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Suzuki–Miyaura Coupling Reactions of Iodo(difluoroenol) Derivatives, Fluorinated Building Blocks Accessible at Near-Ambient Temperatures

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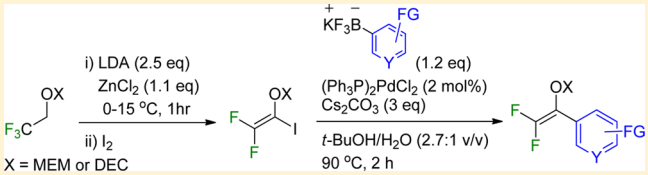
Supporting Information

ABSTRACT: A recently developed method for the near-ambient generation of difluorovinylzinc reagents has facilitated the preparation of 1-(*N*,*N*-diethylcarbamoyloxy)-2,2-difluoro-1-iodoethene and 2,2-difluoro-1-iodo-1-(2′-methoxyethoxymethoxy)ethene. The utility of these reagents has been investigated in Suzuki–Miyaura couplings with a range of potassium trifluoroborate coupling partners, with the scope of successful couplings proving wide. Deiodinated species appeared as significant side products, but a solvent change from *i*-PrOH to *t*-BuOH suppressed the pathway to these species and improved coupling yields.



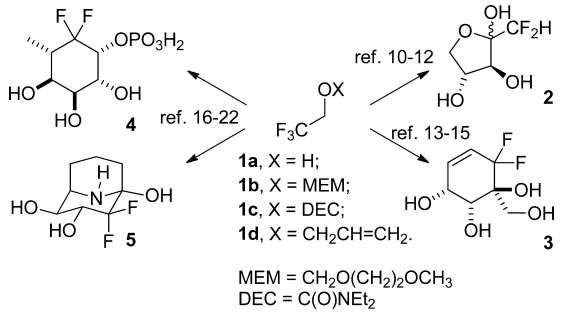
INTRODUCTION

Modern synthetic organic chemistry is subject to an expanding range of pressures which constrain the starting materials it can use and the range of reaction conditions it can deploy. While the use of low-temperature conditions can deliver high selectivity, cryogenic methods are expensive when carried out on a large scale, and reactions which avoid their use are often preferred. It follows that there is considerable interest in carrying out many of the important reactions of synthetic organic chemistry at, or close to, ambient temperatures.

The synthesis of selectively difluorinated molecules is an area of high current activity; recent achievements include new methods for the difluoromethylation of arenes[1] and heteroarenes[2] and novel difluoroenolate chemistry described by Colby et al.[3] which installs a difluoromethylene unit. There are many strategies for the synthesis of difluorinated molecules from building blocks, small commercial molecules which already contain the required fluorine atoms.[4] Trifluoroethanol **1a** is an extremely versatile starting material for the synthesis of a wide range of selectively fluorinated molecules. Protection, followed by dehydrofluorination/metalation begins to transform this bulk chemical into valuable organometallic intermediates.[5−9] In our hands, this approach has been exploited in coupling[10−12] and cycloaddition[13−15] reactions, and rearrangement/ring-closing metathesis sequences[16−22] (Scheme 1) to afford analogues of a range of saccharide, cyclitol, and azasugar natural products including **2**–**5**.

Our work relied on the use of low reaction temperatures, typically −78 °C, though in the case of **1d**, a reaction temperature of −100 °C was required.[16] In some cases, organotin chemistry was used to deliver these difluoroalkenol units into coupling reactions, so we saw the methodology utilizing trifluoroborate **6** published by Katz and co-workers[23] as extremely important and welcome (Figure 1).

Scheme 1. Applications of Building Blocks Derived from Trifluoroethanol



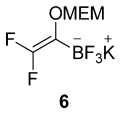


Figure 1. Katz and co-workers' potassium trifluoroborate.

Trifluoroborate **6** was prepared and used in Suzuki–Miyaura couplings;[23] although a low-temperature procedure was still required to prepare **6**, the avoidance of tin reagents was a significant development. We have recently developed a sequence in which dehydrofluorination/metalation chemistry of **1b** and **1c** can be carried out at close to ambient temperature

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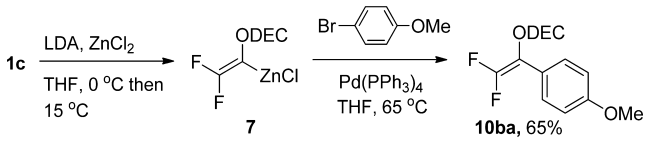
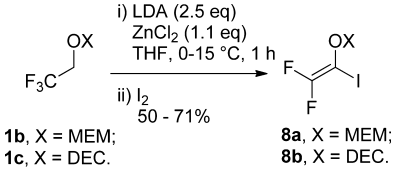
and followed by a Negishi coupling reaction (Scheme 2).[24−26] We were able to use the intermediate organozinc reagents in Negishi coupling reactions to prepare a range of difluorinated alkene products, in high yields in some cases.

Scheme 2. Generation and Negishi Coupling of Vinylzinc Reagent 7



However, there were limitations to Negishi and Suzuki−Miyaura methods, particularly with π-electron-deficient aryl bromides. In some cases, HF addition was observed after product formation, while in other cases coupling was unsuccessful. We sought a method that would avoid low-temperature conditions entirely, tolerate a wider range of coupling partners, and use storable fluorinated intermediates. In this paper, we wish to report complementary Suzuki−Miyaura reactions of iodides **8a** and **8b**, which can be prepared at ice-bath temperature (Scheme 3).

Scheme 3. Ice-Bath Temperature Synthesis of Iodides 8a and 8b



RESULTS AND DISCUSSION

We prepared 5 g batches of known[27] **8b** by this method; 2.5 equiv of LDA was added dropwise to a solution of **1c** and $ZnCl_2$ in THF at 0 °C to afford zinc species **7**. A solution of I_2 in THF was then added via syringe to quench vinylzinc **7**; after workup, the crude iodide was purified by filtration through a plug of silica followed by Kugelrohr distillation to afford iodide **8b** in 71% yield. The preparation of iodide **8a** was less efficient, with 50% the highest yield obtained (for a 3 g batch). The same procedure was observed, but a short contact time between the zinc reagent and iodine was essential for this yield; times of 1 h and longer significantly reduced the yield of iodide **8a** (cf. 25%). Addition of DMPU cosolvent was necessary for a respectable yield of **8a**; the urea cosolvent ensures full conversion of **1b** to the organozinc intermediate.[24] Both iodides were found to be stable after purification and could be stored under N_2 in the refrigerator without decomposition (3 months). Discoloration of the materials was observed when they were stored at room temperature.

We chose potassium trifluoroborate coupling partners to probe the scope of our iodide species in Suzuki−Miyaura coupling because of the reported superior stability and efficacy of these reagents over the more traditional boronic acids, exemplified by the wide range of couplings performed by Molander and co-workers.[28−32] These stable salts were generated in moderate to excellent (51−99%) yields from the boronic acids following literature procedures (Figure 2).[33,34]

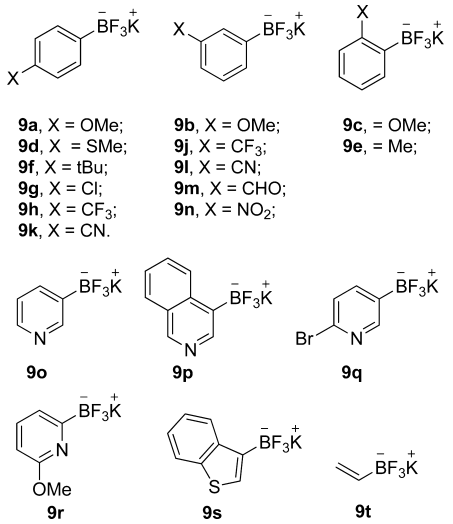
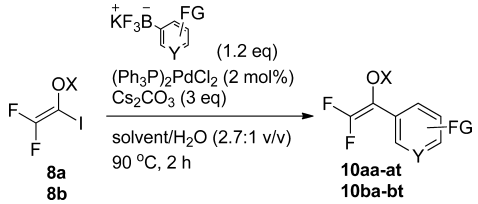


Figure 2. Potassium trifluoroborate coupling partners.

The coupling conditions were based initially on those reported by Molander[31] with a modest excess of boron reagent (1.2 equivalents), $(Ph_3P)_2PdCl_2$ (2 mol %) precatalyst, and Cs_2CO_3 in a toluene/water mixture (2.7:1 v/v); the more stable Pd(II) catalyst was found to be as effective as $Pd(PPh_3)_4$. The excess reagent was required to convert the iodides **8a** and **8b** completely due to difficulty of separating unreacted iodide from the products (Scheme 4).

Scheme 4. Suzuki−Miyaura Coupling of Iodides 8a and 8b



Full conversion of the iodide occurred over 2 h at 90 °C with a number of electron-rich potassium aryltrifluoroborates, producing products in good to excellent yields (Table 1; entries 2, 12, and 14). Not all borates coupled successfully under these conditions, with solubility appearing to be limiting in some cases, prompting a search for more general conditions. To improve borate solubility, more polar solvents were investigated; alcohols were chosen as relatively sustainable candidates.[35] The 3-nitrophenyl borate **9n** was chosen to optimize the reaction conditions as products **10an** and **10bn** are difficult compounds to generate in good yield (as we[24] and others[23,26] have found in previous work). Borate **9n**, iodide **8b**, Cs_2CO_3 (3 equiv), and $(Ph_3P)_2PdCl_2$ (2 mol %) dissolved fully in an alcohol (*n*-PrOH, *i*-PrOH, or *t*-BuOH)/water (2.7:1) mixture at 90 °C. Iodide **8b** was consumed completely in all alcoholic solvent systems, but differing ratios of side products were observed in each case. When *n*-PrOH was used, addition, addition/elimination, and reduced species **11**, **12**, and **13** were generated in a 4:1:10 ratio (Figure 3). Changing to *i*-PrOH removed addition and addition/elimination products **11** and **12**, but **13** was now the major product. Only a small reduction in the amount of **13** produced was observed when the *i*-PrOH was degassed by using the freeze−pump−thaw method.

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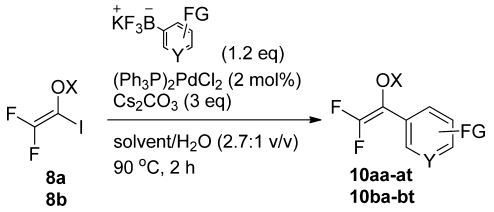
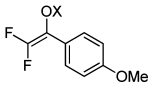
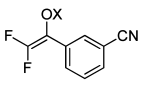
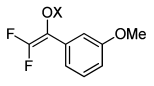
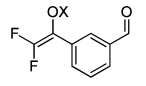
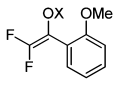
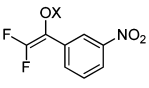
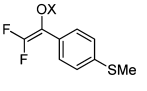
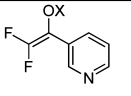
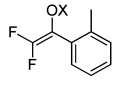
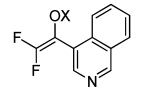
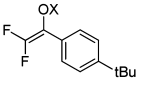
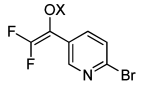
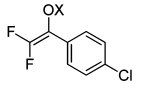
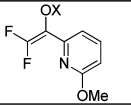
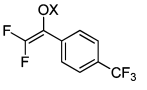
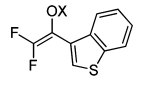
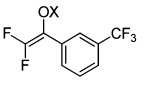
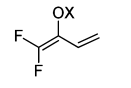
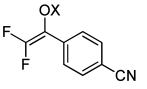
Table 1. Scope of Suzuki–Miyaura Coupling of 8a and 8b with Potassium Trifluoroborate Salts*



Entry	Method	Time (h)	Product and Yield	Entry	Method	Time (h)	Product and Yield
1	3	18	 **10aa**, X = MEM: 87%	21	3	18	 **10al**, X = MEM: 55%
2	1	1	**10ba**, X = DEC: 80%	22	1	2	**10bl**, X = DEC: 61%
3	3	18	 **10ab**, X = MEM: 95%	23	2	2	 **10am**, X = MEM: 67%
4	2	2	**10bb**, X = DEC: 59%	24	2	2	**10bm**, X = DEC: 90%
5	1	2	 **10ac**, X = MEM: 93%	25	3	4	 **10an**, X = MEM: 61%
6	2	2	**10bc**, X = DEC: 59%	26	3	4	**10bn**, X = DEC: 75%
7	3	18	 **10ad**, X = MEM: 62%	27	3	18	 **10ao**, X = MEM: 54%
8	1	2	**10bd**, X = DEC: 93%	28	2	3	**10bo**, X = DEC: 61%
9	3	18	 **10ae**, X = MEM: 95%	29	3	18	 **10ap**, X = MEM: 32%
10	1	2	**10be**, X = DEC: 93%	30	2	2	**10bp**, X = DEC: 44%
11	3	18	 **10af**, X = MEM: 99%	31	3	18	 **10aq**, X = MEM: 32%
12	1	2	**10bf**, X = DEC: 66%	32	3	3	**10bq**, X = DEC: 52%
13	1	2	 **10ag**, X = MEM: 72%	33	3	18	 **10br**, X = DEC: 70%
14	1	2	**10bg**, X = DEC: 88%				
15	1	18	 **10ah**, X = MEM: 88%	34	3	18	 **10as**, X = MEM: 57%
16	1	18	**10bh**, X = DEC: 88%	35	1	2	**10bs**, X = DEC: 57%
17	3	18	 **10aj**, X = MEM: 78%	36	3	18	 **10at**, X = MEM: 27%[a]
18	2	2	**10bj**, X = DEC: 60%	37	3	18	**10bt**, X = DEC: 30%[b]
19	3	18	 **10ak**, X = MEM: 59%				
20	1	18	**10bk**, X = DEC: 62%				

*Method 1: $(Ph_3P)_2PdCl_2$ (2 mol %), Cs_2CO_3 (3 equiv), potassium trifluoroborate (1.2 equiv), toluene/H_2O (2.7:1), 90 °C. Method 2: $(Ph_3P)_2PdCl_2$ (2 mol %), Cs_2CO_3 (3 equiv), potassium trifluoroborate (1.2 equiv), *i*-PrOH/H_2O (freeze–pump–thaw) (2.7:1) 90 °C. Method 3: $(Ph_3P)_2PdCl_2$ (2 mol %), Cs_2CO_3 (3 equiv), potassium trifluoroborate (1.2 equiv), *t*-BuOH/H_2O (2.7:1), 90 °C. [a]Estimated yield: product contaminated with ~1% of **13** and ~1% of **8a**. [b]Estimated yield: product contaminated with ~5% of **13** and ~4% of **8b**.

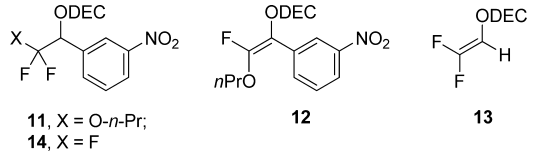


Figure 3. Side products arising from the Suzuki–Miyaura coupling.

Deiodinated **13** could arise from reductive elimination from a palladium hydride complex such as **20**, itself produced from *β*-hydride elimination of palladium alkoxide **19** (Scheme 5). We show key intermediate **15** which partitions between the Suzuki–Miyaura coupling pathway and the reductive pathway. In the former, iodide is displaced by generic boronic acid **16**, formed in situ from the trifluoroborate[36] before transmetalation in a monophosphine cycle.[37] In the latter, alcohol coordination is followed by elimination[38] of HI followed by *β*-hydride elimination[39] to form an hydridopalladium complex; reductive elimination then releases **13**. Similar reactions were reported by Helquist during the palladium-catalyzed dehalogenation of arenes[40] and Buchwald and co-workers[41] in palladium-catalyzed ether formation. Suzuki couplings carried out in solvents which lack protons *α*-to oxygen should therefore be free from formation of **13**, with *t*-BuOH the obvious choice of solvent.

On substitution of *i*-PrOH with *t*-BuOH, the coupling of nitroborate **9n** now proceeded without formation of **13**.

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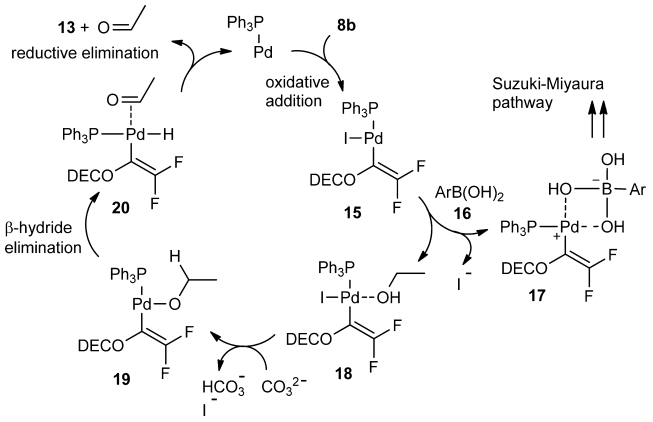
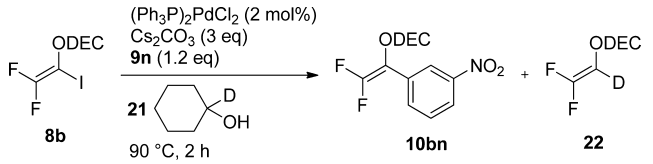
Scheme 5. Proposed Catalytic Cycle for Generation of 13



However, it was necessary to keep the reaction time as short as possible as HF addition product **14** was produced (due to the strong electron-withdrawing effect of the nitro group). This HF addition product was previously observed during our Negishi coupling work[24] and arises from LiF formed during the generation of difluorovinylzinc reagent **7**. Fluoride is also formed from the trifluoroborate salts (vide infra), and HF addition may therefore be a consequence of their use. However, HF addition to afford adducts such as **14** only occurs when the ring is strongly activated by the nitro group. After 18 h, styrene **10bn** and **14** were formed in a 5:1 ratio, with a yield of 55% of **10bn**. Shortening the reaction time to 4 h resulted in an improved yield of 75% of **10bn**. A similar trend was observed when coupling **9n** with **8a**. A yield of 39% of **10an** was improved to 61% after reducing the reaction time from 18 to 4 h.

The β-hydride pathway to **13** was confirmed by carrying out the coupling of **8b** and borate **9n** in 1-deuterio-1-cyclohexanol **21** (Scheme 6).[42]

Scheme 6. Probing the Origin of Product 13



Product **10bn** and deuterated species **22** were produced in a ~3:1 ratio; the ^{19}F NMR chemical shifts of **22** were distinct from those of **13**, and one of the fluorine nuclei showed a splitting pattern consistent with the spin quantum number of deuterium (I = 1) (see the Supporting Information for the spectrum). The same reaction performed in cyclohexanol produced **10bn** and reduced species **13** in a ~4:1 ratio, suggesting strongly that there is no primary kinetic isotope effect on the reaction. Neither β-hydride elimination nor reductive elimination is likely to be the rate-determining step for the side reaction. The different proportions of **13** and **22** may arise from the partitioning of **15** between the two ligand exchange steps in Scheme 5.

The scope of the Suzuki coupling was investigated (Table 1). Several results improved significantly upon our recently published Negishi methodology.[24] All electron-rich borates coupled in good yield with substituents tolerated in all positions of the benzene ring (entries 1–12). Entries 5 and 6 are of particular note as only ~10% of **10bd** could be isolated using our Negishi procedure. Styrenes bearing an electron-withdrawing group generally required the optimized *t*-BuOH conditions and were generated more smoothly and in higher yield than in the complementary Negishi protocol (entries 15–26). Aldehydes **10am** and **10bm**, generated in 67% and 90% yield, are exciting because they could not be generated at all using the Negishi coupling method, and the formyl group is a potential locus for diversity generation. Entries 25 and 26 show formation of the reactive nitro congeners in good yield. Pleasingly, iodides **8a** and **8b** coupled with heteroaryl borates (entries 27–35) to afford species which were inaccessible via the Negishi protocol. Entry 33 is of interest; borate **9r** is a relatively stable species that is effective in coupling reactions,[43] and the pyridine product **10br** contains an activated difluoroalkenyl group, so its stability is pleasing. We also tried to prepare 2-pyridyl trifluoroborate **23** from 2-bromopyridine[44,45] and from commercial **24** (treatment with KHF_2 in aqueous methanol)[33,34] but were unsuccessful on both occasions (Figure 4). A potential alternative coupling partner is Burke's MIDA boronate **25**,[46] but we were unable to secure this species via the published procedure.[47]

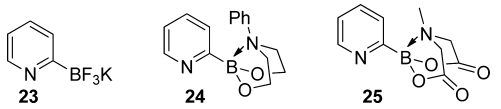


Figure 4. 2-Pyridyl borate **23** and boronate precursors **24** and **25**.

These simple coupling conditions reached their limit of effectiveness when nonaromatic borate coupling partners are introduced. Vinyl borate **9t** coupled with both iodides, but the products were very difficult to separate from unreacted starting material and side products because of their similar R_f's and boiling points. Coupling of alkynyl and alkyl borates has failed to date under these conditions, but efforts to couple sp and sp^3 borates to **8a** and **8b** are ongoing in our laboratory.

A precatalyst loading as low as 0.05 mol % of $(Ph_3P)_2PdCl_2$ was tolerated in the coupling of **9g**; a yield of 80% of **10bg** was obtained. Lowering the catalyst loading to 0.025 mol % resulted in lower (40%) conversion to **10bg**.[48]

A larger (5 mmol) scale coupling of iodide **8b** under the optimized conditions afforded **10bm** in 82% yield after chromatography, further enhancing the utility of this Suzuki–Miyaura coupling protocol.

Suzuki–Miyaura coupling reactions can use a range of boron reagents; boronic acids are currently most readily available from commercial sources, but the range of available potassium trifluoroborate salts is growing. These reagents are easy to prepare from the boronic acids, and they enjoy the distinct advantages[32] of higher integrity and stability over the boronic acids, which can be supplied as complex mixtures (of monomers, dimers, and trimers) and can deborylate on storage and in reactions.[44] Trifluoroborates are structurally unambiguous (making reaction stoichiometries easier to control and reproduce) and nonhygroscopic. They release active boron reagent slowly into solution,[49] which can prevent buildup and decomposition of boronic acids. We therefore prioritized the potassium trifluoroborates as coupling partners for our relatively valuable iodide species **8a** and **8b**. However, we have also examined a selection of freshly purchased boronic acids in Suzuki–Miyaura couplings with iodide **8b** (Table 2).

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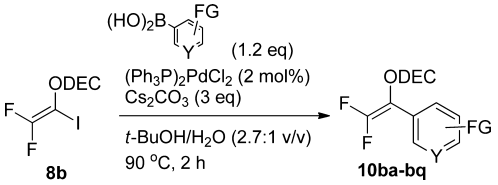
Table 2. Scope of Suzuki–Miyaura Coupling of 8a and 8b with Selected Boronic Acids



entry	boronic acid	product	yield (%)
1	4-OMe	**10ba**	83
2	4-CF_3	**10bh**	92
3	3-CN	**10bl**	74
4	3-formyl	**10bm**	60
5	3-NO_2	**10bn**	75
6	3-pyridyl	**10bo**	0
7	6′-Br-3-pyridyl	**10bp**	25
8	4-isoquinolyl	**10bq**	5

Entries 1–5 show that the boronic acids are also effective coupling partners; entry 5 shows that the HF addition side reaction is avoided with this most activated substrate but the method gives a poor yield for entry 7 and fails entirely for entries 6 and 8 (all boronic acids which deborylate relatively easily[50]). It follows that the substrate scope is wider with the potassium trifluoroborates, and we would recommend these as the boron reagents, particularly if value has been added through synthesis.

In conclusion, we have generated iodo(difluoroenol) derivatives in useful, synthetic amounts using near-ambient temperature conditions. Higher yields of these species were obtained when contact time between the iodide products and iodine was restricted. General conditions for the Suzuki–Miyaura coupling of these species with potassium aryl- and heteroaryltrifluoroborates and boronic acids at low palladium catalyst loading were identified. These protocols yielded product in moderate to excellent yield, overcoming a limitation in scope described in previous publications and signaling a further advance in the coupling of useful difluorovinyl units.[51]

EXPERIMENTAL SECTION

General Experimental Methods. All NMR spectra were recorded on a 400 MHz spectrometer. ^{1}H and ^{13}C NMR spectra were recorded using the deuterated solvent as the lock and the residual solvent as the internal reference. ^{19}F NMR spectra were recorded relative to chlorotrifluoromethane as the external standard. The multiplicities of the spectroscopic data are presented in the following manner: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Homocouplings (H–H, F–F) are given in hertz and specified by *J*; the nuclei involved in heteronuclear couplings are defined with the observed nucleus given first. HRMS measurements were performed using an instrument with an ion trap. GC–MS spectra were obtained on an instrument fitted with a DB5-type column (30 m × 0.25 μm) running a 70–320 °C temperature program, ramp rate 20 °C min^{-1} with helium carrier gas flow at 1 cm^3 min^{-1}. LC–MS measurements (ESI) were recorded on an instrument fitted with a C18 column (50 mm × 2.1 mm i.d. 1.7 μm packing diameter) running at 40 °C. Thin-layer chromatography was performed on precoated aluminum-backed silica gel plates, and visualization was achieved using potassium permanganate staining and UV detection at 254 nm. Column chromatography was performed on silica gel (40–63 μm) using a semi-automated system. IR spectra were recorded on an ATR IR spectrometer. Melting points are uncorrected. Phase separation was accomplished with proprietary fritted phase separators. Hexane was distilled before chromatography. All other materials were used as received unless otherwise stated. 1-(*N*,*N*-diethylcarbamoyloxy)-2,2,2-trifluoroethane was prepared according to the method of Howarth,[52] and 1-(2′-methoxyethoxymethoxy)-2,2,2-trifluoroethane was prepared according to the method of Patel.[53] Iodide **8b** was prepared according to the method of Percy.[24] All trifluoroborates were generated from the commercial boronic acids using the methods of Vedejs[33] and Molander[34] (see the Supporting Information for characterization).

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-iodoethene (**8a**).* *n*-Butyllithium (26.09 mL, 2.3 M, 60 mmol) was added dropwise to a solution of diisopropylamine (8.43 mL, 60 mmol) in THF (20 mL) at 0 °C and the reaction stirred for 30 min at this temperature. The freshly prepared LDA was added dropwise via cannula to a solution of acetal **1b** (3.76 g, 20 mmol), $ZnCl_2$ (3.0 g, 22 mmol), and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (10 mL) in THF (40 mL) at 0 °C. The yellow solution was stirred at 0 °C for 1 h and then 1 h further at room temperature. A solution of iodine (5.08 g in 25 mL THF) was then added via syringe (a slight exotherm was observed, ca. 10 °C) and the orange solution stirred for 10 min. The solution was quenched with aqueous ammonium chloride (60 mL) and extracted with diethyl ether (2 × 100 mL). The organic extracts were combined, washed with saturated sodium sulfite solution (100 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The brown residue was washed through a pad of silica (10% diethyl ether in hexane), concentrated under reduced pressure, and distilled (Kugelrohr, 70 °C/2 mbar) to afford iodide **8a** (2.96 g, 50%) as a colorless oil: R_f (40% diethyl ether in hexane) 0.39; IR ν_{max}(film)/cm^{-1} 2937, 2894, 2829, 1774, 1735, 1457, 1285, 1181, 1155, 1101, 1075, 1026, 963, 911, 847; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.88 (s, 2 H), 3.85–3.82 (m, 2 H), 3.61–3.58 (m, 2 H), 3.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.2 (dd, J_{C-F} 296.4, 278.8), 96.0 (t, J_{C-F} 3.1), 71.0, 68.6, 58.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −89.7 (d, *J* 49.2, 1 F), −100.6 (d, *J* 49.2, 1 F); LRMS (CI) *m*/*z* 262 [M−CH_3O]$^+$; GC (98%) t_R 8.01 min. Compound decomposed before accurate mass spectrometric measurements could be carried out off-site.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-iodoethene (**8b**).* A solution of iodine (2.54 g, 10 mmol in 10 mL of THF) was added dropwise to alkenylzinc reagent **7** (40 mL of a 0.25 M solution in THF) at 15 °C. The reaction mixture was stirred at this temperature overnight. The reaction mixture was quenched with saturated aqueous ammonium chloride (30 mL) and extracted with diethyl ether (2 × 40 mL). The organic extracts were combined, washed with saturated sodium sulfite solution (40 mL), dried ($MgSO_4$), and concentrated under reduced pressure to a brown oil. Distillation afforded iodide **8b** (2.17 g, 71%) as a pale yellow oil: bp 50 °C/2 mmHg (Kugelrohr); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.39–3.25 (m, 4 H), 1.19 (br t, *J* 6.9, 6 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ (ppm) 153.8(dd, J_{C-F} 280.0, 297.7), 151.3, 60.7 (dd, J_{C-F} 58.2, 27.4), 42.9, 42.0, 14.2, 13.2; ^{19}F NMR (400 MHz, $CDCl_3$) δ (ppm) −84.9 (d, *J* 42.3, 1 F), −98.5 (d, *J* 42.3, 1 F). These data are consistent with those reported by Percy and co-workers.[52]

General Coupling Procedure 1. *2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(4″-chlorophenyl)ethene (**10ag**).* A mixture of potassium trifluoroborate **9g** (89 mg, 0.41 mmol), iodide **8a** (100 mg, 0.34 mmol), cesium carbonate (332 mg, 1.0 mmol), and bis(triphenylphosphino)palladium dichloride (4.8 mg, 0.0068 mmol) was taken up in a mixture of toluene (0.75 mL) and H_2O (0.275 mL). The reaction mixture was stirred at 90 °C for 2 h. The reaction mixture was then cooled to room temperature and partitioned between DCM (10 mL) and H_2O (10 mL). The organic phase was separated and dried by passing through a hydrophobic frit. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica (10% diethyl ether in hexane) to afford styrene **10ag** (68 mg, 72%) as a colorless oil: R_f (40% diethyl ether in hexane) 0.44; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44–7.35 (m, 4 H), 4.87 (s, 2 H), 3.88–3.84 (m, 2 H), 3.59–3.54 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) 155.0 (app t, J_{C-F} 290.3), 133.6, 128.3, 128.0 (br d, J_{C-F} 5.8), 127.5 (dd, J_{C-F} 6.0, 3.4), 114.5 (dd, J_{C-F} 35.3, 19.2), 95.0 (t, J_{C-F} 3.0), 71.1, 68.1, 58.5; ^{19}F NMR (376

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MHz, $CDCl_3$) δ (ppm) −97.0 (d, J 54.5, 1 F), −105.4 (d, J 54.5, 1 F). These data were consistent with those reported previously.[20]

General Coupling Procedure 2. *2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(3″-formylphenyl)ethene (**10am**).* A mixture of potassium trifluoroborate **9m** (43 mg, 0.2 mmol), iodide **8a** (50 mg, 0.17 mmol), cesium carbonate (166 mg, 0.51 mmol) and bis(triphenylphosphino)palladium dichloride (2.4 mg, 0.0034 mmol) was taken up in a mixture of degassed (3 x freeze−pump−thaw cycle) *iso*-propanol (0.750 mL) and H_2O (0.275 mL). The reaction mixture was stirred at 90 °C for 2 h. The reaction mixture was then cooled to room temperature and partitioned between DCM (5 mL) and H_2O (5 mL). The organic phase was separated and dried by passing through a hydrophobic frit. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica (10% diethyl ether in hexane) to afford styrene **10am** (31 mg, 67%) as a colorless oil; R_f (40% diethyl ether in hexane) 0.13; IR ν_{max}(film)/cm^{-1} 2924, 2893, 2738, 1698, 1293, 1146, 1070, 1021, 1008, 850, 799, 734, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.05 (s, 1 H), 8.00 (br s, 1 H), 7.85 (dd, J 7.7, 1.23, 1 H), 7.78 - 7.73 (m, 1 H), 7.58 (t, J 7.7, 1 H), 4.92 (br s, 2 H), 3.9−3.87 (m, 2 H), 3.59−3.55 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.3, 155.3 (app t, J_{C-F} 291.5), 136.2, 131.8 (dd, J_{C-F} 6.3, 3.2), 130.9 (br d, J_{C-F} 6.5), 128.8, 128.7, 127.5 (dd, J_{C-F} 6.0, 3.8), 114.4 (dd, J_{C-F} 34.8, 19.2), 95.3 (t, J_{C-F} 3.0), 71.0, 68.2, 58.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −95.7 (d, J 52.6, 1 F), −104.6 (d, J 52.6, 1 F); HRMS (NSI) m/z calcd for $C_{13}H_{18}F_2NO_4$ $[M + NH_4]^+$ 290.1204, Found 290.1202; LRMS (CI) m/z 301 $[M + C_2H_5]^+$; GC (98%) t_R 12.02 min.

General coupling procedure 3. *2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(4″-methoxyphenyl)ethene (**10aa**).* A mixture of potassium trifluoroborate **9a** (27 mg, 0.13 mmol), iodide **8a** (31 mg, 0.11 mmol), cesium carbonate (103 mg, 0.32 mmol), and bis(triphenylphosphino)palladium dichloride (1.5 mg, 0.0021 mmol) was taken up in a mixture of *tert*-butyl alcohol (0.750 mL) and H_2O (0.275 mL). The reaction mixture was stirred at 90 °C for 18 h, cooled to room temperature, and partitioned between DCM (5 mL) and H_2O (5 mL). The organic phase was separated and dried by passing through a hydrophobic frit. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica (10% diethyl ether in hexane) to afford styrene **10aa** (30 mg, 87%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.42−7.38 (m, 2 H), 6.95−6.91 (m, 2 H), 4.88 (s, 2 H), 3.89−3.86 (m, 2 H), 3.84 (s, 3 H), 3.60−3.57 (m, 2 H), 3.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.1, 154.6 (app t, J_{C-F} 287.7), 127.9 (dd, J_{C-F} 5.2, 3.6), 121.5 (br d, J_{C-F} 6.0), 114.8 (dd, J_{C-F} 36.5, 18.6), 113.5, 94.6 (t, J_{C-F} 2.8), 71.1, 67.9, 58.5, 54.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −99.9 (d, J 61.4, 1 F), −108.5 (d, J 61.4, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(3″-methoxyphenyl)ethene (**10ab**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9b** (44 mg, 0.20 mmol) using general procedure 3 to afford **10ab** (53 mg, 95%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.28; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.31 (t, J 8.0, 1 H), 7.08 (dq, J 7.8, J 1.3, 1 H), 7.04−7.02 (m, 1 H), 6.88 (br dd, J 8.3, J 2.5, 1 H), 4.90 (s, 2 H), 3.90−3.86 (m, 2 H), 3.83 (s, 3 H), 3.60−3.56 (m, 2 H), 3.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.2, 155.1 (app t, J_{C-F} 289.9), 130.8 (br d, J_{C-F} 6.1), 129.1, 118.8 (dd, J_{C-F} 5.9, 3.4), 115.0 (dd, J_{C-F} 35.4, 18.4), 113.5, 111.8 (dd, J_{C-F} 5.6, 3.4), 94.9 (t, J_{C-F} 3.1), 71.1, 68.0, 58.5, 54.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −97.6 (d, J 55.6, 1 F), −105.7 (d, J 55.6, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(2″-methoxyphenyl)ethene (**10ac**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9c** (44 mg, 0.20 mmol) using general procedure 1 to afford **10ac** (52 mg, 93%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.28; IR ν_{max}(film)/cm^{-1} 2977, 2939, 2842, 1724, 1497, 1422, 1264, 1142, 982, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.41−7.32 (m, 2 H), 6.99 (dt, J 7.5, J 0.8, 1 H), 6.95 (d, J 8.2, 1 H), 4.80 (s, 2 H), 3.87 (s, 3 H), 3.83−3.79 (m, 2 H), 3.57−3.53 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.4, 154.0 (dd, J_{C-F} 289.4, 281.5), 131.2, 130.4, 119.9, 117.5 (br s), 111.7 (dd, J_{C-F} 42.0, 19.8), 110.7, 93.6, 71.1, 67.4, 58.5, 55.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −100.1 (d, J 60.1, 1 F), −107.7 (d, J 60.1, 1 F); HRMS (NSI) m/z calcd for $C_{13}H_{20}F_2NO_4$ $[M + NH_4]^+$ 292.1355, found 292.1358; LRMS m/z (CI) 275 $[M + H]^+$; GC (98%) t_R 11.32 min.

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(4″-thioanisoyl)-ethene (**10ad**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9d** (47 mg, 0.20 mmol) using general procedure 3 to afford **10ad** (37 mg, 62%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.28; IR ν_{max}(film)/cm^{-1} 2887, 2820, 1730, 1495, 1262, 1178, 1096, 1077, 980, 945, 824; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.41−7.37 (m, 2 H), 7.29−7.25 (m, 2 H), 4.89 (s, 2 H), 3.89−3.86 (m, 2 H), 3.60−3.56 (m, 2 H), 3.40 (s, 3 H), 2.51 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.9 (app t, J_{C-F} 289.1), 138.6, 126.6 (dd, J_{C-F} 5.7, 3.4), 126.0 (br d, J_{C-F} 6.6), 125.8, 114.8 (dd, J_{C-F} 35.0, 18.5), 94.9 (t, J_{C-F} 3.0), 71.1, 68.0, 58.5, 15.0; ^{19}F NMR (400 MHz, $CDCl_3$) δ (ppm) −98.0 (d, J 56.9, 1 F), −106.4 (d, J 56.9, 1 F); HRMS (NSI) m/z calcd for $C_{13}H_{20}F_2NO_3S$ $[M + NH_4]^+$ 308.1127, found 308.1128; LRMS m/z (CI) 319 $[M + C_2H_5]^+$; GC (98%) t_R 12.94 min.

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(2″-methylphenyl)-ethene (**10ae**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9e** (40 mg, 0.20 mmol) using general procedure 3 to afford **10ae** (50 mg, 95%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36−7.19 (m, 4 H), 4.73 (d, J_{H-F} 0.9, 2 H), 3.83−3.79 (m, 2 H), 3.57−3.54 (m, 2 H), 3.40 (s, 3 H), 2.37 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.7 (dd, J_{C-F} 289.9, 280.5), 137.5 (d, J_{C-F} 2.7), 130.2 (t, J_{C-F} 2.7), 129.9, 129.0, 127.5, 125.2, 113.8 (dd, J_{C-F} 42.1, 17.7), 92.8, 71.1, 67.3, 58.5, 18.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −102.2 (d, J 63.6, 1 F), −109.2 (d, J 63.6, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(4″-tert-butylphenyl)ethene (**10af**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9f** (49 mg, 0.20 mmol) using general procedure 3 to afford **10af** (61 mg, 99%) as a colorless oil: R_f (40% diethyl ether in hexane) 0.47; IR ν_{max}(film)/cm^{-1} 2960, 2882, 1722, 1465, 1260, 1154, 1109, 975, 945, 837, 740; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.42 (br s, 4 H), 4.89 (s, 2 H), 3.90−3.87 (m, 2 H), 3.60−3.56 (m, 2 H), 3.40 (s, 3 H), 1.35 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.9 (app t, J_{C-F} 288.4), 150.9, 126.4 (br d, J_{C-F} 6.1), 126.0 (dd, J_{C-F} 5.5, 3.5), 125.0, 115.1 (dd, J_{C-F} 35.5, 18.3), 94.8 (t, J_{C-F} 3.0), 71.1, 68.0, 58.5, 34.1, 30.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −98.7 (d, J 58.0, 1 F), −107.1 (d, J 58.0, 1 F); HRMS (NSI) m/z calcd for $C_{16}H_{26}F_2NO_3$ $[M + NH_4]^+$ 318.1875, found 318.1880; LRMS m/z (CI) 301 $[M + H]^+$; GC (98%) t_R 12.25 min.

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(4″-trifluoromethylphenyl)ethene (**10ah**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9h** (51 mg, 0.20 mmol) using general procedure 1 (90 °C, 18 h) to afford **10ah** (47 mg, 88%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.67 (br d, J 8.6, 2 H), 7.61 (br d, J 8.6, 2 H), 4.90 (s, 2 H), 3.89−3.85 (m, 2 H), 3.58−3.54 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.0 (app t, J_{C-F} 291.9), 133.4 (br d, J_{C-F} 6.4), 129.7 (q, J_{C-F} 32.5), 126.3 (dd, J_{C-F} 6.5, 3.5), 125.0 (q, J_{C-F} 3.0), 123.4 (q, J_{C-F} 271.8), 114.5 (dd, J_{C-F} 34.2, 19.3), 95.4 (t, J_{C-F} 3.0), 71.0, 68.2, 58.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −62.8 (s, 3 F), −94.9 (d, J 50.0, 1 F), −103.6 (d, J 50.0, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(3″-trifluoromethylphenyl)ethene (**10aj**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9j** (51 mg, 0.20 mmol) using general procedure 3 to afford **10aj** (40 mg, 78%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.17; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.76 (br s, 1 H), 7.68 (br d, J 7.8, 1 H), 7.59 (br d, J 7.8, 1 H), 7.53 (t, J 7.8, 1 H), 4.92 (s, 2 H), 3.90−3.86 (m, 2 H), 3.58−3.55 (m, 2 H), 3.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.0 (app t, J_{C-F} 291.3), 130.7 (br d, J_{C-F} 6.4), 130.6 (q, J_{C-F} 32.6), 129.3 (br d, J_{C-F} 4.0), 128.6, 124.4 (d, J_{C-F} 3.5), 123.4 (q, J_{C-F} 272.6), 123.1−122.8 (m), 114.4 (dd, J_{C-F} 34.6, 19.3), 95.4 (t, J_{C-F} 3.2), 71.0, 68.2, 58.5; NMR ^{19}F (376 MHz, $CDCl_3$) δ (ppm) −62.8 (s, 3 F) −95.7 (d, J 51.9, 1 F), −104.5

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(d, *J* 51.9, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(4″-cyanophenyl)-ethene (**10ak**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9k** (43 mg, 0.20 mmol) using general procedure 3 to afford **10ak** (27 mg, 59%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.16; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* 8.5, 2 H), 7.60 (d, *J* 8.5, 2 H), 4.91 (s, 2 H), 3.89−3.86 (m, 2 H), 3.58−3.55 (m, 2 H), 3.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.6 (app t, J_{C-F} 293.8), 134.6 (br d, J_{C-F} 6.8), 131.8, 126.4 (dd, J_{C-F} 7.0, 3.4), 117.9, 114.4 (dd, J_{C-F} 33.7, 19.5), 111.2, 95.6, 71.0, 68.3, 58.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −93.1 (d, *J* 45.5, 1 F), −101.5 (d, *J* 45.5, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(3″-cyanophenyl)-ethene (**10al**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9k** (43 mg, 0.20 mmol) using general procedure 3 to afford **10ak** (25 mg, 55%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.17; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80−7.79 (m, 1 H), 7.74−7.71 (m, 1 H), 7.61 (dt, J 7.8, *J* 1.3, 1 H), 7.52 (t, *J* 7.8, 1 H), 4.91 (s, 2 H), 3.90−3.86 (m, 2 H), 3.59−3.55 (m, 2 H), 3.40 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.4 (app t, J_{C-F} 292.0), 131.4 (dd, J_{C-F} 6.3, 2.2), 131.1, 130.2 (dd, J_{C-F} 6.8, 3.3), 129.6 (dd, J_{C-F} 6.2, 3.9), 129.0, 117.8, 113.9 (dd, J_{C-F} 34.5, 19.8), 112.6, 95.5 (t, J_{C-F} 3.1), 71.0, 68.3, 58.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −94.5 (d, *J* 50.2, 1 F), −103.5 (d, *J* 50.2, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxyethoxymethoxy)-1-(3″-nitrophenyl)-ethene (**10an**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9n** (47 mg, 0.20 mmol) using general procedure 3 (90 °C, 3 h) to afford **10an** (30 mg, 61%) as a colorless oil: R_f (40% diethyl ether in hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.37 (app t, *J* 2.0, 1 H), 8.18 (dd, *J* 8.0, *J* 2.0, 1 H), 7.82 (m, including app d, *J* 8.0, 1 H), 7.59 (app t, *J* 8.0, 1 H), 4.95 (s, 2 H), 3.92−3.88 (m, 2 H), 3.59−3.55 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.5 (app t, J_{C-F} 292.6), 148.1, 131.9 (dd, J_{C-F} 6.5, 2.1), 131.7 (dd, J_{C-F} 6.9, 3.2), 129.1, 122.4, 120.9 (dd, J_{C-F} 6.0, 3.7), 114.1 (dd, J_{C-F} 34.1, 19.5), 95.7 (t, J_{C-F} 3.0), 71.0, 68.3, 58.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −94.1 (d, *J* 49.0, 1 F), −103.0 (d, *J* 49.0, 1 F). These data were consistent with those reported previously.[24]

*2,2-Difluoro-1-(2′-methoxy-ethoxymethoxy)-1-(3-pyridyl) ethene (**10ao**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9o** (38 mg, 0.20 mmol) using general procedure 3 to afford **10ao** (27 mg, 54%) as a yellow oil. R_f (70% diethyl ether in hexane) 0.19; IR ν_{max}(film)/cm^{-1} 2934, 2885, 1731, 1567, 1418, 1267, 1153, 1125, 1099, 1077, 978, 937, 849, 812, 711; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.73 (br s, 1 H), 8.55 (br d, *J* 4.8, 1 H), 7.79−7.75 (m, 1 H), 7.32 (dd, *J* 8.1, 4.8, 1 H), 4.90 (s, 2 H), 3.87−3.84 (m, 2 H), 3.56−3.53 (m, 2 H), 3.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.7 (app t, J_{C-F} 291.8), 149.2, 147.9 (dd, J_{C-F} 6.7, 3.5), 134.0 (dd, J_{C-F} 6.2, 3.3), 126.4 (d, J_{C-F} 6.8), 123.3, 113.6 (dd, J_{C-F} 36.3, 19.7), 95.8 (t, J_{C-F} 3.1), 71.5, 68.7, 59.0; ^{19}F NMR (400 MHz, $CDCl_3$) δ (ppm) −95.3 (d, *J* 52.8, 1 F), −105.0 (d, *J* 52.8, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{11}H_{13}F_2NO_3$ $[M]^+$ 245.0858, found 245.0854; LRMS *m*/*z* (CI) 274 $[M + C_2H_5]^+$; GC (98%) t_R 10.77 min.

*2,2-Difluoro-1-(2′-methoxy-ethoxymethoxy)-1-(4-isoquinolyl) ethene (**10ap**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9p** (48 mg, 0.20 mmol) using general procedure 3 to afford **10ap** (19 mg, 32%) as a pale yellow oil. R_f (70% diethyl ether in hexane) 0.22; IR ν_{max}(film)/cm^{-1} 2932, 2895, 2822, 1752, 1504, 1279, 1193, 1166, 1150, 960, 761, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.30 (s, 1 H), 8.60 (s, 1 H), 8.12 (br d, *J* 8.4, 1 H), 8.04 (br d, *J* 8.4, 1 H), 7.81−7.77 (m, 1 H), 7.71−7.66 (m, 1 H), 4.80 (d, J_{H-F} 0.7, 2 H), 3.82−3.79 (m, 2 H), 3.53−3.50 (m, 2 H), 3.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.0 (dd, J_{C-F} 292.1, 283.5), 153.7, 144.5 (t, J_{C-F} 3.1), 133.9 (d, J_{C-F} 3.1), 130.7, 127.9, 127.6, 127.2, 123.8, 119.7, 111.3 (dd, J_{C-F} 40.8, 21.5), 93.6, 71.0, 67.6, 58.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −98.4 (d, *J* 57.3, 1 F), −107.1 (d, *J* 57.3, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{15}H_{16}F_2NO_3$ $[M + H]^+$ 296.1093, found 296.1096; LRMS *m*/*z* (CI) 324 $[M + C_2H_5]^+$; GC (98%) t_R 13.19 min.

*2,2-Difluoro-1-(2′-methoxy-ethoxymethoxy)-1-(6″-bromo-3-pyridyl) ethene (**10aq**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9q** (54 mg, 0.20 mmol) using general procedure 3 to afford **10aq** (21 mg, 32%) as a yellow oil. R_f (40% diethyl ether in hexane) 0.23; IR ν_{max}(film)/cm^{-1} 2930, 2885, 2820, 1724, 1457, 1271, 1155, 1088, 975, 936, 837; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.49 (d, *J* 2.5, 1 H), 7.65 (ddd, *J* 8.4, *J* 2.5, J_{H-F} 0.9, 1 H), 7.52 (d, *J* 8.4, 1 H), 4.92 (s, 2 H), 3.88−3.85 (m, 2 H), 3.58−3.54 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.3 (app t, J_{C-F} 292.5), 147.7 (dd, J_{C-F} 6.8, 3.5), 141.2, 135.8 (dd, J_{C-F} 6.5, 3.2), 127.5, 125.6 (br d, J_{C-F} 6.6), 112.6 (dd, J_{C-F} 35.8, 20.3), 95.7 (t, J_{C-F} 3.1), 71.1, 68.4, 58.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −94.0 (d, *J* 50.2, 1 F), −103.6 (d, *J* 50.2, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{11}H_{13}BrF_2NO_3$ $[M + H]^+$ 324.0041, found 324.0049; LRMS *m*/*z* (CI) 352 $[M + C_2H_5]^+$; GC (98%) t_R 12.34 min..

*2,2-Difluoro-1-(2′-methoxy-ethoxymethoxy)-1-(3-benzothiophenyl) ethene (**10as**).* Prepared from **8a** (50 mg, 0.17 mmol) and **9s** (49 mg, 0.20 mmol) using general procedure 3 to afford **10as** (35 mg, 57%) as a yellow oil. R_f (40% diethyl ether in hexane) 0.36; IR ν_{max}(film)/cm^{-1} 3103, 2926, 2889, 2822, 1745, 1457, 1429, 1284, 1224, 1114, 1096, 1079, 958, 913, 831, 760, 734; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.98−7.94 (m, 1 H), 7.91−7.87 (m, 1 H), 7.59 (s, 1 H), 7.46−7.38 (m, 2 H), 4.82 (d, J_{H-F} 0.8, 2 H), 3.86−3.83 (m, 2 H), 3.57−3.53 (m, 2 H), 3.39 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.9 (dd, J_{C-F} 290.5, 284.5), 139.4, 137.0 (d, J_{C-F} 3.2), 127.6 (t, J_{C-F} 3.9), 124.3, 124.2, 123.9 (dd, J_{C-F} 5.3), 122.7, 122.2, 110.8 (dd, J_{C-F} 39.9, 19.3), 93.9 (t, J_{C-F} 2.6), 71.1, 67.7, 58.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −99.5 (d, *J* 57.3, 1 F), −107.2 (d, *J* 57.3, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{14}H_{18}F_2NO_3S$ $[M + H]^+$ 318.0970, found 318.0974; LRMS *m*/*z* (CI) 329 $[M + C_2H_5]^+$; GC (98%) t_R 12.98 min.

*1,1-Difluoro-2-(2′-methoxy-ethoxymethoxy)-1,3-butadiene (**10at**).* Prepared from **8a** (549 mg, 1.87 mmol) and **9t** (300 mg, 2.24 mmol) using general procedure 3 to afford **10at** (97 mg, 27%) as a colorless oil after Kugelrohr distillation (100 mbar, 95 °C). R_f (40% diethyl ether in hexane) 0.31; IR ν_{max}(film)/cm^{-1} 2975, 2935, 2889, 1744, 1455, 1366, 1244, 1192, 1162, 1086, 1045, 1024, 983, 896, 849; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.25 (dddd, *J* 17.3, 11.1, J_{H-F} 3.7, 1.6, 1 H), 5.43 (br d, *J* 17.3, 1 H), 5.21−5.17 (m, including app d, *J* 11.2, 1 H), 4.95 (s, 2 H), 3.90−3.87 (m, 2 H), 3.61−3.58 (m, 2 H), 3.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.7 (app t, J_{C-F} 293.5), 123.9 (d, J_{C-F} 4.7), 115.2 (dd, J_{C-F} 35.8, 17.3), 113.3 (dd, J_{C-F} 11.9, 4.4), 95.7 (t, J_{C-F} 3.0), 71.1, 68.1, 58.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −98.1 (d, *J* 54.5, 1 F), −106.6 (dd, *J* 54.5, J_{F-H} 2.7, 1 F); HRMS (APCI) *m*/*z* calcd for $C_8H_{16}F_2NO_3$ $[M + NH_4]^+$ 212.1093, found 212.1092; LRMS *m*/*z* (CI) 195 $[M + H]^+$; GC (98%) t_R 10.48 min.

*1-(N,N-diethylcarbamoyloxy)-2,2-difluoro-1-(4′-methoxyphenyl) ethene (**10ba**).* Prepared from **8b** (137 mg, 0.45 mmol) and **9a** (107 mg, 0.5 mmol) using general procedure 1 (90 °C for 1 h) to afford **10ba** (103 mg, 80%) as a pale yellow oil. R_f (40% diethyl ether in hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.37 (d, *J* 8.9, 2 H), 6.93 (d, *J* 8.9, 2 H), 3.84 (s, 3 H), 3.46 (q, *J* 6.9, 2 H), 3.38 (q, *J* 6.9, 2 H), 1.27 (t, *J* 6.9, 3 H), 1.20 (t, *J* 6.9, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.9, 154.1 (app t, J_{C-F} 288.1), 152.5, 126.6 (dd, J_{C-F} 6.0, 3.3), 122.1 (br d, J_{C-F} 6.3), 113.6, 111.7 (dd, J_{C-F} 38.9, 19.5), 54.8, 42.0, 41.4, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −95.9 (d, *J* 54.5, 1 F), −106.0 (d, *J* 54.5, 1 F). These data were consistent with those reported previously[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(3′-methoxyphenyl)-ethene (**10bb**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9b** (42 mg, 0.2 mmol) using general procedure 2 to afford **10bb** (33 mg, 59%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.31 (app t, *J* 8.1, 1 H), 7.06−7.03 (m, 1 H), 6.98 (br s, 1 H), 6.87 (dd, *J* 8.1, *J* 2.5, 1 H), 3.47 (q, *J* 7.1, 2 H), 3.40 (q, *J* 7.1, 2 H), 1.29 (t, *J* 7.1, 3 H), 1.20 (t, *J* 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.1, 154.5 (app t, J_{C-F} 290.3), 152.4, 131.1 (d, J_{C-F} 6.6), 129.1, 117.4 (dd, J_{C-F} 6.7, 3.5), 113.2, 111.8 (dd, J_{C-F} 37.8, 19.1), 110.8 (dd, J_{C-F} 6.7, 3.6), 54.7, 42.1, 41.5, 13.7, 12.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −93.4 (d, *J* 48.3, 1 F), −103.1 (d, *J*

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48.3, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(2′-methoxyphenyl)-ethene (**10bc**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9c** (42 mg, 0.2 mmol) using general procedure 2 to afford **10bc** (33 mg, 59%) as a yellow oil: R_f (40% diethyl ether in hexane) 0.31; IR ν_{max}(film)/cm^{-1} 2977, 2939, 2842, 1724, 1497, 1437, 1422, 1264, 1142, 982, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.42 (d, J 7.6, 1 H), 7.38−7.33 (m, 1 H), 6.99 (dt, J 7.6, J 0.9, 1 H), 6.94 (d, J 8.4, 1 H), 3.88 (s, 3 H), 3.41−3.29 (m, 4 H), 1.23−1.12 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.8 (d, J_{C-F} 2.4), 154.0 (dd, J_{C-F} 290.1, 284.4), 152.7, 130.3 (t, J_{C-F} 3.0), 130.1, 119.9, 118.4 (br d, J_{C-F} 4.6), 110.7, 108.5 (dd, J_{C-F} 45.1, 20.6), 55.1, 41.9, 41.4, 13.5, 12.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −96.2 (d, J 49.9, 1 F), −104.6 (d, J 49.9, 1 F); HRMS (NSI) m/z calcd for $C_{14}H_{18}F_2NO_3$ $[M + H]^+$ 286.1249, found 286.1253; LRMS m/z (CI) 314 $[M + C_2H_5]^+$; GC (98%) t_R 11.70 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(4′-thioanisoyl)-ethene (**10bd**).* Prepared from **8b** (101 mg, 0.33 mmol) and **9d** (91 mg, 0.4 mmol) using general procedure 1 to afford **10bd** (92 mg, 93%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.21; IR ν_{max}(film)/cm^{-1} 3014, 2947, 1724, 1442, 1166, 1116, 1096, 982, 812, 798, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35 (d, J 8.4, 2 H), 7.27 (d, J 8.4, 2 H), 3.46 (q, J 6.9, 2 H), 3.37 (q, J 6.9, 2 H), 2.50 (s, 3 H), 1.28 (t, J 6.9, 3 H), 1.20 (t, J 6.9, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.3 (app t, J_{C-F} 290.7), 152.4, 138.4, 126.4 (d, J_{C-F} 6.6), 125.9, 125.4 (dd, J_{C-F} 6.4, 3.6), 111.7 (dd, J_{C-F} 38.4, 19.4), 42.1, 41.5, 15.1, 13.7, 12.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −94.1 (d, J 49.9, 1 F), −104.0 (d, J 49.9, 1 F); HRMS (NSI) m/z calcd for $C_{14}H_{18}F_2NO_2S$ $[M + H]^+$ 302.1021 found, 302.1025; LRMS m/z (CI) 302 $[M + H]^+$; GC (98%) t_R 13.42 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(2′-methylphenyl)-ethene (**10be**).* Prepared from **8b** (101 mg, 0.33 mmol) and **9e** (78 mg, 0.4 mmol) using general procedure 1 to afford **10be** (83 mg, 93%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.50; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.42 (br d, J 7.5, 1 H), 7.31−7.19 (m, 3 H), 3.41−3.25 (m, 4 H), 1.23−1.09 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.1 (dd, J_{C-F} 290.0, 282.6), 153.0, 137.8, 130.4, 130.1, 129.3, 129.1 (d, J_{C-F} 4.6), 125.7, 111.1 (dd, J_{C-F} 46.1, 18.8), 42.4, 41.8, 19.5, 14.1, 13.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −97.4 (d, J 53.9, 1 F), −106.2 (d, J 53.9, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(4′-tert-butylphenyl)ethene (**10bf**).* Prepared from **8b** (101 mg, 0.33 mmol) and **9f** (95 mg, 0.4 mmol) using general procedure 1 to afford **10bf** (68 mg, 66%) as a colorless oil: R_f (40% diethyl ether in hexane) 0.25; IR ν_{max}(film)/cm^{-1} 2965, 2872, 1727, 1474, 1420, 1265, 1146, 982, 948, 927, 844, 825, 784, 754; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.43 (d, J 8.5, 2 H), 7.37 (d, J 8.5, 2 H), 3.47 (q, J 7.1, 2 H), 3.39 (q, J 7.1, 2 H), 1.34 (s, 9 H), 1.29 (t, J 6.9, 3 H), 1.21 (t, J 6.9, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.4 (app t, J_{C-F} 289.3), 152.5, 150.7, 126.8 (d, J_{C-F} 6.7), 125.0, 124.7 (dd, J_{C-F} 6.4, 3.4), 111.9 (dd, J_{C-F} 38.6, 19.1), 42.1, 41.5, 34.1, 30.7, 13.6, 12.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −97.4 (d, J 53.9, 1 F), −106.2 (d, J 53.9, 1 F); HRMS (NSI) m/z calcd for $C_{17}H_{24}F_2NO_2$ $[M + H]^+$ 312.1770, found: 312.1771; LRMS m/z (CI) 312 $[M + H]^+$; GC (98%) t_R 12.70 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(4′-chlorophenyl)-ethene (**10bg**).* Prepared from **8b** (101 mg, 0.33 mmol) and **9g** (87 mg, 0.4 mmol) using general procedure 1 to afford **10bg** (84 mg, 88%) as a colorless oil: R_f (40% diethyl ether in hexane) 0.39; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.37 (s, 4 H), 3.46 (q, J 7.0, 2 H), 3.38 (q, J 7.0, 2 H), 1.34 (s, 9 H), 1.28 (t, J 7.1, 3 H), 1.20 (t, J 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.4 (app t, J_{C-F} 291.1), 152.3, 133.5, 128.3 (d, J_{C-F} 5.5), 128.3, 126.3 (dd, J_{C-F} 6.7, 3.5), 111.3 (dd, J_{C-F} 38.7, 20.1), 42.2, 41.5, 13.7, 12.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −93.1 (d, J 47.7, 1 F), −103.1 (d, J 47.7, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(4′-trifluoromethylphenyl)ethene (**10bh**).* Prepared from **8b** (101 mg, 0.33 mmol) and **9h** (100 mg, 0.4 mmol) using general procedure 1 (90 °C for 18 h) to afford **10bh** (94 mg, 88%) as a colorless oil: R_f (40% diethyl ether in hexane) 0.43; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.66 (d, J 8.4, 2 H), 7.55 (d, J 8.4, 2 H), 3.49 (q, J 7.2, 2 H), 3.38 (q, J 7.2, 2 H), 1.30 (t, J 7.1, 3 H), 1.21 (t, J 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.8 (app t, J_{C-F} 292.6), 152.2, 133.5 (br d, J_{C-F} 6.9), 129.5 (q, J_{C-F} 32.5), 125.0−125.2 (m, includes signals for 2(Ar)C−H), 123.4 (q, J_{C-F} 272.6), 111.2 (dd, J_{C-F} 37.8, 19.9), 42.2, 41.6, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −62.9 (s, 3 F), −91.1 (d, J 43.1, 1 F), −101.3 (d, J 43.1, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(3′-trifluoromethylphenyl)ethene (**10bj**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9j** (50 mg, 0.2 mmol) using general procedure 2 to afford **10bj** (32 mg, 60%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.68 (br s, 1 H), 7.63 (br d, J 7.7, 1 H), 7.58 (br d, J 7.7, 1 H), 7.53 (t, J 7.7, 1 H), 3.49 (q, J 7.2, 2 H), 3.39 (q, J 7.2, 2 H), 1.30 (t, J 7.1, 3 H), 1.21 (t, J 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.7 (app t, J_{C-F} 291.0), 152.1, 130.8 (br d, J_{C-F} 6.9), 130.6 (q, J_{C-F} 32.6), 128.6, 128.1 (dd, J_{C-F} 7.0, 3.0), 124.3 (d, J_{C-F} 3.14), 123.2 (q, J_{C-F} 271.2), 121.5−121.8 (m), 111.1 (dd, J_{C-F} 37.3, 19.5), 42.2, 41.6, 13.6, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −63.9 (s, 3 F), −91.7 (d, J 45.3, 1 F), −102.1 (d, J 45.3, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(4′-cyanophenyl)-ethene (**10bk**).* Prepared from **8b** (50 mg, 0.33 mmol) and **9k** (101 mg, 0.4 mmol) using general procedure 1 (90 °C for 18 h) to afford **10bk** (57 mg, 62%) as a pale yellow solid: R_f (40% diethyl ether in hexane) 0.18; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (br d, J 8.3 2 H), 7.53 (br d, J 8.3 2 H), 3.48 (q, J 7.2, 2 H), 3.38 (q, J 7.2, 2 H), 1.29 (t, J 7.2, 3 H), 1.20 (t, J 7.2, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.9 (app t, J_{C-F} 294.0), 152.0, 134.5 (br d, J_{C-F} 7.4), 131.8, 125.2 (dd, J_{C-F} 7.4, 3.7), 117.9, 111.2 (dd, J_{C-F} 37.4, 20.3), 111.1, 42.3, 41.6, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −89.3 (d, J 39.1, 1 F), −99.3 (d, J 39.1, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(3′-cyanophenyl)-ethene (**10bl**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9l** (41 mg, 0.2 mmol) using general procedure 2 to afford **10bl** (28 mg, 61%) as a yellow oil: R_f (40% diethyl ether in hexane) 0.15; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (br d, J 1.1, 1 H), 7.67−7.66 (m, 1 H), 7.60 (app br d, J 7.7, 1 H), 7.52 (app t, J 7.7, 1 H), 3.47 (q, J 7.1, 2 H), 3.40 (q, J 7.1, 2 H), 1.29 (t, J 7.1, 3 H), 1.21 (t, J 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.7 (app t, J_{C-F} 291.7), 152.1, 131.4 (br d, J_{C-F} 7.0), 131.0, 129.1−129.0 (m), 128.4 (dd, J_{C-F} 6.3, 4.0), 117.9, 112.6, 110.6 (dd, J_{C-F} 37.8, 20.2), 42.3, 41.6, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −90.7 (d, J 42.6, 1 F), −101.2 (d, J 42.6, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(3′-formylphenyl)-ethene (**10bm**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9m** (42 mg, 0.2 mmol) using general procedure 2 to afford **10bm** (42 mg, 90%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.17; IR ν_{max}(film)/cm^{-1} 2979, 2941, 1728, 1689, 1424, 1267, 1187, 1142, 1012, 796, 753, 689; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.04 (s, 1 H), 7.93 (br s, 1 H), 7.83 (app br d, J 7.7, 1 H), 7.72−7.69 (m, 1 H), 7.58 (app t, J 7.7, 1 H), 3.49 (q, J 7.1, 2 H), 3.38 (q, J 7.1, 2 H), 1.30 (t, J 7.0, 3 H), 1.20 (t, J 7.0, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.2, 154.7 (app t, J_{C-F} 292.4), 152.2, 136.2, 131.1 (d, J_{C-F} 6.7), 130.6 (dd, J_{C-F} 7.0, 3.4), 128.9, 128.7, 126.1 (dd, J_{C-F} 6.3, 3.9), 111.2 (dd, J_{C-F} 38.1, 19.8), 42.2, 41.6, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −91.8 (d, J 45.3, 1 F), −102.2 (d, J 45.3, 1 F); HRMS (NSI) m/z calcd for $C_{14}H_{19}F_2N_2O_3$ $[M + NH_4]^+$ 301.1358, found 301.1360; LRMS m/z (CI) 284 $[M + H]^+$; GC (98%) t_R 12.40 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(3′-nitrophenyl)-ethene (**10bn**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9n** (45 mg, 0.2 mmol) using general procedure 3 (90 °C for 4 h) to afford **10bn** (37 mg, 75%) as a pale yellow oil: R_f (40% diethyl ether in hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.29 (t, J 2.0, 1 H), 8.18 (dd, J 8.2, J 2.0, 1 H), 7.80−7.77 (m, 1 H), 7.60 (t, J 8.2, 1 H), 3.51 (q,

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J 7.1, 2 H), 3.39 (q, *J* 7.1, 2 H), 1.32 (t, *J* 7.2, 3 H), 1.22 (t, *J* 7.2, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.9 (app t, J_{C-F} 293.2), 152.0, 148.0, 131.9 (br d, J_{C-F} 7.3), 130.6 (dd, J_{C-F} 8.1, 3.5), 129.2, 122.3, 119.8 (dd, J_{C-F} 5.9, 4.4), 110.7 (dd, J_{C-F} 37.5, 20.5), 42.3, 41.6, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −90.3 (d, *J* 42.2, 1 F), −100.7 (d, *J* 42.2, 1 F). These data were consistent with those reported previously.[24]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(3-pyridyl)ethene (**10bo**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9o** (37 mg, 0.2 mmol) using general procedure 2 (90 °C for 3 h) to afford **10bo** (26 mg, 61%) as a colorless oil: R_f (60% diethyl ether in hexane) 0.12; IR ν_{max}(film)/cm^{-1} 2980, 2939, 1737, 1411, 1275, 1150, 82, 706; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.67 (d, *J* 2.2, 1 H), 8.53 (dd, *J* 4.8, 1.4, 1 H), 7.75−7.70 (m, 1 H), 7.31 (ddd, *J* 8.1, *J* 4.8, 0.7, 1 H), 3.44 (q, *J* 6.9, 2 H), 3.35 (q, *J* 7.0, 2 H), 1.26 (t, *J* 7.1, 3 H), 1.18 (t, *J* 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.6 (app t, J_{C-F} 292.3), 152.1, 148.6, 146.3 (dd, J_{C-F} 6.7, 3.8), 132.4 (dd, J_{C-F} 7.1, 3.5), 126.1 (br d, J_{C-F} 6.9), 122.8, 109.8 (dd, J_{C-F} 39.7, 20.1), 42.2, 41.6, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −91.5 (d, *J* 45.4, 1 F), −102.5 (d, *J* 45.4, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{12}H_{15}F_2N_2O_2$ $[M + H]^+$ 257.1096, found 257.1099; LRMS *m*/*z* (CI) 257 $[M + H]^+$; GC (98%) t_R 11.28 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(4-isoquinolyl)-ethene (**10bp**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9p** (46 mg, 0.2 mmol) using general procedure 2 to afford **10bp** (22 mg, 44%) as a colorless oil: R_f (100% diethyl ether) 0.65; IR ν_{max}(film)/cm^{-1} 2979, 2938, 1724, 1422, 1282, 1187, 1142, 1113, 958, 786, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.29 (s, 1 H), 8.70 (s, 1 H), 8.15 (br d, *J* 8.5, 1 H), 8.04 (d, *J* 8.2, 1 H), 7.83−7.78 (m, 1 H), 7.70−7.64 (m, 1 H), 3.38 (q, *J* 6.9, 2 H), 3.29 (q, *J* 7.0, 2 H), 1.18 (t, *J* 7.0, 3 H), 1.12 (t, *J* 7.0, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.6 (dd, J_{C-F} 293.7, 285.1), 153.6, 152.3, 144.3 (t, J_{C-F} 3.0), 133.4, 130.7, 127.8, 127.6, 127.1, 123.6, 120.7 (d, J_{C-F} 4.7), 107.8 (dd, J_{C-F} 45.5, 20.2), 42.0, 41.5, 13.6, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −93.9 (d, *J* 49.1, 1 F), −104.2 (d, *J* 49.1, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{16}H_{17}F_2N_2O_2$ $[M + H]^+$ 307.1253, found 307.1255; LRMS *m*/*z* (CI) 307 $[M + H]^+$; GC (98%) t_R 13.65 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(6′-bromo-3-pyridyl) ethene (**10bq**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9q** (47 mg, 0.17 mmol) using general procedure 3 (90 °C for 3 h) to afford **10bq** (29 mg, 52%) as a pale yellow oil. R_f (40% diethyl ether in hexane) 0.26; IR ν_{max}(film)/cm^{-1} 2979, 2941, 1731, 1461, 1424, 1280, 1148, 1090, 980; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.43 (d, *J* 2.5, 1 H), 7.60 (ddd, *J* 8.4, *J* 2.5, 0.7, 1 H), 7.52 (d, *J* 8.4, 1 H), 3.45 (q, *J* 7.2, 2 H), 3.37 (q, *J* 7.2, 2 H), 1.27 (t, *J* 7.1, 3 H), 1.20 (t, *J* 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.6 (dd, J_{C-F} 293.1, 291.8), 152.0 (t, J_{C-F} 2.9), 146.5 (dd, J_{C-F} 6.5, 4.0), 140.9, 134.8 (dd, J_{C-F} 7.3, 3.3), 127.4, 125.6 (d, J_{C-F} 6.8), 109.3 (dd, J_{C-F} 39.4, 21.5), 42.3, 41.6, 13.7, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −90.4 (d, *J* 43.5, 1 F), −101.3 (d, *J* 43.5, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{12}H_{14}BrF_2N_2O_2$ $[M + H]^+$ 335.0201, found 335.0206; LRMS *m*/*z* (CI) 335 $[M + H]^+$; GC (98%) t_R 12.77 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(6′-methoxy-2-pyridyl)ethene (**10br**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9r** (43 mg, 0.20 mmol) using general procedure 1 to afford **10br** (33 mg, 70%) as a yellow oil: R_f (20% diethyl ether in cyclohexane) 0.1; IR ν_{max}(film)/cm^{-1} 2979, 2341, 1728, 1578, 1466, 1262, 1153, 1047, 800; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.56 (app t, *J* 8.1, 1 H), 6.98 (d, *J* 7.6, 1 H), 6.63 (d, *J* 8.3, 1 H), 3.89 (s, 3 H), 3.48 (q, *J* 7.1 2 H), 3.43 (q, *J* 7.1 2 H), 1.29 (t, *J* 7.1, 3 H) 1.19 (t, *J* 7.1, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 163.4, 156.5 (dd, J_{C-F} 296, 292), 153.1 (t, J_{C-F} 2.4), 146.8 (dd, J_{C-F} 8.8, 3.3), 138.8, 113.4 (dd, J_{C-F} 8.9, 4.4), 112.6 (dd, J_{C-F} 34.3, 18.8), 109.9 (t, J_{C-F} 2.2), 53.1, 42.6, 42.1, 14.2, 13.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −90.6 (d, *J* 34.4, 1 F), −97.9 (d, *J* 34.4, 1 F); HRMS (ESI) *m*/*z* calcd for $C_{13}H_{17}F_2N_2O_3$ $[M + H]^+$ 287.1202, found 287.1196; LRMS *m*/*z* (ESI) 287 $[M + H]^+$; LC (98%) t_R 1.21 min.

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-(3-benzothiophenyl)ethene (**10bs**).* Prepared from **8b** (50 mg, 0.17 mmol) and **9s** (47 mg, 0.2 mmol) using general procedure 1 to afford **10bs** (35 mg, 57%) as a pale brown oil: R_f (40% diethyl ether in hexane) 0.52; IR ν_{max}(film)/cm^{-1} 2977, 2938, 2878, 1726, 1422, 1295, 1215, 1154, 1107, 760, 734; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.95−7.87 (m, 2 H), 7.67 (s, 1 H), 7.47−7.38 (m, 2 H), 3.41 (q, *J* 7.0, 2 H), 3.33 (q, *J* 7.0, 2 H), 1.22 (t, *J* 7.0, 3 H), 1.16 (t, *J* 7.0, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.6 (dd, J_{C-F} 292.2, 284.5), 152.5, 139.3, 136.7 (d, J_{C-F} 2.7), 127.5 (t, J_{C-F} 3.7), 124.8 (d, J_{C-F} 4.9), 124.2, 124.1, 122.3, 122.2, 107.1 (dd, J_{C-F} 44.1, 21.2), 42.0, 41.4, 13.6, 12.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −94.9 (d, *J* 49.4, 1 F), −104.3 (d, *J* 49.4, 1 F); HRMS (NSI) *m*/*z* calcd for $C_{15}H_{16}F_2NO_2S$ $[M + H]^+$ 312.0864, found 312.0862; LRMS *m*/*z* (CI) 312 $[M + H]^+$; GC (98%) t_R 13.37 min.

*1,1-Difluoro-2-(N,N-diethylcarbamoyloxy)-1,3-butadiene (**10bt**).* Prepared from **8b** (569 mg, 1.87 mmol) and **9u** (300 mg, 2.24 mmol) using general procedure 3 to afford **10bu** (113 mg, 30%) as a colorless oil after Kugelrohr distillation (90 °C/100 mbar): R_f (40% diethyl ether in hexane) 0.46; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.36 (dddd, *J* 17.2, 11.2, J_{H-F} 3.4, 1.6, 1 H), 5.23 (d, *J* 17.2, 1 H), 5.19−5.15 (m, including app d, *J* 11.2, 1 H), 3.44−3.32 (m, 4 H), 1.15−1.26 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.3 (dd, J_{C-F} 295.0, 291.0), 152.4, 124.2 (d, J_{C-F} 4.6), 113.2 (dd, J_{C-F} 11.9, 4.3), 112.4 (dd, J_{C-F} 40.6, 18.2), 42.6, 41.9, 14.1, 13.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −95.6 (d, *J* 40.6, 1 F), −105.6 (d, *J* 40.6, 1 F). These data were consistent with those reported previously.[10]

*1-(N,N-Diethylcarbamoyloxy)-2,2-difluoro-1-deuterioethene (**22**).* *n*-Butyllithium (720 μL of a 2 M solution in hexanes) was added dropwise over 2 min to a solution of 1-(*N*,*N*-diethylcarbamoyloxy)-2,2-difluoro-1-(tributylstannyl)ethene (610 mg, 1.30 mmol) in THF (6 mL) with stirring at −78 °C. The reaction solution turned pale yellow after butyllithium addition and was stirred for 45 min at −78 °C. Deuterated methanol (d_4, 53 μL, 1.30 mmol) was added in one portion, and the reaction solution was stirred for a further 1 h at −78 °C and 1 h at room temperature (18 °C). Careful Kugelrohr distillation of the reaction mixture separated the volatile components. Hexane and THF were removed first (18 °C/50 mbar). Deuterated species **22** was then isolated (75 °C/25 mbar) as a colorless oil (97 mg, 41%): IR ν_{max}(film)/cm^{-1} 2982, 2941, 2883, 1726, 1424, 1293, 1275, 1178, 1100, 842, 740, 635; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.38−3.29 (m, 4 H), 1.17 (t, *J* 7.1, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.6 (dd, J_{C-F} 287.9, 274.7), 151.8, 101.2−99.9 (m, including J_{C-F} and J_{C-D}) 42.0, 41.3, 13.4, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −97.5 (dt, *J* 72.8, J_{F-D} 2.3, 1 F), −117.8 (d, *J* 72.8, 1 F); HRMS (APCI) *m*/*z* calcd for $C_7H_{11}DF_2NO_2$ $[M + NH_4]^+$ 198.1159, found 198.1159; LRMS *m*/*z* (CI) 181 $[M + H]^+$; GC (98%) t_R 9.42 min.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedure and characterization for potassium trifluoroborates and ^{1}H, ^{19}F, and ^{13}C NMR spectra and GC−MS chromatograms for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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