Transition Metal-free Synthesis of 2-Substituted Methyl Benzo[*b*]furan-3-carboxylates

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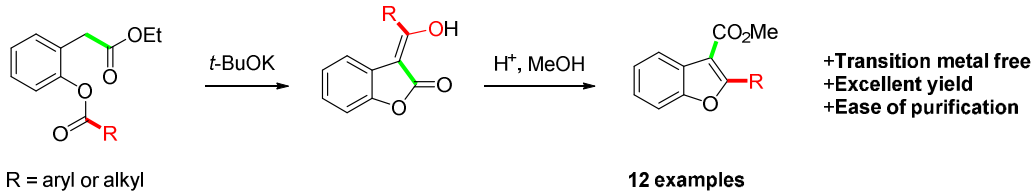
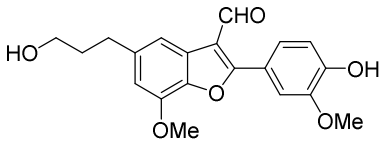
ABSTRACT



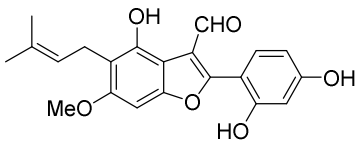
A concise and highly efficient synthetic pathway was developed for 2-substituted methyl benzo[*b*]furan-3-carboxylates. This method provides convenient and cost-effective access for 2-substituted methyl benzo[*b*]furan-3-carboxylates without the use of a transition metal catalyst for synthesis. Furthermore, in most cases, this method gives excellent yields and conventional flash column chromatography is not needed for purification.

Introduction

The 2,3-disubstituted benzo[*b*]furan is a common structure found in numerous natural products. These compounds are known for their various biological activities[1] and there extensive interest for their synthesis (Figure 1).[2,3]



XH-14

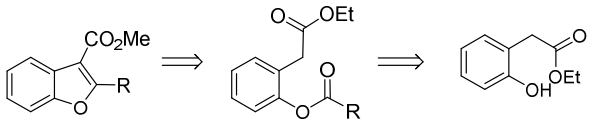


Ebenfuran III

Figure 1. Representative examples of naturally occurring compounds containing 2,3-substituted benzo[*b*]furan structure.

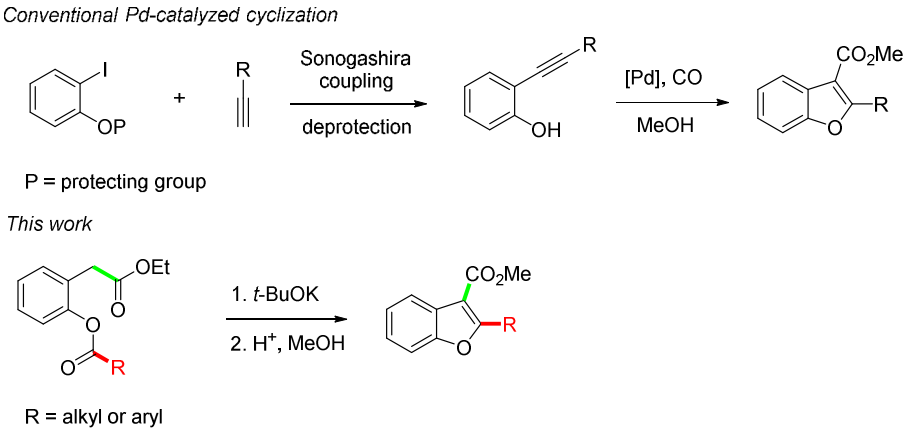
Among the many strategies for the synthesis of the 2,3-disubstituted benzo[*b*]furan skeleton, the most common and widely used method is by transition metal catalyzed cyclization of 2-alkynylphenols.[4] Other popular methods employ Pd-catalyzed cross-coupling of *C*2-halogenated or stannylated benzo[*b*]furans with aryl boronic acids or aryl halides[5] or direct arylation of *C*2- or *C*3-substituted benzo[*b*]furans with aryl halides[6] utilizing C-H activation. Oxidative cross-coupling reactions at the *C*2 position of benzo[*b*]furan[7] and other methods[8] have also been reported recently. Although these methods give generally reasonable results, they require expensive transition metal catalysts for reactions and/or additional purification procedures. For the synthesis of indoles which are nitrogen analogue of benzo[*b*]furan, the original or modified Madelung indole synthesis[9] can be used. However, these Madelung-type methods generally required harsh conditions and it could not be used to synthesize the analogous benzo[*b*]furans. To overcome these shortcomings of previous synthetic strategies, we focused to devise a more effective cyclization reaction for 2,3-disubstituted benzo[*b*]furans without transition metal catalysts. The retrosynthetic strategies focused on affordable and highly effective synthetic approach for the desired product (Scheme 1).

Scheme 1. Retrosynthetic Analysis for 2-Substituted Methyl Benzo[b]furan-3-carboxylate



Herein is reported a simple approach toward the synthesis of 2,3-disubstituted benzo[*b*]furans without the use of transition metal catalysts. We believe this may be a more useful and cost-effective strategy for the synthesis of 2,3-disubstituted benzo[*b*]furans (Scheme 2).

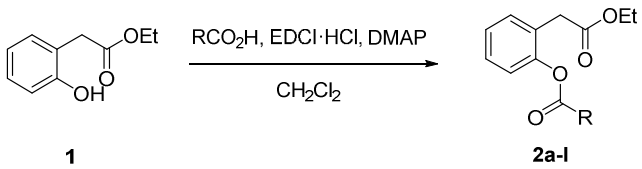
Scheme 2. Comparison Between Pd-catalyzed Cyclization and This Work



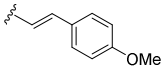
Results and Discussion

To investigate the scope of this synthetic strategy, substrates **2a-l** having various substituents were selected. The substituents encompass aryl groups containing the electron-withdrawing or donating groups in different positions and aliphatic groups with an acidic α-proton. The starting material, ethyl 2-hydroxyphenylacetate (**1**), was obtained from a Fischer esterification reaction (90% yield) using commercially available 2-hydroxyphenylacetic acid, anhydrous ethanol and concentrated sulfuric acid. The substrates **2a-l** were prepared using modified Steglich esterification[10] conditions which is initially employed the DCC-mediated coupling reaction of an alcohol and a carboxylic acid catalyzed by DMAP (Table 1).

Table 1. Synthesis of Various Ethyl (2-Acyloxyphenyl)acetates



1 **2a-l**

product	R	yield (%)[a]
2a	Ph	92
2b	*p*-$MeOC_6H_4$	93
2c	*m*-$MeOC_6H_4$	93
2d	*o*-$MeOC_6H_4$	97
2e	3,4-$(MeO)_2C_6H_3$	83
2f	*p*-FC_6H_4	96
2g	*p*-BrC_6H_4	91
2h	2-naphthyl	92
2i		79
2j	*i*-Bu	96
2k	cyclopropyl	96
2l	cyclohexyl	94

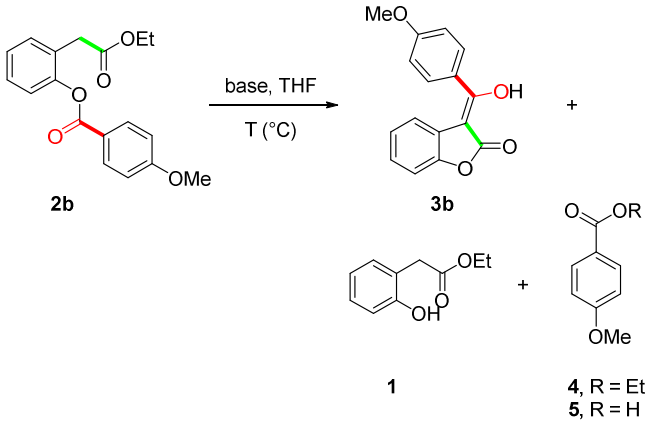
[a]Isolated yield.

In the early stage of study, we used acid chlorides for esterifications of the phenols. However, we found that the crude products were always contaminated with small amount of impurities when acid chlorides were used for esterification and it rendered the purification very laborious. Thus, we decided to use DCC couplings of phenols and carboxylic acids for the acylation of the phenols and it gave better results. However, to obtain pure products from the DCC coupling reaction mixtures, careful column chromatography procedures were required for the removal of dicyclohexylurea, which is an inevitable

by-product formed from DCC. For simple purification of products, we replaced DCC with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI·HCl). We found that the products from these modified conditions were sufficiently pure after filtration through a small plug of silica gel such that excellent yields were obtained and no additional purification procedures were required.

To investigate the optimum reaction conditions for base-mediated cyclization of substrate **2**, compound **2b** was selected and various bases and temperature conditions were tested. The result of the optimization for 3-(hydroxyl(4-methoxyphenyl)methylene)benzo[*b*]furan-2(3*H*)-one is illustrated on Table 2. Under the condition of entry 1, side products **1**, **4** and **5** were isolated, purified and confirmed by the NMR comparison of identical compounds independently prepared from other routes. To minimize the side products, further study focused on lowering the reaction temperature with potassium *t*-butoxide and substituting potassium *t*-butoxide with other bases (sodium hydride, lithium bis(trimethylsilyl)amide). Among these entries, entry 3 gave the best result. Under these conditions, NMR spectra revealed that the desired product **3b** was the sole product of the crude reaction mixture.

Table 2. Optimization of Synthesis of (*Z*)-3-(Hydroxyl(4-methoxyphenyl)methylene)benzo[*b*]furan-2(3*H*)-one (3b)[a]



entry	base	T (°C)	ratio of products (%)[b]			
			3b	**1**	**4**	**5**
1	*t*-BuOK[c]	0 to rt	70	15	5	10

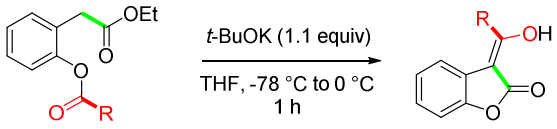
2	*t*-BuOK[c]	-25 to 0	76	12	12	0
3	*t*-BuOK[c]	-78 to 0	100	0	0	0
4	NaH[d]	0 to rt	78	11	11	0
5	NaH[d]	-78 to 0	82	9	9	0
6	LiHMDS[c]	0 to rt	32	34	6	28
7	LiHMDS[c]	-78 to 0	73	13	7	7

[a]All reactions were carried out in 1.0 mmol scale of **2b** with 3 equiv of base in 3 mL of anhydrous THF. [b]Determined by integration of ^{1}H NMR. [c]Used 1.0 M solution in THF. [d]60% dispersion in mineral oil.

Early reaction optimization for 3-(hydroxyl(alkyl)methylene)benzo[*b*]furan-2(3*H*)-one was conducted with an excess amount (3.0 equiv) of *t*-BuOK. However, additional investigations on the stoichiometry of base revealed that a reduced amount of base has no detrimental effect. A slight excess amount (1.1 equiv) of *t*-BuOK gave comparable results with the original conditions.

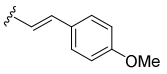
Applying this standard condition to the substrates **2a-l**, gave excellent yields of 3-(hydroxyl(alkyl)methylene)benzo[*b*]furan-2(3*H*)-one products for all entries (Table 3).

Table 3. Synthesis of Various 3-(Hydroxyl(alkyl)methylene)benzo[*b*]furan-2(3*H*)-ones



2a-l **3a-l**

product	R	yield (%)[a]
3a	Ph	87
3b	*p*-MeOC$_6$H$_4$	89
3c	*m*-MeOC$_6$H$_4$	86
3d	*o*-MeOC$_6$H$_4$	77
3e	3,4-(MeO)$_2$C$_6$H$_3$	82
3f	*p*-FC$_6$H$_4$	66

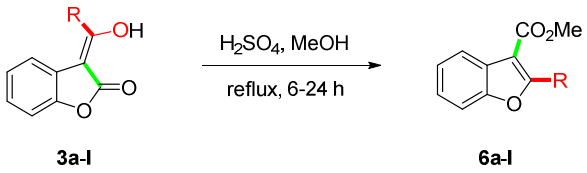
3g	*p*-BrC_6H_4	85
3h	2-naphthyl	88
3i		76
3j	*i*-Bu	91
3k	cyclopropyl	88
3l	cyclohexyl	87

[a]Isolated yield.

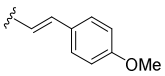
All products could be obtained as purified solids after recrystallization at low temperature (-20 °C). According to the NMR spectra of these products, they existed as enol tautomers almost exclusively and there was little detectable keto tautomer in each. To elucidate the structure of 3-(hydroxyl(alkyl)methylene)benzo[*b*]furan-2(3*H*)-one more clearly, we analyzed the crystal structure of compound **3h** using a single crystal X-ray crystallography technique. (See supporting information for detailed X-Ray crystallographic structure analysis for compound **3h**.)

The compounds **3a-l** were subjected to the methanolysis and dehydrative cyclization process in the presence of concentrated sulfuric acid to give methyl 2-substituted benzo[*b*]furan-3-carboxylates **6a-l** (Table 4). In case of R = aryl, the reaction was completed within 6 h. If R = alkyl, the reaction required longer reaction time (12 h) for completion. In the case of **3i**, which has a conjugated system, it required the longest reaction time (24 h) among these entries.

Table 4. Synthesis of Various 2-Substituted Methyl Benzo[*b*]furan-3-carboxylates



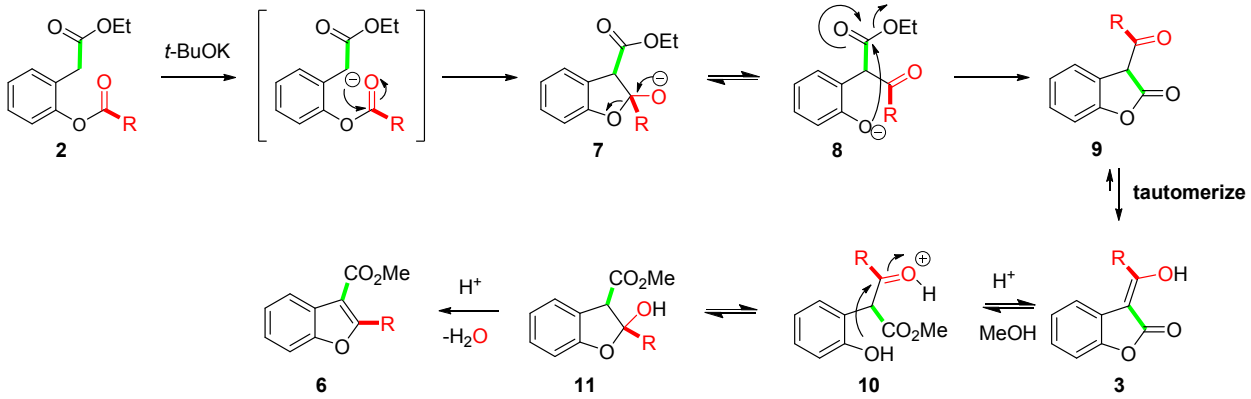
3a-l **6a-l**

product	R	yield (%)[a]
6a	Ph	90
6b	*p*-$MeOC_6H_4$	92
6c	*m*-$MeOC_6H_4$	91
6d	*o*-$MeOC_6H_4$	90
6e	3,4-$(MeO)_2C_6H_3$	92
6f	*p*-FC_6H_4	90
6g	*p*-BrC_6H_4	91
6h	2-naphthyl	87
6i		89
6j	*i*-Bu	85
6k	cyclopropyl	87
6l	cyclohexyl	88

[a]Isolated yield.

This procedure proceeded very cleanly and gave excellent yields and satisfactory purities of products without additional purification procedures. After simple recrystallization of crude products, analytical grade products could be obtained easily. The products **6d** and **6j**, which are oily compounds at rt and therefore impossible to be recrystallized, were purified by column chromatography to obtain analytical grade samples.

Scheme 3. Plausible Mechanism for the Sythesis of 2-Substituted Methyl Benzo[*b*]furan-3-carboxylates



A plausible reaction mechanism for the transformation from **2** to **6** was illustrated on Scheme 3. The proton abstraction from ester **2** gave hemiketal anion **7**. The hemiketal anion **7** transformed to β-ketoester **8**, whose phenolic residue attacked another ester group to give the 3-acylbenzo[*b*]furan-2(3*H*)-one **9**. The resulting 3-acylbenzo[*b*]furan-2(3*H*)-one **9** is immediately tautomerized to give tautomer **3** as a sole product. The enol **3** underwent methanolysis in the presence of methanol and concentrated sulfuric acid to give intermediate **10.** The phenolic oxygen next attacked the carbonyl group of ketone to give the hemiketal **11**. The hemiketal **11** was dehydrated spontaneously in the presence of concentrated sulfuric acid to give the desired 2-substituted methyl benzo[*b*]furan-3-carboxylate **6**.

Conclusion

A new method for synthesizing 2-substituted methyl benzo[*b*]furan-3-carboxylate derivatives has been developed using mild conditions without using any transition metal catalysts. The method is applicable to the preparation of various alkyl or aryl groups at the *C*2. Since our synthetic strategy allows simultaneous installation of a carbonyl substituent at *C*3 and an alkyl or aryl substituent at *C*2, it can be used to introduce other moieties. The products were obtained from 2-hydroxyphenylacetic acid in four steps in very high overall yield. Moreover, in most cases, our strategy has no complicated purification procedure and does not need laborious column chromatography to obtain pure products.

Experimental Section

General Information

All reactions were conducted under inert atmosphere unless otherwise stated. For air and moisture sensitive reactions, all glassware are dried in an convection oven and flame-dried. All solvents and reagents for reaction were purchased from the chemical supplier and used as received. Analytical thin layer chromatography (TLC) was carried out using commercial silica gel 60 TLC plates. NMR spectra were acquired from 400 and 500 MHz spectrometer and chemical shifts were reported as parts per million (ppm) relative to the solvent residual peak ($CDCl_3$ = 7.26 ppm for ^1H NMR, 77.16 ppm for ^{13}C NMR). Coupling constants were reported in Hertz (Hz). Multiplicities of NMR spectra are reported using the following general abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. All melting point values are uncorrected. The high resolution mass spectra were obtained from an ESI+ quadrupole time-of-flight (Q-TOF) mass spectrometer.

Ethyl 2-Hydroxyphenylacetate (1). The mixture of 2-hydroxyphenylacetic acid (2.0 g, 13.1 mmol) and concentrated sulfuric acid (*ca*. 3 mL) in anhydrous ethanol (50 mL) was heated under reflux for 12 h. The resulting mixture was concentrated *in vacuo* and diluted with dichloromethane (20 mL). The organic layer was washed with water (10 mL x 3), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting residue was filtered through a small plug of silica gel with a mixture of EtOAc and *n*-hexane (1:2) to give the product as a low-melting white solid (2.13 g, 90%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.21–7.14 (m, 1H), 7.12 (d, J = 7.4 Hz, 1H), 6.94–6.85 (m, 2H), 4.21 (q, J = 7.1 Hz, 2H), 3.69 (s, 2H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 155.1, 131.0, 129.1, 120.8, 120.7, 117.3, 61.9, 37.7, 14.1. ^1H and ^{13}C NMR spectral data are consistent with previously reported values.[11]

Ethyl (2-Benzoyloxy)phenylacetate (2a). The mixture of ethyl 2-hydroxyphenylacetate (3.60 g, 20.0 mmol), benzoic acid (2.44 g, 20.0 mmol) and DMAP (0.489 g, 4.00 mmol) was suspended in anhydrous

dichloromethane (100 mL). EDCI·HCl (4.21 g, 22.0 mmol) was added to this mixture and stirred for 12 h at rt. The reaction mixture was diluted with dichloromethane and the organic layer was washed with 0.5 N aqueous HCl solution and water followed by a saturated aqueous sodium bicarbonate solution. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The resulting residue was filtered through a small plug of silica gel with a mixture of EtOAc and *n*-hexane (1:2) to give the product as a colorless oil (5.16 g, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.17 (m, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 7.36 (t, J = 7.7 Hz, 2H), 7.28–7.22 (m, 2H), 4.05 (q, J = 7.1 Hz, 2H), 3.63 (s, 2H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 164.6, 149.3, 133.7, 131.4, 130.2, 129.3, 128.7, 128.6, 126.8, 126.2, 122.7, 61.0, 36.6, 14.0. HRMS (ESI$^+$): calcd. for $C_{17}H_{16}NaO_4^+$ $[M + Na]^+$: 307.0946, found 307.0942; Anal. Calcd. For $C_{17}H_{16}O_4$: C, 71.82; H, 5.67, found: C, 71.83; H, 5.68.

Ethyl 2-(4-Methoxybenzoyloxy)phenylacetate (2b). The title compound **2b** (1.62 g, 93%) was obtained from **1** (1.00 g, 5.55 mmol) and *p*-anisic acid (0.842 g, 5.55 mmol) as a colorless oil using a procedure analogous to that described for the preparation of **2a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.9 Hz, 2H), 7.39 (dd, J = 13.3, 4.4 Hz, 2H), 7.30–7.24 (m, 2H), 7.03 (d, J = 8.9 Hz, 2H), 4.10 (q, J = 7.1 Hz, 2H), 3.90 (s, 3H), 3.67 (s, 2H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 164.3, 163.9, 149.4, 132.3, 131.3, 128.4, 126.9, 126.0, 122.7, 121.5, 113.9, 60.9, 55.5, 36.5, 14.0. HRMS (ESI$^+$): calcd. for $C_{18}H_{18}NaO_5^+$ $[M + Na]^+$: 337.1052, found 337.1046; Anal. calcd. for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77, found: C, 68.86; H, 5.73.

Ethyl 2-(3-Methoxybenzoyloxy)phenylacetate (2c). The title compound **2c** (1.62 g, 93%) was obtained from **1** (1.00 g, 5.55 mmol) and *m*-anisic acid (0.842 g, 5.55 mmol) as a colorless oil using a procedure analogous to that described for the preparation of **2a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.7 Hz, 1H), 7.74–7.69 (m, 1H), 7.45–7.34 (m, 3H), 7.28–7.23 (m, 2H), 7.22–7.16 (m, 1H), 4.07 (q,

J = 7.1 Hz, 2H), 3.89 (s, 3H), 3.63 (s, 2H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 164.5, 159.7, 149.3, 131.3, 130.5, 129.6, 128.5, 126.8, 126.2, 122.6, 122.5, 120.2, 114.5, 61.0, 55.5, 36.5, 14.0. HRMS (ESI^+): *m/z* calcd. for $C_{18}H_{18}NaO_5^+$ $[M + Na]^+$: 337.1052, found 337.1046; Anal. calcd. for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77, found: C, 68.82; H, 5.74.

Ethyl 2-(2-Methoxybenzoyloxy)phenylacetate (2d). The title compound **2d** (1.93 g, 97%) was obtained from **1** (1.14 g, 6.30 mmol) and *o*-anisic acid (1.05 g, 6.43 mmol) as a pale yellow oil using a procedure analogous to that described for the preparation of **2a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.6, 1.3 Hz, 1H), 7.56 (td, J = 8.2, 1.7 Hz, 1H), 7.40–7.33 (m, 2H), 7.30–7.22 (m, 2H), 7.06 (t, J = 7.9 Hz, 2H), 4.10 (q, J = 7.1 Hz, 2H), 3.94 (s, 3H), 3.70 (s, 2H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 164.0, 159.8, 149.4, 134.4, 132.3, 131.2, 128.4, 126.8, 126.0, 122.9, 120.2, 118.9, 112.1, 60.9, 56.0, 36.3, 14.1. HRMS (ESI^+): *m/z* calcd. for $C_{18}H_{18}NaO_5^+$ $[M + Na]^+$: 337.1052, found 337.1047; Anal. calcd. for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77, found: C, 68.79; H, 5.76.

Ethyl 2-(3,4-Dimethoxybenzoyloxy)phenylacetate (2e). The title compound **2e** (1.57 g, 83%) was obtained from **1** (1.00 g, 5.55 mmol) and 3,4-dimethoxybenzoic acid (1.01 g, 5.55 mmol) as a white solid using a procedure analogous to that described for the preparation of **2a**: mp 76-77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 8.4, 1.6 Hz, 1H), 7.68 (d, J = 1.5 Hz, 1H), 7.36 (t, J = 7.3 Hz, 2H), 7.27–7.22 (m, 2H), 6.96 (d, J = 8.5 Hz, 1H), 4.06 (q, J = 7.1 Hz, 2H), 3.98 – 3.95 (overlapped s, 6H), 3.62 (s, 2H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 164.4, 153.6, 149.4, 148.8, 131.4, 128.6, 126.9, 126.1, 124.5, 122.8, 121.7, 112.4, 110.4, 61.0, 56.2, 56.1, 36.6, 14.1. HRMS (ESI^+): *m/z* calcd. for $C_{19}H_{20}NaO_6^+$ $[M + Na]^+$: 367.1158, found 367.1152; Anal. calcd. for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85, found: C, 66.27; H, 5.88.

Ethyl 2-(4-Fluorobenzoyloxy)phenylacetate (2f). The title compound **2f** (1.61 g, 96%) was obtained

from **1** (1.00 g, 5.55 mmol) and 4-fluorobenzoic acid (0.777 g, 5.55 mmol) as a pale yellow oil using a procedure analogous to that described for the preparation of **2a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26–8.17 (m, 2H), 7.35 (t, J = 7.9 Hz, 2H), 7.24 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 8.6 Hz, 2H), 4.04 (q, J = 7.1 Hz, 2H), 3.61 (s, 2H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 166.3 (d, $^{1}J_{C\text{-}F}$ = 255.2 Hz), 163.7, 149.2, 132.9 (d, $^{3}J_{C\text{-}F}$ = 9.5 Hz) 131.5, 128.6, 126.8, 126.3, 125.6 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 122.6, 115.9 (d, $^{2}J_{C\text{-}F}$ = 22.1 Hz), 61.0, 36.6, 14.1. HRMS (ESI$^+$): *m/z* calcd. for $C_{17}H_{15}FNaO_4^+$ [M + Na]$^+$: 325.0852, found 325.0847; Anal. calcd. for $C_{17}H_{15}FO_4$: C, 67.54; H, 5.00, found: C, 67.54; H, 5.05.

Ethyl 2-(4-Bromobenzoyloxy)phenylacetate (2g). The title compound **2g** (1.83 g, 91%) was obtained from **1** (1.00g, 5.55 mmol) and 4-bromobenzoic acid (1.11 g, 5.55 mmol) as a white solid using a procedure analogous to that described for the preparation of **2a**: mp 50-51 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8.5 Hz, 2H), 7.35 (t, J = 7.7 Hz, 2H), 7.24 (t, J = 8.5 Hz, 2H), 4.04 (q, J = 7.1 Hz, 2H), 3.60 (s, 2H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 164.0, 149.1, 132.0, 131.7, 131.5, 129.0, 128.6, 128.3, 126.8, 126.4, 122.6, 61.1, 36.6, 14.1. HRMS (ESI$^+$): *m/z* calcd. for $C_{17}H_{15}BrNaO_4^+$ [M + Na]$^+$: 385.0051, found 385.0048; Anal. calcd. for $C_{17}H_{15}BrO_4$: C, 56.22; H, 4.16, found: C, 56.23; H, 4.15.

Ethyl 2-(2-Naphthoyloxy)phenylacetate (2h). The title compound **2h** (1.71 g, 92%) was obtained from **1** (1.00 g, 5.55 mmol) and 2-naphthoic acid (0.955 g, 5.55 mmol) as a white solid using a procedure analogous to that described for the preparation of **2a**: mp 90-91 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.25–8.19 (m, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.95 (dd, J = 12.7, 8.4 Hz, 2H), 7.68–7.57 (m, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.35–7.25 (m, 2H), 4.08 (q, J = 7.1 Hz, 2H), 3.69 (s, 2H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 164.8, 149.4, 135.9, 132.5, 132.0, 131.5, 129.5 128.8, 128.6, 128.5, 127.9, 126.9, 126.9, 126.5, 126.3, 125.5, 122.8, 61.0, 36.7, 14.1. HRMS

(ESI$^+$): *m/z* calcd. for $C_{21}H_{18}NaO_4^+$ $[M + Na]^+$: 357.1103, found 357.1098; Anal. calcd. for $C_{21}H_{18}O_4$: C, 75.43; H, 5.43, found: C, 75.43; H, 5.44.

Ethyl 2-(*trans*-4-Methoxycinnamoyloxy)phenylacetate (2i). The title compound **2i** (1.49 g, 79%) was obtained from **1** (1.00 g, 5.55 mmol) and *trans*-4-methoxycinnamic acid (0.989 g, 5.55 mmol) as a faint yellow solid using a procedure analogous to that described for the preparation of **2a**: mp 92-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 15.9 Hz, 1H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 2H), 7.25–7.17 (m, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.50 (d, *J* = 15.9 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.61 (s, 2H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 165.3, 161.9, 149.4, 146.6, 131.3, 130.2, 128.5, 127.0, 126.9, 126.1, 122.7, 114.6, 114.4, 61.1, 55.6, 36.6, 14.3. HRMS (ESI$^+$): *m/z* calcd. for $C_{20}H_{20}NaO_5^+$ $[M + Na]^+$: 363.1208, found 363.1204; Anal. calcd. for $C_{20}H_{20}O_5$: C, 70.58; H, 5.92, found: C, 70.60; H, 5.89.

Ethyl (2-Isovaleroyloxy)phenylacetate (2j). The title compound **2j** (1.41 g, 96%) was obtained from **1** (1.00 g, 5.55 mmol) and isovaleric acid (0.612 mL, 5.55 mmol) as a colorless oil using a procedure analogous to that described for the preparation of **2a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.55 (s, 2H), 2.46 (d, *J* = 7.2 Hz, 2H), 2.25 (sep, *J* = 6.8 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.06 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 170.8, 149.2, 131.4, 128.5, 126.7, 126.1, 122.6, 61.0, 43.2, 36.5, 25.8, 22.5, 14.2. HRMS (ESI$^+$): *m/z* calcd. for $C_{15}H_{20}NaO_4^+$ $[M + Na]^+$: 287.1259, found 287.1255; Anal. calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63, found: C, 68.10; H, 7.67.

Ethyl (2-Cyclopropanecarbonyloxy)phenylacetate (2k). The title compound **2k** (1.32 g, 96%) was obtained from **1** (1.00 g, 5.55 mmol) and cyclopropanecarboxylic acid (0.501 g, 5.82 mmol) as a colorless oil using a procedure analogous to that described for the preparation of **2a**: ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.19 (td, *J* = 7.6, 1.1 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.56 (s, 2H), 1.89–1.80 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.21–1.16 (m, 2H), 1.06–1.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 170.8, 149.2, 131.3, 128.5, 126.7, 126.1, 122.5, 61.0, 36.5, 14.2, 13.0, 9.2. HRMS (ESI^+): *m/z* calcd. for $C_{14}H_{16}NaO_4^+$ $[M + Na]^+$: 271.0946, found 271.0943; Anal. calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50, found: C, 67.73; H, 6.54.

Ethyl (2-Cyclohexanecarbonyloxy)phenylacetate (2l). The title compound **2l** (1.52 g, 94%) was obtained from **1** (1.00 g, 5.55 mmol) and cyclohexanecarboxylic acid (0.745 g, 5.61 mmol) as a colorless oil using a procedure analogous to that described for the preparation of **2a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.23–7.16 (m, 1H), 7.07 (d, *J* = 8.1 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.54 (s, 2H), 2.57 (tt, *J* = 11.3, 3.6 Hz, 1H), 2.09 (dd, *J* = 13.1, 2.6 Hz, 2H), 1.87–1.79 (m, 2H), 1.73–1.66 (m, 1H), 1.59 (qd, *J* = 12.3, 3.1 Hz, 2H), 1.42–1.26 (m, 3H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 170.8, 149.3, 131.3, 128.5, 126.7, 126.0, 122.5, 61.0, 43.3, 36.4, 29.0, 25.8, 25.5, 14.2. HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{22}NaO_4^+$ $[M + Na]^+$: 313.1416, found 313.1413; Anal. calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64, found: C, 70.33; H, 7.65.

3-(Hydroxyl(phenyl)methylene)benzo[*b*]furan-2(3*H*)-one (3a). A solution of **2a** (1.00 g, 3.52 mmol) in anhydrous THF was cooled to -78 °C. A 1.0 M THF solution of *t*-BuOK (3.87 mL, 3.87 mmol) was added dropwise to this mixture. The reaction mixture was allowed to warm to 0 °C and stirred additionally for 1 h at the same temperature. The reaction mixture was quenched with 1 *N* aqueous HCl solution (5 mL) and diluted with dichloromethane. The aqueous layer was extracted with dichloromethane (10 mL x 3). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude residue was recrystallized with dichloromethane/*n*-hexane at -20 °C to give the product as a greenish yellow solid (0.731 g, 87%): mp 98-99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.44 (br s, 1H), 7.82 (d, *J* = 7.3 Hz, 2H), 7.65-7.55 (m, 3H), 7.25–7.15 (m, 3H),

7.00 (t, J = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 172.1, 150.7, 133.0, 132.4, 128.9, 128.4, 127.2, 123.9, 122.3, 120.0, 111.0, 97.9. HRMS (ESI^+): *m/z* calcd. for $C_{15}H_{10}NaO_3^+$ $[M + Na]^+$: 261.0528, found 261.0523; Anal. calcd. for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23, found: C, 75.63; H, 4.25.

3-(Hydroxyl(4-methoxyphenyl)methylene)benzo[*b*]furan-2(3*H*)-one (3b). The title compound **3b** (0.758 g, 89%) was obtained from **2b** (1.00 g, 3.18 mmol) as a greenish yellow solid using a procedure analogous to that described for the preparation of **3a**: mp 134-135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.50 (br s, 1H), 7.82 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 7.7 Hz, 1H), 7.24-7.16 (m, 2H), 7.08–7.00 (m, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 172.3, 163.0, 150.5, 130.5, 126.8, 125.2, 123.8, 122.7, 119.8, 114.3, 111.0, 96.9, 55.7. HRMS (ESI^+): *m/z* calcd. for $C_{16}H_{12}NaO_4^+$ $[M + Na]^+$: 291.0633, found 291.0631; Anal. calcd. for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51, found: C, 71.67; H, 4.46.

3-(Hydroxyl(3-methoxyphenyl)methylene)benzofuran-2(3*H*)-one (3c). The title compound **3c** (0.734 g, 86%) was obtained from **2c** (1.00 g, 3.18 mmol) as a greenish yellow solid using a procedure analogous to that described for the preparation of **3a**: mp 104-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.43 (br s, 1H), 7.48 (t, J = 7.9 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.32–7.13 (m, 5H), 7.01 (td, J = 7.8, 1.3 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 171.9, 159.9, 150.7, 134.1, 130.1, 127.2, 123.9, 122.2, 120.7, 120.2, 118.5, 113.2, 111.1, 98.0, 55.7. HRMS (ESI^+): *m/z* calcd. for $C_{16}H_{12}NaO_4^+$ $[M + Na]^+$: 291.0633, found 291.0628; Anal. calcd. for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51, found: C, 71.62; H, 4.53.

3-(Hydroxyl(2-methoxyphenyl)methylene)benzofuran-2(3*H*)-one (3d). The title compound **3d** (0.658 g, 77%) was obtained from **2d** (1.00 g, 3.18 mmol) as a greenish yellow solid using a procedure analogous to that described for the preparation of **3a**: mp 145-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.06 (br s, 1H), 7.57 (t, J = 7.9 Hz, 1H), 7.51 (d, J = 7.4 Hz, 1H), 7.14 (m, 4H), 6.95 (t, J = 7.2 Hz, 1H),

6.60 (d, J = 7.7 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 169.6, 157.0, 150.7, 133.1, 129.9, 126.8, 123.8, 122.7, 122.0, 121.0, 120.2, 111.7, 110.7, 99.9, 55.8. HRMS (ESI$^+$): *m/z* calcd. for $C_{16}H_{12}NaO_4^+$ $[M + Na]^+$: 291.0633, found 291.0629; Anal. calcd. for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51, found: C, 71.65; H, 4.51.

3-(3,4-Dimethoxyphenyl(hydroxyl)methylene)benzofuran-2(3*H*)-one (3e). The title compound **3e** (0.711 g, 82%) was obtained from **2e** (1.00 g, 2.90 mmol) as a greenish yellow solid using a procedure analogous to that described for the preparation of **3a**: mp 142-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.51 (br s, 1H), 7.50 (dd, J = 8.3, 1.8 Hz, 1H), 7.39–7.31 (m, 2H), 7.23–7.15 (m, 2H), 7.05–6.99 (m, 2H), 4.00 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 172.1, 152.6, 150.5, 149.1, 126.9, 125.2, 123.7, 122.6, 122.4, 119.9, 111.1, 110.9, 110.8, 96.9, 56.3, 56.2. HRMS (ESI$^+$): *m/z* calcd. for $C_{17}H_{14}NaO_5^+$ $[M + Na]^+$: 321.0739, found 321.0733; Anal. calcd. for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73, found: C, 68.44; H, 4.73.

3-(4-Fluorophenyl(hydroxyl)methylene)benzo[*b*]furan-2(3*H*)-one (3f). The title compound **3f** (0.798 g, 66%) was obtained from **2f** (1.44 g, 4.75 mmol) as a greenish yellow solid using a procedure analogous to that described for the preparation of **3a**: mp 122-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.42 (br s, 1H), 7.85 (dd, J = 8.4, 5.4 Hz, 2H), 7.30–7.16 (m, 5H), 7.02 (t, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 170.8, 165.0 (d, $^1J_{C\text{-}F}$ = 254.0 Hz) 150.7, 130.9 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 129.1 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 127.4, 124.0, 122.1, 119.8, 116.3 (d, $^2J_{C\text{-}F}$ = 22.1 Hz), 111.2, 97.9. HRMS (ESI$^+$): *m/z* calcd. for $C_{15}H_9FNaO_3^+$ $[M + Na]^+$: 279.0433, found 279.0429; Anal. calcd. for $C_{15}H_9FO_3$: C, 70.31; H, 3.54, found: C, 70.12; H, 3.59.

3-(4-Bromophenyl(hydroxyl)methylene)benzo[*b*]furan-2(3*H*)-one (3g). The title compound **3g** (0.740 g, 85%) was obtained from **2g** (1.00 g, 2.75 mmol) as a bright yellow solid using a procedure

analogous to that described for the preparation of **3a**: mp 149-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.38 (br s, 1H), 7.75–7.67 (m, 4H), 7.28–7.16 (m, 3H), 7.03 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 170.5, 150.8, 132.3, 131.8, 130.0, 127.6, 127.0, 124.0, 121.9, 119.9, 111.3, 98.3. HRMS (ESI$^+$): *m/z* calcd. for $C_{15}H_8BrNaO_3^+$ $[M - H + Na]^+$: 337.9555, found 337.9550; Anal. calcd. for $C_{15}H_9BrO_3$: C, 56.81; H, 2.86, found: C, 56.81; H, 2.86.

3-(Hydroxyl(2-naphthyl)methylene)benzo[*b*]furan-2(3*H*)-one (3h). The title compound **3h** (0.759 g, 88%) was obtained from **2h** (1.00 g, 2.99 mmol) as a greenish yellow solid using a procedure analogous to that described for the preparation of **3a**: mp 135-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.54 (s, 1H), 8.37 (s, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 2H), 7.85 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.69–7.59 (m, 2H), 7.27–7.19 (m, 3H), 7.02–6.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 172.1, 150.8, 135.1, 132.6, 130.2, 129.4, 129.0, 128.9, 128.5, 128.1, 127.3, 127.2, 124.5, 123.9, 122.4, 120.0, 111.1, 98.1. HRMS (ESI$^+$): *m/z* calcd. for $C_{19}H_{12}NaO_3^+$ $[M + Na]^+$: 311.0684, found 311.0678; Anal. calcd. for $C_{19}H_{12}O_3$: C, 79.16; H, 4.20, found: C, 79.17; H, 4.20.

3-(Hydroxyl((*E*)-4-methoxystyryl)methylene)benzo[*b*]furan-2(3*H*)-one (3i). The title compound **3i** (0.656 g, 76%) was obtained from **2i** (1.00 g, 2.94 mmol) as an orange solid using a procedure analogous to that described for the preparation of **3a**: mp 136-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.78 (s, 1H), 7.75 (d, *J* = 15.5 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.49–7.43 (m, 1H), 7.26-7.12 (m, 3H), 7.02 (d, *J* = 15.5 Hz, 1H), 6.94 (d, *J* = 8.6 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 167.1, 162.0, 150.7, 142.1, 130.3, 127.6, 126.4, 124.2, 123.0, 120.5, 115.2, 114.7, 111.1, 97.5, 55.6. HRMS (ESI$^+$): *m/z* calcd. for $C_{18}H_{14}NaO_4^+$ $[M + Na]^+$: 317.0790, found 317.0785; Anal. calcd. for $C_{18}H_{14}O_4$: C, 73.46; H, 4.80, found: C, 73.45; H, 4.81.

3-(Hydroxyl(isobutyl)methylene)benzo[*b*]furan-2(3*H*)-one (3j). The title compound **3j** (0.749 g,

91%) was obtained from **2j** (1.00 g, 3.78 mmol) as an off-white solid using a procedure analogous to that described for the preparation of **3a**: mp 68-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.06 (br s, 1H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.27-7.15 (m, 3H), 2.64 (d, *J* = 7.3 Hz, 2H), 2.26 (sep, *J* = 6.8 Hz, 1H), 1.11-1.05 (overlapped s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 173.6, 150.5, 126.5, 124.2, 122.8, 120.1, 111.1, 98.4, 42.6, 27.1, 22.7. HRMS (ESI^+): *m/z* calcd. for $C_{13}H_{14}NaO_3^+$ $[M + Na]^+$: 241.0841, found 241.0834; Anal. calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47, found: C, 71.55; H, 6.48.

3-(Cyclopropyl(hydroxyl)methylene)benzo[*b*]furan-2(3*H*)-one (3k). The title compound **3l** (0.716 g, 88%) was obtained from **2l** (1.00 g, 4.03 mmol) as a white solid using a procedure analogous to that described for the preparation of **3a**: mp 101-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.13 (s, 1H), 7.50–7.43 (m, 1H), 7.25–7.12 (m, 3H), 2.27–2.19 (m, 1H), 1.48–1.40 (m, 2H), 1.26–1.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.2, 173.4, 150.3, 126.0, 124.0, 123.3, 119.5, 111.0, 97.2, 14.5, 10.5. HRMS (ESI^+): *m/z* calcd. for $C_{12}H_9NaO_3^+$ $[M - H + Na]^+$: 224.0449, found 224.0447; Anal. calcd. for $C_{12}H_{10}O_3$: C, 71.28; H, 4.98, found: C, 71.28; H, 4.98.

3-(Cyclohexyl(hydroxyl)methylene)benzo[*b*]furan-2(3*H*)-one (3l). The title compound **3k** (0.732 g, 87%) was obtained from **2k** (1.00 g, 3.44 mmol) as a white solid using a procedure analogous to that described for the preparation of **3a**: mp 100-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.13 (br s, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.25–7.13 (m, 3H), 2.88 (t, *J* = 11.8 Hz, 1H), 1.90 (d, *J* = 11.0 Hz, 4H), 1.78 (d, *J* = 12.4 Hz, 1H), 1.70–1.60 (m, 2H), 1.47–1.25 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.3, 174.0, 150.4, 126.3, 124.2, 122.7, 120.1, 111.1, 96.4, 42.6, 28.6, 26.0, 25.7. HRMS (ESI^+): *m/z* calcd. for $C_{15}H_{16}NaO_3^+$ $[M + Na]^+$: 267.0997, found 267.0992; Anal. calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60, found: C, 73.74; H, 6.62.

Methyl 2-Phenylbenzo[*b*]furan-3-carboxylate (6a). 3a (0.500 g, 2.10 mmol) was suspended in

anhydrous methanol (20 mL) and concentrated sulfuric acid (*ca.* 2 mL) was added carefully to this mixture. The reaction mixture was heated under reflux for 6 h. The reaction mixture was cooled and concentrated under reduced pressure. The resulting residue was diluted with dichloromethane (20 mL) and washed with saturated aqueous sodium bicarbonate solution (20 mL x 3). The organic layer was dried under anhydrous $MgSO_4$ and concentrated *in vacuo*. The resulting residue was recrystallized from *n*-hexane to give **6a** (0.478 g, 90%) as a white solid: mp 79-80 °C (lit. mp[4c,4e] = 77–78 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08–7.99 (m, 3H), 7.59–7.50 (m, 4H), 7.43–7.36 (m, 2H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 160.9, 153.8, 130.3, 129.6, 129.5, 128.2, 127.0, 125.3, 124.1, 122.7, 111.2, 108.8, 51.7. HRMS (ESI^+): *m/z* calcd. for $C_{16}H_{12}NaO_3^+$ $[M + Na]^+$: 275.0684, found 275.0679; Anal. calcd. for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79, found: C, 76.15; H, 4.82. All spectral data are consistent with previously reported values.[4c,4e]

Methyl 2-(4-Methoxyphenyl)benzo[*b*]furan-3-carboxylate (6b). The title compound **6b** (0.484 g. 92%) was obtained from **3b** (0.500 g, 1.86 mmol) as a white solid using a procedure analogous to that described for the preparation of **6a**: mp 80-81 °C. (lit. mp[12] = 78–79 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.00 (m, 3H), 7.54–7.49 (m, 1H), 7.37–7.32 (m, 2H), 7.02 (d, J = 8.9 Hz, 2H), 3.95 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 161.3, 161.3, 153.6, 131.3, 127.3, 125.0, 124.0, 122.7, 122.1, 113.7, 111.1, 107.6, 55.5, 51.7. HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{14}NaO_4^+$ $[M + Na]^+$: 305.0790, found 305.0782; Anal. calcd. for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00, found: C, 72.40; H, 5.03. All spectral data are consistent with previously reported values.[4c,12]

Methyl 2-(3-Methoxyphenyl)benzo[*b*]furan-3-carboxylate (6c). The title compound **6c** (0.479 g, 91%) was obtained from **3c** (0.500 g, 1.86 mmol) as a white solid using a procedure analogous to that described for the preparation of **6a**: mp 79-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–8.03 (m, 1H), 7.69–7.62 (m, 2H), 7.57–7.51 (m, 1H), 7.45–7.34 (m, 3H), 7.08–7.02 (m, 1H), 3.96 (s, 3H), 3.90 (s,

3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 160.5, 159.3, 153.7, 130.8, 129.3, 127.1, 125.4, 124.1, 122.8, 122.0, 116.5, 114.6, 111.2, 109.0, 55.5, 51.8. HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{14}NaO_4^+$ $[M + Na]^+$: 305.0790, found 305.0785; Anal. calcd. for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00, found: C, 72.36; H, 5.02.

Methyl 2-(2-Methoxyphenyl)benzo[*b*]furan-3-carboxylate (6d). The title compound **6d** (0.473 g, 90%) was obtained from **3d** (0.500 g, 1.86 mmol) as a colorless film using a procedure analogous to that described for the preparation of **6a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.03 (m, 1H), 7.62–7.52 (m, 2H), 7.48 (td, *J* = 8.4, 1.6 Hz, 1H), 7.39–7.34 (m, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 3.85–3.82 (overlapped s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 158.2, 157.7, 154.3, 131.8, 131.4, 126.7, 125.0, 123.9, 122.1, 120.4, 119.4, 111.3, 111.2, 111.1, 55.7, 51.6. HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{14}NaO_4^+$ $[M + Na]^+$: 305.0790, found 305.0784; Anal. calcd. For $C_{17}H_{14}O_4$: C, 72.33; H, 5.00, found: C, 72.37; H, 5.04. All spectral data are consistent with previously reported values.[13]

Methyl 2-(3,4-Dimethoxyphenyl)benzo[*b*]furan-3-carboxylate (6e). The title compound **6e** (0.498 g, 92%) was obtained from **3e** (0.500 g, 1.73 mmol) as a white solid using a procedure analogous to that described for the preparation of **6a**: mp 89-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–8.01 (m, 1H), 7.77–7.72 (m, 2H), 7.54–7.49 (m, 1H), 7.36–7.31 (m, 2H), 6.99–6.95 (m, 1H), 3.99 (s, 3H), 3.95 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 160.9, 153.5, 150.9, 148.4, 127.3, 125.1, 124.0, 123.1, 122.7, 122.1, 112.4, 111.0, 110.6, 107.8, 56.1, 56.1, 51.7. HRMS (ESI^+): *m/z* calcd. for $C_{18}H_{16}NaO_5^+$ $[M + Na]^+$: 335.0895, found 335.0889; Anal. calcd. For $C_{18}H_{16}O_5$: C, 69.22; H, 5.16, found: C, 69.26; H, 5.16.

Methyl 2-(4-Fluorophenyl)benzo[*b*]furan-3-carboxylate (6f). The title compound **6f** (0.475 g, 90%) was obtained from **3f** (0.500 g, 1.95 mmol) as a white solid using a procedure analogous to that described for the preparation of **6a**: mp 92-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–8.03 (m, 3H), 7.56–7.50 (m, 1H), 7.40–7.33 (m, 2H), 7.19 (t, *J* = 8.7 Hz, 2H), 3.96 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 164.6, 164.0 (d, *J* = 251.5 Hz), 160.0, 153.8, 131.8 (d, *J* = 8.6 Hz), 127.0, 125.8 (d, *J* = 3.4 Hz), 125.5, 124.2, 122.9, 115.4 (d, *J* = 21.8 Hz), 111.2, 108.7, 51.8. HRMS (ESI^+): *m/z* calcd. for $C_{16}H_{11}FNaO_3^+$ $[M + Na]^+$: 293.0590, found 293.0584; Anal. calcd. for $C_{16}H_{11}FO_3$: C, 71.11; H, 4.10, found: C, 71.18; H, 4.13.

Methyl 2-(4-Bromophenyl)benzo[*b*]furan-3-carboxylate (6g). The title compound **6g** (0.481 g, 91%) was obtained from **3g** (0.500 g, 1.58 mmol) as a white solid using a procedure analogous to that described for the preparation of **6a**: mp 101-102 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08–8.02 (m, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.56–7.51 (m, 1H), 7.41–7.34 (m, 2H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 159.7, 153.8, 131.5, 131.1, 128.5, 127.0, 125.7, 125.0, 124.3, 122.9, 111.3, 109.3, 51.9. HRMS (ESI^+): *m/z* calcd. for $C_{16}H_{11}BrNaO_3^+$ $[M + Na]^+$: 352.9789, found 352.9783; Anal. calcd. for $C_{16}H_{11}BrO_3$: C, 58.03; H, 3.35, found: C, 58.01; H, 3.35.

Methyl 2-(2-Naphthyl)benzo[*b*]furan-3-carboxylate (6h). The title compound **6h** (0.456 g, 87%) was obtained from **3h** (0.500 g, mmol) as a white solid using a procedure analogous to that described for the preparation of **6a**: mp 95-96 °C (lit. mp[4c] = 83–84 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.12–8.07 (m, 2H), 8.00–7.88 (m, 3H), 7.61–7.53 (m, 3H), 7.42–7.36 (m, 2H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 160.9, 154.0, 134.1, 132.9, 130.0, 129.1, 127.8, 127.8, 127.6, 127.3, 127.0, 126.6, 126.2, 125.5, 124.2, 122.8, 111.3, 109.1, 51.8. HRMS (ESI^+): *m/z* calcd. for $C_{20}H_{14}NaO_3^+$ $[M + Na]^+$: 325.0841, found 325.0835; Anal. calcd. for $C_{20}H_{14}O_3$: C, 79.46; H, 4.67, found: C, 79.45; H, 4.64. All spectral data are consistent with previously reported values.[4c]

Methyl (*E*)-2-(4-Methoxystyryl)benzo[*b*]furan-3-carboxylate (6i). The title compound **6i** (0.465 g, 89%) was obtained from **3i** (0.500 g, 1.70 mmol) as a greenish yellow solid using a procedure analogous to that described for the preparation of **6a** and a longer reaction time (24 h): mp 90-91 °C; ^1H NMR

(400 MHz, $CDCl_3$) δ 8.03-7.94 (m, 1H), 7.77 (d, *J* = 16.3 Hz, 1H), 7.60–7.53 (m, 3H), 7.50–7.44 (m, 1H), 7.35–7.28 (m, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 4.00 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 160.7, 160.5, 153.9, 135.5, 129.2, 128.9, 126.8, 125.4, 124.0, 122.3, 114.4, 113.4, 110.8, 108.0, 55.5, 51.7. HRMS (ESI^+): *m/z* calcd. for $C_{19}H_{16}NaO_4^+$ $[M + Na]^+$: 331.0946, found 331.0941; Anal. calcd. for $C_{19}H_{16}O_4$: C, 74.01; H, 5.23, found: C, 74.04; H, 5.16.

Methyl 2-Isobutylbenzo[*b*]furan-3-carboxylate (6j). The title compound **6j** (0.453 g, 85%) was obtained from **3j** (0.500 g, 2.29 mmol) as a colorless oil using a procedure analogous to that described for the preparation of **6a** and a longer reaction time (12 h): ^1H NMR (400 MHz, $CDCl_3$) δ 8.02–7.93 (m, 1H), 7.47–7.40 (m, 1H), 7.32–7.23 (m, 2H), 3.94 (s, 3H), 3.08 (d, *J* = 7.3 Hz, 2H), 2.23 (sep, *J* = 6.8 Hz, 1H), 1.00 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 165.0, 153.7, 126.1, 124.4, 123.8, 122.0, 110.9, 109.2, 51.4, 36.8, 28.4, 22.6. HRMS (ESI^+): *m/z* calcd. for $C_{14}H_{16}NaO_3^+$ $[M + Na]^+$: 255.0997, found 255.0992; Anal. calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94, found: C, 72.35; H, 6.99.

Methyl 2-Cyclopropylbenzo[*b*]furan-3-carboxylate (6k). The title compound **6k** (0.464 g, 87%) was obtained from **3k** (0.500 g, 2.47 mmol) as a white solid using a procedure analogous to that described for the preparation of **6a** and a longer reaction time (12 h): mp 61-62 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95–7.90 (m, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.30–7.20 (m, 2H), 3.96 (s, 3H), 3.10–3.02 (m, 1H), 1.31–1.26 (m, 2H), 1.20–1.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 165.5, 152.8, 126.7, 124.1, 123.8, 121.4, 110.7, 108.3, 51.5, 9.8, 9.7. HRMS (ESI^+): *m/z* calcd. for $C_{13}H_{12}NaO_3^+$ $[M + Na]^+$: 239.0684, found 239.0679; Anal. calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59, found: C, 72.24; H, 5.57.

Methyl 2-Cyclohexylbenzo[*b*]furan-3-carboxylate (6l). The title compound **6l** (0.467 g, 88%) was obtained from **3l** (0.500 g, 2.05 mmol) as a white solid using a procedure analogous to that described for the preparation of **6a** and a longer reaction time (12 h): mp 57-58 °C; ^1H NMR (400 MHz, $CDCl_3$) δ

8.00–7.93 (m, 1H), 7.49–7.42 (m, 1H), 7.33–7.26 (m, 2H), 3.96 (s, 3H), 3.71 (tt, J = 12.0, 3.4 Hz, 1H), 1.97–1.84 (m, 4H), 1.82–1.67 (m, 3H), 1.51–1.26 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 165.1, 153.6, 126.2, 124.3, 123.8, 122.0, 111.1, 107.1, 51.5, 37.4, 30.8, 26.3, 26.0. HRMS (ESI^+): *m/z* calcd. for $C_{16}H_{18}NaO_3^+$ $[M + Na]^+$: 281.1154, found 281.1149; Anal. calcd. for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02, found: C, 74.44; H, 7.11.

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ASSOCIATED CONTENT

SUPPORTING INFORMATION.

^{1}H and ^{13}C NMR spectra of compounds and crystallography data (.cif) of product **3h** (CCDC 1057072). 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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