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Palladium-Catalyzed Tandem Annulation: A Strategy To Construct 2,3-Difunctionalized Benzofuran Derivatives in Ionic Liquids

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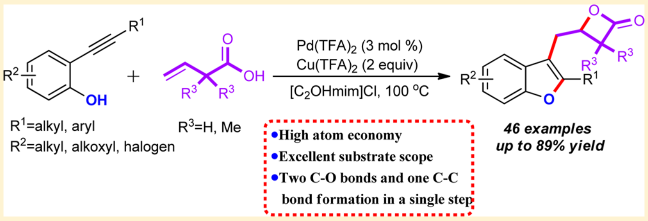
Supporting Information

ABSTRACT: An efficient and ecofriendly method for the construction of 2,3-difunctionalized benzofuran derivatives in moderate to good yields from readily available 2-alkynylphenols has been developed. This tandem annulation process, featuring one pot, three steps, good functional group tolerance, and high atom economy, makes this transformation efficient and practical. Moreover, this protocol is scalable, illustrating its potential applications in synthetic and pharmaceutical chemistry.

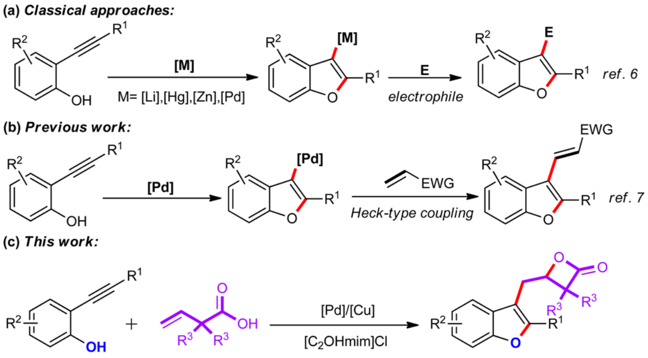


INTRODUCTION

The shortage of resources and the increasing awareness of environmental aspects have changed the major focus of contemporary chemical research to provide desired target molecules via an economical and environmentally benign synthetic route.[1] Toward this end, transition-metal-catalyzed carbon−carbon or carbon−heteroatom bond formation has attracted considerable attention over the past decades, owing to its easy access to highly functionalized complicated molecules in a rather efficient, atom- and step-economical way.[2] Particularly, palladium-catalyzed tandem reaction is now established as a captivating branch of organic chemistry, since such reactions afford unconventional and more elaborated poly- and heterocyclic scaffolds via straightforward and efficient synthetic strategies.[3] Besides, the outstanding potential of palladium-catalyzed tandem processes lies in (i) the diversity of available bond-forming processes, such as C−C, C−O, and C−N bond formations; (ii) high chemo-, regio-, and stereoselectivity; and (iii) great functional-group tolerance. Consequently, palladium-catalyzed tandem processes constitute an efficient strategy to synthesize an increasingly wide range of polyfunctionalized compounds.[4]

In addition, 2,3-difunctionalized benzofurans are attractive synthetic targets because of their remarkable biological activities and potentiality of being pharmaceutical,[5] prompting development of many efficient synthetic methodologies for constructing this scaffold. Undoubtedly, 2-alkynylphenols are the most commonly used precursors to prepare this functionalized core backbone, for instance, cyclization of 2-alkynylphenol to the 3-metallobenzofuran intermediate that reacts further with an electrophile to produce the corresponding 2,3-difunctionalized benzofuran derivatives (Scheme 1, route a).[6] After that, Aurrecoechea and co-workers discovered a new Pd-catalyzed tandem intramolecular oxypalladation/Heck-type coupling between 2-alkynylphenols and alkenes leading to 2,3-difunctionalized benzofuran derivatives (Scheme 1, route b).[7] Despite the significant progress that has been achieved along this line, all these elegant developments suffer from certain limitations such as troublesome operation, harsh reaction conditions, or low yields, prohibiting their wider application in organic synthesis. Therefore, the development of convenient, efficient, and atom-economical synthetic methodologies for the rapid construction of this heterocyclic motif is still highly desirable. In this context, impressive achievements have been made in enhancing the efficiency of transition-metal-catalyzed cross-coupling reaction for the synthesis of 2,3-difunctionalized benzofurans, notably cross-coupling of C2-halogenated or stannylated benzofurans with aryl boronic acids or aryl halides,[8] direct arylation of C2- or C3-substituted benzofurans with aryl halides by C−H activation,[9] oxidative dehydrogenative cross-coupling at the C2 position of benzofurans,[10] and other strategies.[11] More recently, we reported an intermolecular cascade annulation to construct functionalized β- and γ-lactones in ionic liquids.[12] Driven by our interest in nucleopalladation[13] and Pd-catalyzed cross-coupling

Scheme 1. Cyclization of 2-Alkynylphenol to 2,3-Difunctionalized Benzofurans



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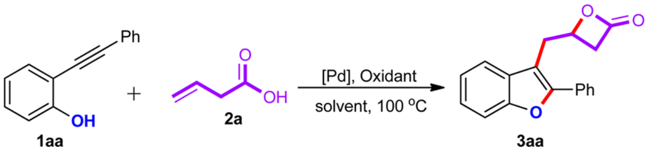
reactions in ionic liquids,[14] herein we disclose an efficient and practical method for the synthesis of 2,3-difunctionalized benzofurans via the Pd-catalyzed intermolecular tandem annulation reaction of 2-alkynylphenol derivatives with vinylacetic acid in ionic liquids (Scheme 1, route c).

RESULTS AND DISCUSSION

Our investigation was initiated by using the reaction of 2-(phenylethynyl)phenol (**1aa**) with but-3-enoic acid (**2a**) as a model system to screen the optimal conditions (Table 1). First, with the combination of $PdCl_2$ and $CuCl_2·2H_2O$ in [C_2OHmim]Cl at 100 °C, the desired product **3aa** was obtained in 23% yield (Table 1, entry 1). The structure of **3aa** was established by ^{1}H NMR, ^{13}C NMR, GC−MS, and HRMS analysis. Subsequently, further exploration of oxidants in the model reaction indicated that $Cu(TFA)_2·xH_2O$ was superior to the others. Other oxidants, such as $Cu(OAc)_2$, $Cu(OTf)_2$, $Cu(OPiv)_2$, and $Cu(hfac)_2·2H_2O$, showed less or no efficiency in terms of chemical yields (Table 1, entries 2−6). Unfortunately, a lower yield of **3aa** was obtained when the reaction was performed under 1 atm of pressure of O_2 (Table 1, entry 8). Furthermore, other palladium catalysts were also examined. Except for $Pd(TFA)_2$, other Pd sources, including $Pd(OAc)_2$, $Pd(PCy_3)_2Cl_2$, $Pd(PhCN)_2Cl_2$, $Pd(acac)_2$, and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, showed low efficiencies (entries 9−13). Replacing [C_2OHmim]Cl with other ionic liquids, such as [Bmim]Cl, [Bmim]BF_4, [Bmim]PF_6, [C_2O_2mim]Cl, and [BuPy]Cl, were ineffective for this transformation, and the reactions gave only low yields.[15] Finally, various conventional solvents, such as DMF, toluene, and 1,4-dioxane, were examined under the same reaction conditions and significantly decreased the yields (entries 14−16).

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	oxidant	solvent	yield[b] (%)
1	$PdCl_2$	$CuCl_2·2H_2O$	[C_2OHmim]Cl	23
2	$PdCl_2$	$Cu(OAc)_2$	[C_2OHmim]Cl	17
3	$PdCl_2$	$Cu(OTf)_2$	[C_2OHmim]Cl	trace
4	$PdCl_2$	$Cu(OPiv)_2$	[C_2OHmim]Cl	trace
5	$PdCl_2$	$Cu(TFA)_2·xH_2O$	[C_2OHmim]Cl	67
6	$PdCl_2$	$Cu(hfac)_2·2H_2O$	[C_2OHmim]Cl	10
7	$Pd(TFA)_2$	$Cu(TFA)_2·xH_2O$	[C_2OHmim]Cl	94 (83)
8	$Pd(TFA)_2$	O_2	[C_2OHmim]Cl	58
9	$Pd(OAc)_2$	$Cu(TFA)_2·xH_2O$	[C_2OHmim]Cl	trace
10	$Pd(PhCN)_2Cl_2$	$Cu(TFA)_2·xH_2O$	[C_2OHmim]Cl	19
11	$Pd(acac)_2$	$Cu(TFA)_2·xH_2O$	[C_2OHmim]Cl	8
12	$Pd(PCy_3)_2Cl_2$	$Cu(TFA)_2·xH_2O$	[C_2OHmim]Cl	52
13	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	$Cu(TFA)_2·xH_2O$	[C_2OHmim]Cl	43
14	$Pd(TFA)_2$	$Cu(TFA)_2·xH_2O$	DMF	trace
15	$Pd(TFA)_2$	$Cu(TFA)_2·xH_2O$	toluene	9
16	$Pd(TFA)_2$	$Cu(TFA)_2·xH_2O$	1,4-dioxane	trace

[a] Unless otherwise noted, all reactions were performed with **1aa** (0.25 mmol), **2a** (0.3 mmol), Pd catalyst (3 mol %), and oxidant (2 equiv) in the indicated solvent (1.0 mL) at 100 °C for 12 h. [b] Determined by GC using dodecane as the internal standard. The value in parentheses is the yield of isolated product. Hfac = hexafluoroacetylacetonate.

With the optimized reaction conditions in hand, we further investigated the scope and generality of this protocol. Representative results are summarized in Table 2. Gratifyingly, a range of 2,3-difunctionalized benzofurans **3** were obtained in moderate to excellent yields. Additionally, reactions employing 2-alkynylphenols **1** with aryl groups attached on the triple bond all worked well to afford the desired products **3**. For instance, a series of para-substituted aryl rings, including some with electron-donating groups (R = alkyl, OMe, Ph, ethylcyclohexyl) and some with electron-withdrawing groups (R = F, Cl, Br), were converted into the corresponding 2,3-difunctionalized benzofurans in moderate to excellent yields (**3aa**−**3al**). Pleasingly, this transformation was compatible with the Cl- and Br-substituted aryl rings, which might allow for further synthetic transformations by transition-metal-catalyzed coupling and other reactions. As for the sterically hindered 2-alkynylphenols **1aa**, **1ae**, and **1ak**, the reaction furnished the corresponding products **3aa** in yields similar to those of **3ae** and **3ak**. These results showed that this new transformation was tolerant toward electronic and steric effects of the aromatic ring. Similarly, 2-alkynylphenols **1** with alkyl groups attached on the triple bond proceeded smoothly to give the products **3** in moderate to good yields (**3am**−**3bc**). Notably, with the carbon chain of alkyl groups extended, the benzofuran derivatives **3an**−**3as** and **3au**−**3ay** were successfully obtained in moderate yields. Afterward, **1az**−**1bc** could be transformed efficiently, which greatly expanded the scope of the products. Besides the wide substrate scope, another impressive feature of the current tandem annulation reaction is its high tolerance for functional groups. For instance, the 2-alkynylphenols containing vinyl or thienyl groups underwent the tandem reaction to give corresponding products **3bd** and **3be** in 78% and 56% yields, respectively. Unfortunately, 2-(pyridin-2-ylethynyl)phenol (**1bf**) failed to afford the desired products. Delightfully, 2,2-dimethylbut-3-enoic acid (**2b**) could be converted into the corresponding products **3bg** in 87% yield as well.

With the positive results above, we next explored the scope of tandem annulation of various substituted phenols with allylic acid (**2a**), which showed high tolerance to the reactions. In general, various substituted 2-alkynylphenols with electron-donating groups (alkyl, alkoxyl) and weakly or moderately electron-withdrawing groups (F, Cl, Br) afforded the corresponding benzofuran derivatives **4a**−**4n** in moderate to excellent yields (Table 3). Importantly, even if a sterically bulky 2-alkynylphenol such as 4-(*tert*-butyl)-2-(phenylethynyl)phenol was used, the corresponding **4e** was obtained in 81% yield. Moreover, this transformation could be successfully extended to a variety of 2,4- and 2,5-disubstituted 2-alkynylphenols, furnishing the corresponding benzofuran derivatives **4f** and **4n** in 76% and 74% yields, respectively.

Based on the results obtained, the tandem annulation reactions of pent-4-enoic acid (**5**) with 2-alkynylphenols were attempted under standard reaction conditions (Scheme 2). When the tandem annulation coupling reagent was 2-(phenylethynyl)-phenol (**1aa**), no benzofuran products **8** were obtained, but **6a** and **7a** were obtained in 84% and 11% yields, respectively. Similarly, when 2-(pent-1-yn-1-yl)phenol (**1ao**) was used as the coupling reagent, the annulation products **6b** (66%) and **7b** (19%) were obtained, respectively. The result obtained indicates the crucial role of the position of the carboxylic acid pattern in the transformation.

To prove the practicality of the present method in the synthesis of benzofuran derivatives, a gram-scale synthesis of **3aa**

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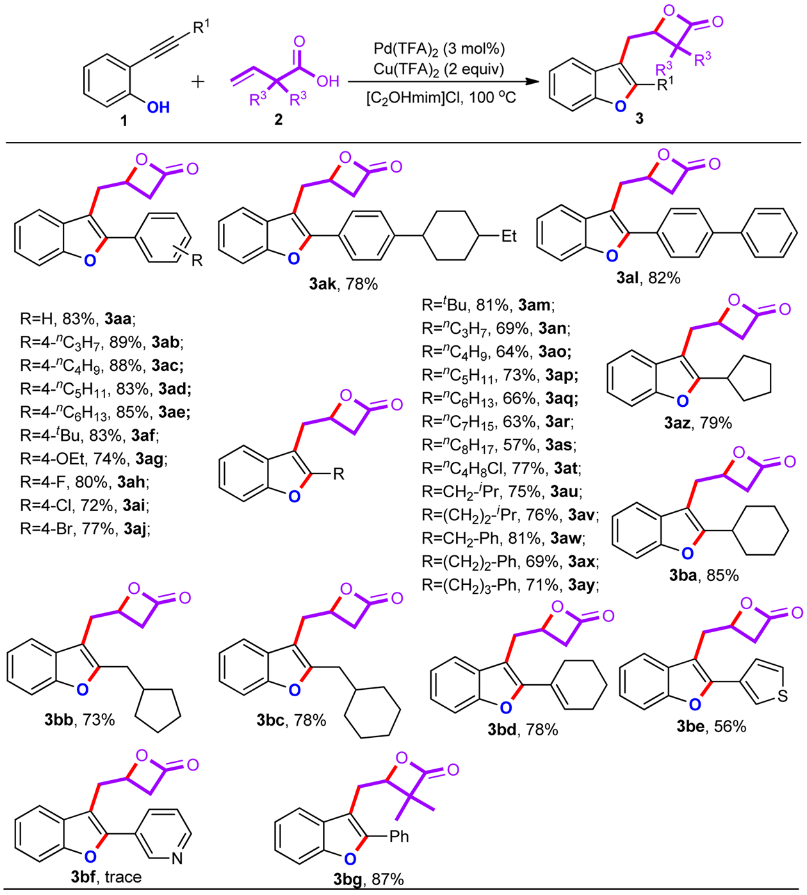
Table 2. Scope of the Reaction of 2-Alkyl-Substituted Phenols with But-3-enoic Acid[a]



[a] Reaction conditions: **1** (0.25 mmol), **2** (0.30 mmol), Pd(TFA)$_2$ (3 mol %), Cu(TFA)$_2$·xH$_2$O (2 equiv), and [C$_2$OHmim]Cl (1 mL) at 100 °C. Reaction was monitored by TLC for the completion of the reaction. Yields referred to isolated yields.

was performed, and the result is shown in Scheme 3. When 0.97 g of **1aa** was utilized, 1.02 g of product **3aa** was obtained in 74% yield.

To extend the applicability of this methodology, we subsequently utilized various 2-(phenylethynyl)anilines **9** with the developed optimal reaction conditions. Disappointingly, 2-(phenylethynyl)aniline (**9a**) and *N*-methyl-2-(phenylethynyl)-aniline (**9b**) failed to afford the desired products and only a complicated mixture was detected by GC−MS. Ultimately, when 4-methyl-*N*-(2-(phenylethynyl)phenyl)benzenesulfonamide (**9c**) was employed to react with **2a** under the standard conditions, only a trace amount of 1-tosyl-1*H*-indole **10c** was detected by GC−MS (Scheme 4).

The aryl halide functionality in the newly formed product enables them to be attractive and versatile synthetic building blocks in a variety of chemical transformations, leading to more complicated organic architectures by the formation of new C−C bonds. Hence, to demonstrate the synthetic utility of this protocol, we further examined the resultant products in the transition-metal-catalyzed cross-coupling reactions (Scheme 5). For instance, the Suzuki−Miyaura cross-coupling reactions of **4l** with phenylboronic acid delivered arylated compounds **11a** in moderate yield.[16] Furthermore, the desulfitative coupling of **4l** occurred uneventfully as well, providing the arylated compounds **11b** in 68% yield.[17] To our satisfaction, **4l** underwent the Negishi coupling to produce the highly functionalized benzofuran derivative **11c** in 63% yield.[16]

Based on the current results and previous literature,[12−14,18] the postulated reaction mechanism is depicted in Scheme 6. Pd complex is initially formed in situ in ionic liquids.[12−14] Then, oxypalladation of 2-alkynylphenols afforded vinyl palladium intermediate **I**.[18] Subsequently, intermediate **I** could undergo Heck-like alkene insertion to produce intermediates **II**. Simultaneously, the alkylpalladium species coordinated to the oxygen atoms of the hydroxyl group and generated the five membered palladacycle intermediate **III**.[12] Finally, a reductive elimination produced the target product and Pd(II) active species was regenerated by the oxidation of Cu(II) for the next cycle.

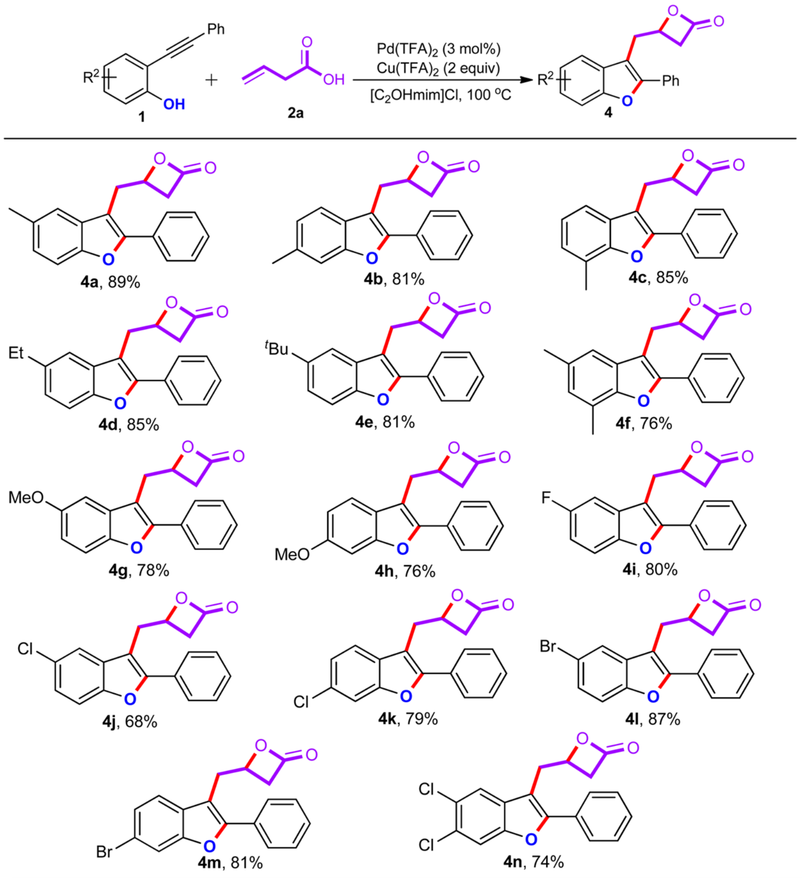
■ CONCLUSION

In conclusion, we have successfully accomplished an attractive strategy for the synthesis of functionalized 2,3-difunctionalized benzofurans via palladium-catalyzed cascade annulation of 2-alkynylphenols with allylic acids in ionic liquids. This cascade annulation process, featuring one pot, three steps, good functional group tolerance, and high atom economy, makes this transformation efficient and practical. Most importantly, the employment of ionic liquids under mild conditions makes this transformation green and environmentally friendly. Furthermore, this protocol should provide an ecofriendly methodology to functionalized benzofurans.

■ EXPERIMENTAL SECTION

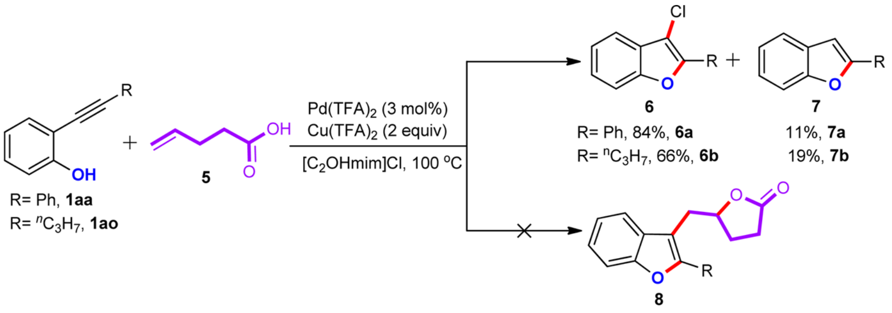
General Methods. Melting points were measured by a melting point instrument and were uncorrected. ^{1}H and ^{13}C NMR spectra were

Table 3. Scope with Regard to But-3-enoic Acid and Substituted Phenols[a]

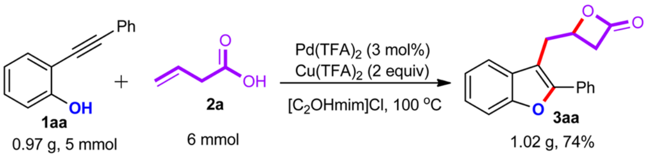


[a]Reaction conditions: **1** (0.25 mmol), **2a** (0.30 mmol), Pd(TFA)$_2$ (3 mol %), Cu(TFA)$_2$·xH$_2$O (2 equiv), and [C$_2$OHmim]Cl (1 mL) at 100 °C. Reaction was monitored by TLC for the completion of the reaction. Yields referred to isolated yields.

Scheme 2. Investigation of Tandem Annulation of Pent-4-enoic Acid with Substituted Phenols

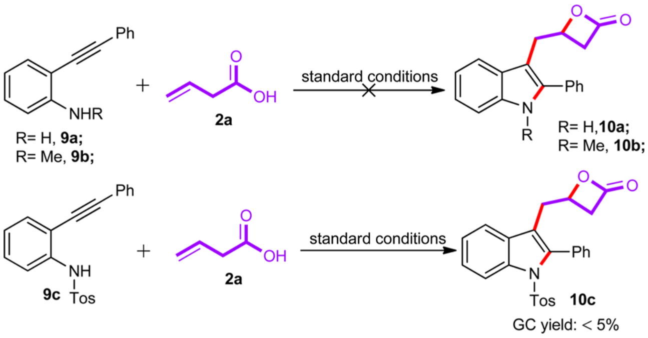


Scheme 3. Gram-Scale Synthesis of 3aa[a]

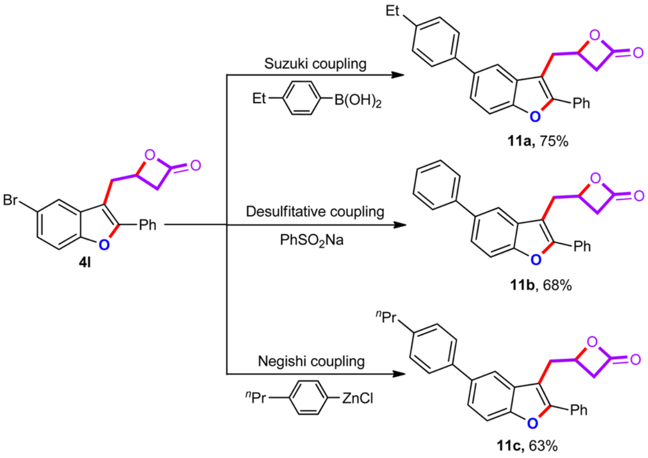


[a]Reaction conditions: **1aa** (5 mmol, 0.97 g), but-3-enoic acid **2a** (6 mmol, 0.52 g), Pd(TFA)$_2$ (3 mol %, 50 mg), Cu(TFA)$_2$·xH$_2$O (2 equiv, 2.89 g), and [C$_2$OHmim]Cl (3 mL) at 100 °C for 28 h. Reaction was monitored by TLC for the completion of the reaction; Yields referred to isolated yields.

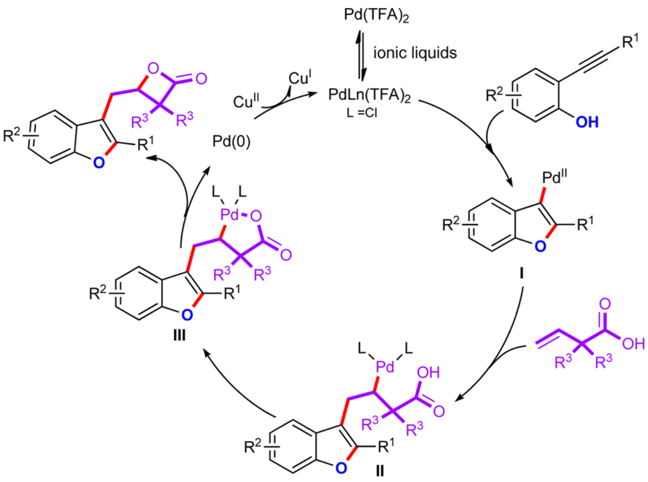
Scheme 4. Investigation of Tandem Annulation of 2a with 2-Alkyl-Substituted Anilines



Scheme 5. Synthetic Transformations of 4l



Scheme 6. Proposed Mechanism



recorded by using a 400 MHz NMR spectrometer. The chemical shifts are referenced to signals at 7.24 and 77.0 ppm, respectively, and chloroform is used as a solvent with TMS as the internal standard. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with an infrared spectrometer. GC−MS was obtained using electron ionization. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). TLC was performed by using commercially available 100−400 mesh silica gel plates (GF254). Unless otherwise noted, all purchased chemicals were used without further purification. The 2-alkynylphenols were prepared according to the literature.[7]

General Procedure for the Synthesis of 2,3-Disubstituted Benzofurans 3 and 4. A mixture of 2-alkynylphenols **1** (0.25 mmol), olefin acids **2** (0.30 mmol), Pd(TFA)$_2$ (2.5 mg, 3 mol %), Cu(TFA)$_2$·xH$_2$O (145 mg, 2 equiv), and ionic liquid (1.0 mL) was placed in a test tube (10 mL) equipped with a magnetic stirring bar. The mixture was stirred under the atmosphere of air at 100 °C. After the reaction was completed, 10 mL of ethyl acetate (3 × 10 mL) was added into the tube. The combined organic layers were washed with brine to neutral, dried over MgSO$_4$, and concentrated in vacuum. Purification of the residue on a preparative TLC afforded the desired products.

*4-((2-Phenylbenzofuran-3-yl)methyl)oxetan-2-one (**3aa**):* yield 83% (57.7 mg) as a yellow solid; mp = 136.6−137.4 °C; R_f 0.34 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.67 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 7.6 Hz, 1H), 7.51 (dt, J = 13.2, 7.6 Hz, 4H), 7.35 (t, J = 8.0 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 5.92 (t, J = 8.0 Hz, 1H), 2.88−2.78 (m, 2H), 2.73−2.59 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.6, 154.5, 153.7, 129.8, 129.5, 128.9, 128.1, 126.7, 124.9, 123.2, 120.6, 113.5, 111.7, 75.9, 29.5, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2922, 1776, 1645, 1515, 1453, 1136, 750; MS (EI) m/z 105, 115, 128, 139, 165, 191, 219, 249, 278; HRMS(ESI) m/z calcd for C$_{18}$H$_{15}$O$_3$ [M + H]$^+$ 279.1016, found 279.1013.

*4-((2-(4-Propylphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**3ab**):* yield 89% (71.2 mg) as a yellow oil; R_f 0.35 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.58 (t, J = 6.8 Hz, 3H), 7.53 (d, J = 8.4 Hz, 1H), 7.33 (t, J = 7.6 Hz, 3H), 7.27 (d, J = 8.0 Hz, 1H), 5.91 (t, J = 8.0 Hz, 1H), 2.86−2.76 (m, 2H), 2.74−2.59 (m, 4H), 1.79−1.64 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.6, 154.4, 154.1, 144.5, 129.1, 128.0, 127.1, 126.8, 124.8, 123.1, 120.4, 112.9, 111.6, 76.0, 37.9, 29.6, 28.6, 24.4, 13.8 ppm; ν_{max}(KBr)/cm^{-1} 3058, 2926, 1766, 1640, 1515, 1416, 1124; MS (EI) m/z 91, 115, 147, 189, 207, 233, 265, 291, 320; HRMS(ESI) m/z calcd for C$_{21}$H$_{21}$O$_3$ [M + H]$^+$ 321.1485, found 321.1483.

*4-((2-(4-Butylphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**3ac**):* yield 88% (73.5 mg) as a yellow oil; R_f 0.35 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.58 (t, J = 7.2 Hz, 3H), 7.53 (d, J = 8.4 Hz, 1H), 7.33 (t, J = 7.2 Hz, 3H), 7.27 (d, J = 7.6 Hz, 1H), 5.91 (t, J = 8.0 Hz, 1H), 2.81 (dd, J = 16.8, 7.6 Hz, 2H), 2.76−2.60 (m, 4H), 1.65 (dt, J = 15.2, 7.6 Hz, 2H), 1.39 (dq, J = 14.6, 7.2 Hz, 2H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 154.4, 154.1, 144.7, 129.0, 128.0, 127.1, 126.8, 124.8, 123.1, 120.4, 112.9, 111.6, 76.0, 35.5, 33.4, 29.6, 28.6, 22.3, 13.9 ppm; ν_{max}(KBr)/cm^{-1} 3055, 2929, 1754, 1637, 1516, 1426, 1128; MS (EI) m/z 115, 131, 145, 187, 199, 217, 229, 272, 281, 334; HRMS(ESI) m/z calcd for C$_{22}$H$_{23}$O$_3$ [M + H]$^+$ 335.1642, found 335.1637.

*4-((2-(4-Pentylphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**3ad**):* yield 83% (72.2 mg) as a yellow oil; R_f 0.37 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.58 (t, J = 7.2 Hz, 3H), 7.53 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.2 Hz, 3H), 7.27 (d, J = 7.6 Hz, 1H), 5.91 (t, J = 8.0 Hz, 1H), 2.81 (dd, J = 16.8, 7.6 Hz, 2H), 2.75−2.58 (m, 4H), 1.73−1.62 (m, 2H), 1.42−1.30 (m, 4H), 0.91 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 154.4, 154.1, 144.8, 129.0, 128.0, 127.1, 126.8, 124.8, 123.1, 120.4, 112.9, 111.6, 76.0, 35.8, 31.5, 30.9, 29.6, 28.6, 22.5, 14.0 ppm; ν_{max}(KBr)/cm^{-1} 3053, 2928, 1755, 1631, 1518, 1426, 1126; MS (EI) m/z 115, 133, 165, 191, 207, 233, 281, 320, 348; HRMS(ESI) m/z calcd for C$_{23}$H$_{25}$O$_3$ [M + H]$^+$ 349.1798, found 349.1795.

*4-((2-(4-Hexylphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**3ae**):* yield 85% (76.9 mg) as a yellow oil; R_f 0.40 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.58 (t, J = 7.2 Hz, 3H), 7.53 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.6 Hz, 3H), 7.27 (d, J = 7.6 Hz, 1H), 5.91 (t, J = 8.0 Hz, 1H), 2.81 (dd, J = 16.8, 7.6 Hz, 2H), 2.74−2.60 (m, 4H), 1.69−1.62 (m, 2H), 1.40−1.30 (m, 6H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 154.4, 154.1, 144.8, 129.0, 128.0, 127.1, 126.8, 124.8, 123.1, 120.4, 112.9, 111.6, 76.0, 35.8, 31.7, 31.3, 29.6, 28.9, 28.6, 22.6, 14.1 ppm; ν_{max}(KBr)/cm^{-1} 3050, 2930, 1748, 1622, 1518, 1424, 1123; MS (EI) m/z 115, 165, 207, 233, 291, 307, 362; HRMS(ESI) m/z calcd for C$_{24}$H$_{27}$O$_3$ [M + H]$^+$ 363.1955, found 363.1952.

*4-((2-(4-(tert-Butyl)phenyl)benzofuran-3-yl)methyl)oxetan-2-one (**3af**):* yield 83% (69.3 mg) as a yellow oil; R_f 0.38 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.59 (t, J = 6.4 Hz, 3H), 7.53 (d, J = 8.4 Hz, 3H), 7.33 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 5.92 (t, J = 8.0 Hz, 1H), 2.86−2.73 (m, 2H), 2.72−2.57 (m, 2H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 154.4, 154.0, 152.9, 127.9, 126.9, 126.8, 125.9, 124.8, 123.1, 120.5, 112.9, 111.6, 76.0, 34.9, 31.2, 29.6, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3057, 2959, 1778, 1619, 1509, 1455, 1400, 1135, 747; MS (EI) m/z 105, 119, 133, 154, 193, 207, 249, 281, 334; HRMS(ESI) m/z calcd for C$_{22}$H$_{22}$NaO$_3$ [M + Na]$^+$ 357.1461, found 357.1458.

*4-((2-(4-Ethoxyphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**3ag**):* yield 74% (59.6 mg) as a yellow solid; mp = 123.4−124.5 °C; R_f 0.41 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.60−7.56 (m, 3H), 7.52 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 6.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 5.88 (t, J = 8.0 Hz, 1H), 4.11 (q, J = 6.8 Hz, 2H), 2.88−2.78 (m, 2H), 2.74−2.60 (m, 2H), 1.46 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 160.0, 154.3, 154.1, 129.6, 126.9, 124.6, 123.1, 122.0, 120.3, 114.9, 112.1, 111.5, 76.1, 63.7, 29.6, 28.5, 14.8 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2923, 1775, 1645, 1546, 1510, 1178, 751; MS (EI) m/z 105, 127, 143, 165, 193, 207, 249, 281, 322; HRMS(EI) m/z calcd for $C_{20}H_{19}O_4$ $[M + H]^+$ 323.1278, found 323.1283.

4-((2-(4-Fluorophenyl)benzofuran-3-yl)methyl)oxetan-2-one ***(3ah)***: yield 80% (59.2 mg) as a yellow solid; mp = 110.6−111.9 °C; R_f 0.42 (petroleum ether/EtOAc 4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.67−7.64 (m, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 7.21 (t, J = 8.0 Hz, 2H), 5.85 (t, J = 8.0 Hz, 1H), 2.88−2.79 (m, 2H), 2.75−2.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 163.4 (J = 249.2 Hz), 154.4, 152.9, 130.1 (J = 8.4 Hz), 126.6, 125.9 (J = 3.2 Hz), 125.1, 123.3, 120.5, 116.2 (J = 21.7 Hz), 113.3, 111.7, 75.7, 29.5, 28.5 ppm; ν_{max}(KBr)/cm^{-1} 3063, 2922, 1775, 1644, 1508, 1453, 1416, 1182, 749; MS (EI) m/z 106, 133, 183, 207, 251, 296; HRMS(EI) m/z calcd for $C_{18}H_{14}FO_3$ $[M + H]^+$ 297.0921, found 297.0922.

4-((2-(4-Chlorophenyl)benzofuran-3-yl)methyl)oxetan-2-one ***(3ai)***: yield 72% (56.2 mg) as a yellow solid; mp = 102.6−103.7 °C; R_f 0.40 (petroleum ether/EtOAc 4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62−7.60 (m, 3H), 7.54 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.41−7.34 (m, 1H), 7.29 (d, J = 7.6 Hz, 1H), 5.87 (t, J = 8.0 Hz, 1H), 2.90−2.78 (m, 2H), 2.74−2.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 154.5, 152.5, 135.7, 130.9, 129.3, 129.2, 128.6, 125.3, 123.4, 120.6, 113.9, 111.7, 75.6, 29.4, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3064, 2923, 1777, 1648, 1483, 1452, 1137, 750; MS (EI) m/z 115, 135, 165, 193, 207, 233, 255, 281, 312; HRMS(EI) m/z calcd for $C_{18}H_{13}ClNaO_3$ $[M + Na]^+$ 335.0445, found 335.0444.

4-((2-(4-Bromophenyl)benzofuran-3-yl)methyl)oxetan-2-one ***(3aj)***: yield 77% (68.5 mg) as a yellow solid; mp = 133.7−134.9 °C; R_f 0.47 (petroleum ether/EtOAc 4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.41−7.34 (m, 2H), 7.29 (d, J = 7.6 Hz, 1H), 5.86 (t, J = 8.0 Hz, 1H), 2.91−2.78 (m, 2H), 2.73−2.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 154.5, 152.5, 138.1, 132.2, 129.5, 128.7, 126.6, 125.3, 123.4, 120.6, 114.0, 111.7, 75.6, 29.4, 28.5 ppm; ν_{max}(KBr)/cm^{-1} 3066, 2921, 1767, 1645, 1485, 1450, 1131, 756; MS (EI) m/z 115, 133, 165, 207, 233, 267, 301, 327, 356; HRMS(EI) m/z calcd for $C_{18}H_{13}BrNaO_3$ $[M + Na]^+$ 378.9940, found 378.9938.

4-((2-(4-(4-Ethylcyclohexyl)phenyl)benzofuran-3-yl)methyl)-oxetan-2-one ***(3ak)***: yield 78% (75.7 mg) as a yellow solid; mp = 130.3−131.3 °C; R_f 0.32 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 3H), 7.52 (d, J = 8.0 Hz, 1H), 7.35 (t, J = 8.0 Hz, 2H), 7.31 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 6.8 Hz, 1H), 5.91 (t, J = 8.0 Hz, 1H), 2.88−2.78 (m, 2H), 2.75−2.61 (m, 2H), 2.57−2.51 (m, 1H), 1.93 (t, J = 11.2 Hz, 4H), 1.53−1.43 (m, 1H), 1.31−1.26 (m, 4H), 1.13−1.03 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.4, 154.1, 149.6, 128.1, 127.5, 127.2, 126.8, 124.7, 123.1, 120.4, 112.9, 111.6, 76.0, 44.6, 39.1, 34.2, 33.1, 30.0, 29.6, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3059, 2921, 1778, 1626, 1514, 1453, 1137, 750; MS (EI) m/z 105, 135, 191, 207, 281, 325, 356, 388; HRMS(EI) m/z calcd for $C_{26}H_{28}NaO_3$ $[M + Na]^+$ 411.1931, found 411.1926.

4-((2-([1,1′-Biphenyl]-4-yl)benzofuran-3-yl)methyl)oxetan-2-one ***(3al)***: yield 82% (72.6 mg) as a yellow solid; mp = 194.3−195.7 °C; R_f 0.31 (petroleum ether/EtOAc 4/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 3H), 7.65 (d, J = 7.2 Hz, 2H), 7.62 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.42−7.37 (m, 2H), 7.35 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 5.98 (t, J = 8.0 Hz, 1H), 2.90−2.80 (m, 2H), 2.78−2.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 154.5, 153.5, 142.3, 140.1, 130.1, 129.0, 128.6, 128.5, 127.6, 127.1, 126.8, 125.0, 123.3, 120.6, 113.6, 111.7, 76.0, 29.5, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3056, 2920, 1775, 1648, 1517, 1500, 1449, 1138, 750; MS (EI) m/z 105, 119, 133, 149, 177, 191, 207, 281, 325, 354; HRMS(EI) m/z calcd for $C_{24}H_{18}NaO_3$ $[M + Na]^+$ 377.1148, found 377.1145.

4-((2-(tert-Butyl)benzofuran-3-yl)methyl)oxetan-2-one ***(3am)***: yield 81% (52.2 mg) as a yellow solid; mp = 101.4−102.8 °C; R_f 0.44 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.6 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 6.07 (t, J = 8.0 Hz, 1H), 2.83−2.71 (m, 2H), 2.58−2.51 (m, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 161.8, 153.3, 127.0, 122.6, 120.4, 111.2, 111.1, 75.9, 30.0, 29.6, 29.2, 27.4 ppm; ν_{max}(KBr)/cm^{-1} 3066, 2967, 1777, 1648, 1517, 1455, 1136, 750; MS (EI) m/z 91, 115, 128, 157, 183, 199, 225, 243, 258; HRMS(EI) m/z calcd for $C_{16}H_{19}O_3$ $[M + H]^+$ 259.1329, found 259.1332.

4-((2-Propylbenzofuran-3-yl)methyl)oxetan-2-one ***(3an)***: yield 69% (42.1 mg) as a yellow oil; R_f 0.44 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.47−7.42 (m, 2H), 7.24−7.18 (m, 2H), 5.68 (t, J = 8.0 Hz, 1H), 2.82−2.72 (m, 4H), 2.56 (dd, J = 16.8, 8.0 Hz, 2H), 1.77 (dq, J = 14.4, 7.2 Hz, 2H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 156.4, 154.2, 126.3, 123.9, 122.8, 119.5, 112.7, 111.2, 75.7, 29.4, 28.9, 28.7, 21.7, 13.7 ppm; ν_{max}(KBr)/cm^{-1} 3055, 2938, 1768, 1649, 1509, 1457, 1400, 1135, 748; MS (EI) m/z 91, 103, 115, 131, 145, 189, 215, 244; HRMS(ESI) m/z calcd for $C_{15}H_{17}O_3$ $[M + H]^+$ 245.1172, found 245.1170.

4-((2-Butylbenzofuran-3-yl)methyl)oxetan-2-one ***(3ao)***: yield 64% (41.3 mg) as a yellow oil; R_f 0.45 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, J = 8.4 Hz, 2H), 7.24−7.18 (m, 2H), 5.68 (t, J = 8.0 Hz, 1H), 2.87−2.68 (m, 4H), 2.56 (dd, J = 16.4, 8.0 Hz, 2H), 1.72 (dt, J = 14.8, 7.2 Hz, 2H), 1.38 (td, J = 14.8, 7.2 Hz, 2H), 0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 155.5, 153.1, 125.2, 122.8, 121.6, 118.3, 111.3, 110.1, 74.5, 29.4, 28.3, 27.8, 25.4, 21.2, 12.6 ppm; ν_{max}(KBr)/cm^{-1} 3056, 2936, 1763, 1645, 1506, 1450, 1400, 1133, 746; MS (EI) m/z 55, 103, 128, 145, 171, 185, 215, 258; HRMS(ESI) m/z calcd for $C_{16}H_{19}O_3$ $[M + H]^+$ 259.1329, found 259.1323.

4-((2-Pentylbenzofuran-3-yl)methyl)oxetan-2-one ***(3ap)***: yield 73% (49.6 mg) as a yellow oil; R_f 0.45 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, J = 8.4 Hz, 2H), 7.24−7.18 (m, 2H), 5.68 (t, J = 8.0 Hz, 1H), 2.83−2.75 (m, 4H), 2.56 (q, J = 8.2 Hz, 2H), 1.77−1.70 (m, 2H), 1.39−1.30 (m, 2H), 0.90 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 156.6, 154.2, 126.3, 123.9, 122.7, 119.5, 112.4, 111.2, 75.7, 31.3, 29.4, 28.9, 28.1, 26.8, 22.4, 13.9 ppm; ν_{max}(KBr)/cm^{-1} 3058, 2938, 1768, 1644, 1506, 1440, 1406, 1130, 748; MS (EI) m/z 91, 128, 145, 187, 217, 243, 272; HRMS(ESI) m/z calcd for $C_{17}H_{21}O_3$ $[M + H]^+$ 273.1485, found 273.1483.

4-((2-Hexylbenzofuran-3-yl)methyl)oxetan-2-one ***(3aq)***: yield 66% (47.2 mg) as a yellow oil; R_f 0.45 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, J = 8.8 Hz, 2H), 7.24−7.18 (m, 2H), 5.67 (t, J = 8.0 Hz, 1H), 2.84−2.70 (m, 4H), 2.55 (q, J = 8.0 Hz, 2H), 1.72 (dd, J = 14.4, 6.8 Hz, 2H), 1.41−1.32 (m, 6H), 0.87 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 156.6, 154.2, 126.3, 123.9, 122.7, 119.5, 112.4, 111.2, 75.7, 31.5, 29.7, 29.4, 28.9, 28.4, 26.8, 22.5, 14.0 ppm; ν_{max}(KBr)/cm^{-1} 3056, 2936, 1766, 1648, 1502, 1445, 1404, 1128, 754; MS (EI) m/z 55, 85, 115, 131, 145, 171, 201, 215, 232, 286; HRMS(ESI) m/z calcd for $C_{18}H_{23}O_3$ $[M + H]^+$ 287.1642, found 287.1640.

4-((2-Heptylbenzofuran-3-yl)methyl)oxetan-2-one ***(3ar)***: yield 63% (47.3 mg) as a yellow oil; R_f 0.46 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, J = 8.8 Hz, 2H), 7.24−7.18 (m, 2H), 5.67 (t, J = 8.0 Hz, 1H), 2.82−2.74 (m, 2H), 2.55 (dd, J = 16.4, 8.0 Hz, 2H), 1.72 (dd, J = 13.2, 6.4 Hz, 2H), 1.33−1.25 (m, 8H), 0.88 (t, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 156.6, 154.2, 126.3, 123.9, 122.7, 119.5, 112.4, 111.2, 75.7, 31.7, 29.4, 29.2, 28.9, 28.8, 28.4, 26.8, 22.6, 14.0 ppm; ν_{max}(KBr)/cm^{-1} 3058, 2938, 1763, 1640, 1508, 1448, 1400, 1129, 756; MS (EI) m/z 55, 85, 118, 131, 171, 207, 215, 245, 281, 300; HRMS(ESI) m/z calcd for $C_{19}H_{25}O_3$ $[M + H]^+$ 301.1798, found 301.1794.

4-((2-Octylbenzofuran-3-yl)methyl)oxetan-2-one ***(3as)***: yield 57% (44.7 mg) as a yellow oil; R_f 0.46 (petroleum ether/EtOAc 5/1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, J = 8.6 Hz, 2H), 7.24−7.18 (m, 2H), 5.67 (t, J = 8.0 Hz, 1H), 2.84−2.71 (m, 4H), 2.56 (q, J = 8.0 Hz, 2H), 1.72 (dd, J = 14.0, 7.0 Hz, 2H), 1.33−1.25 (m, 10H), 0.87 (t, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 156.7, 154.2, 126.3, 123.9, 122.7, 119.5, 112.4, 111.2, 75.7, 31.8, 29.4, 29.3, 29.2, 29.1, 28.9, 28.4, 26.8, 22.6, 14.1 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2940, 1766, 1643, 1500, 1445, 1405, 1134, 758; MS (EI) m/z 55, 77, 91, 115, 145, 187, 215, 229, 259, 281, 314; HRMS(ESI) m/z calcd for $C_{20}H_{27}O_3$ $[M + H]^+$ 315.1955, found 315.1953.

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4-((2-(4-Chlorobutyl)benzofuran-3-yl)methyl)oxetan-2-one (***3at***): yield 77% (56.2 mg) as a yellow oil; R_f 0.41 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45 (t, J = 8.0 Hz, 2H), 7.24−7.19 (m, 2H), 5.68 (t, J = 8.0 Hz, 1H), 3.57 (t, J = 6.0 Hz, 2H), 2.90−2.81 (m, 2H), 2.80−2.72 (m, 2H), 2.64−2.51 (m, 2H), 1.96−1.80 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.6, 155.5, 154.2, 126.2, 124.2, 122.9, 119.5, 112.9, 111.3, 75.5, 44.5, 31.8, 29.3, 28.9, 26.1, 25.7 ppm; ν_{max}(KBr)/cm^{-1} 3050, 2926, 1760, 1644, 1510, 1440, 1400, 1136, 758; MS (EI) m/z 103, 115, 131, 159, 207, 237, 292; HRMS(ESI) m/z calcd for $C_{16}H_{18}ClO_3$ [M + H]$^+$ 293.0939, found 293.0936.

4-((2-Isobutylbenzofuran-3-yl)methyl)oxetan-2-one (***3au***): yield 75% (48.4 mg) as a yellow oil; R_f 0.48 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.47−7.42 (m, 2H), 7.24−7.17 (m, 2H), 5.65 (t, J = 8.0 Hz, 1H), 2.80−2.76 (m, 2H), 2.73−2.63 (m, 2H), 2.62−2.53 (m, 2H), 2.12 (dt, J = 13.6, 6.4 Hz, 2H), 0.98 (dd, J = 11.2, 6.8 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 155.9, 154.3, 126.2, 123.9, 122.8, 119.6, 113.3, 111.2, 75.7, 35.8, 29.5, 28.8, 28.2, 22.5, 22.4 ppm; ν_{max}(KBr)/cm^{-1} 3056, 2934, 1766, 1645, 1506, 1454, 1406, 1138, 749; MS (EI) m/z 103, 115, 131, 145, 171, 215, 258; HRMS(ESI) m/z calcd for $C_{16}H_{19}O_3$ [M + H]$^+$ 259.1329, found 259.1328.

4-((2-Isopentylbenzofuran-3-yl)methyl)oxetan-2-one (***3av***): yield 76% (51.7 mg) as a yellow oil; R_f 0.48 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44 (t, J = 8.0 Hz, 2H), 7.25−7.17 (m, 2H), 5.68 (t, J = 8.0 Hz, 1H), 2.84−2.73 (m, 4H), 2.56 (dd, J = 15.6, 7.6 Hz, 2H), 1.66−1.59 (m, 3H), 0.95 (d, J = 4.0 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 156.8, 154.2, 126.3, 123.9, 122.8, 119.5, 112.2, 111.2, 75.7, 37.5, 29.4, 28.9, 27.7, 24.8, 22.4, 22.3 ppm; ν_{max}(KBr)/cm^{-1} 3055, 2936, 1760, 1648, 1514, 1452, 1400, 1136, 756; MS (EI) m/z 77, 85, 115, 131, 157, 185, 199, 229, 272; HRMS(ESI) m/z calcd for $C_{17}H_{21}O_3$ [M + H]$^+$ 273.1485, found 273.1481.

4-((2-Benzylbenzofuran-3-yl)methyl)oxetan-2-one (***3aw***): yield 81% (51.7 mg) as a yellow oil; R_f 0.46 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.48 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.30 (dd, J = 14.8, 7.6 Hz, 4H), 7.24−7.19 (m, 3H), 5.70 (t, J = 8.0 Hz, 1H), 4.17 (q, J = 16.0 Hz, 2H), 2.74−2.69 (m, 2H), 2.51−2.44 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.6, 154.4, 154.1, 137.0, 128.8, 128.5, 126.9, 126.3, 124.3, 122.9, 119.7, 113.6, 111.4, 75.5, 33.2, 29.3, 28.9 ppm; ν_{max}(KBr)/cm^{-1} 3061, 2922, 1774, 1645, 1515, 1454, 1140, 750; MS (EI) m/z 115, 159, 178, 191, 207, 233, 292; HRMS(ESI) m/z calcd for $C_{19}H_{17}O_3$ [M + H]$^+$ 293.1172, found 293.1170.

4-((2-Phenethylbenzofuran-3-yl)methyl)oxetan-2-one (***3ax***): yield 69% (52.8 mg) as a yellow oil; R_f 0.46 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.47 (d, J = 8.4 Hz, 1H), 7.39 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.24−7.16 (m, 4H), 7.08 (d, J = 7.2 Hz, 2H), 5.36 (t, J = 8.0 Hz, 1H), 3.23−3.07 (m, 2H), 3.04−3.00 (m, 2H), 2.61−2.56 (m, 2H), 2.12 (td, J = 20.0, 10.2 Hz, 1H), 1.96 (dt, J = 12.8, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 154.8, 154.3, 140.5, 128.6, 128.5, 126.4, 126.2, 124.1, 122.8, 119.6, 113.6, 111.2, 75.5, 34.5, 29.3, 29.2, 28.5 ppm; ν_{max}(KBr)/cm^{-1} 3029, 2922, 1775, 1650, 1455, 1140, 748; MS (EI) m/z 103, 128, 145, 187, 215, 246, 281, 306; HRMS(ESI) m/z calcd for $C_{20}H_{19}O_3$ [M + H]$^+$ 307.1329, found 307.1335.

4-((2-(3-Phenylpropyl)benzofuran-3-yl)methyl)oxetan-2-one (***3ay***): yield 71% (56.8 mg) as a yellow oil; R_f 0.48 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45 (t, J = 7.6 Hz, 2H), 7.32−7.27 (m, 3H), 7.20 (t, J = 9.0 Hz, 4H), 5.58 (t, J = 8.0 Hz, 1H), 2.81 (t, J = 7.4 Hz, 2H), 2.77−2.65 (m, 4H), 2.51 (dd, J = 16.0, 7.6 Hz, 2H), 2.10 (qd, J = 11.6, 4.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.6, 156.0, 154.3, 141.3, 128.5, 126.3, 126.1, 124.0, 122.8, 119.5, 112.7, 111.2, 75.5, 35.1, 29.7, 29.4, 28.8, 26.1 ppm; ν_{max}(KBr)/cm^{-1} 3028, 2920, 1776, 1655, 1456, 1146, 756; MS (EI) m/z 91, 119, 131, 146, 193, 207, 253, 281, 320; HRMS(ESI) m/z calcd for $C_{21}H_{21}O_3$ [M + H]$^+$ 321.1485, found 321.1483.

4-((2-Cyclopentylbenzofuran-3-yl)methyl)oxetan-2-one (***3az***): yield 79% (53.3 mg) as a yellow oil; R_f 0.37 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44 (t, J = 8.8 Hz, 2H), 7.25−7.17 (m, 2H), 5.73 (t, J = 8.0 Hz, 1H), 3.33−3.23 (m, 1H), 2.82−2.70 (m, 2H), 2.55 (q, J = 8.0 Hz, 2H), 2.04−1.86 (m, 6H), 1.77−1.69 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 159.2, 154.1, 126.5, 123.8, 122.7, 119.5, 111.5, 111.2, 75.7, 37.2, 32.5, 31.9, 29.5, 29.1, 26.0, 26.0 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2928, 1776, 1648, 1506, 1450, 1144, 756; MS (EI) m/z 91, 115, 141, 169, 197, 215, 241, 270; HRMS(ESI) m/z calcd for $C_{17}H_{19}O_3$ [M + H]$^+$ 271.1329, found 271.1325.

4-((2-Cyclohexylbenzofuran-3-yl)methyl)oxetan-2-one (***3ba***): yield 85% (60.4 mg) as a yellow oil; R_f 0.33 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.48−7.42 (m, 2H), 7.25−7.17 (m, 2H), 5.73 (t, J = 8.0 Hz, 1H), 2.89−2.83 (m, 1H), 2.80−2.71 (m, 2H), 2.60−2.52 (m, 2H), 1.94−1.82 (m, 3H), 1.80−1.72 (m, 4H), 1.41−1.33 (m, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 160.5, 154.1, 126.3, 123.8, 122.7, 119.6, 111.2, 110.7, 75.6, 36.7, 31.9, 31.3, 29.5, 28.9, 26.3, 26.2, 25.7 ppm; ν_{max}(KBr)/cm^{-1} 3063, 2929, 1777, 1649, 1500, 1453, 1141, 752; MS (EI) m/z 91, 115, 145, 183, 211, 241, 256, 284; HRMS(ESI) m/z calcd for $C_{18}H_{21}O_3$ [M + H]$^+$ 285.1485, found 285.1483.

4-((2-(Cyclopentylmethyl)benzofuran-3-yl)methyl)oxetan-2-one (***3bb***): yield 73% (51.8 mg) as a yellow oil; R_f 0.44 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46−7.42 (m, 2H), 7.25−7.18 (m, 2H), 5.67 (t, J = 8.0 Hz, 1H), 2.84−2.71 (m, 4H), 2.56 (dd, J = 18.0, 9.2 Hz, 2H), 2.28 (dt, J = 15.2, 7.8 Hz, 1H), 1.82−1.73 (m, 2H), 1.67−1.54 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 156.5, 154.2, 126.2, 123.9, 122.7, 119.5, 112.6, 111.2, 75.7, 39.5, 32.5, 32.4, 29.7, 29.5, 28.8, 24.9, 24.8 ppm; ν_{max}(KBr)/cm^{-1} 3062, 2928, 1776, 1642, 1454, 1141, 747; MS (EI) m/z 115, 128, 131, 157, 171, 207, 216, 253, 284; HRMS(ESI) m/z calcd for $C_{18}H_{21}O_3$ [M + H]$^+$ 285.1485, found 285.1481.

4-((2-(Cyclohexylmethyl)benzofuran-3-yl)methyl)oxetan-2-one (***3bc***): yield 78% (58.1 mg) as a yellow oil; R_f 0.51 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44 (t, J = 8.4 Hz, 2H), 7.25−7.18 (m, 2H), 5.64 (t, J = 8.0 Hz, 1H), 2.82−2.74 (m, 2H), 2.73−2.61 (m, 2H), 2.56 (dd, J = 20.0, 10.6 Hz, 2H), 1.81−1.64 (m, 5H), 1.18 (dd, J = 24.2, 12.8 Hz, 4H), 1.07−0.94 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 155.6, 154.3, 126.2, 123.9, 122.7, 119.5, 113.3, 111.2, 75.8, 37.4, 34.5, 33.2, 33.1, 29.7, 29.5, 28.8, 26.2, 26.1 ppm; ν_{max}(KBr)/cm^{-1} 3048, 2926, 1777, 1640, 1454, 1145, 748; MS (EI) m/z 115, 128, 131, 157, 171, 216, 254, 298; HRMS(ESI) m/z calcd for $C_{19}H_{23}O_3$ [M + H]$^+$ 299.1642, found 299.1640.

4-((2-(Cyclohex-1-en-1-yl)benzofuran-3-yl)methyl)oxetan-2-one (***3bd***): yield 78% (55.0 mg) as a yellow oil; R_f 0.42 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.50 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 6.12 (s, 1H), 5.83 (t, J = 8.0 Hz, 1H), 2.81−2.77 (m, 2H), 2.64−2.59 (m, 1H), 2.56−2.52 (m, 2H), 2.45−2.34 (m, 1H), 2.32−2.23 (m, 2H), 1.83−1.76 (m, 2H), 1.75−1.68 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.8, 156.1, 153.8, 131.9, 128.4, 126.6, 124.4, 122.8, 120.2, 112.2, 111.3, 76.0, 29.6, 28.8, 26.7, 25.7, 22.3, 21.8 ppm; ν_{max}(KBr)/cm^{-1} 3040, 2931, 1735, 1542, 1452, 1102, 749; MS (EI) m/z 115, 131, 169, 181, 195, 209, 237, 282; HRMS(ESI) m/z calcd for $C_{18}H_{19}O_3$ [M + H]$^+$ 283.1329, found 283.1325.

4-((2-(Thiophen-3-yl)benzofuran-3-yl)methyl)oxetan-2-one (***3be***): yield 56% (39.8 mg) as a yellow solid; mp = 114.4−115.9 °C; R_f 0.28 (petroleum ether/EtOAc 10/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.66 (s, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 5.97 (t, J = 8.0 Hz, 1H), 2.87−2.74 (m, 2H), 2.69−2.61 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 176.6, 154.2, 149.6, 130.7, 126.9, 126.6, 126.5, 124.9, 124.8, 123.3, 120.4, 112.9, 111.5, 75.8, 29.4, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3063, 2922, 1774, 1646, 1515, 1454, 1136, 750; MS (EI) m/z 127, 152, 207, 239, 284; HRMS(ESI) m/z calcd for $C_{16}H_{13}O_3S$ [M + H]$^+$ 285.0580, found 285.0576.

3,3-Dimethyl-4-((2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (***3bg***): yield 87% (66.6 mg) as a yellow solid; mp = 162.6−163.8 °C; R_f 0.43 (petroleum ether/EtOAc 5/1); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.66 (d, J = 7.2 Hz, 2H), 7.58−7.47 (m, 5H), 7.34 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 5.86 (t, J = 8.0 Hz, 1H), 2.66−2.56 (m, 1H), 2.45−2.40 (m, 1H), 1.44 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 181.6, 154.5, 153.6, 129.9, 129.4, 128.9, 128.1, 126.9, 124.9, 123.2, 120.6, 113.3, 111.6, 72.1, 43.5, 40.8, 24.9, 24.4 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2930, 1771, 1646, 1516, 1498, 1119, 748; MS

(EI) m/z 105, 116, 165, 194, 221, 247, 262, 306; HRMS(ESI) m/z calcd for $C_{20}H_{18}NaO_3$ [M + Na]$^+$ 329.1148, found 329.1147.

4-((2-(p-Tolyl)benzofuran-3-yl)methyl)oxetan-2-one (**4a**): yield 89% (64.9 mg) as a yellow solid; mp = 140.5−141.3 °C; R_f 0.53 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dt, J = 17.2, 8.4 Hz, 4H), 7.33 (t, J = 8.0 Hz, 3H), 7.27 (d, J = 8.0 Hz, 1H), 5.90 (t, J = 8.0 Hz, 1H), 2.87−2.74 (m, 2H), 2.69−2.61 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.4, 154.0, 139.8, 129.6, 128.0, 126.9, 126.8, 124.8, 123.1, 120.4, 112.9, 111.6, 76.0, 29.6, 28.6, 21.4 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2921, 1777, 1627, 1567, 1515, 1453, 1138, 749; MS (EI) m/z 109, 115, 133, 165, 178, 207, 233, 247, 292; HRMS(ESI) m/z calcd for $C_{19}H_{17}O_3$ [M + H]$^+$ 293.1172, found 293.1170.

4-((2-(m-Tolyl)benzofuran-3-yl)methyl)oxetan-2-one (**4b**): yield 81% (59.1 mg) as a yellow solid; mp = 128.5−129.8 °C; R_f 0.55 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.0 Hz, 1H), 7.56−7.49 (m, 2H), 7.43 (t, J = 6.4 Hz, 1H), 7.40−7.32 (m, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.92 (t, J = 8.0 Hz, 1H), 2.88−2.78 (m, 2H), 2.75−2.61 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.4, 153.9, 138.8, 130.4, 129.7, 128.8, 128.7, 126.8, 125.3, 124.9, 123.2, 120.5, 113.3, 111.6, 75.9, 29.5, 28.6, 21.5 ppm; ν_{max}(KBr)/cm^{-1} 3097, 2924, 1741, 1629, 1516, 1454, 1414, 1137, 747; MS (EI) m/z 115, 137, 178, 207, 233, 267, 292; HRMS(ESI) m/z calcd for $C_{19}H_{17}O_3$ [M + H]$^+$ 293.1172, found 293.1172.

4-((7-Methyl-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4c**): yield 85% (62.1 mg) as a yellow solid; mp = 116.7−119.2 °C; R_f 0.56 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.40 (dd, J = 15.0, 7.6 Hz, 2H), 7.35 (d, J = 7.2 Hz, 2H), 7.29 (t, J = 7.6 Hz, 2H), 5.55 (t, J = 8.0 Hz, 1H), 2.74 (dt, J = 18.9, 13.6 Hz, 2H), 2.67−2.56 (m, 1H), 2.49 (td, J = 12.0, 6.8 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 154.7, 154.6, 138.6, 130.8, 130.7, 130.1, 128.9, 126.1, 125.8, 124.8, 123.1, 120.3, 114.7, 111.7, 75.8, 29.4, 28.4, 20.1 ppm; ν_{max}(KBr)/cm^{-1} 3038, 2926, 1744, 1628, 1515, 1451, 1410, 1136, 749; MS (EI) m/z 115, 152, 178, 207, 219, 233, 247, 292; HRMS(ESI) m/z calcd for $C_{19}H_{17}O_3$ [M + H]$^+$ 293.1172, found 293.1168.

4-((2-(4-Ethylphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**4d**): yield 85% (65.0 mg) as a yellow solid; mp = 138.8−140.3 °C; R_f 0.59 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 3H), 7.53 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 8.2 Hz, 3H), 7.27 (d, J = 8.0 Hz, 1H), 5.91 (t, J = 8.0 Hz, 1H), 2.88−2.78 (m, 2H), 2.73 (q, J = 7.6 Hz, 2H), 2.69−2.57 (m, 2H), 1.29 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.4, 154.1, 146.0, 128.5, 128.1, 127.1, 126.8, 124.8, 123.1, 120.4, 112.9, 111.6, 76.0, 29.6, 28.8, 28.6, 15.4 ppm; ν_{max}(KBr)/cm^{-1} 3032, 2924, 1776, 1628, 1515, 1454, 1416, 1138, 752; MS (EI) m/z 115, 133, 178, 207, 233, 251, 281, 297, 306; HRMS(ESI) m/z calcd for $C_{20}H_{18}NaO_3$ [M + Na]$^+$ 329.1148, found 329.1146.

4-((2-(4-(tert-Butyl)phenyl)benzofuran-3-yl)methyl)oxetan-2-one (**4e**): yield 81% (67.6 mg) as a yellow solid; mp = 137.9−139.5 °C; R_f 0.62 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, J = 6.4 Hz, 3H), 7.53 (d, J = 8.4 Hz, 3H), 7.33 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 5.92 (t, J = 8.0 Hz, 1H), 2.86−2.73 (m, 2H), 2.72−2.57 (m, 2H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.4, 154.0, 152.9, 127.9, 126.9, 126.8, 125.9, 124.8, 123.1, 120.5, 112.9, 111.6, 76.0, 34.9, 31.2, 29.6, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3057, 2959, 1778, 1619, 1509, 1455, 1400, 1135, 747; MS (EI) m/z 105, 119, 133, 154, 193, 207, 249, 281, 334; HRMS(ESI) m/z calcd for $C_{22}H_{22}NaO_3$ [M + Na]$^+$ 357.1461, found 357.1458.

4-((2-(2,4-Dimethylphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**4f**): yield 76% (58.1 mg) as a yellow solid; mp = 99.3−100.7 °C; R_f 0.61 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.16 (s, 1H), 7.10 (d, J = 7.6 Hz, 1H), 5.54 (t, J = 8.0 Hz, 1H), 2.79−2.67 (m, 2H), 2.64−2.45 (m, 2H), 2.40 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.9, 154.7, 140.2, 138.4, 131.6, 130.7, 126.5, 126.2, 126.0, 124.7, 123.1, 120.2, 114.4, 111.6, 75.9, 29.5, 28.4, 21.3, 20.1 ppm; ν_{max}(KBr)/cm^{-1} 3061, 2924, 1776, 1646, 1516, 1453, 1138, 752; MS (EI) m/z 117, 152, 165, 178, 205, 232, 247, 306; HRMS(ESI) m/z calcd for $C_{20}H_{18}NaO_3$ [M + Na]$^+$ 329.1148, found 329.1145.

4-((2-(4-Methoxyphenyl)benzofuran-3-yl)methyl)oxetan-2-one (**4g**): yield 78% (60.1 mg) as a yellow solid; mp = 118.8−120.1 °C; R_f 0.43 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.56 (m, 3H), 7.52 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 6.4 Hz, 1H), 7.03 (d, J = 8.0 Hz, 2H), 5.88 (t, J = 8.0 Hz, 1H), 3.88 (s, 3H), 2.89−2.75 (m, 2H), 2.73−2.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 160.6, 154.3, 154.0, 129.6, 126.9, 124.6, 123.1, 122.2, 120.3, 114.4, 112.2, 111.5, 76.1, 55.4, 29.6, 28.5 ppm; ν_{max}(KBr)/cm^{-1} 3066, 2921, 1774, 1645, 1511, 1454, 1137, 753; MS (EI) m/z 115, 135, 147, 177, 191, 207, 249, 281, 308; HRMS(ESI) m/z calcd for $C_{19}H_{17}O_4$ [M + H]$^+$ 309.1121, found 309.1120.

4-((6-Methoxy-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4h**): yield 76% (58.5 mg) as a yellow solid; mp = 115.3−116.8 °C; R_f 0.45 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 7.21 (d, J = 6.4 Hz, 2H), 7.01 (d, J = 8.0 Hz, 1H), 5.93 (t, J = 8.0 Hz, 1H), 3.89 (s, 3H), 2.87−2.76 (m, 2H), 2.74−2.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 160.0, 154.4, 153.5, 130.9, 130.0, 126.7, 125.0, 123.2, 120.6, 120.5, 115.2, 113.7, 113.6, 111.7, 75.8, 55.5, 29.5, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2926, 1776, 1642, 1510, 1453, 1138, 758; MS (EI) m/z 126, 145, 165, 181, 207, 249, 279, 308; HRMS(ESI) m/z calcd for $C_{19}H_{17}O_4$ [M + H]$^+$ 309.1121, found 309.1118.

4-((5-Fluoro-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4i**): yield 80% (59.2 mg) as a yellow solid; mp = 194.4−195.7 °C; R_f 0.50 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.2 Hz, 1H), 7.54−7.41 (m, 4H), 7.24−7.19 (m, 1H), 7.06 (t, J = 8.8 Hz, 1H), 5.87 (t, J = 8.0 Hz, 1H), 2.88−2.72 (m, 2H), 2.68−2.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 159.2 (d, J = 238.1 Hz), 155.5, 150.7, 129.6 (d, J = 35.5 Hz), 129.0, 128.1, 127.4, 126.4, 113.7 (d, J = 16.8 Hz), 112.7 (d, J = 26.2 Hz), 112.4 (d, J = 9.6 Hz), 106.3 (d, J = 25.5 Hz), 75.5, 29.4, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3058, 2926, 1768, 1642, 1508, 1450, 1135, 756; MS (EI) m/z 105, 118, 139, 165, 183, 207, 237, 251, 296; HRMS(ESI) m/z calcd for $C_{18}H_{14}FO_3$ [M + H]$^+$ 297.0921, found 297.0918.

4-((5-Chloro-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4j**): yield 68% (53.0 mg) as a yellow solid; mp = 198.7−199.8 °C; R_f 0.56 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.2 Hz, 2H), 7.56−7.45 (m, 5H), 7.30 (d, J = 8.0 Hz, 1H), 5.86 (t, J = 8.0 Hz, 1H), 2.84−2.73 (m, 2H), 2.67−2.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 155.2, 152.9, 129.9, 129.3, 129.0, 128.9, 128.2, 128.1, 125.2, 120.2, 113.1, 112.6, 75.4, 29.4, 28.7 ppm; ν_{max}(KBr)/cm^{-1} 3066, 2924, 1777, 1646, 1516, 1448, 1136, 755; MS (EI) m/z 105, 147, 201, 218, 255, 267, 312; HRMS(ESI) m/z calcd for $C_{18}H_{13}ClNaO_3$ [M + Na]$^+$ 335.0445, found 335.0442.

4-((6-Chloro-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4k**): yield 79% (61.6 mg) as a yellow solid; mp = 173.3−175.0 °C; R_f 0.54 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.6 Hz, 2H), 7.55−7.46 (m, 5H), 7.25 (d, J = 6.8 Hz, 1H), 5.89 (t, J = 8.0 Hz, 1H), 2.88−2.77 (m, 2H), 2.69−2.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 154.5, 154.3, 130.9, 129.8, 129.3, 129.0, 128.0, 125.5, 123.9, 121.2, 113.4, 112.2, 75.6, 29.4, 28.8 ppm; ν_{max}(KBr)/cm^{-1} 3035, 2921, 1741, 1646, 1515, 1464, 1138, 754; MS (EI) m/z 77, 128, 165, 207, 218, 255, 267, 283, 312; HRMS(ESI) m/z calcd for $C_{18}H_{14}ClO_3$ [M + H]$^+$ 313.0626, found 313.0623.

4-((5-Bromo-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4l**): yield 87% (77.4 mg) as a yellow solid; mp = 207.5−208.6 °C; R_f 0.55 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.63 (t, J = 7.6 Hz, 2H), 7.57−7.47 (m, 3H), 7.30 (d, J = 8.0 Hz, 2H), 5.85 (t, J = 8.0 Hz, 1H), 2.87−2.78 (m, 2H), 2.65−2.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 155.0, 153.2, 133.7, 129.9, 129.2, 129.0, 128.2, 128.1, 127.9, 123.2, 116.4, 113.1, 75.4, 29.5, 28.7 ppm; ν_{max}(KBr)/cm^{-1} 3056, 2928, 1756, 1648, 1510, 1442, 1138, 758; MS (EI) m/z 115, 147, 207, 267, 305, 356; HRMS(ESI) m/z calcd for $C_{18}H_{14}BrO_3$ [M + H]$^+$ 357.0121, found 357.0117.

4-((6-Bromo-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4m**): yield 81% (72.1 mg) as a yellow solid; mp = 188.9−189.8 °C; R_f 0.50 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.64 (d, J = 7.2 Hz, 2H), 7.59−7.45 (m, 4H), 7.37 (dd, J = 16.0, 8.0 Hz, 1H), 5.89 (t, J = 8.0 Hz, 1H), 2.80 (dd, J = 10.8,

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7.6 Hz, 2H), 2.61 (dd, J = 17.6, 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 154.7, 154.2, 129.8, 129.0, 128.1, 126.6, 125.9, 121.5, 120.9, 118.3, 115.1, 113.5, 75.5, 29.4, 28.8 ppm; ν_{max}(KBr)/cm^{-1} 3038, 2926, 1740, 1648, 1516, 1468, 1133, 756; MS (EI) m/z 115, 133, 176, 233, 327, 356; HRMS(ESI) m/z calcd for $C_{18}H_{14}BrO_3$ $[M + H]^+$ 357.0121, found 357.0119.

*4-((5,6-Dichloro-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**4n**):* yield 74% (64.0 mg) as a yellow solid; mp = 233.8−234.9 °C; R_f 0.36 (petroleum ether/EtOAc 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.62−7.49 (m, 4H), 7.38 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 7.6 Hz, 1H), 5.86 (t, J = 8.0 Hz, 1H), 2.90−2.76 (m, 2H), 2.73−2.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 154.5, 150.9, 133.8, 133.4, 130.9, 129.7, 127.0, 126.4, 125.6, 123.5, 120.8, 111.8, 75.3, 29.3, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3036, 2928, 1748, 1642, 1519, 1464, 1138, 758; MS (EI) m/z 77, 103, 131, 171, 191, 207, 281, 314, 346; HRMS(ESI) m/z calcd for $C_{18}H_{13}Cl_2O_3$ $[M + H]^+$ 347.0236, found 347.0233.

*3-Chloro-2-phenylbenzofuran (**6a**):*[19] yield 84% (47.9 mg) as a white solid; mp = 68.4−69.8 °C; R_f 0.67 (petroleum ether/EtOAc 100/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (t, J = 8.8 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.23−7.11 (m, 4H), 7.03 (dt, J = 14.4, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 152.0, 130.5, 129.5, 128.6, 128.5, 126.3, 124.9, 123.1, 120.7, 111.3, 107.7 ppm; HRMS(ESI) m/z calcd for $C_{14}H_9ClNaO$ $[M + Na]^+$ 251.0234, found 251.0232.

*3-Chloro-2-propylbenzofuran (**6b**):* yield 66% (32.0 mg) as a yellow oil; R_f 0.71 (petroleum ether/EtOAc 100/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 1H), 7.27−7.25 (m, 1H), 7.21 (d, J = 7.6 Hz, 2H), 2.77 (t, J = 7.2 Hz, 2H), 1.72 (dd, J = 14.8, 7.2 Hz, 2H), 0.93 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 154.3, 131.1, 125.1, 124.5, 123.1, 120.8, 110.9, 29.7, 21.3, 13.7 ppm; ν_{max}(KBr)/cm^{-1} 3026, 2926, 1648, 1510, 1463, 1136; MS (EI) m/z 63, 77, 102, 115, 131, 160, 194; HRMS(ESI) m/z calcd for $C_{11}H_{11}ClNaO$ $[M + Na]^+$ 217.0391, found 217.0388.

*2-Phenylbenzofuran (**7a**):*[18c] yield 11% (5.5 mg) as a white solid; mp = 108.5−109.8 °C; R_f 0.61 (petroleum ether/EtOAc 100/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 7.2 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.35 (d, J = 6.8 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.22 (t, J = 7.2 Hz, 1H), 7.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 154.9, 130.5, 129.3, 128.8, 128.6, 125.0, 124.3, 123.0, 120.9, 111.2, 101.3 ppm.

*2-Propylbenzofuran (**7b**):*[20] yield 19% (7.6 mg) as a yellow oil; R_f 0.64 (petroleum ether/EtOAc 100/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.2 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.17 (dt, J = 13.2, 6.8 Hz, 2H), 6.36 (s, 1H), 2.73 (t, J = 7.6 Hz, 2H), 1.82−1.71 (m, 2H), 1.00 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 154.7, 129.1, 123.0, 122.4, 120.2, 110.7, 101.9, 30.5, 21.1, 13.8 ppm.

General Procedure for the Synthesis of 11a. Following a reported procedure,[16] to a mixture of (4-ethylphenyl)boronic acid (45.0 mg, 0.30 mmol), $Pd(OAc)_2$ (5 mol %), K_3PO_4 (63.5 mg, 0.30 mmol), and Xphos (4.8 mg, 0.01 mmol) in 1 mL of toluene was added a solution of **4l** (35.6 mg, 0.10 mmol) in 1.0 mL of toluene under nitrogen. After stirring at 110 °C for 10 h, the reaction mixture was quenched with water, extracted with ethyl acetate, washed with brine, dried over $MgSO_4$, and concentrated. Column chromatography on silica (petroleum ether/ethyl acetate = 5/1) gave 28.7 mg (yield: 75%) of **11a** as a yellow solid.

*4-((5-(4-Ethylphenyl)-2-phenylbenzofuran-3-yl)methyl)oxetan-2-one (**11a**):* yield 75% (28.7 mg) as a yellow solid; mp = 197.6−198.8 °C; R_f 0.44 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.68 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.55−7.47 (m, 4H), 7.31 (d, J = 8.0 Hz, 2H), 5.93 (t, J = 8.0 Hz, 1H), 2.89−2.79 (m, 2H), 2.77−2.63 (m, 4H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 155.2, 154.0, 143.6, 138.7, 138.3, 129.8, 129.5, 128.9, 128.4, 128.1, 127.3, 125.7, 122.7, 120.6, 113.5, 109.8, 75.9, 29.7, 28.7, 28.5, 15.6 ppm; ν_{max}(KBr)/cm^{-1} 3050, 2928, 1776, 1648, 1516, 1500, 1456, 1418, 1400, 1135, 757; MS (EI) m/z 126, 207, 281, 335, 382; HRMS(EI) m/z calcd for $C_{26}H_{22}NaO_3$ $[M + Na]^+$ 405.1461, found 405.1455.

General Procedure for the Synthesis of 11b. Following a reported procedure,[17] an oven-dried pressure tube (10 mL) was charged with $Pd(OAc)_2$ (1.5 mg, 0.005 mmol), tri-*p*-tolylphosphine (3.0 mg, 0.01 mmol), **4l** (35.6 mg, 0.1 mmol), CH_3ONa (7.6 mg, 0.3 mmol), sodium *p*-toluenesulfinic acid (18.0 mg, 0.1 mmol), and cyclohexane (0.3 mL). The reaction vessel was closed under air, and the resulting solution was stirred at 160 °C for 4 h. After cooling to room temperature, the volatiles were removed under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 5/1) to give the corresponding product **11b** (24.1 mg) as a yellow solid in 68% yield.

*4-((2,5-Diphenylbenzofuran-3-yl)methyl)oxetan-2-one (**11b**):* yield 68% (24.1 mg) as a yellow solid; mp = 195.3−196.8 °C; R_f 0.41 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.61 (d, J = 8.4 Hz, 3H), 7.58−7.50 (m, 4H), 7.49−7.44 (m, 2H), 7.37 (t, J = 7.2 Hz, 1H), 5.93 (t, J = 8.0 Hz, 1H), 2.88−2.79 (m, 2H), 2.77−2.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 154.5, 154.1, 141.4, 137.1, 129.7, 129.6, 128.9, 128.8, 128.2, 127.6, 127.3, 127.1, 124.8, 119.0, 113.5, 111.8, 75.8, 29.6, 28.6 ppm; ν_{max}(KBr)/cm^{-1} 3048, 2926, 1769, 1646, 1515, 1508, 1500, 1456, 1411, 1400, 1136, 758; MS (EI) m/z 133, 163, 191, 207, 281, 354; HRMS(EI) m/z calcd for $C_{24}H_{19}O_3$ $[M +H]^+$ 355.1329, found 355.1326.

General Procedure for the Synthesis of 11c. Following a reported procedure,[16] under nitrogen, $ZnCl_2$ (0.5 M solution in THF; 0.35 mL, 0.16 mmol) was added by syringe to a Schlenk tube. *o*-Tolylmagnesium chloride (1.0 M solution in THF; 0.4 mL, 0.40 mmol) was then added dropwise, and the resulting mixture was stirred at room temperature for 20 min. Next, NMP (0.5 mL) was added by syringe, followed after 5 min by $Pd(P(t\text{-}Bu)_3)_2$ (1.5 mg, 0.003 mmol) and **4l** (35.6 mg, 0.1 mmol). The Schlenk tube was closed at the Teflon stopcock, and the reaction mixture was stirred in a 100 °C oil bath for 2 h. It was then allowed to cool to room temperature, and aqueous HCl was added (1.0 M; 3 mL). The resulting mixture was extracted with Et_2O (2 × 10 mL), and the organic extracts were combined, washed with water (2 × 10 mL), dried ($MgSO_4$), and concentrated, affording a yellow solid. Column chromatography on silica (petroleum ether/ethyl acetate = 5/1) furnished 24.9 mg (63%) of the title compound **11c** as a yellow solid.

*4-((2-(4′-Propyl-[1,1′-biphenyl]-4-yl)benzofuran-3-yl)methyl)-oxetan-2-one (**11c**):* yield 63% (24.9 mg) as a yellow solid; mp = 203.5−204.7 °C; R_f 0.51 (petroleum ether/EtOAc 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 4H), 7.61 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 6.8 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 7.6 Hz, 3H), 5.97 (t, J = 7.6 Hz, 1H), 2.89−2.80 (m, 2H), 2.77−2.69 (m, 2H), 2.67−2.63 (m, 2H), 1.70 (dd, J = 14.8, 7.6 Hz, 2H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 154.5, 153.6, 142.7, 142.3, 137.4, 129.1, 128.4, 128.3, 127.4, 126.9, 126.8, 124.9, 123.2, 120.5, 113.4, 111.7, 75.9, 37.7, 29.5, 28.6, 24.5, 13.9 ppm; ν_{max}(KBr)/cm^{-1} 3058, 2923, 1775, 1648, 1517, 1456, 1428, 1137, 751; MS (EI) m/z 135, 177, 191, 207, 249, 281, 313, 355, 396; HRMS(EI) m/z calcd for $C_{27}H_{25}O_3$ $[M +H]^+$ 397.1798, found 397.1797.

■ ASSOCIATED CONTENT

Supporting Information

Spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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