32−7.27 (m, 2H), 5.82 (t, $J$ = 6.6 Hz, 1H), 4.16 (t, $J$ = 6.6 Hz, 2H), 2.88 (d, $J$ = 6.8 Hz, 2H), 2.69 (s, 3H), 1.64−1.58 (m, 2H), 1.40−1.33 (m, 2H), 0.93 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 170.1, 169.4, 149.3, 139.9, 134.0, 131.1, 123.4, 119.3, 76.1, 65.1, 39.8, 30.5, 19.1, 17.3, 13.7. HRMS calcd for $C_{15}H_{18}O_4^+$ $[M^+]$: 262.1205, found 262.1209.

*3-[(Ethoxycarbonyl)methyl]-7-methylphthalide (**3b**).*[19] White solid (212.7 mg, 91%). mp 49−50 °C. IR (KBr): 2985, 1732, 1166, 1043, 1007, 787, 625 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.56−7.53 (m, 1H), 7.32−7.27 (m, 2H), 5.83 (t, $J$ = 6.6 Hz, 1H), 4.23 (q, $J$ = 7.2 Hz, 2H), 2.88 (d, $J$ = 6.8 Hz, 2H), 2.70 (s, 3H), 1.29 (t, $J$ = 7.0 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 170.1, 169.4, 149.3, 139.9, 134.0, 131.1,



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123.4, 119.3, 76.1, 61.2, 39.8, 17.4, 14.1. HRMS calcd for $C_{13}H_{14}O_4^+$ [$M^+$]: 234.0892, found 234.0885.

*3-[(Ethoxycarbonyl)methyl]-7-methoxyphthalide* (**3c**). Colorless oil (224.8 mg, 90%). IR (neat): 2982, 1766, 1733, 1603, 1488, 1279, 1180, 1038, 799, 691 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.64−7.61 (m, 1H), 7.01 (d, $J$ = 7.2 Hz, 1H), 6.96 (d, $J$ = 8.4 Hz, 1H), 5.81 (t, $J$ = 6.6 Hz, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 4.00 (s, 3H), 2.86 (d, $J$ = 6.8 Hz, 2H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 168.8, 167.4, 158.2, 151.1, 136.1, 113.1, 112.8, 110.7, 75.4, 60.7, 55.6, 39.2, 13.6. HRMS calcd for $C_{13}H_{14}O_5^+$ [$M^+$]: 250.0841, found 250.0823.

*3-[(Ethoxycarbonyl)methyl]-7-nitrophthalide* (**3d**). Yellow solid (230.5 mg, 87%). mp 78−79 °C. IR (KBr): 2945, 1757, 1739, 1596, 1511, 1326, 1268, 1185, 1008, 764, 695 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94 (d, $J$ = 7.6 Hz, 1H), 7.88 (d, $J$ = 7.6 Hz, 1H), 7.85−7.81 (m, 1H), 5.92 (t, $J$ = 6.4 Hz, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 3.04 (dd, $J$ = 16.4, 6.0 Hz, 1H), 2.94 (dd, $J$ = 17.2, 6.8 Hz, 1H), 1.27 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 168.8, 168.2, 151.4, 135.3, 130.9, 126.5, 124.5, 76.0, 61.6, 39.0, 14.1. HRMS calcd for $C_{12}H_{11}NO_6^+$ [$M^+$]: 265.0586, found 265.0569.

*3-[(n-Butoxycarbonyl)methyl]-7-fluorophthalide* (**3e**). Colorless oil (202.4 mg, 76%). IR (neat): 2995, 1767, 1731, 1483, 1274, 1199, 1010, 802, 685 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.72−7.66 (m, 1H), 7.31−7.28 (m, 1H), 7.20 (t, $J$ = 8.2 Hz, 1H), 5.88 (t, $J$ = 6.0 Hz, 1H), 4.16 (t, $J$ = 6.4 Hz, 2H), 2.96 (dd, $J$ = 16.4, 6.4 Hz, 1H), 2.88 (dd, $J$ = 16.8, 6.0 Hz, 1H), 1.64−1.59 (m, 2H), 1.40−1.34 (m, 2H), 0.94 (t, $J$ = 7.0 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 169.1, 166.0, 159.6 (d, $^1J_{C\text{-}F}$ = 263.2 Hz), 151.4, 136.9 (d, $^3J_{C\text{-}F}$ = 6.6 Hz), 118.0 (d, $^3J_{C\text{-}F}$ = 4.2 Hz), 116.5 (d, $^2J_{C\text{-}F}$ = 18.8 Hz), 113.8 (d, $^2J_{C\text{-}F}$ = 14.2 Hz), 76.7, 65.3, 39.3, 30.5, 19.1, 13.6. HRMS calcd for $C_{14}H_{15}FNaO_4^+$ [$M$ + $Na^+$]: 289.0851, found 289.0831.

*3-[(Ethoxycarbonyl)methyl]-7-fluorophthalide* (**3f**).[19] White solid (195.3 mg, 82%). mp 88−89 °C. IR (KBr): 2991, 1762, 1730, 1478, 1264, 1187, 1005, 803, 686 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.71−7.65 (m, 1H), 7.30−7.26 (m, 1H), 7.18 (t, $J$ = 8.6 Hz, 1H), 5.87 (t, $J$ = 6.4 Hz, 1H), 4.20 (q, $J$ = 7.2 Hz, 2H), 2.94 (dd, $J$ = 16.4, 6.8 Hz, 1H), 2.88 (dd, $J$ = 16.0, 5.6 Hz, 1H), 1.26 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 168.5, 159.2 (d, $^1J_{C\text{-}F}$ = 263.3 Hz), 150.9, 136.4, 117.6, 116.1 (d, $^2J_{C\text{-}F}$ = 18.6 Hz), 113.5, 76.1, 60.9, 38.9, 13.6. HRMS calcd for $C_{12}H_{11}FO_4^+$ [$M^+$]: 238.0641, found 238.0647.

*3-[(n-Butoxycarbonylmethyl)]-7-phenylphthalide* (**3g**). Colorless oil (294.5 mg, 91%). IR (neat): 2988, 1757, 1740, 1593, 1471, 1184, 1041, 1010, 764, 698 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.70 (t, $J$ = 7.6 Hz, 1H), 7.55−7.41 (m, 7H), 5.87 (t, $J$ = 6.4 Hz, 1H), 4.17 (t, $J$ = 6.8 Hz, 2H), 2.95−2.92 (m, 2H), 1.65−1.60 (m, 2H), 1.39−1.34 (m, 2H), 0.93 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 169.0, 168.1, 149.7, 142.5, 135.8, 133.6, 130.8, 129.0, 127.9, 127.5, 121.5, 120.3, 75.1, 64.7, 39.3, 30.0, 18.6, 13.2. HRMS calcd for $C_{20}H_{20}NaO_4^+$ [$M$ + $Na^+$]: 347.1259, found 347.1245.

*3-[(Ethoxycarbonyl)methyl]-7-phenylphthalide* (**3h**).[14d] White solid (263.3 mg, 89%). mp 108−109 °C. IR (KBr): 2990, 1756, 1737, 1596, 1473, 1183, 1040, 1009, 763, 697 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.71 (t, $J$ = 7.6 Hz, 1H), 7.55−7.40 (m, 7H), 5.87 (t, $J$ = 6.4 Hz, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 2.95−2.92 (m, 2H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 168.9, 168.2, 149.7, 142.4, 135.8, 133.6, 130.8, 129.0, 128.0, 127.5, 121.5, 120.3, 75.1, 60.8, 39.3, 13.7. HRMS calcd for $C_{18}H_{16}O_4^+$ [$M^+$]: 296.1049, found 296.1042.

*3-[(n-Butoxycarbonylmethyl)]-5,7-dimethylphthalide* (**3i**). Colorless oil (256.5 mg, 93%). IR (neat): 2983, 1760, 1732, 1615, 1379, 1204, 1178, 1022, 863, 687 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.10 (s, 1H), 7.06 (s, 1H), 5.77 (t, $J$ = 6.4 Hz, 1H), 4.17 (t, $J$ = 6.6 Hz, 2H), 2.85 (d, $J$ = 6.4 Hz, 2H), 2.64 (s, 3H), 2.43 (s, 3H), 1.65−1.59 (m, 2H), 1.40−1.34 (m, 2H), 0.94 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 170.2, 169.6, 149.9, 145.2, 139.5, 132.2, 120.9, 119.7, 75.9, 65.1, 39.8, 30.5, 22.0, 19.1, 17.3, 13.7. HRMS calcd for $C_{16}H_{20}O_4^+$ [$M^+$]: 276.1362, found 276.1369.

*3-[(Ethoxycarbonylmethyl)]-5,7-dimethylphthalide* (**3j**).[14d] Colorless oil (220.8 mg, 89%). IR (neat): 2985, 1757, 1730, 1613, 1204, 1078, 1013, 858, 686 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.10 (s, 1H), 7.06 (s, 1H), 5.76 (t, $J$ = 6.4 Hz, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 2.84 (d, $J$ = 6.4 Hz, 2H), 2.64 (s, 3H), 2.43 (s, 3H), 1.28 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 169.6, 169.0, 149.4, 144.6, 139.0, 131.7, 120.5, 119.2, 75.3, 60.7, 39.4, 21.4, 16.7, 13.6. HRMS calcd for $C_{14}H_{16}O_4^+$ [$M^+$]: 248.1049, found 248.1054.

*3-[(Ethoxycarbonylmethyl)]-5,7-dimethoxyphthalide* (**3k**). Colorless oil (237.3 mg, 85%). IR (neat): 2981, 1730, 1603, 1334, 1198, 1154, 1053, 1008, 838, 688 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 6.50 (s, 1H), 6.45 (s, 1H), 5.73 (t, $J$ = 6.4 Hz, 1H), 4.22 (q, $J$ = 7.0 Hz, 2H), 3.96 (s, 3H), 3.89 (s, 3H), 2.87−2.80 (m, 2H), 1.29 (t, $J$ = 7.0 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 169.4, 167.7, 166.9, 159.7, 153.8, 106.6, 99.1, 97.9, 75.6, 61.2, 56.0, 55.9, 39.8, 14.1. HRMS calcd for $C_{14}H_{16}O_6^+$ [$M^+$]: 280.0947, found 280.0925.

*5-Bromo-3-[(n-butoxycarbonyl)methyl]-7-methylphthalide* (**3l**). Colorless oil (303.7 mg, 89%). IR (neat): 2962, 1761, 1714, 1592, 1201, 1183, 1051, 1016, 871, 680 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.47 (s, 2H), 5.77 (t, $J$ = 6.6 Hz, 1H), 4.17 (t, $J$ = 6.6 Hz, 2H), 2.93 (dd, $J$ = 16.4, 6.4 Hz, 1H), 2.83 (dd, $J$ = 16.8, 6.4 Hz, 1H), 2.66 (s, 3H), 1.64−1.57 (m, 2H), 1.40−1.34 (m, 2H), 0.94 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 168.7, 168.6, 150.5, 141.1, 133.9, 128.5, 122.4, 122.1, 75.0, 64.8, 38.9, 30.0, 18.6, 16.7, 13.2. HRMS calcd for $C_{15}H_{17}BrNaO_4^+$ [$M$ + $Na^+$]: 363.0207, found 363.0191.

*5-Bromo-3-[(ethoxycarbonyl)methyl]-7-methylphthalide* (**3m**).[14d] White solid (259.2 mg, 83%). mp 74−75 °C. IR (KBr): 2962, 1761, 1714, 1592, 1201, 1183, 1051, 1016, 871, 680 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.47 (s, 2H), 5.78 (t, $J$ = 6.6 Hz, 1H), 4.22 (q, $J$ = 7.2 Hz, 2H), 2.92 (dd, $J$ = 16.8, 6.8 Hz, 1H), 2.83 (dd, $J$ = 16.8, 6.4 Hz, 1H), 2.66 (s, 3H), 1.29 (t, $J$ = 7.2 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 168.6, 168.5, 150.5, 141.1, 133.9, 128.5, 122.4, 122.1, 75.0, 60.9, 39.0, 16.7, 13.6. HRMS calcd for $C_{13}H_{13}BrO_4^+$ [$M^+$]: 311.9997, found 311.9986.

*3-[(n-Butoxycarbonyl)methyl]-5-methylphthalide* (**3n**). Colorless oil (136.1 mg, 52%). IR (neat): 2968, 1761, 1728, 1598, 1193, 1168, 1052, 1007, 789, 686 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.79 (d, $J$ = 7.6 Hz, 1H), 7.36 (d, $J$ = 7.6 Hz, 1H), 7.29 (s, 1H), 5.84 (t, $J$ = 6.6 Hz, 1H), 4.17 (t, $J$ = 6.8 Hz, 2H), 2.92 (dd, $J$ = 16.4, 7.2 Hz, 1H), 2.87 (dd, $J$ = 14.4, 4.0 Hz, 1H), 2.50 (s, 3H), 1.67−1.59 (m, 2H), 1.42−1.34 (m, 2H), 0.94 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 169.9, 169.4, 149.4, 145.6, 130.7, 125.6, 123.4, 122.4, 76.7, 65.1, 39.6, 30.5, 22.1, 19.1, 13.6. HRMS calcd for $C_{15}H_{18}O_4^+$ [$M^+$]: 262.1205, found 262.1212.

*3-[(n-Butoxycarbonyl)methyl]-5-chlorophthalide* (**3o**). Colorless oil (129.8 mg, 46%). IR (neat): 2968, 1761, 1728, 1598, 1193, 1168, 1052, 1007, 789, 686 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.85 (d, $J$ = 8.4 Hz, 1H), 7.56−7.52 (m, 2H), 5.86 (t, $J$ = 6.6 Hz, 1H), 4.17 (t, $J$ = 6.6 Hz, 2H), 2.99 (dd, $J$ = 16.4, 6.4 Hz, 1H), 2.88 (dd, $J$ = 16.8, 6.8 Hz, 1H), 1.67−1.60 (m, 2H), 1.42−1.34 (m, 2H), 0.94 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 169.1, 168.7, 150.5, 141.0, 130.3, 127.0, 124.5, 122.8, 76.4, 65.3, 39.2, 30.5, 19.1, 13.6. HRMS calcd for $C_{14}H_{15}ClO_4^+$ [$M^+$]: 282.0659, found 282.0647.

*3-[(n-Butoxycarbonyl)methyl]phthalide* (**3p**). Colorless oil (124.3 mg, 50%). IR (neat): 2964, 1756, 1730, 1595, 1203, 1165, 1049, 1009, 787, 688 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.92 (d, $J$ = 7.6 Hz, 1H), 7.71 (t, $J$ = 7.4 Hz, 1H), 7.59−7.51 (m, 2H), 5.91 (t, $J$ = 6.4 Hz, 1H), 4.17 (t, $J$ = 6.8 Hz, 2H), 2.95−2.91 (m, 2H), 1.66−1.59 (m, 2H), 1.42−1.34 (m, 2H), 0.93 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 169.9, 169.3, 148.8, 134.3, 129.5, 126.0, 125.8, 122.1, 76.7, 65.2, 39.5, 30.5, 19.0, 13.6. HRMS calcd for $C_{14}H_{16}O_4^+$ [$M^+$]: 248.1049, found 248.1056.

*3-[(n-Butoxycarbonyl)methyl]-6-methylphthalide* (**3q**). Colorless oil (110.2 mg, 42%). IR (neat): 2960, 1770, 1731, 1626, 1594, 1495, 1060, 1009, 838, 779 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.68 (s, 1H), 7.50 (d, $J$ = 7.6 Hz, 1H), 7.41 (d, $J$ = 7.6 Hz, 1H), 5.84 (t, $J$ = 6.4 Hz, 1H), 4.15 (t, $J$ = 6.6 Hz, 2H), 2.89 (d, $J$ = 6.4 Hz, 2H), 2.47 (s, 3H), 1.66−1.57 (m, 2H), 1.43−1.31 (m, 2H), 0.92 (t, $J$ = 7.4 Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 170.0, 169.3, 146.2, 139.8, 135.4, 126.1, 125.6, 121.8, 76.9, 65.0, 39.6, 30.5, 21.2, 19.0, 13.6. HRMS calcd for $C_{15}H_{18}O_4^+$ [$M^+$]: 262.1205, found 262.1201.

*3-Cyanomethyl-7-methylphthalide* (**3r**).[13b] White solid (173.5 mg, 93%). mp 118−119 °C. IR (KBr): 2965, 2933, 2252, 1753, 1603, 1205, 1040, 1009, 751, 686 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.62 (t, $J$ = 7.6 Hz, 1H), 7.44 (d, $J$ = 7.6 Hz, 1H), 7.38 (d, $J$ = 7.6 Hz, 1H), 5.61 (t, $J$ = 5.8 Hz, 1H), 3.06 (dd, $J$ = 17.2, 5.6 Hz, 1H), 2.96 (dd, $J$ = 16.8, 6.4 Hz,



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1H), 2.71 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 169.0, 147.1, 140.6, 134.6, 132.1, 123.2, 119.4, 115.0, 73.8, 24.0, 17.4. HRMS calcd for $C_{11}H_9NO_2^+$ [$M^+$]: 187.0633, found 187.0639.

*3-Cyanomethyl-7-fluorophthalide (**3s**).* White solid (150.6 mg, 79%). mp 125−126 °C. IR (KBr): 2983, 2253, 1765, 1624, 1482, 1211, 1040, 1011, 805, 681 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.81−7.77 (m, 1H), 7.46 (d, $J$ = 7.6 Hz, 1H), 7.28 (t, $J$ = 8.0 Hz, 1H), 5.71 (t, $J$ = 5.8 Hz, 1H), 3.13 (dd, $J$ = 16.8, 5.2 Hz, 1H), 2.96 (dd, $J$ = 16.8, 6.0 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 164.9 (d, $^3J_{C\text{-}F}$ = 3.0 Hz), 159.8 (d, $^1J_{C\text{-}F}$ = 264.4 Hz), 149.0, 137.7 (d, $^3J_{C\text{-}F}$ = 7.6 Hz), 118.2 (d, $^2J_{C\text{-}F}$ = 20.1 Hz), 117.6 (d, $^2J_{C\text{-}F}$ = 19.2 Hz), 114.6, 113.6 (d, $^3J_{C\text{-}F}$ = 14.5 Hz), 74.5, 23.8. HRMS calcd for $C_{10}H_6FNO_2^+$ [$M^+$]: 191.0383, found 191.0374.

*3-Cyanomethyl-7-phenylphthalide (**3t**).* White solid (224.3 mg, 90%). mp 154−156 °C. IR (KBr): 2978, 2251, 1762, 1619, 1485, 1196, 1042, 1009, 812, 689 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.77 (t, $J$ = 7.6 Hz, 1H), 7.60−7.42 (m, 7H), 5.62 (t, $J$ = 6.0 Hz, 1H), 3.06 (dd, $J$ = 16.8, 5.2 Hz, 1H), 2.99 (dd, $J$ = 16.8, 6.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 167.7, 147.9, 143.4, 135.9, 134.7, 132.2, 129.5, 128.7, 128.1, 121.7, 120.8, 115.0, 73.5, 24.0. HRMS calcd for $C_{16}H_{11}NNaO_2^+$ [$M$ + $Na^+$]: 272.0687, found 272.0663.

*3-Cyanomethyl-7-(trifluoromethyl)phthalide (**3u**).* White solid (195.4 mg, 81%). mp 114−116 °C. IR (KBr): 2976, 2254, 1768, 1312, 1256, 1141, 1122, 1019, 823, 695 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.97−7.85 (m, 3H), 5.74 (t, $J$ = 5.6 Hz, 1H), 3.17 (dd, $J$ = 16.8, 3.2 Hz, 1H), 3.04 (dd, $J$ = 16.8, 6.0 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 164.8, 148.9, 135.0, 129.2 (q, $^2J_{C\text{-}F}$ = 36.4 Hz), 128.1 (q, $^3J_{C\text{-}F}$ = 11.8 Hz), 126.0, 123.1, 121.9 (q, $^1J_{C\text{-}F}$ = 272.2 Hz), 114.6, 74.2, 23.7. HRMS calcd for $C_{11}H_6F_3NNaO_2^+$ [$M$ + $Na^+$]: 264.0248, found 264.0233.

*3-Cyanomethyl-5,7-dimethylphthalide (**3v**).*[14d] White solid (188.7 mg, 94%). mp 137−138 °C. IR (KBr): 2940, 2253, 1749, 1614, 1256, 1208, 1033, 1009, 865, 684 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.22 (s, 1H), 7.18 (s, 1H), 5.54 (t, $J$ = 5.8 Hz, 1H), 3.02 (dd, $J$ = 16.8, 5.2 Hz, 1H), 2.94 (dd, $J$ = 16.8, 6.4 Hz, 1H), 2.64 (s, 3H), 2.47 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 168.5, 147.2, 145.4, 139.6, 132.7, 120.2, 119.3, 114.6, 73.1, 23.5, 21.5, 16.7. HRMS calcd for $C_{12}H_{11}NO_2^+$ [$M^+$]: 201.0790, found 201.0798.

*5-Bromo-3-cyanomethyl-7-methylphthalide (**3w**).* White solid (228.4 mg, 86%). mp 159−161 °C. IR (KBr): 2965, 2251, 1752, 1617, 1246, 1209, 1038, 1011, 863, 694 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.55 (s, 1H), 5.59 (t, $J$ = 5.6 Hz, 1H), 3.04 (d, $J$ = 5.2 Hz, 2H), 2.68 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 168.1, 148.6, 142.2, 135.4, 129.6, 122.9, 122.3, 114.7, 73.4, 23.8, 17.2. HRMS calcd for $C_{11}H_8BrNNaO_2^+$ [$M$ + $Na^+$]: 287.9635, found 287.9629.

*3-Cyanomethyl-5-methylphthalide (**3x**).*[13b] White solid (99.3 mg, 53%). mp 147−148 °C. IR (KBr): 2940, 2250, 1753, 1615, 1346, 1282, 1074, 1013, 842, 689 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, $J$ = 8.0 Hz, 1H), 7.45−7.41 (m, 2H), 5.63 (t, $J$ = 5.8 Hz, 1H), 3.08 (dd, $J$ = 16.8, 5.2 Hz, 1H), 3.00 (dd, $J$ = 16.8, 6.4 Hz, 1H), 2.54 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 168.9, 147.2, 146.4, 131.6, 126.0, 123.1, 122.4, 115.0, 74.4, 23.8, 22.2. HRMS calcd for $C_{11}H_9NO_2^+$ [$M^+$]: 187.0633, found 187.0625.

*5-Chloro-3-cyanomethylphthalide (**3y**).* White solid (103.8 mg, 50%). mp 203−204 °C. IR (KBr): 2944, 2253, 1758, 1611, 1342, 1216, 1063, 1003, 846 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, $J$ = 8.0 Hz, 1H), 7.67−7.61 (m, 2H), 5.66 (t, $J$ = 5.8 Hz, 1H), 3.10 (dd, $J$ = 16.8, 4.8 Hz, 1H), 3.00 (dd, $J$ = 16.8, 6.8 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 167.5, 148.1, 141.8, 131.4, 127.5, 124.3, 122.6, 114.3, 74.1, 23.7. HRMS calcd for $C_{10}H_6ClNO_2^+$ [$M^+$]: 207.0087, found 207.0095.

*3-Cyanomethylphthalide (**3z**).*[13b] White solid (112.6 mg, 65%). mp 113−114 °C. IR (KBr): 2967, 2935, 2252, 1765, 1600, 1347, 1290, 1210, 1054, 991, 746, 719 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, $J$ = 7.6 Hz, 1H), 7.79 (t, $J$ = 7.4 Hz, 1H), 7.68−7.62 (m, 2H), 5.70 (t, $J$ = 5.8 Hz, 1H), 3.10 (dd, $J$ = 16.8, 5.2 Hz, 1H), 3.03 (dd, $J$ = 17.2, 6.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 168.9, 146.6, 134.9, 130.5, 126.3, 125.7, 122.1, 114.9, 74.7, 23.9. HRMS calcd for $C_{10}H_7NO_2^+$ [$M^+$]: 173.0477, found 173.0469.

*3-Cyanomethyl-6-methylphthalide (**3a′**).* White solid (67.5 mg, 36%). mp 153−154 °C. IR (KBr): 2937, 2249, 1749, 1593, 1285, 1153, 1061, 989, 835, 764 cm$^{-1}$. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 7.71 (s, 1H), 7.70−7.61 (m, 2H), 5.88 (t, $J$ = 4.4 Hz, 1H), 3.53 (dd, $J$ = 17.2, 4.4 Hz, 1H), 3.39 (d, $J$ = 5.2 Hz, 1H), 2.45 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 169.1, 145.0, 140.1, 135.7, 125.5, 124.9, 122.6, 116.7, 75.4, 22.8, 20.6. HRMS calcd for $C_{11}H_9NO_2^+$ [$M^+$]: 187.0633, found 187.0636.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01388.

Copies of $^1$H and $^{13}$C NMR spectra for the products (PDF)

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### Notes

The authors declare no competing financial interest.

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