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Regiospecific synthesis of arenofurans via cascade reactions of arenols with Morita–Baylis–Hillman acetates of nitroalkenes and total synthesis of isoparvifuran

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ABSTRACT

A cascade process involving an S_N2' reaction and an intramolecular oxa-Michael addition has been developed by treating Morita–Baylis–Hillman acetates of nitroalkenes with arenols, such as β-naphthols, α-naphthols, and substituted phenols under basic conditions. The products, arenofurans, are formed as single regioisomers in good to excellent yield in most cases. The methodology has been successfully employed for the total synthesis of an anti fungal agent isoparvifuran.

1. Introduction

Furan is a prominent heterocycle in synthesis and in the biological domain.[1] Functionalized and fused furans exhibit a multitude of biological activities.[2] Besides the well-established methods, such as Paal–Knorr synthesis[3] and Feist–Benary synthesis,[4] many transition metal-mediated strategies[5] for the synthesis of furans have appeared in the recent literature. Furans fused to other aromatic rings, in particular, are part of numerous natural products and play a pivotal role in medicinal chemistry.[1,2] Arenofurans have also been employed as fluorescent probes and photosensitizers.[6] Classical methods for the synthesis of fused furans, particularly arenofurans, such as Garst–Spencer annulation of cycloalkanones,[7] Moore–Danheiser rearrangement of cyclobutenones,[8] Nickl–Casiraghi annulation of Li phenolates with allyl halide,[9] Perkin rearrangement of coumarins[10] and Rapp–Stoermer annulation of salicyl aldehydes with α-haloketones[11] found only limited applicability.[12] Many of the recent miscellaneous methods,[13,14] including metal-mediated ones,[13] are much more efficient, but are too substrate specific and often require multistep reaction sequences.

Recently, we have reported the possible application of acetates of Morita–Baylis–Hillman adducts of nitroalkenes **6**[15] as bielectrophiles in the formation of furans **3**, pyrans **4**, and imidazopyridines **1** (Scheme 1).[16] Chen et al. have also reported transformation of **6** to **3** and **4** as well as to cyclopentene derivatives **8**.[17] The strategy involves a cascade Michael-S_N2'-intramolecular Michael sequence that took place under simple and mild conditions. We envisaged that reaction of MBH acetate **6** with phenol **9** in a similar fashion would lead to synthetically and biologically useful highly substituted benzofurans **10**–**12** in a regioselective manner.[18]

2. Results and discussion

At the outset, acetate **6a** was treated with β-naphthol **9a** in the presence of various amine bases (Table 1, entries 1–7). The reactions carried out using DABCO as base in THF, DCM, and toluene and other amine bases, such as DBU, Et_3N, and imidazole in toluene provided the product **10a** only in low yield (entries 1–6). However, diisopropylamine did improve the yield to afford naphthofuran **10a** in 78% yield (entry 7). In principle, amine bases, such as DBU (pKa 12.0), Et_3N, and diisopropylamine (pK_a ~11.0) should be capable of providing the naphthoxide ion via deprotonation of **9a** (pK_a ~9.5) although imidazole (pK_a 7.0) and DABCO (pK_a 8.7), which are much weaker could be less effective. However, the nucleophilic amine bases are also likely to add to the MBH acetate **6a** in a Michael fashion leading to side reactions, the prospects of further improvement in the yield using amine bases appeared remote.

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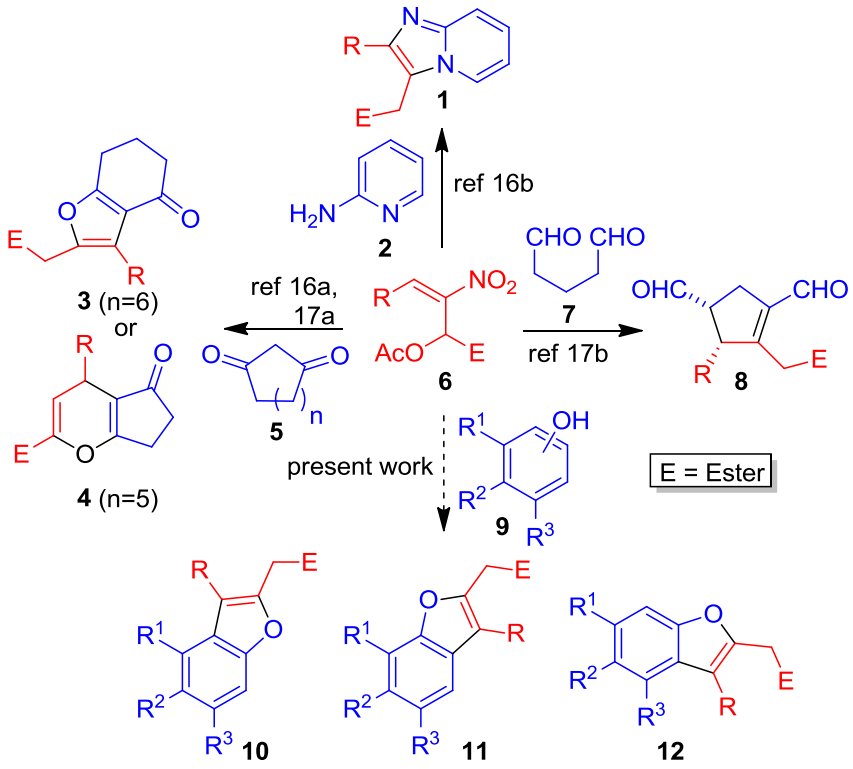
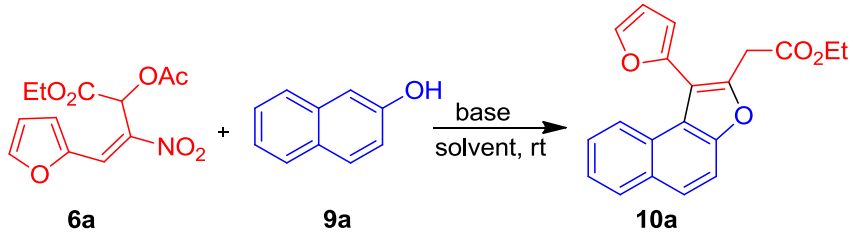


Scheme 1. Cascade reactions of MBH acetate **6**.

Table 1
Screening of bases[a]

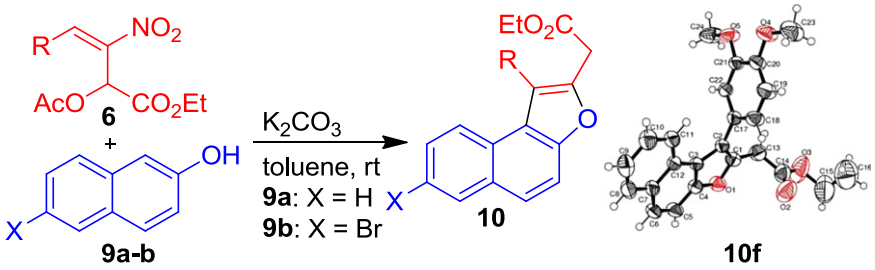


Entry	Base (equiv)	Solvent	Time (h)	% Yield[b]
1	DABCO (1.0)	THF	65	25[c]
2	DABCO (1.0)	DCM	50	35[c]
3	DABCO (1.0)	Toluene	45	35[c]
4	DBU (1.0)	Toluene	24	22[c]
5	Et_3N (1.0)	Toluene	48	41[c]
6	Imidazole (1.0)	Toluene	48	Trace[c]
7	$(i\text{-}Pr)_2NH$ (1.0)	Toluene	80	78
8	LiOH (1.0)	Toluene	96	69
9	K_2CO_3 (1.0)	Toluene	56	89
10	K_2CO_3 (1.5)	Toluene	50	89
11	**K_2CO_3** (2.0)	**Toluene**	**2**	**93**
12	Cs_2CO_3 (2.0)	Toluene	5	93
13	—	Toluene	48	-[d]

Bold entry indicates best condition.
[a] Reactions were carried out with 0.2 mmol of **9a** and 0.26 mmol (1.3 equiv) of **6a**.
[b] Isolated yield after silica gel column chromatography.
[c] Complete conversion of **6a** with considerable decomposition was observed in these cases.
[d] No reaction.

Therefore, we screened LiOH and other alkali metal carbonates (entries 8–12). While LiOH (pK_a 15.7) was less effective (69% yield, entry 8), a dramatic rise in the yield to 89% was observed when K_2CO_3 (pK_a 10.3) was employed (entry 9). This is attributable to the tight ion pair formed by Li^+ with the naphthoxide ion thus reducing its nucleophilicity. Although a marginal rate acceleration was observed with 1.5 equiv of K_2CO_3 with no change in the yield (entry 10), remarkable rate acceleration and further rise in the yield was observed with 2 equiv of K_2CO_3 (2 h, 93%, entry 11). However, a longer reaction time was required for getting comparable yields with 2 equiv of Cs_2CO_3 (5 h, 93%, entry 12). After confirming that base was necessary for the progress of the reaction (entry 13), we proceeded with screening other substrates for the synthesis of various arenofurans (Tables 2–4).

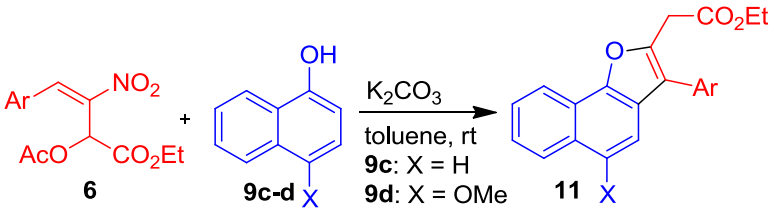
Table 2
Synthesis of naphthofurans **10** via addition of β-naphthols **9a**–**b** to MBH acetates **6**[a]



Entry	**6**, R	**9**	Time (h)	**10**	% Yield[b]
1	**6a**, 2-furyl	**9a**	2	**10a**	93
2	**6b**, 2-thienyl	**9a**	1	**10b**	98
3	**6c**, Ph	**9a**	2	**10c**	92
4	**6d**, 4-MePh	**9a**	1	**10d**	91
5	**6e**, 4-MeOPh	**9a**	7	**10e**	95
6	**6f**, 3,4-$(MeO)_2$Ph	**9a**	1	**10f**[c]	95
7	**6g**, 2,4-$(MeO)_2$Ph	**9a**	1.2	**10g**	87
8	**6h**, 4-ClPh	**9a**	2	**10h**	91
9	**6i**, 2-NO_2Ph	**9a**	3	**10i**	86
10	**6j**, 1-naphthyl	**9a**	1.5	**10j**	81
11	**6k**, PhCH=CH	**9a**	2	**10k**	83
12	**6a**, 2-furyl	**9b**	5	**10l**	94

[a] Reactions were carried out with 0.3 mmol of **9a**–**b**, 0.4 mmol of **6**, and 0.6 mmol of K_2CO_3.
[b] Isolated yield after silica gel column chromatography.
[c] Confirmed by X-ray analysis.

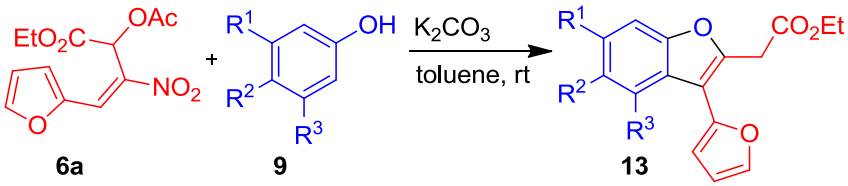
Table 3
Synthesis of naphthofurans **11** via addition of α-naphthol **9c**–**d** to MBH acetates **6**[a]



Entry	**6**, Ar	**9**	Time (h)	**11**	% Yield[b]
1	**6a**, 2-furyl	**9c**	4	**11a**	77
2	**6b**, 2-thienyl	**9c**	3.5	**11b**	90
3	**6c**, Ph	**9c**	5	**11c**	79
4	**6d**, 4-MePh	**9c**	4	**11d**	78
5	**6e**, 4-MeOPh	**9c**	4	**11e**	90
6	**6f**, 3,4-$(OMe)_2$Ph	**9c**	1	**11f**	97
7	**6a**, 2-furyl	**9d**	3	**11g**	65

[a] Reactions were carried out with 0.3 mmol of **9c**–**d**, 0.4 mmol of **6**, and 0.6 mmol of K_2CO_3.
[b] Isolated yield after silica gel column chromatography.

Table 4
Scope of phenols **9**[a]



Entry	**9**	R^1	R^2	R^3	Time (h)	**13**	% Yield[b]
1	**9e**	H	H	H	15	**13a**	22[c]
2	**9f**	OMe	OMe	H	9	**13b**	72
3	**9g**	OMe	OMe	OMe	10	**13c**	73
4	**9h**	$-OCH_2O-$		H	1.5	**13d**	82

[a] Reactions were carried out with 0.3 mmol of **9**, 0.4 mmol of **6a**, and 0.6 mmol of K_2CO_3.
[b] Isolated yield after silica gel column chromatography.
[c] Uncyclized oxa-Michael product **13a′** was isolated in 45% yield.

MBH acetates **6** in which R is heteroaryl, aryl, including fused aryl, and styrenyl, have been treated with β-naphthol **9a** under our optimized conditions (Table 2). No appreciable substituent effect on the rate of reaction or yield was observed in these cases. For instance, acetates **6a**–**b** with heteroaryl groups β to the nitro group afforded furans **10a**–**b** in excellent yield (93 and 98%, respectively, entries 1–2). Furans **10c**–**g** were also obtained in excellent yield (87–95%) from acetates **6c**–**g** with phenyl as well as weakly and strongly electron donating aryl groups (entries 3–7). Weakly and strongly deactivating substituents on the aromatic ring of acetates, e.g., **6h**–**i**, also did not have any adverse effect on the rate of reaction or yield of the products **10h**–**i** (91 and 86%, respectively, entries 8–9). While the yield was marginally lower in the case of a fused aromatic substituent on the acetate, e.g., **6j** (81%, entry 10), acetate **6k** with a styrenyl substituent furnished the product **10k** in excellent yield (83%, entry 11). A substituted β-naphthol **9b**, though required slightly longer duration, also reacted with acetate **6a** to furnish furan **10l** in 94% yield (entry 12).

The structure and regiochemistry of naphthofurans **10** were confirmed by detailed analysis of their spectral data. For instance, an AB quartet in the aromatic region (δ 7.60–7.80) with a *J* value of 8.8–9.1 Hz for the γ, δ protons in all the naphtho[2,1-*b*]furans **10** was indicative of the fusion of furan ring with the naphthalene in an angular fashion. This was further unambiguously established by single crystal X-ray analysis of a representative structure **10f** (see Table 1 and the Experimental section).

Having synthesized a variety of naphtho[2,1-*b*]furans **10** in excellent yield by treating acetates **6a**–**k** with β-naphthols **9a**–**b** (Table 2), we desired to investigate the reactivity of acetates **6** with α-naphthols **9c**–**d** under our optimized conditions in anticipation that the products would be regioisomeric to furans **10** (Table 3). Synthesis of regioisomers of naphthofurans, viz. naphtho[2,1-*b*]furans **10** and naphtho[1,2-*b*]furans **11**, from the same acetates **6** just by switching the commercially available naphthols appeared very attractive. Thus, when selected acetates **6a**–**f** were treated with α-naphthol **9c** under our optimized conditions, naphtho[1,2-*b*]furans **11** were formed in good to excellent yield (Table 3, entries 1–7). Unlike in the reaction of acetates **6** with β-naphthol **9a** where no appreciable effect of substituent on the aryl group was observed (Table 2), strongly electron donating aryl groups in the acetates **6** seemed to favor the formation of furans **11** in greater yield as compared to those with weak electron donating ability (Table 3). Thus the yields of furans **11a** and **11c**–**d** were in the range of 77–79% in the case of acetates **6a** and **6c**–**d**, respectively (entries 1 and 3–4). On the other hand, furans **11b** and **11e**–**f** were formed in 90–97% yield from their corresponding acetates **6b** and **6e**–**f** (entries 2 and 5–6). Reaction of **6a** with methoxynaphthol **9d** was also facile, though the yield of furan **11g** was relatively moderate (65%, entry 7).

Further scope of our methodology was demonstrated by treating a representative acetate **6a** with substituted phenols **9e**–**h** (Table 4). Interestingly, the major product in the reaction of the parent phenol **9e** with acetate **6a** was not the desired furan **13a**, but the oxa-Michael adduct **13a′**, which was formed in 45% yield (entry 1). This is attributable to the poor nucleophilicity of the *ortho*-carbon of phenoxide in the absence of electron donating substituents. On the other hand, phenols with strongly electron donating alkoxy groups **9f**–**h** reacted well with **6a** and delivered furans **13b**–**d** in good to excellent yields (72–82%, entries 2–4).

As for the structure and regiochemistry of naphthofurans **11** and **13**, while the possibility of regioisomers did not arise in naphtho[1,2-*b*]furans **11**, and benzofurans **13a** and **13c**, the regiochemistry of benzofurans **13b** and **13d**–**e** (**13e**: vide infra) is evident from appearance of two singlets in ^{1}H NMR in the range of δ 6.90–7.30.

The proposed mechanism taking phenol **9e** as the representative arenol is shown in Scheme 2. It involves deprotonation of phenol **9e** by K_2CO_3 followed conjugate addition of phenoxide via dearomatization to acetate **6** and concomitant S_N2' substitution of acetate to form intermediate **I**. Intramolecular oxa-Michael addition via rearomatization to the newly formed acrylic ester moiety in **I** in a 5-*exo*-*trig* fashion to form the dihydrofuran intermediate **II** followed by base mediated elimination of HNO_2 from **II** affords arenofuran **13**. The mass spectrometric analysis of the crude reaction mixture for **10b** (Table 2, entry 2) after 20 and 40 min confirmed the intermediacy of **I**/**II** with a characteristic peak appearing at *m*/*z* 383 (M^+), 406 (MNa^+), and 422 (MK^+).[19]

A practical application of our methodology for the first total synthesis of an antifungal agent isoparvifuran **17**, which is isolated from the heartwood of *Dalbergia parviflora*,[20] is outlined in Scheme 3. It begins with the MBH reaction of commercially available nitrostyrene **14** followed by acetylation of the resulting MBH alcohol to provide acetate **6c** in 84% yield. K_2CO_3 mediated addition of phenol **9i** to acetate **6c** under our optimized conditions afforded benzofuran **13e** in 76% yield. Alkaline hydrolysis of the ester group in **13e** proceeded smoothly to provide acid **15** in 93% yield, which was subjected to CaO/NaOH mediated decarboxylation in DMA under reflux conditions to give benzylated isoparvifuran **16** in 80% yield. Debenzylation by hydrogenolysis took place in quantitative yield to deliver the natural product isoparvifuran **17** in an overall yield of 47% for six steps.

3. Conclusions

The synthesis of naphtho[2,1-*b*]furans, naphtho[1,2-*b*]furans, and benzofurans has been carried out via a one-pot cascade process. The steps involved are a base mediated carba-Michael addition of arenols to the MBH acetates of nitroalkenes followed by substitution of acetate in an overall S_N2' reaction and then an intramolecular oxa-Michael addition.[21] The reaction is highly regiospecific in that β-naphthols react with MBH acetates to afford naphtho[2,1-*b*]furans whereas α-naphthols furnish naphtho[1,2-*b*]furans. A practical application of our methodology was demonstrated by synthesizing the antifungal agent isoparvifuran in six simple steps starting from commercially available nitrostyrene in an overall yield of 47%.

4. Experimental section

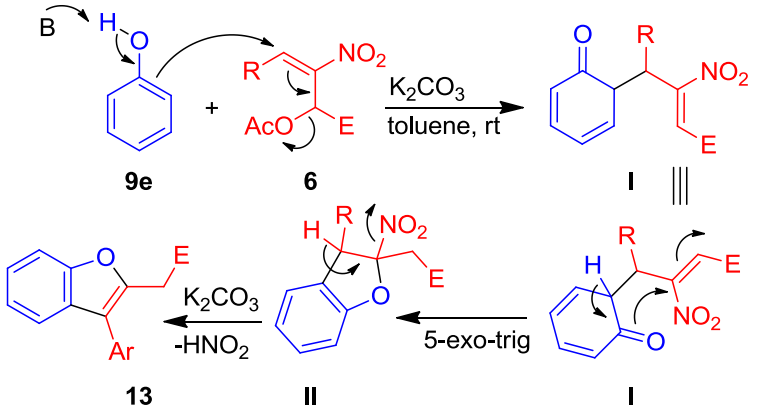
4.1. General

The melting points recorded are uncorrected. NMR spectra (^{1}H, ^{1}H decoupled ^{13}C) were recorded with TMS as the internal standard. The coupling constants (*J* values) are given in Hertz. High resolution mass spectra were recorded under ESI Q-TOF conditions. X-ray data were collected on a diffractometer equipped with graphite monochromated Mo Kα radiation. The structure was solved by direct methods shelxs97 and refined by full-matrix least squares against F^2 using shelxl97 software.

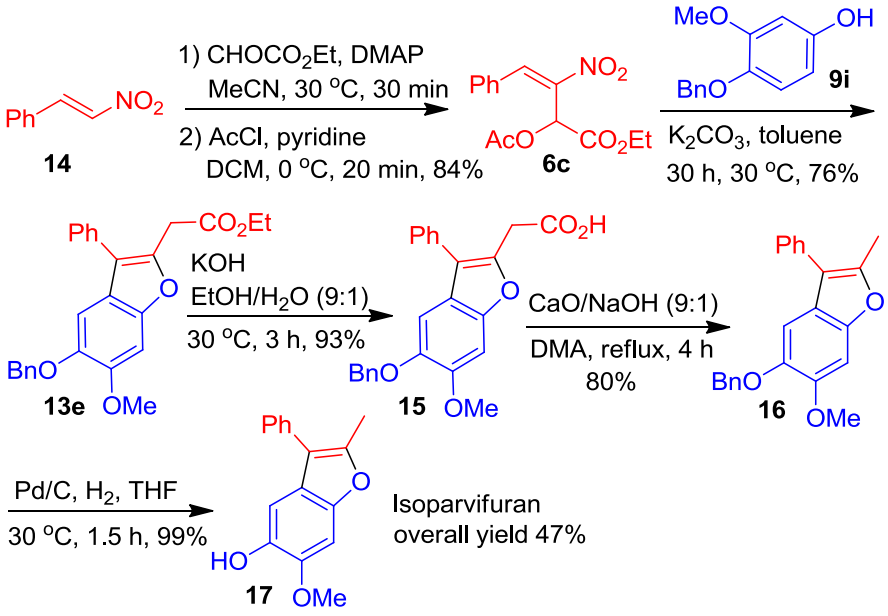
4.2. General procedure for the synthesis of arenofurans 10, 11, and 13

To a stirred solution of naphthol/phenol **9** (0.3 mmol) and K_2CO_3 (0.6 mmol, 2 equiv) in toluene (2 mL) was added MBH acetate **6** (0.4 mmol, 1.3 equiv) at room temperature. After completion of the reaction (monitored by TLC), the solvent was evaporated in vacuo and the crude residue was purified by silica gel column chromatography by gradient elution with ethyl acetate/petroleum ether (1:99 to 7:93).

*4.2.1. Ethyl 2-(1-(furan-2-yl)naphtho[2,1-b]furan-2-yl)acetate (**10a**).* Colorless liquid; yield 89 mg, 93%; R_f 0.60 (20% ethyl acetate/petroleum ether); ν_{max} (liquid film) 3020 (s), 2929 (w), 1736 (s), 1264 (m), 1217 (vs), 759 (vs) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.28 (t, *J* 7.1 Hz, 3H), 3.9 (s, 2H), 4.22 (q, *J* 7.1 Hz, 2H), 6.62–6.65 (m, 2H), 7.44–7.50 (m, 2H) 7.71 (d, *J* 1.0 Hz, 1H), 7.72 (ABq, *J* 8.9 Hz, 2H), 7.92–7.97 (m, 2H); δ_C



Scheme 2. Proposed mechanism for the formation of arenofurans **13**.



Scheme 3. Synthesis of isoparvifuran **17**.

(100 MHz, $CDCl_3$) 14.3, 33.7, 61.7, 111.1, 111.5, 112.1, 112.4, 121.9, 123.8, 124.7, 126.2, 126.5, 127.9, 129.0, 131.0, 143.2, 146.2, 149.2, 152.3, 169.1; MS (ESI) *m/z* (rel intensity) 321 (MH^+, 100), 248 (10), 247 (45); HRMS (ESI) *m/z* found 321.1121 for $C_{20}H_{17}O_4$ (MH^+), requires 321.1127.

*4.2.2. Ethyl 2-(1-(thiophen-2-yl)naphtho[2,1-b]furan-2-yl)acetate (**10b**).* Brown liquid; yield 99 mg, 98%; R_f 0.70 (20% ethyl acetate/petroleum ether); ν_{max} (liquid film) 3021 (s), 2985 (m), 2874 (m), 1729 (vs), 1374 (s), 1248 (vs), 1046 (s), 758 (s), 704 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.28 (t, *J* 7.1 Hz, 3H), 3.86 (s, 2H), 4.22 (q, *J* 7.1 Hz, 2H), 7.24–7.26 (m, 2H), 7.38–7.42 (m, 1H), 7.42–7.48 (m, 1H), 7.55 (d, *J* 4.8 Hz, 1H), 7.72 (ABq, *J* 8.9 Hz, 2H), 7.89–7.95 (m, 2H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.2, 61.6, 112.4, 114.4, 122.4, 123.1, 124.6, 125.9, 126.3, 127.3, 127.7, 128.0, 129.0, 129.2, 131.0, 133.3, 149.0, 151.9, 169.1; MS (ESI) *m/z* (rel intensity) 337 (MH^+, 100), 321 (30), 297 (5), 263 (18); HRMS (ESI) *m/z* found 337.0898 for $C_{20}H_{17}O_3S$ (MH^+), requires 337.0898.

*4.2.3. Ethyl 2-(1-phenylnaphtho[2,1-b]furan-2-yl)acetate (**10c**).* Colorless solid; yield 91 mg, 92%; mp 93–96 °C; R_f 0.73 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3021 (m), 2929 (w), 1736 (s), 1217 (s), 759 (vs), 704 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.26 (t, *J* 7.1 Hz, 3H), 3.77 (s, 2H), 4.19 (q, *J* 7.1 Hz, 2H), 7.26–7.33 (m, 1H), 7.36–7.42 (m, 1H), 7.48–7.56 (m, 5H), 7.71 (ABq, *J* 8.9 Hz, 2H), 7.76 (d, *J* 8.3 Hz, 1H), 7.92 (d, *J* 8.0 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.1, 61.5, 121.8, 122.1, 123.2, 124.4, 125.6, 126.0, 128.1, 128.2, 128.4, 128.9, 129.0, 130.6, 130.9, 133.4, 147.0, 152.0, 169.4; MS (ESI) *m/z* (rel intensity) 331 (MH^+, 100), 321 (50), 308 (8), 257 (17), 247 (8); HRMS (ESI) *m/z* found 331.1337 for $C_{22}H_{19}O_3$ (MH^+), requires 331.1334.

*4.2.4. Ethyl 2-(1-p-tolylnaphtho[2,1-b]furan-2-yl)acetate (**10d**).* Brown solid; yield 94 mg, 91%; mp 94–96 °C; R_f 0.63 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3020 (m), 2925 (w), 1735 (m), 1216 (s), 759 (vs), 669 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.26 (t, *J* 7.1 Hz, 3H), 2.49 (s, 3H), 3.76 (s, 2H), 4.18 (q, *J* 7.1 Hz, 2H), 7.28–7.34 (m, 3H), 7.38–7.44 (m, 3H), 7.69 (ABq, *J* 8.9 Hz, 2H), 7.80 (d, *J* 8.3 Hz, 1H), 7.92 (d, *J* 8.1 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 21.6, 33.2, 61.5, 112.5, 121.7, 122.2, 123.3, 124.3, 125.6, 126.0, 128.9, 129.0, 129.6, 130.2, 130.4, 130.9, 137.9, 147.0, 152.0, 169.5; MS (ESI) *m/z* (rel intensity) 345 (MH^+, 100), 343 (27), 271 (36), 215 (10), 214 (49); HRMS (ESI) *m/z* found 345.1494 for $C_{23}H_{21}O_3$ (MH^+), requires 345.1491.

*4.2.5. Ethyl 2-(1-(4-methoxyphenyl)naphtho[2,1-b]furan-2-yl)acetate (**10e**).* Colorless solid; yield 102 mg, 95%; mp 65–67 °C; R_f 0.70 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2979 (w), 2928 (w), 1738 (s), 1602 (w), 1511 (m), 1393 (w), 1286 (m), 1247 (s), 1178 (m),

1033 (m), 805 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.27 (t, *J* 7.0 Hz, 3H), 3.77 (s, 2H), 3.92 (s, 3H), 4.20 (q, *J* 7.0 Hz, 2H), 7.07 (d, *J* 8.6 Hz, 2H), 7.30–7.36 (m, 1H), 7.38–7.44 (m, 1H), 7.47 (d, *J* 8.6 Hz, 2H), 7.70 (ABq, *J* 8.8 Hz, 2H), 7.81 (d, *J* 8.0 Hz, 1H), 7.92 (d, *J* 7.8 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.2, 55.5, 61.5, 112.5, 114.3, 121.4, 122.3, 123.3, 124.3, 125.4, 125.6, 126.0, 128.3, 129.0, 130.9, 131.7, 147.0, 151.9, 159.6, 169.5; MS (ESI) *m*/*z* (rel intensity) 361 (MH^+, 100), 360 (M^+, 5), 297 (6), 287 (12); HRMS (ESI) *m*/*z* found 361.1447 for $C_{23}H_{21}O_4$ (MH^+), requires 361.1440.

*4.2.6. Ethyl 2-(1-(3,4-dimethoxyphenyl)naphtho[2,1-b]furan-2-yl) acetate (**10f**).* Colorless solid; yield 111 mg, 95%; mp 123–125 °C; R_f 0.4 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3021 (s), 1735 (s), 1250 (s), 1217 (s), 1098 (m), 758 (vs), 669 (w) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.26 (t, *J* 7.1 Hz, 3H), 3.77 (s, 2H), 3.86 (s, 3H), 3.98 (s, 3H), 4.18 (q, *J* 7.1 Hz, 2H), 7.06 (ABq, *J* 7.1 Hz, 2H, the lower half further split into d, *J* 1.6 Hz), 7.07–7.09 (d, *J* 1.6 Hz, 1H), 7.29–7.33 (m, 1H), 7.37–7.42 (m, 1H), 7.69 (ABq, *J* 8.9 Hz, 2H), 7.84 (d, *J* 8.3 Hz, 1H), 7.90 (d, *J* 8.0 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.2, 56.0, 61.5, 111.4, 112.5, 113.6, 121.6, 122.1, 122.8, 123.3, 124.4, 125.6, 126.0, 128.2, 129.0, 130.9, 147.0, 148.9, 149.0, 151.9, 169.5; MS (ESI) *m*/*z* (rel intensity) 391 (MH^+, 100), 385 (8), 317 (9), 79 (11); HRMS (ESI) *m*/*z* found 391.1541 for $C_{24}H_{23}O_5$ (MH^+), requires 391.1545; selected X-ray data (CCDC 930323): $C_{48}H_{44}O_{10}$, *M*=780.83, Monoclinic, space group *P*21/*n*, *a*=7.9520(4) Å, *b*=8.7362(4) Å, *c*=29.4465(16) Å, α=90°, β=96.652(5)°, γ=90°, *V*=2031.88(18) $Å^3$, D_c=1.276 Mg/m^3, *Z*=2, *F*(000)=824, λ=0.71073 Å, μ=0.089 mm^{-1}, total/unique reflections=23,711/6796 [*R*(int)=0.0365], *T*=150(2) K, θ range=3.13–32.50°, final *R* [$I>2\sigma(I)$]: *R*1=0.0777, *wR*2=0.2152, *R* (all data): *R*1=0.1312, *wR*2=0.2579.

*4.2.7. Ethyl 2-(1-(2,4-dimethoxyphenyl)naphtho[2,1-b]furan-2-yl) acetate (**10g**).* Colorless liquid; yield 102 mg, 87%; R_f 0.46 (20% ethyl acetate/petroleum ether); ν_{max} (liquid film) 2936 (w), 1738 (vs), 1603 (vs), 1579 (s), 1507 (m), 1464 (m), 1304 (m), 1209 (s), 1158 (m), 1031 (s), 805 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.25 (t, *J* 7.1 Hz, 3H), 3.66 (s, 3H), 3.82 (ABq, *J* 16.6 Hz, 2H), 3.92 (s, 3H), 4.17, 4.18 (two overlapped q, *J* 7.1 Hz, 2H), 6.62–6.65 (m, 2H), 7.28–7.40 (m, 3H), 7.68 (ABq, *J* 9.1 Hz, 3H), 7.89 (d, *J* 8.1 Hz, 1H); benzylic CH_2 appears as ABq presumably due to atropisomerism; δ_C (100 MHz, $CDCl_3$) 14.3, 33.3, 55.6, 61.4, 99.1, 104.6, 112.6, 114.4, 117.5, 122.8, 123.2, 124.1, 125.2, 125.8, 128.6, 128.7, 130.8, 132.8, 147.2, 152.0, 159.0, 161.4, 169.6; MS (ESI) *m*/*z* (rel intensity) 391 (MH^+, 100), 317 (12), 252 (15), 73 (19); HRMS (ESI) *m*/*z* found 391.1549 for $C_{24}H_{23}O_5$ (MH^+), requires 391.1545.

*4.2.8. Ethyl 2-(1-(4-chlorophenyl)naphtho[2,1-b]furan-2-yl)acetate (**10h**).* Colorless solid; yield 99 mg, 91%; mp 73–75 °C; R_f 0.63 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3054 (w), 2984 (w), 1738 (s), 1491 (w), 1393 (w), 1265 (m), 807 (m), 740 (s), 704 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.27 (t, *J* 7.1 Hz, 3H), 3.75 (s, 2H), 4.19 (q, *J* 7.1 Hz, 2H), 7.32–7.36 (m, 1H), 7.40–7.44 (m, 1H), 7.48–7.53 (m, 4H), 7.71 (ABq, *J* 8.9 Hz, 4H), 7.73 (d, *J* 7.9 Hz, 1H), 7.93 (d, *J* 8.0 Hz, 1 Hz); δ_C (100 MHz, $CDCl_3$) 14.3, 33.1, 61.6, 112.5, 120.7, 121.8, 123.1, 124.5, 125.9, 126.2, 128.1, 129.1, 129.2, 130.9, 131.9, 132.0, 134.3, 147.1, 152.1, 169.3; MS (ESI) *m*/*z* (rel intensity) 365 (MH^+, 100), 345 (60), 321 (6), 297 (9), 291 (12), 271 (8); HRMS (ESI) *m*/*z* found 365.0953 for $C_{22}H_{18}O_3Cl$ (MH^+), requires 365.0944.

*4.2.9. Ethyl 2-(1-(2-nitrophenyl)naphtho[2,1-b]furan-2-yl)acetate (**10i**).* Brown solid; yield 97 mg, 86%; mp 105–107 °C; R_f 0.43 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3055 (w), 2986 (w), 2927 (w), 1736 (m), 1530 (m), 1351 (w), 1266 (s), 1028 (w), 740 (s) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.22 (t, *J* 7.1 Hz, 3H), 3.69 (ABq, *J* 16.4 Hz, 2H), 4.10–4.18 (m, 2H), 7.25–7.31 (m, 2H), 7.39 (ddd, *J* 8.1, 6.2, 1.9 Hz, 1H), 7.62 (dd, *J* 7.4, 1.5 Hz, 1H), 7.68–7.73 (m, 1H), 7.72 (ABq, *J* 8.9 Hz, 2H), 7.76–7.79 (m, 1H), 7.92 (d, *J* 8.0 Hz, 1H), 8.19 (dd, *J* 8.0, 1.3 Hz, 1H); Benzylic CH_2 appears as ABq presumably due to atropisomerism; δ_C (100 MHz, $CDCl_3$) 14.2, 33.3, 61.7, 112.5, 117.0, 122.3, 122.6, 124.5, 125.0, 126.0, 126.4, 127.9, 128.2, 129.1, 129.9, 130.9, 133.4, 133.7, 146.9, 150.0, 152.0, 168.7; MS (ESI) *m*/*z* (rel intensity) 398 (MNa^+, 100), 376 (MH^+, 85), 302 (35), 263 (15), 262 (79); HRMS (ESI) *m*/*z* found 376.1189 for $C_{22}H_{18}NO_5$ (MH^+), requires 376.1185.

*4.2.10. Ethyl 2-(1-(naphthalen-1-yl)naphtho[2,1-b]furan-2-yl)acetate (**10j**).* Light yellow solid; yield 92 mg, 81%; mp 80–82 °C; R_f 0.60 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3057 (w), 1739 (vs), 1623 (w), 1384 (w), 1265 (m), 1190 (s), 1156 (m), 1029 (m), 804 (s), 780 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.16 (t, *J* 7.1 Hz, 3H), 3.69 (ABq, *J* 16.6 Hz, 2H), 4.09 (two overlapped q, *J* 7.1 Hz, 2H), 7.02–7.07 (m, 1H), 7.11 (d, *J* 8.4 Hz, 1H), 7.29–7.33 (m, 2H), 7.48–7.54 (m, 1H), 7.59–7.64 (m, 2H), 7.66–7.68 (m, 1H), 7.76 (ABq, *J* 9.1 Hz, 2H), 7.89 (d, *J* 8.1 Hz, 1H), 7.97 (d, *J* 8.2 Hz, 1H), 8.01–8.04 (m, 1H); δ_C (100 MHz, $CDCl_3$) 14.2, 33.3, 61.5, 112.6, 119.5, 123.2, 123.3, 124.4, 125.8, 125.9, 126.2, 126.3, 126.4, 126.7, 128.1, 128.5, 128.7, 128.8, 129.0, 130.8, 130.9, 133.1, 133.9, 147.8, 152.2, 169.3; MS (ESI) *m*/*z* (rel intensity) 381 (MH^+, 100), 380 (M^+, 5), 307 (14), 253 (5); HRMS (ESI) *m*/*z* found 381.1497 for $C_{26}H_{21}O_3$ (MH^+), requires 381.1491.

*4.2.11. (E)-Ethyl 2-(1-styrylnaphtho[2,1-b]furan-2-yl)acetate (**10k**).* Colorless solid; yield 88 mg, 83%; mp 103–105 °C; R_f 0.56 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3020 (m), 2959 (m), 2929 (m), 1735 (s), 1265 (s), 1217 (s), 759 (vs) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.32 (t, *J* 7.1 Hz, 3H), 4.00 (s, 2H), 4.26 (q, *J* 7.1 Hz, 2H), 6.97 (d, *J* 16.1 Hz, 1H), 7.34–7.38 (m, 1H), 7.43–7.58 (m, 4H), 7.54 (d, *J* 16.1 Hz, 1H), 7.61–7.63 (m, 2H), 7.69 (ABq, *J* 8.9 Hz, 2H), 7.95 (d, *J* 7.8 Hz, 1H), 8.37 (d, *J* 8.3 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.4, 33.8, 61.7, 112.5, 119.6, 119.8, 122.0, 123.7, 124.5, 125.8, 126.5, 126.8, 128.2, 128.6, 129.0, 129.1, 131.0, 134.4, 137.2, 146.6, 152.0, 169.5; MS (ESI) *m*/*z* (rel intensity) 357 (MH^+, 100), 283 (22), 279 (11), 167 (8), 149 (8); HRMS (ESI) *m*/*z* found 357.1496 for $C_{24}H_{21}O_3$ (MH^+), requires 357.1491.

*4.2.12. Ethyl 2-(7-bromo-1-(furan-2-yl)naphtho[2,1-b]furan-2-yl) acetate (**10l**).* Yellow solid; yield 112 mg, 94%; mp 79–81 °C; R_f 0.63 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3020 (s), 2928 (w), 2854 (w), 1734 (s), 1504 (w), 1422 (w), 1216 (vs), 1021 (m), 929 (w), 759 (vs) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.27 (t, *J* 7.1 Hz, 3H), 3.90 (s, 2H), 4.21 (q, *J* 7.1 Hz, 2H), 6.61–6.63 (m, 2H), 7.05 (dd, *J* 8.8, 2.0 Hz, 1H), 7.64 (ABq, *J* 9.0 Hz, 2H), 7.69 (dd, *J* 1.7, 1.0 Hz, 1H), 7.80 (d, *J* 8.8 Hz, 1H), 8.05 (d, *J* 2.0 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.7, 61.8, 111.2, 111.6, 112.0, 113.4, 118.4, 122.0, 125.2, 125.6, 126.3, 129.7, 130.9, 132.3, 143.3, 145.7, 149.7, 152.2, 168.9; MS (ESI) *m*/*z* (rel intensity) 401 ($[MH+2]^+$, 100), 399 (MH^+, 98), 391 (95), 326 (22), 317 (40); HRMS (ESI) *m*/*z* found 399.0220 for $C_{20}H_{16}BrO_4$ (MH^+), requires 399.0232.

*4.2.13. Ethyl 2-(3-(furan-2-yl)naphtho[1,2-b]furan-2-yl)acetate (**11a**).* Colorless solid; yield 74 mg, 77%; mp 60–63 °C; R_f 0.70 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2917 (w), 2852 (w), 1736 (vs), 1645 (w), 1461 (w), 1381 (m), 1265 (m), 1178 (m), 1029 (m), 810 (m), 748 (s) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.28 (t, *J* 7.0 Hz, 3H), 4.23 (s, 2H), 4.25 (q, *J* 7.0 Hz, 2H), 6.58 (d, *J* 1.5 Hz, 1H), 6.72 (d, *J* 3.1 Hz, 1H), 7.49–7.55 (m, 1H), 7.58–7.62 (m, 2H), 7.72 (d, *J* 8.8 Hz, 1H), 7.92 (d, *J* 8.8 Hz, 2H), 7.95 (d, *J* 9.6 Hz, 1H), 8.33 (d, *J* 8.2 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 34.6, 61.6, 107.3, 111.4, 111.8, 119.1, 120.3, 121.2, 121.8, 123.9, 125.5, 126.5, 128.4, 131.6, 142.0, 146.3, 147.6, 150.0, 169.3; MS (ESI) *m*/*z* (rel intensity) 321 (MH^+, 100), 247 (11), 208 (6), 158 (5); HRMS (ESI) *m*/*z* found 321.1139 for $C_{20}H_{16}O_4$ (MH^+), requires 321.1127.

*4.2.14. Ethyl 2-(3-(thiophen-2-yl)naphtho[1,2-b]furan-2-yl)acetate (**11b**).* Yellow liquid; yield 90 mg, 90%; R_f 0.67 (20% ethyl acetate/petroleum ether); ν_{max} (liquid film) 3063 (w), 2981 (m), 2928 (m), 1736 (vs), 1383 (m), 1370 (m), 1188 (s), 1027 (m), 810 (m), 753 (s),

699 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.27 (t, *J* 7.1 Hz, 3H), 4.07 (s, 2H), 4.23 (q, *J* 7.1 Hz, 2H), 7.17–7.19 (m, 1H), 7.31–7.32 (m, 1H), 7.41–7.42 (m, 1H), 7.47–7.50 (m, 1H), 7.56–7.60 (m, 1H), 7.75 (ABq, *J* 8.6 Hz, 2H), 7.92 (d, *J* 8.1 Hz, 1H), 8.31 (d, *J* 8.2 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 34.0, 61.7, 114.9, 118.7, 120.3, 121.2, 123.4, 123.9, 125.5, 125.7, 126.4, 126.6, 127.9, 128.5, 131.7, 133.2, 146.7, 150.0, 169.2; MS (ESI) *m*/*z* (rel intensity) 337 (MH^+, 89), 318 (30), 317 (100), 298 (23), 253 (20), 233 (16), 214 (16); HRMS (ESI) *m*/*z* found 337.0887 for $C_{20}H_{17}O_3S$ (MH^+), requires 337.0898.

*4.2.15. Ethyl 2-(3-phenylnaphtho[1,2-b]furan-2-yl)acetate (**11c**).* Yellow liquid; yield 78 mg, 79%; R_f 0.73 (20% ethyl acetate/petroleum ether); ν_{max} (liquid film) 3059 (w), 2981 (w), 2929 (w), 1740 (vs), 1381 (m), 1258 (m), 1190 (m), 1028 (m), 812 (m), 748 (s), 701 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.30 (t, *J* 7.1 Hz, 3H), 3.98 (s, 2H), 4.24 (q, *J* 7.1 Hz, 2H), 7.41–7.48 (m, 1H), 7.50–7.55 (m, 3H), 7.58–7.66 (m, 3H), 7.67–7.69 (unresolved m, 2H), 7.94 (d, *J* 8.1 Hz, 1H), 8.34 (d, *J* 8.2 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.4, 33.7, 61.6, 118.7, 120.3, 121.2, 121.4, 123.7, 123.8, 125.3, 126.5, 127.7, 128.5, 129.1, 129.2, 131.7, 132.2, 146.2, 150.1, 169.6; MS (ESI) *m*/*z* (rel intensity) 331 (MH^+, 100), 307 (5), 297 (5), 258 (5), 257 (16); HRMS (ESI) *m*/*z* found 331.1337 for $C_{22}H_{19}O_3$ (MH^+), requires 331.1334.

*4.2.16. Ethyl 2-(3-p-tolylnaphtho[1,2-b]furan-2-yl)acetate (**11d**).* Yellow solid; yield 80 mg, 78%; mp 71–73 °C; R_f 0.66 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3022 (m), 2983 (m), 2926 (m), 1737 (s), 1513 (w), 1382 (m), 1258 (m), 1216 (s), 812 (m), 758 (vs) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.29 (t, *J* 7.1 Hz, 3H), 2.44 (s, 3H), 3.96 (s, 2H), 4.23 (q, *J* 7.0 Hz, 2H), 7.40 (ABq, *J* 7.7 Hz, 4H), 7.47–7.49 (m, 1H), 7.58–7.62 (m, 1H), 7.64–7.70 (m, 2H), 7.93 (d, *J* 8.0 Hz, 1H), 8.33 (d, *J* 8.1 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 21.5, 33.7, 61.6, 118.7, 120.3, 121.1, 121.4, 123.6, 123.9, 125.3, 126.4, 128.4, 129.1, 129.2, 129.8, 131.6, 137.5, 146.0, 150.0, 169.6; MS (ESI) *m*/*z* (rel intensity) 345 (MH^+, 100), 343 (19), 322 (14), 321 (60), 271 (23), 247 (19); HRMS (ESI) *m*/*z* found 345.1501 for $C_{23}H_{21}O_3$ (MH^+), requires 345.1491.

*4.2.17. Ethyl 2-(3-(4-methoxyphenyl)naphtho[1,2-b]furan-2-yl)acetate (**11e**).* Colorless solid; yield 97 mg, 90%; mp 86–88 °C; R_f 0.56 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2932 (m), 2835 (w), 1736 (s), 1604 (w), 1512 (m), 1380 (m), 1289 (m), 1251 (s), 1179 (s), 1035 (m), 812 (m), 753 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.29 (t, *J* 7.1 Hz, 3H), 3.88 (s, 3H), 3.95 (s, 2H), 4.24 (q, *J* 7.1 Hz, 2H), 7.06 (dt, *J* 8.8, 2.1 Hz, 2H), 7.47–7.52 (m, 1H), 7.53 (dt, *J* 8.8, 2.1 Hz, 2H), 7.57–7.63 (m, 1H), 7.66 (ABq, *J* 8.5 Hz, 2H), 7.93 (d, *J* 8.1 Hz, 1H), 8.33 (d, *J* 8.2 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.7, 55.5, 61.6, 114.5, 118.7, 120.3, 120.8, 121.4, 123.5, 123.9, 124.4, 125.2, 126.4, 128.4, 130.4, 131.6, 145.8, 150.0, 159.3, 169.7; MS (ESI) *m*/*z* (rel intensity) 361 (MH^+, 100), 301 (7), 298 (14), 297 (42), 287 (17); HRMS (ESI) *m*/*z* found 361.1445 for $C_{23}H_{21}O_4$ (MH^+), requires 361.1440.

*4.2.18. Ethyl 2-(3-(3,4-dimethoxyphenyl)naphtho[1,2-b]furan-2-yl) acetate (**11f**).* Colorless solid; yield 113 mg, 97%; mp 82–84 °C; R_f 0.40 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2928 (s), 2855 (m), 1738 (vs), 1515 (s), 1464 (m), 1381 (m), 1261 (vs), 1028 (s), 754 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.29 (t, *J* 7.1 Hz, 3H), 3.94 (s, 3H), 3.96 (s, 3H), 3.97 (s, 2H), 4.24 (q, *J* 7.1 Hz, 2H), 7.02 (d, *J* 8.0 Hz, 1H), 7.14–7.17 (m, 2H), 7.47–7.52 (m, 1H), 7.57–7.62 (m, 1H), 7.67 (ABq, *J* 8.7 Hz, 2H), 7.93 (d, *J* 8.1 Hz, 1H), 8.33 (d, *J* 8.2 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.8, 56.1, 61.6, 111.7, 112.4, 118.6, 120.3, 121.0, 121.4, 121.5, 123.6, 123.8, 124.7, 125.3, 126.5, 128.4, 131.6, 145.8, 148.7, 149.3, 150.0, 169.7; MS (ESI) *m*/*z* (rel intensity) 391 (MH^+, 100), 390 (M^+, 6), 317 (6), 297 (13), 235 (5); HRMS (ESI) *m*/*z* found 391.1561 for $C_{24}H_{23}O_5$ (MH^+), requires 391.1545.

*4.2.19. Ethyl 2-(3-(furan-2-yl)-5-methoxynaphtho[1,2-b]furan-2-yl) acetate (**11g**).* Colorless solid; yield 65 mg, 65%; mp 70–72 °C; R_f 0.56 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2928 (w), 1738 (vs), 1645 (m), 1589 (m), 1381 (m), 1225 (m), 1159 (m), 763 (s), 736 (s) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.26 (t, *J* 7.1 Hz, 3H), 4.06 (s, 3H), 4.14 (s, 2H), 4.21 (q, *J* 7.1 Hz, 2H), 6.57 (dd, *J* 3.2, 1.8 Hz, 1H), 6.66 (d, *J* 3.2 Hz, 1H), 7.18 (s, 1H), 7.47–7.51 (m, 1H), 7.58–7.62 (m, 2H), 8.23 (d, *J* 8.2 Hz, 1H), 8.31 (d, *J* 8.4 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 34.7, 56.1, 61.6, 96.5, 107.1, 111.4, 112.1, 120.0, 121.3, 121.6, 123.2, 124.2, 124.9, 127.2, 142.0, 145.0, 146.3, 147.8, 152.6, 169.3; MS (ESI) *m*/*z* (rel intensity) 351 (MH^+, 100), 350 (M^+, 4), 277 (3); HRMS (ESI) *m*/*z* found 351.1236 for $C_{21}H_{19}O_5$ (MH^+), requires 351.1232.

*4.2.20. Ethyl 2-(3-(furan-2-yl)-6,7-dihydrobenzofuran-2-yl)acetate (**13a**).* Colorless liquid; yield 17 mg, 22%; R_f 0.63 (20% ethyl acetate/petroleum ether); ν_{max} (liquid film) 3020 (s), 2927 (w), 1735 (m), 1265 (m), 1216 (vs), 1026 (w), 910 (vs), 755 (vs) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.26 (t, *J* 7.1 Hz, 3H), 4.11 (s, 2H), 4.21 (q, *J* 7.1 Hz, 2H), 6.54 (dd, *J* 3.3, 1.6 Hz, 1H), 6.67 (d, *J* 3.3 Hz, 1H), 7.28–7.35 (m, 2H), 7.47–7.49 (m, 1H), 7.54 (d, *J* 1.6 Hz, 1H), 7.82–7.85 (m, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 34.6, 61.6, 107.3, 110.7, 111.4, 111.5, 120.8, 123.3, 124.8, 126.3, 142.0, 147.1, 147.4, 154.5, 169.1; MS (ESI) *m*/*z* (rel intensity) 271 (MH^+, 100), 225 (6), 198 (8), 197 (65); HRMS (ESI) *m*/*z* found 271.0971 for $C_{16}H_{15}O_4$ (MH^+), requires 271.0970.

*4.2.21. Ethyl 4-(furan-2-yl)-3-nitro-4-phenoxybut-2-enoate (**13a′**).* Yellow solid; yield 43 mg, 45%; mp 76–78 °C; R_f 0.4 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2973 (w), 1763 (s), 1649 (m), 1519 (m), 1494 (m), 1319 (vs), 1215 (vs), 1061 (m), 1025 (m), 756 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.25 (t, *J* 7.1 Hz, 3H), 4.29 (ABqq, *J* 17.8, 7.1 Hz, 2H), 6.59 (s, 1H), 6.60 (dd, *J* 3.6, 1.8 Hz, 1H), 6.96–7.20 (m, 3H), 7.04 (d, *J* 3.6 Hz, 1H), 7.22–7.26 (m, 2H), 7.61 (d, *J* 1.8 Hz, 1H), 8.02 (s, 1H); δ_C (100 MHz, $CDCl_3$) 14.2, 62.5, 72.4, 113.8, 116.8, 122.8, 123.5, 125.0, 129.6, 142.1, 146.3, 148.1, 157.6, 167.8; MS (ESI) *m*/*z* (rel intensity) 341 ($MHNa^+$, 21), 340 (MNa^+, 100), 337 (22), 335 (18), 272 (22), 244 (20), 225 (24), 224 (31); HRMS (ESI) *m*/*z* found 341.0871for $C_{16}H_{16}O_6Na$ ($MHNa^+$), requires 341.0875.

*4.2.22. Ethyl 2-(3-(furan-2-yl)-4,5-dimethoxybenzofuran-2-yl)acetate (**13b**).* Colorless solid; yield 73 mg, 72%; mp 85–87 °C; R_f 0.59 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2927 (m), 1737 (m), 1489 (m), 1325 (w), 1219 (m), 1031 (m), 758 (vs) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.25 (t, *J* 7.1 Hz, 3H), 3.92 (s, 3H), 3.96 (s, 3H), 4.03 (s, 2H), 4.20 (q, *J* 7.1 Hz, 2H), 6.54 (dd, *J* 3.2, 1.6 Hz, 1H), 6.60 (d, *J* 3.2 Hz, 1H), 7.03 (s, 1H), 7.25 (s, 1H), 7.54 (d, *J* 1.6 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 34.5, 56.4, 56.7, 61.6, 95.4, 102.3, 107.0, 110.8, 111.4, 118.2, 141.9, 146.0, 146.9, 147.7, 148.3, 149.2, 169.3; MS (ESI) *m*/*z* (rel intensity) 331 (MH^+, 100), 330 (M^+, 5), 257 (13); HRMS (ESI) *m*/*z* found 331.1170 for $C_{18}H_{19}O_6$ (MH^+), requires 331.1182.

*4.2.23. Ethyl 2-(3-(furan-2-yl)-4,5,6-trimethoxybenzofuran-2-yl)acetate (**13c**).* Colorless solid; yield 78 mg, 73%; mp 79–81 °C; R_f 0.65 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2936 (m), 1739 (vs), 1621 (m), 1469 (s), 1155 (m), 1053 (m), 1020 (w), 757 (s) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.26 (t, *J* 7.1 Hz, 3H), 3.83 (s, 3H), 3.88 (s, 3H), 3.89 (s, 3H), 4.00 (s, 2H), 4.19 (q, *J* 7.1 Hz, 2H), 6.50 (dd, *J* 3.3, 1.8 Hz, 1H), 6.82 (s, 1H), 6.84 (dd, *J* 3.3, 0.7 Hz, 1H), 7.50 (dd, *J* 1.8, 0.7 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 34.4, 56.4, 61.5, 61.8, 91.5, 110.0, 110.3, 111.4, 113.1, 139.3, 142.0, 146.9, 151.4, 152.5, 169.5; MS (ESI) *m*/*z* (rel intensity) 361 (MH^+, 100), 360 (M^+, 11), 297 (4), 287 (9); HRMS (ESI) *m*/*z* found 361.1281 for $C_{19}H_{21}O_7$ (MH^+), requires 361.1287.

*4.2.24. Ethyl 2-(8-(furan-2-yl)benzofuro[5,4-d][1,3]dioxol-7-yl)acetate (**13d**).* Colorless solid; yield 77 mg, 82%; mp 67–69 °C; R_f 0.56 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 2932 (w), 1739 (vs), 1621 (w), 1463 (m), 1370 (w), 1324 (m), 1196 (m), 1155 (s), 1035 (s), 738 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.25 (t, *J* 7.0 Hz, 3H), 4.02 (s, 2H), 4.20 (q, *J* 7.0 Hz, 2H), 5.97 (s, 2H), 6.50–6.52 (unresolved m, 1H),

6.56 (d, *J* 2.7 Hz, 1H), 6.95 (s, 1H), 7.20 (s, 1H), 7.51 (unresolved m, 1H); δ_C (100 MHz, $CDCl_3$) 14.3, 34.4, 61.5, 93.5, 99.4, 101.5, 106.9, 111.0, 111.3, 119.4, 141.8, 144.9, 146.3, 146.4, 147.4, 149.6, 169.2; MS (ESI) *m*/*z* (rel intensity) 315 (MH^+, 100), 314 (M^+, 7), 247 (4), 241 (17); HRMS (ESI) *m*/*z* found 315.0879 for $C_{17}H_{15}O_6$ (MH^+), requires 315.0869.

*4.2.25. Ethyl 2-(5-(benzyloxy)-6-methoxy-3-phenylbenzofuran-2-yl) acetate (**13e**).* Light yellow solid; yield 45 mg, 76%; mp 102–104 °C; R_f 0.46 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3062 (w), 2981 (w), 2938 (w), 1737 (vs), 1619 (m), 1489 (vs), 1452 (s), 1327 (m), 1266 (m), 1191 (m), 1164 (m), 737 (vs), 703 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.28 (t, *J* 7.1 Hz, 3H), 3.82 (s, 2H), 3.93 (s, 3H), 4.21 (q, *J* 7.1 Hz, 2H), 5.12 (s, 2H), 7.08 (s, 1H), 7.09 (s, 1H), 7.29–7.34 (m, 1H), 7.35–7.41 (3H), 7.43–7.50 (m, 6H); δ_C (100 MHz, $CDCl_3$) 14.3, 33.6, 56.6, 61.6, 72.3, 95.9, 105.3, 120.0, 120.2, 127.6, 127.8, 128.0, 128.6, 128.9, 129.1, 132.3, 137.4, 145.7, 149.1, 149.6, 169.6; MS (ESI) *m*/*z* (rel intensity) 439 (MNa^+, 80), 417 (MH^+, 100), 401 (7), 335 (9), 158 (5); HRMS (ESI) *m*/*z* found 417.1712 for $C_{26}H_{25}O_5$ (MH^+), requires 417.1702.

*4.2.26. 2-(5-(Benzyloxy)-6-methoxy-3-phenylbenzofuran-2-yl)acetic acid (**15**).* To a stirred solution of benzofuran **13e** (0.28 mmol, 117 mg) in EtOH/H_2O (9:1) was added KOH (32 mg, 0.56 mmol) at room temperature. The stirring was continued till the starting material was fully consumed (3–4 h). Then Amberlyst 15 acid resin (56 mg) was added and the reaction mixture was stirred for 10–15 min in order to neutralize the excess KOH. The resin was filtered through a pad of Celite and the solvent was evaporated in vacuo. The acid isolated was sufficiently pure for further reaction. Colorless solid; yield 101 mg, 93%; mp 135–137 °C; R_f 0.13 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3060 (w), 2931 (m), 2588 (br w), 1718 (s), 1620 (m), 1557 (w), 1489 (s), 1451 (s), 1313 (m), 1163 (m), 1123 (m), 1021 (s), 744 (s), 703 (s) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.85 (s, 2H), 3.92 (s, 3H), 5.12 (s, 2H), 7.06 (s, 1H), 7.07 (s, 1H), 7.28–7.33 (m, 1H), 7.34–7.41 (m, 3H), 7.41–7.49 (m, 6H); δ_C (100 MHz, $CDCl_3$) 33.2, 56.5, 72.2, 95.9, 105.3, 120.1, 120.4, 127.7, 127.8, 128.0, 128.7, 128.9, 129.2, 132.0, 137.3, 144.8, 145.8, 149.2, 149.7, 175.5; MS (ESI) *m*/*z* (rel intensity) 389 (MH^+, 100), 367 (31), 359 (52), 345 (23), 343 (26), 320 (10), 267 (7); HRMS (ESI) *m*/*z* found 389.1406 for $C_{24}H_{21}O_5$ (MH^+), requires 389.1389.

*4.2.27. 5-(Benzyloxy)-6-methoxy-2-methyl-3-phenylbenzofuran (**16**).* To a stirred solution of benzofuran carboxylic acid **15** (78 mg, 0.2 mmol) in dimethylacetamide (5 mL) were added CaO/NaOH (9:1, 74 mg) and the resulting mixture was refluxed for 4 h. The reaction mixture was cooled to ambient temperature and diluted with ether. The organic phase was subsequently washed with water (3×5 mL) and dried over anhyd Na_2SO_4. The combined organic layers were concentrated in vacuo and the residue was purified by silica gel column chromatography (1% EtOAc/petroleum ether). White solid; yield 55 mg, 80%; mp 131–133 °C; R_f 0.60 (20% ethyl acetate/petroleum ether); ν_{max} (KBr) 3063 (w), 2921 (s), 2850 (m), 1634 (m), 1486 (vs), 1455 (vs), 1310 (m), 1265 (vs), 1204 (s), 1185 (s), 1164 (vs), 1091 (s), 806 (m), 738 (vs), 699 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.51 (s, 3H), 3.94 (s, 3H), 5.13 (s, 2H), 7.06 (s, 1H), 7.09 (s, 1H), 7.30–7.35 (m, 1H), 7.36–7.44 (m, 5H), 7.45–7.50 (m, 4H); δ_C (100 MHz, $CDCl_3$) 13.0, 56.6, 72.3, 95.8, 105.1, 116.9, 120.7, 127.0, 127.8, 128.0, 128.6, 128.8, 128.9, 133.2, 137.5, 145.5, 148.4, 149.1, 150.4; MS (ESI) *m*/*z* (rel intensity) 345 (MH^+, 100), 331 (71), 317 (8), 295 (8), 276 (18), 262 (13), 254 (8), 236 (8), 91 (8); HRMS (ESI) *m*/*z* found 345.1483 for $C_{23}H_{21}O_3$ (MH^+), requires 345.1491.

*4.2.28. 6-Methoxy-2-methyl-3-phenylbenzofuran-5-ol (Isoparvifuran) (**17**).*[20a] To a stirred solution of decarboxylated benzofuran **16** (80 mg, 0.23 mmol) in dry THF (2 mL) was added 10% Pd/C (10 mg). After stirring for 1.5 h at room temperature under H_2 (balloon) atmosphere, the reaction mixture was filtered through a Celite pad and concentrated in vacuo to afford pure product **17**. White solid; yield 59 mg, 99%; mp 118–120 °C (lit[20a] 121–122 °C); ν_{max} (KBr) 3433 (br m), 2917 (w), 2849 (w), 1619 (s), 1485 (vs), 1439 (m), 1362 (m), 1312 (vs), 1266 (m), 1198 (m), 1156 (m), 1026 (m), 761 (vs), 704 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.52 (s, 3H), 3.93 (s, 3H), 5.61 (br s, 1H), 7.02 (s, 1H), 7.15 (s, 1H), 7.35–7.38 (m, 1H), 7.47–7.52 (m, 4H); δ_C (100 MHz, $CDCl_3$) 13.0, 56.5, 94.5, 103.7, 116.9, 121.5, 126.9, 128.8, 133.1, 142.6, 144.7, 148.1, 150.4; MS (ESI) *m*/*z* (rel intensity) 277 (MNa^+, 45), 255 (MH^+, 100), 227 (4), 223 (8); HRMS (ESI) *m*/*z* found 255.1018 for $C_{16}H_{15}O_3$ (MH^+), requires 255.1021. Consistent with literature.[20a]

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Supplementary data

Copies of NMR spectra for all the new/relevant compounds. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.04.023.

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