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Methylenation of Perfluoroalkyl Ketones using a Peterson Olefination Approach

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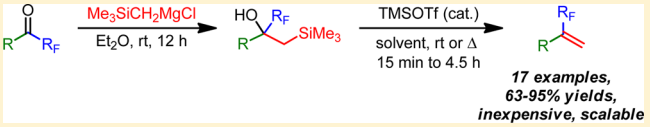
Supporting Information

ABSTRACT: An operationally simple, inexpensive, and rapid route for the olefination of a wide array of trifluoromethyl ketones to yield 3,3,3-trifluoromethylpropenes is reported. Using a Peterson olefination approach, the reaction gives good to excellent yields of the alkene products and can be performed without purification of the β-hydroxysilyl intermediate. The reaction can be extended to other perfluoroalkyl substituents and is easily scaled up. The alkenes prepared can be readily transformed into a variety of other perfluoroalkyl-containing compounds.



INTRODUCTION

The incorporation of the trifluoromethyl group ($-CF_3$) into organic molecules has garnered much attention because of its ability to enhance the metabolic stability and membrane permeability of the parent molecule while also serving as a bioisostere for several functionalities.[1] In addition to these properties, its strongly electron withdrawing nature allows it to impart significant changes to the reactivity of the functional groups to which it is attached. As such, many medicinally relevant molecules not only feature this moiety, but also capitalize on the unique chemistry of trifluoromethyl-bearing compounds in synthetic strategies.

One class of compounds that greatly benefits from CF_3 substitution is alkenes. Of particular interest is the 3,3,3-trifluoropropenyl ($CF_3CR{=}CR-$) moiety, which is attractive to medicinal chemistry as an isostere to certain amino acid groups[2] and to agrochemistry[3] as key intermediates in the synthesis of potent insecticides (or in some cases, insecticides themselves). Macrocycles containing this moiety, such as 26-trifluoro-(*E*)-9,10-dehydroepothilone,[4] are promising anticancer compounds, while conjugating the 3,3,3-trifluoropropenyl group into higher order π systems yields potential organic light-emitting diodes (OLEDs).[5]

The synthetic approach taken to prepare trifluoromethyl-functionalized alkenes is highly dependent on the location of the CF_3 group on the alkene. In the case of β-CF_3 alkenes, such as β-trifluoromethylstyrene derivatives, several strategies have been reported.[3a,6] Of note are two recent reports by Buchwald[6a] and Prakash,[6b] which contrast two distinct approaches to CF_3 alkene construction: via direct trifluoromethylation of activated alkenes or by transition-metal-mediated cross coupling using simple CF_3 alkenyl building blocks, respectively.

α-CF_3 alkenes can be accessed by the methylenation of trifluoromethyl ketones (TFMKs) or by transition-metal coupling (Figure 1). In the case of the former, classical approaches employing Wittig chemistry[7] or a modified Julia approach[8] have been utilized. A protocol using Wilkinson's catalyst, $ClRh(PPh_3)_3$, has also been developed.[9] However, excess PPh_3 and (trimethylsilyl)diazomethane are required, limiting scalability. Alternatively, arenes can be coupled with 2-bromo-3,3,3-trifluoroprop-1-ene using Suzuki,[10] Negishi,[11] or Kumada[12,13] coupling reactions. While useful, these methods are limited to preparing α-CF_3 styryl derivatives. Another metal-mediated methodology involves conversion of (trifluoromethyl)trimethylsilane into $CuCF_3$ and then using this for trifluoromethylation of activated and nonactivated alkenyl halides in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) as a chelating solvent.[14]

Building on our successes in developing methods to access various TFMKs,[15] we envisioned that constructing α-perfluoroalkyl alkenes by dehydrative desilylation in a Peterson[16] manner might offer an attractive alternative to the established protocols. To the best of our knowledge, no such approach had been reported previously. Such a methodology has several advantages over current approaches: (1) it would be metal- and phosphine-free, (2) it would avoid the use of highly toxic (trimethylsilyl)diazomethane, (3) the process would be scalable, and (4) the reaction conditions would be mild. We therefore decided to pursue this potential methodology and report our findings here.

RESULTS AND DISCUSSION

We began our investigation by first constructing a representative α-trifluoromethyl β-hydroxysilyl alcohol, **2a**. With this alcohol in hand, we explored a variety of Lewis acid catalysts to promote dehydrative desilylation to yield the desired alkene **3a**

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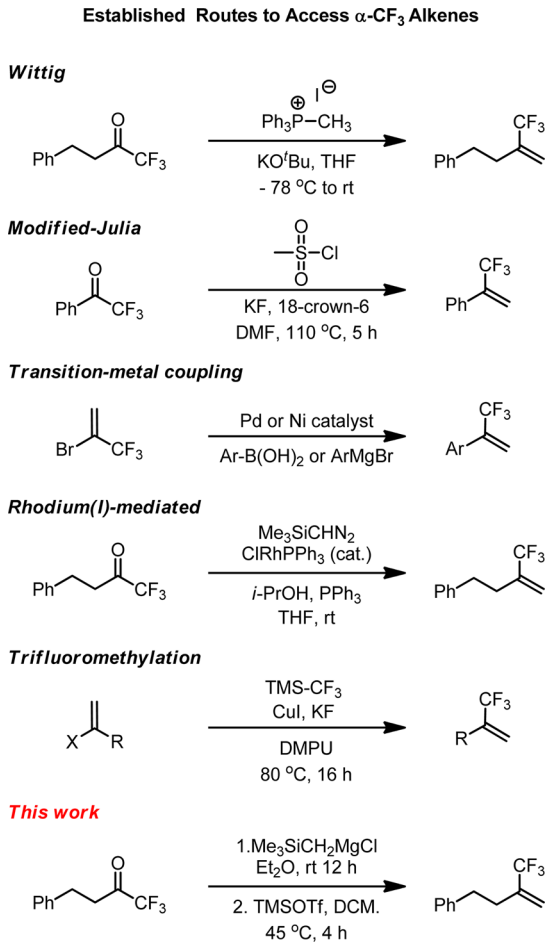


Figure 1. Strategies to access α-CF_3 alkenes from TFMKs.

(Table 1). Initially, we hoped to use the crude ethereal mixture of **2a** obtained after workup and treat it with hydrochloric acid to facilitate elimination (Table 1, entry 1). However, we did not observe any elimination in this case, so we opted to use crude but solvent-free carbinol for our remaining trials. We screened a variety of protic and aprotic Lewis acids to evaluate the propensity for dehydrative desilylation. Surprisingly, **2a** proved remarkably resistant to this transformation with nearly all traditional Lewis acids, giving little to no **3a** (entries 2−9). This is in stark contrast to traditional Peterson olefination reactions which proceed easily using HCl or other standard Lewis acids.[14] The combined effect of diminished oxygen nucleophilicity and high activation barrier for E2-like elimination likley makes the olefination process too energetically unfavorable (Figure 2).[14] To circumvent this, we turned to a more powerful

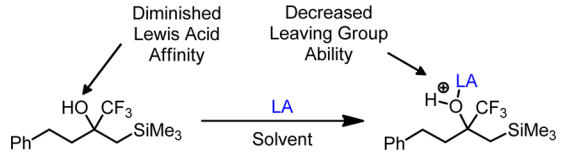
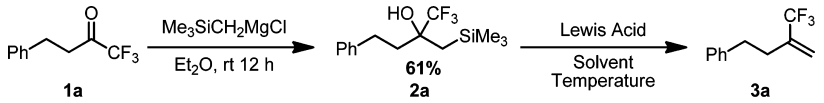


Figure 2. Possible explanation for resistance to dehydrative desilylation.

catalyst, TMSOTf, and encountered success, albeit with low conversion. Solvent had a significant role, with dichloromethane being superior to the more Lewis basic diethyl ether and acetonitrile. To expedite elimination, we chose to heat the reaction to reflux and slightly increase the loading of TMSOTf from 0.10 to 0.15 equiv, allowing complete conversion to the desired alkene in 4 h.

With the optimized reaction conditions in hand, we explored the scope of this process. We were pleased to find that our protocol could be extended to a range of functionalities. Electron-rich (Table 2, entries 1−3 and 5) and electron-poor arenes (entry 4) were both tolerated under our reaction conditions, though with a significant disparity in reactivity. Electron-rich and electron-neutral arenes underwent elimina-

Table 1. Catalyst Screen for Dehydrative Desilylation[a]



1a 2a 3a

entry	solvent	Lewis acid cat.	temp. (°C)	time (h)	conversion (%)[b]
1[c]	Et_2O	2 M HCl	25	1.0	0
2	DCM	$Sc(OTf)_3$	25	0.5	0
3	DCM	$Gd(OTf)_3$	25	0.5	0
4	DCM	$Mg(OTf)_2$	25	0.5	0
5	DCM	TFA	25	0.5	0
6	DCM	p-TSA	25	0.5	0
7	DCM	$SnCl_4$	25	0.5	0
8	DCM	$BF_3{\cdot}OEt_2$	25	0.5	0
9	DCM	TfOH	25	0.5	trace
10	Et_2O	TMSOTf	25	1.0	0
11	MeCN	TMSOTf	25	0.5	0
12	DCE	TMSOTf	25	0.5	9
13	DCM	TMSOTf	25	0.5	16
14	DCM	TMSOTf	45	0.5	30
15[d]	DCM	TMSOTf	45	1.0	55
16[d]	DCM	TMSOTf	45	4.0	100 (74)[e]

[a]Reaction conditions unless otherwise noted: **2a** (0.3 mmol, 1 equiv), catalyst (0.03 mmol, 0.1 equiv), solvent (1.5 mL). [b]Conversion determined by ^{1}H NMR. [c]0.5 equiv of catalyst used. [d]0.15 equiv of catalyst used. [e]The value in parentheses indicates the isolated yield of **3a**.

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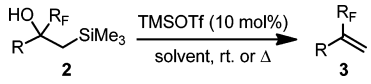
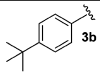
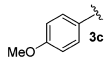
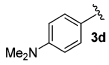
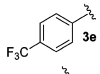
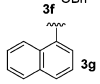
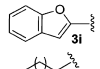
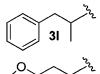
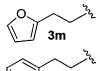
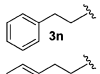
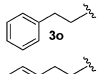
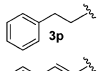
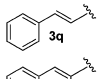
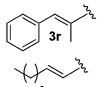
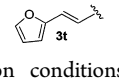
Table 2. Scope of Methylenation of Various TMFKs[a]



entry	R	R_F	temp. (°C)	time (min)	yield (%)[b]
1	 3b	CF_3	25	15	86
2	 3c	CF_3	25	15	80 (88)[c]
3[d,e]	 3d	CF_3	90	270	95
4	 3e	CF_3	45	240	63
5	 3f	CF_3	25	15	85
6	 3g	CF_3	25	15	91
7[d]	 3h	CF_3	90	270	-[f]
8	 3i	CF_3	25	15	86
9	 3j	CF_3	45	240	88
10	3k	CF_3	45	240	65
11	 3l	CF_3	45	240	84
12	 3m	CF_3	-78	60	-[g]
13	 3n	CF_2CF_3	90	240	84
14[d]	 3o	CF_2H	25	15	92
15	 3p	CFH_2	25	15	72
16	 3q	CF_3	25	15	80
17	 3r	CF_3	25	15	86
18	 3s	CF_3	25	60	85
19	 3t	CF_3	25	30	-[g]

[a]Reaction conditions unless otherwise noted: alcohol (1 equiv), TMSOTf (0.15 equiv), CH_2Cl_2 (0.2 M in alcohol). [b]Isolated yields. [c]The value in parentheses indicates the isolated yield of alkene on a 57 mmol scale. [d]Performed in DCE. [e]0.3 equiv of TMSOTf was used. [f]No reaction even at 2 equiv TMSOTf loading. [g]Extensive polymerization.

tion in as little as 15 min at room temperature, while electron-poor arenes required our original optimized conditions. An exception to this trend is **2d** (entry 3). This substrate behaved much like an electron-poor arene, requiring a significantly higher reaction temperature and catalyst loading to reach completion. This reversal of reactivity can likely be attributed to protonation of the dimethylamino group during the course of the reaction, thereby preventing electron donation into the ring system. Heteroarenes (Table 1, entries 7 and 8) showed a similar, more pronounced disparity in reactivity based on the electronics of the ring system. We attribute the failure of the pyridyl system (entry 7) to a rationale similar to that for the dimethylaniline case. The protonation (or silylation) of the nitrogen combined with the inherent deactivation of the pyridyl ring prohibited dehydrative desilylation.

We also explored aliphatic carbinols, finding that unbranched and branched examples were amenable to dehydrative desilylation (Table 2, entries 9–11). A representative furyl system (entry 12) was also screened in these trials. However, extensive polymerization occurred when attempting dehydrative desilylation of this substrate, even at lower temperatures and catalyst loadings. We next turned our attention to different perfluoroalkyl groups (entries 13–15). As one might expect, the more destabilizing α-CF_2CF_3 group required higher temperatures to facilitate elimination; hence, 1,2-dichloroethane (DCE) was employed as the solvent. Likewise, the less destabilized α-CF_2H and α-CFH_2 carbinols underwent dehydrative desilylation more rapidly than their trifluoromethyl congeners.

We also investigated whether conjugated dienes could be accessed via this methodology, and we met with mixed success. While cinnamyl-derived and straight-chain dienes (Table 2, entries 16–18) could be prepared in good yield, the furyl-substituted alkene (entry 19) gave the same result as its saturated counterpart (entry 12), namely, polymerization. Finally, it should be noted that, in nearly all cases, the intermediate carbinol can be carried directly to the dehydrative desilylation reaction without need for further purification. Additionally, this process can be scaled up substantially (entry 2, 57 mmol scale) without compromising the yield.

Representative Reactions Utilizing CF_3 Alkenes. To probe the utility of the alkene products prepared in this study, we conducted several derivatization reactions using **3c** as a representative alkene (Scheme 1). We selected reactions that would either provide potentially valuable synthons for further elaboration or demonstrate key functionalizations that capitalize on the unique electronic nature of the 3,3,3-trifluoropropenyl system. We first explored difluoromethylcyclopropanation using the conditions recently disclosed by Hu and Prakash.[17] We were pleased to find that we could obtain the highly fluorinated cyclopropane **4c** in excellent yield. Next, we sought to convert our representative alkene into a potential partner for cross-coupling processes. We successfully prepared the vinyl bromide **5c** in similarly good yield using a modified literature protocol.[18] Next, on the basis of reports by Bégué and Bonnet-Delpon,[19] we sought to access functionalized *gem*-difluoroalkenes by treatment of **3c** with the appropriate organolithium species. While we were unable to react phenyllithium successfully with **3c**, treatment with lithiated piperidine successfully led to amination and the generation of difluoroalkene **6c** in good yield. Finally, we subjected **3c** to dihydroxylation using traditional Upjohn conditions.[20] This too was successful, giving the diol **7c** in 85% yield.

CONCLUSIONS

In summary, we have disclosed an operationally simple, effective, and user-friendly methodology for the preparation of α-perfluoroalkyl-functionalized alkenes by the dehydrative desilylation of α-trifluoromethyl β-hydroxysilyl carbinol using TMSOTf. The reaction is compatible with a range of functionalities, and the alkene products can be obtained in good to excellent yields. The reaction is scalable and minimal product purification is required. Finally, these alkenes can be used to access other valuable fluorinated products.

EXPERIMENTAL SECTION

General Considerations. All chemical transformations requiring inert atmospheric conditions or vacuum distillation utilized Schlenk

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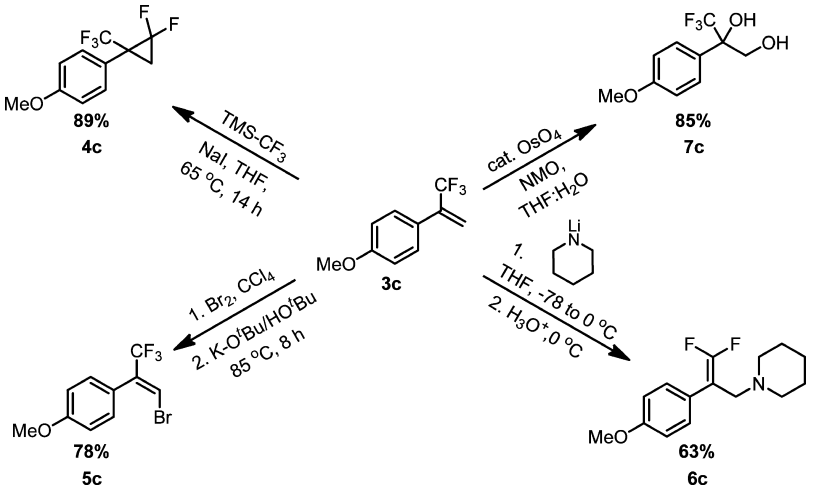
Scheme 1. Applications of α-CF_3-Substituted Alkenes



line techniques with a three- or four-port dual-bank manifold. Nitrogen was used to provide such an atmosphere. NMR spectra (^{1}H, ^{13}C, ^{19}F) were obtained at 298 K. ^{1}H NMR spectra obtained in $CDCl_3$ were referenced to residual nondeuterated chloroform (7.26 ppm) in the deuterated solvent. ^{13}C NMR spectra obtained in $CDCl_3$ were referenced to chloroform (77.3 ppm). ^{19}F NMR spectra were referenced to hexafluorobenzene (−164.9 ppm).[21] Reactions were monitored by a gas chromatograph attached to a mass spectrometer, ^{1}H NMR, and/or TLC on silica gel plates (60 Å porosity, 250 μm thickness). High-resolution mass spectra were performed on either a TOF-DART instrument in positive direct analysis in real time (DART) ionization method, using PEG as the internal standard, or an ESI ionization source. IR spectra were obtained using an ATR accessory. TLC analysis was performed using Hex/EtOAc as the eluent and visualized using permanganate stain, *p*-anisaldehyde stain, Seebach's stain, and/or UV light. Flash chromatography and silica plugs utilized flash silica gel (60 Å porosity, 32−63 μm) or an automated flash chromatography unit.

Chemicals. Deuterated NMR solvents ($CDCl_3$) were stored over 4 Å molecular sieves and K_2CO_3. Unless otherwise specified, all aldehydes were purchased from commercial sources and used without further purification. 2-(Benzyloxy)benzaldehyde[22] and benzofuran-2-carbaldehyde[23] were prepared according to literature protocols. Trifluoromethyl ketone (TFMK) substrates **1a−c,g,k,s** were prepared as in our previously published protocol.[15b] TFMK substrates **1e,f,h−j,l−n,q,r,t** were prepared as in our previously published protocol.[15a,c] To prepare the requisite trifluoromethyl carbinols for the latter TFMK synthesis, aldehydes were treated with Me_3Si-CF_3 using our outlined protocol, which is a modification of the procedure outlined by Prakash.[15a,24] The oxoammonium salt 4-acetamido-2,2,6,6-tetramethyl-1-oxopiperidin-1-ium tetrafluoroborate required for the latter oxidation route was prepared according to our recently published protocol.[25] 1-(4-(Dimethylamino)phenyl)-2,2,2-trifluoroethanone[26] (**1d**), 1,1-difluoro-4-phenylbutan-2-one[27] (**1o**), and 1-fluoro-4-phenylbutan-2-one[28] (**1n**) substrates were prepared according to literature protocols.

General Procedure for the Grignard Reaction of Perfluoroalkyl Ketones using ((Trimethylsilyl)methyl)magnesium Chloride. *1,1,1-Trifluoro-4-phenyl-2-((trimethylsilyl)methyl)butan-2-ol (**2a**).* The following is a modification of the procedure outlined by O'Doherty.[29] In a 100 mL round-bottom flask were added crushed magnesium turnings (0.6807 g, 28 mmol, 1.4 equiv) and a stirbar. The flask was sealed with a rubber septum, the atmosphere was evacuated from the flask via an inlet needle, and the flask was flame-dried under vacuum.[30] The flask was flushed with nitrogen and placed in a room-temperature oil bath. (Chloromethyl)trimethylsilane (2.9125 g, 24 mmol, 1.2 equiv) dissolved in anhydrous Et_2O (14 mL) was added to the flask dropwise[31] via an addition funnel atop a reflux condenser. The reaction mixture was heated to reflux for 1.5 h while under a N_2 atmosphere. The reaction mixture gradually became cloudy and then dark gray. After this time the flask was cooled to 0 °C in an ice bath for 10 min. Subsequently 1,1,1-trifluoro-4-phenylbutan-2-one (**1a**; 4.00 g, 20 mmol, 1 equiv) dissolved in anhydrous Et_2O was added to the flask dropwise. Ten minutes after completion of this addition, the ice bath was removed and the solution was stirred at room temperature for 12 h. After this time, the solution was was quenched with 0.5 M aqueous HCl (20 mL) and transferred to a separatory funnel. The phases were separated, and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with saturated $NaHCO_3$ (∼150 mL) and brine (∼150 mL) and then dried with Na_2SO_4. The solvent was removed in vacuo by rotary evaporation to give the pure carbinol **2a** (3.552 g, 61%) as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.16 (s, 9 H), 1.16 (d, J = 15.16 Hz, 1 H), 1.27 (d, J = 15.16 Hz, 1 H), 1.90 (s, 1 H), 1.99−2.08 (m, 2 H), 2.72−2.81 (m, 2 H), 7.19−7.26 (m, 3 H), 7.28−7.36 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.5 (CH_3), 23.6 (CH_2), 29.9 (CH_2), 38.8 (CH_2), 76.4 (q, J_{C-C-F} = 27.90 Hz, C), 126.5 (CH), 127.0 (q, J_{C-F} = 286.1 Hz, CF_3), 128.6 (CH), 128.9 (CH), 141.5 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −84.13; GC-MS (EI) 290 ([M]$^+$, 2%) 200 (10%), 161 (39%), 146 (6%), 129 (7%), 91 (100%), 77 (15%), 73 (27%); HRMS (DART) calcd for $C_{14}H_{21}F_3OSi$ [M + NH_4]$^+$ 308.1658, found 308.1665.

*2-(4-(tert-Butyl)phenyl)-1,1,1-trifluoro-2-((trimethylsilyl)methyl)-butan-2-ol (**2b**).* **2b** (1.491 g, 76%) was prepared according to the representative procedure for the synthesis of **2a** from 1-(4-(*tert*-butyl)phenyl)-2,2,2-trifluoroethanone (**1b**; 1.42 g, 6.17 mmol), affording the pure α-perfluoroalkyl β-trimethylsilyl carbinol as a clear, orange oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) −0.17 (s, 9 H), 1.34 (s, 9 H), 1.47 (d, J = 14.82 Hz, 1 H), 1.65 (d, J = 14.98 Hz, 1 H), 2.33 (s, 1 H), 7.40 (d, J = 8.20 Hz, 2 H), 7.48 (d, J = 8.20 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 0.01 (CH_3), 25.3 (CH_2), 31.6 (CH_3), 34.77 (C), 77.6 (q, J_{C-C-F} = 28.8 Hz, C), 125.3 (CH), 126.1 (CH), 126.3 (q, J_{C-F} = 285.7 Hz, CF_3), 135.4 (C), 151.6 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −85.06; GC-MS (EI) 228 ([M]$^+$, 20%), 213 (100%), 185 (45%), 164 (4%), 151 (4%), 129 (5%), 128 (8%), 115 (11%), 69 (2%), 41 (6%); HRMS (DART) calcd for $C_{16}H_{25}F_3OSi$ [M + NH_4]$^+$ 336.1970, found 336.1955.

*1,1,1-Trifluoro-2-(4-methoxyphenyl)-3-(trimethylsilyl)propan-2-ol (**2c**).* **2c** (3.683 g, 85%) was prepared according to the representative procedure for the synthesis of **2a** from 2,2,2-trifluoro-1-(4-methoxyphenyl)ethanone (**1c**; 3.023 g, 14.8 mmol), affording the pure carbinol as a pale yellow solid (mp 63−65 °C): ^{1}H NMR ($CDCl_3$, 300 MHz; δ, ppm) −0.16 (s, 9 H), 1.38−1.48 (m, 1 H), 1.63 (d, J = 15.17 Hz, 1 H), 2.26 (s, 1 H), 3.82 (s, 3 H), 6.86−6.94 (m, 2 H), 7.46 (d, J = 9.22 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 0.1 (CH_3), 25.1 (CH_2), 55.5 (CH_3), 77.4 (q, J_{C-C-F} = 28.8 Hz, C), 113.7 (CH), 126.2 (q, J_{C-F} = 284.8 Hz, CF_3), 127.8 (CH), 130.4 (C), 159.8 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −85.47; GC-MS

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(EI) 202 ([M]$^+$, 98%), 186 (5%), 159 (7%), 133 (100%), 118 (13%), 109 (30%), 103 (11%), 89 (16%), 69 (5%), 63 (13%); HRMS (DART) calcd for $C_{13}H_{19}F_3O_2Si$ [M − OH]$^+$ 275.1079, found 275.1080.

*2-(4-(Dimethylamino)phenyl)-1,1,1-trifluoro-3-(trimethylsilyl)-propan-2-ol (**2d**).* **2d** (4.463 g, 91%) was prepared according to the representative procedure for the synthesis of **2a** from 1-(4-(dimethylamino)phenyl)-2,2,2-trifluoroethanone (**1d**; 3.475 g, 16 mmol), affording the pure carbinol as a clear, orange oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) −0.16 (s, 9 H), 1.47 (d, J = 14.92 Hz, 1 H), 1.67 (d, J = 15.16 Hz, 1 H), 2.41 (s, 1 H), 2.94−3.04 (m, 6 H), 6.75 (d, J = 9.05 Hz, 2 H), 7.41 (d, J = 8.80 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.2 (CH_3), 24.8 (CH_2), 40.6 (CH_3), 77.3 (q, J_{C-C-F} = 28.6 Hz, C), 112.1 (CH), 126.4 (q, J_{C-F} = 286.1 Hz, CF_3), 125.8 (CH), 127.3 (C), 150.6 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −85.24; GC-MS (EI) 305 ([M]$^+$, 18%), 287 (4%), 236 (40%), 220 (20%), 214 (22%), 196 (12%), 178 (9%), 146 (100%), 75 (12%), 73 (10%); HRMS (ESI+) calcd for $C_{14}H_{22}F_3NOSi$ [M + H]$^+$ 306.1501, found 306.1479.

*1,1,1-Trifluoro-2-(4-(trifluoromethyl)phenyl)-3-(trimethylsilyl)-propan-2-ol (**2e**).* **2e** (1.978 g, 91%) was prepared according to the representative procedure for the synthesis of **2a** from 2,2,2-trifluoro-1-(4-(trifluoromethyl)phenyl)ethanone (**1e**; 1.600 g, 6.6 mmol), affording the pure carbinol as a clear, pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) −0.17 (s, 9 H), 1.46−1.53 (m, 1 H), 1.63−1.71 (m, 1 H), 2.40 (s, 1 H), 7.66 (d, J = 8.80 Hz, 2 H), 7.72 (d, J = 8.31 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.01 (CH_3), 25.3 (CH_2), 77.6 (q, J_{C-C-F} = 29.3 Hz, C), 124.3 (q, J_{C-F} = 272.2 Hz, CF_3), 125.8 (q, J_{C-F} = 286.8 Hz, CF_3), 125.4 (q, J_{C-C-F} = 3.7 Hz, CH), 127.2 (d, $J_{C-C-C-C-F}$ = 1.5 Hz, CH), 131.0 (q, J_{C-C-F} = 33.0 Hz, C), 142.3 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −84.90 (s, 3 F), −65.72 (s, 3 F); GC-MS (EI) 240 ([M]$^+$, 86%), 221 (40%), 201 (4%), 171 (100%), 169 (14%), 151 (95%), 145 (12%), 102 (15%), 75 (12%), 69 (12%), 50 (5%); HRMS (DART) calcd for $C_{13}H_{16}F_6OSi$ [M + HF]$^+$ 350.0937, found 350.0978; FTIR (cm^{-1}, neat, ATR) 3622, 2958, 2362, 1622, 1327, 1168, 1129, 841.

*2-(2-(Benzyloxy)phenyl)-1,1,1-trifluoro-3-(trimethylsilyl)propan-2-ol (**2f**).* **2f** (3.250 g, 79%) was prepared according to the representative procedure for the synthesis of **2a** from 1-(2-(benzyloxy)phenyl)-2,2,2-trifluoroethanone (**1f**; 3.097 g, 11.13 mmol), affording the pure carbinol as a cloudy, pale yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) −0.07 (s, 9 H), 1.52 (d, J = 14.98 Hz, 1 H), 1.68 (dd, J = 14.82, 2.84 Hz, 1 H), 5.18 (d, J = 2.36 Hz, 2 H), 6.23−6.40 (m, 1 H), 7.02−7.11 (m, 2 H), 7.32−7.41 (m, 3 H), 7.41−7.49 (m, 4 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 0.5 (CH_3), 23.2 (CH_2), 72.2 (CH_2), 79.6 (q, J_{C-C-F} = 29.7 Hz, C), 114.3 (CH), 121.8 (CH), 126.5 (q, J_{C-F} = 287.4 Hz, CF_3), 126.1 (CH), 128.0 (CH), 128.9 (CH), 129.2 (CH), 130.4 (CH), 130.8 (C), 135.8 (C), 157.9 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −85.44; GC-MS (EI) 368 ([M]$^+$, 10%), 260 (16%), 175 (12%), 149 (23%), 91 (100%), 75 (10%), 65 (9%); HRMS (DART) calcd for $C_{19}H_{23}F_3O_2Si$ [M − OH]$^+$ 351.1392, found 351.1438.

*1,1,1-Trifluoro-2-(naphthalen-1-yl)-3-(trimethylsilyl)propan-2-ol (**2g**).* **2g** (2.618 g, 79%) was prepared according to the representative procedure for the synthesis of **2a** from 2,2,2-trifluoro-1-(naphthalen-1-yl)ethanone (**1g**; 2.386 g, 10.64 mmol), affording the pure carbinol as a cloudy, pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) −0.16 (s, 9 H), 1.69 (d, J = 15.41 Hz, 1 H), 2.23 (d, J = 15.41 Hz, 1 H), 2.60 (s, 1 H), 7.43−7.58 (m, 3 H), 7.74−7.84 (m, 1 H), 7.89 (d, J = 7.82 Hz, 2 H), 8.73−8.95 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.2 (CH_3), 26.7 (CH_2), 80.5 (q, J_{C-C-F} = 29.3 Hz, C), 126.6 (q, J_{C-F} = 286.8 Hz, CF_3), 124.6 (CH), 125.6 (CH), 126.1 (CH), 127.0 (q, $J_{C-C-C-F}$ = 1.5 Hz, C), 127.4 (br s, CH) 129.4 (CH), 130.7 (CH), 131.9 (C), 133.9 (C), 135.2 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −82.01; GC-MS (EI) 312 ([M]$^+$, 13%), 243 (26%), 227 (12%), 201 (8%), 183 (30%), 153 (100%), 127 (10%), 115 (5%), 73 (13%); HRMS (DART) calcd for $C_{16}H_{19}F_3OSi$ [M]$^+$ 312.1157, found 312.1183.

*1,1,1-Trifluoro-2-(pyridin-2-yl)-3-(trimethylsilyl)propan-2-ol (**2h**).* **2h** (1.266 g, 23%) was prepared according to the representative procedure for the synthesis of **2a** from 2,2,2-trifluoro-1-(pyridin-2-yl)ethanone (**1h**; 3.600 g, 21 mmol),[32] affording the pure carbinol as a clear, brown oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) −0.23 (s, 9 H), 1.43 (d, J = 14.92 Hz, 1 H), 1.71 (d, J = 14.67 Hz, 1 H), 6.39 (s, 1 H), 7.31−7.37 (m, 1 H), 7.53 (dd, J = 8.07, 0.98 Hz, 1 H), 7.78 (td, J = 7.70, 1.59 Hz, 1 H), 8.57 (dq, J = 4.89, 0.82 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) −0.1 (CH_3), 23.1 (CH_2), 76.3 (q, J_{C-C-F} = 28.6 Hz, C), 125.9 (q, J_{C-F} = 286.1 Hz, CF_3), 122.1 (q, $J_{C-C-C-C-F}$ = 2.2 Hz, CH) 124.0 (CH), 137.6 (CH), 147.4 (CH), 155.9 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −84.71; GC-MS (EI) 263 ([M]$^+$, 15%), 248 (24%), 242 (17%), 194 (26%), 190 (12%), 178 (35%), 154 (100%), 150 (13%), 134 (42%), 104 (62%), 78 (30%), 73 (30%), 45 (11%); HRMS (ESI+) calcd for $C_{11}H_{16}F_3NOSi$ [M + H]$^+$ 264.1032, found 264.1056.

*2-(Benzofuran-2-yl)-1,1,1-trifluoro-3-(trimethylsilyl)propan-2-ol (**2i**).* **2i** (1.937 g, 94%) was prepared according to the representative procedure for the synthesis of **2a** from 1-(benzofuran-2-yl)-2,2,2-trifluoroethanone (**1i**; 1.450 g, 6.8 mmol), affording the pure carbinol as a clear, pale yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) −0.09 (s, 9 H), 1.48−1.57 (m, 1 H), 1.63 (s, 1 H), 2.89 (s, 1 H), 6.82 (d, J = 0.73 Hz, 1 H), 7.23−7.36 (m, 2 H), 7.48−7.53 (m, 1 H), 7.57−7.61 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) −0.2 (CH_3), 22.5 (CH), 75.5 (q, J_{C-C-F} = 30.8 Hz, C), 105.6 (CH), 111.7 (CH), 125.2 (q, J_{C-F} = 286.1 Hz, CF_3), 121.7 (CH), 123.5 (CH), 125.2 (CH), 128.1 (C), 153.9 (C), 155.0 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −85.44; GC-MS (EI) 302 ([M]$^+$, 16%), 233 (36%), 212 (28%), 193 (41%), 165 (4%), 143 (100%), 131 (7%), 115 (25%), 73 (19%); HRMS (DART) calcd for $C_{14}H_{17}F_3O_2Si$ [M − CF_3]$^+$ 233.0993, found 233.1025.

*1,1,1-Trifluoro-2-((trimethylsilyl)methyl)tridecan-2-ol (**2j**).* **2j** (3.416 g, 90%) was prepared according to the representative procedure for the synthesis of **2a** from 1,1,1-trifluorotridecan-2-one (**1j**; 2.800 g, 11.1 mmol), affording the pure carbinol as a clear, pale yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) 0.06 (s, 9 H), 0.85−0.91 (m, 3 H), 1.06 (d, J = 15.13 Hz, 1 H), 1.15 (d, J = 15.13 Hz, 1 H), 1.23−1.34 (m, 16 H), 1.35−1.45 (m, 2 H), 1.60−1.74 (m, 2 H), 1.76−2.01 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 0.4 (CH_3), 14.4 (CH_3), 23.0 (CH_2), 23.3 (CH_2), 23.5 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 29.9 (2 × CH_2), 29.9 (CH_2), 30.3 (CH_2), 32.2 (CH_2), 37.0 (CH_2), 76.5 (q, J_{C-C-F} = 28.0 Hz, C), 127.1 (q, J_{C-F} = 285.7 Hz, CF_3); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −84.31; GC-MS (EI) 340 ([M]$^+$, 2%), 222 (3%), 193 (5%), 180 (5%), 165 (7%), 151 (7%), 140 (5%), 131 (7%), 125 (6%), 111 (30%), 103 (10%), 97 (49%), 89 (12%), 83 (48%), 70 (65%), 57 (91%), 43 (100%); HRMS (DART) calcd for $C_{17}H_{35}F_3OSi$ [M + NH_4]$^+$ 358.2753, found 358.2759.

*3-Cyclohexyl-1,1,1-trifluoro-2-((trimethylsilyl)methyl)propan-2-ol (**2k**).* **2k** (2.728 g, 89%) was prepared according to the representative procedure for the synthesis of **2a** from 3-cyclohexyl-1,1,1-trifluoropropan-2-one (**1k**; 2.100 g, 10.8 mmol), affording the pure carbinol as a clear, pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.10 (s, 9 H), 0.91−1.36 (m, 8 H), 1.52−1.60 (m, 2 H), 1.60−1.74 (m, 4 H), 1.76 (s, 1 H), 1.83−1.93 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.4 (CH_3), 24.4 (CH_2), 26.4 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 33.3 (CH), 35.2 (CH_2), 35.6 (CH_2), 43.7 (CH_2), 77.0 (q, J_{C-C-F} = 27.9 Hz, C), 127.0 (q, J_{C-F} = 286.1 Hz, CF_3); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −84.53; GC-MS (EI) 282 ([M]$^+$, 2%), 213 (3%), 153 (10%), 133 (26%), 131 (11%), 125 (8%), 111 (13%), 83 (100%), 73 (77%); HRMS (DART) calcd for $C_{13}H_{25}F_3OSi$ [M + H]$^+$ 283.1705, found 283.1701.

*1,1,1-Trifluoro-3-methyl-4-phenyl-2-((trimethylsilyl)methyl)-butan-2-ol (**2l**).* **2l** (1.9725 g, 88%) was prepared according to the representative procedure for the synthesis of **2a** from 1,1,1-trifluoro-3-methyl-4-phenylbutan-2-one (**1l**; 1.600 g, 7.9 mmol), affording the pure carbinol as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.20 (apparent doublet, J = 5.38 Hz, 9 H), 0.94 (t, J = 7.58 Hz, 3 H), 1.09−1.27 (m, 2 H), 2.05 (br s, 1 H), 2.10−2.34 (m, 2 H), 3.23 (t, J = 11.70 Hz, 1 H), 7.18−7.28 (m, 3 H), 7.30−7.37 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.5 (CH_3), 0.5 (CH_3), 13.9 (q, $J_{C-C-C-C-F}$ = 2.2 Hz, CH_3), 14.0 (d, $J_{C-C-C-C-F}$ = 1.5 Hz, CH_3), 20.1 (CH_2), 21.8 (CH_2), 37.4 (d, $J_{C-C-C-F}$ = 1.5 Hz, CH) 37.6 (d,

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$J_{C-C-C-F}$ = 2.2 Hz, CH) 42.7 (CH_2), 43.1 (CH_2), 78.7 (q, J_{C-C-F} = 26.4 Hz, C), 79.0 (q, J_{C-C-F} = 26.4 Hz, C), 127.3 (q, J_{C-F} = 287.6 Hz, CF_3), 127.4 (q, J_{C-F} = 287.6 Hz, CF_3), 141.0 (C), 141.3 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −79.49 (s, 3 F), −78.92 (s, 3 F); GC-MS (EI) 304 ([M]$^+$, 4%), 214 (4%), 194 (6%), 175 (16%), 147 (4%), 117 (6%), 91 (100%), 73 (24%); HRMS (DART) calcd for $C_{15}H_{23}F_3OSi$ [M + NH_4]$^+$ 322.1814, found 322.1849.

*1,1,1-Trifluoro-4-(furan-2-yl)-2-((trimethylsilyl)methyl)butan-2-ol (**2m**).* **2m** (5.280 g, 73%) was prepared according to the representative procedure for the synthesis of **2a** from 1,1,1-trifluoro-4-(furan-2-yl)butan-2-one (**1m**; 4.9956 g, 26 mmol), affording the pure carbinol as a clear, brown oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.12 (s, 9 H), 1.06−1.15 (m, 1 H), 1.16−1.24 (m, 1 H), 1.92 (s, 1 H), 2.02−2.12 (m, 2 H), 2.79 (dd, J = 10.39, 6.48 Hz, 2 H), 6.02 (d, J = 3.18 Hz, 1 H), 6.29 (dd, J = 3.18, 1.96 Hz, 1 H), 7.32 (d, J = 1.22 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.3 (CH_3), 22.4 (CH_2), 23.5 (CH_2), 34.9 (CH_2), 76.1 (q, J = 28.6 Hz, C), 105.4 (CH), 110.5 (CH), 126.9 (q, J = 286.1 Hz, CF_3), 141.5 (CH), 155.1 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −84.07; GC-MS (EI) 280 ([M]$^+$, 5%), 262 (8%), 170 (21%), 151 (9%), 141 (4%), 123 (11%), 103 (9%), 94 (14%), 81 (100%), 73 (44%), 53 (17%), 45 (10%); HRMS (DART) calcd for $C_{12}H_{19}F_3O_2Si$ [M + H]$^+$ 281.1185, found 281.1179.

*1,1,1,2,2-Pentafluoro-5-phenyl-3-((trimethylsilyl)methyl)pentan-3-ol (**2n**).* **2n** (1.508 g, 93%) was prepared according to the representative procedure for the synthesis of **2a** from 1,1,1,2,2-pentafluoro-5-phenylpentan-3-one (**1n**; 1.200 g, 4.76 mmol), affording the pure carbinol as a clear, yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.19 (s, 8 H), 1.19−1.27 (m, 1 H), 1.33−1.41 (m, 1 H), 2.03 (s, 1 H), 2.10 (dd, J = 11.25, 6.11 Hz, 2 H), 2.72−2.83 (m, 2 H), 7.19−7.25 (m, 3 H), 7.30−7.37 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.7 (CH_3), 23.5 (CH_2), 30.0 (br s, CH_2) 39.2 (CH_2), 77.3 (t, J_{C-C-F} = 22.70 Hz, C), 115.9 (tq, J_{C-F} = 261.2, 34.5 Hz, CF_2) 119.9 (qt, J_{C-F} = 288.3, 37.4 Hz, CF_3), 126.5 (CH), 128.6 (CH), 128.9 (CH), 141.4 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −125.31 to −123.20 (m, 2 F), −80.98 (s, 3 F); GC-MS (EI) 340 ([M]$^+$, 4%), 250 (11%), 231 (9%), 211 (8%), 191 (5%), 161 (9%), 129 (7%), 119 (3%), 105 (8%), 91 (100%), 73 (28%); HRMS (DART) calcd for $C_{15}H_{21}F_5OSi$ [M + NH_4]$^+$ 358.1626, found 358.1640.

*1,1-Difluoro-4-phenyl-2-((trimethylsilyl)methyl)butan-2-ol (**2o**).* **2o** (4.7627 g, 92%) was prepared according to the representative procedure for the synthesis of **2a** from 1,1-difluoro-4-phenylbutan-2-one (**1o**; 3.500 g, 19 mmol), affording the pure carbinol as a clear, orange oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.14 (s, 9 H), 1.09 (d, J = 11.74 Hz, 2 H), 1.75 (s, 1 H), 1.89−1.98 (m, 2 H), 2.69−2.80 (m, 2 H), 5.62 (t, J = 57.00 Hz, 1 H), 7.17−7.24 (m, 3 H), 7.27−7.34 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.7 (CH_3), 23.3 (CH_2), 29.6 (CH_2), 38.7 (t, $J_{C-C-C-F}$ = 1.8 Hz, CH_2), 75.5 (t, J_{C-C-F} = 21.3 Hz, C), 117.9 (t, J_{C-F} = 248.7 Hz, CF_2H) 126.3 (CH), 128.6 (CH), 128.8 (CH), 142.0 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −134.72 (dd, J = 276.56, 55.86 Hz, 1 F), −133.29 (dd, J = 276.57, 57.22 Hz, 1 F); GC-MS (EI) 272 ([M]$^+$, 3%), 254 (2%), 221 (6%), 182 (8%), 162 (10%), 143 (45%), 128 (16%), 104 (11%), 91 (100%), 73 (31%), 65 (8%), 47 (7%); HRMS (DART) calcd for $C_{14}H_{22}F_2OSi$ [M + NH_4]$^+$ 290.1752, found 290.1770.

*1-Fluoro-4-phenyl-2-((trimethylsilyl)methyl)butan-2-ol (**2p**).* **2p** (1.98 g, 52%) was prepared according to the representative procedure for the synthesis of **2a** from 1-fluoro-4-phenylbutan-2-one (**1p**; 2.49 g, 15 mmol), with the following modification. (a) Further purification was accomplished by FCC (gradient Hex to 95/5 Hex/EtOAc to 9/1 Hex/EtOAc). The pure carbinol was obtained as an off-white semisolid: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.20 (s, 9 H), 1.07 (apparent quartet of doublets, J = 12.00, 2.00 Hz, 2 H), 1.95 (dd, J = 11.25, 6.11 Hz, 2 H), 2.04 (s, 1 H), 2.77 (apparent doublet of doublets, J = 10.88, 5.80 Hz, 2 H), 4.33 (dq, J = 47.80, 8.60 Hz, 2 H), 7.27 (m, 3 H), 7.36 (apparent triplet, J = 7.20 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.7 (CH_3), 25.3 (d, $J_{C-C-C-C-F}$ = 3.1 Hz, CH_2), 30.5 (CH_2), 40.9 (d, $J_{C-C-C-C-F}$ = 3.3 Hz, CH_2), 74.7 (d, J_{C-C-F} = 17.6 Hz, C), 89.3 (d, J_{C-F} = 174.1 Hz, CFH_2) 126.2 (CH), 128.5 (CH), 128.7 (CH), 142.2 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −227.55 (t, J = 47.70 Hz); GC-MS (EI) 254 ([M]$^+$, 1%), 236 (2%), 221 (8%), 164 (4%), 149 (10%), 145 (18%), 129 (29%), 117 (19%), 104 (12%), 91 (100%), 75 (29%), 65 (11%), 57 (15%), 45 (9%); HRMS (DART) calcd for $C_{14}H_{23}FOSi$ [M + NH_4]$^+$ 272.1846, found 272.1842.

*(E)-1,1,1-Trifluoro-4-phenyl-2-((trimethylsilyl)methyl)but-3-en-2-ol (**2q**).* **2q** (3.514 g, 81%) was prepared according to the representative procedure for the synthesis of **2a** from (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one (**1q**; 2.900 g, 15 mmol) with the following modification. (a) A gradient was used (pentane to 95/5 pentane/EtOAc) when eluting off the silica gel plug.[33] The pure carbinol was obtained as a pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.04 (s, 9 H), 1.23−1.41 (m, 2 H), 2.16 (s, 1 H), 6.21 (d, J = 16.14 Hz, 1 H), 6.85 (d, J = 16.14 Hz, 1 H), 7.26−7.48 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.5 (CH_3), 24.1 (CH_2), 76.8 (q, J_{C-C-F} = 29.3 Hz, C), 125.9 (q, J_{C-F} = 286.1 Hz, CF_3), 127.0 (CH), 128.5 (CH), 129.0 (CH), 131.8 (CH 136.1 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −86.05; GC-MS (EI) 288 ([M]$^+$, 3%), 219 (53%), 203 (10%), 177 (12%), 159 (45%), 129 (100%), 115 (9%), 73 (22%), 69 (1%); HRMS (DART) calcd for $C_{14}H_{19}F_3OSi$ [M − CF_3]$^+$ 219.1205, found 219.1198.

*(E)-1,1,1-Trifluoro-3-methyl-4-phenyl-2-((trimethylsilyl)methyl)-but-3-en-2-ol (**2r**).* **2r** (3.150 g, 87%) was prepared according to the representative procedure for the synthesis of **2a** from (*E*)-1,1,1-trifluoro-3-methyl-4-phenylbut-3-en-2-one (**1r**; 2.570 g, 12 mmol), affording the pure carbinol as a clear, pale yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) 0.15 (s, 9 H), 1.33 (d, J = 14.98 Hz, 1 H), 1.53 (d, J = 15.13 Hz, 1 H), 1.95 (s, 3 H), 2.21 (s, 1 H), 6.93 (s, 1 H), 7.30 (d, J = 7.09 Hz, 3 H), 7.37−7.44 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 0.3 (CH_3), 15.2 (CH_3), 22.6 (CH_2), 79.0 (q, J_{C-C-F} = 28.0 Hz, C), 126.3 (q, J_{C-F} = 287.4 Hz, CF_3), 127.1 (CH), 128.5 (CH), 128.8 (CH), 129.3 (CH), 135.2 (C), 137.6 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −83.65; GC-MS (EI) 302 ([M]$^+$, 9%), 233 (99%), 217 (11%), 197 (14%), 177 (19%), 173 (35%), 143 (100%), 128 (78%), 115 (39%), 91 (16%), 73 (40%), 69 (2%); HRMS (DART) calcd for $C_{15}H_{21}F_3OSi$ [M − OH]$^+$ 285.1286, found 285.1277.

*(E)-1,1,1-Trifluoro-2-((trimethylsilyl)methyl)dodec-3-en-2-ol (**2s**).* **2s** (2.339 g, 92%) was prepared according to the representative procedure for the synthesis of **2a** from (*E*)-1,1,1-trifluorododec-3-en-2-one (**1s**; 1.820 g, 8.19 mmol), affording the pure carbinol as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.07−0.11 (m, 9 H), 0.87−0.96 (m, 3 H), 1.13 (d, J = 14.92 Hz, 1 H), 1.26 (d, J = 14.92 Hz, 1 H), 1.32 (s, 8 H), 1.39−1.51 (m, 2 H), 2.05−2.09 (m, 1 H), 2.12 (d, J = 7.09 Hz, 2 H), 5.51 (d, J = 15.65 Hz, 1 H), 5.92 (d, J = 15.65 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.5 (CH_3), 14.3 (CH_3), 22.9 (CH_2), 23.7 (CH_2), 29.1 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 32.1 (CH_2), 32.4 (CH_2), 76.3 (q, J_{C-C-F} = 28.6 Hz, C), 126.0 (q, J_{C-F} = 285.4 Hz, CF_3), 128.0 (CH), 133.3 (CH); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −86.47; GC-MS (EI) 324 ([M]$^+$, 2%), 251 (8%), 224 (3%), 177 (4%), 139 (11%), 115 (11%), 97 (16%), 84 (32%), 73 (15%), 69 (71%), 56 (81%), 43 (100%); HRMS (DART) calcd for $C_{16}H_{31}F_3OSi$ [M − H]$^+$ 323.2018, found 323.2014.

*(E)-1,1,1-Trifluoro-4-(furan-2-yl)-2-((trimethylsilyl)methyl)but-3-en-2-ol (**2t**).* **2t** (1.627 g, 61%) was prepared according to the representative procedure for the synthesis of **2a** from (*E*)-1,1,1-trifluoro-4-(furan-2-yl)but-3-en-2-one (**1t**; 1.82 g, 9.47 mmol) with the following modification. (a) A gradient was used (pentane to 95/5 pentane/EtOAc) when eluting off the silica gel plug.[15] The pure carbinol was obtained as a clear, brown oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.04−0.12 (m, 9 H), 1.25 (d, J = 14.92 Hz, 1 H), 1.32 (d, J = 14.67 Hz, 1 H), 2.18 (br s, 1 H), 6.16 (d, J = 15.89 Hz, 1 H), 6.33 (d, J = 3.18 Hz, 1 H), 6.40 (dd, J = 3.30, 1.83 Hz, 1 H), 6.66 (d, J = 15.89 Hz, 1 H), 7.38 (d, J = 1.47 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 0.4 (CH_3), 24.3 (CH_2), 76.6 (q, J_{C-C-F} = 29.3 Hz, C), 109.7 (CH), 111.7 (CH), 120.3 (CH), 125.9 (q, J_{C-F} = 285.4 Hz, CF_3), 125.5 (CH), 143.0 (CH), 152.0 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −85.93; GC-MS (EI) 278 ([M]$^+$, 29%), 209 (83%), 193 (19%), 188 (10%), 170 (12%), 159 (11%), 149 (14%), 141 (7%), 119 (100%), 109 (10%), 91 (69%), 81 (10%), 77 (26%), 73 (68%), 65

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(15%), 55 (21%); HRMS (DART) calcd for $C_{12}H_{17}F_3O_2Si$ $[M + H]^+$ 279.1028, found 279.1032.

General Procedure for Alkene Synthesis. *(3-(Trifluoromethyl)-but-3-en-1-yl)benzene (**3a**).*[7] In a 100 mL one-neck round-bottom flask equipped with a stirbar were added the carbinol **2a** (1.45 g, 5 mmol, 1 equiv) and CH_2Cl_2 (25 mL, 0.2 M in the alcohol).[34] The solution was cooled to 0 °C via an ice−water bath and stirred for 10 min at this temperature. After this time, TMSOTf (0.167 g, 0.14 mL, 0.15 equiv) was added to the flask dropwise over 1 min. The flask was then equipped with a reflux condenser and heated to reflux for 4 h.[35] After this time, the flask was cooled to room temperature and quenched with 50 mL of aqueous saturated $NaHCO_3$. The reaction mixture was transferred to a separatory funnel and diluted with pentane (∼150 mL). The layers were separated, and the aqueous layer was extracted with pentane (3 × 75 mL). The combined organic layers were washed with brine (∼150 mL) and dried with Na_2SO_4. The solvent was removed in vacuo by rotary evaporation. The crude product was gently added atop a silica gel plug and eluted with pentane[36] (2−3 column volumes). The solvent was removed in vacuo by rotary evaporation, affording the pure alkene (0.745 g, 74%) as a clear, colorless oil.: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 2.53 (t, J = 8.07 Hz, 2 H), 2.81−2.89 (m, 2 H), 5.30 (d, J = 1.22 Hz, 1 H), 5.69 (s, 1 H), 7.18−7.25 (m, 3 H), 7.28−7.35 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 31.5 (CH_2), 34.1 (CH_2), 118.5 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 124.1 (q, J_{C-F} = 273.6 Hz, CF_3), 126.5 (CH), 128.7 (CH), 128.8 (CH), 138.1 (q, J_{C-C-F} = 29.3 Hz, C), 140.9 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −71.49; GC-MS (EI) 200 ($[M]^+$, 24%), 161 (6%), 128 (4%), 115 (4%), 91 (100%), 69 (4%), 51 (5%).

*1-(tert-Butyl)-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (**3b**).*[12] **3b** (0.868 g, 86%) was prepared according to the representative procedure for the synthesis of **3a** from 2-(4-(*tert*-butyl)phenyl)-1,1,1-trifluoro-3-(trimethylsilyl)propan-2-ol (**2b**; 1.40 g, 4.4 mmol), with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 1.38−1.40 (m, 9 H), 5.80 (q, J = 1.70 Hz, 1 H), 5.96 (q, J = 1.40 Hz, 1 H), 7.46 (s, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 31.5 (CH_3), 34.9 (C), 119.85 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 123.8 (q, J_{C-F} = 273.8 Hz, CF_3), 125.8 (CH), 127.3 (CH), 131.0 (C), 139.1 (q, J_{C-C-F} = 30.5 Hz, C), 152.5 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −67.87; GC-MS (EI) 228 ($[M]^+$, 20%), 213 (100%), 185 (45%), 128 (8%), 115 (11%), 77 (4%), 69 (2%).

*1-Methoxy-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (**3c**).*[37] **3c** (0.811 g, 80%) was prepared according to the representative procedure for the synthesis of **3a** from 1,1,1-trifluoro-2-(4-methoxyphenyl)-3-(trimethylsilyl)propan-2-ol (**2c**; 1.46 g, 5 mmol, with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 3.82−3.85 (m, 3 H), 5.71 (q, J = 1.71 Hz, 1 H), 5.86−5.90 (m, 1 H), 6.89−6.95 (m, 2 H), 7.42 (d, J = 8.31 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 55.5 (CH_3), 114.2 (CH), 119.1 (q, $J_{C-C-C-F}$ = 5.6 Hz, CH_2), 123.8 (q, J_{C-F} = 273.2 Hz, CF_3), 126.3 (CH), 128.91 (C), 138.7 (q, J_{C-C-F} = 30.1 Hz, C), 160.5 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −67.91; GC-MS (EI) 202 ($[M]^+$, 98%), 183 (5%), 159 (7%), 133 (100%), 118 (13%), 109 (30%), 103 (11%), 89 (16%), 69 (5%), 63 (13%).

*N,N-Dimethyl-4-(3,3,3-trifluoroprop-1-en-2-yl)aniline (**3d**).* **3d** (1.33 g, 95%) was prepared according to the representative procedure for the synthesis of **3a** from 2-(4-(dimethylamino)phenyl)-1,1,1-trifluoro-3-(trimethylsilyl)propan-2-ol (**2d**; 1.99 g, 6.5 mmol) with the following modifications. (a) The reaction mixture was heated at reflux in DCE for 4.5 h. (b) A 0.3 equiv amount of TMSOTf was used. (c) A silica gel plug was not required. The pure CF_3 alkene was obtained as an orange, crystalline solid (mp 49−50 °C): ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 3.01 (s, 6 H), 5.69 (d, J = 1.71 Hz, 1 H), 5.80 (d, J = 0.98 Hz, 1 H), 6.73 (d, J = 9.05 Hz, 2 H), 7.40 (d, J = 8.56 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 40.5 (CH_3), 112.2 (CH), 116.8 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 124.1 (q, J_{C-F} = 274.4 Hz, CF_3), 121.4 (C), 128.3 (CH), 138.7 (q, J_{C-C-F} = 29.3 Hz, C), 151.00 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −67.52; GC-MS (EI) 215 ($[M]^+$, 100%), 199 (19%), 151 (7%), 146 (23%), 130 (11%), 102 (8%), 69 (4%); HRMS (ESI+), calcd for $C_{11}H_{12}F_3N$ $[M + H]^+$ 216.1000, found 216.0984.

*1-(Trifluoromethyl)-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (**3e**).*[8] **3e** (0.759 g, 63%) was prepared according to the representative procedure for the synthesis of **3a** from 1,1,1-trifluoro-2-(4-(trifluoromethyl)phenyl)-3-(trimethylsilyl)propan-2-ol (**2e**; 1.65 g, 5 mmol), affording the pure CF_3 alkene as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 5.85 (q, J = 1.47 Hz, 1 H), 6.04−6.10 (m, 1 H), 7.55−7.61 (m, 2 H), 7.63−7.69 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 122.4 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 123.3 (q, J_{C-F} = 272.9 Hz, CF_3), 124.2 (q, J_{C-F} = 272.2 Hz, CF_3), 125.9 (q, $J_{C-C-C-F}$ = 3.7 Hz, CH) 128.2 (d, $J_{C-C-C-C-F}$ = 1.5 Hz, CH) 131.4 (q, J_{C-C-F} = 32.3 Hz, C), 137.4 (C), 138.4 (q, J_{C-C-F} = 30.8 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −68.01 (s, 3 F), −66.03 (s, 3 F); GC-MS (EI) 240 ($[M]^+$, 86%), 221 (40%), 201 (4%), 171 (100%), 169 (14%), 151 (95%), 145 (12%), 102 (15%), 75 (12%), 69 (12%).

*1-(Benzyloxy)-2-(3,3,3-trifluoroprop-1-en-2-yl)benzene (**3f**).* **3f** (1.18 g, 85%) was prepared according to the representative procedure for the synthesis of **3a** from 2-(2-(benzyloxy)phenyl)-1,1,1-trifluoro-3-(trimethylsilyl)propan-2-ol (**2f**; 1.84 g, 5 mmol), with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, pale yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 5.07 (s, 2 H), 5.64 (d, J = 1.19 Hz, 1 H), 6.07 (d, J = 1.19 Hz, 1 H), 6.90−6.98 (m, 2 H), 7.19−7.39 (m, 7 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 70.6 (CH_2), 113.0 (CH), 120.9 (C), 123.5 (q, J_{C-F} = 273.6 Hz, CF_3), 123.7 (q, $J_{C-C-C-F}$ = 5.1 Hz, CH_2), 124.0 (CH), 127.3 (CH), 128.1 (CH), 128.8 (CH), 130.5 (CH), 131.1 (CH), 136.3 (q, J_{C-C-F} = 31.5 Hz, C), 137.2 (CH), 156.8 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −68.49; GC-MS (EI) 279 ($[M]^+$, 7%), 258 (4%), 209 (2%), 186 (5%), 118 (3%), 109 (7%), 91 (100%), 69 (12%); HRMS (DART) calcd for $C_{16}H_{13}F_3O$ $[M + NH_4]^+$ 296.1262, found 296.1279.

*1-(3,3,3-Trifluoroprop-1-en-2-yl)naphthalene (**3g**).*[11] **3g** (1.01 g, 91%) was prepared according to the representative procedure for the synthesis of **3a** from 1,1,1-trifluoro-2-(naphthalen-1-yl)-3-(trimethylsilyl)propan-2-ol (**2g**; 1.56 g, 5 mmol), with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 5.72 (d, J = 0.98 Hz, 1 H), 6.39 (d, J = 1.47 Hz, 1 H), 7.47−7.62 (m, 4 H), 7.87−7.97 (m, 2 H), 7.98−8.06 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 123.5 (q, J_{C-F} = 273.6 Hz, CF_3), 124.4 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 125.2 (CH), 125.6 (CH), 126.4 (CH), 126.9 (CH), 127.7 (CH), 128.6 (CH), 129.6 (CH), 131.8 (C), 132.4 (C), 134.0 (C), 137.6 (q, J_{C-C-F} = 31.2 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −69.79; GC-MS (EI) 222 ($[M]^+$, 39%), 201 (22%), 183 (7%), 153 (100%), 151 (20%), 126 (6%), 69 (5%).

*2-(3,3,3-Trifluoroprop-1-en-2-yl)benzofuran (**3i**).* **3i** (0.967 g, 86%) was prepared according to the representative procedure for the synthesis of **3a** from 2-(benzofuran-2-yl)-1,1,1-trifluoro-3-(trimethylsilyl)propan-2-ol (**2i**; 1.60 g, 5.3 mmol), with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) 6.06 (s, 1 H), 6.36 (s, 1 H), 6.97 (s, 1 H), 7.32 (t, J = 7.60 Hz, 1 H), 7.41 (t, J = 7.40 Hz, 1 H), 7.55 (d, J = 8.20 Hz, 1 H), 7.65 (d, J = 7.72 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 106.5 (q, $J_{C-C-C-C-F}$ = 1.7 Hz, CH) 111.4 (CH), 118.3 (q, $J_{C-C-C-F}$ = 5.1 Hz, CH_2), 122.8 (q, J_{C-F} = 272.1 Hz, CF_3), 122.0 (CH), 123.6 (CH), 126.0 (CH), 128.7 (C), 129.7 (q, J_{C-C-F} = 32.2 Hz, C), 148.7 (C), 155.0 (C), ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −68.70; GC-MS (EI) 212 ($[M]^+$, 100%), 183 (3%), 143 (54%), 133 (7%), 115 (49%), 89 (9%), 69 (6%); HRMS (DART) calcd for $C_{11}H_7F_3O$ $[M]^+$ 212.0449, found 212.0443.

*2-(Trifluoromethyl)tridec-1-ene (**3j**).* **3j** (1.10 g, 88%) was prepared according to the representative procedure for the synthesis of **3a** from 1,1,1-trifluoro-2-((trimethylsilyl)methyl)tridecan-2-ol (**2j**; 1.70 g, 5 mmol), affording the pure CF_3 alkene as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) 0.89 (t, J = 7.10 Hz, 3 H), 1.21−1.38 (m,

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16 H), 1.47−1.56 (m, 2 H), 2.19 (t, J = 7.80 Hz, 2 H), 5.29 (q, J = 1.40 Hz, 1 H), 5.65 (d, J = 1.42 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 14.4 (CH_3), 23.0 (CH_2), 27.7 (CH_2), 29.4 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.9 (CH_2), 29.9 (CH_2), 30.0 (CH_2), 32.2 (CH_2), 117.5 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 124.2 (q, J_{C-F} = 273.8 Hz, CF_3), 139.1 (q, J_{C-C-F} = 28.8 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −71.75; GC-MS (EI) 250 ([M]$^+$, 2%), 194 (4%), 165 (7%), 131 (7%), 111 (30%), 97 (49%), 83 (48%), 70 (65%), 57 (91%), 43 (100%); HRMS (DART) calcd for $C_{14}H_{25}F_3$ [M − C_4H_9]$^+$ 193.1199, found 193.1233; FTIR (cm^{-1}, neat, ATR) 2926, 2855, 1467, 1168, 1125, 937, 792, 637.

*(2-(Trifluoromethyl)allyl)cyclohexane (**3k**).* **3k** (0.622 g, 65%) was prepared according to the representative procedure for the synthesis of **3a** from 3-cyclohexyl-1,1,1-trifluoro-2-((trimethylsilyl)methyl)propan-2-ol (**2k**; 1.42 g, 5 mmol), affording the pure CF_3 alkene as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.82−0.93 (m, 2 H), 1.10−1.31 (m, 3 H), 1.46−1.57 (m, 1 H), 1.63−1.79 (m, 5 H), 2.08 (d, J = 7.25 Hz, 2 H), 5.27 (s, 1 H), 5.69 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 26.4 (CH_2), 26.7 (CH_2), 33.3 (CH_2), 35.9 (CH), 38.1 (CH_2), 119.1 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 124.2 (q, J_{C-F} = 273.8 Hz, CF_3), 137.2 (q, J_{C-C-F} = 28.8 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −71.39; GC-MS (EI) 192 ([M]$^+$, 3%), 153 (3%), 133 (6%), 127 (2%), 115 (3%), 109 (6%), 83 (100%), 69 (4%), 55 (70%), 41 (22%); HRMS (DART) calcd for $C_{10}H_{15}F_3$ [M − C_3H_4 + H]$^+$: 153.0891, found 153.0917; FTIR (cm^{-1}, neat, ATR) 2926, 2854, 1450, 1167, 1123, 936, 842.

*(2-Methyl-3-(trifluoromethyl)but-3-en-1-yl)benzene (**3l**).* **3l** (0.900 g, 84%) was prepared according to the representative procedure for the synthesis of **3a** from 1,1,1-trifluoro-3-methyl-4-phenyl-2-((trimethylsilyl)methyl)butan-2-ol (**2l**; 1.52 g, 5 mmol), affording the pure CF_3 alkene as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 1.17 (d, J = 6.85 Hz, 3 H), 2.64 (dd, J = 13.33, 8.93 Hz, 1 H), 2.74−2.84 (m, 1 H), 3.03 (dd, J = 13.45, 5.38 Hz, 1 H), 5.39−5.44 (m, 1 H), 5.81 (q, J = 1.47 Hz, 1 H), 7.21−7.26 (m, 2 H), 7.26−7.31 (m, 1 H), 7.33−7.39 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 19.8 (CH_3), 35.7 (CH), 42.9 (CH_2), 117.7 (q, J_{C-F} = 5.9 Hz, CH_2), 124.5 (q, J_{C-F} = 274.4 Hz, CF_3), 126.5 (CH), 128.6 (CH), 129.5 (CH), 140.0 (C), 143.7 (q, J_{C-C-F} = 27.9 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −70.44; GC-MS (EI) 214 ([M]$^+$, 11%), 175 (5%), 128 (6%), 91 (100%), 69 (7%); HRMS (DART) calcd for $C_{12}H_{13}F_3$ [M + H]$^+$ 215.1048, found 215.1032.

*(4,4,5,5,5-Pentafluoro-3-methylenepentyl)benzene (**3n**).* **3n** (0.772 g, 75%) was prepared according to the representative procedure for the synthesis of **3a** from 1,1,1,2,2-pentafluoro-5-phenyl-3-((trimethylsilyl)methyl)pentan-3-ol (**2n**; 1.40 g, 4.11 mmol), with the following modification. (a) The reaction mixture was heated for 4 h at reflux in DCE. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 2.58 (t, J = 8.07 Hz, 2 H), 2.90 (t, J = 7.80 Hz, 2 H), 5.54 (s, 1 H), 5.78 (s, 1 H), 7.23−7.31 (m, 3 H), 7.33−7.40 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 31.7 (CH_2), 34.5 (CH_2), 113.7 (tq, J_{C-F} = 253.1, J_{C-C-F} = 37.4 Hz, CF_2) 119.5 (qt, J_{C-F} = 286.8, J_{C-C-F} = 38.9 Hz, CF_3), 121.3 (t, $J_{C-C-C-F}$ = 8.8 Hz, CH_2), 126.6 (CH), 128.7 (CH), 128.8 (CH), 137.6 (t, J_{C-C-F} = 21.3 Hz, C), 140.8 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −119.29 (s, 2 F), −86.87 (s, 3 F); GC-MS (EI) 250 ([M]$^+$, 25%), 211 (5%), 191 (3%), 91 (100%), 69 (3%), 65 (13%); HRMS (DART) calcd for $C_{12}H_{11}F_5$ [M − $C_5H_6F_5$ - H]$^+$ 91.0548, found 91.0579; FTIR (cm^{-1}, neat, ATR) 3066, 3030, 2931, 2362, 1605, 1453, 1332, 1202, 1122, 1023, 940, 698.

*(3-(Difluoromethyl)but-3-en-1-yl)benzene (**3o**).*[9] **3o** (0.838 g, 92%) was prepared according to the representative procedure for the synthesis of **3a** from 1,1-difluoro-4-phenyl-2-((trimethylsilyl)-methyl)butan-2-ol (**2o**; 1.36 g, 5 mmol), with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 2.58 (t, J = 8.07 Hz, 2 H), 2.92 (t, J = 8.30 Hz, 2 H), 5.26−5.31 (m, 1 H), 5.44 (s, 1 H), 6.09 (t, J = 56.00 Hz, 1 H), 7.26−7.33 (m, 3 H), 7.34−7.42 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 30.5 (t, $J_{C-C-C-F}$ = 1.5 Hz, CH_2), 34.2 (CH_2), 117.8 (q, J_{C-F} = 237.7 Hz, CF_2H) 117.9 (t, J = 10.00 Hz, CH_2), 126.4 (CH), 128.7 (CH), 128.7 (CH), 141.4 (C), 142.3 (t, J = 20.5 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −118.44 (d, J = 55.86 Hz); GC-MS (EI) 182 ([M]$^+$, 20%), 128 (3%), 115 (3%), 104 (2%), 91 (100%), 77 (4%), 65 (16%), 51 (8%).

*(3-(Fluoromethyl)but-3-en-1-yl)benzene (**3p**).* **3p** (0.709 g, 72%) was prepared according to the representative procedure for the synthesis of **3a** from 1-fluoro-4-phenyl-2-((trimethylsilyl)methyl)-butan-2-ol (**2p** ; 1.53 g, 6 mmol), with the following modifications. (a) The reaction mixture was stirred for 15 min at room temperature. (b) Further purification was accomplished by FCC utilizing hexanes as an eluent. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 2.45 (t, J = 7.90 Hz, 2 H), 2.83 (t, J = 8.50 Hz, 2 H), 4.83 (dq, J = 47.54, 0.60 Hz, 2 H), 5.04 (ddt, J = 2.03, 1.35, 0.69 Hz, 1 H), 5.15 (qspt, J = 2.00, 1.30 Hz, 1 H), 7.19−7.25 (m, 3 H), 7.28−7.35 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 34.2 (d, $J_{C-C-C-F}$ = 1.9 Hz, CH_2), 34.3 (CH_2), 85.7 (d, J_{C-F} = 167.8 Hz, CH_2F) 113.4 (d, $J_{C-C-C-F}$ = 10.4 Hz, CH_2), 126.2 (CH), 128.6 (CH), 128.6 (CH), 141.8 (C), 144.4 (d, J_{C-C-F} = 14.5 Hz, CH); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −218.52 (td, J = 47.70); GC-MS (EI) 164 ([M]$^+$, 100%), 144 (6%), 131 (22%), 129 (19%), 115 (14%), 104 (17%), 77 (13%), 59 (3%); HRMS (DART) calcd for $C_{11}H_{13}F$ [M − F]$^+$ 145.1017, found 145.1023.

*(E)-(3-(Trifluoromethyl)buta-1,3-dien-1-yl)benzene (**3q**).*[37] **3q** (4.09 g, 85%) was prepared according to the representative procedure for the synthesis of **3a** from (*E*)-1,1,1-trifluoro-4-phenyl-2-((trimethylsilyl)methyl)but-3-en-2-ol (**2q**; 7.00 g, 24.3 mmol), with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 5.70 (d, J = 30.64 Hz, 1 H), 6.66 (d, J = 16.36 Hz, 1 H), 6.89 (d, J = 16.66 Hz, 1 H), 7.23−7.47 (m, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 119.4 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH2) 121.8 (CH), 123.4 (q, J_{C-F} = 274.4 Hz, CF_3), 127.1 (CH), 128.8 (CH), 129.0 (CH), 133.2 (CH), 136.8 (q, J_{C-C-F} = 30.1 Hz, C), 136.5 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −68.91; GC-MS (EI) 198 ([M]$^+$, 33%), 177 (24%), 159 (5%), 129 (100%), 127 (22%), 102 (7%), 77 (8%), 69 (7%), 51 (9%).

*(E)-(2-Methyl-3-(trifluoromethyl)buta-1,3-dien-1-yl)benzene (**3r**).* **3r** (0.914 g, 86%) was prepared according to the representative procedure for the synthesis of **3a** from (*E*)-1,1,1-trifluoro-3-methyl-4-phenyl-2-((trimethylsilyl)methyl)but-3-en-2-ol (**2r**; 1.51 g, 5 mmol), with the following modification. (a) The reaction mixture was stirred for 15 min at room temperature. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 500 MHz; δ, ppm) 2.08 (s, 3 H), 5.68 (d, J = 1.58 Hz, 1 H), 5.87 (s, 1 H), 6.86 (s, 1 H), 7.28−7.35 (m, 3 H), 7.38−7.43 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz; δ, ppm) 16.5 (CH_3), 119.0 (q, $J_{C-C-C-F}$ = 5.9 Hz, CH_2), 123.7 (q, J_{C-F} = 275.5 Hz, CF_3), 127.4 (CH), 128.5 (CH), 129.6 (CH), 130.8 (CH), 131.4 (C), 137.4 (C), 141.4 (q, J_{C-C-F} = 28.8 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −66.26; GC-MS (EI) 212 ([M]$^+$, 23%), 197 (31%), 191 (12%), 177 (59%), 143 (100%), 128 (92%), 115 (31%), 91 (9%), 69 (7%); HRMS (DART) calcd for $C_{12}H_{11}F_3$ [M + H]$^+$ 213.0891, found 213.0900.

*(E)-2-(Trifluoromethyl)undeca-1,3-diene (**3s**).* **3s** (0.936 g, 85%) was prepared according to the representative procedure for the synthesis of **3a** from (*E*)-1,1,1-trifluoro-2-((trimethylsilyl)methyl)-dodec-3-en-2-ol (**2s**; 1.55 g, 5 mmol), with the following modification. (a) The reaction mixture was stirred for 1 h at room temperature. The pure CF_3 alkene was obtained as a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 0.85−0.94 (m, 3 H), 1.30 (s, 8 H), 1.38−1.50 (m, 2 H), 2.14 (q, J = 6.85 Hz, 2 H), 5.43 (s, 1 H), 5.59 (s, 1 H), 5.93−6.12 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 14.3 (CH_3), 23.0 (CH_2), 29.2 (CH_2), 29.5 (CH_2), 32.1 (CH_2), 33.6 (CH_2), 117.4 (q, $J_{C-C-C-F}$ = 5.4 Hz, CH_2), 123.5 (q, J_{C-F} = 274.4 Hz, CF_3), 123.3 (CH), 136.4 (CH), 136.9 (q, J_{C-C-F} = 29.7 Hz, C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −69.48; GC-MS (EI) 234 ([M]$^+$, 2%), 220 (24%), 191 (13%), 178 (15%), 164 (46%), 149 (40%), 136 (35%), 127 (21%), 122 (23%), 115 (85%), 109 (33%), 95 (100%), 81 (35%), 69 (82%), 56 (86%), 41 (94%); HRMS (DART) calcd for $C_{12}H_{19}F_3$ [M − C_4H_9]$^+$ 163.0729, found 163.0745; FTIR (cm^{-1}, neat, ATR) 2957, 2927, 2855, 1467, 1305, 1207, 1165, 967.

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Application Reactions Utilizing α-CF_3 Alkenes. *Cyclopropanation: 1-(2,2-Difluoro-1-(trifluoromethyl)cyclopropyl)-4-methoxybenzene (**4c**).* This protocol is a modification of the procedure outlined by Prakash.[17] In a 25 mL screw top vial equipped with a stirbar were added **3c** (1.01 g, 5 mmol, 1 equiv), NaI (0.150, 1 mmol, 0.2 equiv), and anhydrous THF (7.2 mL, 0.7 M in the alkene). The contents of the vial were stirred for 5 min, and after this time $TMSCF_3$ (1.78 g, 12.5 mmol, 2.5 equiv) was added all at once to the vial. The vial was sealed and heated to 65 °C. The progress of the reaction was monitored by GC/MS. After 12 h the reaction appeared to stall and the vial was (after cooling) charged with more NaI (0.075 g, 0.5 mmol, 0.1 equiv) and $TMSCF_3$ (0.355 g, 2.5 mmol, 0.5 equiv). The solution was heated to 65 °C, and after 6 h the reaction was judged to be complete. The solution was cooled to room temperature, and the solvent was removed in vacuo by rotary evaporation[38] to give an off-yellow semisolid. The solid material was taken up in Et_2O (∼100 mL) and deionized water (∼100 mL) and transferred to a separatory funnel. The phases were separated, and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic layers were washed with saturated aqueous sodium thiosulfate (∼100 mL), saturated aqueous $NaHCO_3$ (∼100 mL), deionized water (∼100 mL), and finally brine (∼150 mL). The organic layer was dried with Na_2SO_4, and the solvent was removed in vacuo by rotary evaporation. The crude product was adhered to silica gel using ∼1.5 wt equiv of silica gel (relative to the theoretical yield). The dry-packed material was gently added atop a silica gel plug. The plug was eluted with a 95/5 by volume mixture of Hex/EtOAc (2−3 column volumes). The solvent was removed in vacuo by rotary evaporation, affording the pure cyclopropane (1.12 g, 89%) as a clear, yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 1.85−1.94 (m, 1 H), 2.29 (s, 1 H), 3.82 (s, 3 H), 6.90−6.96 (m, 2 H), 7.35 (d, J = 8.80 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 20.1 (ddt, J_{C-C-F} = 10.8, 7.2, 3.1 Hz, CH_2), 36.4 (qdd, J = 33.9, 12.7, 9.9 Hz, C), 55.3 (CH_3), 109.9 (ddq, J = 292.0, 285.3, 3.1 Hz, CF_2) 114.5 (CH), 121.2 (C), 124.0 (qd, J_{C-F} = 275.1, 2.9 Hz, CF_3), 132.4 (d, $J_{C-C-C-C-F}$ = 2.2 Hz, CH) 160.8 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −141.23 (dquind, J = 160.76, 13.60, 4.08 Hz, 1 F), −132.06 (dqd, J = 160.77, 7.50, 4.10 Hz, 1 F), −69.82 (dd, J = 13.63, 2.72 Hz, 3 F); GC-MS (EI) 252 ([M]$^+$, 29%), 231 (4%), 202 (7%), 183 (100%), 169 (11%), 163 (26%), 151 (9%), 145 (9%), 133 (30%), 109 (8%), 69 (4%); HRMS (DART), calcd for $C_{11}H_9F_5O$ [M + H]$^+$ 253.0652, found 253.0662.

*Bromination Elimination: 1-(1-Bromo-3,3,3-trifluoroprop-1-en-2-yl)-4-methoxybenzene (**5c**).* This protocol is a modification of the procedure outlined by Zuilhof.[18] In a 50 mL one-neck round-bottom flask equipped with a stirbar were added **3c** (1.21 g, 6 mmol, 1 equiv) and CCl_4 (6 mL, 1 M in the alkene). The flask was sealed with a rubber septum and placed under an N_2 atmosphere via an inlet needle. The flask was cooled to 0 °C in an ice bath, and after 5 min Br_2 (1.055 g, 0.34 mL, 6.6 mmol, 1.1 equiv) was added to the flask dropwise via a syringe. Five minutes after complete addition, the flask was warmed to room temperature over 10 min. After this time, the solvent was removed in vacuo by rotary evaporation. The crude semisolid material was taken up in ^{t}BuOH (21 mL) and the solution stirred for 5 min. After this time, KO^{t}Bu (0.741 g, 6.6 mmol, 1.1 equiv) was added to the flask and was refluxed for 1 h. After this time the reaction appeared to have stalled[39] and an additional loading of KO^{t}Bu (0.741 g, 6.6 mmol, 1.1 equiv) was added. The reaction was refluxed for an additional 6 h, and complete conversion was achieved. After this time, the solution was cooled to room temperature and deionized water (∼20 mL) was added to the reaction mixture. The solution was transferred to a separatory funnel and extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with deionized water (2 × 100 mL) and brine (∼150 mL). The organic layer was dried with Na_2SO_4, and the solvent was removed in vacuo to give the pure bromide (1.32 g, 78%) as a light brown oil: ^{1}H NMR ($CDCl_3$, 400 MHz, *E* isomer; δ, ppm) 3.85 (s, 3 H), 6.94−6.99 (m, 2 H), 7.25−7.29 (m, 2 H), 7.30 (q, J = 1.71 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz, *E* isomer; δ, ppm) 55.4 (CH_3), 114.3 (C), 116.6 (q, $J_{C-C-C-F}$ = 7.1 Hz, CH) 122.7 (q, J_{C-F} = 275.8 Hz, CF_3), 123.9 (CH), 130.8 (C), 136.3 (q, J_{C-C-F} = 30.1 Hz, C), 160.6 (C); ^{19}F NMR ($CDCl_3$, 377 MHz, *E* isomer; δ, ppm) −68.15; GC-MS (EI, *E* isomer) 281 ([M]$^+$, 100%), 279 (99%), 211 (24%), 201 (10%), 186 (15%), 181 (20%), 169 (10%), 158 (39%), 151 (12%), 138 (13%), 117 (24%), 89 (35%), 75 (10%), 69 (13%), 63 (21%); ^{1}H NMR ($CDCl_3$, 400 MHz, *Z* isomer; δ, ppm) 3.83 (s, 3 H), 6.77 (s, 1 H), 6.90 (d, J = 8.80 Hz, 2 H), 7.20−7.24 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz, *Z* isomer; δ, ppm) 55.5 (CH_3), 113.0 (q, $J_{C-C-C-F}$ = 3.7 Hz, CH) 114.2 (CH), 122.9 (q, J_{C-F} = 275.8 Hz, CF_3), 123.9 (CH), 129.9 (C), 137.2 (q, J_{C-C-F} = 31.5 Hz, C), 160.6 (C); ^{19}F NMR ($CDCl_3$, 377 MHz, *Z* isomer; δ, ppm) −62.87; GC-MS (EI, *Z* isomer) 281 ([M]$^+$, 99%), 279 (100%), 213 (18%), 211 (13%), 201 (7%), 186 (11%), 181 (15%), 169 (7%), 158 (29%), 151 (9%), 138 (9%), 117 (17%), 89 (26%), 75 (8%), 69 (9%), 63 (16%); HRMS (DART) calcd for $C_{10}H_8BrF_3O$ [M + H]$^+$ 280.9789, found 280.9802.

*gem-Difluoroalkene Synthesis: 1-(3,3-Difluoro-2-(4-methoxyphenyl)allyl)piperidine (**6c**).* This protocol is a modification of the procedure outlined by Bonnet-Delpon.[19] In a flame-dried flask equipped with a stirbar, rubber septum, and N_2 inlet needle were added piperidine (0.685 g, 0.795 mL, 8.05 mmol, 1.15 equiv) and anhydrous THF (47 mL, 0.15 M in the olefin). The flask was cooled to −78 °C via a dry ice/acetone bath and, after cooling for 10 min, a 2.5 M solution of *n*-BuLi (3.2 mL, 8.05 mmol, 1.15 equiv) in hexanes was added dropwise to the flask over 5 min. The solution was stirred at −78 °C for 1 h and gradually became cloudy and white. After this time, **3c** (1.42 g, 7 mmol, 1 equiv) was added to the flask dropwise over 5 min. The solution was stirred at −78 °C for 1 h and after this time was warmed to 0 °C in an ice−water bath. The solution was stirred at 0 °C for 1 h and then was poured into a separatory funnel containing saturated aqueous NH_4Cl (∼100 mL). The biphasic mixture was diluted with Et_2O (∼100 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 50 mL) and the combined organic layers were washed with deionized water (∼100 mL), followed by brine (∼150 mL). The combined organic layers were dried with Na_2SO_4. The solvent was removed in vacuo to give the crude difluoroalkene as an orange-tinged oil. Further purification was accomplished by FCC (gradient Hex to 7/3 Hex/EtOAc) to give the pure difluoroalkene (1.17 g, 63%) as a light yellow-orange oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 1.41 (br sxt, J = 4.90 Hz, 2 H), 1.53 (quin, J = 5.56 Hz, 4 H), 2.38 (br t, J = 4.70 Hz, 4 H), 3.22 (dd, J = 3.07, 1.75 Hz, 2 H), 3.81 (s, 3 H), 6.88 (dt, J = 8.81, 2.90 Hz, 2 H), 7.43 (dd, J = 8.86, 1.07 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 24.6 (CH_2), 26.2 (CH_2), 54.2 (CH_2), 55.3 (CH_2), 56.5 (d, $J_{C-C-C-F}$ = 3.9 Hz, CH_2), 89.4 (dd, J_{C-C-F} 18.7, 11.8 Hz, C), 113.9 (CH), 126.6 (t, $J_{C-C-C-F}$ = 3.5 Hz, C), 129.7 (t, $J_{C-C-C-C-F}$ = 3.4 Hz, CH) 155.3 (dd, J_{C-F} = 292.1, 288.0 Hz, CF_2) 158.9 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −93.19 (d, J = 39.51 Hz, 1 F), −92.88 (d, J = 39.51 Hz, 1 F); GC-MS (EI) 267 ([M]$^+$, 4%), 224 (1%), 184 (62%), 169 (4%), 151 (4%), 140 (5%), 133 (21%), 118 (5%), 98 (100%), 70 (5%); HRMS (DART), calcd for $C_{15}H_{19}F_2NO$ [M + H]$^+$ 268.1513, found 268.1536.

*Dihydroxylation: 3,3,3-Trifluoro-2-(4-methoxyphenyl)propane-1,2-diol (**7c**).* In a 50 mL one-neck round-bottom flask were added **3c** (1.21 g, 6 mmol, 1 equiv), THF (4.5 mL), and deionized water (1.5 mL). The flask was cooled to 0 °C in an ice bath. After cooling for 10 min, 50% w/w NMO in H_2O (2.76 g, 12 mmol, 2 equiv) was added to the flask followed by 4% w/w OsO_4 (Caution! Toxic!) in H_2O (3.814 g, 3.37 mL, 0.6 mmol, 0.1 equiv). Five minutes after this addition, the ice bath was removed and the solution was stirred at room temperature overnight. After 24 h, the reaction appeared to have stalled[39] and an additional loading of NMO (2.76 g, 12 mmol, 2 equiv) and OsO_4 (3.814 g, 3.37 mL, 0.6 mmol, 0.1 equiv) was added. The reaction mixture was stirred for an additional 24 h and after this time was judged to be complete. The solution was transferred to a separatory funnel and diluted with deionized water (∼100 mL) and Et_2O (∼100 mL). The phases were separated, and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine (∼150 mL) and dried with Na_2SO_4. The solvent was removed in vacuo to give the crude diol as a thick, dark brown oil. The crude product was adhered to silica gel using ∼1.5 wt equiv silica gel (relative to the theoretical yield). The dry-packed material was gently added atop a silica gel plug. The plug was eluted

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with EtOAc. The solvent was removed in vacuo by rotary evaporation, affording the pure diol (1.20 g, 85%) as a clear, brown oil: ^{1}H NMR ($CDCl_3$, 400 MHz; δ, ppm) 3.82 (s, 3 H), 3.88 (dd, J = 11.98, 1.47 Hz, 1 H), 4.25 (d, J = 11.98 Hz, 1 H), 6.89−6.97 (m, 2 H), 7.48 (d, J = 8.56 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz; δ, ppm) 55.5 (CH_3), 65.0 (q, $J_{C-C-C-F}$ = 1.5 Hz, CH_2), 76.3 (q, J_{C-C-F} = 27.9 Hz, C), 114.2 (CH), 125.4 (q, J_{C-F} = 286.1 Hz, CF_3), 127.5 (CH), 127.7 (q, $J_{C-C-C-F}$ = 1.5 Hz, C), 160.2 (C); ^{19}F NMR ($CDCl_3$, 377 MHz; δ, ppm) −80.64; GC-MS (EI) 236 ([M]$^+$, 16%), 205 (100%), 135 (89%), 121 (13%), 108 (21%), 92 (10%), 77 (15%), 69 (3%); HRMS (ESI+), calcd for $C_{10}H_{11}F_3O_3$ [M + NH_4]$^+$ 254.1004, found 254.1022.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra of the compounds. 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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■ REFERENCES

(1) (a) Meanwell, N. A. *J. Med. Chem.* **2011**, *54*, 2529. (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320. (c) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359. (d) Vorbrueggen, H. *Helv. Chim. Acta* **2011**, *94*, 947. (e) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881. (f) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214.

(2) (a) Wipf, P.; Henninger, T. C.; Geib, S. J. *J. Org. Chem.* **1998**, *63*, 6088. (b) Xiao, J.; Weisblum, B.; Wipf, P. *J. Am. Chem. Soc.* **2005**, *127*, 5742. (c) Maes, V.; Tourwé, D. Aspects of Peptidomimetics. In *Peptide and Protein Design for Biopharmaceutical Applications*; Wiley: Chichester, U.K., 2009. (d) Inokuchi, E.; Narumi, T.; Niida, A.; Kobayashi, K.; Tomita, K.; Oishi, S.; Ohno, H.; Fujii, N. *J. Org. Chem.* **2008**, *73*, 3942. (e) Kobayashi, K.; Narumi, T.; Oishi, S.; Ohno, H.; Fujii, N. *J. Org. Chem.* **2009**, *74*, 4626. (f) Fustero, S.; Chiva, G.; Piera, J.; Sanz-Cervera, J. F.; Volonterio, A.; Zanda, M.; Ramirez de Arellano, C. *J. Org. Chem.* **2009**, *74*, 3122.

(3) (a) Kobayashi, T.; Eda, T.; Tamura, O.; Ishibashi, H. *J. Org. Chem.* **2002**, *67*, 3156. (b) Cassayre, J. Y.; Renold, P.; El Qacemi, M.; Pitterna, T.; Toueg, J. C. (Syngenta Crop Protection LLC) U.S. Patent 20120238517 A1, 2012. (c) Ikeda, E.; Komoda, M.; Maeda, K.; Mita, T.; Toyama, K.-I.; Yamada, Y. (Nissan Chemical Industries, Ltd.) European Patent EP 2199287 A1, 2010.

(4) (a) Rivkin, A.; Yoshimura, F.; Gabarda, A. E.; Cho, Y. S.; Chou, T.-C.; Dong, H.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2004**, *126*, 10913. (b) Wu, K.-D.; Cho, Y. S.; Katz, J.; Ponomarev, V.; Chen-Kiang, S.; Danishefsky, S. J.; Moore, M. A. S. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 10640. (c) Rivkin, A.; Chou, T.-C.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 2838.

(5) Shimizu, M.; Takeda, Y.; Higashi, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 3653.

(6) (a) Parsons, A. T.; Senecal, T. D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 2947. (b) Prakash, G. K. S.; Krishnan, H. S.; Jog, P. V.; Iyer, A. P.; Olah, G. A. *Org. Lett.* **2012**, *14*, 1146. (c) Iqbal, N.; Choi, S.; Kim, E.; Cho, E. J. *J. Org. Chem.* **2012**, *77*, 11383. (d) Yasu, Y.; Koike, T.; Akita, M. *Chem. Commun.* **2013**, *49*, 2037. (e) Hanamoto, T.; Morita, N.; Shindo, K. *Eur. J. Org. Chem.* **2003**, 4279.

(7) Representative example of this strategy: Ichikawa, J.; Yokota, M.; Kudo, T.; Umezaki, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 4870.

(8) Nader, B. S.; Cordova, J. A.; Reese, K. E.; Powell, C. L. *J. Org. Chem.* **1994**, *59*, 2898.

(9) Lebel, H.; Paquet, V. *Org. Lett.* **2002**, *4*, 1671.

(10) Pan, R.-q.; Liu, X.-x.; Deng, M.-z. *J. Fluorine Chem.* **1999**, *95*, 167.

(11) Jiang, B.; Xu, Y. *J. Org. Chem.* **1991**, *56*, 7336.

(12) Kobayashi, O.; Uraguchi, D.; Yamakawa, T. *J. Fluorine Chem.* **2009**, *130*, 591.

(13) Kobayashi, O.; Uraguchi, D.; Yamakawa, T. *J. Mol. Catal. B* **2009**, *302*, 7.

(14) Hafner, A.; Bräse, S. *Adv. Synth. Catal.* **2011**, *353*, 3044−.

(15) (a) Kelly, C. B.; Mercadante, M. A.; Hamlin, T. A.; Fletcher, M. H.; Leadbeater, N. E. *J. Org. Chem.* **2012**, *77*, 8131. (b) Rudzinski, D. M.; Kelly, C. B.; Leadbeater, N. E. *Chem. Commun.* **2012**, *48*, 9610. (c) Hamlin, T. A.; Kelly, C. B.; Leadbeater, N. E. *Eur. J. Org. Chem.* **2013**, 3658.

(16) Seminal work: Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. Recent review: van Staden, L. F.; Gravestock, D.; Ager, D. J. *Chem. Soc. Rev.* **2002**, *31*, 195.

(17) Wang, F.; Luo, T.; Hu, J.; Wang, Y.; Krishnan, H. S.; Jog, P. V.; Ganesh, S. K.; Prakash, G. K. S.; Olah, G. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 7153.

(18) Alem, K. v.; Belder, G.; Lodder, G.; Zuilhof, H. *J. Org. Chem.* **2005**, *70*, 179.

(19) (a) Begue, J.-P.; Bonnet-Delpon, D.; Rock, M. H. *Tetrahedron Lett.* **1995**, *36*, 5003. (b) Begue, J.-P.; Bonnet-Delpon, D.; Rock, M. H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1409.

(20) (a) Schneider, W. P.; McIntosh, A. V. (Upjohn) U.S. Patent 2769824. (b) VanRheennen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *17*, 1973.

(21) Ravikumar, I.; Saha, S.; Ghosh, P. *Chem. Commun.* **2011**, *47*, 4721.

(22) McQuaid, K. M.; Long, J. Z.; Sames, D. *Org. Lett.* **2009**, *11*, 2972.

(23) Korthals, K. A.; Wulff, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 2898.

(24) Krishnamurti, R.; Bellew, D. R.; Prakash, G. K. S. *J. Org. Chem.* **1991**, *56*, 984.

(25) Mercadante, M. A.; Kelly, C. B.; Bobbitt, J. M.; Tilley, L. J.; Leadbeater, N. E. *Nat. Protoc.* **2013**, *8*, 666.

(26) Sheppard, W. A. *J. Am. Chem. Soc.* **1965**, *87*, 2410.

(27) Kitazume, T.; Asai, M.; Tsukamoto, T.; Yamazaki, T. *J. Fluorine Chem.* **1992**, *56*, 271.

(28) Grassi, D.; Li, H.; Alexakis, A. *Chem. Commun.* **2012**, *48*, 11404.

(29) Haukaas, M. H.; O'Doherty, G. A. *Org. Lett.* **2001**, *3*, 401.

(30) The flask and addition funnel were flame-dried a total of three times with cooling in between via N_2.

(31) Care should be taken during this addition. If addition is too fast, the reaction mixture will exotherm quite vigorously.

(32) Note that this ketone required rigorous drying before use. We found that azeotropic removal of water using benzene and a Dean−Stark apparatus followed by rapid solvent removal and immediate use proved optimal.

(33) We observed both 1,2- and 1,4-addition. These two species were determined to be separable by TLC, and therefore FCC was performed.

(34) Hexanes can also be used in place of CH_2Cl_2.

(35) It is recommended that, when attempting dehydrative desilylation using this protocol on substrates not outlined here, the reaction be monitored by TLC, NMR, or GC/MS to determine reaction progress. The rate and success of dehydrative desilylation of these CF_3 alcohols are dependent on the stability of the theoretical α-CF_3 cation. Hence, α-aryl or α-alkenyl carbinols typically do not require heating and the reactions can be conducted at room

temperature over very short periods of time. However, α-alkyl or electron-deficient α-aryl substitution demands heating. In some cases alternative solvents (i.e., DCE) are needed to access high temperature ranges.
(36) Hexanes can also be used.
(37) Jiang, B.; Xu, Y. *Tetrahedron Lett.* **1992**, *33*, 511.
(38) Note that, due to the volatility of highly fluorinated species, it is *imperative* that higher pressures (40 mmHg or greater) and low water bath temperature (less than 32 °C) be used during rotary evaporation to ensure good yields.
(39) Reaction progress determined by ^{1}H NMR.