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Metal and Oxidant Free Bronsted Acid-mediated Cascade Reaction to Substituted-benzofurans

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Abstract: Substituted hydroxy-benzofurans are easily accessible by treatment of resorcinols and 1,2-diaza-1,3-dienes under acidic conditions. The reaction happens through an uncommon Michael reaction between aromatic derivatives as aromatic C(sp²)-H nucleophiles and 1,2-diaza-1,3-dienes as acceptors. Also the behavior of different phenols and 2-naphthol was investigated.

Introduction

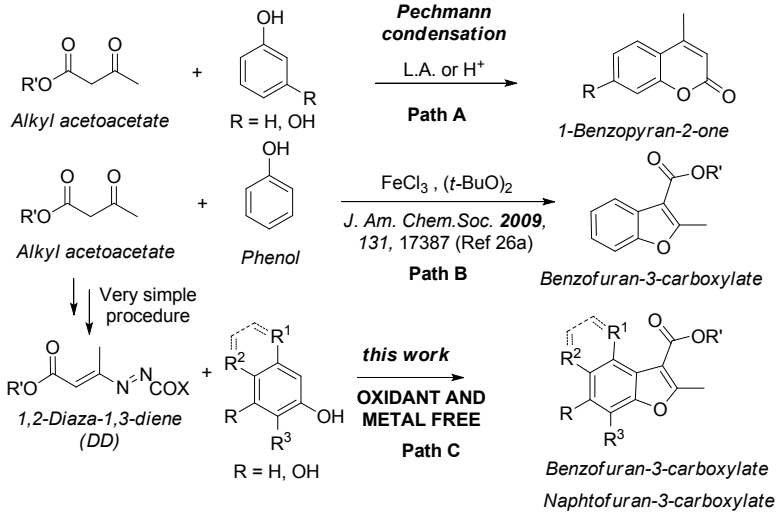
Michael's reaction is a formidable tool available for the synthetic chemist to form new bonds.[1] The mild conditions, the high yields obtained, the perfect atom economy, the high tolerance to other functions, the possibility to easily create carbon-carbon,[2] carbon-nitrogen,[3] carbon-oxygen,[4] carbon-sulfur,[5] carbon-selenium,[6] and carbon-phosphorus bonds[7] are the main reasons for the success of this reaction. In the formation of the carbon-carbon bond, the nucleophile is usually an sp^3 carbon activated by one or two electron withdrawing groups in α position. The use of sp carbons,[8] or aromatic sp^2 carbons as nucleophiles is much less frequent, usually requiring harsh reaction conditions or complicate work-up procedure and are limited in the substrate scope. In particular, few examples of nucleophilic aromatic carbons are present in literature: recently Werner reports an interesting tris(pentafluorophenyl)-borane catalyzed addition of aniline derivatives to α,β-unsaturated ketones.[9] Franzén and Bah describe the addition of *N*,*N*-dimethylaniline to 4-oxobutanoates with carbocationic catalysts,[10] while Bertrand proposes a cationic anti-Bredt di(amino)carbene gold(I) complex catalyzed hydroarylation of enones with *N*,*N*-dialkyl aniline.[11] Regarding the use of phenols and the resorcinols, recently Katiyar suggests the trifluoro acetic catalyzed construction of 4*H*-chromenes via Michael addition of phenols to benzylidene oxobutanoates;[12] Ajavakom synthesizes dihydroquinolines through initial Michael addition of aminophenol to methyl propiolate using CuI as catalyst,[13] while Bodalski reports the self-catalyzed Michael reactions of selected hydroxy arenes with dicyclohexylammonium acrylates bearing electron withdrawing groups at the C-2 carbon atom.[14] Two other examples have been previously reported by our group: the synthesis of cynnolines and pyrazolones by the initial addition of the strongly activated 1,3,5-tris(dialkylamino)benzene derivatives to 1,2-diaza-1,3-dienes (DDs),[15a] and very

recently the access to otherwise inaccessible hydrazone structures through an umpolung approach that involves the Michael-type reaction between anilino substrates and DDs.[15b]

On the other hand, benzofuran is a recurring structure in many biologically active compounds, both of natural and synthetic origin.[16] Consequently, the development of its new synthetic pathways is the subject of considerable attention by organic chemists.[17] Usually, the syntheses are catalyzed by different transition metals such as palladium,[18] platinum,[19] rhodium,[20] ruthenium,[21] copper,[22] zinc,[23] silver,[24] gold,[25] and iron.[26]

Among these last approaches, the use of phenols and β-ketoesters in the iron-catalyzed oxidative variation of the Pechmann condensation (Figure 1, Path B), in which benzofurans are created instead of coumarins (1-benzopyrans or 2*H*-chromen-2-one, Figure 1, Path A), represents an elegant access to this pentatomic heterocyclic target.[26a] Here we report a metal and oxidant free Brønsted acid-mediated cascade reaction to substituted-benzofurans employing resorcinols or 2-naphthol and DDs (Figure 1, Path C). Considering that the DDs are easily generated from β-ketoesters,[27] also this method can be considered as a Pechmann variation in which the first step of the reactions sequence is a Michael type addition of an sp^2 carbon to the azo-ene of the DDs.

Figure 1. Phenol- or resorcinol- derivatives as precursors of 1-benzopyran-2-ones or benzofuran-3-carboxylate.

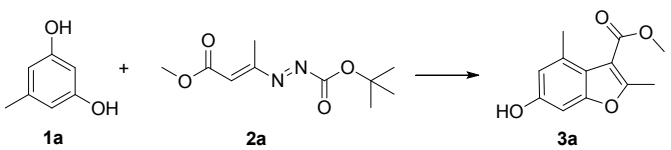


Results and Discussion

Our studies began on the reaction between the 5-methylbenzene-1,3-diol (orcinol)[28] **1a** and DD **2a** chosen as representative model (Table 1). **1a** and **2a** do not react in toluene also under reflux. Then, our attention was focused on identifying an effective catalyst or promoter. To tentatively raise the nucleophilicity of the resorcinol **1a**, some bases such as K_2CO_3, MeONa, DIPEA, and DBU were tested in tetrahydrofuran (Table 1, entries 1–4). Unfortunately, in these latter cases, only complicated mixtures were obtained. We have therefore undertaken a different approach testing different Lewis acids such as $ZnCl_2$, $CuCl_2$, CuI, $FeCl_3$,

SmI_3, $Y(OTf)_3$, $Sc(OTf)_3$, $InBr_3$, $Bi(OTf)_3$, $ZnBr_2$, $SnCl_2$, $CuSO_4$, in toluene at room temperature (Table 1, entries 5–16). It is known that the coordination between the Lewis acid and the azo-ene enhances the electrophilicity of the DD **2**.[29] Monitoring these reactions by TLC analysis, we observed a similar pattern in all cases that is the initial formation of a first spot, that partially turns into a less polar product that was identified as the desired benzofuran **3a**. All attempts to isolate the first intermediate failed. On the basis of our previous experience,[30] we hypothesized that initially an hydrazonic adduct is formed (Scheme 3), which subsequently intramolecularly cyclizes producing the furanic ring. The best result was obtained using the $CuCl_2$, but the yield was poor (23%, entry 6). An increase of the temperature was investigated to tentatively convert completely the initial intermediate. Performing the reaction at 70 °C, or refluxing it, the yields were increased even if remained unsatisfactory (26%, 33%, entries 17, 18, respectively). Better results were obtained by initially conducting the reaction at room temperature (until the disappearance of the reagents), thus refluxing it (41%, entry 19). We then tested different molar ratios of the starting materials: when two equivalents of DDs **2a** were employed, the reaction yield did not improve (31%, entry 20). Unfortunately, in this case, the DD **2a** reacts with itself by means of [4+2] cycloaddition,[31] and the yield of **3a** does not increase significantly. By reacting two equivalents of resorcinol **1a**, the benzofuran **3a** was formed with 50% yield (entry 21). Analyzing the reaction, we can deduce that to produce the desired benzofuran **3a**, an elimination of the hydrazinic counterpart of the DDs occurs. To facilitate the release in the reaction medium of the corresponding *tert*-butyl carbazate, a more polar solvent such as a mixture of acetonitrile/acetone (95/5) together with the addition of an equivalent of Amberlyst 15H were tested. The role of the acetone is to trap the carbazate forming the corresponding hydrazonic derivative.[32] With satisfaction, we have noted that under these conditions **3a** was obtained in 82% yield (entry 22). Finally, we tested also the reaction under the same conditions, but without the addition of the $CuCl_2$: with surprise and considerable pleasure, we have isolated the desired **3a** in 83% (entry 23). Then, the Amberlyst 15H is able itself to effectively promote the formation of the benzofuran, avoiding the use of metal catalysts with all connected drawbacks such as toxicity, higher cost, the eventual necessity of complex ligands and threshold values in pharmaceutical products. It is noteworthy that the reaction between the 2-chloro acetoacetate (DDs' precursors) and **1a** does not provide **3a** either using Lewis acids or Amberlyst 15H.

Table 1. Reaction conditions optimization.



1a **2a** **3a**

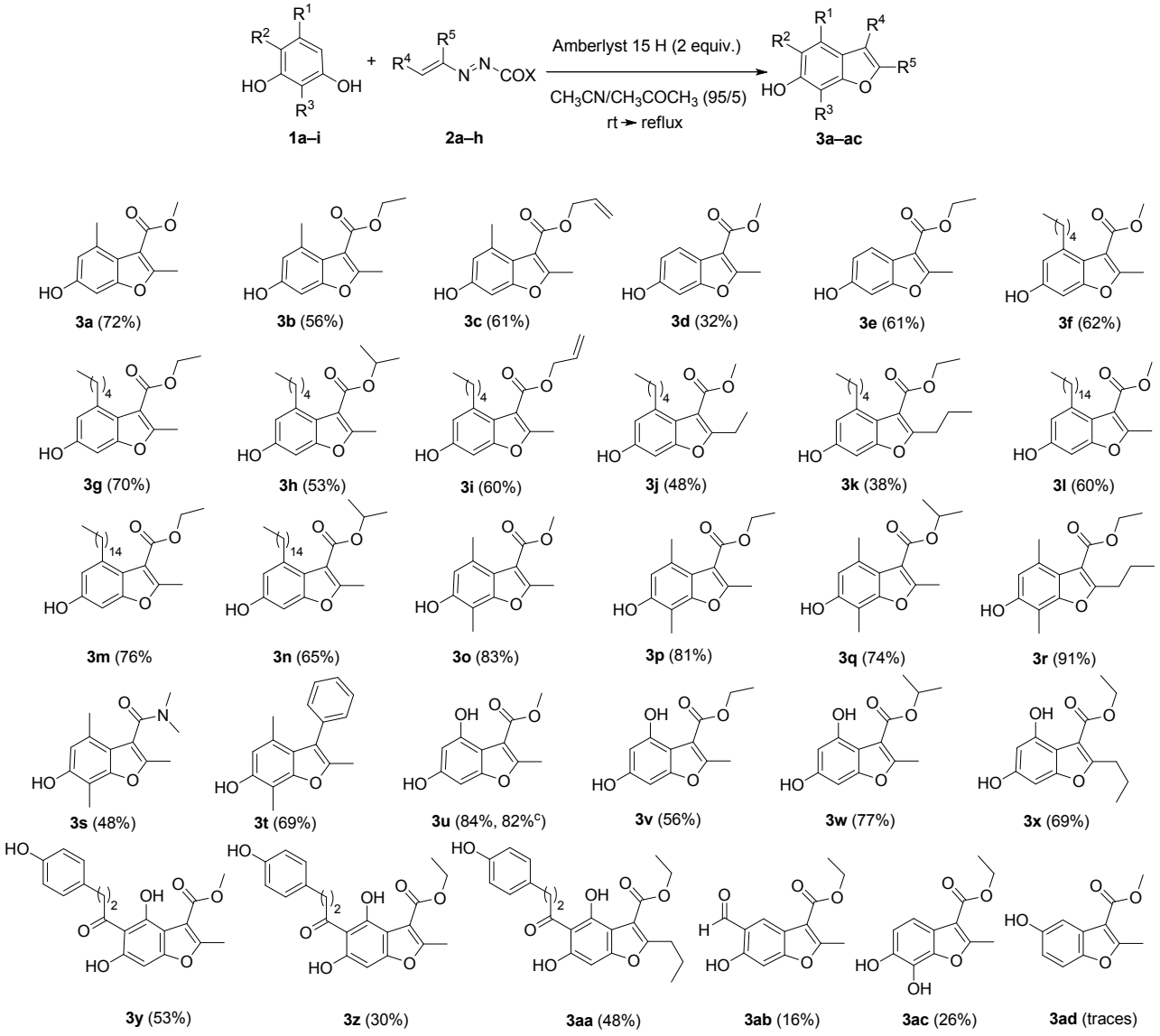
Entry[a]	Solvent	T (C°)	Catalyst/promoter	Ratio **1a**/**2a**	Yields (%)[b]
1	THF	r.t.	K_2CO_3[c]	1/1	-[d]

2	THF	r.t.	MeONa[e]	1/1	-[d]
3	THF	r.t.	DIPEA[e]	1/1	-[d]
4	THF	r.t.	DBU[f]	1/1	-[d]
5	Toluene	r.t.	$ZnCl_2$[g]	1/1	17
6	Toluene	r.t.	$CuCl_2$[g]	1/1	23
7	Toluene	r.t.	CuI[g]	1/1	-[d]
8	Toluene	r.t.	$FeCl_3$[g]	1/1	19
9	Toluene	r.t.	SmI_3[g]	1/1	12
10	Toluene	r.t.	$Y(OTf)_3$[g]	1/1	16
11	Toluene	r.t.	$Sc(OTf)_3$[g]	1/1	8
12	Toluene	r.t.	$InBr_3$[g]	1/1	-[d]
13	Toluene	r.t.	$Bi(OTf)_3$[g]	1/1	9
14	Toluene	r.t.	$ZnBr_2$[g]	1/1	-[d]
15	Toluene	r.t.	$SnCl_2$[g]	1/1	12
16	Toluene	r.t.	$CuSO_4$[g]	1/1	-[d]
17	Toluene	70	$CuCl_2$[g]	1/1	26
18	Toluene	reflux	$CuCl_2$[g]	1/1	33
19[h]	Toluene	rt→reflux	$CuCl_2$[g]	1/1	41
20[h]	Toluene	rt→reflux	$CuCl_2$[g]	1/2	31
21[h]	Toluene	rt→reflux	$CuCl_2$[g]	2/1	50
22[h]	Acetonitrile/acetone[i]	rt→reflux	$CuCl_2$[g]/Amberlyst 15H[j]	2/1	82
23[h]	Acetonitrile/acetone[i]	rt→reflux	Amberlyst 15H[j]	2/1	83

[a] The reactions were conducted on 0.2 mmol scale in 2.0 mL of solvent. [b] Isolated yields. [c] 2.0 equiv. [d] Complicated mixture. [e] 1.0 equiv. [f] 0.5 equiv. [g] 0.2 equiv. [h] The reaction was conducted at room temperature until the disappearance of the limiting reagent, thus refluxing the reaction until the complete disappearance of the intermediate. [i] acetonitrile/acetone 95/5 (v/v). [j] 2.0 equiv.

Identified the optimal conditions, the reaction scope was extented to the benzene-1,3-diol (resorcinol) **1b**[33,34] and to different other alkyl-resorcinols[35] such as 5-pentylbenzene-1,3-diol (5-pentyl resorcinol or olivetol) **1c**,[36] 5-pentadecilbenzene-1,3-diol (5-pentadecilresorcinol, or adipostatin A) **1d**,[37] 2,5-dimethylbenzene-1,3-diol (2,5-dimethyl resorcinol or β-orcinol) **1e**, benzene-1,3,5-triol (phloroglucinol) **1f**,[38] phloretin **1g**,[39] 2,4-dihydroxybenzaldehyde (β-resorcinolaldehyde) **1h** and 3,4,5-trihydroxybenzoic acid (gallic acid) **1i**.[40,41]

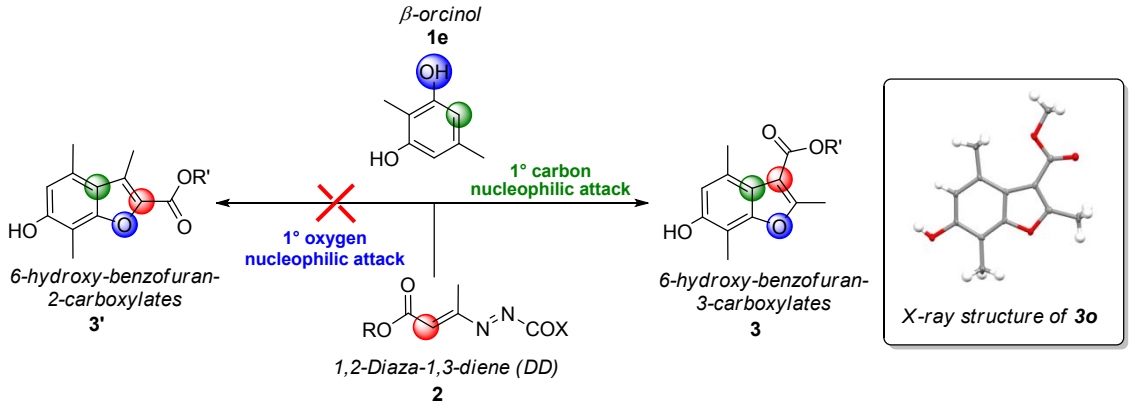
Table 2: Substrate scope[a,b]



[a] *Reaction conditions:* ***1*** *(1.0 mmol),* ***2*** *(0.5 mmol), Amberlyst 15H (2.0 equiv.), acetonitrile/acetone (95/5), 5 mL, 25 °C, 0.5 h, then reflux, 4.0 h.* [b] *Isolated yields.* [c] ***3u*** *(1.452 g) was obtained in 8.0 mmol scale (referred to* ***1a****).*

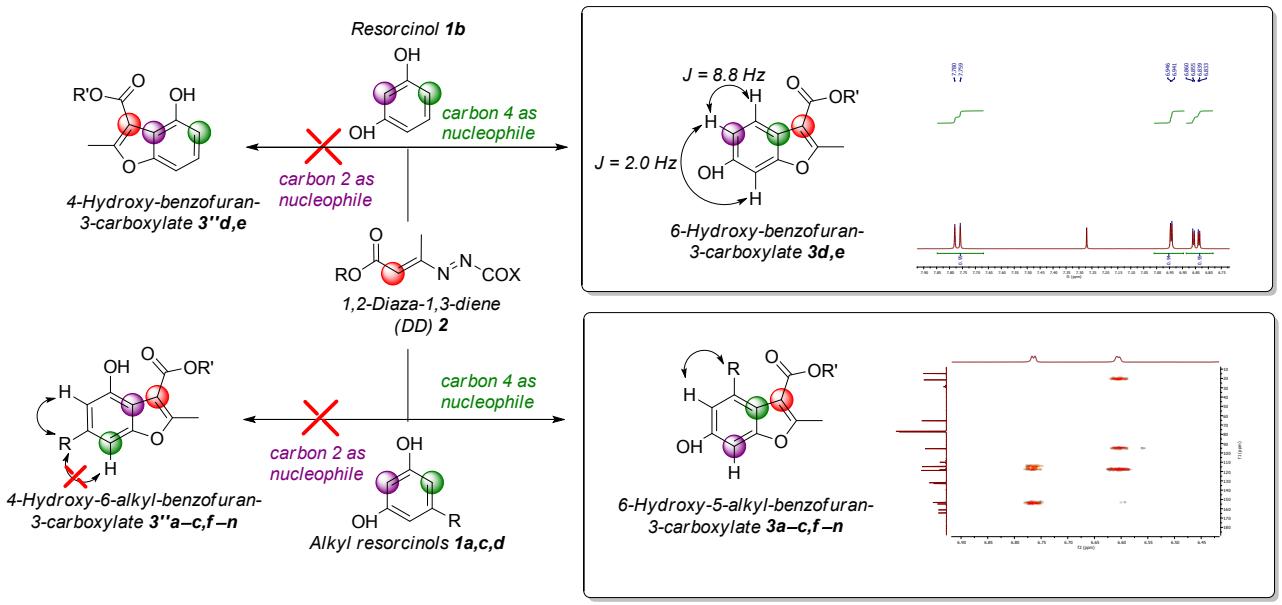
Different benzofurans **3a**–**3ac** were easily obtained in moderate to good yields (Table 2) by means of a cyclization that involves the formation of new carbon-oxygen and carbon-carbon bonds. The reaction was performed on a gram scale, yielding the desired product **3u** without loss of yield (82%). Depending on the number and the positions of the substituents on the aromatic ring of **1**, different regioisomers can be obtained (Schemes 1, and 2).

Scheme 1. Possible regioisomers generated by a first nucleophilic attack of the oxygen or carbon.



To determine the exact concatenation leading to the formation of the furanic ring, we assume that the first reactive center of DDs is the carbon in position 4 of the azo-enic system that behaves as Michael acceptor (highlighted in red in Scheme 1).[27] Depending on whether the first nucleophilic attack is due to carbon or oxygen, the two regioisomers 6-hydroxy-benzofuran-3-carboxylate **3** or 6-hydroxy-benzofuran-2-carboxylate **3'** can be obtained, respectively. The X-ray analysis of compound **3o** unequivocally confirms that the carbon-carbon bond is the first formed, validating that the Michael reaction between DDs **2** and resorcinols **1** occurs via aromatic C(sp^2) nucleophiles (Scheme 2).[42] On the other hand, in the cases of the resorcinol **1b** and alkyl resorcinols **1a,c,d**, also the carbon that acts as nucleophile must be individuated. The more activated pronucleophile sp^2 carbons of the resorcinol derivatives are in position 2 and 4. Then, the isomers 4-hydroxy- or 6-hydroxy-benzofuran-3-carboxylates **3''** or **3**, can be produced respectively. In the case of benzofurans **3d,e** derived from the resorcinol **1b**, the splitting pattern together with ^{1}H NMR coupling constants of 8.8 Hz and 2.0 Hz clearly indicate that the 6-hydroxy-benzofuran-3-carboxylate **3** is the regioisomer generated. In the benzofurans **3a–c**,**f–n**, obtained from the alkyl resorcinols **1a,c,d**, the splitting pattern and the H-H coupling constants do not provide information to determine the exact regioselectivity which, however, can be established by heteronuclear H-C correlations. The HMBC experiments conducted on compounds **3a–c,f–n** clearly indicate that only one of the two residual aromatic protons correlates with aliphatic carbon, effectively excluding the formation of the 4-hydroxy-6-alkyl-benzofuran regioisomer **3''a–c,f–n**. Then in these cases, the sp^2 carbon in position 4 (highlighted in green) of the alkyl resorcinols acts as nucleophile despite the steric hindrance of the alkyl residue (**1a**: R = CH_3, **1c**: R = C_5H_{11}, **1d**: R = $C_{15}H_{31}$, Scheme 2).

Scheme 2. Possible regioisomers generated by nucleophilic attack of the aromatic carbon in position 2 or 4.



The structures of benzofurans **3y–3aa** deriving from the phloretin **1g** were determined by 2D-NMR experiments. The absence of coupling constants between the aromatic protons indicates that the ethyl 5-formyl-6-hydroxy-2-methylbenzofuran-3-carboxylate **3ab** is the regioisomer obtained employing the β-resorcinolaldehyde **1h** as reagent. The substituents on the aromatic ring play a decisive role: from Table 1, it can be noted that electron donor groups favor the reaction. The position of the substituents on the aromatic ring is also crucial: the reaction occurs when the two hydroxyl groups are in meta. In this case, the activating effect of the two electron donor groups converges on the same sp^2 carbon. On the contrary, the reaction between the 1,4-benzenediol **1j** and DDs **2a** furnished a complicate reaction mixture where only minimal traces of the corresponding benzofuran **3ad** are present (Table 2). Here, the synergic activating effect of the two hydroxyl groups is missing.

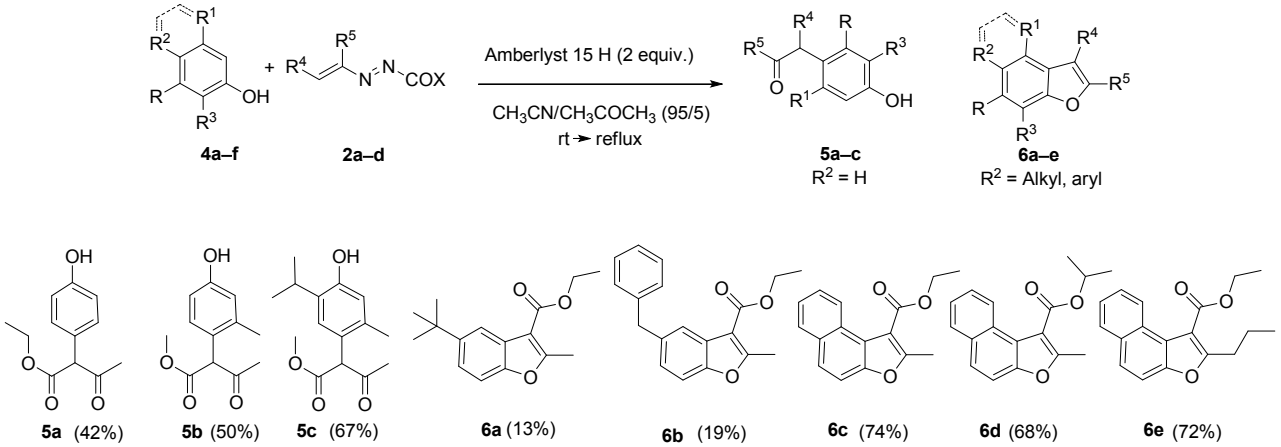
Yields decrease by inserting electron withdrawing groups on the aromatic ring as in the case of phloretin **1g**, and resorcinolaldehyde **1h** (compounds **3y-3ab**, Table 1). A particular behavior was observed in the reaction of the gallic acid **1i**: together with the formation of the furan ring, a decarboxylation reaction occurs leading to the formation of the ethyl 6,7-dihydroxy-2-methylbenzofuran-3-carboxylate **3ac** (Table 1).[43]

Under the same conditions, also the reactivity of the phenol derivatives **4a–e** and 2-naphthol **4f** was investigated. The reactions of phenol **4a** or *ortho*-, and *meta*-substituted phenols **4b,c** with DDs **2a,b** furnished the alkyl 2-(4-hydroxyphenyl)-3-oxobutanoates **5a–c** confirming that the carbon-carbon bond is initially formed (Table 3). The general trend observed in the previous reactions is confirmed: greater number of electron donor substituents improve the yields.

Probably for steric reasons, the sp^2 carbon in *para* to the hydroxyl function is privileged as nucleophile site, and furthermore it could be noted that the acid reaction conditions promote the hydrolysis of the hydrazonic

function. To favor the cyclization, the 4-*tert*-butyl- and 4-benzyl-phenols **4d,e**, blocked in *para* position, were tested obtaining the corresponding benzofurans **6a,b** but only in 13 and 19% yields (Table 3). A different behavior was observed when the 2-naphthol **4f**[44] was employed as starting material: the electronic features of the polycyclic system enhance the nucleophilicity of the sp^2 carbon in position one and the corresponding naphtho[2,1-*b*]furan-1-carboxylates **6c–e** were obtained in good yields (68–74%, Table 3).

Table 3: Reaction between phenols **4a–e** or 2-naphthol **4f** and DDs **2a–d**.[a,b]



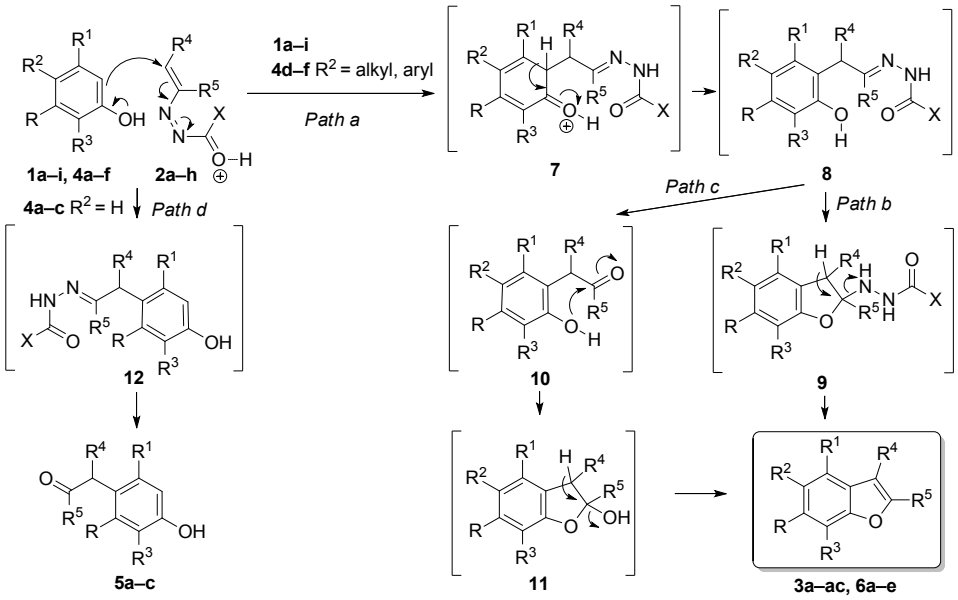
*[a] Reaction conditions: **4** (1.0 mmol), **2** (0.5 mmol), Amberlyst 15H (2.0 equiv.), acetonitrile/acetone (95/5), 5 mL, 25 °C, 0.5 h, then reflux, 4.0 h. [b] Isolated yields.*

The plausible mechanism for the formation of the benzofurans **3a–ac**,**6a–e** (Scheme 3, Path a) involves the preliminary nucleophilic attack of the activated aromatic carbon of **1a–i** onto the terminal carbon atom of the azo-ene system of the DDs **2a–h** with consequent formation of the α-functionalized hydrazone intermediates **7**. The restoration of the benzene aromaticity via [1,3] proton shift triggers the formation of the dihydrobenzofuran **8** due to the nucleophilic attack of oxygen on the hydrazonic function (Scheme 3, Path b). The final elimination of the hydrazine residue provides the desired benzofurans **3a–ac**, **6a,b** or naphthofurans **6c–e**.

Considering the reaction between DDs **2a,b** and phenols **4a–c** (Scheme 3, Path d), in which the *para* position is free, the aromatic C(sp^2) in position 4 acts as nucleophile leading to the corresponding α-aryl hydrazone intermediates **12**. As in this case the ring closure is impossible, the hydrazonic function is hydrolyzed to the corresponding ketone furnishing the alkyl 2-(4-hydroxyphenyl)-3-oxobutanoates **5a–c** that are in equilibrium with their enolic tautomeric form.

Even in the formation of the benzofurans **3** it is not excluded that the hydrazonic function can be preliminarily hydrolyzed, and the second nucleophilic attack can involve the ketonic moiety (Scheme 3, Path c). However, in both cases, the acid reaction environment initially activates the DDs making them better electrophiles, and also promotes the ring closure activating the hydrazone/ketone moiety and facilitating the final elimination of the hydrazine/water portion.

Scheme 3. Plausible mechanism of reaction.



Conclusion

In conclusion, we have developed a metal- and oxidant-free annulation between resorcinols or naphthol and 1,2-diaza-1,3-dienes for the preparation of hydroxy-benzofuran-3-carboxylates or napthofuran-3-carboxylates with complete regioselectivity.

A wide range of resorcinols was employed and the reaction exhibited good functional group tolerance and scalability. The selection of the starting materials enables the choice up to five different variations in the architecture of the final products. The absence of metal catalysts, as well as the easy work-up procedure together with the robustness, represent the key strength of this new approach to benzofurans. New carbon-carbon and carbon-oxygen couplings determine the construction of the benzofuran ring. The resorcinol frameworks act as a double nucleophile: the studies have confirmed that the aromatic carbon firstly operates. Then this reaction represents also a rare example of a Michael reaction between aromatic derivatives as aromatic C(sp^2)-H nucleophiles and 1,2-diaza-1,3-dienes as acceptors under mild conditions.

Experimental section

General experimental details.

All the commercially available reagents and solvents were used without further purification. 1,2-Diaza-1,3-dienes **2a–h** were synthesized as a mixture of *E/Z* isomers as previously reported.[45] Chromatographic purification of compounds was carried out on silica gel (60–200 μm). TLC analysis was performed on pre-loaded (0.25 mm) glass supported silica gel plates (Kieselgel 60); compounds were visualized by exposure to UV light and by dipping the plates in 1% $Ce(SO_4)\cdot 4H_2O$, 2.5% $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ in 10% sulphuric acid followed by heating on a hot plate. All ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz,

respectively, using [D_6]DMSO or $CDCl_3$ as solvent. Chemical shift (δ scale) are reported in parts per million (ppm) relative to the central peak of the solvent and are sorted in ascending order within each group. The following abbreviations are used to describe peak patterns where appropriate: s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, q = quartet, sex = sextet, sept = septet, m = multiplet and br = broad signal. All coupling constants (J value) are given in Hertz [Hz]. The multiplicities in ^{13}C NMR spectra were obtained using HMQC experiments to aid in assignment (q = methyl, t = methylene, d = methine, s = quaternary). FT-IR spectra were obtained as Nujol mulls. High-and low-resolution mass spectroscopy was performed on a Micromass Q-ToF Micro mass spectrometer (Micromass, Manchester, UK) using an ESI source. Melting points were determined in open capillary tubes and are uncorrected. Elemental analyses were within ± 0.4 of the theoretical values (C, H, N).

General procedure for the synthesis of hydroxy-benzofuran-3-carboxylates 3a–3ac, alkyl 2-(4-hydroxyphenyl)-3-oxobutanoates 5a–c or napthofuran-3-carboxylates 6a–c.

To a solution of resorcinols **1a–l** (1.0 mmol) or phenols **4a–e** (1.0 mmol) or 2-naphthol **4f** (1.0 mmol) in acetonitrile/acetone (95/5, v/v, 5.0 mL), 1,2-diaza-1,3-dienes **2a–h** (0.5 mmol.) and Amberlyst 15H (dry form, 2.0 equiv.) were added and the reaction mixture was softly stirred at room temperature until the disappearance of the limiting reagent **2** (0.5 h). A TLC analysis (elution mixture cyclohexane: ethyl acetate, 70 : 30) shows the formation of a new intermediate (R*f* = 0.35). At this point, the reaction mixture was refluxed under softly magnetical stirring until the complete disappearance of the intermediate (4.0 h, TLC analysis: elution mixture: cyclohexane : ethyl acetate, 70 : 30). The reaction mixtures were cooled at room temperature, the Amberlyst 15H was removed by filtration and the solvents were evaporated under reduced pressure. The obtained crude was then purified by column chromatography on silica gel (elution mixture: cyclohexane : ethyl acetate, 90 : 10) and the pure products **3a–3ac, 5a–c, 6a–c** were precipitated in ethyl ether/petrol ether.

Methyl 6-hydroxy-2,4-dimethylbenzofuran-3-carboxylate 3a.

3a was isolated by column chromatography on silica gel (acetate/cyclohexane) in 72% yield (159 mg). White solid; mp: 126–128 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.59 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 5.27 (brs, 1H, OH), 6.61 (dd, 1H, *J*= 2.0 Hz, *J*= 0.8 Hz, Ph), 6.76 (dd, 1H, *J*= 2.0 Hz, *J*= 0.4 Hz, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.6 (q), 21.4 (q), 51.4 (q), 95.4 (d), 110.0 (s), 114.7 (d), 118.2 (s), 132.9 (s), 153.1 (s), 154.8 (s), 161.1 (s), 165.2 (s); IR (nujol): ν_{max} = 3328, 1678 cm^{-1}; MS *m/z* (ESI): 221 ($M + H^+$); anal. calcd. for $C_{12}H_{12}O_4$ (220.22): C 65.45, H 5.49; found: C 65.57, H 5.44.

Ethyl 6-hydroxy-2,4-dimethylbenzofuran-3-carboxylate 3b.

3b was isolated by column chromatography on silica gel (acetate/cyclohexane) in 56% yield (132 mg). White solid; mp: 130–132 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.14 (t, 3H, *J*= 6.8 Hz), 2.59 (s, 3H), 2.64 (s, 3H), 4.39 (q, 2H, *J*= 7.2 Hz), 5.73 (brs, 1H), 6.61 (dd, 1H, *J*= 2.0 Hz, *J*= 0.4 Hz), 6.76 (d, 1H, *J*= 2.0

Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.3, 14.6, 21.5, 60.7, 95.4, 110.3, 114.7, 118.1, 132.8, 153.3, 154.8, 161.0, 165.0; IR (nujol): ν_{max} = 3338, 1688 cm^{-1}; MS *m/z* (ESI): 235 (M + H$^+$); anal. calcd. for $C_{13}H_{14}O_4$ (234.25): C 66.66, H 6.02; found: C 66.57, H 6.05.

Allyl 6-hydroxy-2,4-dimethylbenzofuran-3-carboxylate 3c.

3c was isolated by column chromatography on silica gel (acetate/cyclohexane) in 61% yield (150 mg). White solid; mp: 82–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.59 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 4.83 (dt, 2H, *J*= 6.0 Hz, *J*= 0.8 Hz, O*CH*$_2$CHCH$_2$), 5.31 (dq, 1H, *J*= 10.4 Hz, *J*= 1.2 Hz, OCH$_2$CH*CH*$_2$), 5.37 (brs, 1H, OH), 5.42 (dq, 1H, *J*= 17.2 Hz, *J*= 1.2 Hz, OCH$_2$CH*CH*$_2$), 6.01–6.11 (m, 1H, OCH$_2$*CH*CH$_2$), 6.60 (d, 1H, *J*= 2.0 Hz, Hz, Ph), 6.76 (d, 1H, *J*= 2.0 Hz, Hz, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.7 (q), 21.5 (q), 65.4 (t), 95.4 (d), 110.0 (s), 114.7 (d), 118.1 (s), 118.8 (t), 132.1 (d), 132.9 (s), 153.2 (s), 154.8 (s), 161.2 (s), 164.5 (s); IR (nujol): ν_{max} = 3414, 1702, 1672 cm^{-1}; MS *m/z* (ESI): 247 (M + H$^+$); anal. calcd. for $C_{14}H_{14}O_4$ (246.09): C 68.28, H 5.73; found: C 68.16, H 5.77.

Methyl 6-hydroxy-2-methylbenzofuran-3-carboxylate 3d.[46]

3d was isolated by column chromatography on silica gel (acetate/cyclohexane) in 32% yield (66 mg). Pale yellow solid; mp: 138–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.73 (s, 3H), 3.95 (s, 3H), 5.46 (brs, 1H), 6.85 (dd, 1H, *J*= 8.4 Hz, *J*= 2.4 Hz), 6.95 (d, 1H, *J*= 2.0 Hz), 7.76 (d, 1H, *J*= 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.3, 51.5, 98.0, 108.7, 112.6, 119.5, 121.9, 153.6, 154.4, 162.9, 165.2; IR (nujol): ν_{max} = 3406, 3328, 1689 cm^{-1}; MS *m/z* (ESI): 207 (M + H$^+$); anal. calcd. for $C_{11}H_{10}O_4$ (206.19): C 64.07, H 4.89; found: C 63.95, H 4.94.

Ethyl 6-hydroxy-2-methylbenzofuran-3-carboxylate 3e.

3e was isolated by column chromatography on silica gel (acetate/cyclohexane) in 61% yield (134 mg). White solid; mp: 140–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.44 (t, 3H, *J*= 7.2 Hz, OCH$_2$*CH*$_3$), 2.73 (s, 3H, CH_3), 4.41 (t, 2H, *J*= 7.2 Hz, O*CH*$_2$CH$_3$), 5.49 (brs, 1H, OH), 6.85 (dd, 1H, *J*= 8.4 Hz, *J*= 2.0 Hz, Ph), 6.94 (d, 1H, *J*= 2.0 Hz, Ph), 7.76 (d, 1H, *J*= 8.4 Hz, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.3 (q), 14.4 (q), 60.3 (t), 97.9 (d), 108.8 (s), 112.6 (d), 119.6 (s), 122.0 (d), 153.6 (s), 154.4 (s), 162.7 (s), 164.7 (s); IR (nujol): ν_{max} = 3312, 1672, cm^{-1}; MS *m/z* (ESI): 221 (M + H$^+$); anal. calcd. for $C_{12}H_{12}O_4$ (220.07): C 65.45, H 5.49; found: C 65.58, H 5.42.

Methyl 6-hydroxy-2-methyl-4-pentylbenzofuran-3-carboxylate 3f.

3f was isolated by column chromatography on silica gel (acetate/cyclohexane) in 62% yield (171 mg). Pale brown solid; mp: 52–54 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.87 (t, 3H, *J*= 6.8 Hz, CH$_2$(CH$_2$)$_3$*CH*$_3$), 1.29–1.33 (m, 4H, CH$_2$CH$_2$*(CH*$_2$*)*$_2$CH$_3$), 1.48–1.55 (m, 2H, CH$_2$*CH*$_2$(CH$_2$)$_2$CH$_3$), 2.62 (s, 3H, CH_3), 2.95 (t, 2H, *J*= 8.0 Hz, *CH*$_2$(CH$_2$)$_3$CH$_3$), 3.92 (s, 3H, OCH$_3$), 5.87 (brs, 1H, OH), 6.63 (d, 1H, *J*= 2.4 Hz, Ph), 6.78 (d, 1H, *J*= 2.4 Hz, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0 (q), 14.6 (q), 22.6 (t), 31.1 (t), 31.7 (t),

34.2 (t), 51.6 (q), 95.5 (d), 110.0 (s), 113.8 (d), 117.2 (s), 138.0 (s), 153.4 (s), 155.0 (s), 160.9 (s), 165.6 (s); IR (nujol): ν_{max} = 3440, 1709, 1631 cm^{-1}; MS *m/z* (ESI): 277 (M + H^+); anal. calcd. for $C_{16}H_{20}O_4$ (276.14): C 69.54, H 7.30; found: C 69.68, H 7.28.

Ethyl 6-hydroxy-2-methyl-4-pentylbenzofuran-3-carboxylate 3g.

3g was isolated by column chromatography on silica gel (acetate/cyclohexane) in 70% yield (202 mg). Pale yellow solid; mp: 56–58 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.86 (t, 3H, *J*= 6.8 Hz), 1.26–1.31 (m, 4H), 1.42 (t, 3H, *J*= 7.2 Hz,), 1.49-1.56 (m, 2H), 2.62 (s, 3H), 2.99 (t, 2H, *J*= 8.0 Hz), 4.40 (q, 2H, *J*= 7.2 Hz), 5.78 (brs, 1H), 6.63 (d, 1H, *J*= 2.0 Hz), 6.77 (d, 1H, *J*= 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0, 14.3, 14.6, 22.6, 31.0, 31.6, 34.1, 60.8, 95.5, 110.3, 113.7, 117.3, 138.0, 153.3, 155.0, 160.6, 165.2; IR (nujol): ν_{max} = 3330, 1674, 1662 cm^{-1}; MS *m/z* (ESI): 291 (M + H^+); anal. calcd. for $C_{17}H_{22}O_4$ (290,35): C 70.32, H 7.64; found: C 70.45, H 7.58.

Isopropyl 6-hydroxy-2-methyl-4-pentylbenzofuran-3-carboxylate 3h.

3h was isolated by column chromatography on silica gel (acetate/cyclohexane) in 53% yield (161 mg) . Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.87 (t, 3H, *J*= 6.8 Hz), 1.29–1.33 (m, 4H), 1.40 (d, 6H, *J*= 6.4 Hz), 1.50–1.57 (m, 2H), 2.61 (s, 3H), 3.03 (t, 2H, *J*= 8.0 Hz), 4.83 (brs, 1H), 5.28 (ept, 1H, *J*= 6.4 Hz), 6.61 (d, 1H, *J*= 2.4 Hz), 6.76 (d, 1H, *J*= 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0, 14.6, 22.0, 22.7, 31.0, 31.5, 34.0, 68.2, 95.4, 110.8, 113.4, 117.6, 138.1, 153.0, 154.9, 160.0, 164.4; IR (nujol): ν_{max} = 3409, 1685 cm^{-1}; MS *m/z* (ESI): 305 (M + H^+); anal. calcd. for $C_{18}H_{24}O_4$ (304.38): C 71.03, H 7.95; found: C 71.15, H 7.91.

Allyl 6-hydroxy-2-methyl-4-pentylbenzofuran-3-carboxylate 3i.

3i was isolated by column chromatography on silica gel (acetate/cyclohexane) in 60% yield (182 mg). Pale brown oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.85–0.88 (m, 3H, $CH_2(CH_2)_3CH_3$), 1.27-1.32 (m, 4H, $CH_2CH_2(CH_2)_2CH_3$), 1.48-1.58 (m, 2H, $CH_2CH_2(CH_2)_2CH_3$), 2.63 (s, 3H, CH_3), 2.98 (t, 2H, *J*= 8.0 Hz, $CH_2(CH_2)_3CH_3$), 4.84 (dt, 2H, *J*= 5.6 Hz, *J*= 1.6 Hz,$OCH_2CH{=}CH_2$), 5.31 (dq, 1H, *J*= 10.4 Hz, *J*= 1.2 Hz, $OCH_2(CH{=}CH_2)$, 5.42 (dq, 1H, *J*= 17.2 Hz, *J*= 1.2 Hz, $OCH_2(CH{=}CH_2)$, 5.76 (brs, 1H, OH), 6.01-6.11 (m, 1H, $OCH_2(CH{=}CH_2)$, 6.63 (d, 1H, *J*= 2.4 Hz, Ph), 6.78 (d, 1H, *J*= 2.4 Hz, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0 (q), 14.7 (q), 22.6 (q), 31.0 (t), 31.6 (t), 34.1 (t), 65.6 (t), 95.5 (d), 110.0 (s), 113.8 (d), 117.1 (s), 118.9 (t), 131.9 (d), 137.9 (s), 153.4 (s), 155.0 (s), 160.8 (s), 164.9 (s); IR (nujol): ν_{max} = 3387, 1702 cm^{-1}; MS *m/z* (ESI): 303 (M + H^+); anal. calcd. for $C_{18}H_{22}O_4$ (302.36): C 71.50, H 7.33; found: C 71.59, H 7.28.

Methyl 2-ethyl-6-hydroxy-4pentylbenzofuran-3-carboxylate 3j.

3j was isolated by column chromatography on silica gel (acetate/cyclohexane) in 48% yield (139 mg). Pale brown oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.88 (t, 3H, *J*= 6.8 Hz), 1.28–1.33 (m, 7H), 1.49–1.56 (m, 2H), 2.92–3.04 (m, 4H), 3.92 (s, 3H), 5.93 (brs, 1H), 6.64 (d, 1H, *J*= 2.4 Hz), 6.79 (d, 1H, *J*= 2.0 Hz);

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.4, 14.0, 21.8, 22.6, 31.1, 31.7, 34.2, 51.6, 95.6, 109.1, 113.7, 117.3, 138.0, 153.3, 155.0, 165.3, 165.6; IR (nujol): ν_{max} = 3411, 1687 cm^{-1}; MS *m/z* (ESI): 291 (M + H$^+$); anal. calcd. for $C_{17}H_{22}O_4$ (290.35): C 70.32, H 7.64; found: C 70.19, H 7.68.

Ethyl 6-hydroxy-4-pentyl-2-propylbenzofuran-3-carboxylate 3k.

3k was isolated by column chromatography on silica gel (acetate/cyclohexane) in 38% yield (121 mg). Pale brown oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.87 (t, 3H, *J*= 7.2 Hz), 0.99 (t, 3H, *J*= 7.6 Hz), 1.29–1.32 (m, 4H), 1.42 (t, 3H, *J*= 7.2 Hz), 1.49–1.57 (m, 2H), 1.77 (sex, 2H, *J*= 7.6 Hz), 2.94-2.99 (m, 4H), 4.40 (q, 2H, *J*= 7.2 Hz), 5.92 (brs, 1H), 6.64 (d, 1H, *J*= 2.0 Hz), 6.79 (d, 1H, *J*= 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.8, 14.0, 14.2, 21.6, 22.6, 30.2, 30.9, 31.6, 34.0, 60.8, 95.6, 110.1, 113.6, 117.2, 137.9, 153.4, 155.0, 163.8, 165.4; IR (nujol): ν_{max} = 3394, 1707 cm^{-1}; MS *m/z* (ESI): 319 (M + H$^+$); anal. calcd. for $C_{19}H_{26}O_4$ (318.41): C 71.67, H 8.23; found: C 71.58, H 8.26.

Methyl 6-hydroxy-2-methyl-4-pentadecylbenzofuran-3-carboxylate 3l.

3l was isolated by column chromatography on silica gel (acetate/cyclohexane) in 60% yield (249 mg). White solid; mp: 80–83 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, 3H, *J*= 6.8 Hz), 1.25–1.35 (m, 24H), 1.49–1.56 (m, 2H), 2.63 (s, 3H), 2.97 (t, 2H, *J*= 8.0 Hz), 3.92 (s, 3H), 5.40 (brs, 1H), 6.63 (d, 1H, *J*= 2.0 Hz), 6.78 (d, 1H, *J*= 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1, 14.6, 22.7, 29.4, 29.6, 29.6, 29.6, 29.7, 31.5, 31.9, 34.3, 51.6, 95.5, 110.0, 113.8, 117.3, 138.0, 153.3, 155.0, 160.9, 165.5; IR (nujol): ν_{max} = 3226, 1729, 1703 cm^{-1}; MS *m/z* (ESI): 417 (M + H$^+$); anal. calcd. for $C_{26}H_{40}O_4$ (416.59): C 74.96, H 9.68; found: C 75.08, H 9.63.

Ethyl 6-hydroxy-2-methyl-4-pentadecylbenzofuran-3-carboxylate 3m.

3m was isolated by column chromatography on silica gel (acetate/cyclohexane) in 76% yield (328 mg). White solid; mp: 65–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, 3H, *J*= 7.2 Hz), 1.24–1.32 (m, 24H), 1.42 (t, 3H, *J*= 7.2 Hz), 1.49–1.56 (m, 2H), 2.62 (s, 3H), 3.00 (t, 2H, *J*= 8.0 Hz), 4.39 (q, 2H, *J*= 7.2 Hz), 5.16 (brs, 1H), 6.62 (d, 1H, *J*= 2.4 Hz), 6.77 (d, 1H, *J*= 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1, 14.4, 14.6, 22.7, 29.3, 29.4, 29.6, 29.7, 29.7, 31.9, 34.2, 60.7, 95.5, 110.4, 113.6, 117.5, 138.1, 153.2, 155.0, 160.5, 165.0; IR (nujol): ν_{max} = 3287, 1698, cm^{-1}; MS *m/z* (ESI): 431 (M + H$^+$); anal. calcd. for $C_{27}H_{42}O_4$ (430.62): C 75.31, H 9.83; found: C 75.16, H 9.89.

Isopropyl 6-hydroxy-2-methyl-4-pentadecylbenzofuran-3-carboxylate 3n.

3n was isolated by column chromatography on silica gel (acetate/cyclohexane) in 65% yield (289 mg). White solid; mp: 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, 3H, *J*= 6.8 Hz, $CH_2(CH_2)_{13}\mathit{CH_3}$), 1.24–1.33 (m, 24H, $CH_2CH_2\mathit{(CH_2)_{12}}CH_3$), 1.40 (d, 6H, *J*= 6.4 Hz, $OCH(\mathit{CH_3})_2$), 1.49–1.56 (m, 2H, $CH_2\mathit{CH_2}(CH_2)_{12}CH_3$), 2.61 (s, 3H, CH_3), 3.03 (t, 2H, *J*= 8.0 Hz, $\mathit{CH_2}(CH_2)_{13}CH_3$), 4.83 (brs, 1H, OH), 5.28 (sept, 1H, *J*= 6.4 Hz, $OCH(\mathit{CH_3})_2$), 6.61 (d, 1H, *J*= 2.4 Hz, Ph), 6.76 (d, 1H, *J*= 2.0 Hz, Ph); ^{13}C

NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1 (q), 14.6 (q), 22.0 (q), 22.7 (t), 29.4 (t), 29.4 (t), 29.6 (t), 29.7 (t), 29.7 (t), 31.3 (t), 31.9 (t), 34.0 (t), 68.2 (d), 95.4 (d), 110.8 (s), 113.4 (d), 117.7 (s), 138.1 (s), 153.1 (s), 155.0 (s), 160.0 (s), 164.4 (s); IR (nujol): ν_{max} = 3353, 1684 cm^{-1}; HRMS (ESI) calcd. for $C_{28}H_{45}O_4$ $[M + H]^+$: 445.3318; found: 445.3294.

Methyl 6-hydroxy-2,4,7-trimethylbenzofuran-3-carboxylate 3o.

3o was isolated by column chromatography on silica gel (acetate/cyclohexane) in 83% yield (194 mg). White solid; mp: 156–158 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.33 (s, 3H, CH_3), 2.55 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 3.90 (s, 3H, O*CH*$_3$), 4.79 (brs, 1H, OH), 6.58 (s, 1H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.0 (q), 14.7 (q), 21.1 (q), 51.3 (q), 104.3 (s), 110.3 (s), 114.4 (d), 117.7 (s), 129.2 (s), 150.8 (s), 153.8 (s), 161.0 (s), 165.3 (s); IR (nujol): ν_{max} = 3364, 1678 cm^{-1}; MS *m/z* (ESI): 235 $(M + H^+)$; anal. calcd. for $C_{13}H_{14}O_4$ (234.09): C 66.66, H 6.02; found: C 66.54, H 6.08.

Ethyl 6-hydroxy-2,4,7-trimethylbenzofuran-3-carboxylate 3p.

3p was isolated by column chromatography on silica gel (acetate/cyclohexane) in 81% yield (202 mg). White solid; mp: 129–131 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.41 (t, 3H, *J*= 7.2 Hz), 2.33 (s, 3H), 2.55 (s, 3H), 2.66 (s, 3H), 4.39 (q, 2H, *J*= 7.2 Hz), 5.22 (brs, 1H), 6.57 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.0, 14.3, 14.7, 21.2, 60.5, 104.3, 110.6, 114.4, 117.6, 129.1, 150.9, 153.8, 160.9, 165.1; IR (nujol): ν_{max} = 3358, 1668 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}O_4$ $[M + H]^+$: 249.1127; found: 249.1151.

Isopropyl 6-hydroxy-2,4,7-trimethylbenzofuran-3-carboxylate 3q.

3q was isolated by column chromatography on silica gel (acetate/cyclohexane) in 74% yield (194 mg). White solid; mp: 122–124 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.40 (d, 6H, *J*= 6.4 Hz), 2.33 (s, 3H), 2.55 (s, 3H), 2.66 (s, 3H), 4.97 (brs, 1H), 5.29 (sept, 1H, *J*= 6.4 Hz), 6.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.0, 14.6, 21.3, 22.0, 68.2, 104.3, 111.0, 114.3, 117.7, 129.0, 150.9, 153.8, 160.6, 164.6; IR (nujol): ν_{max} = 3430 cm^{-1}; MS *m/z* (ESI): 263 $(M + H^+)$; anal. calcd. for $C_{15}H_{18}O_4$ (262.30): C 68.68, H 6.92; found: C 68.77, H 6.88.

Ethyl 6-hydroxy-4,7-dimethyl-2-propylbenzofuran-3-carboxylate 3r.

3r was isolated by column chromatography on silica gel (acetate/cyclohexane) in 91% yield (251 mg). White solid; mp: 87–88 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.01 (t, 3H, *J*= 7.2 Hz, CH_2CH_2*CH*$_3$), 1.42 (t, 3H, *J*= 7.2 Hz, OCH_2*CH*$_3$), 1.80 (sex, 2H, *J*= 7.2 Hz, CH_2*CH*$_2CH_3$), 2.34 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 3.02 (t, 2H, *J*= 7.6 Hz, *CH*$_2CH_2CH_3$), 4.40 (q, 2H, *J*= 7.2 Hz, O*CH*$_2CH_3$), 5.49 (brs, 1H, OH), 6.58 (s, 1H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.0 (q), 13.8 (q), 14.2 (q), 21.1 (q), 21.6 (t), 30.2 (t), 60.6 (t), 104.5 (s), 110.3 (s), 114.4 (d), 117.6 (s), 129.1 (s), 151.0 (s), 153.8 (s), 164.3 (s), 165.2 (s); IR (nujol): ν_{max} = 3379, cm^{-1}; MS *m/z* (ESI): 277 $(M + H^+)$; anal. calcd. for $C_{16}H_{20}O_4$ (276.14): C 69.54, H 7.30; found: C 69.43, H 7.35.

6-Hydroxy-*N*,*N*,2,4,7-pentamethylbenzofuran-3-carboxamide 3s.

3s was isolated by column chromatography on silica gel (acetate/cyclohexane) in 48% yield (118 mg). Pale brown solid; mp: 188–190 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.17 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.87 (s, 3H, NCH_3), 3.02 (s, 3H, NCH_3), 6.55 (s, 1H, Ph), 9.21 (s, 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 8.3 (q), 12.4 (q), 17.4 (q), 34.1 (q), 37.7 (q), 103.8 (s), 112.8 (d), 117.1 (s), 126.3 (s), 149.2 (s), 152.4 (s), 153.4 (s), 165.4 (s); IR (nujol): ν_{max} = 3287, 1636 cm^{-1}; MS *m/z* (ESI): 248 (M + H$^+$); anal. calcd. for $C_{14}H_{17}NO_3$ (247.29): C 68.00, H 6.93, N 5.66; found: C 67.86, H 6.98, N 5.73.

2,4,7-Trimethyl-3-phenylbenzofuran-6-ol 3t.

3t was isolated by column chromatography on silica gel (acetate/cyclohexane) in 69% yield (174 mg). Pale yellow solid; mp: 119–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.04 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 4.30 (brs, 1H, OH), 6.48 (s, 1H, Ph), 7.34–7.45 (m, 5H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.0 (q), 12.2 (q), 19.0 (q), 104.3 (s), 112.8 (d), 118.0 (s), 121.0 (s), 127.1 (d), 128.0 (d), 128.1 (s), 130.7 (d), 134.4 (s), 150.3 (s), 150.4 (s), 153.7 (s); IR (nujol): ν_{max} = 3262 cm^{-1}; MS *m/z* (ESI): 253 (M + H$^+$); anal. calcd. for $C_{17}H_{16}O_2$ (252.31): C 80.93, H 6.39; found: C 81.06, H 6.33.

Methyl 4,6-dihydroxy-2-methylbenzofuran-3-carboxylate 3u.

3u was isolated by column chromatography on silica gel (acetate/cyclohexane) in 84% yield (187 mg) or in 82% (1.452 g starting from 8.0 mmol of **1a**). White solid; mp: 186–188 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.60 (s, 3H), 3.92 (s, 3H), 6.16 (d, 1H, *J*= 2.0 Hz), 6.41 (d, 1H, *J*= 2.0 Hz), 9.61 (s, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4, 53.0, 89.4, 98.7, 105.4, 108.0, 150.3, 155.2, 157.3, 160.8, 167.7; IR (nujol): ν_{max} = 3399, 3081, 1663 cm^{-1}; MS *m/z* (ESI): 223 (M + H$^+$); anal. calcd. for $C_{11}H_{10}O_5$ (222.20): C 59.46, H 4.54; found: C 59.59, H 4.49.

Ethyl 4,6-dihydroxy-2-methylbenzofuran-3-carboxylate 3v.

3v was isolated by column chromatography on silica gel (acetate/cyclohexane) in 56% yield (133 mg). White solid; mp: 194–196 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.36 (t, 3H, *J*= 7.2 Hz), 2.63 (s, 3H), 4.39 (q, 2H, *J*= 7.2 Hz), 6.16 (d, 1H, *J*= 1.6 Hz), 6.42 (d, 1H, *J*= 2.0 Hz), 9.61 (s, 1H), 10.30 (s, 1H); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.9, 14.5, 62.1, 89.4, 98.7, 105.4, 108.2, 150.3, 155.2, 157.3, 160.8, 167.3; IR (nujol): ν_{max} = 3398, 3393, 1651 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}O_5$ [M + H]$^+$: 237.0763; found: 237.0764.

Isopropyl 4,6-dihydroxy-2-methylbenzofuran-3-carboxylate 3w.

3w was isolated by column chromatography on silica gel (acetate/cyclohexane) in 77% yield (192 mg). White solid; mp: 158–160 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.36 (d, 6H, *J*= 6.4 Hz), 2.62 (s,

3H), 5.19 (sept, 1H, *J*= 6.4 Hz), 6.15 (d, 1H, *J*= 1.6 Hz), 6.41 (d, 1H, *J*= 2.0 Hz), 9.57 (s, 1H), 10.32 (s, 1H); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 14.5, 21.5, 70.2, 89.4, 98.6, 105.4, 108.4, 150.3, 155.2, 157.3, 160.6, 167.8; IR (nujol): ν_{max} = 3418, 3066, 1650 cm^{-1}; MS *m/z* (ESI): 251 (M + H$^+$); anal. calcd. for $C_{13}H_{14}O_5$ (250.25): C 62.39, H 5.64; found: C 62.35, H 5.60.

Ethyl 4,6-dihydroxy-2-propylbenzofuran-3-carboxylate 3x.

3x was isolated by column chromatography on silica gel (acetate/cyclohexane) in 69% yield (182 mg). White solid; mp: 136–138 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 0.93 (t, 3H, *J*= 7.2 Hz), 1.35 (t, 3H, *J*= 7.2 Hz), 1.70 (sex, 2H, *J*= 7.2 Hz), 3.00 (t, 2H, *J*= 7.2 Hz), 4.39 (q, 2H, *J*= 7.2 Hz), 6.16 (d, 1H, *J*= 2.0 Hz), 6.43 (d, 1H, *J*= 2.0 Hz), 9.62 (s, 1H), 10.35 (s, 1H); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.6, 13.8, 21.2, 29.8, 62.1, 89.5, 98.7, 105.3, 108.1, 150.5, 155.3, 157.4, 164.1, 167.2; IR (nujol): ν_{max} = 3407, 3080, 1668 cm^{-1}; MS *m/z* (ESI): 265 (M + H$^+$); anal. calcd. for $C_{14}H_{16}O_5$ (264.27): C 63.63, H 6.10; found: C 63.54, H 6.12.

Methyl 4,6-dihydroxy-5-(3-(4-hydroxyphenyl) propanoyl)-2-methylbenzofuran-3-carboxylate 3y.

3y was isolated by column chromatography on silica gel (acetate/cyclohexane) in 53% yield (196 mg). White solid; mp: 176–178 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 2.66 (s, 3H, *CH$_3$*), 2.86 (t, 2H, *J*= 7.6 Hz, CH$_2$*CH$_2$*), 3.34 (t, 2H, *J*= 7.6 Hz, *CH$_2$*CH$_2$), 3.96 (s, 3H, OCH$_3$), 6.22 (s, 1H, Ph), 6.88 (d, 2H, *J*= 7.6 Hz, Ph), 7.06 (d, 2H, *J*= 7.6 Hz, Ph), 9.15 (s, 1H, OH), 11.44 (s, 1H, OH), 13.18 (s, 1H, OH); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 14.4 (q), 28.8 (q), 43.3 (t), 53.4 (q), 99.0 (d), 100.6 (s), 106.9 (s), 108.4 (s), 115.0 (d), 129.0 (d), 130.9 (s), 153.7 (s), 155.4 (s), 156.8 (s), 161.2 (s), 164.0 (s), 167.5 (s), 201.6 (s); IR (nujol): ν_{max} = 3430, 1663 cm^{-1}; MS *m/z* (ESI): 371 (M + H$^+$); anal. calcd. for $C_{20}H_{18}O_7$ (370.35): C 64.86, H 4.90; found: C 65.01, H 4.84.

Ethyl 4,6-dihydroxy-5-(3-(4-hydroxyphenyl) propanoyl)-2-methylbenzofuran-3-carboxylate 3z.

3z was isolated by column chromatography on silica gel (acetate/cyclohexane) in 30% yield (115 mg). White solid; mp: 166–168 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 1.37 (t, 3H, *J*= 7.2 Hz), 2.65 (s, 3H), 2.85 (t, 2H, *J*= 7.6 Hz), 3.33 (t, 2H, *J*= 7.6 Hz), 4.41 (q, 2H, *J*= 7.2 Hz), 6.20 (s, 1H), 6.67 (d, 2H, *J*= 8.8 Hz), 7.06 (d, 2H, *J*= 8.4 Hz), 9.16 (s, 1H), 11.48 (s, 1H), 13.18 (s, 1H); ^{13}C NMR (100 MHz, DMSO$_{d6}$, 25 °C): δ = 13.8, 14.5, 28.8, 43.9, 62.6, 99.0, 100.5, 106.9, 108.5, 115.1, 129.1, 130.9, 153.6, 155.5, 156.8, 161.2, 164.1, 167.1, 201.6; IR (nujol): ν_{max} = 3443, 1689 cm^{-1}; MS *m/z* (ESI): 385 (M + H$^+$); anal. calcd. for $C_{21}H_{20}O_7$ (384.38): C 65.62, H 5.24; found: C 65.74, H 5.20.

Ethyl 4,6-dihydroxy-5-(3-(4-hydroxyphenyl) propanoyl)-2-propylbenzofuran-3-carboxylate 3aa.

3aa was isolated by column chromatography on silica gel (acetate/cyclohexane) in 48% yield (198 mg). White solid; mp: 166–168 °C; ^{1}H NMR (400 MHz, DMSO$_{d6}$, 25 °C): δ = 0.91 (t, 3H, *J*= 7.6 Hz, CH$_2$CH$_2$*CH$_3$*), 1.36 (t, 3H, *J*= 7.2 Hz, OCH$_2$*CH$_3$*), 1.70 (sex, 2H, *J*= 7.2 Hz, CH$_2$*CH$_2$*CH$_3$), 2.85 (t, 2H, *J*= 7.6

Hz, CH_2CH_2), 3.02 (t, 2H, *J*= 7.6 Hz, $CH_2CH_2CH_3$), 3.34 (t, 2H, *J*= 7.6 Hz, CH_2CH_2), 4.41 (q, 2H, *J*= 7.2 Hz, OCH_2CH_3), 6.21 (s, 1H, Ph), 6.67 (d, 2H, *J*= 8.4 Hz, Ph), 7.05 (d, 2H, *J*= 8.4 Hz, Ph), 9.18 (s, 1H, OH), 11.53 (s, 1H, OH), 13.20 (s, 1H, OH); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 13.6 (q), 13.8 (q), 20.6 (t), 28.8 (t), 29.7 (t), 43.9 (t), 62.7 (t), 99.0 (d), 100.5 (s), 106.9 (s), 108.5 (s), 115.1 (d), 129.0 (d), 130.9 (s), 153.8 (s), 155.5 (s), 157.1 (s), 164.2 (s), 164.3 (s), 167.1 (s), 201.7(s); IR (nujol): ν_{max} = 3430, 1658 cm^{-1}; MS *m/z* (ESI): 413 (M + H$^+$); anal. calcd. for $C_{23}H_{24}O_7$ (412.43): C 66.98, H 5.87; found: C 66.85, H 5.94.

Ethyl 5-formyl-6-hydroxy-2-methylbenzofuran-3-carboxylate 3ab.

3ab was isolated by column chromatography on silica gel (acetate/cyclohexane) in 16% yield (40 mg). White solid; mp: 136–138 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.46 (t, 3H, *J*= 7.2 Hz, OCH_2CH_3), 2.75 (s, 3H, CH_3), 4.44 (q, 2H, *J*= 7.2 Hz, OCH_2CH_3), 6.99 (s, 1H, Ph), 8.13 (s, 1H, Ph), 9.98 (s, 1H, COH), 11.22 (s, 1H, OH); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 14.4 (q), 14.4 (q), 60.6 (t), 99.2 (d), 109.0 (s), 118.5 (s), 119.9 (s), 128.1 (d), 158.3 (s), 160.2 (s), 163.7 (s), 164.4 (s), 196.4 (s); IR (nujol): ν_{max} = 3413, 1738 cm^{-1}; MS *m/z* (ESI): 249 (M + H$^+$); anal. calcd. for $C_{13}H_{12}O_5$ (248.23): C 62.90, H 4.87; found: C 63.01, H 4.84.

Ethyl 6,7-dihydroxy-2-methylbenzofuran-3-carboxylate 3ac.

3ac was isolated by column chromatography on silica gel (acetate/cyclohexane) in 66% yield (156 mg). Pale yellow solid; mp: 120–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.44 (t, 3H, *J*= 7.2 Hz), 2.74 (s, 3H), 4.40 (q, 2H, *J*= 7.2 Hz), 5.45 (brs, 2H), 6.90 (d, 1H, *J*= 8.4 Hz), 7.36 (d, 1H, *J*= 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.3, 29.7, 60.4, 109.5, 112.8, 112.9, 121.0, 128.5, 141.0, 142.3, 163.0, 164.6; IR (nujol): ν_{max} = 3375, 3231, 1742 cm^{-1}; MS *m/z* (ESI): 237 (M + H$^+$); anal. calcd. for $C_{12}H_{12}O_5$ (236.22): C 61.01, H 5.12; found: C 60.89, H 5.19.

Ethyl 2-(4-hydroxyphenyl)-3-oxobutanoate 5a.[47]

5a was isolated by column chromatography on silica gel (acetate/cyclohexane) in 42% yield (93 mg). The enolic form (E) constitutes the 76% of the mixture and the ketonic form (K) the remaining 24% (determined by ^{1}H-NMR). Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.0 (q, 3H, *J*= 7.2 Hz, E), 1.28 (q, 3H, *J*= 7.2 Hz, K), 1.86 (s, 3H, E), 2.18 (s, 3H, K), 4.15–4.27 (m, 2H, E, K), 4,63 (s, 1H, K), 5.37 (brs, 1H, E), 5.68 (brs, 1H, K), 6.62 (s, 1H, K), 6.80 (d, 1H, *J*= 8.4 Hz, E), 6.81 (d, 1H, *J*= 8.4 Hz, K), 7.01 (d, 1H, *J*= 8.4 Hz, E), 7.19 (d, 1H, *J*= 8.4 Hz, K), 13.1 (s, 1H, E); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0, 14.2, 19.8, 28.7, 60.6, 61.8, 64.8, 103.7, 115.0, 116.0, 124.3, 127.4, 130.5, 130.6, 132.4, 154.6, 156,0, 169.2, 172.8, 173.9, 202.6.

Methyl 2-(4-hydroxy-2-methylphenyl)-3-oxobutanoate 5b.

5b was isolated by column chromatography on silica gel (acetate/cyclohexane) in 50% yield (111 mg). The enolic form (E) constitutes the 63% of the mixture and the ketonic form (K) the remaining 37% (determined

by ^{1}H-NMR). Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.77 (s, 3H, E), 2.10 (s, 3H, E), 2.17 (s, 3H, K), 2.28 (s, 3H, K), 3.68 (s, 3H, E), 3.77 (s, 3H, K), 4,86 (s, 1H, K), 5.34 (brs, 1H, E), 5.57 (brs, 1H, K), 6.64-6.73 (m, 2H, E, K), 6.91 (d, 1H, *J*= 8.0 Hz, E), 7.13 (d, 1H, *J*= 8.4 Hz, K), 12.9 (s, 1H, E); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 19.4, 19.7, 19.8, 28.7, 51.7, 52.6, 61.4, 102.1, 112.8, 113.7, 116.7, 117.7, 123.3, 126.8, 130.2, 132.6, 138.4, 139.7, 155.1, 155.7, 169.8, 173.1, 174.0, 202.8. HRMS (ESI) calcd. for $C_{12}H_{15}O_4$ $[M + H]^+$: 223.0970; found: 239.0966.

Methyl 2-(4-hydroxy-5-isopropyl-2-methylphenyl)-3-oxobutanoate 5c.

5c was isolated by column chromatography on silica gel (acetate/cyclohexane) in 67% yield (261 mg). The enolic form (E) constitutes the 76% of the mixture and the ketonic form (K) the remaining 24% (determined by ^{1}H-NMR). Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.22–1.26 (m, 6H, E, K), 1.77 (d, 3H, *J*= 0.8 Hz, E), 2.07 (s, 3H, E), 2.17 (s, 3H, K), 2.26 (s, 3H, K), 3.13–3.20 (m, 1H, E, K), 3.70 (s, 3H, E), 3.77 (s, 3H, K), 4,84 (s, 1H, K), 5.00 (brs, 1H, E), 5.15 (brs, 1H, K), 6.62 (s, 1H, K), 6.63 (s, 1H, E), 6.87 (s, 1H, E), 7.08 (s, 1H, K), 13.0 (d, 1H, *J*= 0.4 Hz, E); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 19.2, 19.3, 19.5, 22.5, 22.5, 22.8, 26.7, 26.9, 28.6, 51.8,52.5, 61.7, 102.4, 116.6, 117.6, 123.4, 126.7, 127.3, 129.5, 131.8, 132.7, 135.2, 136.4, 152.1, 152.7, 169.8, 173.2, 174.0, 202.8. HRMS (ESI) calcd. for $C_{15}H_{21}O_4$ $[M + H]^+$: 265.1440; found: 265.1449.

Ethyl 5-(*tert*-butyl)-2-methylbenzofuran-3-carboxylate 6a.

6a was isolated by column chromatography on silica gel (acetate/cyclohexane) in 13% yield (34 mg). Pale yellow solid; mp: 50–52 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.39, (s, 9H), 1.47 (t, 3H, *J*= 7.2 Hz), 2.76 (s, 3H), 4.43 (q, 2H, *J*= 7.2 Hz), 7.35 (s, 1H), 7.35 (s, 1H), 8.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4, 14.5, 31.8, 34.8, 60.2, 109.0, 110.0, 117.9, 122.1, 125.9, 146.8, 151.8, 163.6, 164.7; IR (nujol): ν_{max} = 1720, cm^{-1}; MS *m/z* (ESI): 261 ($M + H^+$); anal. calcd. for $C_{16}H_{20}O_3$ (260.33): C 73.82, H 7.74; found: C 73.69, H 7.80.

Ethyl 5-benzyl-2-methylbenzofuran-3-carboxylate 6b.

6b was isolated by column chromatography on silica gel (acetate/cyclohexane) in 19% yield (56 mg). Pale yellow solid; mp: 74–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.41 (t, 3H, *J*= 7.2 Hz), 2.76 (s, 3H), 4.10 (s, 2H), 4.39 (q, 2H, *J*= 7.2 Hz), 7.11 (dd, 1H, *J*= 8.4 Hz, *J*= 1.6 Hz), 7.18–7.23 (m, 3H), 7.28–7.34 (m, 3H), 7.79 (d, 1H, *J*= 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.4, 14.5, 41.9, 60.2, 109.0, 110.6, 121.7, 125.3, 126.0, 126.4, 128.4, 128.9, 136.7, 141.5, 152.4, 163.8, 164.5; IR (nujol): ν_{max} = 1743 cm^{-1}; MS *m/z* (ESI): 295 ($M + H^+$); anal. calcd. for $C_{19}H_{18}O_3$ (294.34): C 77.53, H 6.16; found: C 77.69, H 6.09.

Ethyl 2-methylnaphtho[2,1-*b*]furan-1-carboxylate 6c.

6c was isolated by column chromatography on silica gel (acetate/cyclohexane) in 74% yield (188 mg). White solid; mp:84–86 °C; ^{1}H NMR (400 MHz, $DMSO_{d6}$, 25 °C): δ = 1.50 (t, 3H, *J*= 7.2 Hz), 2.79 (s, 3H), 4.52 (q,

2H, *J*= 7.2 Hz), 7.51 (ddd, 1H, *J*= 8.0 Hz, *J*= 6.8 Hz, *J*= 1.2 Hz), 7.59 (d, 1H, *J*= 8.0 Hz), 7.61 (ddd, 1H, *J*= 8.4 Hz, *J*= 6.8 Hz, *J*= 1.6 Hz), 7.74 (d, 1H, *J*= 8.8 Hz), 7.93 (d, 1H, *J*= 9.2 Hz), 9.22 (d, 1H, *J*= 8.4 Hz); ^{13}C NMR (100 MHz, $DMSO_{d6}$, 25 °C): δ = 14.4, 15.3, 60.8, 111.6, 111.8, 120.4, 124.6, 126.0, 126.2, 126.3, 127.8, 128.7, 131.3, 151.4, 161.3, 165.0; IR (nujol): ν_{max} = 1724, 1703 cm^{-1}; MS *m/z* (ESI): 255 (M + H$^+$); anal. calcd. for $C_{16}H_{14}O_3$ (254.28): C 75.57, H 5.55; found: C 75.48, H 5.59.

Isopropyl 2-methylnaphtho[2,1-*b*]furan-1-carboxylate 6d.

was isolated by column chromatography on silica gel (acetate/cyclohexane) in 68% yield (182 mg). White solid; mp: 79–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.49 (d, 6H, *J*= 6.4 Hz, OCH$(CH_3)_2$), 2.79 (s, 3H, CH_3), 5.43 (sept, 1H, *J*= 6.4 Hz, O$CH(CH_3)_2$), 7.51 (ddd, 1H, *J*= 8.0 Hz, *J*= 6.8 Hz, *J*= 1.2 Hz, Ar), 7.59 (d, 1H, *J*= 8.8 Hz, Ar), 7.61 (ddd, 1H, *J*= 8.4 Hz, *J*= 6.8 Hz, *J*= 1.6 Hz, Ar), 7.74 (d, 1H, *J*= 9.2 Hz, Ar), 7.93 (d, 1H, *J*= 8.0 Hz, Ar), 9.24 (d, 1H, *J*= 8.4 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 15.3 (q), 22.1 (q), 68.4 (d), 111.6 (d), 112.2 (s), 120.5 (s), 124.6 (d), 126.1 (d), 126.2(d), 126.2 (d), 127.9 (s), 128.7 (d), 131.3 (s), 151.5 (s), 161.1 (s), 164.6 (s); IR (nujol): ν_{max} = 1705 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{17}O_3$ [M + H]$^+$: 269.1178; found: 269.1178.

Ethyl 2-propylnaphtho[2,1-*b*]furan-1-carboxylate 6e.

6e was isolated by column chromatography on silica gel (acetate/cyclohexane) in 72% yield (203 mg). Pale yellow solid; mp: 48–50 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.05 (t, 3H, *J*= 7.6 Hz), 1.50 (t, 3H, *J*= 7.2 Hz), 1.87 (sex, 2H, *J*= 7.6 Hz), 3.15 (t, 2H), 4.52 (q, 2H, *J*= 7.2 Hz), 7.51 (ddd, 1H, *J*= 8.0 Hz, *J*= 6.8 Hz, *J*= 1.2 Hz), 7.62 (d, 1H, *J*= 9.2 Hz,), 7.61 (ddd, 1H, *J*= 8.4 Hz, *J*= 6.8 Hz, *J*= 1.6 Hz), 7.75 (d, 1H, *J*= 8.8 Hz), 7.94 (d, 1H, *J*= 8.0 Hz), 9.15 (d, 1H, *J*= 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 14.3, 21.8, 30.8, 60.8, 111.5, 111.7, 120.3, 124.6, 125.9, 126.2, 126.3, 127.8, 128.7, 131.2, 151.5, 164.8, 165.1; IR (nujol): ν_{max} = 1709 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{19}O_3$ [M + H]$^+$: 283.1334; found: 283.1325.

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Supporting Information

Structures of starting materials (Figure S1), detailed reaction mechanism of gallic acid **1i** (Figure S2), ^{1}H- and ^{13}C- NMR spectra of benzofurans **3a–ac**, **6a,b**, alkyl 2-(4-hydroxyphenyl)-3-oxobutanoates **5a–c**, naphthofurans **6c–e**, and crystal data of compounds **3o**.

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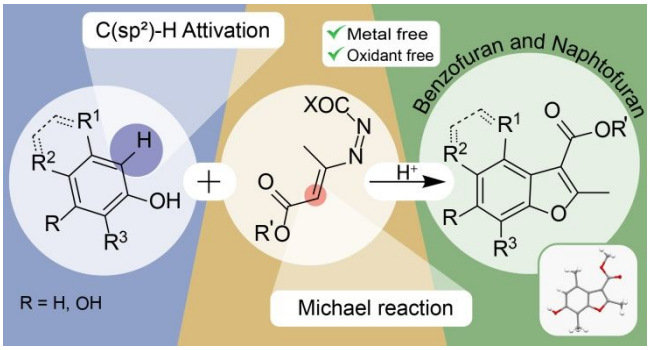
C(sp²)-H Attivation
Metal free
Oxidant free
Benzofuran and Naphtofuran
R = H, OH
Michael reaction