JOC The Journal of Organic Chemistry

Article

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Synthesis of α-Fluoro-α-nitroarylacetates via Vicarious Nucleophilic Substitution of Hydrogen

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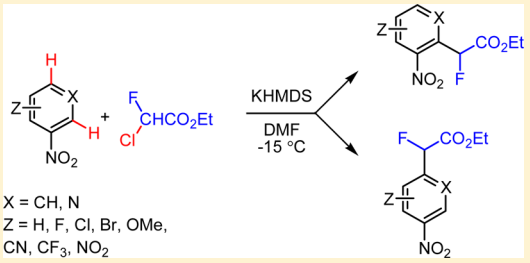
Supporting Information

ABSTRACT: Readily available ethyl chlorofluoroacetate, when treated with a strong base, forms an α-chloro-α-fluorocarbanion that adds to nitroarenes at a position *ortho* or *para* to the nitro group with formation of anionic σ^H adducts. Subsequent base-induced β-elimination of HCl proceeds selectively to give nitrobenzylic α-fluorocarbanions and, upon protonation, ethyl α-fluoro-α-nitroarylacetates.



INTRODUCTION

Owing to the unique properties of fluorine atom, high electrophilicity, small atomic radius, and high energy of C−F bonds, the presence of fluorine in organic molecules affects substantially their physicochemical and biological properties; hence, a significant proportion of new pharmaceuticals and agrochemicals contain fluorine.[1] As a consequence, synthesis of fluoroorganic compounds is of great interest, and it is widely studied.[2] One of the main approaches to the synthesis of desired fluoroorganic molecules is introduction of fluorinated substituents into aromatic rings.[3] Recently, a new method for synthesis of ethyl α-fluoro-α-arylacetates and α-fluorobenzyl phenyl sulfone was reported via nickel-catalyzed reaction of arylboronic acids with ethyl bromofluoroacetate and fluoroiodomethyl phenyl sulfone (Scheme 1).[4] The latter reaction was also used for synthesis of substituted benzyl fluorides via controlled reduction of the α-fluorobenzyl sulfones.

Synthesis of a few ethyl α-fluoro-α-(*o*-nitroaryl)acetates was recently published via a multistep reaction sequence: S_NAr of fluorine in *o*-fluoronitrobenzenes by the carbanion of diethyl fluoromalonate, hydrolysis of the obtained diethyl fluoro(*o*-nitroaryl)malonates, decarboxylation, and esterification (Scheme 1).[5]

In this paper, we present a much simpler synthesis of esters of α-fluoro-α-arylacetic acids that contain a nitro group in the ring via vicarious nucleophilic substitution of hydrogen (VNS) in nitroarenes with ethyl chlorofluoroacetate (Scheme 1).

VNS is a general reaction between α-halocarbanions and electron-deficient arenes, particularly nitroarenes. It proceeds via addition of the carbanions to the nitroaromatic rings at positions *ortho* or *para* to the nitro group occupied by hydrogen to form anionic σ^H adducts. Subsequent base-induced β-elimination of hydrogen halide produces nitrobenzylic carbanions of the products. Further protonation gives products of substitution of hydrogen with the carbanion moiety.[6] It should be stressed that addition of carbanions to halonitroarenes proceeds faster at positions occupied by hydrogen than at those occupied by halogen. Therefore, VNS of hydrogen also proceeds efficiently with *o*- and *p*-halonitroarenes and even in 2,4-dinitrofluorobenzene without competing S_NAr of the halogens.[7] A variety of α-halocarbanions generated from esters of chloro- and dichloroacetic acids, α-chloronitriles, and even haloforms enter the VNS reaction.[6,8]

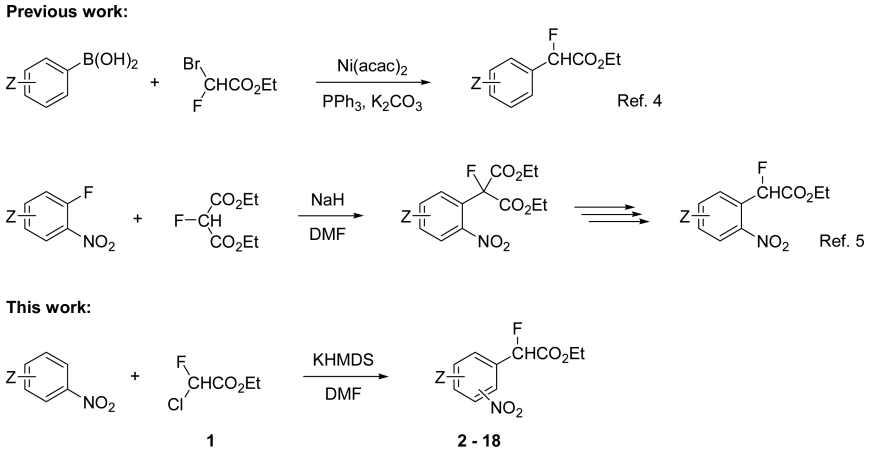
Taking into account that base-induced β-elimination of HCl proceeds usually much faster than HF, we expected that carbanion generated by deprotonation of commercially available ethyl chlorofluoroacetate should react with nitroarenes via addition at positions occupied by hydrogen to form σ^H adducts. Subsequent reaction of the σ^H adducts with a base should result in selective β-elimination of HCl rather than HF with formation of esters of α-nitroaryl-α-fluoroacetic acids as ultimate products.

Surprisingly, reactions of carbanions generated by deprotonation of ethyl chlorofluoroacetate are unknown, although other reactions of this ester are reported.[9] There is an example of alkylation of the carbanion of *tert*-butyl chlorofluoroacetate with allyl bromide[10a] and of mercuration of carbanion of methyl chlorofluoroacetate.[10b] We have also found only one report of a reaction of a carbanion of analogous ethyl bromofluoroacetate generated by deprotonation of the ester. Treatment of a solution of this ester and diarylnitrones in THF at −78 °C with KHMDS (potassium hexamethyldisilazide) results in addition of the α-fluoro-α-bromocarbanion to the electron-deficient C═N double bond. Further elimination of Br^- and nitrosobenzene gives substituted ethyl α-fluoroacrylates.[11] On the other hand, it was reported that the attempted Michael addition of a carbanion generated by base-induced deprotonation of ethyl bromofluoroacetate was unsuccessful.[12] Carbanion of ethyl bromofluoroacetate for the Darzens reaction with ketones

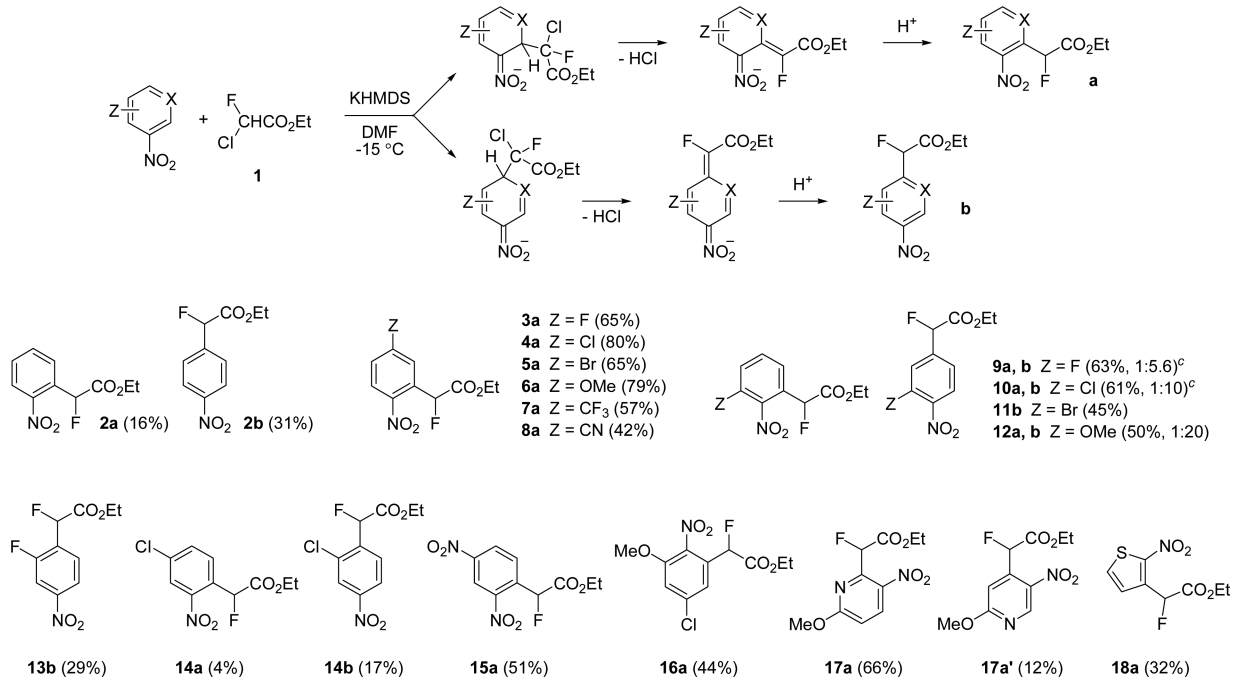
Received: September 9, 2016
Published: October 26, 2016

DOI: 10.1021/acs.joc.6b02219
J. Org. Chem. 2016, 81, 11751−11757

Scheme 1. Preparation of Esters of α-Fluoro-α-arylacetic Acids



Scheme 2. VNS Reactions of Nitroarenes with 1[a,b]



[a]Reaction conditions: nitroarene (1 equiv) and **1** (1 equiv) in DMF were added dropwise to KHMDS (3 equiv) in DMF cooled to −15 °C and then stirred for 30 min. [b]Yields of isolated products without optimization of individual examples. [c]Regioisomers not separated.

to give α-fluorooxiranes was generated not via deprotonation of the ester but via debromination of ethyl dibromofluoroacetate with diethylzinc.[13] Recently, reactions of carbanions of ethyl fluoroacetate, α-fluoroalkanoates, and α-fluoro-substituted ethyl arylacetates with imines were reported.[14] In light of the above reports, the chance for VNS with carbanion of ethyl chlorofluoroacetate **1** appeared doubtful.

RESULTS AND DISCUSSION

To our satisfaction, when a solution of **1** and *p*-chloronitrobenzene in THF was added to a solution of 3 molar equiv of *t*-BuOK in DMF at −20 °C, typical conditions for VNS with α-chloroesters, strong coloration of the reaction mixture, characteristic for nitrobenzylic carbanions, was observed. Upon acidification of the mixture, the expected product, ethyl α-fluoro-α-(2-nitro-5-chlorophenyl)acetate, was isolated in moderate yield of 40%. The product was contaminated with *tert*-butyl ester due to partial trans-esterification. After some experimentation, we found that the reaction gives much better yields when carried out in DMF in the presence of KHMDS instead of *t*-BuOK. On the other hand, inferior results are obtained at temperatures lower than −15 °C.

Thus, when a solution of *p*-chloronitrobenzene and **1** (molar ration 1:1) in DMF was added to a solution of KHMDS in DMF at −15 °C and the resulting mixture was stirred at this temperature for 15 min, upon standard workup the desired product was obtained in 63% yield. Under similar conditions, nitrobenzene and a series of substituted nitrobenzenes gave the esters of α-fluoro-α-(*o*- and *p*-nitroaryl)acetic acids, usually with good yields. The results of the reactions are presented in Scheme 2.

As we expected, the reaction of **1** with nitrobenzene **2** resulted in the formation of two isomeric products of

DOI: 10.1021/acs.joc.6b02219
J. Org. Chem. 2016, 81, 11751−11757

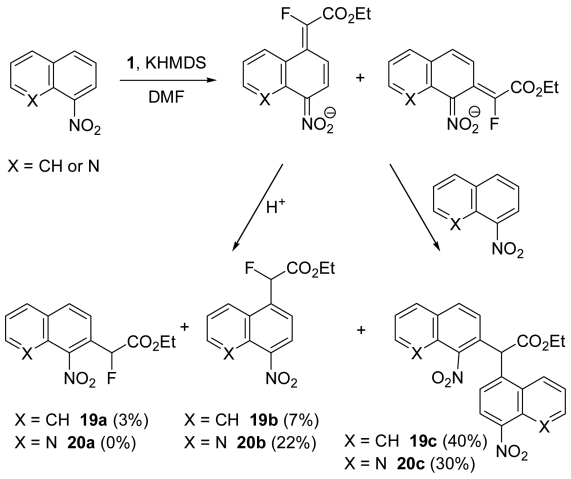
substitution in the *ortho* (**2a**) and *para* (**2b**) positions in moderate yield. In spite of the methinic character of the carbanion $\mathbf{1}^-$, due to the small atomic radius of fluorine, $\mathbf{1}^-$ is not sterically demanding, and the ratio of **2a** and **2b** is 1:2. On the other hand, VNS in nitrobenzene with carbanion of ethyl dichloroacetate proceeds only in the *para* position.[8b] Nitrobenzenes *para*-substituted with electron-withdrawing and electron-donating groups react with **1** satisfactorily to give the expected products of substitution in the position *ortho* to the nitro group (**3a**−**8a**) in moderate to good yields. To some extent, moderate yields were associated with incomplete consumption of the starting nitroarene, but formation of decomposition products could be observed as well. It is difficult to correlate the yields with the nature of substituents present in the nitroarene ring. However, correlation of the rates of the first reaction step, that is, nucleophilic addition of a model carbanion of chloromethyl phenyl sulfone to variously substituted nitroarenes, with the Hammett constants has been reported by us previously.[7a] It should be mentioned that the reaction of **1** with *p*-fluoro nitrobenzene proceeds exclusively as VNS of hydrogen without traces of conventional S_NAr of fluorine. Interestingly, the reaction of $\mathbf{1}^-$ with 2-fluoronitrobenzene proceeds also exclusively as VNS of hydrogen giving products of substitution at the *ortho* and *para* positions in a ratio of 1:5. In our previous quantitative studies of rates of the addition of methylenic carbanion of $PhSO_2CH_2Cl$ to nitroarenes we observed that rates of the addition of this carbanion to 2-fluoronitrobenzene at positions 2-, 4-, and 6- are almost equal.[7a]

Observation that VNS of hydrogen in *o*- and *p*-halonitrobenzenes to give esters **3**−**5** and **9**−**11** proceeds faster than conventional S_NAr of halogen confirms the recently formulated, corrected mechanism of nucleophilic aromatic substitution in nitroarenes.[15]

Interesting results gave the VNS reaction of $\mathbf{1}^-$ with 1-nitronaphthalene (Scheme 3). Apart from the expected products of substitution at positions 2- (**19a**) and 4- (**19b**) in a ratio of 1:2.2, the third product **19c** was formed that did not contain fluorine (yields of **19a**, **19b**, and **19c** of 11%, 24%, and 23%, respectively). On the basis of NMR and MS analysis, we have found that this unexpected compound was the product of double VNS reaction: ethyl *α*-(1-nitronaphth-2-yl)-*α*-(1-nitronaphth-4-yl)acetate (Scheme 3). Product **19c** was apparently formed via addition of the *α*-fluoro carbanion of **19a** to 1-nitronaphthalene at position 4 and base-induced *β*-elimination of HF from the σ^H adduct. In order to confirm this supposition, the reaction of **1** with 1-nitronaphthalene was repeated with a double excess of the latter reactant. In this case, the selectivity of the reaction toward formation of bis(arylated) product increased as the compounds **19a**, **19b**, and **19c** were formed in 3%, 7%, and 40% yield, respectively. A similar product has been observed in the reaction of $\mathbf{1}^-$ with 8-nitroquinoline as ethyl *α*-(8-nitroquinolin-5-yl)-*α*-(8-nitroquinolin-7-yl)acetate **20c** has been obtained in 30% yield, together with ethyl *α*-(8-nitroquinolin-5-yl)acetate **20b** (22%; Scheme 3). It was the first case where such double-VNS reactions were observed. In previous papers, we and other authors reported that reaction of *α*,*α*-dichlorocarbanions of dichloroacetates and carbanions of haloforms react with nitroarenes to give *α*-chloronitrobenzylic and *α*,*α*-dichloronitrobenzylic carbanions that upon protonation give the expected VNS products. No further reactions of these intermediate *α*-chloronitrobenzylic carbanions with nitroarenes have been observed. The double VNS of carbanion of **1** occurs perhaps due to high activity of bicyclic nitroarenes in electrophilic addition to the ring as well as smaller steric requirements of *α*-fluorocarbanions and their higher nucleophility resulting from weaker carbanion-stabilizing effect of fluorine compared with chlorine.

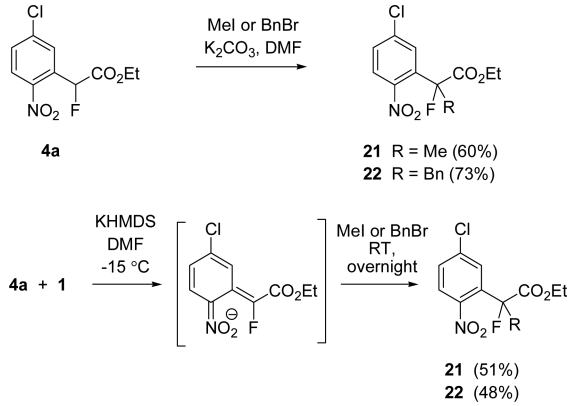
The carbanions of ethyl *α*-fluoro-*α*-nitroarylacetates formed in the VNS reaction of **1** are sufficiently stable to enter subsequent reactions, even with moderately active electrophilic partners, to provide *α*-nitroaryl esters with a quaternary center substituted with fluorine atom. For instance, they can be alkylated with ethyl iodide and benzyl bromide to form esters of higher *α*-fluoro acids (Scheme 4). The reaction can be performed as a one-pot process as quenching the reaction mixture after the VNS stage with an alkylating agent instead of HCl gives the same products **21** and **22** in moderate yields (Scheme 4, bottom).

Scheme 3. Reactions of Bicyclic Electron-Deficient Arenes with 1[a]



[a]Reaction conditions: nitroarene (2 equiv) and **1** (1 equiv) in DMF were added dropwise to KHMDS (3 equiv) in DMF cooled to −15 °C and then stirred for 30 min.

Scheme 4. Alkylation of Ethyl *α*-Fluoro-*α*-nitroarylacetates



CONCLUSIONS

Ethyl chlorofluoroacetate under treatment with a strong base, *t*-BuOK or KHMDS in DMF, is deprotonated to form *α*-chloro-*α*-fluorocarbanion. This carbanion is sufficiently stable and

DOI: 10.1021/acs.joc.6b02219
J. Org. Chem. 2016, 81, 11751−11757

active to add to nitroaromatic rings with the formation of σ^H adducts that in the presence of a base undergo selective β-elmination of HCl (rather than HF) to form nitrobenzylic α-fluorocarbanions. Their protonation leads to the products of vicarious nucleophilic substitution: ethyl α-fluoro-α-(*o*- and *p*-nitroaryl)acetates. Nitroarenes that are very prone to nucleophilic addition to the ring, such as nitronaphthalene, can add to the initially formed nitrobenzylic α-fluorocarbanions to form products of double-VNS reactions: esters of bis-(nitroaryl)acetic acids. Besides protonation, α-fluorocarbanions of the products can be directly quenched by alkyl halides to give esters of α-fluoro-α-nitroarylalkanoic acids. Although our method is limited to electron-deficient nitroarenes and the substitution can result in formation of isomeric products, it is simpler than other reported methods.

EXPERIMENTAL SECTION

The ^{1}H and ^{13}C NMR spectra were recorded at a temperature of 298 K in $CDCl_3$ solutions with a 500 MHz spectrometer (500, 125, and 470 MHz for ^{1}H, ^{13}C, and ^{19}F, respectively) or 400 MHz (400, 100, and 376 MHz for ^{1}H, ^{13}C, and ^{19}F, respectively). The ^{1}H and ^{13}C NMR chemical shifts are given relative to the TMS signal at 0.0 ppm and relative to $CFCl_3$ for ^{19}F spectra. Mass spectra and HRMS measurements were obtained using a mass spectrometer equipped with an electrospray ion source and q-TOF type mass analyzer (ES+) or a magnetic sector mass spectrometer equipped with an electron impact (EI) ion source and the EBE double-focusing geometry mass analyzer. IR spectra were obtained from DCM film using a FT-IR spectrometer. Melting point temperatures were measured at a heating rate of 5 °C/min and are uncorrected. Column chromatography was performed using silica gel 60 (0.040−0.063 mm). Thin-layer chromatography was performed on precoated silica gel plates and visualized under a UV lamp. For column chromatography, hexanes/ethyl acetate and hexanes/Et_2O mixtures were used as eluents. Hexanes were distilled before use. Dry DMF and ethyl chlorofluoroacetate and other reagents were commercial and used as received.

General Procedure for Preparation of Ethyl α-Fluoro-α-nitroarylacetates. A solution of KHMDS (3 mmol, 598 mg) in dry DMF (3 mL) was placed in a Schlenk flask under argon atmosphere and cooled to −15 °C. A solution of ethyl chlorofluoroacetate **1** (1 mmol, 141 mg, 116 μL) and nitroarene (1 mmol) in dry DMF (1 mL) was added dropwise. The reaction mixture was stirred at −15 °C for 30 min and poured into ice-cold 1 M HCl (20 mL). The product was extracted with AcOEt (3 × 15 mL), and the combined organic layers washed with brine (3 × 30 mL) and dried (Na_2SO_4). After evaporation of solvent, the crude products were purified using column chromatography on silica gel with hexanes−AcOEt 5:1 as eluent. Isomeric products could be more readily separated with hexanes−Et_2O 10:1 or 5:1 eluent.

Ethyl 2-fluoro-2-(2-nitrophenyl)acetate (**2a**): 36 mg (16%) yield; bright yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.2 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.74 (t, J = 7.2 Hz, 1H), 7.59 (m, 1H), 6.62 (d, $^2J_{HF}$ = 46.7 Hz, 1H), 4.31−4.20 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8 (d, J_{CF} = 24.7 Hz), 147.1, 134.2 (d, J_{CF} = 1.8 Hz), 130.5 (d, J_{CF} = 21.3 Hz), 130.1 (d, J_{CF} = 1.4 Hz), 127.7 (d, J_{CF} = 14.5 Hz), 125.3, 86.7 (d, J_{CF} = 184.1 Hz), 62.6, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −187.97 (d, $^2J_{FH}$ = 46.6 Hz); IR (DCM) ν_{max} 2986, 2940, 1749, 1531, 1351, 1215, 1024 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_{10}FNO_4Na$ [M + Na]$^+$ 250.0492, found 250.0491.

Ethyl 2-fluoro-2-(4-nitrophenyl)acetate (**2b**): 71 mg (31%) yield; bright yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 9.0 Hz, 2H), 5.89 (d, $^2J_{HF}$ = 47.3 Hz, 1H), 4.32−4.20 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4 (d, J_{CF} = 26.3 Hz), 148.7, 141.0 (d, J_{CF} = 20.7 Hz), 127.2 (d, J_{CF} = 7.1 Hz), 124.0, 88.3 (d, J_{CF} = 189.1 Hz), 62.6, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ −185.89 (d, $^2J_{FH}$ = 47.3 Hz); HRMS (ES+) calcd for $C_{10}H_{10}FNO_4Na$ [M + Na]$^+$ 250.0492, found 250.0488; IR (DCM) ν_{max} 3115, 3085, 2985, 1761, 1529, 1350, 1217, 1077, 1016, 858, 736 cm^{-1}. Anal. Calcd for $C_{10}H_{10}FNO_4$: C, 52.87; H, 4.44; F, 8.36; N, 6.17. Found: C, 52.96; H, 4.52; F, 8.45; N, 6.07.

Ethyl 2-fluoro-2-(5-fluoro-2-nitrophenyl)acetate (**3a**): 159 mg (65%) yield; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (ddd, J = 9.1, 4.9, 0.9 Hz, 1H), 7.50 (dd, J = 9.0, 2.7 Hz, 1H), 7.25 (m, 1H), 6.62 (d, $^2J_{HF}$ = 46.8 Hz, 1H), 4.7 (q, J = 7.2 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8 (d, J_{CF} = 24.1 Hz), 165.5 (dd, J_{CF} = 258.8 Hz, 2.7 Hz), 142.8, 134.3 (dd, J_{CF} = 21.7 Hz, 9.2 Hz), 128.2 (d, J_{CF} = 9.9 Hz), 116.7 (d, J_{CF} = 23.5 Hz), 114.9 (dd, J_{CF} = 26.2 Hz, 17.2 Hz), 86.7 (d, J_{CF} = 185.0 Hz), 62.6, 13.8; ^{19}F NMR (470 MHz, $CDCl_3$) δ −100.68 to −100.76 (m, 1F), −187.93 (d, $^2J_{FH}$ = 46.8 Hz, 1F); IR (DCM) ν_{max} 3123, 3087, 2986, 2938, 1751, 1593, 1533, 1350, 1275, 1232, 1031, 841 cm^{-1}. HRMS (ES+) calcd for $C_{10}H_9F_2NO_4Na$ [M + Na]$^+$ 268.0397, found 268.0394.

Ethyl 2-(5-chloro-2-nitrophenyl)-2-fluoroacetate (**4a**): 209 mg (80%) yield; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, J = 8.9, 0.9 Hz, 1H), 7.78 (d, J = 2.2 Hz, 1H), 7.55 (dd, J = 8.8, 2.1 Hz, 1H), 6.60 (d, $^2J_{HF}$ = 46.7 Hz, 1H), 4.26 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (d, J_{CF} = 24.2 Hz), 145.0, 141.3 (d, J_{CF} = 2.5 Hz), 132.6 (d, J_{CF} = 21.5 Hz), 129.9, 127.8 (d, J_{CF} = 16.9 Hz), 126.8, 86.6 (d, J_{CF} = 185.6 Hz), 62.9, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −191.05 (d, $^2J_{FH}$ = 46.7 Hz); IR (DCM) ν_{max} 3111, 2985, 2940, 1748, 1608, 1574, 1530, 1346, 1212, 1112, 1024, 845 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_9ClFNO_4Na$ [M + Na]$^+$ 284.0102, found 284.0099. Anal. Calcd for $C_{10}H_9ClFNO_4$ C, 45.91; H, 3.47; Cl, 13.55; F, 7.26; N, 5.35. Found: C, 45.87; H, 3.50; Cl, 13.61; F, 7.24; N, 5.43.

Ethyl 2-(5-bromo-2-nitrophenyl)-2-fluoroacetate (**5a**): 199 mg (65%) yield; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.7, 0.9 Hz, 1H), 7.94 (d, J = 2.0 Hz, 1H), 7.72 (dd, J = 8.8, 2.1 Hz, 1H), 6.60 (d, $^2J_{HF}$ = 46.7 Hz, 1H), 4.26 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (d, J_{CF} = 24.1 Hz), 145.6, 133.2, 132.5 (d, J_{CF} = 21.3 Hz), 130.8 (d, J_{CF} = 16.8 Hz), 129.7 (d, J_{CF} = 2.4 Hz), 126.7, 86.5 (d, J_{CF} = 185.6 Hz), 62.9, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −188.53 (d, $^2J_{FH}$ = 46.7 Hz); IR (DCM) ν_{max} 3108, 2984, 1749, 1568, 1530, 1352, 1211, 1097, 1024, 849 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_9BrFNO_4Na$ [M + Na]$^+$ 327.9597, found 327.9589. Anal. Calcd for $C_{10}H_9BrFNO_4$: C, 39.24; H, 2.96; Br, 26.10; F, 6.21; N, 4.58. Found: C, 39.35; H, 2.78; Br, 25.90; F, 6.13; N, 4.73.

Ethyl 2-fluoro-2-(5-methoxy-2-nitrophenyl)acetate (**6a**): 203 mg (79%) yield; yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, J = 9.1, 0.9 Hz, 1H), 7.23 (d, J = 2.7 Hz, 1H), 6.99 (dd, J = 9.2, 2.8 Hz, 1H), 6.62 (d, $^2J_{HF}$ = 47.0 Hz, 1H), 4.25 (m, 2H), 3.93 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5 (d, J_{CF} = 24.4 Hz), 164.3 (d, J_{CF} = 2.3 Hz), 139.7, 133.8 (d, J_{CF} = 20.6 Hz), 128.1, 114.7, 112.4 (d, J_{CF} = 17.2 Hz), 87.4 (d, J_{CF} = 183.2 Hz), 62.5, 56.3, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ −187.40 (d, $^2J_{FH}$ = 47.0 Hz); IR (DCM) ν_{max} 2984, 2942, 1750, 1584, 1519, 1344, 1293, 1240, 1092, 1024, 837 cm^{-1}; HRMS (EI+) calcd for $C_{11}H_{12}FNO_5$ [M]$^+$ 257.0700, found 257.0710. Anal. Calcd for $C_{11}H_{12}FNO_5$: C, 51.37; H, 4.70; F, 7.39; N, 5.45. Found: C, 51.35; H, 4.55; N, 5.55; F, 7.54.

Ethyl 2-fluoro-2-(2-nitro-5-(trifluoromethyl)phenyl)acetate (**7a**): 148 mg (50%) yield; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 8.5 Hz, 1H), 8.07 (s, 1H), 7.86 (dd, J = 8.6, 1.7 Hz, 1H), 6.66 (d, $^2J_{HF}$ = 46.6 Hz, 1H), 4.27 (m, 2H), 1.29 (d, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9 (d, J_{CF} = 24.2 Hz), 148.7, 135.8 (q, J_{CF} = 34.3 Hz), 131.8 (d, J_{CF} = 21.7 Hz), 127.2 (d, J_{CF} = 2.9 Hz), 125.9, 125.0 (m), 122.8 (q, J_{CF} = 273.4 Hz), 86.4 (d, J_{CF} = 186.6 Hz), 63.0, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.27 (s, 3F), −189.32 (d, $^2J_{FH}$ = 46.7 Hz, 1F); IR (DCM) ν_{max} 3120, 3093, 2984, 2944, 2846, 1750, 1585, 1519, 1345, 1293, 1241, 1205, 1092, 1024, 837, 752 cm^{-1}; HRMS (ES+) calcd for $C_{11}H_9F_4NO_4Na$ [M + Na]$^+$ 318.0365, found 318.0356. Anal. Calcd for $C_{11}H_9F_4NO_4$: C, 44.76; H, 3.07; F, 25.74; N, 4.75. Found: C, 45.01; H, 3.17; F, 25.83; N, 4.88.

Ethyl 2-(5-cyano-2-nitrophenyl)-2-fluoroacetate (**8a**): 106 mg (42%) yield; yellow crystals (hexanes/CH_2Cl_2); mp 36−37 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 1.5 Hz, 1H), 7.89 (dd, J = 8.4, 1.8 Hz, 1H), 6.63 (d, $^2J_{HF}$ = 46.6 Hz, 1H), 4.28 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$)

DOI: 10.1021/acs.joc.6b02219
J. Org. Chem. 2016, 81, 11751−11757

δ 165.6 (d, J_{CF} = 24.0 Hz), 148.9, 133.7, 132.2 (d, J_{CF} = 21.8 Hz), 131.5 (d, J_{CF} = 16.7 Hz), 126.0, 118.2 (d, J_{CF} = 2.4 Hz), 116.5, 86.2 (d, J_{CF} = 187.3 Hz), 63.2, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −189.64 (d, $^2J_{FH}$ = 46.5 Hz); IR (DCM) ν_{max} 3117, 3088, 3051, 2987, 2239, 1748, 1536, 1352, 1231, 1200, 1097, 1021, 849 cm^{-1}; HRMS (ES+) calcd for $C_{11}H_9FN_2O_4Na$ $[M + Na]^+$ 275.0444, found 275.0441. Anal. Calcd for $C_{11}H_9FN_2O_4$: C, 52.39; H, 3.60; F, 7.53; N, 11.11. Found: C, 52.41; H, 3.80; N, 11.12; F, 7.68.

*Ethyl 2-fluoro-2-(3-fluoro-2-nitrophenyl)acetate (**9a**) and ethyl 2-fluoro-2-(3-fluoro-4-nitrophenyl)acetate (**9b**):* 154 mg (63%) yield; **9a**:**9b** ratio 1:5.6; bright yellow oil; IR (DCM) ν_{max} 3061, 2987, 2941, 1764, 1606, 1535, 1353, 1274, 1208, 1081, 1021, 841, 749 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_9F_2NO_4Na$ $[M + Na]^+$ 268.0397, found 268.0396. Anal. Calcd for $C_{10}H_9F_2NO_4$: C, 48.99; H, 3.70; F, 15.50; N, 5.71. Found: C, 49.16; H, 3.48; F, 15.35; N, 5.64. **9a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (td, J = 8.2, 5.0 Hz, 1H), 7.48 (m, 1H), 7.35 (ddd, J = 9.5, 8.6, 1.1 Hz, 1H), 6.25 (d, $^2J_{HF}$ = 46.0 Hz, 1H), 4.34−4.18 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (d, J_{CF} = 26.4 Hz), 154.5 (d, J_{CF} = 261.3 Hz), 133.0 (d, J_{CF} = 8.5 Hz), 130.0 (d, J_{CF} = 21.7 Hz), 126.6, 122.7 (dd, J_{CF} = 10.9, 3.5 Hz), 118.5 (d, J_{CF} = 19.9 Hz), 84.5 (d, J_{CF} = 188.5 Hz), 62.8, 13.8; ^{19}F NMR (470 MHz, $CDCl_3$) δ −120.42 (m), −188.00 (dd, J_{FH} = 45.9, 2.3 Hz). **9b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (t, J = 7.8 Hz, 1H), 7.49−7.42 (m, 2H), 5.86 (d, $^2J_{HF}$ = 47.2 Hz, 1H), 4.34−4.18 (m, 2H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6 (d, J_{CF} = 25.9 Hz), 155.4 (d, J_{CF} = 266.6 Hz), 142.3 (dd, J_{CF} = 21.5, 8.0 Hz), 137.7, 126.6 (d, J_{CF} = 2.1 Hz), 121.9 (dd, J_{CF} = 7.3, 4.4 Hz), 116.1 (dd, J_{CF} = 22.8, 8.1 Hz), 87.5 (d, J_{CF} = 190.5 Hz), 62.7, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −115.76 (dd, J_{FH} = 10.4, 7.7 Hz), −187.22 (d, $^2J_{FH}$ = 47.2 Hz).

*Ethyl 2-(3-chloro-2-nitrophenyl)-2-fluoroacetate (**10a**) and ethyl 2-(3-chloro-4-nitrophenyl)-2-fluoroacetate (**10b**):* 160 mg (61%) yield; **10a**:**10b** ratio 1:10; bright yellow oil; IR (DCM) ν_{max} 3105, 2986, 1763, 1535, 1356, 1218, 1090, 1021, 835 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_9FClNO_4Na$ $[M + Na]^+$ 284.0102, found 284.0094. Anal. Calcd for $C_{10}H_9ClFNO_4$: C, 45.91; H, 3.47; Cl, 13.55; F, 7.26; N, 5.35. Found: C, 46.11; H, 3.59; Cl, 13.39; F, 7.31; N, 5.52. **10b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 1.8 Hz, 1H), 7.54 (m, 1H), 5.83 (d, $^2J_{HF}$ = 47.1 Hz, 1H), 4.35−4.19 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl3) δ 166.9 (d, J_{CF} = 26.3 Hz), 148.4, 139.9 (d, J_{CF} = 21.4 Hz), 129.5 (d, J_{CF} = 8.0 Hz), 127.8, 126.0, 125.3 (d, J_{CF} = 7.2 Hz), 87.6 (d, J_{CF} = 190.6 Hz), 62.8, 14.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ −186.75 (d, $^2J_{FH}$ = 47.1 Hz).

*Ethyl 2-(3-bromo-4-nitrophenyl)-2-fluoroacetate (**11b**):* 138 mg (45%) yield; bright yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89−7.84 (m, 2H), 7.60−7.55 (m, 1H), 5.83 (d, $^2J_{HF}$ = 47.1 Hz, 1H), 4.34−4.20 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9 (d, J_{CF} = 26.1 Hz), 150.2, 139.8 (d, J_{CF} = 21.3 Hz), 132.7 (d, J_{CF} = 7.9 Hz), 126.01, 125.96, 115.0, 87.5 (d, J_{CF} = 190.4 Hz), 62.8, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ −186.55 (d, $^2J_{FH}$ = 47.1 Hz); IR (DCM) ν_{max} 2984, 2916, 2849, 1758, 1582, 1532, 1470, 1339, 1263, 1214, 1078, 1017, 832, 743 cm^{-1}; HRMS (ES+) $C_{10}H_9BrFNO_4Na$ $[M + Na]^+$ calcd 327.9597, found 327.9591. Anal. Calcd for $C_{10}H_9BrFNO_4$: C, 39.24; H, 2.96; Br, 26.11; F, 6.21; N, 4.58. Found: C, 39.44; H, 2.72; Br, 26.19; F, 6.28; N, 4.64.

*Ethyl 2-fluoro-2-(3-methoxy-4-nitrophenyl)acetate (**12b**):* yield 48%, 123 mg; bright yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J = 8.4, 1.0 Hz, 1H), 7.22 (d, J = 1.6 Hz, 1H), 7.13 (dm, J = 8.3, 1H), 5.82 (d, $^2J_{HF}$ = 47.3 Hz, 1H), 4.33−4.20 (m, 2H), 3.98 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3 (d, J_{CF} = 26.4 Hz), 153.1, 140.4 (d, J_{CF} = 21.1 Hz), 140.2, 126.0, 117.8 (d, J_{CF} = 6.9 Hz), 110.9 (d, J_{CF} = 8.1 Hz), 88.2 (d, J_{CF} = 189.3 Hz), 62.4, 56.7, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −185.59 (d, $^2J_{FH}$ = 47.3 Hz); IR (DCM) ν_{max} 2984, 2947, 1761, 1613, 1527, 1356, 1286, 1210, 1082, 1027, 847 cm^{-1}; HRMS (ES+) $C_{11}H_{12}FNO_5Na$ $[M + Na]^+$ calcd 280.0597, found 280.0594. Anal. Calcd for $C_{11}H_{12}FNO_5$: C, 51.36; H, 4.70; F, 7.39; N, 5.45. Found: C, 51.47; H, 4.80; F, 7.17; N, 5.50.

*Ethyl 2-fluoro-2-(2-fluoro-4-nitrophenyl)acetate (**13b**):* 71 mg (29%) yield; colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (dd, J = 8.5, 2.2 Hz, 1H), 8.01 (ddd, J = 9.3, 2.2, 1.2 Hz, 1H), 7.71 (dd, J = 8.5, 6.8 Hz, 1H), 6.11 (d, $^2J_{HF}$ = 46.5 Hz, 1H), 4.34−4.19 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.6 (dd, J_{CF} = 26.4, 1.5 Hz), 159.7 (dd, J_{CF} = 255.1, 4.6 Hz), 149.5 (d, J_{CF} = 8.8 Hz), 129.4 (dd, J_{CF} = 6.5, 3.2 Hz), 129.0 (dd, J_{CF} = 21.5, 14.3 Hz), 119.8 (d, J_{CF} = 3.9 Hz), 112.0 (d, J_{CF} = 26.5 Hz), 83.0 (dd, J_{CF} = 187.3, 2.8 Hz), 62.8, 14.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ −112.28 (dd, J_{FH} = 9.1, 6.9 Hz), −186.24 (d, $^2J_{FH}$ = 46.5 Hz); IR (DCM) ν_{max} 3116, 3090, 2986, 1765, 1537, 1355, 1235, 1065, 812, 742 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_9F_2NO_4Na$ $[M + Na]^+$ 268.0397, found 268.0394. Anal. Calcd for $C_{10}H_9F_2NO_4$: C, 48.99; H, 3.70; N, 5.71. Found: C, 49.10; H, 3.75; N, 5.57.

*Ethyl 2-fluoro-2-(3-chloro-2-nitrophenyl)acetate (**14a**):* 10 mg (4%) yield; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.72 (d, J = 8.3 Hz, 1H), 7.69 (dd, J = 8.3 Hz, 1.7 Hz, 1H), 6.56 (d, $^2J_{HF}$ = 46.7 Hz, 1H), 4.24 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (d, J_{CF} = 24.9 Hz), 136.0 (d, J_{CF} = 2.2 Hz), 134.1 (d, J_{CF} = 2.2 Hz), 128.9, 128.8, 128.7, 125.3, 86.3 (d, J_{CF} = 184.9 Hz), 62.6, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −188.19 (d, $^2J_{FH}$ = 46.3 Hz); IR (DCM) ν_{max} 2985, 1750, 1540, 1352, 1214, 1022, 892 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_9ClFNO_4Na$ $[M + Na]^+$ 284.0102, found 284.0099. Anal. Calcd for $C_{10}H_9ClFNO_4$: C, 45.91; H, 3.47; Cl, 13.55; F, 7.26; N, 5.35. Found: C, 46.32; H, 3.59; Cl, 13.82; F, 7.23; N, 5.28.

*Ethyl 2-fluoro-2-(2-chloro-4-nitrophenyl)acetate (**14b**):* 44 mg (17%) yield; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (dd, J = 2.0, 1.2 Hz, 1H), 8.19 (dd, J = 8.6, 2.2 Hz, 1H), 7.74 (d, J = 8.6 Hz, 1H), 6.23 (d, $^2J_{HF}$ = 46.3 Hz, 1H), 4.34−4.20 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6 (d, J_{CF} = 26.5 Hz), 148.9, 139.1 (d, J_{CF} = 21.2 Hz), 134.3 (d, J_{CF} = 4.6 Hz), 129.2 (d, J_{CF} = 7.9 Hz), 125.2, 122.3, 85.8 (d, J_{CF} = 186.8 Hz), 62.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −184.48 (dd, J_{FH} = 46.3 Hz, 5.5 Hz); IR (DCM) ν_{max} 2916, 2849, 1735, 1526, 1344, 1190, 1015, 732 cm^{-1}; HRMS (ES+) calcd for $C_{10}H_9ClFNO_4Na$ $[M + Na]^+$ 284.0102, found 284.0104. Anal. Calcd for $C_{10}H_9ClFNO_4$: C, 45.91; H, 3.47; Cl, 13.55; F, 7.26; N, 5.35. Found: C, 46.31; H, 3.77; Cl, 13.88; F, 7.35; N, 5.36.

*Ethyl 2-(2,4-dinitrophenyl)-2-fluoroacetate (**15a**):* 138 mg (51%) yield; bright yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.95 (dd, J = 2.1, 1.1 Hz, 1H), 8.57 (dd, J = 8.7, 2.3 Hz, 1H), 8.04 (d, J = 8.6 Hz, 1H), 6.70 (d, $^2J_{HF}$ = 46.7 Hz, 1H), 4.29−4.20 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.4 (d, J_{CF} = 24.1 Hz), 148.3, 147.1, 136.7 (d, J_{CF} = 21.5 Hz), 129.0 (d, J_{CF} = 16.7 Hz), 128.2 (d, J_{CF} = 2.4 Hz), 120.6, 86.6 (d, J_{CF} = 187.3 Hz), 63.2, 13.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ −189.28 (d, $^2J_{FH}$ = 46.7 Hz); IR (DCM) ν_{max} 3106, 3061, 2986, 2924, 2852, 2306, 1747, 1607, 1539, 1348, 1265, 1214, 1018, 738 cm^{-1}; HRMS (ES+) $C_{10}H_9FN_2O_6Na$ $[M + Na]^+$ calcd 295.0342, found 295.0336. Anal. Calcd for $C_{10}H_9FN_2O_6$: C, 44.13; H, 3.33; F, 6.98; N, 10.29. Found: C, 44.29; H, 3.18; F, 6.84; N, 10.01.

*Ethyl 2-(5-chloro-3-methoxy-2-nitrophenyl)-2-fluoroacetate (**16a**):* 128 mg (44%) yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 2.0 Hz, 1H), 7.08 (d, J = 2.0 Hz, 1H), 5.97 (d, $^2J_{HF}$ = 46.2 Hz, 1H), 4.22 (m, 2H), 3.91 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1 (d, J_{CF} = 26.4 Hz), 152.4, 138.0, 137.9, 129.7 (d, J_{CF} = 22.7 Hz), 118.7 (d, J_{CF} = 10.3 Hz), 114.5, 84.3 (d, J_{CF} = 189.3 Hz), 62.8, 57.0, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −186.50 (d, $^2J_{FH}$ = 46.3 Hz); IR (DCM) ν_{max} 3484, 3111, 2985, 2940, 2909, 2872, 1748, 1608, 1574, 1530, 1346, 1212 cm^{-1}; HRMS (ES+) calcd for $C_{11}H_{11}FClNO_5Na$ $[M + Na]^+$ 314.0207, found 314.0200. Anal. Calcd for $C_{11}H_{11}FClNO_5$: C, 45.30; H, 3.80; F, 6.51; Cl, 12.16; N, 4.80. Found: C, 45.34; H, 3.84; F, 6.57; Cl, 12.00; N, 4.80.

*Ethyl 2-fluoro-2-(6-methoxy-3-nitropyrid-2-yl)acetate (**17a**):* 170 mg (66%) yield; yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (dd, J = 9.0, 0.8 Hz, 1H), 6.91 (dd, J = 9.0, 1.1 Hz, 1H), 6.55 (d, $^2J_{HF}$ = 46.5 Hz, 1H), 4.37−4.26 (m, 2H), 4.03 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6 (d, J_{CF} = 24.7 Hz), 165.5, 147.9 (d, J_{CF} = 18.8 Hz), 139.3, 136.5 (d, J_{CF} = 1.1 Hz), 113.0 (d, J_{CF} = 2.5 Hz), 87.1 (d, J_{CF} = 190.0 Hz), 62.31, 55.13, 14.26; ^{19}F NMR (470 MHz, $CDCl_3$) δ −185.01 (d, $^2J_{FH}$ = 48.4 Hz); IR (DCM) ν_{max} 3094,

DOI: 10.1021/acs.joc.6b02219
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2988, 2943, 2871, 1769, 1599, 1525, 1478, 1340, 1294, 1218, 1074, 1026, 845 cm^{-1}; HRMS (ES+) $C_{10}H_{11}FN_2O_5Na$ $[M + Na]^+$ calcd 281.0550, found 281.0548. Anal. Calcd for $C_{10}H_{11}FN_2O_5$: C, 46.52; H, 4.29; F, 7.36; N, 10.85. Found: C, 46.78; H, 4.49; F, 7.51; N, 10.76.

*Ethyl 2-fluoro-2-(2-methoxy-5-nitropyrid-4-yl)acetate (**17a′**):* 31 mg (12%) yield; yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.06 (s, 1H), 6.58 (d, $^2J_{HF}$ = 47.0 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.07 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6 (d, J_{CF} = 2.9 Hz), 165.4 (d, J_{CF} = 23.4 Hz), 146.7, 142.4 (d, J_{CF} = 21.6 Hz), 137.7, 108.8 (d, J_{CF} = 16.9 Hz), 86.8 (d, J_{CF} = 186.0 Hz), 62.9, 55.2, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −191.16 (d, $^2J_{FH}$ = 47.0 Hz); IR (DCM) ν_{max} 2988, 1751, 1616, 1561, 1523, 1348, 1243, 1113, 1021, 848 cm^{-1}; HRMS (ES+) $C_{10}H_{12}FN_2O_5$ $[M + H]^+$ calcd 259.0730, found 259.0724. Anal. Calcd for $C_{10}H_{11}FN_2O_5$: C, 46.52; H, 4.29; F, 7.36; N, 10.85. Found: C, 46.50; H, 4.34; F, 7.45; N, 10.83.

*Ethyl 2-fluoro-2-(2-nitrothiene-4-yl)acetate (**18a**):* 75 mg (32%); dark yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 5.6 Hz, 1H), 7.24 (d, J = 5.6 Hz, 1H), 6.67 (dd, $^2J_{HF}$ = 46.2 Hz, 1H), 4.35−4.19 (m, 2H), 1.30−1.26 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (d, J_{CF} = 25.7 Hz), 148.4, 136.4 (d, J_{CF} = 24.5 Hz), 131.1, 127.0 (d, J_{CF} = 7.2 Hz), 84.5 (d, J_{CF} = 183.4 Hz), 62.6, 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −184.09 (d, $^2J_{FH}$ = 46.7 Hz); IR (DCM) ν_{max} 3116, 2985, 1754, 1510, 1340, 1211, 1065, 1022, 816, 767, 722 cm^{-1}; HRMS $C_8H_7FNO_4S$ $[M - H]^-$ calcd 232.0080, found 232.0079.

*Ethyl 2-fluoro-2-(1-nitronaphthalen-2-yl)acetate (**19a**):* 8 mg (3%) yield; pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 8.7 Hz, 1H), 7.96−7.92 (m, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.71−7.62 (m, 3H), 6.18 (d, $^2J_{HF}$ = 46.3 Hz, 1H), 4.32−4.17 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9 (d, J_{CF} = 27.1 Hz), 146.8, 134.3 (d, J_{CF} = 1.4 Hz), 132.0, 129.4, 128.5, 128.32, 124.6, 124.7, 122.7 (d, J_{CF} = 8.2 Hz), 122.7, 85.0 (d, J_{CF} = 186.6 Hz), 62.7, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −184.05 (d, $^2J_{FH}$ = 46.2 Hz); IR (DCM) ν_{max} 3064, 2985, 2938, 1764, 1533, 1361, 1212, 1071, 1020, 866, 815, 753 cm^{-1}; HRMS (EI+) $C_{14}H_{12}FNO_4$ $[M]^+$ calcd 277.0750, found 277.0751. Anal. Calcd for $C_{14}H_{12}FNO_4$: C, 60.65; H, 4.36; F, 6.85; N, 5.05. Found: C, 60.74; H, 4.52; F, 7.05; N, 5.22.

*Ethyl 2-fluoro-2-(4-nitronaphthalen-1-yl)acetate (**19b**):* 19 mg (7%) yield, 88 mg; pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, J = 8.3 Hz, 1H), 8.30 (d, J = 8.1 Hz, 1H), 8.15 (d, J = 7.9 Hz, 1H), 7.79−7.69 (m, 3H), 6.41 (d, $^2J_{HF}$ = 46.7 Hz, 1H), 4.33−4.15 (m, 2H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6 (d, J_{CF} = 26.5 Hz), 148.4, 136.2 (d, J_{CF} = 18.8 Hz), 131.34, 131.32, 129.3, 128.3, 124.7 (d, J_{CF} = 9.5 Hz), 124.3 (d, J_{CF} = 2.0 Hz), 123.6, 122.4, 87.8 (d, J_{CF} = 187.9 Hz), 62.5, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −181.07 (d, $^2J_{FH}$ = 47.0 Hz); IR (DCM) ν_{max} 3090, 2984, 2916, 2848, 1759, 1524, 1345, 1211, 1054, 766 cm^{-1}; HRMS (EI+) $C_{14}H_{11}FNO_4$ $[M - H]^+$ calcd 276.0672, found 276.0671.

*Ethyl 2-(4-nitronaphthalen-1-yl)-2-(1-nitronaphthalen-2-yl)-acetate (**19c**):* 172 mg (40%) yield; pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J = 8.6 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.91−7.85 (m, 2H), 7.83 (d, J = 8.5 Hz, 1H), 7.72−7.66 (m, 2H), 7.65−7.56 (m, 3H), 7.20 (d, J = 8.7 Hz, 1H), 6.01 (s, 1H), 4.39−4.25 (m, 2H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 147.8, 147.4, 134.0, 133.5, 132.4, 131.4, 129.4, 129.3, 128.7, 128.3, 128.1, 126.4, 125.7, 125.6, 124.9, 124.6, 124.0, 123.7, 122.8, 122.0, 62.4, 49.8, 14.2. IR (DCM) ν_{max} 3063, 2982, 2933, 1738, 1525, 1345, 1184, 767 cm^{-1}; HRMS (ES+) $C_{24}H_{18}N_2O_6Na$ $[M + Na]^+$ calcd 453.1063, found 453.1057. Anal. Calcd for $C_{24}H_{18}N_2O_6$: C, 66,97; H, 4.22; N, 6,51. Found: C, 66.76; H, 4.35; N, 6.34.

*Ethyl 2-fluoro-2-(8-nitroquinolin-5-yl)acetate (**20b**):* 61 mg (22%) yield; pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 9.04 (dd, J = 4.2, 1.7 Hz, 1H), 8.26 (dd, J = 8.3, 1.7 Hz, 1H), 8.04 (d, J = 8.6 Hz, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.59 (1H, dd, J = 8.3, 4.2 Hz, 1H), 6.12 (d, $^2J_{HF}$ = 46.2 Hz, 1H), 4.29 (dq, J = 10.8, 7.1 Hz, 1H), 4.21 (dq, J = 10.8, 7.1 Hz, 1H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4 (d, J_{CF} = 27.9 Hz), 153.0, 152.6, 139.3, 135.8, 130.6, 129.2, 126.5 (d, J_{CF} = 22.7 Hz), 123.6, 123.4 (d, J_{CF} = 7.3 Hz), 84.4 (d, J_{CF} = 187.8 Hz), 62.7, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −184.21 (d, $^2J_{FH}$ = 46.3 Hz); IR (DCM) ν_{max} 2983, 2926, 1765, 1539, 1372, 1219, 1078, 1020, 847, 795 cm^{-1}; HRMS (ES+) $C_{13}H_{11}FN_2O_4Na$ $[M + Na]^+$ calcd 301.0601, found 301.0599.

*Ethyl 2-(8-nitroquinolin-5-yl)-2-(8-nitroquinolin-7-yl)acetate (**20c**):* 130 mg (30%), pink crystals (hexanes/CH_2Cl_2); mp >200 °C dec; ^1H NMR (500 MHz, $CDCl_3$) δ 9.05 (m, 2H), 8.37 (dd, J = 8.8, 1.4, 1H), 8.23 (dd, J = 8.4, 1.6 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.4, 4.2 Hz, 1H), 7.55 (dd, J = 8.8 Hz, 4.2 Hz, 1H), 7.30 (d, J = 8.6 Hz, 1H), 5.97 (s, 1H), 4.37 (dq, J = 10.8, 7.2 Hz, 1H), 4.31 (dq, J = 10.8, 7.0 Hz, 1H), 1.32 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5, 152.9, 152.5, 148.8, 148.0, 140.0, 139.4, 136.5, 135.8, 131.7, 130.1, 128.4, 128.3, 127.6, 126.2, 125.4, 123.6, 123.4, 122.5, 62.8, 48.4, 14.0. IR (DCM) ν_{max} 3054, 2983, 1737, 1535, 1355, 1184, 1020, 841, 788, 736 cm^{-1}; HRMS (ES+) $C_{22}H_{17}N_4O_6$ $[M + H]^+$ calcd 433.1148, found 433.1138. Anal. Calcd for $C_{22}H_{16}N_4O_6$: C, 61.11; H, 3.73; N, 12.96. Found: C, 61.18; H, 3.67; N, 12.94.

General Procedure for Preparation of Ethyl α-Alkyl-α-fluoro-α-nitroarylacetates 21 and 22. Dry K_2CO_3 (1.5 mmol, 207 mg) and DMF (3 mL) were placed in a round-bottom flask. Ester **4a** (0.5 mmol, 131 mg) and benzyl bromide (1 mmol, 171 mg, 119 μL) or methyl iodide (1 mmol, 142 mg, 62 μL) were added, and the reaction mixture was stirred vigorously overnight at rt. The mixture was then diluted with water (10 mL) and extracted with AcOEt (3 × 10 mL). Combined organic extracts were washed with brine (3 × 10 mL), dried (Na_2SO_4), and evaporated. The crude products were purified by column chromatography on silica gel with hexanes/Et_2O 10:1 then 5:1 as eluent.

*Ethyl 2-(5-chloro-2-nitrophenyl)-2-fluoropropionate (**21**):* 83 mg (60%) yield; pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 8.7 Hz, 1H), 7.81 (d, J = 2.3 Hz, 1H), 7.52 (dd, J = 8.7, 2.3 Hz, 1H), 4.25 (m, 2H), 2.01 (d, $^3J_{HF}$ = 24.6 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8 (d, J_{CF} = 23.6 Hz), 144.7 (d, J_{CF} = 2.3 Hz), 140.7 (d, J_{CF} = 2.9 Hz), 137.5 (d, J_{CF} = 23.1 Hz), 129.5, 127.8 (d, J_{CF} = 19.1 Hz), 126.7, 95.0 (d, J_{CF} = 178.6 Hz), 62.5, 24.0 (d, J_{CF} = 25.4 Hz), 13.8; ^{19}F NMR (470 MHz, $CDCl_3$) δ −140.83 (q, $^3J_{FH}$ = 24.9 Hz); IR (DCM) ν_{max} 3112, 2985, 2943, 1759, 1531, 1347, 1297, 1234, 1134, 1017, 907, 862 cm^{-1}; HRMS (ES+) calcd for $C_{11}H_{11}FClNO_4Na$ $[M + Na]^+$ 298.0258, found 298.0260. Anal. Calcd for $C_{11}H_{11}FClNO_4$: C, 47.93; H, 4.02; F, 6.89; Cl, 12.86; N, 5.08. Found: C, 47.90; H, 4.19; F, 6.84; Cl, 12.73; N, 5.27.

*Ethyl 2-(5-chloro-2-nitrophenyl)-2-fluoro-3-phenylpropionate (**22**):* 128 mg (73%); pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.7 Hz, 1H), 7.38 (dd, J = 8.6, 2.2 Hz, 1H), 7.20 (d, J = 2.3 Hz, 1H), 7.16 (m, 3H), 6.91 (d, J = 7.8 Hz, 2H), 4.27 (dq, J = 10.7, 7.1 Hz, 1H), 4.23 (dq, J = 10.8, 7.1 Hz, 1H), 3.90 (dd, $^3J_{HF}$ = 18.3, $^2J_{HH}$ = 14.9 Hz, 1H), 3.63 (dd, $^3J_{HF}$ = 38.3, $^2J_{HH}$ = 14.9 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8 (d, J_{CF} = 23.8 Hz), 144.8, 140.0 (d, J_{CF} = 2.9 Hz), 135.1 (d, J_{CF} = 23.5 Hz), 133.5, 130.6 (d, J_{CF} = 1.5 Hz), 129.2 (d, J_{CF} = 2.9 Hz), 129.0, 128.1, 127.3, 126.2, 96.8 (d, J_{CF} = 181.9 Hz), 62.6, 41.7 (d, J_{CF} = 22.7 Hz), 13.8; ^{19}F NMR (470 MHz, $CDCl_3$) δ −147.34 (dd, $^3J_{FH}$ = 38.1, 18.3 Hz); IR (DCM) ν_{max} 3032, 2984, 1755, 1527, 1348, 1247, 1173, 1042, 863, 734, 701 cm^{-1}; HRMS (ES+) calcd for $C_{17}H_{15}FClNO_4Na$ $[M + Na]^+$ 374.0571, found 374.0576. Anal. Calcd for $C_{17}H_{15}FClNO_4$: C, 58.05; H, 4.30; F, 5.40; Cl, 10.08; N, 3.98. Found: C, 58.13; H, 4.50; F, 5.23; Cl, 9.97; N, 3.78.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02219.

^1H, ^{13}C, and ^{19}F NMR spectra of compounds **2**−**22** (PDF)

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DOI: 10.1021/acs.joc.6b02219
J. Org. Chem. 2016, 81, 11751−11757

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Science Centre (Grant No. UMO-2014/15/B/ST5/02180).

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DOI: 10.1021/acs.joc.6b02219
J. Org. Chem. 2016, 81, 11751−11757