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Indium-Promoted Reformatsky Reaction: A Straightforward Access to β-Amino and β-Hydroxy α,α-Difluoro Carbonyl Compounds

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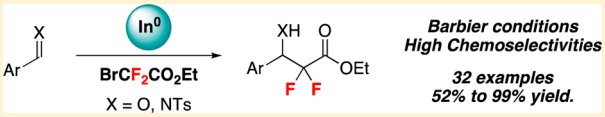
Supporting Information

ABSTRACT: A versatile and practical methodology to access β-amino and β-hydroxy α,α-difluoro carbonyl compounds using indium metal is described. This methodology has been successfully applied to a broad range of substrates including aldehydes, ketones, and imines, affording the corresponding and highly valuable *gem*-difluoro esters. The wide substrate scope highlights the chemoselectivity of the process.

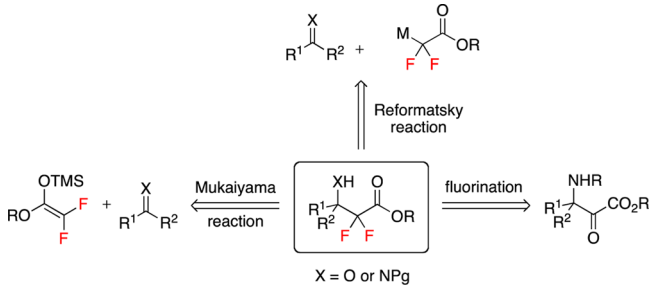


INTRODUCTION

Fluorinated molecules are of utmost interest in medicinal[1] and agrochemical research.[2] The unique properties of the fluorine atom, such as its electronegativity and its small ionic radius, strongly affect several molecular properties.[3] For instance the lipophilicity, the bioavailability, and the metabolic stability of a drug might be enhanced with the introduction of fluorine atoms onto its backbone. This remarkable ability to modify those properties is demonstrated by the presence of at least one fluorine atom in almost 20% of all pharmaceuticals and 30% of all agrochemicals.[1] Therefore, it is not surprising that the introduction of fluorine atoms into molecules is becoming a remarkable challenge, and several efforts were recently devoted to develop straightforward access to fluorinated molecules.[4] Among all of these fluorinated molecules, β-amino and β-hydroxy *gem*-difluorocarbonyl compounds are important compounds and relevant building blocks for the synthesis of more complex fluorinated molecules and biomolecules. For example, α,α-difluorinated β-amino acids are often used for the conformational analysis of peptides or as enzymes inhibitors,[5] while β-hydroxy α,α-difluorinated esters are important building blocks for the synthesis of fluorinated peptides[6] and other bioactive compounds.[7]

The introduction of highly relevant *gem*-difluoromethylene units is usually achieved by fluorination of the corresponding ketones using DAST or Deoxofluor,[8] by addition of fluorinated building blocks to an aldehyde or an imine through a Mukaiyama addition reaction of an unstable fluorinated silicon enolate,[9] or fluorinated Reformatsky-type reagents (Scheme 1). The latter strategy mainly uses zinc metal to perform the Reformatsky process, and it is still hampered by several major drawbacks.[10,11] First, the preparation of unstable organozinc reagents usually requires specific and sometimes difficult-to-control protocols to enhance the reactivity of the zinc metal .[12] Second, the use of large excesses of the organometallic reagent in combination with several additives such as AgOAc or Et_2AlCl,[10c] Cp_2TiCl_2,[11b] and CuCl[11e] poses a significant problem in terms of atom economy. To ensure good conversions of desired fluorinated Reformatsky adducts, exotic activation protocols or unusual reaction conditions are used. Sonication has been found helpful to enhance the reactivity of the electrophile and to extend the half-life of the unstable Reformatsky reagent.[13] An electrochemical process involving a sacrificial Zn anode and a nickel catalyst has been reported by Périchon and co-workers.[14]

Scheme 1. Classical Methods for the Synthesis of β-Amino and β-Hydroxy α,α-Difluoro Carbonyl Compounds



The other preferred pathway to the Reformatsky adduct is the Honda–Reformatsky reaction (Scheme 2).[15] This methodology uses an excess of expensive and pyrophoric Et_2Zn along with a catalytic amount of $RhCl(PPh_3)_3$ (Wilkinson's catalyst). Although this catalytic process does not require the use of activated zinc metal, it can be severely affected by a lack of selectivity due to radical side reactions. In fact, depending on the reaction solvent, α,β-unsaturated ketones might afford either 1,2- or 1,3-adducts.

To tackle these major drawbacks, we speculated that indium metal might be a convenient and practical alternative to zinc. Indium metal gives numerous advantages compared to others

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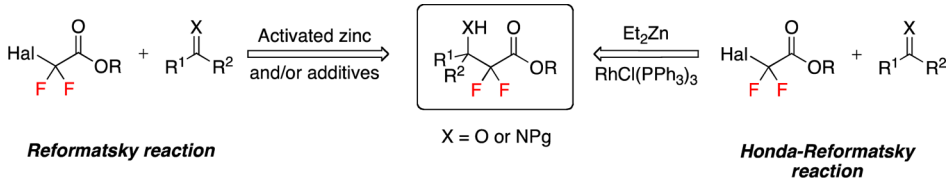
Scheme 2. Reformatsky and Honda−Reformatsky Reaction with $BrCF_2CO_2Et$



metals. First, indium(0) is stable and easy to handle, and in contrast to zinc it does not require any prior-to-use activation. Moreover, indium-mediated addition reactions can be performed under Barbier conditions, thus providing a practical procedure that does not require an initial generation of an organometallic species.[16] Additionally, the low toxicity of indium metal and its associated reagents,[17] combined with the broad functional group tolerance and the impressive level of chemoselectivity, makes it very appealing from a synthetic point of view.

Extensive use of indium in allylation, crotylation, propargylation, and allenylation reactions of aldehydes, ketones, and imines have been reported.[18] For example, Yus and co-workers recently described an elegant In(0)-promoted diastereoselective allylation reaction of imines.[19] It should be noted that In(0) has been previously used in Reformatsky reactions with aldehydes and ketones.[20] Interestingly, when the reaction was carried out with an imine as the electrophile, lower yields were obtained with In(0) compared to that with Zn.[20i] Pioneering results on the In-promoted Reformatsky reactions were reported by Rieke using In(0) generated from potassium and $InCl_3$.[20a] Later, Araki[20b−d] showed that commercially available indium metal was suitable and extended the scope of those reactions. During the past decade, Baba[20e−g] reported the use of mixtures of In(0) and In(I) and remarkably enhanced the diastereoselectivity of the reaction. This elegant work showed that both In(I) and In(III) enolates were formed in the reaction media, and the authors proposed the In(I) enolate to be the most reactive organometallic species.[20f,21]

To the best of our knowledge, the In(0)-mediated Reformatsky reaction with halo-*gem*-difluoroacetate has not been investigated to date. Thus, taking into account the appealing properties of In(0), we decided to explore this new pathway to access *β*-amino and *β*-hydroxy *α*,*α*-difluoro carbonyl compounds. Herein we report a straightforward and practical access to the Reformatsky adduct using indium metal.

RESULTS AND DISCUSSION

Initially, the aldol-type Reformatsky reaction was carried out with benzaldehyde using 1.05 equiv of indium metal and 1.05 equiv of ethyl bromodifluoroacetate in THF at room temperature, and after 18 h the desired product **2a** was formed in a modest 24% conversion . To our delight, increasing the reaction temperature to 60 °C led to a complete conversion, and **2a** was isolated in 76% yield (Scheme 3). Remarkably, a further screening revealed that the reaction could be performed in several organic solvents without erosion of the reaction yield.[22] With this optimized reaction condition, we extended the reaction scope using several aldehydes and ketones (Table 1).

Scheme 3. Initial Experiments

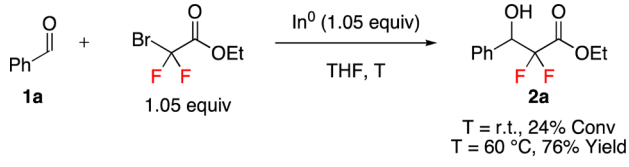
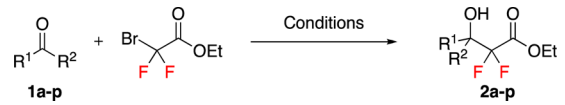


Table 1. Indium-Mediated Reformatsky Reaction with Aldehyde and Ketones[a]



entry	R^1	R^2	product	yield (%)[b]
1	C_6H_5	H	**2a**	76
2	2-Me-C_6H_5	H	**2b**	60
3	1-naphthyl	H	**2c**	61
4	4-Br-C_6H_4	H	**2d**	72
5	3,4-Cl_2-C_6H_4	H	**2e**	69
6	4-CF_3-C_6H_4	H	**2f**	91
7	4-CN-C_6H_4	H	**2g**	66
8	4-CO_2Me-C_6H_4	H	**2h**	52
9	3-OH-C_6H_4	H	**2i**	63
10	3,4-(OCH_2O)-C_6H_4	H	**2j**	61
11[c]	(*E*)-C_6H_5-CH_2=CH_2	C_6H_5	**2k**	68
12[c]	C_6H_5	Me	**2l**	66
13[c]	C_6H_5	Et	**2m**	99
14[c]	*α*-tetralone		**2n**	84
15[c]	3-thienyl	Me	**2o**	69
16[c]	C_6H_5	CH_2CH_2Cl	**2p**	91

[a]Conditions: **1** (0.5 mmol), $BrCF_2CO_2Et$ (1.05 equiv), In^0 (1.05 equiv), THF (1 mL), 60 °C, 6 h. [b]Isolated yield. [c]1.5 equiv of In^0 and $BrCF_2CO_2Et$ were used, and the reaction time was extended to 12 h.

We were pleased to find that our practical process could be applied to a broad range of aromatic aldehydes.[23] Halogens substituents (**2d**, **2e**, entries 4 and 5) as well the CF_3 group (entry 6) were tolerated. Nitrile and ester groups were also compatible with the reaction conditions (entries 7 and 8). These last results further highlight the high level of chemoselectivity of this reaction. Impressively, a phenolic hydrogen did not affect the reaction, and the corresponding adduct **2i** was obtained in good yield (entry 9). Ketones reacted smoothly, but a slight excess of indium metal (1.5 equiv) and ethyl bromodifluoroacetate (1.5 equiv) was used to ensure complete conversions after 18 h. Under these modified reaction conditions, the corresponding tertiary alcohols **2l**−**p** were isolated in good to excellent yields. In contrast with the Honda−Reformatsky reaction, *α*,*β*-unsaturated ketones such as chalcone gave exclusively the 1,2-adduct **2k** in good yield (entry 11), while the Rh-catalyzed Honda−Reformatsky reaction affords a mixture of 1,2- and 1,3-adduct.[15] Remarkably, an aliphatic chlorinated substituent was compatible and the corresponding 1,2-addition product **2p** was obtained in

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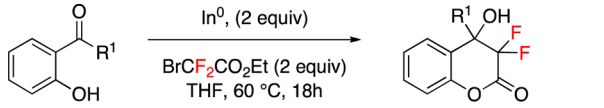
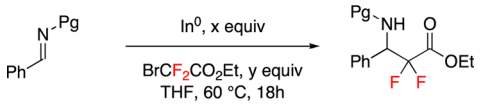
excellent yield (entry 16). Having evaluated the scope of the In-promoted Refomatsky process, we speculated that 2′-hydroxy ketones could undergo a subsequent cyclization, allowing the formation of the corresponding fluorinated lactones. Thus, using 2′-hydroxy ketones **3a** and **3b**, we were pleased to observe the one-pot formation of the *gem*-difluorinated lactones **4a** and **4b** in 41% and 48% yields, respectively (Scheme 4).

Scheme 4. Synthesis of Fluorinated Lactones



A further extension of our methodology would be represented by the Mannich-type Reformatsky reaction. The success of this strategy would give easy access to highly valuable *gem*-difluorinated *β*-amino esters. First, using the reaction conditions previously established, a survey of N-protecting groups revealed the sulfonamide protecting group to be ideal, and the corresponding adduct was obtained in 58% conversion after 18 h (Table 2, entry 3). Interestingly, no traces of the corresponding *gem*-difluoro-*β*-lactam were detected. This is in contrast to the Zn-mediated Reformatsky addition[24] and the previous indium-based reactions.[20i] A further increase of the indium and ethyl bromodifluoroacetate, from 1 to 2 equiv, led to a full conversion, and the desired adduct was isolated as the sole product in 70% yield (entry 4). It should be noted that the amount of indium and bromodifluoro ester could be reduced to 1.5 equiv by extension of the reaction time from 18 h to 24 h (entry 9).

Table 2. Optimization of the Mannich-Type Reformatsky Reaction[a]

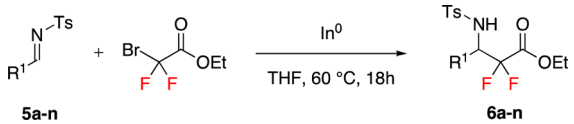


entry	Pg	*x*	*y*	conv[b] (%)[c]
1	Ph	1.05	1	13
2[d]	4-OMePh	1.05	1	16
3	SO_2Ph	1.05	1	58
4	SO_2Ph	2.0	2.0	100 (70)
5	SO_2Ph	1.5	2.0	92
6	SO_2Ph	1.05	2.0	58
7	SO_2Ph	1.05	1.5	59
8	SO_2Ph	1.5	1.5	93
9[e]	SO_2Ph	1.5	1.5	100 (71)

[a]Conditions: imine (0.5 mmol), In^0 (*x* equiv), $BrCF_2CO_2Et$ (*y* equiv), THF (1 mL), 60 °C, 18 h. [b]Determined by ^1H and ^{19}F NMR using an internal standard. [c]Isolated yield. [d]Imine was formed in situ. [e]Reaction time: 24 h.

With these optimized conditions in hand, the reaction scope was successfully extended to several *N*-Ts aldimines (Table 3). Substrates bearing a halogen substituent were suitable, and the corresponding products were isolated in excellent yield (entries 6−8). Nitrile and ester functionalities were also compatible, and the corresponding products were obtained in good yield (entries 9 and 10). Heteroaromatic aldimines proved to be suitable substrates yielding the corresponding *β*-amino-*gem*-difluoro esters (entries 11−13). The *α*,*β*-unsaturated imine derived from cinnamaldehyde was also a suitable substrate, affording exclusively the 1,2-adduct in 73% yield (entry 14). Unfortunately, our methodology could not be extended to *N*-Tos ketimines.[25]

Table 3. Indium-Mediated Reformatsky Reaction with *N*-Ts Imine[a]



entry	R^1	product	yield (%)[b]
1[c]	Ph	**6a**	70
2	4-OMe-C_6H_4	**6b**	68
3	1-naphthyl	**6c**	80
4	3,4-OCH_2O-C_6H_4	**6d**	71
5	4-CF_3-C_6H_4	**6e**	75
6	4-Br-C_6H_4	**6f**	81
7	4-Cl-C_6H_4	**6g**	85
8	3,4-Cl C_6H_3	**6h**	81
9	4-CN-C_6H_4	**6i**	73
10	4-CO_2Me-C_6H_4	**6j**	65
11	3-furyl	**6k**	72
12	2-thienyl	**6l**	69
13	3-pyridyl	**6m**	76
14	cinnamyl	**6n**	73

[a]Conditions: imine (0.5 mmol), In^0 (2 equiv), $BrCF_2CO_2Et$ (2 equiv), THF (1 mL), 60 °C, 18 h. [b]Isolated yield. [c]*N*-benzensulfonylimine was used instead of *N*-Ts imine.

To highlight the high chemoselectivity of our methodology, we performed competition reactions between aldehyde, ketone, and imine starting materials (Scheme 5). The reaction in the presence of benzaldehyde and *N*-benzenesulfonylimine revealed that the aldehyde reacts faster than the imine. When benzaldehyde was reacted in the presence of acetophenone, a similar trend was observed, with ketones reacting faster than imines. These initial experiments clearly highlight the high chemoselectivity of the organoindium reagents.

We next sought to extend our methodology, employing the highly valuable ethyl bromofluoroacetate. The resulting *α*-fluoro *β*-amino esters are of great interest for the development of fluorinated analogues of *β*-amino *α*-hydroxy esters and for conformational studies of *β*-amino acids.[26] Using our optimized conditions, the reaction proceeded smoothly and the Mannich adduct **7** was isolated in 78% yield as an inseparable 1.6:1 mixture of diastereoisomers (Scheme 6). Further attempts to improve the diastereoselectivity were unsuccessful.[27]

Presumably, the observed low diastereoselectivity arises from the presence of a mixture of *E* and *Z* In-enolate.[28] Unfortunately, all our attempts to characterize the indium reagents or to quantify the *E*/*Z* ratio by use of ^1H or ^{19}F NMR spectroscopy were unsuccessful. Nevertheless, to get information about the reaction pathway and to demonstrate the practicability of our methodology, reactions were carried out with commercially available InCl and unactivated Zn in place of In(0) (Scheme 7).

Interestingly, when unactivated Zn was used instead of In(0), a significant drop of reactivity was observed. After 14 h only 43% of the corresponding product was detected by ^{19}F NMR. This result clearly points out the advantage to use indium metal

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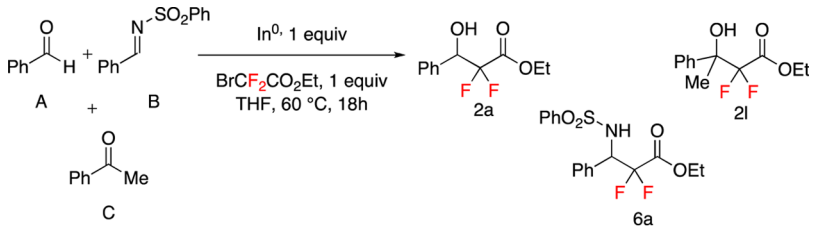
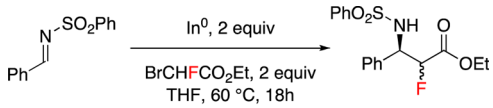
Scheme 5. Competition Reactions[a]



A	B	C	2a	6a	2l
1 equiv	1 equiv	0 equiv	87	13	-
1 equiv	0 equiv	1 equiv	85	-	15
0 equiv	1 equiv	1 equiv	-	20	80

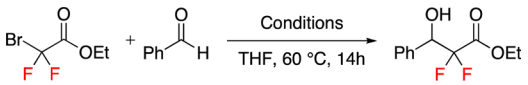
[a]Ratios were determined by ^{19}F NMR using $C_6H_5CF_3$ as an internal standard.

Scheme 6. Addition of Ethyl Bromofluoroacetate to *N*-Sulfonylimine



7
79% yield
syn/*anti*: 1.6: 1

Scheme 7. Test Experiments



Conditions: In(0) : 76%
unactivated Zn: 43%
InCl: 79%

instead of Zn. When InCl was used, the reaction proceeded smoothly, affording the Reformatsky adduct in 79% NMR yield (vs 76% isolated yield with In(0)). According to Baba's observations,[20f] this result might be explained by invoking the formation of an In(I) enolate, which might then react with the electrophile. Therefore, in analogy to Baba's proposal, the following tentative mechanism was envisaged (Figure 1). The reaction of indium metal with ethyl bromodifluoroacetate in THF affords a mixture of In(III) and In(I) enolate. The latter reacts faster with the electrophile, affording the Reformatsky adduct. Although a radical process cannot be ruled out, we assume that the radical derived from ethyl bromodifluoroacetate would not be sufficiently nucleophilic to react with aldehydes, ketones, or imines.[29]

■ CONCLUSION

In summary, a straightforward and practical access to α-hydroxy and α-amino *gem*-difluoroesters has been reported using indium(0) as the metal. The remarkable functional group tolerance associated with the unique properties of indium allowed the extension of this methodology to a broad selection of substrates in good to excellent yields. This method allows a straightforward access to highly valuable β-amino and β-hydroxy *gem*-difluorinated carbonyl compounds.

■ EXPERIMENTAL SECTION

Residual $CHCl_3$ served as internal standard (δ = 7.26) for ^1H NMR, $CFCl_3$ served as internal standard (δ = 0.0) for ^{19}F NMR, and $CDCl_3$ served as internal standard (δ = 77.16) for ^{13}C NMR. Flash chromatography was performed with silica gel (0.063−0.200 mm). Analytical thin layer chromatography (TLC) was performed on silica gel aluminum plates with F-254 indicator and visualized by UV fluorescence and/or staining with $KMnO_4$ or PMA. THF was distilled over Na/benzophenone prior to use. HRMS analyses were performed under ESI conditions with a micro-TOF detector. All experiments were conducted under nitrogen atmosphere in oven-dried glassware with magnetic stirring using standard Schlenk techniques. All aldehydes were recrystallized, distilled, or filtered through basic alumina prior to use. All ketones were used as received. *N*-Tos-aldimines were prepared according to literature methods[30] and recrystallized from a boiling mixture of petroleum ether and ethyl acetate prior to use.

Reformatsky Reaction with Aldehyde. To a solution of In^0 (powder, 0.55 mmol, 60 mg) and the corresponding aldehyde (0.5 mmol) in THF (1 mL) was added $BrCF_2CO_2Et$ (0.55 mmol, 64 μL). The resulting mixture was stirred at 60 °C for 6 h and then cooled to room temperature. The solution was quenched with aqueous HCl (0.5 M, 5 mL) and extracted with DCM (three times). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography (SiO_2, petroleum ether/EtOAc) to afford the corresponding β-hydroxy *gem*-difluoroesters **2a**−**j**.

Ethyl 2,2-Difluoro-3-hydroxy-3-phenylpropionate ***2a.*** Compound **2a** was obtained as a colorless oil in 76% yield (87 mg), after flash chromatography (SiO_2, cyclohexane/EtOAc, 4:1, R_f = 0.30 cyclohexane/EtOAc 4:1). ^1H NMR (300 MHz, $CDCl_3$): 7.47−7.39 (m, 5H), 5.24−5.14 (m, 1H), 4.32 (q, 2H, J = 7.1 Hz), 2.62 (dd, 1H, J = 5.3 Hz, J = 0.4 Hz), 1.30 (t, 3H, J = 7.1 Hz) ^{13}C NMR (75 MHz, $CDCl_3$): 163.7 (dd, J = 32.4 Hz, J = 30.8 Hz), 134.6 (d, J = 2.0 Hz), 129.3, 128.5, 127.8, 113.9 (dd, J = 259.2 Hz, J = 254.1 Hz), 73.8 (dd, J = 27.8 Hz, J = 24.4 Hz), 63.3, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −113.9 (dd, 1F, J = 262.4 Hz J = 8.0 Hz), −120.4 (dd, 1F, J = 262.4 Hz J = 15.3 Hz). IR (cm^{-1}): 2989, 1755, 1456, 1376, 1192, 1092, 856,

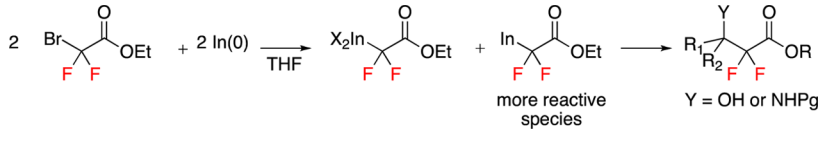


Figure 1. Proposed mechanism.

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718, 698. HRMS (ESI−): calcd for [M − H] $C_{11}H_{11}F_2O_3$: 229.0676, found: 229.0671 (−2.1 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(2-methylphenyl)propionate ***2b***. Compound **2b** was obtained as a colorless oil in 60% yield (73 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc, 19:1 to 9:1, R_f = 0.54 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.54−7.51 (m, 1H), 7.26−7.24 (m, 2H), 7.19−7.16 (m, 1H), 5.46 (dt, 1H, J = 16.8 Hz, J = 5.1 Hz), 4.31 (q, 2H, J = 7.1 Hz), 2.53 (d, 1H, J = 5.4 Hz), 2.38 (s, 3H), 1.29 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.9 (t, J = 31.8 Hz), 137.0, 133.1,130.7, 129.2, 127.6 (d, J = 1.5 Hz), 126.3, 114.3 (t, J = 256.9 Hz), 69.8 (dd, J = 28.9 Hz, J = 24.0 Hz), 63.3, 19.6, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$): −112.8 (d, 1F, J = 263.6 Hz), −121.4 (d, 1F, J = 263.6 Hz). IR (cm^{-1}): 3216, 1759, 1294, 1121, 1058, 1002, 831, 731. HRMS (ESI−): calcd for [M − H] $C_{12}H_{13}F_2O_3$: 243.0833, found: 243.0829 (+1.6 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(1-naphthyl)propionate ***2c***. Compound **2c** was obtained as a yellow oil in 61% yield (86 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1, R_f = 0.50 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 8.12−8.09 (m, 1H), 7.89 (d, 2H, J = 8.0 Hz), 7.79 (d, 1H, J = 7.2 Hz), 7.59−7.49 (m, 3H), 6.11−6.02 (m, 1H), 4.27 (q, 2H, J = 7.1 Hz), 2.87 (d, 1H, J = 5.1 Hz), 1.23 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.8 (t, J = 31.8 Hz), 133.7, 131.5, 130.8 (d, J = 1.6 Hz), 130.0, 129.0, 126.7, 126.3, 125.9, 125.3, 123.3 (t, J = 1.3 Hz), 114.4 (t, J = 257.3 Hz), 69.9 (dd, J = 28.3 Hz, J = 24.4 Hz), 63.3, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −112.9 (d, J = 261.03 Hz), −120.1 (d, J = 260.85 Hz). IR (cm^{-1}): 3493, 1755, 1305, 1081, 1065, 788. HRMS (ESI^-): calcd for [M − H] $C_{15}H_{13}F_2O_3$: 279.0833, found: 279.0835 (+ 0.7 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(4-bromophenyl)propionate ***2d***. Compound **2d** was obtained as a pale yellow oil in 72% yield (111 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1, R_f = 0.50 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.51 (d, 2H, J = 8.4 Hz), 7.31 (d, 2H, J = 8.3 Hz), 5.13 (ddd, 1H, J = 15.3 Hz, J = 7.4 Hz, J = 5.3 Hz), 4.30 (q, 2H, J = 7.1 Hz), 2.94 (d, 1H, J = 5.2 Hz), 1.30 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.5 (t, J = 31.6 Hz), 133.6 (d, J = 1.7 Hz), 131.7, 129.5, 123.6, 113.5 (t, J = 257.2 Hz), 73.3 (dd, J = 28.0 Hz, J = 24.4 Hz), 63.4, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$): −113.7 (d, J = 264.0 Hz), −121.1 (J = 264.3 Hz). IR (cm^{-1}): 3218, 1768, 1289, 1118, 1066, 1009, 833, 734. HRMS (ESI^-): calcd for [M − H] $C_{11}H_{10}F_2O_3Br$: 306.9781, found: 306.9778 (−1.0 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(3,4-dichlorophenyl)propionate ***2e***. Compound **2e** was obtained as a white solid in 69% yield (103 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1, R_f = 0.61 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.55 (d, 1H, J = 1.5 Hz), 7.45 (d, 1H, J = 8.3 Hz), 7.29−7.26 (m, 1H), 5.14 (ddd, 1H, J = 15.2 Hz, J = 7.0 Hz, J = 5.3 Hz), 4.32 (q, 2H, J = 7.1 Hz), 3.05 (d, 1H, J = 5.2 Hz), 1.31 (t, 3H, J = 7.15 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.4 (t, J = 31.5 Hz), 134.7 (d, J = 1.4 Hz), 133.6, 132.8, 130.5, 129.8 (d, J = 1.3 Hz), 127.1, 113.4 (t, J = 257.6 Hz), 72.7 (dd, J = 28.4 Hz J = 24.6 Hz), 63.6, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$): −113.1 (dd, J = 265.9 Hz, J = 7.21 Hz), −121.1 (dd, J = 265.8 Hz J = 15.26 Hz). IR (cm^{-1}): 3431, 1764, 1466, 1302, 1181, 1120, 1000, 850, 757, 679. HRMS (ESI−): calcd for [M − H] $C_{11}H_9Cl_2F_2O_3$: 296.9897, found: 296.9904 (+ 2.3 ppm). Mp: 74−75 °C.

Ethyl 2,2-Difluoro-3-hydroxy-3-(4-trifluoromethylphenyl)-propionate ***2f***. Compound **2f** was obtained as a white solid in 91% yield (135 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1 to 4:1 to 7:3). ^{1}H NMR (300 MHz, $CDCl_3$): 7.65 (d, 2H, J = 8.4 Hz), 7.58 (d, 2H, J = 8.3 Hz), 5.29−5.20 (m, 1H), 4.31 (q, 2H, J = 7.1 Hz), 3.03 (d, 1H, J = 5.2 Hz), 1.29 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.4 (dd, J = 32.2 Hz, J = 30.8 Hz), 138.5, 131.5 (q, J = 32.63 Hz), 128.3 (d, J = 1.0 Hz), 125.5 (q, J = 3.8 Hz), 124.1 (d, J = 272.3 Hz), 113.5 (dd, J = 260.7 Hz, J = 254.7 Hz), 73.31 (dd,, J = 28.1 Hz, J = 24.5 Hz), 63.5, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −63.3, −113.2 (dd, J = 266.3 Hz, J = 7.2 Hz), −121.1 (dd, J = 266.3 Hz, J = 15.4 Hz). IR (cm^{-1}): 3217, 1767, 1320, 1161, 1065, 1016, 836, 709, 543. HRMS (ESI^-): calcd for [M − H] $C_{12}H_{10}F_5O_3$: 297.0550, found: 297.0545 (−1.7 ppm). Mp: 99−100 °C.

Ethyl 2,2-Difluoro-3-hydroxy-3-(4-cyanophenyl)propionate ***2g***. Compound **2g** was obtained as a colorless oil in 66% yield (84 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1 to 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.65 (d, 2H, J = 8.3 Hz), 7.57 (d, 1H, J = 8.1 Hz), 5.23 (dt, J = 15.7 Hz, J = 6.1 Hz), 4.31 (q, 2H, J = 7.1 Hz), 3.52 (d, 1H, J = 5.4 Hz), 1.29 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.3 (t, J = 31.5 Hz), 140.1 (J = 1.0 Hz), 132.1, 128.6, 118.5, 113.4 (t, J = 254.5 Hz), 112.8, 72.9 (dd, J = 28.4 Hz, J = 24.5 Hz), 63.5, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −112.2 (dd, J = 265.5 Hz, J = 6.9 Hz), −121.2 (dd, J = 265.5 Hz, J = 15.9 Hz). IR (cm^{-1}): 3434, 2232, 1756, 1315, 1190, 1102, 1071, 565. HRMS (ESI−): calcd for [M − H] $C_{12}H_{10}F_2NO_3$: 254.0629, found: 254.0624 (−2.0 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(4-methylbenzoate)propionate ***2h***. Compound **2h** was obtained as a pale yellow oil in 52% yield (75 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1 to 4:1, R_f = 0.34 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 8.01 (d, J = 8.2 Hz), 7.51 (d, J = 8.2 Hz), 5.27−5.18 (m, 1H), 4.30 (q, 2H, J = 7.1 Hz), 3.90 (s, 3H), 3.26 (d, 1H, J = 5.2 Hz), 1.28 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 166.9, 163.4 (t, J = 31.5 Hz), 139.6 (d, J = 1.6 Hz), 130.9, 129.7, 127.9, 113.7 (t, J = 257.4 Hz), 73.4 (dd, J = 28.0 Hz, J = 24.4 Hz), 63.4, 52.4, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$): −113.4 (d, J = 264.2 Hz), −120.9 (d, J = 265.5 Hz). IR (cm^{-1}): 3461, 1758, 1721, 1438, 1278, 1104, 1071, 1019, 731. HRMS (ESI+): calcd for [M + NH_4] $C_{13}H_{18}F_2NO_5$: 306.1153 found: 306.1154 (+0.3 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(3-hydroxyphenyl)propionate ***2i***. Compound **2i** was obtained as a colorless oil in 63% yield (78 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 17:1 to 4:1, R_f = 0.23 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.27−7.20 (m, 1H), 6.95 (d, 2H, J = 7.4 Hz), 6.85 (dd, 1H, J = 7.4 Hz, J = 1.7 Hz), 6.00 (brs, 1H), 5.14−5.07 (m, 1H), 4.30 (q, 2H, J = 7.1 Hz), 3.38 (brs, 1H), 1.29 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.9 (t, J = 31.6 Hz), 155.9, 136.2 (d, J = 2.0 Hz), 129.6, 120.3, 116.6, 114.7, 113.9 (t, J = 259.3 Hz), 73.7 (dd, J = 27.7 Hz, J = 24.5 Hz), 63.5, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −114.4 (d, J = 260.6 Hz), −120.6 (d, J = 260.6 Hz). IR (cm^{-1}): 3401, 1750, 1593, 1458, 1095, 1071, 771. HRMS (ESI−): calcd for [M − H] $C_{11}H_{11}F_2O_4$: 245.0625, found: 245.0632 (+2.9 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(3,4-methylenedioxyphenyl)-propionate ***2j***. Compound **2j** was obtained as a yellow oil in 61% yield (83 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1 to 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 6.94 (s, 1H), 6.87 (d, 1H, J = 8.1 Hz), 6.79 (d, 1H, J = 8.0 Hz), 5.96 (d, 2H), 5.11−5.02 (m, 1H), 4.31 (q, 2H, J = 7.1 Hz), 2.81 (d, 1H, J = 4.9 Hz), 1.31 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.7 (t, J = 31.7 Hz), 148.5, 148.0, 128.3 (d, J = 2.1 Hz), 121.8 (d, J = 0.9 Hz), 113.8 (t, J = 258.7 Hz), 108.2, 108.2 (t, J = 1.5 Hz), 101.4, 73.7 (dd, J = 27.9 Hz, J = 24.2 Hz), 63.2, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$): −114.6 (dd, J = 261.3 Hz, J = 8.1 Hz), −121.0 (dd, J = 261.3 Hz, J = 15.1 Hz). IR (cm^{-1}): 3503, 1755, 1505, 1489, 1489, 1306, 1244, 1096, 1067, 1036, 926, 853, 791, 712, 547. HRMS (ESI−): calcd for [M − H] $C_{12}H_{11}F_2O_5$: 273.0575, found: 273.0569 (−2.2 ppm).

Reformatsky Reaction with Ketone. To a solution of In^0 (powder, 0.75 mmol, 90 mg) and the corresponding ketones (0.5 mmol) in THF (1 mL) was added $BrCF_2CO_2Et$ (0.75 mmol, 96 μL). The resulting mixture was stirred at 60 °C for 12 h and then cooled to room temperature. The solution was quenched with aqueous HCl (0.5 M, 5 mL) and extracted with DCM (three times). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography (SiO_2, petroleum ether/EtOAc) to afford the corresponding β-hydroxy *gem*-difluoroester **2k−p** and **4a,b**.

Ethyl 2,2-Difluoro-3-hydroxy-3,5-diphenylpent-4-enoate ***2k***. Compound **2k** was obtained as a viscous pale yellow oil in 68% yield (113 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1 to 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.59 (d, 2H, J = 7.3 Hz), 7.39−7.21 (m, 8H), 6.80 (m, 2H), 4.15 (q, 2H, J = 7.1 Hz), 3.47 (brs, 1H), 1.10 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$):

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136.6 (t, J = 32.0 Hz), 138.1, 136.1, 132.7 (d, J = 1.2 Hz), 128.7, 128.6, 128.4, 128.3, 127.0, 126.9 (t, J = 1.9 Hz), 126.8 (d, J = 2.5 Hz), 114.4 (t, J = 262.8 Hz), 77.9 (t, J = 24.0 Hz), 63.3, 13.8. ^{19}F NMR (282 MHz, $CDCl_3$): −114.8 (d, J = 16.9 Hz). IR (cm^{-1}): 3496, 1756, 1603, 1454, 1373, 1095, 1004, 975, 745, 687. HRMS (ESI−): calcd for [M − H] $C_{19}H_{17}F_2O_3$: 331.1146, found: 331.1148 (+0.6 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-phenylbutanoate ***2l***. Compound **2l** was obtained as a yellow oil in 66% yield (80 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.52 (d, 2H, J = 7.2 Hz), 7.40−7.32 (m, 3H), 4.15 (q, 2H, J = 7.1 Hz), 3.11 (s, 1H), 1.75 (s, 3H), 1.12 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.7 (t, J = 32.2 Hz), 139.7 (d, J = 1.3 Hz), 128.4, 128.3, 126.1 (t, J = 1.7 Hz), 114.9 (t, J = 261.4), 76.1 (t, J = 24.5 Hz), 63.1, 23.4 (d, J = 2.6 Hz), 13.8. ^{19}F NMR (282 MHz, $CDCl_3$): −116.0 (d, J = 15.1 Hz). IR (cm^{-1}): 1753, 1307, 1126, 1106, 1036, 761, 699. HRMS (ESI^-): calcd for [M − H] $C_{12}H_{13}F_2O_3$: 243.0833, found: 243.0841 (+3.3 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-phenylpentanoate ***2m***. Compound **2m** was obtained as a white solid in 99% yield (128 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1, R_f = 0.35 petroleum ether/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.49 (d, 2H, J = 7.5 Hz), 7.38−7.29 (m, 3H), 4.11 (q, 2H, J = 7.1 Hz), 3.09 (s, 1H), 2.28−2.04 (m, 2H), 1.07 (t, 3H, J = 7.1 Hz), 0.76 (t, 3H, J = 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.7 (t, J = 31.8 Hz), 137.4, 128.2, 128.1, 126.6 (t, J = 1.8 Hz), 115.3 (t, J = 260.1 Hz), 78.6 (t, J = 23.4 Hz), 62.9, 27.2 (t, J = 2.2 Hz), 13.6, 6.7. ^{19}F NMR (282 MHz, $CDCl_3$): −116.3. IR (cm^{-1}): 3501, 2979, 1756, 1454, 1310, 1157, 1128, 1109, 989, 831, 759. HRMS (ESI−): calcd for [M − H] $C_{13}H_{15}F_2O_3$: 257.0989, found: 257.0998 (+3.5 ppm). Mp: 44−45 °C.

Ethyl 1-(Hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl)-1,1-difluoroacetate ***2n***. Compound **2n** was obtained as a colorless oil in 84% yield (114 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.66 (d, 1H, J = 7.2 Hz), 7.29−7.20 (m, 2H), 7.15−7.12 (m, 1H), 4.27 (qd, 2H, J = 7.1 Hz, J = 1.9 Hz), 2.85−2.69 (m, 3H), 2.35−2.23 (m, 1H), 2.04−1.95 (m, 2H), 1.89−1.77 (m, 1H), 1.23 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.8 (t, J = 32.4 Hz), 138.9, 133.7 (d, J = 1.4 Hz), 129.1, 128.7, 127.8 (t, J = 3.4 Hz), 126.2, 116.0 (t, J = 261.0 Hz), 73.6 (t, J = 22.6 Hz), 33.2 (t, J = 1.6 Hz), 29.5, 18.7 (t, J = 1.8 Hz), 13.8. ^{19}F NMR (282 MHz, $CDCl_3$): −112.3 (d, J = 257.3 Hz), −113.9 (d, J = 257.3 Hz). IR (cm^{-1}): 3500, 1754, 1451, 1372, 1305, 1123, 1017, 760, 729. HRMS (ESI+): calcd for [M + NH_4] $C_{14}H_{20}F_2NO_3$: 288.1411, found: 288.1407 (−1.4 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-(3-thienyl)butyrate ***2o***. Compound **2o** was obtained as a yellow oil in 69% yield (86 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 4:1, R_f = 0.34 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.33−7.28 (m, 2H), 7.12 (dd, 1H, J = 5.0 Hz, J = 0.8 Hz), 4.19 (q, 2H, J = 7.1 Hz), 3.25 (s, 1H), 1.17 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.7 (t, J = 32.1 Hz), 141.6 (d, J = 2.1 Hz), 126.2 (t, J = 2.1 Hz), 126.à, 122.7 (t, J = 1.6 Hz), 114.6 (t, J = 261.3 Hz), 75.3 (t, J = 25.3 Hz), 63.1, 23.3, 13.8. ^{19}F NMR (282 MHz, $CDCl_3$): −115.8 (d, J = 257.9 Hz), −116.5 (d, J = 257.9 Hz). IR (cm^{-1}): 3510, 1753, 1308, 1106, 1035, 792, 657. HRMS (ESI−): calcd for [M − H] $C_{10}H_{11}F_2SO_3$: 249.0397, found: 249.0390 (−2.8 ppm).

Ethyl 2,2-Difluoro-3-hydroxy-3-phenyl-5-chloropentanoate ***2p***. Compound **2p** was obtained as a white solid in 91% yield (133 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1, R_f = 0.45 petroleum ether/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.48 (d, 2H, J = 7.4 Hz), 7.42−7.32 (m, 3H), 4.11 (q, 2H, J = 7.1 Hz), 3.56 (td, 1H, J = 10.2 Hz, J = 6.8 Hz), 3.49 (s, 1H), 3.21 (td, 1H, J = 10.2 Hz, J = 6.2 Hz), 2.70−2.55 (m, 2H), 1.06 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 163.3 (t, J = 31.6 Hz), 136.5 (d, J = 2.5 Hz), 128.7, 128.6, 126.3 (t, J = 2.1 Hz), 114.4 (t, J = 262.9 Hz), 77.8 (t, J = 23.5 Hz), 63.2, 39.0, 37.8, 13.6. ^{19}F NMR (282 MHz, $CDCl_3$): −115.6 (d, J = 258.6 Hz), −116.8 (d, J = 258.6 Hz). IR (cm^{-1}): 3440, 1746, 1449, 1321, 1180, 947, 767, 701, 610. HRMS (ESI^-): calcd for [M − H] $C_{13}H_{14}F_2O_3Cl$: 291.0600, found: 291.0608 (+2.7 ppm). Mp: 73−74 °C.

4-Hydroxy-4-ethyl-3,3-difluoro-3,4-dihydrocoumarin ***4a***. Compound **4a** was obtained as a white solid in 41% yield (47 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.62 (d, 1H, J = 8.1 Hz), 7.55−7.49 (m, 1H), 7.38−7.33 (m, 2H), 2.89 (qd, 2H, J = 7.6 Hz, J = 2.3 Hz), 1.31 (t, 3H, J = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 155.4 (d, J = 30.3 Hz), 150.9 (d, J = 2.7 Hz), 145.2, 141.9, 136.4 (d, J = 12.7 Hz), 130.7, 125.1, 124.6, 117.4, 17.8 (d, J = 2.8 Hz), 13.1 (d, J = 1.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): −136.80. IR (cm^{-1}): 2983, 1727, 1649, 1448, 1150, 1093, 775, 754, 459. HRMS (ESI^-): calcd for [M + OH]$^-$ $C_{11}H_{11}F_2O_4$: 245.0625, found: 245.0631 (+2.4 ppm). Mp: 69−70 °C.

4-Hydroxy-4-phenethyl-3,3-difluoro-3,4-dihydrocoumarin ***4b***. Compound **4b** was obtained as a white solid in 48% yield (73 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.56 (d, 1H, J = 8.1 Hz), 7.51−7.46 (m, 1H), 7.34−7.25 (m, 4H), 7.21−7.17 (m, 3H), 3.14−3.08 (m, 2H), 2.95−2.90 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): 155.2 (d, J = 30.2 Hz), 150.8 (d, J = 2.72 Hz), 142.9 (d, J = 253.0 Hz), 139.9, 134.0 (d, J = 12.7 Hz), 130.7 (d, J = 2.7 Hz), 128.8, 128.4, 126.9, 125.1, 124.6 (d, J = 6.1 Hz), 118.8 (d, J = 3.1 Hz), 117.4 (d, J = 1.4 Hz), 34.6 (d, J = 1.8 Hz), 18.4 (d, J = 1.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): −135.19. IR (cm^{-1}): 1731, 1601, 1448, 1146, 1098, 902, 748, 716, 698, 454. HRMS (ESI^-): calcd for [M + OH]$^-$ $C_{17}H_{15}F_2O_4$: 321.0938, found: 321.0944 (+1.9 ppm). Mp: 101−102 °C.

Reformatsky Reaction with Aldimine. To a solution of In^0 (powder, 1.0 mmol, 120 mg) and aldimine (0.5 mmol) in THF (1 mL) was added $BrCF_2CO_2Et$ (1.0 mmol, 0.128 mL). The resulting mixture was stirred at 60 °C for 18 h and then cooled to room temperature. The solution was quenched with HCl (0.5 M, 5 mL) and extracted with DCM. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (SiO_2, petroleum ether/EtOAc) to afford the Mannich adducts **6a**−**n**.

Ethyl 2,2-Difluoro-3-(benzenesulfonylamino)-3-phenylpropionate ***6a***. Compound **6a** was obtained as a white solid in 70% yield (129 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85: 15, R_f = 0.36 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.67 (d, 2H, J = 7.7 Hz), 7.41 (t, 1H, J = 7.4 Hz), 7.28 (t, 2H, J = 7.6 Hz), 7.22−7.11 (m, 5H), 5.91 (d, 1H, J = 10.2 Hz), 5.05 (dt, 1H, J = 16.5 Hz, J = 9.8 Hz), 4.22 (q, 2H, J = 7.1 Hz), 1.25 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.7 (t, J = 31.5 Hz), 140.1, 132.7, 131.7 (d, J = 2.0 Hz), 129.1, 128.8, 128.6, 128.3, 127.0, 113.7 (t, J = 257.8 Hz), 63.5, 59.8 (dd, J = 27.4 Hz, J = 23.6 Hz), 13.8. ^{19}F NMR (282 MHz, $CDCl_3$): −111.6 (dd, J = 258.4 Hz, J = 9.5 Hz), −115.6 (dd, J = 258.4 Hz, J = 16.5 Hz). IR (cm^{-1}): 3242, 1758, 1337, 1165, 1063, 717, 685, 543. HRMS (ESI+): calcd for [M + H] $C_{17}H_{18}F_2SNO_4$: 370.0925, found: 370.0916 (−2.4 ppm). Mp: 109−110 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(4-methoxyphenyl)propionate ***6b***. Compound **6b** was obtained as a viscous colorless oil in 68% yield (140 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 4:1 to 7:3). ^{1}H NMR (300 MHz, $CDCl_3$): 7.54 (d, 2H, J = 8.3 Hz), 7.10 (d, 2H, J = 8.1 Hz), 7.04 (d, 2H, J = 8.7 Hz), 6.70 (d, 2H, J = 8.7 Hz), 5.63 (d, 1H, J = 9.9 Hz), 4.96 (dt, 1H, J = 16.1 Hz, J = 10.0 Hz), 4.21 (q, 2H, J = 7.1 Hz), 3.74 (s, 3H), 2.33 (s, 3H), 1.25 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.8 (t, J = 31.6 Hz), 160.1, 143.6, 137.3, 129.6, 129.5, 127.2, 124.0 (d, J = 2.2 Hz), 114.0, 113.8 (t, J = 254.9 Hz), 63.5, 59.3 (dd, J = 26.9 Hz, J = 23.8 Hz), 55.4, 21.5, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −112.1 (dd, J = 257.6 Hz, J = 10.1 Hz), 115.3 (dd, J = 257.6 Hz, J = 16.1 Hz). IR (cm^{-1}): 3255, 1774, 1613, 1518, 1441, 1330, 1258, 1160, 912, 808, 666, 544. HRMS (ESI+): calcd for [M + H] $C_{19}H_{22}F_2NSO_5$: 414.1187, found: 414.1182 (−1.2 ppm).

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(1-naphthyl)propionate ***6c***. Compound **6c** was obtained as a viscous yellow oil in 80% yield (173 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 4:1, R_f = 0.24 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.93 (d, 2H, J = 8.5 Hz), 7.68 (d, 1H, J = 7.6 Hz), 7.62 (d, 1H, J = 8.1 Hz), 7.50−7.37 (m, 2H), 7.29−7.26 (m, 3H), 7.17 (dd, 1H, J = 8.5 Hz, J = 6.9 Hz), 6.66 (d, 2H, J = 8.1 Hz), 5.98−5.85

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(m, 2H), 4.18−4.07 (m, 2H), 2.05 (s, 3H), 1.10 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.7 (t, J = 31.7 Hz), 143.3, 136.6, 133.5, 131.6, 129.6, 129.0, 128.7, 128.4 (d, J = 1.7 Hz), 127.0, 126.9, 126.1, 125.1, 122.7, 114.1 (t, J = 257.7 Hz), 63.6, 54.2 (dd, J = 28.0 Hz, J = 23.5 Hz), 21.3, 13.8. ^{19}F NMR (282 MHz, $CDCl_3$): −110.7 (d br, J = 262.0 Hz), −114.4 (d br, J = 257.0 Hz). IR (cm^{-1}): 1774, 1331, 1199, 1051, 773, 555, 407. HRMS (ESI+): calcd for [M + H] $C_{22}H_{22}F_2NSO_4$: 434.1238, found: 434.1227 (−2.5 ppm).

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(3,4-methylenedioxyphenyl)propionate ***6d***. Compound **6d** was obtained as a yellow solid in 71% yield (152 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 4:1 to 7:3). ^{1}H NMR (300 MHz, $CDCl_3$): 7.52 (d, 2H, J = 8.3 Hz), 7.11 (d, 2H, J = 8.0 Hz), 6.59 (m, 3H), 5.98 (d, 1H, J = 10.1 Hz), 5.87 (dd, 1H, J = 3.8 Hz, J = 1.3 Hz), 4.96−4.87 (m, 1H), 4.23 (q, 2H, J = 7.1 Hz), 2.33 (s, 3H), 1.27 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.7 (t, J = 31.6 Hz), 148.2, 147.8, 143.6, 137.2, 129.4, 127.2, 125.5 (d, J = 2.1 Hz), 122.7, 113.6 (t, J = 257.5 Hz), 108.4, 108.2, 101.4, 63.6, 59.5 (dd, J = 27.4 Hz, J = 23.5 Hz), 21.5, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −111.8 (dd, J = 257.3 Hz, J = 9.6 Hz), −115.7 (dd, J = 257.3 Hz, J = 16.6 Hz). IR (cm^{-1}): 1774, 1443, 1324, 1246, 1161, 1040, 917, 808, 670, 542. HRMS (ESI+): calcd for [M + H] $C_{19}H_{20}F_2NSO_6$: 428.0979, found: 428.0988 (+2.1 ppm). Mp: 107−108 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(4-trifluoromethylphenyl)propionate ***6e***. Compound **6e** was obtained as a white solid in 75% yield (170 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 9:1, R_f = 0.36 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.49 (d, 2H, J = 8.3 Hz), 7.41 (d, 2H, J = 8.2 Hz), 7.25 (d, 2H, J = 7.8 Hz), 7.05 (d, 2H, J = 8.1 Hz), 5.95 (d, 1H, J = 10.2 Hz), 5.16−5.04 (m, 1H), 4.27 (q, 2H, J = 7.1 Hz), 2.30 (s, 3H), 1.29 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.4 (t, J = 31.5 Hz), 144.1, 136.8, 135.8, 131.1 (q, J = 32.7 Hz), 129.5, 129.1, 127.1, 125.4 (q, J = 3.7 Hz), 123.9 (d, J = 272.3 Hz), 113.4 (t, J = 258.2 Hz), 63.9, 59.4 (dd, J = 28.7 Hz, J = 23.4 Hz), 21.3, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −63.4, (dd, J = 260.8 Hz, J = 7.9 Hz), (dd, J = 260.8 Hz, J = 17.9 Hz). IR (cm^{-1}): 3228, 1761, 1449, 1325, 1162, 1061, 807, 668, 553. HRMS (ESI+): calcd for [M + H] $C_{19}H_{19}F_5NSO_4$: 452.0955, found: 452.0954 (−0.2 ppm). Mp: 134−135 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(4-bromophenyl)propionate ***6f***. Compound **6f** was obtained as a white solid in 81% yield (187 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85:15, R_f = 0.36 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.52 (d, 2H, J = 8.3 Hz), 7.30 (d, 2H, J = 8.4 Hz), 7.10 (d, 2H, J = 8.2 Hz), 7.00 (d, 2H, J = 8.4 Hz), 5.92 (d, 1H, J = 10.1 Hz), 5.05−4.93 (m, 1H), 4.24 (q, 2H, J = 7.1 Hz), 2.35 (s, 3H), 1.28 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.5 (t, J = 31.6 Hz), 144.0, 136.9, 131.8, 130.9 (d, J = 1.7 Hz), 130.1, 129.6, 127.1, 123.4, 113.4 (t, J = 257.9 Hz), 63.8, 59.3 (dd, J = 28.0 Hz, J = 23.6 Hz), 21.6, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −111.0 (dd, J = 259.8 Hz, J = 8.9 Hz), −116.2 (dd, J = 259.8 Hz, J = 17.1 Hz). IR (cm^{-1}): 3228, 1764, 1447, 1338, 1163, 1067, 794, 668, 552. HRMS (ESI+): calcd for [M + H] $C_{18}H_{19}BrF_2NSO_4$: 462.0186, found: 462.0183 (−0.6 ppm). Mp: 131−132 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(4-chlorophenyl)propionate ***6g***. Compound **6g** was obtained as a white solid in 85% yield (177 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85:15, R_f = 0.33 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.53 (d, 2H, J = 8.3 Hz), 7.17−7.05 (m, 6H), 5.90 (d, 1H, J = 10.0 Hz), 5.00 (dt, 1H, J = 17.0 Hz, J = 9.4 Hz), 4.24 (q, 2H, J = 7.1 Hz), 2.35 (s, 3H), 1.27 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.5 (t, J = 31.6 Hz), 144.0, 137.0, 135.2, 130.4 (d, J = 1.7 Hz), 129.8, 129.6, 128.8, 127.1, 113.4 (t, J = 256.0 Hz), 63.7, 59.2 (dd, J = 27.9 Hz, J = 23.7 Hz), 21.6, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −110.5 (dd, J = 259.7 Hz, J = 8.8 Hz), −115.7 (dd, J = 259.7 Hz, J = 16.9 Hz). IR (cm^{-1}): 3228, 1767, 1446, 1318, 1162, 1118, 1066, 911, 806, 551. HRMS (ESI+): calcd for [M + H] $C_{18}H_{19}F_2ClNSO_4$: 418.0691, found: 418.0676 (−3.6 ppm). Mp: 121−122 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(3,4-dichlorophenyl)propionate ***6h***. Compound **6h** was obtained as a white solid in 81% yield (183 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85:15, R_f = 0.29 petroleum ether/EtOAc 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): 7.51 (d, 2H, J = 8.3 Hz), 7.25 (d, 1H, J = 8.3 Hz), 7.12−7.10 (m, 3H), 7.05−7.02 (m, 1H), 7.11 (d, 1H, J = 10.2 Hz), 4.97 (ddd, 1H, J = 17.9 Hz, J = 10.0 Hz, J = 7.9 Hz), 4.29 (q, 2H, J = 7.1 Hz), 2.35 (s, 3H), 1.31 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.4 (t, J = 31.5 Hz), 144.3, 136.7, 133.5, 132.8, 131.9 (d, J = 1.2 Hz), 130.6, 130.6, 129.6, 127.8, 113.2 (t, J = 258.1 Hz), 63.9, 58.9 (dd, J = 28.8 Hz, J = 23.6 Hz), 21.5, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −110.2 (dd, J = 260.8 Hz, J = 7.9 Hz), −116.9 (dd, J = 260.8 Hz, J = 17.8 Hz). IR (cm^{-1}): 3237, 1756, 1469, 1459, 1344, 1215, 1167, 1071, 807, 682, 534. HRMS (ESI+): calcd for [M + H] $C_{18}H_{18}Cl_2F_2NSO_4$: 452.0302, found: 452.0304 (+0.4 ppm). Mp: 117−118 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(4-cyanophenyl)propionate ***6i***. Compound **6i** was obtained as a white solid in 73% yield (149 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 7:3). ^{1}H NMR (300 MHz, $CDCl_3$): 7.51 (m, 2H), 7.31−7.26 (m, 2H), 7.12 (d, 2H, J = 8.1 Hz), 6.11 (dd, 1H, J = 10.2 Hz, J = 0.1 Hz), 5.15−5.03 (m, 1H), 4.25 (q, 2H, J = 7.1 Hz), 2.35 (s, 3H), 1.29 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.2 (t, J = 31.2 Hz), 144.3, 137.2 (d, J = 1.1 Hz), 136.8, 132.3, 129.7, 129.3, 127.1, 118.1, 113.2 (t, J = 258.3 Hz), 113.0, 64.0, 59.3 (dd, J = 28.5 Hz, J = 23.7 Hz), 21.6, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −109.8 (dd, J = 261.6 Hz, J = 7.6 Hz), −116.7 (dd, J = 261.6 Hz, J = 17.6 Hz). IR (cm^{-1}): 3256, 2245, 1174, 1448, 1332, 1283, 1163, 1088, 917, 836, 666, 549. HRMS (ESI+): calcd for [M + H] $C_{19}H_{19}F_2N_2SO_4$: 409.1034, found: 409.1020 (−3.4 ppm). Mp: 171−172 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(4-methoxycarbonylphenyl)propionate ***6j***. Compound **6j** was obtained as a white solid in 65% yield (143 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85:15 to 7:3). ^{1}H NMR (300 MHz, $CDCl_3$): 7.83 (d, 2H, J = 8.4 Hz), 7.52 (d, 2H, J = 8.3 Hz), 7.23 (d, 2H, J = 8.2 Hz), 7.05 (d, 2H, J = 8.0 Hz), 6.23 (d, 1H, J = 10.3 Hz), 5.09 (dt, 1H, J = 17.7 Hz, J = 9.0 Hz), 4.24 (q, 2H, J = 7.1 Hz), 3.89 (s, 3H), 2.28 (s, 3H), 1.27 (t, 3H, J = 7.1 Hz).. ^{13}C NMR (75 MHz, $CDCl_3$): 166.5, 162.4 (t, J = 31.5 Hz), 143.9, 137.0, 136.8, 130.7, 129.7, 129.5, 128.8, 127.1, 113.5 (t, J = 258.2 Hz), 63.7, 59.5 (dd, J = 28.0 Hz, J = 23.6 Hz), 52.4, 21.4, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −110.1 (dd, J = 259.5 Hz, J = 8.5 Hz), −115.7 (ddd, J = 259.5 Hz, J = 17.3 Hz, J = 2.6 Hz). IR (cm^{-1}): 1768, 1703, 1446, 1346, 1285, 1190, 1115, 1071, 1013, 906, 817, 701, 671. HRMS (ESI+): calcd for [M + H] $C_{20}H_{22}F_2NSO_6$: 442.1136, found: 442.1143 (+1.6 ppm). Mp: 156−157 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(3-furyl)propionate ***6k***. Compound **6k** was obtained as a white solid in 72% yield (134 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85:15). ^{1}H NMR (300 MHz, $CDCl_3$): 7.65 (d, 2H, J = 8.3 Hz), 7.25−7.20 (m, 4H), 6.22 (s, 1H), 5.54 (d, 1H, J = 10.0 Hz), 5.02 (dt, 2H, J = 15.5 Hz, J = 9.8 Hz), 4.24 (qd, 2H, J = 7.1 Hz, J = 1.9 Hz), 2.38 (s, 3H), 1.28 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.6 (t, J = 31.6 Hz), 143.9, 143.8, 141.7, 137.3, 129.7, 127.2, 117.6 (d, J = 2.6 Hz), 113.5 (t, J = 257.5 Hz), 109.2, 63.6, 52.5 (dd, J = 28.0 Hz, J = 25.2 Hz), 21.6, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −111.9 (dd, J = 259.7 Hz, J = 9.7 Hz), −115.5 (dd, J = 259.7 Hz, J = 15.6 Hz). IR (cm^{-1}): 1773, 1448, 1321, 1247, 1161, 1040, 918, 808, 669, 551. HRMS (ESI+): calcd for [M + H] $C_{16}H_{18}F_2NSO_5$: 374.0874, found: 374.0881 (+1.9 ppm). Mp: 79−80 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(2-thienyl)propionate ***6l***. Compound **6l** was obtained as a white solid in 69% yield (134 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85:15). ^{1}H NMR (300 MHz, $CDCl_3$): 7.60 (d, 2H, J = 8.3 Hz), 7.20 (dd, 1H, J = 5.0 Hz, J = 1.2 Hz), 7.18−7.15 (m, 2H), 6.89−6.88 (m, 1H), 6.83 (dd, 1H, J = 5.0 Hz, J = 3.6 Hz), 5.48 (d, 1H, J = 10.0 Hz), 5.33 (dt, 1H, J = 15.1 Hz, J = 9.6 Hz), 4.25 (q, 2H, J = 7.1 Hz), 2.36 (s, 3H), 1.27 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.4 (t, J = 31.7 Hz), 143.8, 137.2, 134.1 (d, J = 2.1 Hz), 129.6, 128.4, 127.2 (2C), 127.0, 113.1 (t, J = 258.3 Hz), 63.7, 55.7 (dd, J = 27.9 Hz, J = 25.3 Hz), 21.6, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −111.6 (dd, J = 258.8 Hz, J = 9.2 Hz), −115.2 (dd, J = 258.8 Hz, J = 15.1 Hz). IR

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(cm^{-1}): 3240, 1775, 1444, 1328, 1289, 1160, 1066, 912, 809, 725, 685, 539. HRMS (ESI+): calcd for [M + H] $C_{16}H_{18}F_2NS_2O_4$: 390.0645, found: 390.0650 (+1.3 ppm). Mp: 123−124 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-3-(3-pyridyl)-propionate **6m**. Compound **6m** was obtained as a yellow solid in 76% yield (146 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 1:1 to 2:3, R_f = 0.22 petroleum ether/EtOAc 1:1). ^1H NMR (300 MHz, $CDCl_3$): 8.50 (dd, 1H, J = 4.7 Hz, J = 1.3 Hz), 8.41 (d, 1H, J = 1.8 Hz), 7.56−7.50 (m, 3H), 7.17−7.11 (m, 3H), 6.08 (d, 1H, J = 9.9 Hz), 5.14−5.02 (m, 1H), 4.26 (q, 2H, J = 7.1 Hz), 2.33 (s, 3H), 1.29 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.3 (t, J = 31.4 Hz), 150.2, 149.7, 144.1, 136.9, 135.8, 129.7, 128.3, 127.1, 123.6, 113.4 (t, J = 258.2 Hz), 63.9, 57.8 (dd, J = 28.7 Hz, J = 23.9 Hz), 21.6, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −110.1 (dd, J = 261.3 Hz, J = 8.2 Hz), −116.6 (dd, J = 261.3 Hz, J = 17.7 Hz). IR (cm^{-1}): 2926, 1756 1597, 1482, 1437, 1330, 1292, 1154, 1064, 806, 739, 669, 542. HRMS (ESI+): calcd for [M + H] $C_{17}H_{19}F_2N_2SO_4$: 385.1034, found: 385.1031 (−0.8 ppm). Mp: 172−173 °C.

Ethyl 2,2-Difluoro-3-(p-tolylsulfonylamino)-5-phenylpent-4-enoate **6n**. Compound **6n** was obtained as a yellow solid in 73% yield (149 mg), after flash chromatography (SiO_2, petroleum ether/EtOAc 85:15, R_f = 0.30 petroleum ether/EtOAc 4:1). ^1H NMR (300 MHz, $CDCl_3$): 7.73 (d, 2H, J = 8.3 Hz), 7.30−7.25 (m, 3H), 7.20 (d, 2H, J = 8.1 Hz), 7.16−7.13 (m, 2H), 6.37 (d, 1H, J = 15.9 Hz), 5.80 (dd, 1H, J = 15.9 Hz, J = 7.6 Hz), 5.08 (d, 1H, J = 9.9 Hz), 4.70−4.56 (m, 1H), 4.33−4.23 (m, 2H), 2.28 (s, 3H), 1.32 (t, 3H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 162.6 (t, J = 31.6 Hz), 144.1, 137.6, 137.1, 135.3, 129.8, 128.7, 128.7, 127.4,126.8, 118.7 (dd, J = 3.1 Hz, J = 1.7 Hz), 113.6 (t, J = 257.4 Hz), 63.6, 58.6 (dd, J = 27.9 Hz, J = 24.6 Hz), 21.5, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$): −111.6 (dd, J = 260.7 Hz, J = 8.6 Hz), −116.9 (dd, J = 260.7 Hz, J = 15.3 Hz). IR (cm^{-1}): 3228, 1773, 1444, 1337, 1159, 1074, 967, 815, 745, 667, 541. HRMS (ESI+): calcd for [M + H] $C_{20}H_{22}F_2NSO_4$: 410.1238, found: 410.1237 (−0.2 ppm). Mp: 124−125 °C.

Ethyl 2-Fluoro-3-(benzenesulfonylamino)-3-phenylpropionate **7**. Compound **7** was obtained as a yellow oil in 79% yield (138 mg, dr = 1.6:1), after flash chromatography (SiO_2, petroleum ether/EtOAc 7:3). ^1H NMR (300 MHz, $CDCl_3$): 7.64−7.56 (m, 5H), 7.38−7.30 (m, 3H), 7.27−7.18 (m, 6H), 7.11−7.03 (m, 10H), 6.99−6.97 (m, 2H), 5.85 (d, 1.6H, J = 9.5 Hz), 5.80 (d, 1H, J = 9.1 Hz), 5.14 (dd, 1H, J_{H-F} = 48.7 Hz, J = 3.7 Hz), 5.02−4.77 (m, 4.5H), 4.13−3.94 (m, 5.2H), 1.16 (t, 4.8H), 0.99 (t, 3H) ^{13}C NMR (75 MHz, $CDCl_3$): 167.0 (d, J = 24.6 Hz), 166.5 (d, J = 23.0 Hz), 140.4, 140.2, 135.6, 134.0, 132.7, 132.5, 129.0, 128.8, 128.7, 128.7, 128.6, 128.4, 127.8, 127.8, 127.1, 127.0, 90.96 (d, J = 193.7 Hz), 90.66 (d, J = 194.1 Hz), 62.4, 61.9, 58.8 (d, J = 3.9 Hz), 58.5 (d, J = 3.6 Hz), 14.1, 13.9. ^{19}F NMR (282 MHz, $CDCl_3$): −201.5 (dd, J = 47.5 Hz, J = 25.3 Hz), −202.3 (dd, J = 48.7 Hz, J = 26.2 Hz). IR (cm^{-1}): 1771, 1438, 1341, 1154, 971, 812, 741, 540. HRMS (ESI+): calcd for [M + H] $C_{18}H_{21}FNSO_4$: 366.1175, found: 366.1168 (−1.9 ppm).

Competition Reaction (Scheme 5). To a solution of In^0 (powder, 0.5 mmol, 58 mg), benzaldehyde (0.5 mmol), and the corresponding aldimine (0.5 mmol) in THF (1 mL) was added $BrCF_2CO_2Et$ (0.5 mmol, 64 μL). The resulting mixture was stirred at 60 °C for 18 h and then cooled to room temperature. After a usual workup, ratios were determined by ^{19}F NMR using $C_6H_5CF_3$ as an internal standard.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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