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Palladium-catalyzed decarboxylative C3-acylation of benzofurans and benzothiophenes with α-oxocarboxylic acids via direct sp^2 C–H bond activation

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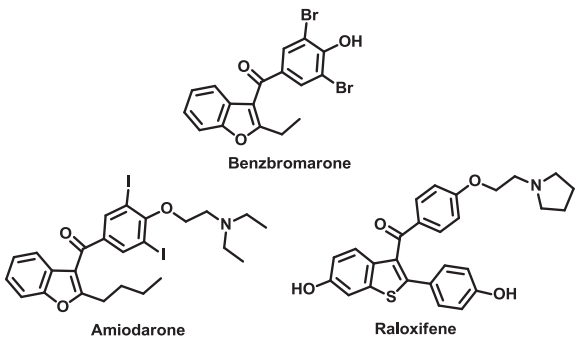
ABSTRACT

An efficient approach to decarboxylative C3-acylation of benzothiophenes or benzofurans with α-oxocarboxylic acids via palladium-catalyzed C–H bond activation was developed. This method was compatible with a variety of functional groups and provided an attractive route to 3-acylbenzothiophenes and 3-acylbenzofurans in good to high yields.

1. Introduction

The (hetero)aryl ketones are fundamental building blocks for natural products, medicinally-relevant molecules, and organic functional materials.[1] More specifically, acylbenzothiophene and acylbenzofuran have attracted considerable attention in the pharmaceutical chemistry.[2] For example, the 3-acylbenzofuran derivatives, benzbromarone, and amiodarone (Scheme 1), are employed as the uricosuricagent[3] and antiarrhythmic agents,[4] respectively. The aryl-benzothiophenyl ketone, raloxifene (Scheme 1), can be used as the vasodilator.[5] There are numerous synthetic approaches[6] to C2 or C3-acyl benzofuran and benzothiophene derivatives, including palladium-catalyzed cross-coupling reaction of arylboronic acids, carbon monoxide, and aryl iodides,[6a] photoreactions of arenecarbothioamides with benzofuran or benzothiophene in benzene,[6b] reduction, S-alkylation, re-oxidation, and cyclization of 2-mercaptobenzoic acids,[6c] reaction of benzothiophene with carboxylic acids and trifluoroacetic anhydride in the presence of H_3PO_4,[6d] reaction of *o*-thioalkyl and *o*-thioaryl substituted phenyl radicals with alkynes.[6e] Reaction of thiophenol with *n*-BuLi, dimethylformamide, and chloroacetone provided 2-acetylbenzothiophene.[6f] These methods required, a multistep synthesis of starting material, or the use of toxic carbon monoxide, unstable diazo compounds, and pyrophoric *n*-BuLi, and led to the formation of a mixture of regioisomers. Traditionally, the simple and straightforward method for the synthesis of acylbenzothiophenes or benzofurans appeared to be the Friedel–Crafts acylation reactions,[7] which, however, involved the use of excess $AlCl_3$, had poor regioselectivity, and led to the formation of environmentally harmful gaseous HCl. Therefore, screening out simple and practical



Scheme 1. Some structures of bioactive 3-acylbenzofuran and 3-acylbenzothiophene derivatives.

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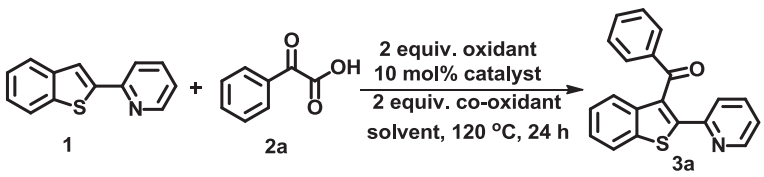
processes for the syntheses of acylbenzofuran and acylbenzothiophene remains a great challenge.

In the past decade, the decarboxylative acylation of unactivated arenes through metal-catalyzed C–H activation using α-oxocarboxylic acids as acylating resources[8] has been an attractive synthetic method for the formation of aryl ketones. Such methods did not require the use of stoichiometric organometallic coupling reagents and gave rise to CO_2 instead of toxic metal compounds. Ge and co-workers disclosed Pd-catalyzed decarboxylative C(sp^2)–H acylation of acetanilides, or 2-phenylpyridines or benzoic acids with α-oxocarboxylic acids.[9] After that the metal-mediated decarboxylative *ortho*-acylation of *O*-methyl ketoximes, phenylacetamides, *O*-phenyl carbamates, *O*-methyl oximes, azoxybenzenes, azobenzenes, 2-aryloxypyridines, cyclic enamides, (benzyl)(aryl)sulfane, and 2-phosphorylbiphenyl with α-oxocarboxylic acids have been reported.[10] As far as the decarboxylative acylation of heteroarenes by C–H functionalization is concerned, only indole, azole and their derivatives[11] have been explored. Although the decarboxylative arylation of benzofuran or benzothiophene has been well explored,[12] the Pd-catalyzed decarboxylative acylation of C(sp^2)–H bond has never been reported. Very recently, Beller and co-workers[13a] reported ruthenium-catalyzed carbonylative direct acylation of five-membered and condensed heterocycles with toxic carbon monoxide and aryliodides in moderate to good yields. Han and Pan et al.[13b] have demonstrated Pd-catalyzed C3-acylation of benzofurans and benzothiophenes by dehydrogenative coupling reaction using unstable aldehydes as acylating agents and chlorobenzene as a solvent. These limitations prompted chemists to develop new convenient methodology to get 3-acylbenzofurans and 3-acylbenzofurans. As an extension of our project on the oxidative decarboxylative coupling reactions,[14] we herein report an alternative protocol to achieve the C3-acylation of benzofuran and benzothiophene with the α-oxocarboxylic acid via palladium-catalyzed C(sp^2)–H activation.

2. Results and discussion

Our investigation started with the decarboxylative cross-coupling reaction of 2-(benzothiophen-2-yl)pyridine (**1**) and 2-oxophenylacetic acid (**2a**) in the presence of 10 mol % $Pd(PPh_3)_4$ with Ag_2CO_3 (2 equiv) as a decarboxylative reagent, $K_2S_2O_8$ (2 equiv) as the co-oxidant in 1,4-dioxane/HOAc/DMSO at 120 °C under air (Table 1). After 21 h, the desired product phenyl(2-(pyridin-2-yl)benzothiophen-3-yl)methanone (**3a**) could be obtained in 84% yield (entry 1). Encouraged by this initial result, we began to optimize the reaction conditions with respect to different palladium catalysts, oxidants, and solvents. The screening of catalysts indicated that for catalyzing the decarboxylative cross-coupling reactions of **1** with **2a**, $Pd(PPh_3)_4$ (entry 1) was more effective than $Pd(TFA)_2$ (TFA=trifluoroacetate), $PdCl_2$, $Pd(OAc)_2$, and $Pd_2(dba)_3$ (dba=dibenzylideneacetone) (entries 2–5). For the oxidants, Ag_2O (entry 6) seemed better than Ag_2CO_3 (entry 1), AgOAc and $Cu(OAc)_2$ (entries 7 and 8). It was noted that the yield of resulting product was dramatically increased from 87% to 96% (entry 5) when tetrabutyl ammonium bromide (TBAB) was added into the catalytic system (entry 10). The control experiments showed that $Pd(PPh_3)_4$, Ag_2O, and $K_2S_2O_8$ were required for this coupling reaction. As shown in Table 1 (entries 14–18), a strong solvent dependence of the acylation was observed. The yield of the desired product was very low in the absence of one of these three reagents. Solvent screening revealed that the optimal results could be obtained with a co-solvent of 1,4-dioxane/AcOH/DMSO in a volume ratio of 7.5:1.5:1, providing the product (**3a**) in 96% yield. The yield of **3a** decreased with reduced amount of Ag_2O or $K_2S_2O_8$. Therefore, the optimal reaction conditions were finally established as follow: 10 mol % $Pd(PPh_3)_4$, 2.0 equiv of Ag_2O, 2.0 equiv of $K_2S_2O_8$, and 1.0 equiv of TBAB in 7.5:1.5:1 1,4-dioxane/HOAc/DMSO at 120 °C under air.

Table 1
Optimization of the reaction conditions for the decarboxylative C3-acylation of 2-(benzothiophen-2-yl)pyridine with α-oxocarboxylic acid[a]



Entry	Cat.	Oxidant	Co-oxidant	Additive	1,4-Dioxane/HOAc/DMSO	Yield[b] (%)
1	$Pd(PPh_3)_4$	Ag_2CO_3	$K_2S_2O_8$		7.5:1.5:1	84
2	$Pd(TFA)_2$	Ag_2CO_3	$K_2S_2O_8$		7.5:1.5:1	79
3	$PdCl_2$	Ag_2CO_3	$K_2S_2O_8$		7.5:1.5:1	76
4	$Pd(OAc)_2$	Ag_2CO_3	$K_2S_2O_8$		7.5:1.5:1	73
5	$Pd_2(dba)_3$	Ag_2CO_3	$K_2S_2O_8$		7.5:1.5:1	78
6	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$		7.5:1.5:1	87
7	$Pd(PPh_3)_4$	AgOAc	$K_2S_2O_8$		7.5:1.5:1	40
8	$Pd(PPh_3)_4$	$Cu(OAc)_2$	$K_2S_2O_8$		7.5:1.5:1	28
9	$Pd(PPh_3)_4$	Ag_2O	$(NH_4)_2S_2O_8$		7.5:1.5:1	26
10	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	7.5:1.5:1	96
11		Ag_2O	$K_2S_2O_8$	TBAB	7.5:1.5:1	16
12	$Pd(PPh_3)_4$		$K_2S_2O_8$	TBAB	7.5:1.5:1	7
13	$Pd(PPh_3)_4$	Ag_2O		TBAB	7.5:1.5:1	28
14	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	1,4-Dioxane	22
15	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	DMSO	14
16	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	HOAc	15
17	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	7:2:1	73
18	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	4:1:—	62
19[c]	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	7.5:1.5:1	58
20[d]	$Pd(PPh_3)_4$	Ag_2O	$K_2S_2O_8$	TBAB	7.5:1.5:1	69

[a] Reaction conditions: **1** (0.1 mmol), **2a** (0.2 mmol), palladium reagent (0.01 mmol), oxidant (0.2 mmol), co-oxidant (0.2 mmol), 1.0 equiv of tetrabutyl ammonium bromide (TBAB), solvent (1.5 mL), 120 °C, 21 h.
[b] GC yields.
[c] Ag_2O (1.0 equiv).
[d] $K_2S_2O_8$ (1.0 equiv).

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With the optimized reaction conditions in hand, we turned our attention to investigate the scope of the decarboxylative acylation of 2-(benzothiophen-2-yl)pyridine with α-oxocarboxylic acids. The compatibility of substituted phenylglyoxylic acids was summarized in Table 2. Various 2-arylglyoxylic acids containing different functional groups in the aromatic ring showed high reactivity to give the corresponding products in good to high yields (**3a**–**3m**). Interestingly, high yields could be obtained with *p*-fiuoro (**3e**), *p*-chloro (**3f**), *p*-bromo (**3g**), and *m*-bromo (**3h**) substituted phenylglyoxylic acids, although it was not surprising that halogens were tolerated under the reaction conditions. However, the reaction did not show any obvious electronic preference. The electron-rich and electron-deficient 2-arylglyoxylic acids afforded the corresponding 3-acylbenzothiophene products **3b**–**3j** in 76–95% yield. Meanwhile, 2-(naphthalen-2-yl)-2-oxoacetic acid underwent the reaction smoothly to give the product **3k** in 84% yield. It is noteworthy that the heterocyclic α-keto acids such as 2-thienylglyoxylic acid and 2-furylglyoxylic acid also provided bisheteroaryl ketone products (**3l** and **3m**) in moderate yields (64% and 67%).

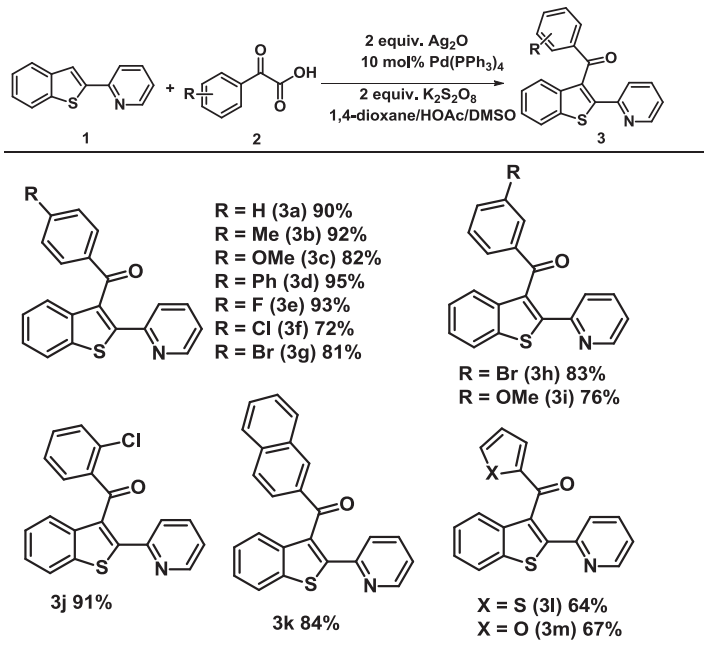
Encouraged by the high efficiency for the reactions of 2-(benzothiophen-2-yl)pyridine with α-oxocarboxylic acids described above, we also investigated the decarboxylative acylation reactions of 2-(benzofuran-2-yl)pyridine (**4**) with various phenylglyoxylic acids under the optimal reaction conditions. The reaction of **4** and **2a** catalyzed by $Pd(PPh_3)_4$ in the presence of Ag_2CO_3 and $K_2S_2O_8$ in 1,4-dioxane/HOAc/DMSO produced phenyl(2-(pyridin-2-yl)benzofuran-3-yl)methanone in 71% yield. When Ag_2CO_3 was replaced by Ag_2O, the similar reaction gave the product in 78% yield. In the case of the solvent, the reaction carried out in 1,4-dioxane/HOAc/DMF gave higher yields (90%) than that in 1,4-dioxane/HOAc/DMSO. The 2-arylglyoxylic acids containing different functional groups in the aromatic ring also showed good reactivity to give the products in good to high yields (**5a**–**5m**), using Ag_2CO_3 as a decarboxylative reagent, $K_2S_2O_8$ as a co-oxidant in 1,4-dioxane/HOAc/DMF (v/v/v=7.5:1.5:1) at 120 °C in air. The electron-rich and -neutral 2-arylglyoxylic acids proceeded smoothly to form the corresponding 3-acylbenzofurans in more than 90% isolated yields (**5a**–**5d** and **5i**). However, the moderate yields were observed for 2-arylglyoxylic acids with electron-withdrawing groups such as fluoro (**5e**, 77%), chloro (**5f**, 71%) or bromo groups (**5g**, 73%; **5h**, 71%). It seemed that the *o*-substituted chloro group on phenyl rings of 2-oxophenylacetic acid did not hamper the decarboxylative acylation reaction (**5j**, 90%). For the heteroaromatic α-oxocarboxylic acids such as 2-thienylglyoxylic acid and 2-furylglyoxylic acid, the corresponding 2-thienyl- and 2-furyl-benzofuryl ketones were obtained in 74% and 79% isolated yields, respectively (Table 3).

According to the previous reports,[10,11] we propose the possible catalytic reaction mechanism (Scheme 2) to account for the aforementioned results. Firstly, the *ortho*-palladation of **1** or **4** with Pd(II) to provide the five-membered palladacycle intermediate **I**. Secondly, the intermediate **I** reacts with the intermediate **II**, which is formed from the silver-mediated decarboxylation of **2**, to generate the acyl–Pd(II) intermediate **III**. Thirdly, the intermediate **III** undergoes the reductive elimination to produce the desired ketone product and Pd(0). Finally, the regenerated Pd(0) catalyst can be re-oxidized into the active Pd(II) catalyst with $K_2S_2O_8$, thereby furnishing the catalytic cycle.

3. Conclusions

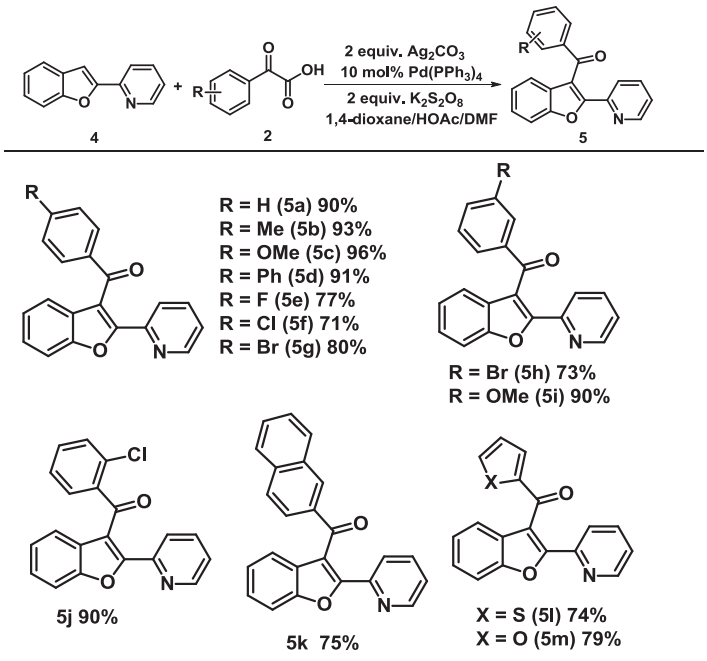
In summary, we have demonstrated an efficient approach to the decarboxylative C3-acylation of benzofurans and benzothiophenes with α-oxocarboxylic acids via palladium-catalyzed C–H activation. The remarkable features of this methodology include good product yields and wide tolerance of various functional groups. It provides a highly versatile alternative to the existing methods for building the biologically important C3-acylated benzofuran and benzothiophene units. It is also applicable to the synthesis of more pharmacologically important benzofuran and benzothiophene derivatives.

Table 2
Palladium-catalyzed C3-acylation of 2-(benzo[*b*]thiophen-2-yl)pyridine with α-oxocarboxylic acids[a]



[a] Reaction conditions: **1** (0.1 mmol), **2** (0.2 mmol), $Pd(PPh_3)_4$ (0.01 mmol), Ag_2O (0.2 mmol), $K_2S_2O_8$ (0.2 mmol), 1,4-dioxane/HOAc/DMSO (7.5/1.5/1, 1.5 mL), 120 °C, 21 h; isolated yield.

Table 3
Palladium-catalyzed C3-acylation of 2-(benzofuran-2-yl)pyridine with α-oxocarboxylic acids[a]

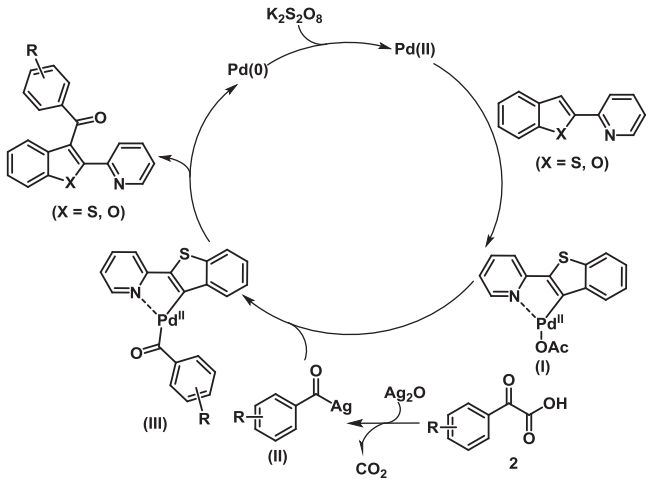


[a] Reaction conditions: **4** (0.1 mmol), **2** (0.2 mmol), $Pd(PPh_3)_4$ (0.01 mmol), Ag_2CO_3 (0.2 mmol), $K_2S_2O_8$ (0.2 mmol), 1,4-dioxane/HOAc/DMF (7.5/1.5/1, 1.5 mL), 120 °C, 21 h; isolated yield.

4. Experimental

4.1. General

All reactions were performed under air atmosphere unless stated otherwise. Commercially available reagents were used as received without purification. Pyridine was distilled from CaH_2. 2-(Benzo[*b*]thiophen-2-yl)pyridine and 2-(benzofuran-2-yl)pyridine were prepared according to the literature.[13b] α-Oxocarboxylic acids were synthesized according to the reported method.[15] Column chromatography was carried out on silica gel (300–400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a Varian NITYplus-400. $CDCl_3$ and DMSO-d_6 were used as deuterated solvents. The chemical shifts δ were reported as parts per million (ppm) relative to, respectively, the TMS as the internal standard. Resonance patterns were reported with the notations of s (singlet), d (doublet), and m (multiplet). In addition, coupling constants *J* were reported in hertz (Hz). The uncorrected melting points were re-determined on a Mel-Temp II apparatus.



Scheme 2. The proposed reaction mechanism.

4.2. General procedure for the acylation of benzothiophene or benzofuran with α-oxocarboxylic acid

A sealed reaction tube equipped with a magnetic stirring bar was charged with 2-(benzothiophen-2-yl)pyridine (0.1 mmol), α-oxocarboxylic acids (0.2 mmol), $K_2S_2O_8$ (0.2 mmol), tetrabutyl ammonium bromide (TBAB) (0.1 mmol), Ag_2O (0.2 mmol), and $Pd(PPh_3)_4$ (0.01 mmol) in 1,4-dioxane/HOAc/DMSO (1.5 mL; v/v/v=7.5:1.5:1). The reaction mixture was stirred vigorously at 120 °C in an oil bath for 21 h. Then it was cooled to room temperature and diluted with ethyl acetate and filtered. After the filtrate was concentrated under reduced pressure, the residue was purified through the flash column chromatography on silica gel to afford the desired products.

*4.2.1. 2-(Benzo[b]thiophen-2-yl)pyridine (**1**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.65–8.63 (m, 1H), 7.88–7.86 (m, 2H), 7.82–7.80 (m, 2H), 7.76–7.73 (m, 1H), 7.38–7.33 (m, 2H), 7.23–7.20 (m, 1H). ^{13}C NMR (400 MHz, $CDCl_3$): δ=152.5, 149.6, 144.6, 140.8, 140.6, 136.9, 125.2, 124.6, 124.3, 122.7, 122.7, 121.4, 119.8 ppm.

*4.2.2. 2-(Benzofuran-2-yl)pyridine (**4**).* ^{1}H NMR (400 MHz, DMSO-d_6): δ=8.65–8.63 (m, 1H), 7.88–7.86 (m, 2H), 7.82–7.80 (m, 2H), 7.76–7.73 (m, 1H), 7.38–7.33 (m, 2H), 7.23–7.20 (m, 1H) ppm. ^{13}C NMR (400 MHz, DMSO-d_6): δ=155.3, 155.1, 150.4, 148.7, 137.7, 128.9, 125.8, 123.9, 123.9, 122.3, 120.0, 111.9, 105.2 ppm.

*4.2.3. Phenyl(2-(pyridine-2-yl)benzo[b]thiophen-3-yl)methanone (**3a**).* Yellow solid. Mp 74–75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.48–8.47 (m, 1H), 7.92 (d, *J*=4.0 Hz, 1H), 7.87 (d, *J*=4.0 Hz, 2H),

7.63 (d, *J*=8.0 Hz, 1H), 7.52–7.46 (m, 2H), 7.43–7.39 (m, 2H), 7.36–7.32 (m, 3H), 7.09–7.07 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=194.8, 151.2, 149.5, 143.8, 139.6, 139.5, 137.5, 136.5, 133.5, 133.1, 129.7, 128.6, 125.7, 125.1, 123.7, 122.8, 122.7, 122.3 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=316.1; found: 316.1.

*4.2.4. (2-(Pyridin-2-yl)benzo[b]thiophen-3-yl)(p-tolyl)methanone (**3b**).* Yellow solid. Mp 104–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.52 (d, *J*=4.0 Hz, 1H), 7.91 (d, *J*=8.0 Hz, 1H), 7.78 (d, *J*=8.0 Hz, 2H), 7.58 (d, *J*=8.0 Hz, 1H), 7.51–7.49 (m, 1H), 7.45–7.30 (m, 3H), 7.15–7.08 (m, 3H), 2.34 (s, 3H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=194.6, 151.2, 149.4, 144.7, 143.3, 139.6, 139.5, 136.6, 134.9, 133.4, 129.9, 129.4, 125.7, 125.0, 123.7, 123.8, 122.7, 122.3, 21.7 ppm. LC-MS (EI): *m*/*z* calcd $[M+1]^+$=330.1; found: 330.1.

*4.2.5. (4-Methoxyphenyl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3c**).* Yellow solid. Mp 99–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.54–8.53 (m, 1H), 7.91 (d, *J*=8.0 Hz, 1H), 7.86 (d, *J*=8.0 Hz, 2H), 7.58 (d, *J*=8.0 Hz, 1H), 7.54–7.51 (m, 1H), 7.46–7.44 (m, 1H), 7.39 (t, *J*=8.0 Hz, 1H), 7.34–7.31 (m, 1H), 7.13–7.10 (m, 1H), 6.82 (d, *J*=8.0 Hz, 2H), 3.80 (s, 3H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=193.5, 164.0, 151.2, 149.4, 143.0, 139.7, 139.6, 136.6, 133.4, 132.2, 130.3, 125.6, 123.0, 123.6, 122.8, 122.6, 122.3, 113.9, 55.4 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=346.1; found: 346.1.

*4.2.6. [1,1′-Biphenyl](2-(pyridin-2-yl)benzo[b]thiophen-3-yl)methanone (**3d**).* White solid. Mp 134–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.54 (d, *J*=4.0 Hz, 1H), 7.95–7.93 (m, 3H), 7.67–7.65 (m, 1H), 7.58–7.56 (m, 5H), 7.50–7.35 (m, 6H), 7.14–7.11 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=194.3, 150.9, 149.2, 146.1, 143.1, 139.6, 139.6, 139.5, 136.9, 136.1, 133.5, 130.3, 128.9, 128.3, 127.2, 125.8, 125.2, 123.7, 123.0, 123.0, 122.4 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=392.1; found: 392.1.

*4.2.7. (4-Fluorophenyl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3e**).* Yellow solid. Mp 169–170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.60–8.58 (m, 1H), 7.93–7.91 (m, 1H), 7.77 (t, *J*=8.0 Hz, 1H), 7.68–7.65 (m, 2H), 7.62–7.60 (m, 1H), 7.49–7.48 (m, 1H), 7.45–7.41 (m, 1H), 7.32–7.28 (m, 1H), 7.25–7.24 (m, 1H), 7.00–7.98 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=193.1, 165.9 (d, *J*=254.0 Hz), 150.9, 149.3, 143.3, 139.4 (d, *J*=17.0 Hz), 136.9, 134.0 (d, *J*=3.0 Hz), 133.0, 132.3 (d, *J*=10.0 Hz), 125.9, 125.3, 123.6, 123.0, 122.9, 122.4, 115.9, 115.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=334.1; found: 334.0.

*4.2.8. (4-Chlorophenyl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3f**).* White solid. Mp 129–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.47–8.46 (m, 1H), 7.92 (d, *J*=8.0 Hz, 1H), 7.80 (d, *J*=8.0 Hz, 2H), 7.63–7.55 (m, 2H), 7.46–7.34 (m, 3H), 7.30 (d, *J*=8.0 Hz, 2H), 7.14–7.11 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=193.3, 150.8, 149.2, 143.2, 139.8, 139.5, 139.3, 137.0, 136.0, 132.9, 130.9, 128.9, 125.9, 125.3, 123.6, 123.1, 122.9, 122.4 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=350.0; found: 350.0.

*4.2.9. (4-Bromophenyl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3g**).* White solid. Mp 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.46 (d, *J*=4.0 Hz, 1H), 7.92 (d, *J*=8.0 Hz, 1H), 7.73–7.71 (m, 2H), 7.63–7.56 (m, 2H), 7.48–7.34 (m, 5H), 7.14–7.11 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=195.5, 150.8, 149.2, 143.3, 139.5, 139.3, 136.9, 136.4, 132.9, 131.9, 131.0, 128.6, 125.9, 125.3, 123.6, 123.0, 122.8, 122.4 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=394.0; found: 394.0.

*4.2.10. (3-Bromophenyl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3h**).* Yellow solid. Mp 117–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.44–8.43 (m, 1H), 8.04 (s, 1H), 7.92 (d, *J*=8.0 Hz, 1H), 7.70–7.64 (m, 2H), 7.57 (t, *J*=8.0 Hz, 2H), 7.45–7.35 (m, 3H), 7.18–7.15 (m, 1H), 7.11–7.08 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=193.18, 150.8, 149.3, 143.8, 139.5, 139.4, 139.3, 136.8, 136.0, 132.6, 132.0, 130.1, 128.3, 125.9, 125.4, 123.6, 123.0, 122.8, 122.7, 122.4 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=394.0; found: 394.0.

*4.2.11. (3-Methoxyphenyl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3i**).* Yellow solid. Mp 137–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.51–8.50 (m, 1H), 7.92 (d, *J*=4.0 Hz, 1H), 7.64 (d, *J*=4.0 Hz, 1H), 7.55–7.51 (m, 2H), 7.45–7.39 (m, 2H), 7.36–7.33 (m, 2H), 7.19 (t, *J*=4.0 Hz, 1H), 7.12–7.10 (m, 1H), 7.04–7.02 (m, 1H), 3.79 (s, 3H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=194.5, 159.8, 151.1, 149.3, 143.5, 139.5, 139.5, 138.8, 136.7, 133.3, 129.6, 125.8, 125.1, 123.7, 122.9, 122.9, 122.8, 122.3, 120.4, 113.0, 55.4 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=346.1; found: 346.1.

*4.2.12. (2-Chlorophenyl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3j**).* Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.49–8.48 (m, 1H), 8.00–7.98 (m, 1H), 7.91–7.90 (m, 1H), 7.58–7.55 (m, 1H), 7.49–7.47 (m, 1H), 7.45–7.43 (m, 2H), 7.41 (d, *J*=8.0 Hz, 1H), 7.29–7.26 (m, 1H), 7.22–7.19 (m, 1H), 7.09 (t, *J*=4.0 Hz, 1H), 7.07–7.04 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=191.5, 150.8, 149.0, 147.0, 139.2, 139.1, 138.3, 136.5, 133.5, 133.2, 132.1, 131.4, 130.7, 126.3, 125.9, 125.6, 124.2, 123.9, 122.1, 122.2 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=350.0; found: 350.0.

*4.2.13. (Naphthalen-2-yl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl) methanone (**3k**).* Yellow solid. Mp 100–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.43–8.41 (m, 1H), 8.16 (d, *J*=8.0 Hz, 1H), 7.88 (d, *J*=8.0 Hz, 2H), 7.82–7.78 (m, 1H), 7.73–7.63 (m, 6H), 7.58–7.49 (m, 3H), 7.45–7.41 (m, 1H), 7.30–7.27 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=193.2, 167.1, 150.4, 149.9, 143.3, 139.2, 139.1, 138.0, 136.6, 132.8, 132.5, 132.2, 131.8, 131.2, 130.5, 128.2, 127.4, 126.6, 126.1, 124.0, 123.4, 122.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=366.1; found: 366.1.

*4.2.14. (2-(Pyridin-2-yl)benzo[b]thiophen-3-yl)(thiophen-2-yl)methanone (**3l**).* Yellow solid. Mp 47–49 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.58–8.57 (m, 1H), 7.91 (d, *J*=8.0 Hz, 1H), 7.74 (d, *J*=8.0 Hz, 1H), 7.64–7.57 (m, 2H), 7.54–7.52 (m, 1H), 7.44–7.36 (m, 3H), 7.18–7.15 (m, 1H), 6.93–6.91 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=186.6, 151.1, 149.4, 144.7, 143.8, 139.5, 139.3, 136.8, 135.4, 135.2, 132.8, 128.3, 125.8, 125.1, 123.6, 123.0, 123.0, 122.3 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=322.0; found: 322.0.

*4.2.15. (Furan-2-yl)(2-(pyridin-2-yl)benzo[b]thiophen-3-yl)methanone (**3m**).* Yellow solid. Mp 108–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.58–8.57 (m, 1H), 7.91 (d, *J*=8.0 Hz, 1H), 7.81 (d, *J*=8.0 Hz, 1H), 7.61 (t, *J*=8.0 Hz, 1H), 7.51–7.48 (m, 2H), 7.42–7.40 (m, 2H), 7.19–7.16 (m, 1H), 6.92–6.91 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=180.8, 152.9, 151.2, 149.2, 147.5, 144.5, 139.5, 139.2, 137.1, 132.1, 125.9, 125.3, 123.6, 123.3, 123.1, 122.3, 121.0, 112.5 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=306.1; found: 306.0.

*4.2.16. Phenyl(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5a**).* Yellow solid. Mp 146–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.43–8.42 (m, 1H), 7.90 (d, *J*=8.0 Hz, 2H), 7.84 (d, *J*=8.0 Hz, 1H), 7.70–7.64 (m, 2H), 7.56–7.48 (m, 2H), 7.43–7.34 (m, 3H), 7.30–7.28 (m, 1H), 7.17–7.14 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=192.4, 154.3, 153.2, 149.6, 147.9, 138.0, 136.7, 133.1, 129.6, 128.4, 128.2, 126.2, 124.0, 123.5, 122.2, 121.4, 118.6, 111.7 ppm. LC-MS (EI): *m*/*z* calcd $[M+1]^+$=300.1; found: 300.1.

*4.2.17. (2-(Pyridin-2-yl)benzofuran-3-yl)(p-tolyl)methanone (**5b**).* Yellow solid. Mp 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.50–8.49 (m, 1H), 7.86 (d, *J*=8.0 Hz, 1H), 7.82 (d, *J*=4.0 Hz, 2H), 7.72–7.69 (m, 1H), 7.65 (d, *J*=4.0 Hz, 1H), 7.49 (d, *J*=4.0 Hz, 1H),

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7.41–7.39 (m, 1H), 7.27–7.25 (m, 1H), 7.20–7.16 (m, 3H), 2.37 (s, 3H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=191.9, 154.2, 152.7, 149.3, 147.7, 144.2, 137.0, 135.3, 129.8, 129.2, 128.2, 126.2, 123.9, 123.4, 122.2, 121.4, 119.1, 111.7, 21.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=314.1; found: 314.1.

*4.2.18. (4-Methoxyphenyl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5c**).* Yellow solid. Mp 44–45 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.53–8.52 (m, 1H), 7.91 (d, *J*=4.0 Hz, 2H), 7.86 (d, *J*=8.0 Hz, 1H), 7.73–7.69 (m, 1H), 7.65 (d, *J*=8.0 Hz, 1H), 7.49 (d, *J*=8.0 Hz, 1H), 7.40 (t, *J*=8.0 Hz, 1H), 7.28–7.25 (m, 1H), 7.21–7.19 (m, 1H), 6.87–6.84 (m, 2H), 3.83 (s, 3H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=190.8, 163.8, 154.2, 152.4, 149.4, 147.8, 136.9, 132.1, 130.8, 128.3, 126.2, 123.9, 123.4, 121.3, 119.0, 113.7, 113.6, 111.7, 55.5 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=330.1; found: 330.1.

*4.2.19. [1,1′-Biphenyl](2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5d**).* Yellow solid. Mp 129–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.46–8.45 (m, 1H), 7.98 (d, *J*=8.0 Hz, 2H), 7.87 (d, *J*=8.0 Hz, 1H), 7.71–7.64 (m, 2H), 7.59–7.56 (m, 5H), 7.45–7.37 (m, 4H), 7.31–7.25 (m, 1H), 7.17–7.14 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=191.9, 154.2, 153.2, 149.4, 147.8, 145.7, 139.8, 136.8, 136.7, 130.2, 128.9, 128.2, 127.2, 127.0, 126.2, 124.0, 123.5, 122.1, 121.4, 118.7, 111.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=376.1; found: 376.1.

*4.2.20. (4-Fluorophenyl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5e**).* Yellow solid. Mp 151–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.40–8.39 (m, 1H), 7.95–7.91 (m, 2H), 7.85 (d, *J*=8.0 Hz, 1H), 7.70 (t, *J*=8.0 Hz, 1H), 7.63 (d, *J*=8.0 Hz, 1H), 7.55 (d, *J*=8.0 Hz, 1H), 7.41 (t, *J*=8.0 Hz, 1H), 7.31–7.26 (m, 1H), 7.17–7.14 (m, 1H), 7.02 (t, *J*=8.0 Hz, 2H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=190.8, 165.7 (d, *J*=253.0 Hz), 154.2, 153.4, 149.5, 147.8, 136.7, 134.5 (d, *J*=3.0 Hz), 132.1 (d, *J*=9.0 Hz), 128.1, 126.2, 124.1, 123.5, 122.0, 121.2, 118.2, 115.5 (d, *J*=22.0 Hz), 116.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=318.1; found: 318.1.

*4.2.21. (4-Chlorophenyl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5f**).* Yellow solid. Mp 160–162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.37–8.36 (m, 1H), 7.87–7.83 (m, 3H), 7.70 (t, *J*=8.0 Hz, 1H), 7.63 (d, *J*=8.0 Hz, 1H), 7.55 (d, *J*=8.0 Hz, 1H), 7.41 (t, *J*=8.0 Hz, 1H), 7.33–7.29 (m, 3H), 7.17–7.13 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=191.2, 154.2, 153.6, 149.6, 147.9, 139.3, 136.5, 136.5, 130.8, 128.7, 128.1, 126.2, 124.1, 123.5, 121.8, 121.2, 117.9, 111.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=334.1; found: 334.0.

*4.2.22. (4-Bromophenyl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5g**).* Yellow solid. Mp 147–149 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.37 (br, 1H), 7.87–7.86 (m, 1H), 7.76 (d, *J*=8.0 Hz, 2H), 7.71 (t, *J*=4.0 Hz, 1H), 7.63 (d, *J*=8.0 Hz, 1H), 7.56–7.55 (m, 1H), 7.59 (d, *J*=8.0 Hz, 2H), 7.43–7.40 (m, 1H), 7.31–7.28 (m, 1H), 7.16 (t, *J*=4.0 Hz, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=191.4, 154.3, 153.7, 149.6, 147.9, 137.0, 136.5, 131.7, 130.9, 128.1, 126.2, 124.1, 123.5, 121.7, 121.2, 117.8, 111.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=378.0; found: 378.0.

*4.2.23. (3-Bromophenyl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5h**).* Yellow solid. Mp 112–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.38–8.36 (m, 1H), 8.05–8.04 (m, 1H), 7.88–7.86 (m, 1H), 7.76–7.70 (m, 2H), 7.65–7.58 (m, 3H), 7.45–7.41 (m, 1H), 7.33–7.26 (m, 1H), 7.22–7.15 (m, 2H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=190.9, 154.3, 154.0, 149.4, 147.7, 140.0, 136.6, 135.7, 132.1, 129.9, 128.1, 128.0, 126.3, 124.2, 123.6, 122.6, 121.9, 121.2, 117.8, 111.7 ppm. LC-MS (EI): *m*/*z* calcd $[M+1]^+$=378.0; found: 378.0.

*4.2.24. (3-Methoxyphenyl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5i**).* Yellow solid. Mp 103–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.46–8.45 (m, 1H), 7.83–7.81 (m, 1H), 7.70–7.63 (m, 2H), 7.57–7.55 (m, 1H), 7.52 (s, 1H), 7.42–7.40 (m, 2H), 7.31–7.29 (m, 1H), 7.23–7.15 (m, 2H), 7.06–7.04 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=192.1, 159.7, 154.2, 153.6, 149.5, 148.0, 139.3, 136.5, 129.3, 128.2, 126.1, 124.0, 123.4, 122.7, 122.1, 121.4, 120.0, 118.5, 113.0, 111.6, 55.4 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=330.1; found: 330.1.

*4.2.25. (2-Chlorophenyl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5j**).* Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.44–8.43 (m, 1H), 7.83 (d, *J*=8.0 Hz, 1H), 7.79 (d, *J*=4.0 Hz, 1H), 7.70–7.67 (m, 1H), 7.64 (d, *J*=4.0 Hz, 1H), 7.47–7.46 (m, 1H), 7.43 (t, *J*=4.0 Hz, 1H), 7.36–7.33 (m, 1H), 7.31–7.30 (m, 1H), 7.27–7.24 (m, 1H), 7.19–7.17 (m, 1H), 7.13 (t, *J*=4.0 Hz, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=190.6, 156.5, 154.3, 148.8, 147.4, 139.3, 136.7, 132.3, 131.6, 130.4, 130.2, 127.2, 126.4, 126.3, 124.5, 123.9, 123.6, 122.1, 119.3, 111.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=334.1; found: 334.0.

*4.2.26. (Naphthalen-2-yl)(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5k**).* Yellow solid. Mp 116–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.88–8.86 (m, 1H), 8.12–8.11 (m, 1H), 7.86 (d, *J*=8.0 Hz, 2H), 7.74–7.62 (m, 5H), 7.58–7.54 (m, 1H), 7.50–7.40 (m, 2H), 7.33–7.30 (m, 1H), 7.19 (t, *J*=8.0 Hz, 1H), 7.00–6.97 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=193.8, 155.4, 154.2, 149.3, 147.9, 136.8, 136.1, 133.7, 132.5, 131.0, 129.4, 128.2, 128.18, 127.9, 126.4, 126.1, 126.1, 124.2, 124.1, 123.3, 122.4, 121.7, 120.4, 111.6 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=350.1; found: 350.1.

*4.2.27. (2-(Pyridin-2-yl)benzofuran-3-yl)(thiophen-2-yl)methanone (**5l**).* Yellow solid, mp 133–134 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.60–8.58 (m, 1H), 7.93–7.91 (m, 1H), 7.77 (t, *J*=8.0 Hz, 1H), 7.68–7.65 (m, 2H), 7.62–7.60 (m, 1H), 7.49–7.48 (m, 1H), 7.42–7.41 (m, 1H), 7.32–7.29 (m, 1H), 7.25–7.24 (m, 1H), 7.00–6.98 (m, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=184.0, 154.2, 152.5, 149.3, 147.5, 144.8, 137.3, 134.8, 134.7, 128.1, 127.9, 126.4, 124.1, 123.7, 122.4, 121.3, 119.0, 111.8 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=306.1; found: 306.0.

*4.2.28. Furan-2-yl(2-(pyridin-2-yl)benzofuran-3-yl)methanone (**5m**).* Yellow solid, mp 143–144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.1–8.49 (m, 1H), 7.89 (d, *J*=8.0 Hz, 1H), 7.72 (t, *J*=8.0 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 1H), 7.62 (d, *J*=8.0 Hz, 1H), 7.47 (br s, 1H), 7.41 (t, *J*=8.0 Hz, 1H), 7.33–7.30 (m, 1H), 7.22–7.19 (m, 1H), 7.07–7.06 (m, 1H), 6.44 (br s, 1H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ=178.9, 154.2, 153.9, 153.2, 149.4, 148.0, 146.8, 136.9, 127.8, 126.2, 124.1, 123.5, 122.2, 121.3, 119.6, 117.8, 112.4, 111.7 ppm. LC–MS (EI): *m*/*z* calcd $[M+1]^+$=290.1; found: 290.0.

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Supplementary data

The ^{1}H and ^{13}C NMR spectra for the isolated products. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.12.095.

References and notes

1. (a) Dadiboyena, S. *Eur. J. Med. Chem.* **2012**, *51*, 17; (b) Waterman, P. G.; Mohammad, I. *J. Chem. Soc., Chem. Commun.* **1984**, 1280; (c) Matsumoto, K.; Choshi, T.; Hourai, M.; Zamami, Y.; Sasaki, K.; Abe, T.; Ishikura, M.; Hatae, N.; Iwamura, T.; Tohyama, S.; Nobuhiro, J.; Hibino, S. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 4762; (d) Clive, D. L. J.; Cheng, P. *Tetrahedron* **2013**, *69*, 5067; (e) Cheng, P.; Clive, D. L. J.; Fernandopulle, S.; Chen, Z. *Chem. Commun.* **2013**, 558; (f) Yamanaka, K.; Ryan, K. S.; Gulder, T. A. M.; Hughes, C. C.; Moore, B. S. *J. Am. Chem. Soc.* **2012**, *134*, 12434; (g) Nicolaou, K. C.; Simmons, N. L.; Chen, J. S.; Haste, N. M.; Nizet, V. *Tetrahedron Lett.* **2011**, *52*, 2041; (h) Kanakis, A. A.; Sarli, V. *Org. Lett.* **2010**, *12*, 4872.
2. (a) Jiang, X.; Liu, W.; Zhang, W.; Jiang, F.; Gao, Z.; Zhuang, H.; Fu, L. *Eur. J. Med. Chem.* **2011**, *46*, 3526; (b) Flynn, B. L.; Gill, G. S.; Grobelny, D. W.; Chaplin, J. H.; Paul, D.; Leske, A. F.; Lavranos, T. C.; Chalmers, D. K.; Charman, S. A.; Kostewicz, E.; Shackleford, D. M.; Morizzi, J.; Hamel, E.; Jung, M. K.; Kremmidiotis, G. *J. Med. Chem.* **2011**, *54*, 6014.
3. Heel, R. C.; Brogden, R. N.; Speight, T. M.; Avery, G. S. *Drugs* **1977**, *14*, 349.
4. Mason, J. J. *N. Engl. J. Med.* **1987**, *316*, 455.
5. Balfour, J. A.; Goa, K. L. *Drug Aging* **1998**, *12*, 335.
6. (a) Ishiyama, T.; Kizaki, H.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1993**, *34*, 7595; (b) Oda, K.; Machida, M. *Chem. Pharm. Bull.* **1993**, *41*, 1299; (c) Gallagher, T.; Pardoe, D. A.; Porter, R. A. *Tetrahedron Lett.* **2000**, *41*, 5415; (d) Pal, S.; Khan, M. A.; Bindu, P.; Dubey, P. *Beilstein J. Org. Chem.* **2007**, *3*, 35; (e) Leardini, R.; Pedulli, G. F.; Tundo, A.; Zanardi, G. *J. Chem. Soc., Chem. Commun.* **1985**, 1390; (f) Basha, A.; Brooks, D. W. *J. Org. Chem.* **1993**, *58*, 1293.
7. (a) Mitsumori, S.; Tsuri, T.; Honma, T.; Hiramatsu, Y.; Okada, T.; Hashizume, H.; Kida, S.; Inagaki, M.; Arimura, A.; Yasui, K. *J. Med. Chem.* **2003**, *46*, 2446; (b) Gaertner, R. *J. Am. Chem. Soc.* **1952**, *74*, 2185.
8. (a) Gooßen, L. J.; Rudolphi, F.; Oppel, C.; Rodríguez, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 3043; (b) Li, M. Z.; Wang, C.; Ge, H. B. *Org. Lett.* **2011**, *13*, 2062.
9. (a) Fang, P.; Li, M. Z.; Ge, H. B. *J. Am. Chem. Soc.* **2010**, *132*, 11898; (b) Li, M. Z.; Ge, H. B. *Org. Lett.* **2010**, *12*, 3464; (c) Miao, J.; Ge, H. B. *Org. Lett.* **2013**, *15*, 2930.
10. (a) Kim, M.; Park, J.; Sharma, S.; Kim, A.; Park, E.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Chem. Commun.* **2013**, 925; (b) Park, J.; Kim, M.; Sharma, S.; Park, E.; Kim, A.; Lee, S. H.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Chem. Commun.* **2013**, 1654; (c) Sharma, S.; Kim, A.; Park, E.; Park, J.; Kim, M.; Kwak, J. H.; Lee, S. H.; Jung, Y. H.; Kim, I. S. *Adv. Synth. Catal.* **2013**, *355*, 667; (d) Yang, Z. Y.; Chen, X.; Liu, J. D.; Gui, Q. W.; Xie, K.; Li, M. M.; Tan, Z. *Chem. Commun.* **2013**, 1560; (e) Li, H. J.; Li, P. H.; Zhao, Q.; Wang, L. *Chem. Commun.* **2013**, 9170; (f) Li, Z. Y.; Li, D. D.; Wang, G. W. *J. Org. Chem.* **2013**, *78*, 10414; (g) Yao, J.; Feng, R.; Wu, Z.; Liu, Z.; Zhang, Y. *Adv. Synth. Catal.* **2013**, *355*, 1517; (h) Wang, H.; Guo, L. N.; Duan, X. H. *Org. Lett.* **2012**, *14*, 4358; (i) Xu, B.; Liu, W.; Kuang, C. X. *Eur. J. Org. Chem.* **2014**, 2576; (j) Ma, Y. N.; Tian, Q. P.; Zhang, H. Y.; Zhou, A. X.; Yang, S. D. *Org. Chem. Front.* **2014**, *1*, 284.
11. (a) Yu, L.; Li, P. P.; Wang, L. *Chem. Commun.* **2013**, 2368; (b) Wang, C. P.; Wang, S. Y.; Li, H.; Yan, J. B.; Chi, H. J.; Chen, X. C.; Zhang, Z. Q. *Org. Biomol. Chem.* **2014**, *12*, 1721; (c) Pan, C. D.; Jin, H. M.; Liu, X.; Cheng, Y. Y.; Zhu, C. J. *Chem. Commun.* **2013**, 2933; (d) Yang, K.; Zhang, C.; Wang, P.; Zhang, Y.; Ge, H. B. *Chem.—Eur. J.* **2014**, *20*, 7241.
12. (a) Roger, J.; Gottumukkala, A. L.; Doucet, H. *ChemCatChem* **2010**, *2*, 20 and references cited therein; (b) Tang, D.-T. D.; Collins, K. D.; Ernst, J. B.; Glorius, F. *Angew. Chem., Int. Ed.* **2014**, *53*, 1809; (c) Wu, Y.; Wang, J.; Mao, F.; Kwong, F. Y. *Chem. Asian J.* **2014**, *9*, 26; (d) Funaki, K.; Sato, T.; Oi, S. *Org. Lett.* **2012**, *14*, 6186; (e) Biajoli, A. F. P.; Penha, E. T. d.; Correia, C. R. D. *RSC Adv.* **2012**, *2*, 11930.
13. (a) Pospech, J.; Tlili, A.; Spannenberg, A.; Neumann, H.; Beller, M. *Chem.—Eur. J.* **2014**, *20*, 3135; (b) Zhao, J. C.; Fang, H.; Xie, C.; Han, J. L.; Li, G. G.; Pan, Y. *Asian J. Org. Chem.* **2013**, *2*, 1044.
14. (a) Liu, D. X.; Li, F. L.; Li, H. X.; Gong, W. J.; Gao, J.; Lang, J. P. *Eur. J. Org. Chem.* **2014**, 4817; (b) Liu, D. X.; Li, F. L.; Li, H. X.; Gao, J.; Lang, J. P. *Tetrahedron* **2014**, *70*, 2416.
15. Zhuang, J.; Wang, C. Q.; Xie, F.; Zhang, W. B. *Tetrahedron* **2009**, *65*, 9797.

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