

Synthesis of fluorine containing 3-cyano/ethoxycarbonyl-2-ethyl-benzo[b]furans via microwave assisted tandem intramolecular Wittig and Claisen rearrangement reactions†

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Dedicated to Dr. A.V. Rama Rao on the occasion of his 70th birthday
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Abstract

Microwave irradiation of [$\{2\text{-(fluorophenoxy)propanoyl}\}$ -(cyano/ethoxy-carbonyl) methylene] triphenylphosphoranes resulted in the exclusive formation of fluoro-substituted 2-ethyl-benzo[b]furan-3-carbonitriles and ethyl 2-ethyl-benzo[b]furan-3-carboxylic acid esters, respectively, along with triphenylphosphine oxide. The aryl propargylic ethers formed initially by the intramolecular Wittig reaction of the ylides underwent Claisen rearrangement reaction under the same reaction conditions and the resulting *ortho*-allenyl phenol intermediates cyclised to yield benzofurans.

Keywords: [$\{2\text{-(Aryloxy)propanoyl}\}$ -(cyano/ethoxycarbonyl) methylene] triphenylphosphoranes, Claisen rearrangement, intramolecular Wittig reaction, *ortho*-allenylphenol, 2-ethyl-benzo[b]furan-3-carbonitrile, ethyl 2-ethyl-benzo[b]furan-3-carboxylate

Introduction

Benzo[b]furans have wide applications as pharmaceutical and agrochemical intermediates.^{1,2} A large number of benzo[b]furan derivatives with physiological and pharma-cological properties were isolated from natural sources.³⁻⁶ They were usually synthesized by condensation reactions involving *o*-hydroxybenzaldehyde or phenolic substrates,^{1,6-9} Claisen rearrangement reaction of aryl propargylic ethers,¹⁰⁻¹² intramolecular Wittig reaction of *o*-hydroxyphenacylidetriphenylphosphoranes,^{13,14} flash vacuum pyrolysis of α -acyl-*o*-methoxybenzylidene-triphenylphosphoranes,¹⁵ tandem intramolecular Wittig and Claisen rearrangement reactions¹⁶⁻¹⁹ and a host of other methods.¹ 2-Ethyl-benzo[b]furan and its

analogues were used as drug intermediates in the treatment of pathological syndromes of cardiovascular system, such as of angina pectoris, hypertension and arrhythmias.^{20,21}

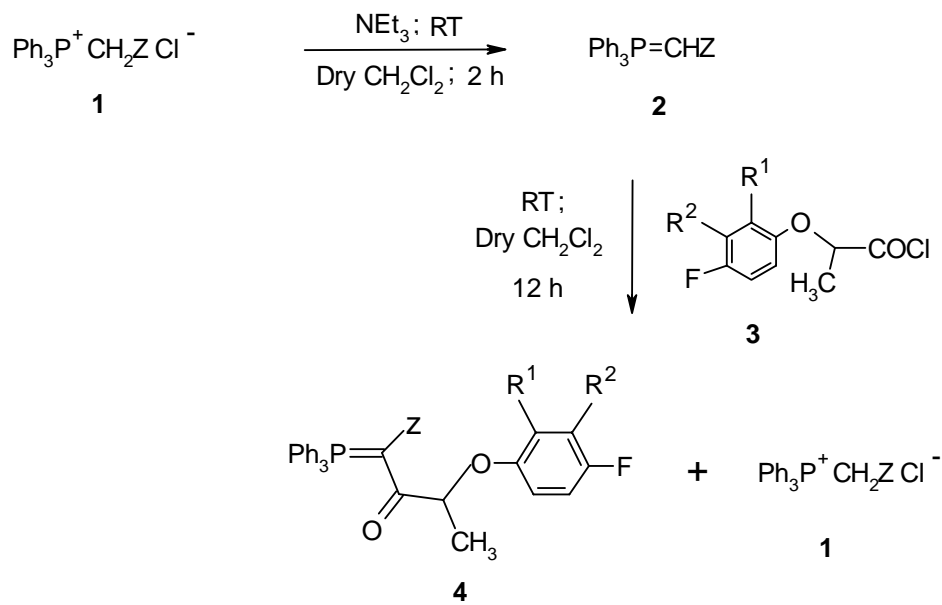
Thermolysis of [(aryloxyacetyl)-(cyano)methylene]triphenylphosphoranes was reported to yield either 4-cyano-2H-chromenes or 3-cyano-2-methyl-benzo[b]furans.¹⁶⁻¹⁸ The reaction was carried out at high temperatures and sometimes accompanied by the formation of the corresponding phenol due to decomposition of the intermediates and resulted in a lower yield of either 2H-chromene or 2-methyl-benzo[b]furan.

The regioselectivity for the 2H-chromene or benzo[b]furan derivatives depended on the nature of substituents present on the aryloxy-moiety. Earlier, we have reported an improved synthesis of fluorine containing disubstituted alkynes by microwave induced intramolecular Wittig reaction of [acyl-(cyano / ethoxycarbonyl)methylene]triphenylphosphoranes,²² where in, the problems associated with prolonged heating were avoided. We have successfully adopted this technique for the synthesis of various benzo[b]furan derivatives.¹⁹ The advantages of microwave technology over conventional methods in heterocyclic synthesis have been recently reviewed.²³ In the present study, we wish to report a regioselective and efficient one pot synthesis of halogen containing 3-cyano/ethoxycarbonyl-2-ethyl-benzo[b]furan derivatives **8a-f** by the microwave assisted tandem intramolecular Wittig and Claisen rearrangement reactions of the corresponding [{2-(aryloxy)propanoyl}-(cyano / ethoxycarbonyl) methylene]triphenylphosphoranes **4a-f**.

Results and Discussion

Cyano/ethoxycarbonyl-methyltriphenylphosphonium chloride **1a/1e** was reacted with triethylamine to generate the corresponding [(cyano / ethoxycarbonyl)methylene] triphenylphosphorane **2a/2e**.²² The latter on treatment with 2-(aryloxy)propanoyl chlorides **3a-d**²⁴ underwent transylidation reaction¹⁶⁻¹⁹ to give equimolar amounts of the respective phosphoranes **4a-f** and the phosphonium salt **1a/1e**. All the fluorine containing [{2-(aryloxy)propanoyl}-(cyano / ethoxycarbonyl)methylene]triphenylphosphoranes **4a-f** reported here (**Scheme-1**) were prepared for the first time and were well characterized.

The oxo-ylides **4a-f** were subjected to controlled microwave irradiation, individually, for 6-9 min to carry out intramolecular Wittig reaction.^{19,22} The product mixture from each of the experiments was purified by column chromatography over silica gel to isolate the new compounds free from triphenylphosphine oxide **6**, an expected common product in all the cases.



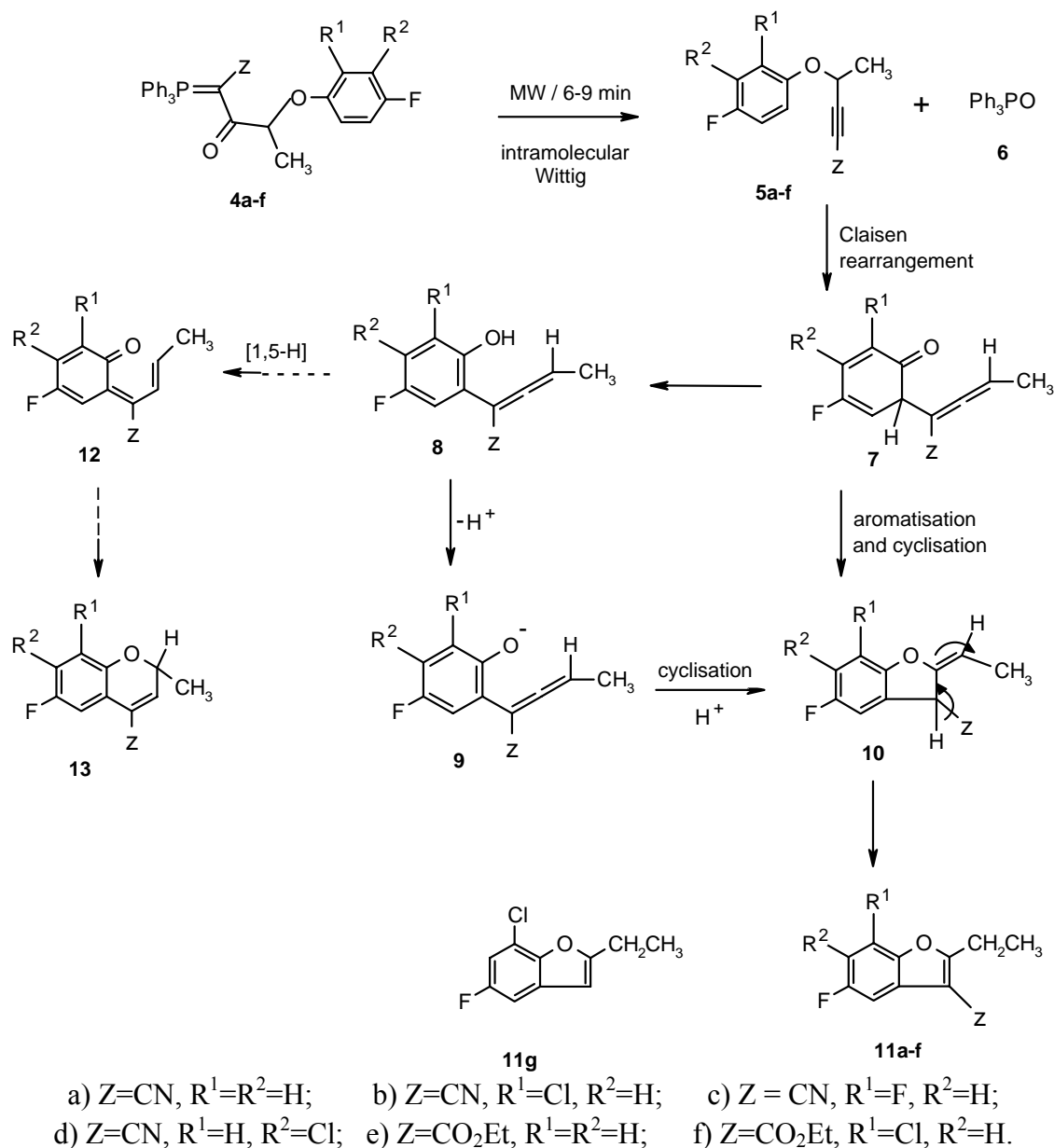
- a) Z=CN, R¹=R²=H; b) Z=CN, R¹=Cl, R²=H; c) Z = CN, R¹=F, R²=H;
 d) Z=CN, R¹=H, R²=Cl; e) Z=CO₂Et, R¹=R²=H; f) Z=CO₂Et, R¹=Cl, R²=H.

Scheme 1

[{2-(Aryloxy)propanoyl}-(cyano)methylene]triphenylphosphoranes **4a-d** on microwave irradiation furnished a new product in each case, in over 80 percent yield, along with triphenylphosphine oxide **6**. The formation of triphenylphosphine oxide **6** was the direct result of an intramolecular Wittig reaction of the oxo-ylides **4a-d**. The IR spectra of the products revealed the presence of a nitrile group around 2230 cm⁻¹. The ¹H NMR spectra of all the products showed the presence of an ethyl group attached to an aromatic ring [around δ 1.4 (t, 3H) and 3.0 ppm (q, 2H)], which was not present in the parent oxo-ylides **4a-d**. Microwave irradiation of [{2-(4-fluoro-phenoxy)propanoyl}-(ethoxycarbonyl)methylene]triphenylphosphorane **4e** resulted in a single new product in 83 percent yield, while [{2-(2-chloro-4-fluorophenoxy)propanoyl}-(ethoxycarbonyl)methylene] triphenylphosphorane **4f** gave two new compounds in 78 and 8 percent isolated yield respectively. The IR spectra of these products also did not contain absorption bands due to acetylenic triple bond. The ester carbonyl absorption band was observed at 1735 cm⁻¹ for the product of **4e** and at 1715 cm⁻¹ for the major product of **4f**. The ¹H NMR spectra of these two products revealed the presence of a -CH₂CH₃ group [around δ 1.4 (t, 3H) and 3.2 ppm (q, 2H)] attached to an aromatic ring and a -OCH₂CH₃ group [around δ 1.3 (t, 3H) and 4.4 ppm (q, 2H)] each.

From the above data, it was clear that all the oxo-ylides **4a-f** underwent intramolecular Wittig reaction resulting initially, in the formation of the corresponding 4-aryloxy-but-2-ynenitrile **5a-d** or ethyl 4-aryloxy-but-2-ynoic acid ester **5e-f** along with triphenylphosphine oxide **6**. It was presumed that the acetylenic compounds **5a-f** under microwave irradiation conditions underwent Claisen rearrangement to give the *ortho*-allenylphenol intermediates **8** via the

allenylcyclohexadienone **7** (scheme 2). The allenylphenol **8** could cyclise leading to 2-ethylbenzo[b]furan derivatives **11a-f**. Other alternative pathway available for **8** is to undergo [1,5-H] shift, followed by an electrocyclic ring closure¹⁶ of the expected open chain dienone **12** to generate 4-substituted-2-methyl-2H-chromene derivative **13**. Although, the transformation of *ortho*-allenylphenol **8** into an *ortho*-quinone monomethide intermediate **12** is a symmetry allowed 1,5-sigmatropic reaction/rearrangement, it involves dearomatisation. The absence of methyl, olefinic and O-allylic protons in ¹H NMR spectra rule-out 2-methyl-2H-chromene structure **13** for the products. The spectral data agree very well with the 2-ethylbenzo[b]furan-3-carbonitrile **11a-d** or ethyl 2-ethylbenzo[b]furan-3-carboxylic acid ester **11e-f** structures for the respective compounds (Table-1). The sequence of probable reactions are depicted in Scheme 2.



Scheme 2

Table1. Synthesis of 2-ethyl-benzo[b]furans **8**

Entry	Ylide	Z	R ₁	R ₂	Time (Min.)	Product	Yield (%)
1.	4a	CN	H	H	8	11a	85
2.	4b	CN	Cl	H	9	11b	86
3.	4c	CN	F	H	7	11c	81
4.	4d	CN	H	Cl	9	11d	83
5.	4e	COOEt	H	H	7	11e	83
6.	4f	COOEt	Cl	H	6	11f	72
7.	4f	H	Cl	H	6	11g	8

Claisen rearrangement of aryl propargylic ethers **5a-f** results in the *ortho*-allenylcyclohexadienone intermediate **7**, which enolises to a more stable *ortho*-allenylphenol intermediates **8a-f**. Enolisation of **7** to **8** is a favored step because of aromatisation. The presence of electron-withdrawing substituents and a polar medium was reported¹¹ to enhance the acidity of the phenolic intermediates **8**. The halogen substituents on the phenyl ring, polar medium in the form of triphenylphosphine oxide and microwave energy could be favouring dissociation of the allenylphenol **8** into a phenolate anion **9**. The α,β -unsaturated nitrile or ester group present in **9** enhances the electrophilicity of the allenyl carbon, favouring intramolecular nucleophilic addition of the phenolate anion on to this carbon leading to the 2-alkylidene-2,3-dihydrobenzofuran **10** formation. Alternatively, under the influence of microwave energy, the dihydrobenzofuran **10** could have been formed directly from the enone **7** by simultaneous aromatisation and cyclisation as depicted in scheme 2. This type of cyclisation was reported in the flash vacuum pyrolysis of phenyl propargyl ether leading to the formation of dihydrobenzofuran.²⁵ The dihydrobenzofuran **10** rearranges to give more stable 2,3-disubstituted-benzo[b]furans **11a-f**. The regioselectivity observed in the case of **11d** was attributed to the highly electronegative and bulky chlorine in 4-(3-chloro-4-fluorophenoxy)but-2-ynenitrile intermediate **5d** which favoured the Claisen rearrangement occurring away from it rather than towards itself.

In the present investigation, several new [{2-(fluorophenoxy)propanoyl}-(cyano/ethoxycarbonyl) methylene] triphenylphosphoranes were prepared in excellent yield by the transylidation reaction of [(cyano/ethoxycarbonyl) methylene] triphenylphosphorane with the corresponding 2-(fluorophenoxy)propanoyl chloride. These oxo-ylides underwent tandem intramolecular Wittig and Claisen rearrangement and cyclisation reactions under controlled microwave irradiation, to generate fluorine containing 3-cyano / ethoxycarbonyl-2-ethyl-benzo[b]furans in good yield. This is a convenient and efficient method for the synthesis of 2,3-disubstituted benzo[b]furans under solvent free conditions.

Experimental Section

General Procedures. Melting points were determined in open glass capillaries on a Fisher Johnes melting point apparatus and are uncorrected. IR spectra were recorded on FT-IR Perkin-Elmer 1310 infrared spectrophotometer. ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded on Varian Gemini spectrometer in CDCl_3 solvent using TMS as internal standard. Mass spectra were recorded on a VG-micro mass 7070H instrument at 70eV. Elemental analyses were carried out on Elemental Vario EL (Germany) apparatus. Microwave irradiations were carried out using thick walled glass tube fitted with teflon screw cap (Aldrich, Ace pressure tube, 10.2 cm, 15 ml) in a domestic microwave oven (BPL BMO 700T).

General procedure for the synthesis of **[[2-(aryloxy)propanoyl]-(cyano/ ethoxycarbonyl) methylene]triphenylphosphoranes (4a-f)**

To a well stirred suspension of (cyano)methyltriphenylphosphoniumchloride/(ethoxycarbonyl) methyltriphenyl phosphonium chloride (2 mmol) in dry dichloromethane (8 ml) placed in a two necked round bottom flask equipped with a dropping funnel and a nitrogen balloon adopter, cooled to 10-15 °C, a solution of triethylamine (2 mmol) in dry dichloromethane (3 ml) was added dropwise and the reaction mixture was stirred for another 1h to generate the [(cyano) methylene] triphenylphosphoranes / [(ethoxycarbonyl) methylene] triphenylphosphorane. A solution of aryloxypropanoyl chloride (1 mmol) in dichloromethane (3 ml) was added slowly through the dropping funnel to the reaction mixture and the stirring continued for another 12 h at room temperature. The reaction mixture was diluted with dichloromethane (10 ml) and washed with water (2x15 ml). The organic layer was separated and dried over anhydrous sodium sulphate. The solvent was removed on rotavapor and the crude product was purified by recrystallisation from a 1:4 mixture of hexane and ethyl acetate. The yields based on the acid chloride were given along with the physical properties for the individual phosphoranes **4a-f**.

[[2-(4-Fluorophenoxy)propanoyl]-(cyano) methylene] triphenylphosphorane (4a). Solid (87.2%), mp. 159 °C; δ_{H} (200 MHz, CDCl_3): 1.68 (d, 3H, $J=7.3$ Hz), 5.15 (q, 1H, $J=7.3$ Hz), 6.87-6.96 (m, 4H), 7.43-7.54 (unresolved, 10H) and 7.59-7.68 (m, 5H); IR ν_{max} (cm^{-1}): 3047, 2175, 1602, 1487, 1196, 1104; MS (EI) m/z : 467 (M^+ , 1), 329 (33), 328 (100), 278 (60), 277 (90), 262 (3); Anal. calcd. for $\text{C}_{29}\text{H}_{23}\text{FNO}_2\text{P}$: C, 74.51; H, 4.96; N, 3.00. Found: C, 74.52; H, 4.98; N, 2.98%.

[[2-(2-Chloro-4-fluorophenoxy)propanoyl]-(cyano)methylene]triphenyl-phosphorane (4b). Solid (88.9%), mp. 199 °C; δ_{H} (200 MHz, CDCl_3): 1.69 (d, 3H, $J=7.3$ Hz), 5.11 (q, 1H, $J=7.3$ Hz), 6.78-6.84 (m, 1H) 6.90-7.02 (m, 2H), 7.42-7.55 (unresolved, 10H) and 7.58-7.69 (m, 5H); IR ν_{max} (cm^{-1}): 3055, 2170, 1595, 1489, 1096; MS (FAB) m/z : 502 (MH^+ , 9), 328 (100), 279 (14), 262 (8); Anal. calcd. for $\text{C}_{29}\text{H}_{22}\text{ClFNO}_2\text{P}$: C, 69.40; H, 4.42; N, 2.79. Found: C, 69.40; H, 4.39; N, 2.80%.

[[2-(3-Chloro-4-fluorophenoxy)propanoyl]-(cyano)methylene] triphenylphosphorane (4c). Solid (85.3%), mp. 186-188 °C; δ_{H} (200 MHz, CDCl_3): 1.74 (d, 3H, $J=7.3$ Hz), 5.24 (q, 1H, $J=7.3$ Hz), 6.79-6.94 (m, 2H), 7.08 (m, 1H) and 7.43-7.72 (unresolved, 15H); IR ν_{max} (cm^{-1}): 3048, 2923,

2174, 1586, 1485, 1106; MS (FAB) m/z : 502 (MH^+ , 6), 328 (40), 281 (10), 147 (70), 73 (100); Anal. calcd. for $C_{29}H_{22}ClFNO_2P$: C, 69.40; H, 4.42; N, 2.79. Found: C, 69.39; H, 4.41; N, 2.80%.

[[2-(2,4-Difluorophenoxy)propanoyl]-(cyano) methylene] triphenylphosphorane (4d). Solid (86.5%), mp. 133 °C; δ_H (200 MHz, $CDCl_3$): 1.68 (d, 3H, $J=7.3$ Hz), 5.15 (q, 1H, $J=7.3$ Hz), 6.87-6.96 (m, 4H), 7.43-7.54 (unresolved, 10H) and 7.59-7.68 (m, 5H); IR ν_{max} (cm^{-1}): 3049, 2182, 1585, 1102; MS (FAB) m/z : 486 (MH^+), 328, 278; Anal. calcd. for $C_{29}H_{22}F_2NO_2P$: C, 71.75; H, 4.57; N, 2.89. Found: C, 71.77; H, 4.56; N, 2.88%.

[[2-(4-Fluorophenoxy)propanoyl]-(ethoxycarbonyl)methylene]triphenylphosphorane (4e). Solid (85.4%), mp. 143 °C; δ_H (200 MHz, $CDCl_3$): 0.69 (t, 1H, $J=7.1$ Hz), 1.57 (d, 1H, $J=7.3$ Hz), 3.76 (q, 2H, $J=7.1$ Hz), 5.88 (q, 1H, $J=7.3$ Hz), 6.72-6.85 (m, 4H), 7.39-7.76 (unresolved, 10H) and 7.60-7.68 (m, 5H); IR ν_{max} (cm^{-1}): 3056, 1654, 1582, 1492, 1191, 1102; MS (FAB) m/z : 515 (MH^+ , 44), 469 (13), 403 (28), 375 (100), 279 (24); Anal. calcd. for $C_{31}H_{28}FO_4P$: C, 72.36; H, 5.49. Found: C, 72.37; H, 5.49%.

[[2-(2-Chloro-4-fluorophenoxy)propanoyl]-(ethoxycarbonyl)methylene]triphenylphosphorane (4f). Solid (86.3%), mp. 156 °C; δ_H (200 MHz, $CDCl_3$): 0.69 (t, 3H, $J=7.1$ Hz), 1.64 (d, 3H, $J=7.3$ Hz), 3.74 (q, 1H, $J=7.1$ Hz), 5.52 (q, 1H, 7.3 Hz), 6.69-6.75 (m, 2H), 6.96-7.05 (m, 1H), and 7.35-7.68 (unresolved, 15H); IR ν_{max} (cm^{-1}): 2989, 1643, 1585, 1489, 1090; MS (FAB) m/z : 549 (MH^+ , 25), 520 (33), 505 (39), 375 (100), 278 (76); Anal. calcd. for $C_{31}H_{27}ClFO_4P$: C, 67.82; H, 4.96. Found: C, 67.84, H, 4.97%.

General procedure for the synthesis of 3-cyano/ethoxycarbonyl-2-ethyl-benzo[b] furans (11a-f)

Suitably substituted [$\{2-(4\text{-Fluorophenoxy})\text{propanoyl}\}$ -(cyano/ethoxycarbonyl) methylene] triphenylphosphorane **1** (2.0 g) was taken in a sealed tube and subjected to controlled microwave irradiation for a specified time at 600 watts microwave power. The dark brown reaction mixture was cooled to room temperature, dissolved in dichloromethane (10 ml) and purified by column chromatography on silica gel (100-200 mesh) using hexane as eluent. Concentration of the initial fractions afforded 3-cyano/ethoxycarbonyl-2-ethyl-benzo[b]furan **8a-f**. The later fractions eluted with a 1: 1 mixture of hexane and ethyl acetate contained triphenylphosphine oxide. The reaction time and yield of the products are given in Table 1.

3-Cyano-2-ethyl-5-fluoro-benzo[b]furan (11a). Solid, mp. 45 °C; δ_H (200 MHz, $CDCl_3$): 1.42 (t, 3H, $J=7.0$ Hz), 3.03 (q, 2H, 7.0 Hz), 7.05 (ddd, 1H, $^3J_{H-H}=9.0$ Hz, $^3J_{H-F}=8.7$ Hz, $^4J_{H-H}=2.6$ Hz, $C_6\text{-H}$), 7.3 (dd, 1H, $^3J_{H-F}=7.9$ Hz, $^4J_{H-H}=2.6$ Hz, $C_4\text{-H}$) and 7.41 (dd, 1H, $^3J_{H-H}=9.1$ Hz, $^4J_{H-F}=4.1$ Hz, $C_7\text{-H}$); IR ν_{max} (cm^{-1}): 3042, 2919, 2225, 1475, 1173; MS (EI) m/z : 189 (42), 174 (100), 141 (76), 91 (78); Anal. calcd. for $C_{11}H_8FNO$: C, 69.84, H, 4.26; N, 7.40. Found C, 69.81; H, 4.27; N, 7.41%.

7-Chloro-3-cyano-2-ethyl-5-fluoro-benzo[b]furan (11b). Solid, mp. 101 °C; δ_H (200 MHz, $CDCl_3$): 1.52 (t, 3H, $J=7.1$ Hz), 3.07 (q, 2H, $J=7.1$ Hz), 7.14 (dd, 1H, $^3J_{H-F}=8.5$ Hz, $^4J_{H-H}=2.6$ Hz, $C_6\text{-H}$) and 7.25 (dd, 1H, $^3J_{H-F}=8.6$ Hz, $^4J_{H-H}=2.6$ Hz, $C_4\text{-H}$); IR ν_{max} (cm^{-1}): 3050, 2926, 2230,

1479, 1184; MS (EI) m/z : 223 (M^+ , 70), 208 (100), 146 (90); Anal. calcd. for $C_{11}H_7ClFNO$: C, 59.08; H, 3.16; N, 6.26. Found C, 59.08; H, 3.15; N, 6.27%.

3-Cyano-5, 7-difluoro-2-ethyl-benzo[b]furan (11c). Solid, mp. 54-56 °C; δ_H (200 MHz, $CDCl_3$): 1.53 (t, 6H, $J=7.0$ Hz), 3.94 (q, 1H, $J=7.0$ Hz), 6.91 (ddd, 1H, $^3J_{H-F}=9.6$ Hz, $^3J_{H-F}=9.6$ Hz, $^4J_{H-H}=2.3$ Hz, C_6-H) and 7.15 (dd, 1H, $^3J_{H-F}=8.2$ Hz, $^4J_{H-H}=2.3$ Hz, C_4-H); IR ν_{max} (cm^{-1}): 3041, 2925, 2226, 1475, 1103; MS (EI) m/z : 207 (M^+ , 65), 182 (100); Anal. calcd. for $C_{11}H_7F_2NO$: C, 63.77; H, 3.41; N, 6.76. Found C, 63.71; H, 3.47, 6.79%.

6-Chloro-3-cyano-2-ethyl-5-fluoro-benzo[b]furan (11d). Solid, mp. 96-97 °C; δ_H (200 MHz, $CDCl_3$): 1.43 (t, 3H, $J=7.0$ Hz), 3.01 (q, 2H, $J=7.0$ Hz), 7.39 (d, 1H, $^3J_{H-F}=8.1$ Hz, C_4-H) and 7.54 (d, 1H, $^4J_{H-F}=6.0$ Hz, C_7-H); IR ν_{max} (cm^{-1}): 3053, 2924, 2235, 1476, 1104; MS (EI) m/z : 223 (M^+ , 40), 208 (100); Anal. calcd. for $C_{11}H_7ClFNO$: C, 59.08; H, 3.16; N, 6.26. Found C, 59.09; H, 3.13; N, 6.26%.

3-Ethoxycarbonyl-2-ethyl-5-fluoro benzo[b]furan (11e). Solid, mp. 50 °C; δ_H (200 MHz, $CDCl_3$): 1.37 (t, 3H, $J=7.0$ Hz), 1.46 (t, 3H, $J=7.1$ Hz), 3.2 (q, 2H, $J=7.0$ Hz), 4.4 (q, 2H, $J=7.1$ Hz), 6.92 (ddd, 1H, $^3J_{H-H}=9.0$ Hz, $^3J_{H-F}=8.7$ Hz, $^4J_{H-H}=2.6$ Hz, C_6-H), 7.34 (dd, 1H, $^3J_{H-H}=9.1$ Hz, $^4J_{H-F}=4.1$ Hz, C_7-H) and 7.58 (dd, 1H, $^3J_{H-F}=7.9$ Hz, $^4J_{H-H}=2.6$ Hz, C_4-H); δ_C (50 MHz, $CDCl_3$): 9.9 (s, $-CH_2-CH_3$) 12.4 (s, $-OCH_2CH_3$), 19.8 (s, CH_2 on C_2), 58.3 (s, OCH_2), 105.8 (d, $^2J_{C-F}=26.4$ Hz, C_4), 106.5 (s, C_3), 109.5 (d, $^3J_{C-F}=9.6$ Hz, C_7), 109.9 (d, $^2J_{C-F}=26.6$ Hz, C_6), 125.4 (d, $^3J_{C-F}=11.2$ Hz, C_9), 147.8 (s, C_8), 157.9 (d, $^1J_{C-F}=238.8$ Hz, C_5), 161.9 (s, $-COO-$) and 168.0 (s, C_2); IR ν_{max} (cm^{-1}): 2925, 1735, 1465, 1165; MS (EI) m/z : 236 (M^+ , 29), 207 (41), 191 (100), 149 (25); Anal. calcd. for $C_{13}H_{13}FO_3$: C, 66.09; H, 5.55. Found: C, 66.12; H, 5.53%.

7-Chloro-ethoxycarbonyl-2-ethyl-5-fluoro-benzo[b]furan (11f). Liquid; δ_H (200 MHz, $CDCl_3$): 1.3 (t, 3H, $J=7.0$ Hz), 1.46 (t, 3H, $J=7.1$ Hz), 3.25 (q, 2H, $J=7.0$ Hz), 4.4 (q, 2H, $J=7.1$ Hz), 7.05 (dd, 1H, $^3J_{H-F}=8.6$ Hz, $^4J_{H-H}=2.6$ Hz, C_6-H) and 7.52 (dd, 1H, $^3J_{H-F}=8.6$ Hz, $^4J_{H-H}=2.6$ Hz, C_4-H); IR ν_{max} (cm^{-1}): 3048, 2930, 1715, 1486, 1197; MS (EI) m/z : 270 (M^+ , 75), 241 (100), 227 (33), 225 (92), 196 (10); Anal. calcd. for $C_{13}H_{12}ClFO_3$: C, 57.68; H, 4.47; Found: C, 57.70; H, 4.47%.

7-Chloro-2-ethyl-5-fluoro-benzo[b]furan (11g). Liquid; δ_H (200 MHz, $CDCl_3$): 1.39 (t, 3H, $J=7.0$ Hz), 2.86 (q, 2H, $J=7.0$ Hz), 6.38 (s, 1H, C_3-H), 6.98 (dd, 1H, $^3J_{H-F}=8.6$ Hz, $^4J_{H-H}=2.6$ Hz, C_6-H) and 7.07 (dd, 1H, $^3J_{H-F}=8.6$ Hz, $^4J_{H-H}=2.6$ Hz, C_4-H); IR ν_{max} (cm^{-1}): 3051, 2925, 1479, 1186; MS (EI) m/z : 198 (M^+ , 33), 183 (65); Anal. calcd. for $C_{10}H_8ClFO$: C, 60.47; H, 4.06. Found: C, 60.47; H, 4.08%.

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24. Fluorophenol (41 mmole) and 50% aqueous 2-chloro-propanoic acid (41 mmol) were refluxed with 33% aqueous sodium hydroxide (82 mmol, 10 ml) solution for 3h. The reaction mixture is cooled and neutralized with 5% dilute HCl (15 ml). The precipitated 2-

fluorophenoxy-propanoic acid was filtered, washed with water (2x20 ml) and dried (yield: 88-94%). The fluorophenoxypropanoic acid was refluxed with 2 equivalents of thionyl chloride in hexane (10 ml) for 1-2 h. After removing hexane and excess thionyl chloride, pure fluoroaryloxypropanoyl chloride was obtained by distillation under reduced pressure (yield: 81-85%).

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