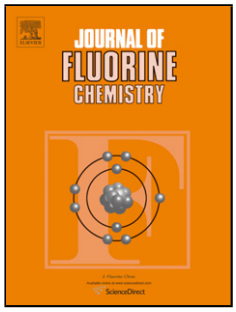

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Facile synthesis of 2-fluoroindenones *via* a Knoevenagel condensation/palladium-catalyzed annulation

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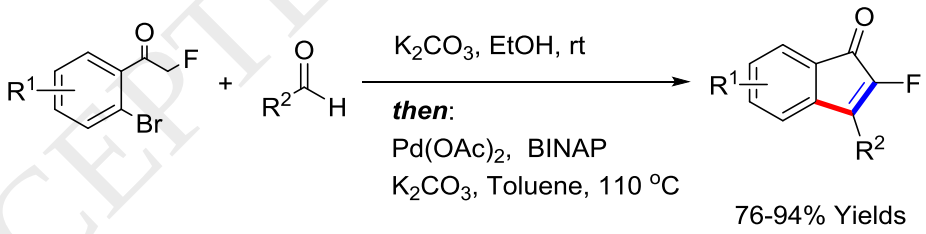
Graphical abstract



Highlights

- Domino reaction leading to 2-fluoroindenones
- No need of toxic CO gas
- Simple ortho-bromoketones and aldehydes were used

Abstract: An efficient synthesis of 2-fluoroindenones was developed starting from simple *o*-bromo-2-fluroethenones and aldehydes. This domino reaction involved Knoevenagel condensation and intramolecular Heck coupling cyclization. A variety of 2-fluoroindenones were generated in good to excellent yields.

Keywords: 2-Fluoroindenones, Domino reaction, Knoevenagel condensation, Intramolecular Heck cyclization

1. Introduction

Indenones are important carbocyclic compounds that are core moieties in a variety of natural products and biological active molecules [1]. For example, a structural analogue of indenone **A** is used as a fluorescent binding agent to estrogen receptors [2], neo-lignin **B** was isolated from Virolasebifera plant fruits [3], and compound **C** is a structural analogue of the selective COX-2 inhibitor nimesulide [4]. Compound **D**, as a hit toward agonists of peroxisome proliferator-activated receptor γ (PPAR γ), has displayed the most active agonistic activity with an EC_{50} value of 50 nM (Fig. 1) [5].

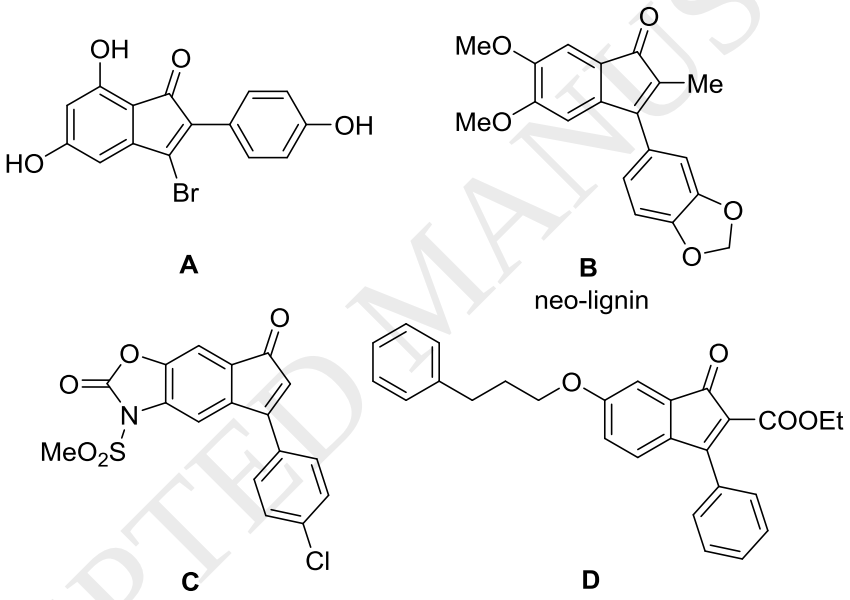
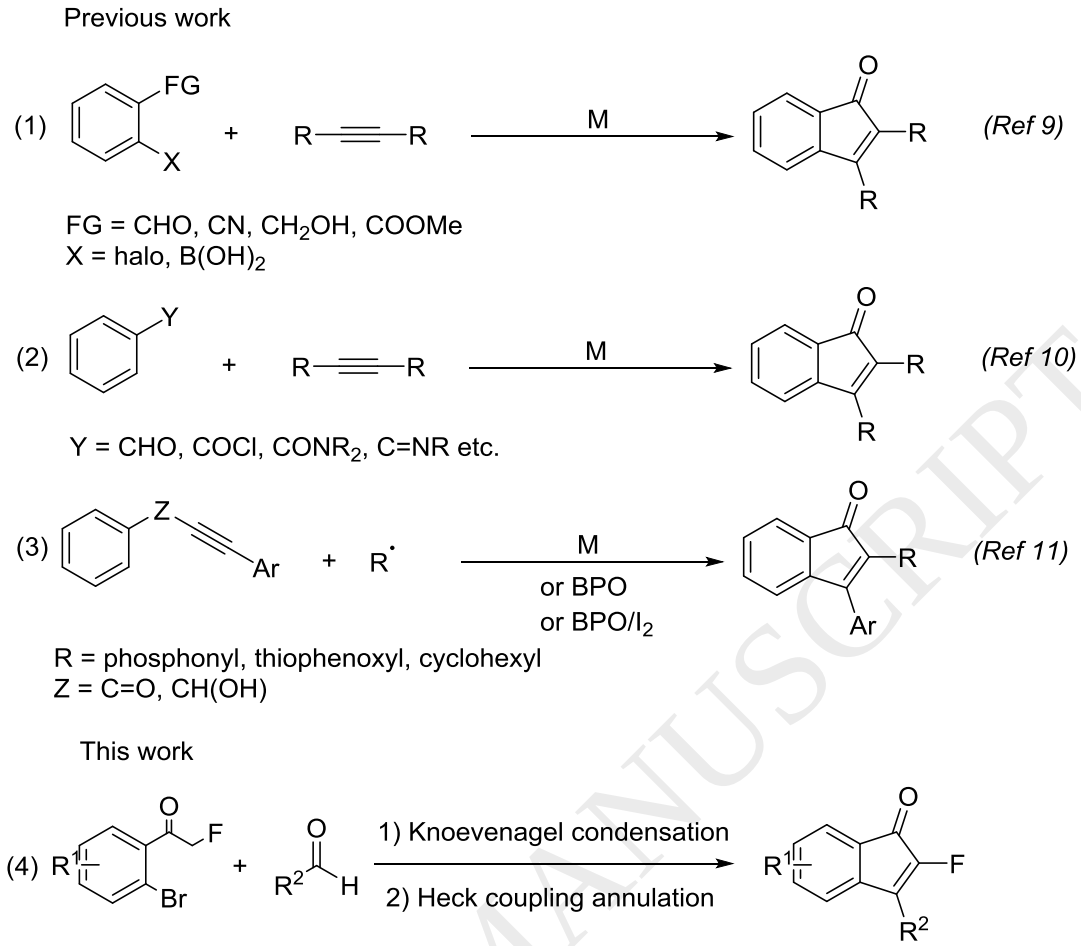


Figure 1. Compounds containing an indenone core.

On account of their importance, various methods have been developed to access indenones over the past decades. Although traditional indenone syntheses have largely relied upon Friedel-Crafts cyclizations [6] and the addition of Grignard reagents to 2-substituted indandiones [7], a number of transition-metal-catalyzed annulations of alkynes were accomplished using carbon monoxide (CO) as carbonylating agent [8], while annulations of internal alkynes with ortho-bifunctionalized arenes have also

been established (Scheme 1, Eq. 1) [9]. In recently years, guided by powerful C-H activation technologies, rhodium [10a-10e], rhenium [10f], cobalt [10g] and ruthenium [10h] catalyzed direct annulations of benzoyl chlorides, benzimides, benzamides, azomethines, arylnitrones and benzaldehydes with alkynes have been established (Scheme 1, Eq. 2). On the other hand, radical-mediated cyclizations were also reported (Scheme 1, Eq. 3) [11].

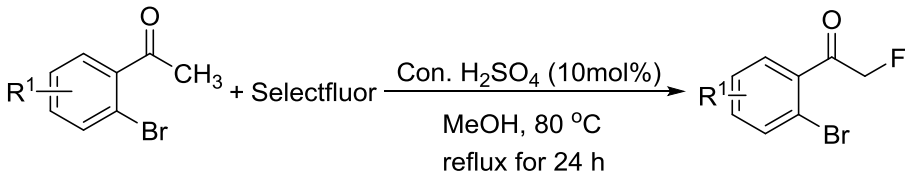
Introduction of fluorine atoms has become a crucial strategy in drug design [12]. The judicious incorporation fluorine atoms or fluorine-containing units on specific positions of biologically active organic molecules can significantly affect their pKa, conformation, intrinsic potency, pharmacokinetic properties and membrane permeability [13]. To the best of our knowledge, there are few 2-fluoroindenone examples reported in literature [14]. Herein, we describe an efficient domino process for the synthesis of 2-fluoroindenones starting from *o*-bromoketones and aldehydes (Scheme 1, Eq. 4).



Scheme 1. Synthetic strategies to indenones

2. Results and discussion

According to a previous method [15], 1-(2-bromoaryl)-2-fluoroethanones **2** were easily prepared from 1-(2-bromoaryl) ethanones **1** using Selectfluor as fluorination reagent in methanol (Scheme 2).

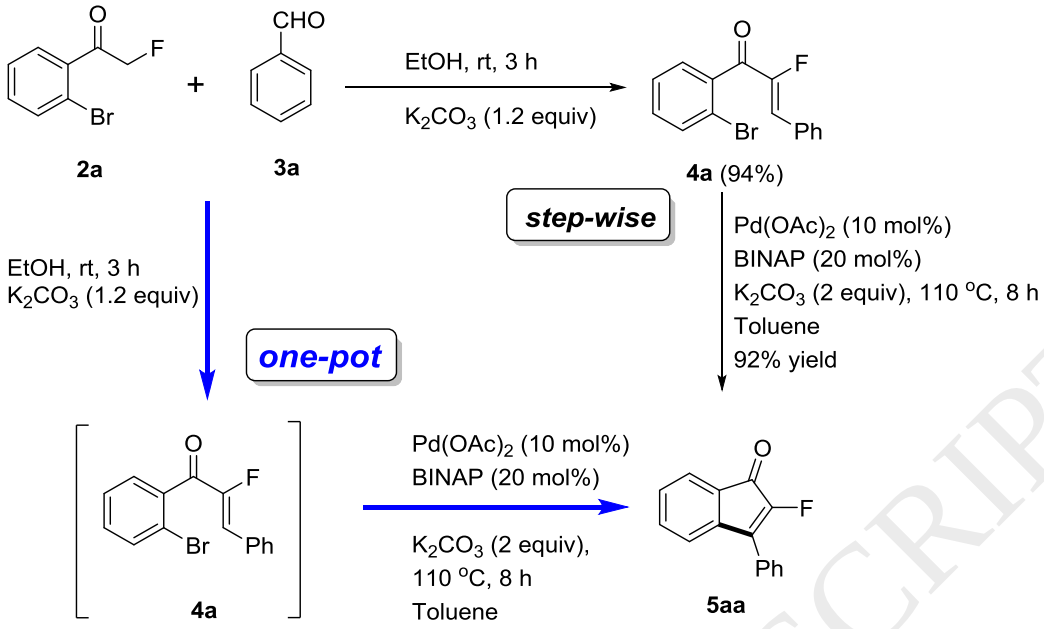


1 **2**

2a, R^1 = H, 88%
2b, R^1 = Cl, 76%
2c, R^1 = F, 78%

Scheme 2. Synthesis of 1-(2-bromoaryl)-2-fluoroethanones **2**

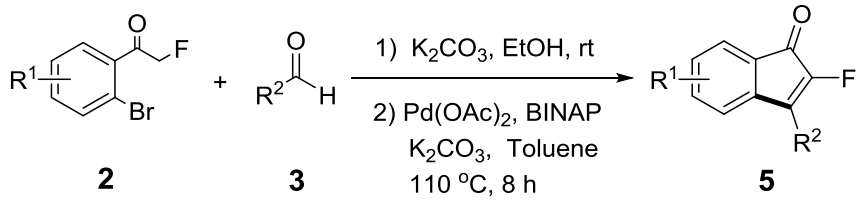
With substrates **2** in hand, we initially examined the reaction of 1-(2-bromophenyl)-2-fluoroethanone **2a** and benzaldehyde **3a**. With 1.2 equiv of K_2CO_3 in ethanol at room temperature, the Knoevenagel condensation reaction was carried out in 94% yield. Then, the isolated **4a** was subjected to a Pd-catalyzed intramolecular Heck coupling cyclization. By a careful, systematic examination of the influence of a variety of catalysts, ligands, bases and solvent, the optimal intramolecular Heck coupling reaction for the formation of the 2-fluoroindenone **5aa** was found to be 10 mol% $Pd(OAc)_2$, 20 mol% BINAP, 2 equiv of K_2CO_3 at 110 ^oC in toluene for 8 hours (92% yield). With these encouraging results, we performed a condensation reaction and a subsequent intramolecular Heck reaction in a one-pot manner. However, the overall yield was significant affected by the different solvents in two steps. To our delight, after evaporating the ethanol under vacuum after the Knoevenagel condensation step, the desired 2-fluoroindenone **5aa** was obtained in 91% overall yield (Scheme 3).



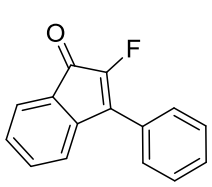
Scheme 3. Step-wise and one-pot synthesis of 2-fluoroindenone **5aa**

With these accomplishments, we then investigated the scope of this domino protocol between various 1-(2-bromoaryl)-2-fluoroethanones **2** and aldehydes **3** (Table 1). Gratifyingly, the reaction was amenable and afforded the 2-fluoroindenones **5aa**−**5cf** in good to excellent yields. Delightfully, the reaction proceeded smoothly with electron-withdrawing fluorine atom (**5ah**), as well as electron-donating alkyl (**5ab** and **5ag**), OMe (**5ac** and **5ad**), N, N-dimethyl (**5ae**) substituents on the aromatic ring of benzaldehydes. The reaction was also successful with electron-deactivating (F, Cl) atoms on the aromatic ring of 1-(2-bromoaryl)-2-fluoroethanones.

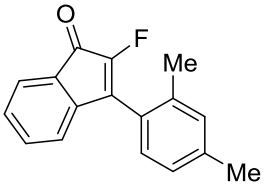
Table 1. Scope of domino cyclization synthesis of 2-fluoroindenones **5**[a,b]



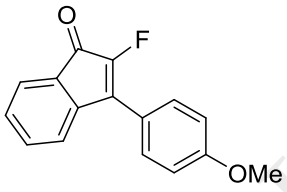
2 **3** **5**



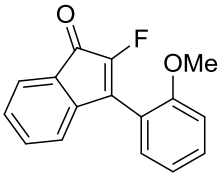
5aa (91%)



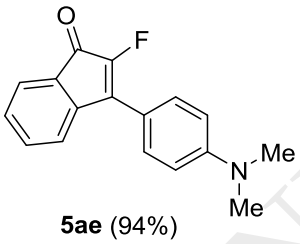
5ab (92%)



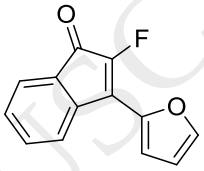
5ac (93%)



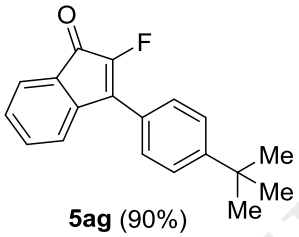
5ad (93%)



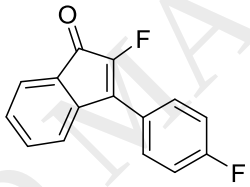
5ae (94%)



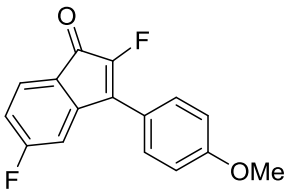
5af (94%)



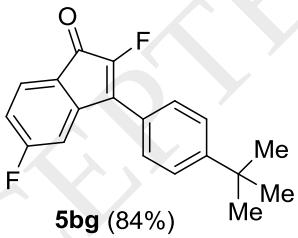
5ag (90%)



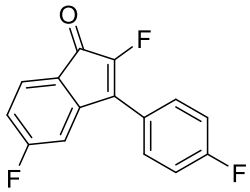
5ah (88%)



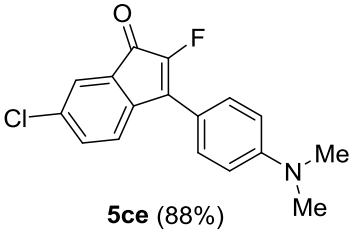
5bc (83%)



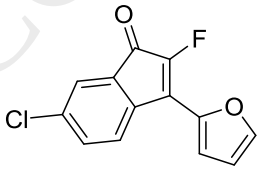
5bg (84%)



5bh (76%)



5ce (88%)



5cf (85%)

[a] Reaction conditions: 1) 1.1 equiv **2**, 1 equiv aldehyde **3**, 1.2 equiv K_2CO_3, ethanol (2 mL), rt, 3 h; 2) 10 mol% $Pd(OAc)_2$, 20 mol% BINAP, 2.0 equiv K_2CO_3, toluene (3

mL), 110 ^{o}C, 8 h.

[b] Isolated yield.

3. Conclusion

In summary, we have developed a convenient domino protocol via Knoevenagel condensation followed by intermolecular Heck annulation. Using 1-(2-bromoaryl)-2-fluoroethanones and aldehydes as readily materials, varieties of 2-fluoroindenones can be achieve in good to excellent yields.

4. Experimental

4.1. General

All reactions were carried out in oven-dried glassware under nitrogen atmosphere. All commercially available reagents were used without further purification, unless specified otherwise.

All new compounds were characterized by ^{1}H NMR,^{19}F NMR, ^{13}C NMR and IR spectroscopy , in addition to high-resolution mass spectroscopy. High-resolution mass spectra were carried out on a Finnigan GC-MS-4021 spectrometer. ^{1}H (400MHz) and ^{13}C (101MHz) NMR spectra were recorded on a BrukerAM-400 spectrometer with Me_4Si as an internal standard. ^{19}F NMR spectra were obtained on a BrukerAM-400 (376MHz) spectrometer in $CDCl_3$ with $CFCl_3$ as an external standard, in which downfield shifts were designated as negative. All chemical shifts (δ) were expressed in parts per million and coupling constants (*J*) are given in hertz.

4.2. General procedure for Domino reaction of 1-(2-bromoaryl)-2-fluoroethanones and aldehydes

A suspension of 1-(2-bromoaryl)-2-fluroethanones **2** (0.33 mmol, 1.1 equiv), aldehydes **3** (0.3 mmol, 1 equiv) and K_2CO_3 (0.36 mmol, 1.2 equiv) in ethanol (2 mL) was stirred at room temperature for 3 h. When the reaction was completed (monitored by TLC), the solvent was removed in vacuum. Then, $Pd(OAc)_2$ (0.03 mmol, 10%), BINAP (0.06 mmol, 20%), K_2CO_3 (0.6 mmol, 2.0 equiv) in toluene (3 mL) was added, and the mixture was stirred under N_2 atmosphere at 110 ^oC for 8 h. The crude product was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate as eluent.

*4.2.1. 2-fluoro-3-phenyl-inden-1-one(**5aa**)*

Yellow solid. m.p.: 85.7-86.7 ^oC. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 6.4 Hz, 2H), 7.54-7.45 (m, 3H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.25-7.17 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.41 (d, *J* = 24.0Hz), 151.41 (d, *J* = 292.1 Hz), 140.54, 135.54, 134.10, 130.33, 128.97, 128.74, 128.55, 128.25, 126.79, 123.25, 121.73 (d, *J* = 8.0 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -150.47 (s, 1F). IR (neat, cm^{-1}): 1726, 1631, 1599, 1494, 1446, 960, 690. MS (EI): m/z(%) 77 (3), 165 (3), 196 (34), 224 (100, M^+). HRMS: Calcd. for $C_{15}H_9FO$: 224.0637; found: 224.0639.

*4.2.2. 3-(2,4-dimethylphenyl)-2-fluoro-inden-1-one(**5ab**)*

Orange solid. m.p.: 95.1-95.4 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53-7.43 (m, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.30-7.25 (m, 2H), 7.23 (d, *J* = 9.6 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.2 Hz, 1H), 2.42 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 186.58 (d, *J* = 23.1 Hz), 150.17 (d, *J* = 290.4 Hz), 140.78, 138.93, 135.93, 135.09, 133.24, 130.80, 127.56, 126.78, 125.58, 125.44, 123.68, 121.93, 120.61 (d, *J* = 7.9 Hz), 20.31, 19.11. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -144.78 (s, 1F). IR (neat, cm^{-1}): 2924, 1719, 1603, 1530, 1451, 1432, 957, 710. MS (EI): m/z(%) 77 (4), 183 (38), 203 (16), 209 (58), 252 (100, M^{+}). HRMS: Calcd. for $C_{17}H_{13}FO$: 252.0950; found: 252.0951.

*4.2.3. 2-fluoro-3-(4-methoxyphenyl)-inden-1-one(5**ac**)*

Orange solid. m.p.: 150.6-150.8 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 7.1 Hz, 1H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 7.1 Hz, 1H), 7.32-7.24 (m, 1H), 7.12-7.01 (m, 2H), 3.93 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 186.23 (d, *J* = 22.1 Hz), 160.17, 149.89 (d, *J* = 289.1 Hz), 139.43, 134.51, 132.81, 128.98, 127.63, 126.14, 121.95, 120.68 (d, *J* = 7.9 Hz), 119.96, 113.44, 54.41. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -151.91 (s, 1F). IR (neat, cm^{-1}): 2922, 1734, 1602, 1514, 1461, 1451, 912, 718. MS (EI): m/z(%) 77 (4), 183 (38), 211 (19), 239 (19), 254 (100, M^{+}). HRMS: Calcd. for $C_{16}H_{11}FO_2$: 254.0743; found: 254.0744.

*4.2.4. 2-fluoro-3-(2-methoxyphenyl)-inden-1-one(5**ad**)*

Orange solid. m.p.: 153.8-154.4 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50-7.37 (m, 3H), 7.31 (d, *J* = 15.0 Hz, 1H), 7.19 (t, *J* = 7.0 Hz, 1H), 7.11-7.02 (m, 2H), 6.96 (d, *J* = 7.3 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.79 (d, *J* = 22.9 Hz), 157.37, 151.79 (d, *J* = 292.2 Hz), 141.50, 134.12, 133.55, 131.54, 129.59, 128.27, 126.49, 122.72, 121.93 (d, *J* = 7.8 Hz), 120.61, 117.39, 111.57, 55.59. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -144.24 (s, 1F). IR (neat, cm^{-1}): 2912, 1735, 1604, 1508, 1472, 1450, 928, 709. MS (EI): m/z(%) 77 (4), 183 (38), 211 (19), 239 (19), 254 (100, M^{+}). HRMS: Calcd. for $C_{16}H_{11}FO_2$: 254.0743; found: 254.0744.

*4.2.5. 3-(4-(dimethylamino)phenyl)-2-fluoro-inden-1-one(5**ae**)*

Purplish red solid. m.p.: 110.6 -110.8 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.9 Hz, 2H), 7.48-7.30 (m, 3H), 7.23 (d, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 9.0 Hz, 2H), 3.07 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 185.94 (d, *J* = 21.2 Hz), 150.49, 149.24 (d, *J* = 284.8 Hz), 139.38, 135.46, 132.30, 128.94, 127.39, 126.90, 121.40, 120.82 (d, *J* = 7.8 Hz), 114.98, 110.67, 39.03. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -153.66 (s, 1F). IR (neat, cm^{-1}): 2918, 1707, 1603, 1526, 1484, 1442, 959, 702. MS (EI): m/z(%) 175 (3), 223 (4), 251 (14), 267 (100, M^{+}). HRMS: Calcd. for $C_{17}H_{14}FNO$: 267.1059; found: 267.1058.

*4.2.6. 2-fluoro-3-(furan-2-yl)-inden-1-one(5**af**)*

Orange solid. m.p.: 168.0-168.5 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85-7.77 (m, 1H), 7.74 (d, *J* = 2.2 Hz, 1H), 7.48-7.38 (m, 2H), 7.26 (s, 1H), 7.22-7.17 (m, 1H), 6.69 (dd, *J* = 3.8, 1.9 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 186.14 (d, *J* = 20.7 Hz), 149.23 (d, *J* = 293.7 Hz), 145.26, 142.51, 137.99, 134.08, 128.90, 127.20, 125.26, 123.48 (d, *J* = 7.9 Hz), 122.85, 117.31, 113.14. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -144.90 (s, 1F). IR (neat, cm^{-1}): 2962, 2849, 2351, 1724, 1597, 1473, 1420, 803, 743. MS (EI): m/z(%) 157 (33), 221 (3), 214 (100, M^{+}). HRMS: Calcd. for $C_{13}H_7FO_2$: 214.0430; found: 214.0431.

*4.2.7. 3-(4-(tert-butyl)phenyl)-2-fluoro-inden-1-one(5**ag**)*

Yellow solid. m.p.: 175.8-176.5 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 8.4 Hz, 2H), 7.58-7.51 (m, 2H), 7.47-7.43 (m, 1H), 7.39-7.34 (m, 1H), 7.31 (d, *J* = 7.0 Hz, 1H), 7.26-7.19 (m, 1H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.44 (d, *J* = 22.1 Hz), 153.89, 151.29 (d, *J* = 291.89 Hz), 140.54, 135.65, 133.96, 128.64, 128.08, 126.97, 125.93, 125.69, 123.09, 121.81 (d, *J* = 8.0 Hz), 35.03, 31.17. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -150.93 (s, 1F). IR (neat, cm^{-1}): 2962, 2849, 2351, 1724, 1597, 1473, 1420, 803, 743. MS (EI): m/z(%) 77 (3), 220 (34), 238 (5), 280 (100, M^{+}). HRMS: Calcd. for $C_{19}H_{17}FO$: 280.1029; found: 280.1263.

*4.2.8. 2-fluoro-3-(4-fluorophenyl)-1H-inden-1-one(5**ah**)*

Orange solid. m.p.: 166.0-166.4 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73-7.54 (m, 2H), 7.50-7.44 (m, 1H), 7.38 (td, *J* = 7.6, 7.1, 1.5 Hz, 1H), 7.29-7.20 (m, 2H),

7.20-7.13 (m, 1H), 6.95 (t, *J* = 8.6 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.76 (d, *J* = 18.4 Hz), 161.88 (d, *J* = 248.7 Hz), 151.00(d, *J* = 287.8 Hz), 136.30, 131.43 (d, *J* = 8.2 Hz), 129.06, 127.79, 125.07, 121.53 (d, *J* = 8.1 Hz), 116.40, 116.18, 115.65, 115.44. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -108.54 – -108.66 (m, 1F), -150.51(s, 1F). IR (neat, cm^{-1}): 1738, 1606, 1510, 1479, 1449, 910, 677. MS (EI): m/z(%) 194 (7), 214 (35), 242 (100, M^+). HRMS: Calcd. for $C_{15}H_8F_2O$: 242.0544; found: 242.0543.

*4.2.9. 2,5-difluoro-3-(4-methoxyphenyl)-inden-1-one(5**bc**)*

Orange solid. m.p.: 154.9-155.6 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 8.8 Hz, 2H), 7.36 (dd, *J* = 7.9, 5.3 Hz, 1H), 6.97 (d, *J* = 8.9 Hz, 3H), 6.79 (ddd, *J* = 8.9, 8.0, 2.2 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 184.51 (d, *J* = 22.3 Hz), 165.36 (d, *J* = 255.1 Hz), 160.31, 150.29 (d, *J* = 292.5 Hz), 142.88, 132.63 (d, *J* = 9.3 Hz), 128.80, 123.98 (d, *J* = 9.9 Hz), 121.86, 119.38, 113.59, 110.26, 54.41. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -102.01 (td, *J* = 9.8, 5.5 Hz, 1F), -148.45(s, 1F). IR (neat, cm^{-1}): 2963, 1713, 1637, 1599, 1510, 1460, 945, 798. MS (EI): m/z(%) 175 (3), 223 (4), 251 (14), 267 (100, M^+). HRMS: Calcd. for $C_{16}H_{10}F_2O_2$: 267.1059; found: 267.1058.

*4.2.10. 3-(4-(tert-butyl)phenyl)-2,5-difluoro-inden-1-one(5**bg**)*

Orange solid. m.p.: 171.9-172.8 ºC. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (m, *J* = 9.0, 5.3, 1.5 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.47 (d, *J* = 7.1 Hz, 1H), 7.35 (d, *J* =

8.5 Hz, 2H), 7.05 (t, *J* = 8.6 Hz, 1H), 6.78 (d, *J* = 36.8 Hz, 1H), 1.24 (s, 9H). 13C NMR (101 MHz, Chloroform-*d*) δ 185.39 (d, *J* = 22.8 Hz), 162.08 (d, *J* = 249.4 Hz), 151.78 (d, *J* = 292.6 Hz), 131.28 (d, *J* = 8.0 Hz), 130.28, 130.19, 125.48 (d, *J* = 10.4 Hz), 118.01, 117.78, 116.59, 116.37, 115.96, 115.74, 35.03, 31.17. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.71 – -101.87 (m, 1F), -147.43 (s, 1F). IR (neat, cm^{-1}): 2926, 1707, 1606, 1516, 1480, 1439, 1366, 1359, 940, 701. MS (EI): m/z(%) 77 (3), 220 (34), 238 (5), 298 (100, M^+). HRMS: Calcd. for $C_{19}H_{16}F_2O$: 298.1169; found: 298.1170.

*4.2.11. 2,5-difluoro-3-(4-fluorophenyl)-inden-1-one(5**bh**)*

Yellow solid. m.p.: 170.0-170.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (dd, *J* = 8.6, 5.3 Hz, 1H), 7.08-7.02 (m, 2H), 6.91 (t, *J* = 8.6 Hz, 3H), 6.87-6.83 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.54 (d, *J* = 22.2 Hz), 162.72 (d, *J* = 253.3 Hz), 162.32 (d, *J* = 255.8 Hz), 151.93 (d, *J* = 287.8 Hz), 131.27 (d, *J* = 8.1 Hz), 128.38 (d, *J* = 3.5 Hz), 127.95 (d, *J* = 10.7 Hz), 118.03, 117.80, 115.97, 115.76, 114.52, 114.29. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -96.15 (td, *J* = 9.3, 5.8 Hz, 1F), -112.77 – -112.87 (m, 1F), -189.88 (s, 1F). IR (neat, cm^{-1}): 1738, 1607, 1511, 1477, 1450, 910, 678. MS (EI): m/z(%), 212 (12), 232 (42), 260 (100, M^+). HRMS: Calcd. for $C_{15}H_7F_3O$: 260.0449; found: 260.0451.

*4.2.12. 4-chloro-3-(4-(dimethylamino)phenyl)-2-fluoro-inden-1-one(5**ce**)*

Burgundy solid. m.p.: 162.4-163.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65-7.54 (m, 2H), 7.31 (s, 1H), 7.25 (d, *J* = 3.1 Hz, 1H), 7.19 (s, 1H), 6.79-6.62 (m, 2H), 3.01 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 186.29 (d, *J* = 27.2 Hz), 152.30 (d, *J* = 280.7 Hz), 151.54, 138.81, 134.50, 132.80, 132.09, 129.63, 129.16, 127.23, 123.02 (d, *J* = 8.0 Hz), 118.79, 111.80, 40.04. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -152.43 (s, 1F). IR (neat, cm^{-1}): 2959, 2918, 1707, 1606, 1526, 1453, 1416, 979, 731. MS (EI): m/z(%) 121 (5), 194 (9), 285 (14), 301 (100, M^{+}). HRMS: Calcd. for $C_{17}H_{13}ClFNO$: 303.0670; found: 303.0671.

*4.2.13. 4-chloro-2-fluoro-3-(furan-2-yl)-inden-1-one(5**cf**)*

Orange solid. m.p.: 167.5-168.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (dd, *J* = 4.9, 3.0 Hz, 2H), 7.44-7.38 (m, 2H), 7.22 (d, *J* = 3.7 Hz, 1H), 6.71 (dd, *J* = 3.8, 1.9 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ186.45 (d, *J* = 26.6 Hz), 148.61(d, *J* = 290.88 Hz), 145.62, 135.87, 134.96, 133.10, 129.83, 124.55 (d, *J* = 8.4 Hz), 123.46, 118.03, 117.92, 113.37, 113.02. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -143.85 (s, 1F). IR (neat, cm^{-1}): 2958, 2852, 2361, 1723, 1595, 1462, 1423, 803, 744. MS (EI): m/z(%) 157 (33), 221 (3), 248 (100, M^{+}). HRMS: Calcd. for $C_{13}H_{6}ClFO_{2}$: 248.0040; found: 248.0041.

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