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Synthetic Utilization of 2-Chloro-1,1,1,2-tetrafluoroethane

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Abstract: β-Substituted α-fluoro-α,β-unsaturated carboxylic acids have been successfully synthesized, usually in a (*Z*)-stereospecific manner by way of a stepwise or a one-pot three-step procedure starting from 2-chloro-1,1,1,2-tetrafluoroethane (HCFC-124), one of the major byproducts of the industrial process for tetrafluoroethene formation from chlorofluoromethane (HCFC-22).

Keywords: allylic alcohols · carboxylic acids · fluorine · hydrochlorofluorocarbons (HCFCs) · sigmatropic rearrangement

Introduction

The hydrochlorofluorocarbon (HCFC) 2-chloro-1,1,1,2-tetrafluoroethane (HCFC-134/**1c**) is produced as one of the side products of the industrial process for the formation of tetrafluoroethylene from chlorodifluoromethane (HCFC-22). Taking limited amounts of fluorine sources, ozone layer depletion, and the global warming characteristics of **1c** into account, it is quite important to consider its efficient consumption from a synthetic point of view. However, to our surprise, almost all articles[1] and patents[2] thus far have concentrated on its conversion to the corresponding hydrofluorocarbons (HFCs) 1,1,2,2-tetrafluoroethane (HFC-134) and pentafluoroethane (HFC-125), or fluorinated C2-alkene derivatives. This prompted us to develop new and efficient transformations into synthetically useful intermediates. Among a variety of materials, our attention was focused on β-substituted α-fluoro-α,β-unsaturated carboxylic acids **8**[3,4] because of their utility as constituents of biologically active substances.[5] However, their preparation has sometimes suffered from stereoisomer contamination.[3] In this article, we disclose detailed reactions of the anion of **1c** with a variety of carbonyl compounds and transformation of the resultant fluorinated alcohols **5** into the respective fluorinated acids **8**, mostly in a *Z*-stereospecific manner. This process was performed not only in successive fashion, but also in a one-pot three-step sequence. The last step offers a better chance to decrease the amount of solvent and base required.

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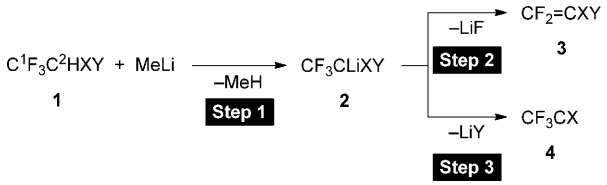
Results and Discussion

Theoretical comparison of HCFC-124 (1c) with HFC-134a (1a) and HCFC-133a (1b): A literature search based on the related HCFC or HFC families indicated that proper generation of anions is possible from CF_3CHXY, in which both X and Y are halogens, by the action of a typical strong base, such as *n*BuLi. Conversely, the subsequent ready elimination of a fluorine atom from the CF_3 group is usually observed when X = H and Y = halogen. For clarification of this discrepancy, theoretical calculations were performed[6] for **1c** and the structurally related compounds, CF_3CH_2F (**1a**) and CF_3CH_2Cl (**1b**). The results are summarized in Table 1. We have calculated the thermodynamic stability of substrates **1**, lithiated intermediates **2** (after proton abstraction from **1** by monomeric MeLi as the simplified model base), terminally difluorinated ethenes **3** (obtained by β-elimination of fluoride from **2**), and carbenes **4** (obtained by α-elimination of chloride from **2**). Initial lithiation (Table 1, step 1) seemed to proceed smoothly due to an energetic preference (ΔE = 15 to 30 kcal mol^{-1}) for the combination of species **2** and methane when compared with the substrate pair **1** and MeLi. A considerably high energy barrier was estimated for the formation of **4** (Table 1, step 3) because of the significant instability of **4** with respect to **2**. On the other hand, β-elimination from **2** (Table 1, step 2) was expected to furnish the thermodynamically more favorable ethenes **3**, which bear two fluorine atoms at the terminal carbon atom, with low activation energies of up to only 7 kcal mol^{-1}. Deprotonation of **1a** by *n*BuLi constructed **3a**, in accordance with the computational result. The vinylic proton of **3a** was further abstracted and the resultant anion could be eventually trapped with appropriate carbonyl compounds to give fluorinated allylic alcohols.[4,7] Intramolecular interaction of Li···F (206.0 pm) in **2a** seemed to be one of the major promoters for conversion to **3a**, which, as a result, would effect a 9.4 pm elongation of the C–F···Li bond. Although **1b** energetically preferred transformation to lithiated **2b** rather than **3b** (by 4 kcal mol^{-1} on the basis of the present calculation, either in Et_2O or THF), **2b** is in fact known to follow

Table 1. Computational results for compounds **1a–c**.[a]



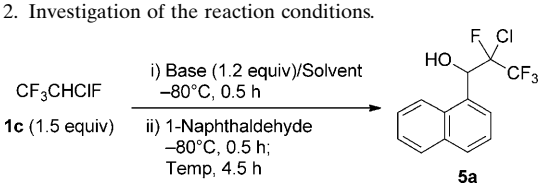
Compound	X	Y	Solvent	ΔE [kcal mol^{-1}]				Charge on **2**[b]			
				CF_3CLiXY (**2**)	TS_{step2}	$F_2C{=}XY$ (**3**)	CF_3CX(**4**)	C^1	C^2	X	Y
1a	H	F	none	−21.652	2.671	−9.354	57.349	0.971	−0.413	0.178	−0.495
			Et_2O	−15.002	1.186	−23.130	47.632				
			THF	−14.151	0.869	−24.015	47.234				
1b	H	Cl	none	−25.920	1.104	−7.550	57.995	0.995	−0.779	0.205	−0.200
			Et_2O	−22.179	5.365	−18.346	46.082				
			THF	−22.239	6.051	−18.300	45.117				
1c	F	Cl	none	−28.289	7.186	−1.715	34.704	0.947	−0.145	−0.383	−0.284
			Et_2O	−26.620	4.980	−9.055	25.168				
			THF	−26.948	4.798	−8.590	25.091				

[a] Calculations were carried out by Gaussian 03W at the B3LYP/6–31+G* level of theory. Solvent effect was estimated by the single point calculation for the fully optimized conformers by using the SCI-PCM (self-consistent isodensity polarized continuum model) method. [b] Charges were obtained by natural bond orbital analysis.

the same β-elimination as **2a** by treatment with *n*BuLi.[8] This experimental fact is a reflection of the higher negative charge localized on C2, which might render anion **2b** less stable and promote the irreversible elimination of LiF. A weak Li···F contact (264.7 pm) and elongated C–F···Li bond (4.4 pm) were also observed for **2b**. However, in the case of **1c**, in addition to the substantial energetic stability of lithiated **2c** relative to **3c** and **4c**, a much lower level of negative charge was accumulated on C2; a result of effective electron delocalization over two electronegative elements attached to the same carbon atom. These computational results led to a strong expectation that the anion from **1c** would be utilized experimentally in a successful manner.[9]

Formation of fluorinated alcohols 5 by the reaction of 1c with carbonyl compounds: With these computational results in hand, the efficiency of proton abstraction from **1c** was first investigated by use of a variety of bases. The results, compared after trapping the generated anion with 1-naphthaldehyde, are collected in Table 2. A similar yield of the desired alcohol **5a** was obtained after treatment with *n*BuLi, *s*BuLi, or lithium diisopropylamine (LDA) (Table 2, entries 1, 2, and 4). MeLi was found to be less potent and EtMgBr did not work at all for the present purpose (Table 2, entries 3 and 5). Despite only moderate success, it is notable that the same adduct **5a** was formed in 39% yield after potassium *tert*-butoxide treatment (Table 2, entry 6), while the corresponding in situ prepared Li and Na alkoxides proved to be totally insufficient for abstraction of the proton in **1c**. The more polar solvent THF furnished a sluggish result, with the formation of a variety of products indicated by ^{19}F NMR spectroscopy. An Et_2O/hexane (1:9) mixed solvent did not work efficiently (Table 2, entry 8), so we determined the initial conditions (Table 2, entry 1) as the best for this reaction, after a brief check of the reaction temperature (Table 2, entry 9).

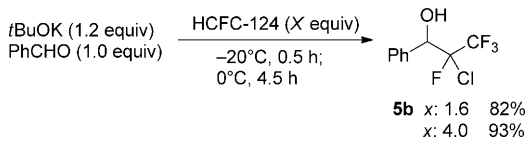
Table 2. Investigation of the reaction conditions.



	Base	Solvent	T [°C]	Yield[a] [%]
1	*n*BuLi	Et_2O	−80 to 0	76 (73)[b]
2	*s*BuLi	Et_2O	−80 to 0	64
3	MeLi	Et_2O	−80 to 0	22
4	LDA	Et_2O	−80 to 0	64
5	EtMgBr	Et_2O	−80 to 0	–[c]
6	*t*BuOK	Et_2O	−80 to 0	39
7	*n*BuLi	THF	−80	trace
8	*n*BuLi	Et_2O/hex[d]	−80	10
9	*n*BuLi	Et_2O	−80	72

[a] Calculated by ^{19}F NMR spectroscopy on the basis of 1-naphthaldehyde. [b] Isolated yield. [c] 76% of 1-(1-naphthyl)propanol was obtained. [d] Et_2O/hexane = 1:9.

Compared with *n*BuLi, an easy-to-handle base like *t*BuOK was quite advantageous and, thus, its potential was further investigated. Extensive studies on the reaction parameters attained, at most, 40% chemical yield of **5b** when PhCHO was used as the electrophile under similar conditions as described in Table 2. Our working hypothesis that this result would stem from the instability of the anion of **1c** with potassium as the counter cation[10] led us to generate this active species in the presence of electrophiles so as to enable its capture as quickly as possible. To our delight, construction of **5b** was realized in 76% yield by addition of **1c** (1.6 equiv) to a mixture of *t*BuOK (1.2 equiv) and benzaldehyde (1 equiv) at −20 °C, followed by 5 h stirring at the same temperature. As shown in Scheme 1, further improvement was also possible by changing the reaction tempera-

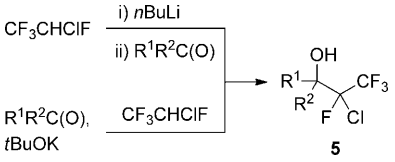


Scheme 1. Formation of **5b** by reaction with *t*BuOK.

ture (−20 °C, 0.5 h, then −80 to 0 °C, 4.5 h; 82 % yield) or increasing the amount of **1c** employed (4 equiv; 93 % yield).

Utilization of the two different established reaction protocols with a variety of electrophiles led to successful conversion of **1c** into tetrafluorinated alcohols **5**; the results are summarized in Table 3. The *n*BuLi- and *t*BuOK-mediated

Table 3. Preparation of alcohols **5**.

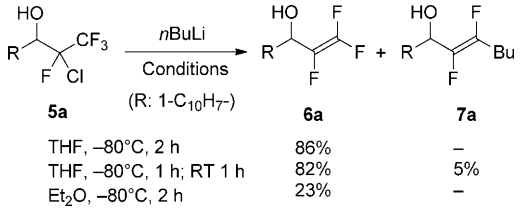


	R^1	R^2	Product	Isolated yield [%] (d.r.)[a] *n*BuLi	*t*BuOK
1	1-$C_{10}H_7$	H	**5a**	73 (61:39)	–[b]
2	Ph	H	**5b**	83 (60:40)	83[c] (51:49)
3	*p*-$MeOC_6H_4$	H	**5c**	89 (57:43)	82 (51:49)
4	*p*-$H_3CC_6H_4$	H	**5d**	90 (59:41)	82 (51:49)
5	*p*-$F_3CC_6H_4$	H	**5e**	72 (60:40)	33 (56:44)
6	C_9H_{19}	H	**5f**	74 (52:48)	trace
7	$PhCH_2CH_2$	H	**5g**	81 (51:49)	–[b]
8	(*E*)-PhCH=CH	H	**5h**	82 (56:44)	12[d] (54:46)
9	Ph	CH_3	**5i**	85 (40:60)	0

[a] Diastereomeric ratio (d.r.) was determined by ^{19}F NMR spectroscopy. [b] Not attempted. [c] 87 % isolated yield was obtained after reaction in THF at −40 °C for 1 h. [d] Yield was determined by ^{19}F NMR spectroscopy.

pathways usually recorded similar yields of **5**, but there are some points worth noting for the latter system) electrophiles with the carbonyl α proton were not applicable (Table 3, entries 6, 7, and 9), due to the requirement for premixing of the carbonyl compound with *t*BuOK; 2) the strongly electron-withdrawing nature of the CF_3 group in *p*-$(F_3C)C_6H_4CHO$ was likely to promote the Cannizzaro reaction, which decreased the chemical yield to some extent[11] when compared to the *n*BuLi-mediated protocol (Table 3, entry 5).

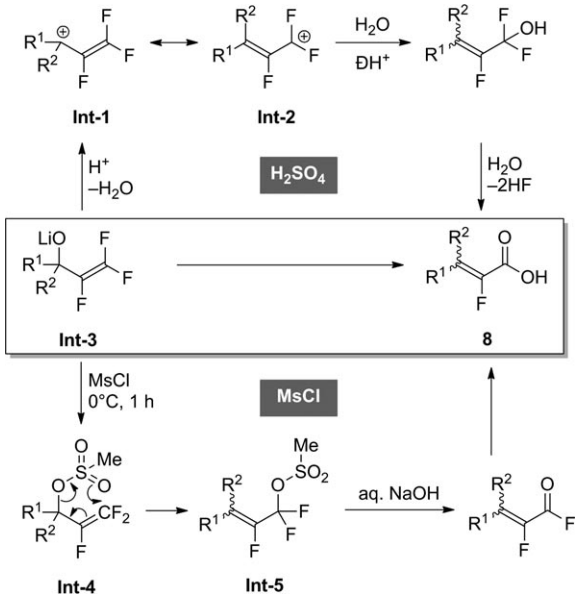
Conversion of alcohols 5 into α-fluoro-α,β-unsaturated carboxylic acids 8 by acid hydrolysis: Having successfully synthesized alcohols **5**, we next studied their transformation to trifluorinated allylic alcohols **6**. It has already been reported[9c,f] that a CF_3 group rendered the geminal halogen atoms ready to accept nucleophilic attack of *n*BuLi due to its strong electron-withdrawing ability adequately stabilizing the resultant anion. Such intermediates would experience subsequent defluorination to form **6**. In fact, treatment of **5a** with *n*BuLi in THF at −80 °C smoothly affected dechlorodefluorination to furnish the corresponding allylic alcohol **6a** in 86 % yield, while the same conditions in the less polar solvent Et_2O led to a drastic reduction in the amount of **6a** formed (Scheme 2). Raising the reaction temperature was



Scheme 2. Formation of allylic alcohol **6a**.

found to permit the undesired entry of a butyl moiety, to some extent, at the terminal fluorinated carbon atom and **7a** was produced as a byproduct.[4b,8a] It was also clarified that instability of **6a**,[12] especially under vacuum in a rotary evaporator, sometimes invoked an abrupt reaction in the flask (indicated by, for example, sudden colorization) to give a complex mixture of unidentified materials. Due to these characteristics of **6a**, we decided to progress to the subsequent hydrolysis step, to obtain the corresponding α-fluoro-α,β-unsaturated carboxylic acids **8**, without further purification of this labile alcohol.

Successful conversion to the desired acids **8** was realized by quenching the reaction mixture that contained the allylic alkoxide **Int-3** (Scheme 3) by addition of an aqueous solution of H_2SO_4 (1:1 v/v)[13] then stirring for 24 h at ambient temperature.[14] However, **5e**–**5g** (Table 4, entries 5–7) were found to be inappropriate substrates under these conditions. In the case of **5f**, the same treatment furnished a crude mix-



Scheme 3. Plausible mechanism for conversion of **Int-3** to **8**.

Table 4. Preparation of α-fluoro-α,β-unsaturated carboxylic acids **8**.

	R^1	R^2	Product	Yield[a] [%]	Selectivity[b] [%]
1	1-$C_{10}H_7$	H	**8a**	53 (64)	>99 (>99)
2	Ph	H	**8b**	65 (72)	>99 (>99)
3	*p*-$MeOC_6H_4$	H	**8c**	72 (72)	>99 (>99)
4	*p*-$H_3CC_6H_4$	H	**8d**	89 (70)	>99 (>99)
5	*p*-$F_3CC_6H_4$	H	**8e**	– (71)[c]	– (>99)
6	C_9H_{19}	H	**8f**	– (59)[d]	– (>99)
7	$PhCH_2CH_2$	H	**8g**	– (80)[d]	– (>99)
8	(*E*)-PhCH=CH	H	**8h**	26[e] (31)[e]	87 (>99)
9	Ph	CH_3	**8i**	87 (70)	62 (73)

[a] Isolated yield obtained after acid hydrolysis. The value in parentheses represents the yield obtained after mesylate-mediated [3,3]-sigmatropic rearrangement. [b] Percentage of the (*Z*)-isomer obtained. [c] NaOH hydrolysis for 2 h. [d] NaOH hydrolysis for 5 d. [e] Determined by ^{19}F NMR spectroscopy.

ture from which three sets of peaks were observed by ^{19}F NMR spectroscopy: one was recovered **5f** (23% yield by ^{19}F NMR spectroscopy), the other two were attributed to the allylic alcohols **6f** and **7f** (41 and 12% yield by ^{19}F NMR spectroscopy, respectively) on the basis of the typical olefinic *trans* F–F couplings ($J>100$ Hz)[15,16] and the presence of only one additional peak for the former (the terminal fluorine atom). A similar situation was found for the crude mixture obtained from **5e**. These facts indicated that an extra stabilizing factor was required for the conversion from **Int-3** to **8**. Thus, substrates with electron-rich aromatic substituents as R^1 were considered to effectively stabilize **Int-1**, while this was not the case for substrates with electron-withdrawing groups on the benzene ring, for example, **5e**. Alkyl moieties as R^1, as in **5f** and **5g**, are also inappropriate for effective electronic donation to the cationic center. Because these problems stemmed from the inherent structures of the substrates, we have explored a different strategy for the construction of the desired compounds **8**.

Conversion of alcohols 5 into α-fluoro-α,β-unsaturated carboxylic acids 8 by [3,3]-sigmatropic rearrangement of sulfonates: To address the problem encountered above, [3,3]-sigmatropic rearrangement of mesylates[17] was selected as an alternative pathway; chemistry previously developed by our group for the similar terminally difluorinated allylic alcohols. Computational analysis of this route was first carried out (Figure 1)[7] and it was found that the energy barrier of the transition state **TS**-(*Z*) for transformation of the model species **6j** (R=Me; Scheme 2) into the more stable (by 14.11 kcal mol^{-1}) product (*Z*)-**Int-5j** (R^1=Me, R^2=H; Scheme 3) was 23.54 kcal mol^{-1}. The other transition state **TS**-(*E*) and the resultant stereoisomeric product (*E*)-**Int-5j** (R^1=H, R^2=Me; Scheme 3) were found to be 2.68 and 3.16 kcal mol^{-1} destabilized with respect to **TS**-(*Z*) and (*Z*)-**Int-5j**, respectively. The height of the **TS**-(*Z*) energy barrier

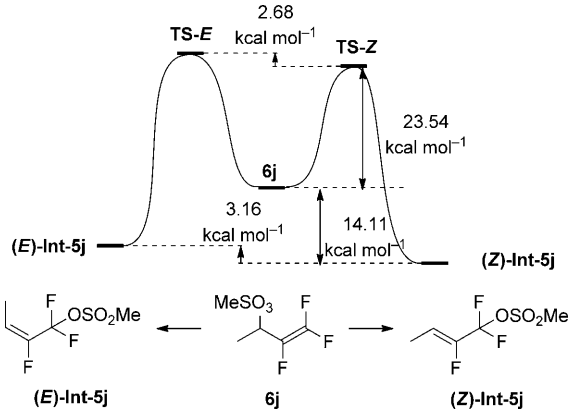


Figure 1. Energy profile for the [3,3]-sigmatropic rearrangement.

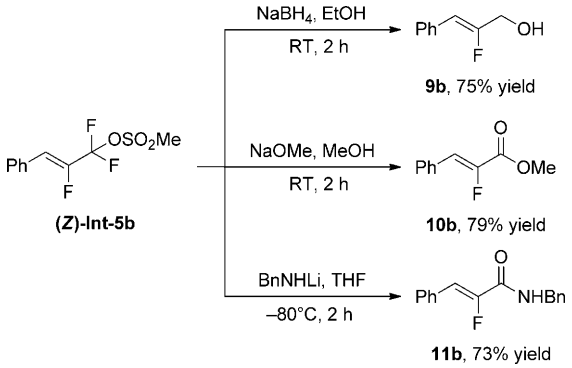
and the energetic difference ($\Delta\Delta E^{\neq}$) between the diastereomeric transition states led us to expect that the present reaction should proceed without significant difficulty to afford the desired α-fluoro-α,β-unsaturated carboxylic acids **8** in a highly *Z*-selective manner.

With these computational results in hand, appropriate reaction conditions were investigated for this unique rearrangement. Quenching the mixture that contained the lithium alkoxide **Int-3** by addition of mesyl chloride at −80°C, followed by 1 h stirring at 0°C, effected its smooth conversion to **Int-5**[18] after the initial mesylate formation from **Int-3**.

Similar to our previous work,[17] the rearrangement from **Int-4** (Scheme 3) proceeded in an extremely facile manner so this intermediate was undetected at any stage of the reaction. Subsequent attack by hydroxide at the positively charged sulfonate sulfur atom and the successive elimination of fluoride furnished the acid fluoride, which eventually produced the desired acid **8** under the conditions employed. The usual S_N2 type reaction to **Int-5** was not likely to be occur because two electronegative fluorine atoms bent toward the incoming OH^- to some extent would refuse the approach of this nucleophile. At this biphasic hydrolysis step, it was demonstrated that the presence of a catalytic amount of quaternary ammonium salt was crucial for attainment of better results. For example, **8b** was produced in 72% yield (Table 4, entry 2) but the yield was reduced to only 44% without the catalyst. Employment of DMF as the solvent for this hydrolysis stage (**Int-5** into **8**) facilitated the NaOH-mediated conversion and afforded the desired product **8** in 95% yield. However, the requirement for THF as the solvent for conversion of **5** to **6**, because of the use of *n*BuLi, gave the disadvantage of a two-step process from **5** to **8**, which included concentration of the solution that contained the relatively labile compound **6**. Thus, we eventually chose the convenient one-pot procedure in THF.

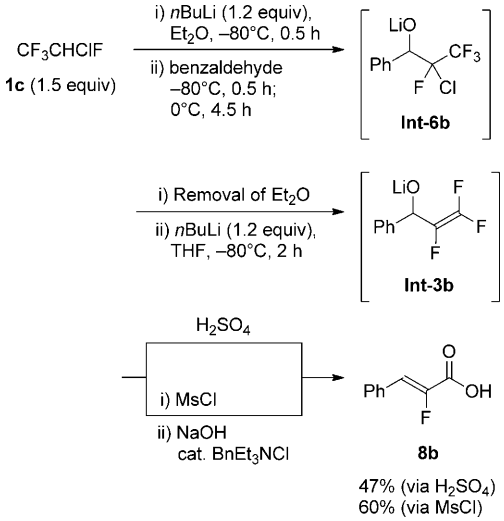
The rearrangement pathway manifested similar efficiency to the acid hydrolysis pathway (Table 4, entries 1–4) for construction of the desired acids **8a–d**. Moreover, formation of the acids **8e–h** in good to high yields by rearrangement

(Table 4, entries 5–8) was pleasing because the acid-mediated pathway failed in this respect. An additional advantage of the rearrangement method is the versatility of intermediate **Int-5**. If other nucleophiles behave in a similar manner to the hydroxide ion **Int-5** should accept further attack by a nucleophile after transformation to the corresponding acid fluoride (Scheme 3). This is actually the case, and addition of $NaBH_4$, NaOMe, or BnNHLi readily furnished the corresponding allylic alcohol **9b**,[19] α,β-unsaturated ester **10b**,[19,20] and amide **11b**, respectively, in 70–79% yield (Scheme 4).



Scheme 4. Reaction of the rearranged mesylate with nucleophiles.

Finally, we have modified the stepwise route to **8** from **1c** to a one-pot method for effective reduction of the amounts of bases and solvents employed, as well as the number of time-consuming isolation protocols. The first condensation with benzaldehyde, under the conditions determined above, furnished the corresponding lithium alkoxide **Int-6b**, which was treated with another equivalent of *n*BuLi after exchange of the solvent from Et_2O to THF. **Int-3b** thus formed was directly hydrolyzed with aqueous solution of H_2SO_4, or an aqueous solution NaOH after reaction with mesyl chloride, to afford the desired α-fluoro-α,β-unsaturated carboxylic acid (*Z*)-**8b** in 47 and 60% overall yield, respectively (Scheme 5).



Scheme 5. One-pot synthesis of **8b**.

Conclusion

In addition to our calculations which, different from HFC-134a (**1a**) and HCFC-133a (**1b**), clarified the stability of the anionic species generated from deprotonation of 2-chloro-1,1,1,2-tetrafluoroethane (HCFC-124, **1c**), we have successfully demonstrated the facile transformation of **1c** to the synthetically useful intermediates, α-fluoro-α,β-unsaturated carboxylic acids (**8**), usually in a *Z*-specific fashion. The one-pot sequence for conversion of **1c** to **8b** was quite efficient for effective reduction of both the amount of base and solvent employed without detriment to the yield of the product.

Experimental Section

General methods: All reactions were carried out under an argon atmosphere in oven-dried glassware, with magnetic stirring. Analytical TLC was routinely used for monitoring reactions (hexane/EtOAc). Spherical neutral silica gel (63–210 μm) was employed for column chromatography. Anhydrous Et_2O, THF, and CH_2Cl_2 were purchased and used without further purification. ^1H (300.40 MHz), ^{13}C (75.45 Hz), and ^{19}F NMR spectra (282.65 Hz) were recorded on a JEOL AL 300 spectrometer in $CDCl_3$, unless otherwise noted, and chemical shifts (δ) were recorded in parts per million (ppm), downfield from internal tetramethylsilane (Me_4Si: $\delta = 0.00$ ppm for ^1H and ^{13}C NMR spectra) or hexafluorobenzene (C_6F_6: $\delta = -163.00$ ppm for ^{19}F NMR spectra). Data are reported in the following order: multiplicity [(s) singlet; (d) doublet; (t) triplet; (q) quartet; (quint) quintet; (sex) sextet; (m) multiplet; (br) broad peak], coupling constants (Hz), number of protons. IR spectra were obtained on a JASCO A-302 spectrometer and are reported in wavenumbers (cm^{-1}). Elemental analyses were performed with a Perkin–Elmer Series II CHNS/O analyzer. Electrospray ionization (ESI) mass spectrometry was performed on a Thermofisher Exactive spectrometer in both negative and positive ionization modes.

General workup: The quenched aqueous layer was extracted three times with EtOAc and the obtained organic layer was treated with anhydrous Na_2SO_4. Filtration and evaporation of the organic layer gave crude materials.

Typical procedure for the preparation of 1-substituted 2-chloro-2,3,3,3-tetrafluoropropanol (5)

With nBuLi as base: *n*BuLi (15.0 mL, 24.0 mmol, 1.6 M in hexanes) and benzaldehyde (1.99 mL, 19.6 mmol) were added successively to a solution of **1c** (3.0 mL, 30.0 mmol) in diethyl ether (50 mL) at −80 °C. After stirring for 0.5 h at −80 °C, then 4.5 h at 0 °C, the reaction mixture was quenched with a 1 M aqueous solution of HCl (40 mL). The mixture was extracted with EtOAc (3×100 mL) and the unreacted aldehyde was removed by washing the combined organic layers with a 30% aqueous solution $NaHSO_3$ (50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give a crude oil. Purification by silica gel column chromatography (CH_2Cl_2) furnished **5b** (83%, 3.962 g, 16.3 mmol), diastereomeric ratio (d.r.) = 61:39.

With tBuOK as base: HCFC **1c** (2.1 mL, 21.0 mmol) was added to a solution of *t*BuOK (0.678 g, 5.0 mmol) and benzaldehyde (0.51 mL, 5.0 mmol) in diethyl ether (20 mL) at −20 °C. After stirring for 0.5 h at −20 °C, followed by 0 °C for 4.5 h, the reaction mixture was quenched with a 1 M aqueous solution of HCl. General workup and purification by

silica gel column chromatography (CH_2Cl_2) furnished **5b** (84%, 1.012 g, 4.2 mmol), d.r. = 51:49.

Data for ***5b***: R_f = 0.58 (CH_2Cl_2); b.p. 95 °C (0.1 kPa); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.60 (br s, 1H; minor), 3.62 (br s, 1H; major), 5.12 (dd, J = 15.6, 4.5 Hz, 1H; minor), 5.24 (t, J = 6.0 Hz, 1H; major), 7.35–7.40 (m, 3H; major + minor), 7.41–7.46 ppm (m, 2H; major + minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 73.6 (d, J = 26.6 Hz; major), 75.4 (d, J = 21.1 Hz; minor), 107.4 (dq, J = 252.5, 33.5 Hz; major), 107.7 (dq, J = 258.0, 33.5 Hz; minor), 120.6 (qd, J = 285.3, 31.6 Hz; minor), 120.9 (qd, J = 284.7, 31.0 Hz; major), 128.0 (major), 128.1 (minor), 128.2 (major), 128.4 (minor), 129.5 (major), 129.6 (minor), 134.6 (minor), 134.8 ppm (major); ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −136.55–−136.43 (m, 1F; minor), −130.98 (quint, J = 6.8 Hz, 1F; major), −79.54 (d, J = 6.8 Hz, 3F; major), −78.16 ppm (d, J = 4.5 Hz, 3F; minor); IR (neat): $\tilde{\nu}$ = 600, 650, 690, 720, 730, 800, 930, 980, 1020, 1040, 1080, 1170, 1190, 1270, 1370, 1440, 1480, 1580, 2850, 3000, 3350 cm^{-1}; elemental analysis calcd (%) for $C_9H_7ClF_4O$: C 44.56, H 2.91; found: C 44.56, H 2.91.

Compound 5a: Prepared with *n*BuLi: yield = 73%, d.r. = 61:39. R_f = 0.58 (CH_2Cl_2); b.p. 125 °C (0.4 kPa); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.64 (d, J = 5.1 Hz, 1H; major), 2.71 (d, J = 5.1 Hz, 1H; minor), 6.09 (dd, J = 5.3, 18.1 Hz, 1H; minor), 6.26 (dd, J = 3.9, 4.5 Hz, 1H; major), 7.25–8.11 ppm (m, 7H; major + minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 68.2 (d, J = 27.9 Hz; major), 70.6 (d, J = 21.1 Hz; minor), 107.3 (dq, J = 262.5, 34.5 Hz; major), 108.3 (dq, J = 252.3, 33.9 Hz; minor), 114.6–133.7 ppm (m; major + minor); ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −139.82–−139.78 (m, 1F; minor), −129.05 (s, 1F; major), −80.05 (d, J = 6.2 Hz, 3F; major), −78.29 ppm (d, J = 4.5 Hz, 3F; minor); IR (neat): $\tilde{\nu}$ = 620, 690, 720, 740, 780, 860, 940, 1050, 1080, 1100, 1120, 1190, 1280, 1320, 1360, 1400, 1510, 1600, 1660, 3050, 3400 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_9ClF_4O$: C 53.35, H 3.10; found: C 53.63, H 3.33.

Compound 5c: Prepared with *n*BuLi: yield = 89%, d.r. = 57:43; prepared with *t*BuOK: yield = 85%, d.r. = 51:49. R_f = 0.63 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.62 (br s, 1H; major + minor), 3.70 (s, 3H; major + minor), 5.01 (dd, J = 4.8, 15.3 Hz, 1H; minor), 5.12 (t, J = 6.0 Hz, 1H; major), 6.81–6.86 (m, 2H), 7.30 ppm (d, J = 8.4 Hz, 2H; major + minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 55.0 (major + minor), 73.1 (d, J = 27.2 Hz; major), 74.9 (d, J = 21.1 Hz; minor), 107.5 (dq, J = 251.9, 33.5 Hz; major), 107.8 (dq, J = 258.8, 33.0 Hz; minor), 113.6 (major), 113.7 (minor), 120.6 (qd, J = 284.9, 31.8 Hz; minor), 120.8 (qd, J = 285.2, 30.6 Hz; major), 127.1 (minor), 129.3 (d, J = 6.0 Hz; major), 129.5 (major + minor), 160.2 (major), 160.2 ppm (minor); ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −135.6–−135.49 (m, 1F; minor), −130.74 (quint, J = 6.8 Hz, 1F; major), −79.17 (d, J = 6.8 Hz, 3F; major), −77.92 ppm (d, J = 4.5 Hz, 3F; minor); IR (neat): $\tilde{\nu}$ = 408, 418, 426, 436, 447, 462, 556, 589, 631, 668, 720, 730, 770, 790, 834, 933, 951, 1031, 1079, 1118, 1214, 1254, 1304, 1444, 1466, 1516, 1587, 1614, 2843, 2913, 2941, 2963,3010, 3460 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_9ClF_4O_2$: C 44.06, H 3.33; found: C 43.73, H 3.64.

Compound 5d: Prepared with *n*BuLi: yield = 90%, d.r. = 60:40; prepared with *t*BuOK: yield = 82%, d.r. = 51:49. R_f = 0.63 (CH_2Cl_2); b.p. 120 °C (0.1 kPa); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.35 (s, 3H; major + minor), 3.03 (d, J = 5.4 Hz, 1H; major), 3.06 (d, J = 5.1 Hz, 1H; minor), 5.07 (dd, J = 15.4, 5.1 Hz, 1H; minor), 5.18 (t, J = 6.0 Hz, 1H; major), 7.16–7.20 (m, 2H; major + minor), 7.32 ppm (dd, J = 2.1, 8.1 Hz, 2H; major + minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.0 (major + minor), 73.4 (d, J = 27.3 Hz; major), 75.3 (d, J = 21.1 Hz; minor), 107.4 (dq, J = 252.5, 33.5 Hz; major), 107.6 (dq, J = 225.1, 33.5 Hz; minor), 120.5 (qd, J = 285.4, 31.7 Hz; minor), 120.8 (qd, J = 285.3, 30.4 Hz, major), 127.8 (major), 127.9 (minor), 128.1 (major + minor), 129.0 (major + minor), 129.1 (major + minor), 131.8 (major + minor), 139.5 (major), 139.7 ppm (minor); ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −136.50–−136.38 (m, 1F; minor), −131.16 (quint, J = 6.8 Hz, 1F; major), −79.54 (d, J = 6.8 Hz, 3F; major), −78.20 ppm (d, J = 4.5 Hz, 3F; minor); IR (neat): $\tilde{\nu}$ = 630, 660, 690, 710, 760, 800, 830, 910, 970, 1010, 1050, 1080, 1150, 1250, 1360, 1500, 1600, 2850, 3300 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_9ClF_4O$: C 46.80, H 3.53; found: C 46.95, H 3.60.

Compound 5e: Prepared with *n*BuLi: yield = 72%, d.r. = 59:41; prepared with *t*BuOK: yield = 33%, d.r. = 56:44. R_f = 0.62 (CH_2Cl_2); m.p. 50.0–51.0 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.60 (d, J = 5.7 Hz, 1H; major), 3.68 (d, J = 4.8 Hz, 1H; minor), 5.21 (dd, J = 4.8, 14.7 Hz, 1H; minor), 5.32 (t, J = 6.0 Hz, 1H; major), 7.56–7.59 (m, 2H; major + minor), 7.63–7.67 ppm (m, 2H; major + minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 73.0 (d, J = 26.7 Hz; major), 74.9 (d, J = 21.7 Hz; minor), 106.9 (dq, J = 253.4, 34.1 Hz; major), 107.1 (dq, J = 258.0, 34.1 Hz; minor), 120.4 (qd, J = 284.8, 31.7 Hz; minor), 120.6 (qd, J = 285.0, 30.7 Hz; major), 123.7 (q, J = 271.7 Hz; minor), 123.8 (q, J = 271.7 Hz; major), 125.0–125.3 (m; major + minor), 128.3 (d, J = 1.9 Hz; major), 128.6 (minor), 131.7 (q, J = 32.7 Hz; major), 131.8 (q, J = 32.7 Hz; minor), 138.20 (minor), 138.34 ppm (major); ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −136.81–−136.70 (m, 1F; minor), −131.38 (quint, J = 6.8 Hz, 1F; major), −79.87 (d, J = 6.8 Hz, 3F; major), −78.42 (d, J = 6.8 Hz, 3F; minor), −64.36 (s, 3F; minor), −64.30 ppm (s, 3F; major); IR ($CHCl_3$): $\tilde{\nu}$ = 590, 620, 640, 660, 720, 830, 930, 1020, 1060, 1100, 1160, 1280, 1320, 1410, 1610, 2900, 3000, 3400 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_6ClF_7O$: C 38.67, H 1.95; found: C 38.56, H 1.96.

Compound 5f: Prepared with *n*BuLi: yield = 74%; d.r. = 52:48. R_f = 0.63 (CH_2Cl_2); b.p. 114 °C (0.1 kPa); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.88 (t, J = 6.8 Hz, 3H), 1.20–1.44 (m, 13H), 1.52–1.83 (m, 3H), 1.86 (d, J = 8.7 Hz, 1H), 2.08 (d, J = 8.7 Hz, 1H), 4.04–4.16 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.8, 22.7, 25.4, 25.5, 29.3, 29.4, 29.4, 29.6, 29.7, 30.4, 32.0, 72.1 (d, J = 26.6 Hz), 73.3 (d, J = 21.05 Hz), 108.5 (dq, J = 255.5, 34.2 Hz), 108.8 (dq, J = 254.3, 33.5 Hz), 120.8 (qd, J = 252.5, 31.6 Hz), 120.9 ppm (qd, J = 284.7, 31.0 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −134.52–−134.41 (m, 1F), −132.26–−132.17 (m, 1F), −79.83 (d, J = 6.8 Hz, 3F), −78.54 ppm (d, J = 6.8 Hz, 3F); IR (neat): $\tilde{\nu}$ = 670, 710,720, 920, 1050, 1110, 1140, 1190, 1290, 1370, 1450, 1640, 2850, 2910, 3130 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{21}ClF_4O$: C 49.23, H 7.23; found: C 49.52, H 7.03.

Compound 5g: Prepared with *n*BuLi: yield = 81%; d.r. = 51:49. R_f = 0.61 (CH_2Cl_2); b.p. 105 °C (0.2 kPa); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.86–2.02 (m, 1H), 2.07–2.19 (m, 2H), 2.09 (d, J = 8.4 Hz, 1H), 2.30 (d, J = 6.9 Hz, 1H), 2.68–2.79 (m, 2H), 2.90–3.01 (m, 1H), 4.04–4.12 (m, 1H), 7.20–7.33 ppm (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz, major diastereoisomer): δ = 31.1 (d, J = 1.9 Hz), 31.8, 71.4 (d, J = 26.6 Hz), 72.4 (d, J = 21.1 Hz), 108.4 (dq, J = 254.3, 34.1 Hz), 120.6 (qd, J = 284.7, 32.2 Hz), 120.8 (qd, J = 285.4, 31.0 Hz), 126.3, 128.3, 128.5, 128.6, 140.3, 140.4 ppm; ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −134.63–−134.52 (m, 1F), −132.11 (s, 1F), −79.78 (d, J = 6.8 Hz, 3F), −78.59 ppm (d, J = 4.5 Hz, 3F); IR (neat): $\tilde{\nu}$ = 700, 740, 830, 920, 1030, 1060, 1120, 1180, 1290, 1360, 1440, 1490, 1590, 2880, 2920, 3020, 3400 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{11}ClF_4O$: C 48.81, H 4.10; found: C 48.84, H 4.18.

Compound 5h: Prepared with *n*BuLi: yield = 82%; d.r. = 56:44. R_f = 0.56 (CH_2Cl_2); b.p. 115 °C (0.1 kPa); m.p. 38.0–39.5 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.53 (d, J = 7.2 Hz, 1H; minor), 2.69 (d, J = 6.3 Hz, 1H; major), 4.74–4.87 (m, 1H; major + minor), 6.15–6.30 (m, 1H; major + minor), 6.77–6.84 (m, 1H; major + minor), 7.22–7.38 ppm (m, 5H; major + minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 73.4 (d, J = 27.2 Hz; minor), 74.5 (d, J = 21.7 Hz; major), 107.6 (dq, J = 254.3, 33.5 Hz; minor), 107.8 (dq, J = 256.8, 34.2 Hz; major), 120.6 (qd, J = 285.3, 31.0 Hz; major), 120.8 (qd, J = 285.3, 31.0 Hz; minor), 121.3 (d, J = 4.4 Hz), 121.6, 127.0, 128.8, 128.9, 135.4 (major), 135.5 (minor), 136.4, 137.0 ppm; ^{19}F NMR ($CDCl_3$, 283 MHz): δ = −134.03 (dq, J = 12.5, 6.8 Hz, 1F; minor), −131.94 (quint, J = 6.9 Hz, 1F; major), −79.40 (d, J = 7.1 Hz, 3F; major), −78.49 ppm (d, J = 6.8 Hz, 3F; minor); IR (neat): $\tilde{\nu}$ = 680, 730, 740, 840, 930, 960, 1020, 1060, 1100, 1180, 1280, 1380, 1440, 1490, 1580, 1650, 3040, 3340 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_9ClF_4O$: C 49.18, H 3.38; found: C 49.12, H 3.46.

Compound 5i: Prepared with *n*BuLi: yield = 85%; d.r. = 40:60; R_f = 0.60 (CH_2Cl_2); b.p. 100 °C (0.1 kPa); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.87–1.88 (m, 3H; major + minor), 2.79 (s, 1H; minor), 2.88 (s, 1H; major), 7.31–7.39 (m, 3H; major + minor), 7.54–7.59 ppm (m, 2H; major + minor); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.4 (quint, J = 1.9 Hz; major), 26.1 (quint, J = 1.8 Hz; minor), 77.1 (d, J = 21.7 Hz; minor), 77.8 (d, J = 21.7 Hz; major), 110.1 (dq, J = 260.5, 32.9 Hz; major), 111.2 (dq, J = 262.3, 32.8 Hz; minor), 120.8 (qd, J = 286.6, 32.3 Hz; minor), 121.0 (qd, J = 286.6, 32.2 Hz; major), 126.5 (d, J = 1.3 Hz; minor), 126.6 (d, J = 1.9 Hz;

major), 127.9 (major), 128.0 (minor), 128.4 (minor), 128.4 (major), 139.0 (minor), 139.6 ppm (major); ^{19}F NMR ($CDCl_3$, 283 MHz): $\delta = -130.96$ (q, $J = 6.8$ Hz, 1F; major), −130.36 (q, $J = 7.5$ Hz, 1F; minor), −74.93 (d, $J = 7.1$ Hz, 3F; minor), −74.75 ppm (d, $J = 6.8$ Hz, 3F; major); IR (neat): $\tilde{\nu} =$ 620, 650, 710, 740, 760, 800, 920, 940, 990, 1040, 1080, 1140, 1200, 1290, 1340, 1390, 1460, 1510, 1560, 3000, 3050, 3500 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_9ClF_4O$: C 46.80, H 3.53; found: C 46.98, H 3.66.

Compound Int-5b: *n*BuLi (0.90 mL, 1.3 mmol, 1.40 M in hexanes) was added to a solution of **5b** (0.290 g, 0.99 mmol) in THF (5 mL) at −80 °C. The reaction mixture was stirred for 30 min at −80 °C, then *n*BuLi (0.90 mL, 1.3 mmol, 1.40 M in hexanes) was added to the mixture, which was stirred at −80 °C for 2 h. Methanesulfonyl chloride (0.16 mL, 2.0 mmol) was added and the mixture was stirred for 1 h at 0 °C. General workup and purification by silica gel column chromatography (CH_2Cl_2/hexane = 1:1) furnished (*Z*)-**Int-5b** (81 %, 0.212 g, 0.80 mmol). $R_f = 0.69$ (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 3.33$ (s, 3H), 6.40 (d, $J =$ 36.0 Hz, 1H), 7.26–7.44 (m, 2H), 7.53–7.58 ppm (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 44.3$, 111.7 (q, $J = 3.3$ Hz), 116.7 (td, $J = 270.2$, 39.2 Hz), 128.65 (d, $J = 32.8$ Hz), 128.71, 129.5, 129.6 (d, $J = 9.9$ Hz), 145.3 ppm (dt, $J = 266.9$, 35.8 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz): $\delta =$ −132.21 (dt, $J = 35.7$, 12.0 Hz, 1F), −74.69 ppm (d, $J = 13.8$ Hz, 2F); IR (neat): $\tilde{\nu} = 518$, 693, 760, 876, 964, 1050, 1081, 1147, 1203, 1280, 1301, 1333, 1390, 1420, 1453, 1497, 1700, 2944, 3033; elemental analysis calcd (%) for $C_{10}H_9F_3O_3S$: C 45.11; H 3.41. found: C 44.68; H 3.67.

Compound 8a[4c,21]

Procedure for H_2SO_4 hydrolysis: *n*BuLi (1.0 mL, 1.2 mmol, 1.20 M in hexanes) was added to a solution of **5b** (0.282 g, 1.02 mmol) in THF (5 mL) at −80 °C. The reaction mixture was stirred for 30 min at −80 °C, then *n*BuLi (1.0 mL, 1.2 mmol, 1.20 M in hexanes) was added and the mixture was stirred at −80 °C for 2 h. A 1:1 *c*H_2SO_4/H_2O solution (3.0 mL) was added and the mixture was stirred for 24 h at RT. General workup furnished (*Z*)-**8a** (53 %, 0.118 g, 0.55 mmol).

Procedure for mesylate rearrangement: *n*BuLi (1.5 mL 2.4 mmol, 1.60 M in hexanes) was added to a solution of **5b** (0.273 g, 0.99 mmol) in THF (3 mL) at −80 °C. The reaction mixture was stirred for 2 h at −80 °C, then methanesulfonyl chloride (0.125 mL, 1.61 mmol) was added and stirring was continued for 1 h at 0 °C. A 6 M aqueous solution of NaOH (1.0 mL) and benzyltriethylammonium chloride (0.022 g, 0.097 mmol) were added and the mixture was stirred for 1 h at RT. General workup furnished (*Z*)-**8a** (64 %, 0.138 g, 0.63 mmol).

*Data for (Z)-**8a***: ^{1}H NMR ([D$_6$]acetone, 300 MHz): $\delta = 7.57$–7.69 (m, 3H), 7.74 (d, $J = 33.3$ Hz, 1H), 7.96–8.02 (m, 3H), 8.15 ppm (d, $J =$ 8.1 Hz, 1H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta = 114.5$ (d, $J = 4.4$ Hz), 124.3, 126.3, 127.0, 127.8, 128.0 (d, $J = 3.8$ Hz), 129.3 (d, $J = 10.6$ Hz), 129.6, 130.8, 132.1, 134.5, 148.9 (d, $J = 266.0$ Hz), 162.2 ppm (d, $J =$ 32.9 Hz); ^{19}F NMR ([D$_6$]acetone, 283 MHz): $\delta = -123.99$ ppm (d, $J =$ 34.2 Hz).

Compound 8b:[21a,b] Prepared by H_2SO_4 hydrolysis: yield = 65 %, *Z* isomer only; prepared by mesylate rearrangement: yield = 72 %, *Z* isomer only.

One-pot procedure A: *n*BuLi (3.75 mL, 6.0 mmol, 1.6 M in hexanes) was added to a flask, and a large portion of hexane was removed under reduced pressure. Et_2O (20 mL) and **1c** (1.50 mL, 15.0 mmol) were added to the flask at −80 °C. After 30 min stirring at −80 °C benzaldehyde (0.51 mL, 5.0 mmol) was added. The mixture was stirred for 30 min at −80 °C, then 4.5 h at 0 °C. The solvent was evaporated under reduced pressure, THF (20 mL) was added and the mixture was cooled to −80 °C. *n*BuLi (3.75 mL, 6.0 mmol, 1.6 M in hexanes) was added the mixture was stirred for 2 h at −80 °C. A 1:1 (v/v) *c*H_2SO_4/H_2O solution (10 mL) was added and stirring was continued for 24 h at RT. General workup furnished (*Z*)-**8b** (58 %, 0.483 g, 2.9 mmol).

One-pot procedure B: *n*BuLi (4.28 mL, 5.9 mmol, 1.40 M in hexanes) was added to a solution of **1c** (1.50 mL, 15.0 mmol) in Et_2O (20 mL) at −80 °C. After stirring for 30 min at −80 °C, benzaldehyde (0.51 mL, 5.0 mmol) was added. After stirring for 30 min at −80 °C and 4.5 h at 0 °C the solvent was evaporated under reduced pressure. THF (20 mL) was added and the solution was cooled to −80 °C. *n*BuLi (4.28 mL, 5.9 mmol, 1.40 M in hexanes) was added and the mixture was stirred for 2 h at −80 °C. Methanesulfonyl chloride (0.75 mL, 8.0 mmol) was added at 0 °C. The mixture was stirred for 1 h at 0 °C, then a 6 M aqueous solution of NaOH (5.0 mL) and benzyltriethylammonium chloride (0.114 g, 0.50 mmol) were added and stirring was continued for 1 h at RT. General workup furnished (*Z*)-**8b** (60 %, 0.497 g, 3.0 mmol).

*Data for (Z)-**8b***: ^{1}H NMR ([D$_6$]acetone, 300 MHz): $\delta = 7.05$ (d, $J =$ 35.7 Hz, 1H), 7.39–7.49 (m, 3H), 7.70–7.75 (m, 2H), 11.02 ppm (brs, 1H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta = 118.1$ (d, $J = 5.0$ Hz), 129.6, 130.5 (d, $J = 3.1$ Hz), 131.0 (d, $J = 8.1$ Hz), 132.2 (d, $J = 3.8$ Hz), 147.9 (d, $J = 264.2$ Hz), 162.3 ppm (d, $J = 35.3$ Hz); ^{19}F NMR ([D$_6$]acetone, 283 MHz): $\delta = -123.99$ ppm (d, $J = 36.5$ Hz).

Compound 8c:[21a,b] Prepared by H_2SO_4 hydrolysis: yield = 72 %, *Z* isomer only; prepared by mesylate rearrangement: yield = 72 %, *Z* isomer only. ^{1}H NMR ([D$_6$]acetone, 300 MHz): $\delta = 3.86$ (s, 3H), 6.92–7.04 (m, 3H), 7.68–7.71 ppm (m, 2H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta =$ 55.7, 115.2, 118.0 (d, $J = 5.0$ Hz), 124.6 (d, $J = 4.4$ Hz), 132.8 (d, $J =$ 8.1 Hz), 146.7 (d, $J = 259.2$ Hz), 161.8 (d, $J = 3.1$ Hz), 162.4 ppm (d, $J =$ 34.7 Hz); ^{19}F NMR ([D$_6$]acetone, 283 MHz): $\delta = -127.11$ ppm (d, $J =$ 34.2 Hz).

Compound 8d:[4c,21b] Prepared by H_2SO_4 hydrolysis: yield = 89 %, *Z* isomer only; prepared by mesylate rearrangement: yield = 70 %, *Z* isomer only. ^{1}H NMR ([D$_6$]acetone, 300 MHz): $\delta = 2.32$ (s, 3H), 6.96 (d, $J = 36.0$ Hz, 1H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.57 (d, $J = 8.4$ Hz, 2H), 10.23 ppm (brs, 1H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta = 21.4$, 118.1 (d, $J = 5.0$ Hz), 129.3 (d, $J = 4.3$ Hz), 130.4, 130.5 (d, $J = 8.1$ Hz), 140.8 (d, $J =$ 2.5 Hz), 147.5 (d, $J = 262.9$ Hz), 162.3 ppm (d, $J = 34.8$ Hz); ^{19}F NMR ([D$_6$]acetone, 283 MHz): $\delta = -124.99$ ppm (d, $J = 36.7$ Hz).

Compound 8e: Prepared by mesylate rearrangement: yield = 71 %, *Z* isomer only. M.p. 203.5–206.0 °C; ^{1}H NMR ([D$_6$]acetone, 300 MHz): $\delta =$ 7.13 (d, $J = 34.8$ Hz, 1H), 7.80 (d, $J = 8.1$ Hz, 2H), 7.94 (d, $J = 8.4$ Hz, 2H), 10.09 ppm (brs, 1H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta = 116.4$ (d, $J = 4.4$ Hz), 125.0 (q, $J = 271.1$ Hz), 126.5 (q, $J = 3.7$ Hz), 131.1 (d, $J =$ 2.5 Hz), 131.5 (d, $J = 8.7$ Hz), 136.0 (d, $J = 2.4$ Hz), 149.4 (d, $J = 269.2$ Hz), 161.9 ppm (d, $J = 35.3$ Hz); ^{19}F NMR ([D$_6$]acetone, 283 MHz): $\delta =$ −120.44 (d, $J = 34.2$ Hz, 1F), −61.79 ppm (s, 3F); IR (KBr): $\tilde{\nu} = 722$, 775, 839, 1013, 1062, 1129, 1176, 1271, 1319, 1439, 1664, 1708, 2524, 2615, 2683, 2859, 2925, 3079, 3439 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_6F_4O_2$: C 51.30, H 2.58; found: C 51.04, H 2.87.

Compound 8f: Prepared by mesylate rearrangement: yield = 59 %, *Z* isomer only. M.p. 48.5–51.0 °C; ^{1}H NMR ([D$_6$]acetone, 300 MHz): $\delta =$ 0.88 (t, $J = 6.8$ Hz, 3H), 1.21–1.35 (m, 12H), 1.46 (quint, $J = 6.8$ Hz, 2H), 2.28 (qd, $J = 7.4$, 2.0 Hz, 2H), 6.28 ppm (dt, $J = 32.8$, 7.9 Hz, 1H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta = 14.4$, 23.3, 24.7 (d, $J = 3.1$ Hz), 29.0 (d, $J = 1.9$ Hz), 29.3–30.6 (m), 32.6, 121.3 (d, $J = 11.8$ Hz), 148.8 (d, $J =$ 252.5 Hz), 161.8 ppm (d, $J = 36.6$ Hz); ^{19}F NMR ([D$_6$]acetone, 283 MHz): $\delta = -133.29$ ppm (d, $J = 31.9$ Hz); IR (CH_2Cl_2): $\tilde{\nu} = 739$, 847, 922, 1096, 1266, 1443, 1469, 1672, 1704, 2359, 2852, 2920, 3080 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{12}H_{20}FO_2$: 215.1447, $[M-H]^+$; found: 215.1446.

Compound 8g: Prepared by mesylate rearrangement: yield = 80 %, *Z* isomer only. M.p. 98.0–102.0 °C; ^{1}H NMR ([D$_6$]acetone, 300 MHz): $\delta =$ 2.57–2.65 (m, 2H), 2.76–2.81 (m, 2H), 5.79 (brs, 1H), 6.29 (td, $J = 7.7$, 32.5 Hz, 1H), 7.18–7.33 ppm (m, 5H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta = 26.6$ (d, $J = 2.4$ Hz), 34.8 (d, $J = 2.5$ Hz), 120.5 (d, $J = 13.0$ Hz), 126.9, 129.2 (d, $J = 6.2$ Hz), 141.7, 148.9 (d, $J = 253.1$ Hz), 161.7 ppm (d, $J =$ 36.6 Hz); ^{19}F NMR ([D$_6$]acetone, 283 MHz): $\delta = -131.84$ ppm (d, $J =$ 31.9 Hz); IR (CH_2Cl_2): $\tilde{\nu} = 696$, 745, 837, 921, 991, 1114, 1186, 1281, 1451, 1667, 1691, 2867, 2939, 3025, 3066 cm^{-1}; elemental analysis calcd (%) $C_{11}H_{11}FO_2$: C 68.03, H 5.71; found: C 67.98, H 5.66.

Compound 8i:[21a,b] Prepared by H_2SO_4 hydrolysis: yield = 87 %, *E*/*Z* = 38:62; prepared by mesylate rearrangement: yield = 70 %, *E*/*Z* = 27:73. ^{1}H NMR ([D$_6$]acetone, 300 MHz, *Z* isomer): $\delta = 2.46$ (d, $J = 3.6$ Hz, 3H), 7.20–7.60 ppm (m, 5H); ^{1}H NMR ([D$_6$]acetone, 300 MHz, *E* isomer): $\delta =$ 2.15 (d, $J = 4.8$ Hz, 3H), 7.20–7.60 ppm (m, 5H); ^{13}C NMR ([D$_6$]acetone, 75 MHz): $\delta = 18.5$ (d, $J = 1.3$ Hz; *Z*), 19.4 (d, $J = 6.8$ Hz; *E*), 128.36, 128.40 (d, $J = 3.1$ Hz), 128.6, 128.7 (d, $J = 3.1$ Hz), 129.06, 129.10, 138.6 (d, $J =$ 1.8 Hz; *Z*), 139.4 (d, $J = 5.6$ Hz; *E*), 144.2 (d, $J = 252.2$ Hz; *Z*), 145.1 (d, $J = 251.2$ Hz; *E*), 161.4 (d, $J = 36.6$ Hz; *E*), 162.9 ppm (d, $J = 35.3$ Hz; *Z*);

^{19}F NMR ([D$_6$]acetone, 283 MHz, *Z* isomer): $\delta = -124.79$ ppm (s); ^{19}F NMR ([D$_6$]acetone, 283 MHz, *E* isomer): $\delta = -123.03$ ppm (q, $J =$ 4.5 Hz).

Compound 9b:[19] $NaBH_4$ (0.034 g, 0.91 mmol) was added to a solution of **Int-5b** (0.080 g, 0.30 mmol) in EtOH (5 mL) at 0 °C and the mixture was stirred for 2 h at RT. The reaction was quenched with a 1 M aqueous solution of HCl. General workup and purification by silica gel column chromatography afforded the allylic alcohol (*Z*)-**9b** (75 %, 0.034 g, 0.22 mmol). $R_f = 0.24$ (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.87$ (br s, 1H), 4.29 (d, $J = 14.4$ Hz, 2H), 5.78 (d, $J = 38.8$ Hz, 1H), 7.22–7.28 (m, 1H), 7.34 (t, $J = 7.5$ Hz, 2H), 7.51 ppm (d, $J = 7.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 61.6$ (d, $J = 32.2$ Hz), 107.4 (d, $J = 6.2$ Hz), 127.4 (d, $J = 2.5$ Hz), 128.4, 128.6 (d, $J = 7.5$ Hz), 132.6 (d, $J = 2.5$ Hz), 158.1 ppm (d, $J = 266.0$ Hz); ^{19}F NMR ($CDCl_3$, 283 MHz): $\delta = -114.74$ ppm (td, $J =$ 13.7, 38.7 Hz).

Compound 10b:[19,20] NaOMe (0.082 g, 1.5 mmol) was added to a solution of **Int-5b** (0.132 g, 0.49 mmol) in MeOH (5 mL) at 0 °C and the mixture was stirred for 2 h at RT. The reaction was quenched with a 1 M aqueous solution of HCl (3 mL). General workup and purification by silica gel column chromatography afforded the allylic alcohol (*Z*)-**10b** (79 %, 0.071 g, 0.39 mmol). $R_f = 0.55$ (hexane/EtOAc = 4:1); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 3.90$ (s, 3H), 6.93 (d, $J = 35.1$ Hz, 1H), 7.23–7.44 (m, 3H), 7.62–7.66 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 52.5$, 117.6 (d, $J = 4.4$ Hz), 128.7, 129.6 (d, $J = 3.1$ Hz), 130.2 (d, $J = 8.7$ Hz), 130.9 (d, $J =$ 4.4 Hz), 144.7 (d, $J = 266.7$ Hz), 161.7 ppm (d, $J = 34.1$ Hz); ^{19}F NMR ($CDCl_3$, 283 MHz): $\delta = -126.90$ ppm (d, $J = 36.4$ Hz).

Compound 11b: *n*BuLi (0.93 mL, 1.5 mmol, 1.6 M in hexanes) was added to benzylamine (0.164 mL, 1.5 mmol) in THF (2 mL) at −80 °C and the mixture was stirred for 30 min at −80 °C. The lithium benzylamine salt solution was added to a solution of **Int-5b** (0.132 g, 5.0 mmol) in THF (3 mL) at −80 °C and the mixture was stirred for 2 h −80 °C. The reaction was quenched with a 1 M aqueous solution of HCl (3 mL). General workup and purification by silica gel column chromatography afforded the allylic alcohol (*Z*)-**11b** (73 %, 0.092 g, 0.36 mmol). M.p. 122.5–124.0 °C; $R_f = 0.54$ (hexane/EtOAc = 2:1); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 4.59$ (d, $J = 6.0$ Hz, 2H), 6.68 (br s, 1H), 6.99 (d, $J = 37.0$ Hz, 1H), 7.27–7.42 (m, 3H), 7.58–7.62 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 43.6$, 113.9 (d, $J = 4.4$ Hz), 127.7, 127.9, 128.7, 128.8, 129.18, 129.21, 130.1 (d, $J = 8.1$ Hz), 131.3 (d, $J = 3.7$ Hz), 149.9 (d, $J = 274.7$ Hz), 160.4 ppm (d, $J = 29.8$ Hz); ^{19}F NMR ($CDCl_3$, 283 MHz): $\delta =$ −131.02 ppm (d, $J = 38.7$ Hz); IR (CH_2Cl_2): $\tilde{\nu} = 689$, 753, 1328, 1535, 1644, 2337, 2360, 2925, 3331 cm^{-1}; elemental analysis calcd (%) for $C_{16}H_{15}FNO$: C 75.28, H 5.53, N 5.49; found: C 75.12, H 5.83, N 5.45.

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