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Palladium-catalyzed alkenylation of fluoro-substituted furans via C–H activation to form tetrasubstituted furans

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ABSTRACT

A palladium-catalyzed oxidative Heck reaction of fluoro-substituted furans with alkenes was developed to afford tetrasubstituted furans in moderate to good yields.

1. Introduction

The C–C bond formation through catalytic direct activation of normally inert C–H bond is of a privileged way in that such process precludes the need for a prior functionalization step of the reactant, making the overall chemical transformation highly efficient and atom-economic. In this rapidly developing field, the oxidative Heck reaction via direct C–H activation has gain tremendous interests during the past decades.[1] To date, most strategies deal with electron-rich arenes,[2–5] in which an electrophilic attack of a Pd(II) complex to the reactant is usually involved as a key step. Probably due to the difficulty for electron-deficient arenes to undergo this step and their poor coordination with Pd catalysts, reports using these substrates are relatively rare.[6] In together, these prior works have demonstrated the power of this methodology in the construction of molecules from simple starting material.

On the other hand, vinylated or arylated furans as well as thiophenes are of interest for their photo- and electrochemical properties as well as biological activities.[7] Although direct vinylations of furans and thiophenes via Pd-catalyzed direct C–H activation have been reported recently,[4d,8] such processes are restricted to the electronically favored 2- and/or 5-positions of the heterocycles. Moreover, in contrast to a very recent report on the direct vinylation of perfluoroarenes,[9] no reports have dealt with the fluorinated counterparts of these five-membered heterocycles. Based on our previous study on the direct arylation of 3-fluorofurans,[10] we reasoned that the direct vinylation at the C4-position of furans may be also possible and would allow an atom-economical access to vinylated tetrasubstituted furans. Herein, we present the details of this study.

2. Results and discussion

Initially, the reaction between fluoro-substituted furan **1a** and butyl acrylate **2a** was chosen as the model reaction for the optimization of reaction conditions (Table 1). Of the several palladium sources examined, $Pd(OAc)_2$ showed the best reactivity, giving the product **3a** in 65% yield in DMF with $Cu(OAc)_2$ as the oxidant (Table 1, entry 6). In order to improve the yield further, several other solvents and oxidants were screened but all with inferior results. *t*-BuOOBz was first tried but no reaction took place (entry 15), then some silver salts were tested in this reaction but the yield was not improved apparently (entries 16–18).[2–5] Moreover, some ligands were added to the system to improve the yield, but they showed low efficiency (entries 19–20).[2–5] Since positive effects of the use of lithium salts, such as LiOAc and LiCl have been observed in related previous studies,[4d] we also tried these two additives and were pleased to find that the addition of 3 equiv of LiCl enhanced the

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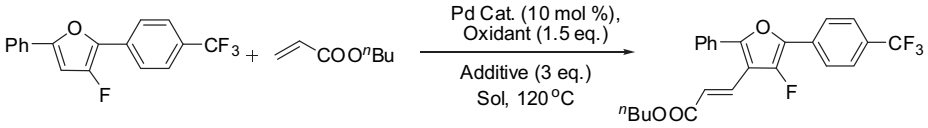
Table 1
Optimization of reaction conditions for the coupling reaction of **1a** and butyl acrylate **2a**[a]



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

Entry	Pd Cat.	Oxidant	Additive	Solvent	Yield[b] (%)
1	$PdCl_2$+AgOTf	$Cu(OAc)_2$	None	DMF	46
2	$PdCl_2$	$Cu(OAc)_2$	None	DMF	52
3	$PdCl_2(CH_3CN)_2$	$Cu(OAc)_2$	None	DMF	54
4	$PdCl_2(PPh_3)_2$	$Cu(OAc)_2$	None	DMF	47
5	$Pd_2(dba)_3$	$Cu(OAc)_2$	None	DMF	42
6	$Pd(OAc)_2$	$Cu(OAc)_2$	None	DMF	65
7	$Pd(OAc)_2$	$Cu(OAc)_2$	None	CH_3CN	45
8	$Pd(OAc)_2$	$Cu(OAc)_2$	None	AcOH	38
9	$Pd(OAc)_2$	$Cu(OAc)_2$	None	DME	35
10	$Pd(OAc)_2$	$Cu(OAc)_2$	None	1,4-Dioxane	47
11	$Pd(OAc)_2$	$Cu(OAc)_2$	None	DMA	61
12	$Pd(OAc)_2$	$Cu(OAc)_2$	None	Toluene	46
13	$Pd(OAc)_2$	$Cu(OAc)_2$	None	DMSO	58
14	$Pd(OAc)_2$	$Cu(OAc)_2$	None	NMP	21
15	$Pd(OAc)_2$	*t*-BuOOBz	None	DMF	NR
16	$Pd(OAc)_2$	Ag_2CO_3	None	DMF	18
17	$Pd(OAc)_2$	Ag_2O	None	DMF	37
18	$Pd(OAc)_2$	AgOAc	None	DMF	35
19	$Pd(OAc)_2$	$Cu(OAc)_2$	PPh_3	DMF	52
20	$Pd(OAc)_2$	$Cu(OAc)_2$	Pyridine	DMF	47
21	$Pd(OAc)_2$	$Cu(OAc)_2$	LiOAc	DMF	63
22	$Pd(OAc)_2$	$Cu(OAc)_2$	LiCl	DMF	73

[a] Unless otherwise specified, the reaction was carried on 0.1 mmol scale in 0.8 mL of solvent.
[b] Isolated yield after flash column chromatography.

yield of **3a** to 73% (entry 22). It is speculated that the addition of lithium chloride is to provide the ligand to prevent the deactivation of Pd(0) to non-reactive metallic species.[11]

Having established the optimal conditions for the oxidative Heck reaction of fluoro-substituted furans **1a** with butyl acrylate **2a**, we next explored the scope of the substrates and representative results are listed in Table 2. The examination of different acrylates revealed that relative bulkier substituents, such as *n*- or *t*-butyl group were more favored than methyl or ethyl groups in this reaction (Table 2, entries 1–4). For substrates **1b**–**e** bearing different R^1 substituents, moderate to good yields were consistently obtained irrespective of the electronic nature of the substituents on the arene ring (entries 5–8). Notably, when R^2 was an alkyl group, the reaction still proceeded smoothly to give the desired product in 61% yield (entry 9). Moreover, in addition to acrylic esters, styrenes also proved suitable reaction partners in this reaction system, and the desired products were obtained in good yields from their reactions with furan **1a** (entries 10–12). However, when (*E*)-ethyl but-2-enoate with a non-terminal C–C double bond was subjected to the same reaction conditions, no reaction was detected.

A plausible mechanism for the direct coupling reaction of fluoro-substituted furans **1** with acrylate **2** is illustrated in Scheme 1. The first step may involve electrophilic attack of $Pd(OAc)_2$ to **1** to form intermediate **I**.[2–5] Next, coordination of the complex **I** with alkene **2** followed by *syn* insertion gives intermediate **II**, which then underwent β-hydrogen elimination to give the product **3** and a Pd (0) species. The latter then would be re-oxidized to Pd(II) by the oxidant to complete the catalytic cycle.

3. Conclusion

In summary, we have realized direct alkenylation of fluoro-substituted furans at the C4-position via C–H activation using a Pd $(OAc)_2$–$Cu(OAc)_2$–LiCl system. This protocol provides an easy access to functionalized tetrasubstituted fluorinated furans.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded at 300 and 100 MHz, respectively, with TMS as the internal standard. ^{19}F NMR spectra were recorded at 282 MHz with $CFCl_3$ as the external standard. IR spectra were recorded in cm^{-1}. Melting points were uncorrected. All solvents were distilled prior to use unless otherwise noted. All reactions sensitive to moisture or oxygen were conducted under an atmosphere of nitrogen or argon.

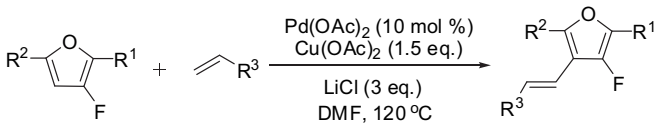
Compounds **1a**–**f** were prepared according to known procedures.[10]

*4.1.1. 3-Fluoro-5-phenyl-2-(4-(trifluoromethyl)phenyl)furan (**1a**).* White solid; IR (CH_2Cl_2 film): 1695, 1628, 1410, 1331, 1115, 1067, 920, 841, 689 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.84–7.82 (m, 2H), 7.71–7.64 (m, 4H), 7.45–7.25 (m, 3H), 6.68 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 151.8 (d, ^1J=245.2 Hz), 151.4 (d, ^3J=8.7 Hz), 134.6 (d, ^2J=20.4 Hz), 132.1 (m), 129.8 (m), 128.9, 128.6, 125.7 (q), 124.3 (q, ^1J=270.5 Hz), 123.9, 123.3, 123.2, 99.3 (d, ^2J=19.7 Hz) ppm; ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−62.9, −158.6 ppm; MS (EI) (*m*/*z*): 306 (M^+); Anal. Calcd for $C_{17}H_{10}F_4O$: C, 66.67; H, 3.29. Found: C, 66.62; H, 3.65.

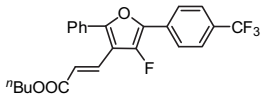
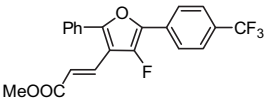
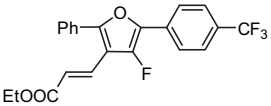
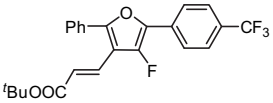
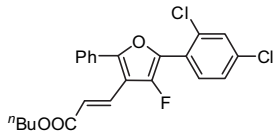
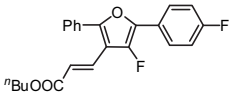
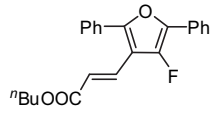
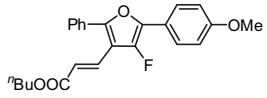
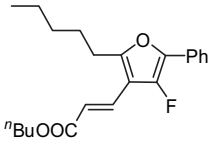
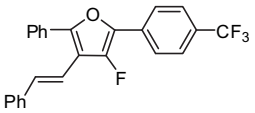
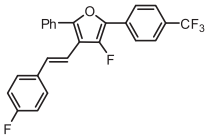
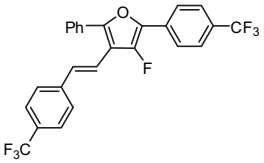
4.2. General procedure for the oxidative Heck reaction of 1 with 2

A mixture of compound **1** (0.1 mmol), $Pd(OAc)_2$ (2.25 mg, 0.01 mmol), $Cu(OAc)_2$ (27 mg, 0.15 mmol), and LiCl (12.6 mg,

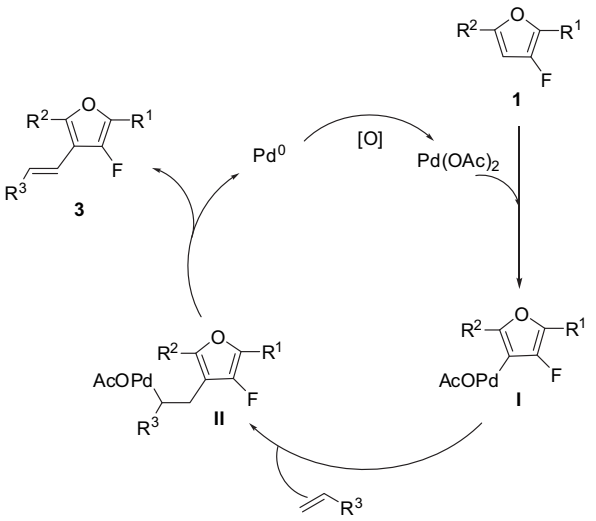
Table 2
The Heck reaction of fluorine-substitute furans **1** with alkenes **2**[a]



1 **2** **3**

Entry	R^1	R^2	R^3	Product	Yield[b] (%)
1	4-CF_3–C_6H_4 (**1a**)	Ph	COO^{n}Bu	 **3a**	72
2	4-CF_3–C_6H_4 (**1a**)	Ph	COOMe	 **3b**	44
3	4-CF_3–C_6H_4 (**1a**)	Ph	COOEt	 **3c**	53
4	4-CF_3–C_6H_4 (**1a**)	Ph	COO^{t}Bu	 **3d**	65
5	2,4-Cl_2–C_6H_3(**1b**)	Ph	COO^{n}Bu	 **3e**	65
6	4-F–C_6H_4(**1c**)	Ph	COO^{n}Bu	 **3f**	76
7	Ph (**1d**)	Ph	COO^{n}Bu	 **3g**	67
8	4-MeO–C_6H_4(**1e**)	Ph	COO^{n}Bu	 **3h**	66
9	Ph(**1f**)	C_5H_{11}	COO^{n}Bu	 **3i**	61
10	4-CF_3–C_6H_4(**1a**)	Ph	Ph	 **3j**	76
11	4-CF_3–C_6H_4(**1a**)	Ph	4-F–C_6H_4	 **3k**	91
12	4-CF_3–C_6H_4(**1a**)	Ph	4-CF_3–C_6H_4	 **3l**	74

[a] Unless otherwise specified, the reaction was carried on 0.1 mmol scale in 0.8 mL of solvent. The reaction time was 24 h.
[b] Isolated yield after flash column chromatography.



Scheme 1. A plausible mechanism for the reaction.

0.3 mmol) in 0.8 mL of DMF was stirred for 20 min at rt before **2** (0.3 mmol) was added to the system via a microsyringe. Then the mixture was heated to 120 °C for 24 h. After cooling to rt, the reaction was quenched by adding saturated aqueous NH_4Cl. After extraction with Et_2O and drying with Na_2SO_4, the organic layer was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel to afford the desired products.

*4.2.1. (E)-Butyl 3-(4-fluoro-2-phenyl-5-(4-(trifluoromethyl)phenyl)-furan-3-yl)acrylate (**3a**).* Yield: 72%; yellow oil; IR (CH_2Cl_2 film): 2960, 2873, 1717, 1644, 1618, 1325, 1067, 1017, 842 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.70–7.34 (m, 9H), 7.24–7.17 (m, 1H), 6.53 (d, 1H, J=16 0.2 Hz), 4.14 (t, 2H, J=6.8 Hz), 1.63–1.61 (m, 2H), 1.39–1.34 (m, 2H), 0.89 (t, 3H, J=6.8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 167.0, 151.8 (d, ^3J=6.6 Hz), 149.6 (d, ^1J=260.3 Hz), 135.3 (d, ^2J=19.0 Hz), 131.6 (m), 131.3 (m), 129.7, 129.4, 129.3, 129.1, 127.3, 125.8 (m), 124.1 (q, J=269.8 Hz), 123.7 (d, J=5.1 Hz), 121.4 (d. J=7.3 Hz), 110.1 (d, J=13.1 Hz), 64.6, 30.8, 19.2, 13.7 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−63.0, −159.1 ppm; MS (EI) (m/z): 432 (M^+); HRMS calcd for $C_{24}H_{20}F_4O_3$: 432.1349, found: 432.1345.

*4.2.2. (E)-Methyl 3-(4-fluoro-2-phenyl-5-(4-(trifluoromethyl)phenyl)furan-3-yl)acrylate (**3b**).* Yield: 44%; light yellow solid; mp: 101–102 °C; IR: 2948, 1719, 1641, 1614, 1448, 1328, 1171, 1065, 848, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.88–7.80 (d, 2H), 7.78–7.67 (m, 5H), 7.53–7.49 (m, 3H), 6.63 (d, 1H, J=16.2 Hz), 3.83 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 167.4, 151.9 (d, ^3J=6.6 Hz), 149.6 (d, ^1J=260.3 Hz), 135.4 (d, ^2J=19.0 Hz), 131.9 (m), 131.4 (m), 129.7, 129.5, 129.3, 129.1, 127.3, 125.8 (q), 124.1 (q, J=273.4 Hz), 123.8 (d, J=5.9 Hz), 120.9 (d, J=6.6 Hz), 111.0 (d, ^2J=12.4 Hz), 51.8 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−63.0, −159.1 ppm; MS (ESI): 413.1 ($M+Na^+$); HRMS calcd for $C_{21}H_{14}F_4O_3$: 390.0879, found: 413.0771 ([$M+Na^+$]).

*4.2.3. (E)-Ethyl 3-(4-fluoro-2-phenyl-5-(4-(trifluoromethyl)phenyl)-furan-3-yl)acrylate (**3c**).* Yield: 53%; white solid; mp: 57–60 °C; IR: 3403, 2975, 1711, 1644, 1453, 1328, 1112, 1064, 841, 692, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.81–7.60 (m, 7H), 7.48–7.39 (m, 3H), 6.55 (d, 1H, J=16.5 Hz), 4.20 (q, 2H, J=6.9 Hz), 1.28 (t, 3H, J=6.9 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 166.9, 151.8 (d, ^3J=6.5 Hz), 149.6 (d, ^1J=161 Hz), 135.3 (d, ^2J=19.7 Hz), 131.6 (q), 131.3 (q), 126.7, 129.4, 129.3, 129.1, 127.3, 125.8 (q), 124.1 (q, J=269.8 Hz), 123.7 (d, J=5.1 Hz), 121.4 (d, J=6.5 Hz), 111.1 (d, ^2J=13.1 Hz), 60.7, 14.3 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−63.0, −159.1 ppm; MS (ESI): 405.2 ($M+H^+$); HRMS calcd for $C_{22}H_{16}F_4O_3$: 404.1036, found: 427.0928 ([$M+Na^+$]).

*4.2.4. (E)-tert-Butyl 3-(4-fluoro-2-phenyl-5-(4-(trifluoromethyl)phenyl)furan-3-yl)acrylate (**3d**).* Yield: 65%; light yellow solid; IR: 3420, 2924, 1613, 1504, 1451, 1325, 1166, 1064, 960, 834 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.80–7.77 (m, 2H), 7.63–7.60 (m, 5H), 7.44–7.40 (m, 3H), 6.48 (d, 1H, J=15.9 Hz), 1.47 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 166.3, 151.6 (d, ^3J=6.5 Hz), 149.7 (d, ^1J=261.0 Hz), 135.2 (d, ^2J=19.7 Hz), 131.4 (q), 130.6 (q), 129.6, 129.4, 129.1, 127.2, 125.8 (q), 124.1 (q, J=269.8 Hz), 123.7 (d, J=5.9 Hz), 123.2 (d, J=7.3 Hz), 111.1 (d, ^2J=13.2 Hz), 80.8, 28.1 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−63.0, −158.9 ppm; MS (ESI): 455.2 ($M+Na^+$); HRMS calcd for $C_{24}H_{20}F_4O_3$: 432.1349, found: 455.1241 ([$M+Na^+$]).

*4.2.5. (E)-Butyl 3-(5-(2,4-dichlorophenyl)-4-fluoro-2-phenylfuran-3-yl)acrylate (**3e**).* Yield: 65%; white solid; mp: 52–54 °C; IR: 2957, 1723, 1649, 1475, 1310, 1268, 1186, 1055, 850, 683 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.71–7.66 (d, 1H), 7.60–7.58 (m, 2H), 7.48–7.35 (m, 5H), 7.27–7.25 (d, 1H), 6.53 (d, 1H, J=16.0 Hz) 4.14 (t, 2H, J=6.8 Hz), 1.61 (m, 2H, J=7.2 Hz), 1.35 (m, 2H, J=7.2 Hz), 0.89 (m, 3H, J=7.2 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 167.1, 152.4 (d, ^3J=6.6 Hz), 148.8 (d, ^1J=259.6 Hz), 135.2, 133.7 (d, ^2J=21.2 Hz), 133.8, 131.9, 130.6, 129.6, 129.5, 129.1, 127.3, 125.5 (d, J=4.4 Hz), 121.1 (d, J=7.3 Hz), 110.4 (d, ^2J=13.9 Hz), 64.5, 30.8, 19.2, 13.8 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−156.2 ppm; MS (ESI): 455.2 ($M+Na^+$); HRMS calcd for $C_{23}H_{19}Cl_2FO_3$: 432.0695, found: 455.0588 ([$M+Na^+$]).

*4.2.6. (E)-Butyl 3-(4-fluoro-5-(4-fluorophenyl)-2-phenylfuran-3-yl)-acrylate (**3f**).* Yield: 76%; white solid; mp: 73–74 °C; IR: 2967, 1706, 1640, 1510, 1308, 1262, 1188, 1019, 840, 681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.69–7.63 (m, 3H), 7.60–7.57 (m, 2H), 7.41–7.33 (m, 3H), 7.08–7.04 (t, 2H), 6.52 (d, 1H, J=16.0 Hz) 4.14 (t, 2H, J=6.8 Hz), 1.61 (m, 2H, J=7.2 Hz), 1.35 (m, 2H, J=7.2 Hz), 0.89 (m, 3H, J=7.2 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 167.2, 162.1 (d, ^1J=248.7 Hz), 150.8 (d, ^3J=5.9 Hz), 148.0 (d, ^1J=258.1 Hz), 135.9 (d, ^2J=19.7 Hz), 132.1, 129.6, 129.4, 129.0, 127.2, 125.7 (dd), 124.5 (m), 120.9 (d, J=7.3 Hz), 116.0 (d, J=21.9 Hz), 110.9 (d, ^2J=13.1 Hz), 64.5, 30.8, 19.2, 13.7 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−113.3, −163.0 ppm; MS (ESI): 405.2 ($M+Na^+$); HRMS calcd for $C_{23}H_{20}F_2O_3$: 383.1381, found: 383.1453.

*4.2.7. (E)-Butyl 3-(4-fluoro-2,5-diphenylfuran-3-yl)acrylate (**3g**).* Yield: 67%; light oil; IR (CH_2Cl_2 film): 2958, 1712, 1640, 1441, 1289, 1249, 1180, 764, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.70–7.35 (m, 9H), 7.24–7.17 (m, 1H), 6.53 (d, 1H, J=16.0 Hz), 4.14 (t, 2H, J=6.8 Hz), 1.62 (m, 2H, J=2.8 Hz), 1.36 (m, 2H, J=6.4 Hz), 0.89 (m, 3H, J=7.6 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 167.2, 150.9 (d, ^3J=6.6 Hz), 148.4 (d, ^1J=258.1 Hz), 136.7 (d, ^2J=19.7 Hz), 132.2 (d, J=3.6 Hz), 129.7, 129.3, 129.0, 128.9, 128.2 (d, J=5.1 Hz), 127.8, 127.2, 123.8 (d, J=5.1 Hz), 120.8 (d, J=6.7 Hz), 111.1 (d, J=12.9 Hz), 64.5, 30.8, 19.2, 13.8 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−162.1 ppm; MS (EI) (m/z): 364 (M^+); HRMS calcd for $C_{23}H_{21}FO_3$: 364.1475, found: 364.1479.

*4.2.8. (E)-Butyl 3-(4-fluoro-5-(4-methoxyphenyl)-2-phenylfuran-3-yl)acrylate (**3h**).* Yield: 66%; white solid; mp: 55–57 °C; IR: 2959, 1714, 1628, 1510, 1462, 1253, 1176, 1032, 831, 767 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.78 (s, 1H), 7.75–7.66 (m, 4H), 7.51–7.50 (m, 2H), 7.44–7.40 (m, 1H), 6.99 (d, 2H, J=8.0 Hz) 6.61 (d, 1H, J=16.0 Hz), 4.22 (t, 2H, J=8.0 Hz), 3.86 (s, 3H), 1.71 (m, 2H, J=8.0 Hz), 1.45 (m, 2H, J=8.0 Hz), 0.98 (m, 3H, J=8.0 Hz) ppm. ^{13}C NMR

(100 MHz, $CDCl_3$) 167.3, 159.2, 150.2 (*d*, ^3J=6.5 Hz), 147.3 (d, ^1J=255.2 Hz), 136.8 (d, ^2J=19.6 Hz), 132.4, 129.9, 129.1, 129.0, 127.1, 125.4 (d, *J*=5.1 Hz), 121.1 (d, *J*=5.2 Hz), 120.5 (d, *J*=7.3 Hz), 114.4, 111.1 (d, ^2J=12.9 Hz), 64.5, 55.4, 30.8, 19.2, 13.8 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−164.8 ppm; MS (EI) (*m*/*z*): 394 (M^+); HRMS calcd for $C_{24}H_{23}FO_4$: 394.1580, found: 394.1578.

*4.2.9. (E)-Butyl 3-(4-fluoro-2-pentyl-5-phenylfuran-3-yl)acrylate (**3i**).* Yield: 61%; oil; IR (CH_2Cl_2 film): 2957, 2928, 1716, 1650, 1443, 1287, 1174, 975, 761 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.67−7.65 (m, 2H), 7.47−7.39 (m, 3H), 7.27−7.24 (m, 1H), 6.44 (d, 1H, *J*=16.0 Hz), 4.20 (m, 2H, *J*=6.8 Hz), 2.74 (m, 2H, *J*=7.6 Hz), 1.72−1.65 (m, 4H), 1.47−1.42 (m, 2H), 1.41−1.25 (m, 4H), 0.98−0.87 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 167.5, 155.6 (d, ^3J=5.9 Hz), 147.7 (d, ^1J=257.3 Hz), 135.7 (d, ^2J=20.4 Hz), 131.8, 128.7, 128.5 (d, *J*=5.2 Hz), 127.3, 123.5 (d, *J*=5.8 Hz), 118.3 (d, *J*=6.6 Hz), 110.7 (d, ^2J=13.1 Hz), 64.4, 31.2, 30.8, 27.9, 27.0, 22.3, 19.2, 13.9, 13.7 ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−163.7 ppm; MS (EI) (*m*/*z*): 358 (M^+); HRMS calcd for $C_{22}H_{27}FO_3$: 358.1944, found: 358.1946.

*4.2.10. (E)-3-Fluoro-5-phenyl-4-styryl-2-(4-(trifluoromethyl)phenyl)-furan (**3j**).* Yield: 76%; white solid; mp: 128−130 °C; IR: 3404, 1617, 1491, 1448, 1325, 1173, 1110, 837, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.79−7.77 (m, 2H), 7.63−7.58 (m, 4H), 7.43−7.39 (m, 4H), 7.36−7.32 (m, 1H), 7.30−7.28 (m, 1H), 7.27−7.00 (m, 3H), 6.99−6.96 (d, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 150.1 (d, ^1J=258.9 Hz), 148.7 (d, ^3J=7.3 Hz), 137.3, 134.8 (d, ^2J=19.7 Hz), 132.67, 132.61, 131.9 (m), 130.4, 128.9, 128.8, 128.0, 126.8, 126.5, 125.8 (q), 124.2 (q, ^1J=280 Hz), 123.6 (d, *J*=5.6 Hz), 115.8 (d, *J*=3.6 Hz), 113.1 (d, ^2J=13.1 Hz) ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−62.3, −158.7 ppm; MS (EI) (*m*/*z*): 408 (M^+); HRMS calcd for $C_{25}H_{16}F_4O$: 408.1137, found: 408.1136.

*4.2.11. (E)-Butyl 3-(4-fluoro-5-(4-methoxyphenyl)-2-phenylfuran-3-yl)acrylate (**3k**).* Yield: 91%; white solid; mp: 118−120 °C; IR: 3420, 3054, 2925, 1613, 1448, 1416, 1328, 1118, 834, 761 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.76−7.74 (m, 2H), 7.58 (s, 4H), 7.43−7.34 (m, 5H), 7.15−7.09 (d, 1H), 6.99−6.83 (d, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 162.6 (d, ^1J=246.4 Hz), 150.0 (d, ^1J=261.7 Hz), 148.6 (d, ^3J=8.8 Hz), 134.8 (d, ^2J=19.7 Hz), 134.5 (d, *J*=3.7 Hz), 131.8 (q), 131.6, 131.3 (q), 130.4, 129.0, 128.8, 128.2, 128.0, 126.8, 125.8 (q, *J*=3.7 Hz), 124.2 (q, ^1J=280.5 Hz), 115.8 (d, *J*=19.5 Hz), 115.5 (d, *J*=3.7 Hz), 112.9 (d, ^2J=13.1 Hz) ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−62.9, −113.9, −159.4 ppm; MS (EI) (*m*/*z*): 426 (M^+); HRMS calcd for $C_{25}H_{15}F_5O$ 426.1043, found: 426.1049.

*4.2.12. (E)-3-Fluoro-5-phenyl-2-(4-(trifluoromethyl)phenyl)-4-(4-(trifluoromethyl)styryl)furan (**3l**).* Yield: 74%; oil; IR (CH_2Cl_2 film): 3411, 2966, 1714, 1639, 1451, 1328, 1181, 1115, 837 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.87−7.84 (d, 2H), 7.69−7.44 (m, 11H), 7.30−7.25 (m, 1H), 7.16−7.10 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 149.8 (d, ^1J=258.9 Hz), 149.4 (d, ^3J=6.5 Hz), 140.7, 135.0 (d, ^2J=18.9 Hz), 130.84, 130.77, 130.2, 129.1, 129.0, 127.0, 126.5, 125.9−125.7 (m), 124.19 (q, *J*=269.8 Hz), 124.11 (q, *J*=270.5 Hz), 123.7 (d, *J*=5.8 Hz), 118.4 (d, *J*=3.6 Hz), 112.6 (d, *J*=12.4 Hz) ppm. ^{19}F NMR (282.3 MHz, $CDCl_3$): δ=−62.9, −159.4 ppm; MS (EI) (*m*/*z*): 476 (M^+); HRMS calcd for $C_{26}H_{15}F_7O$ 476.1011, found: 476.1016.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.08.064. These data include MOL files and InChIKeys of the most important compounds described in this article.

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