Photocatalytic defluorinative α-aminoalkylation of allylic difluorides

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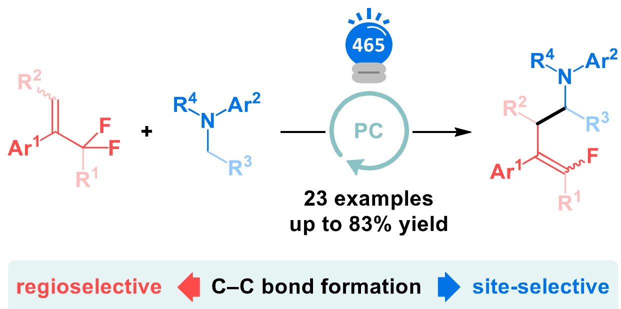
Supporting Information Placeholder



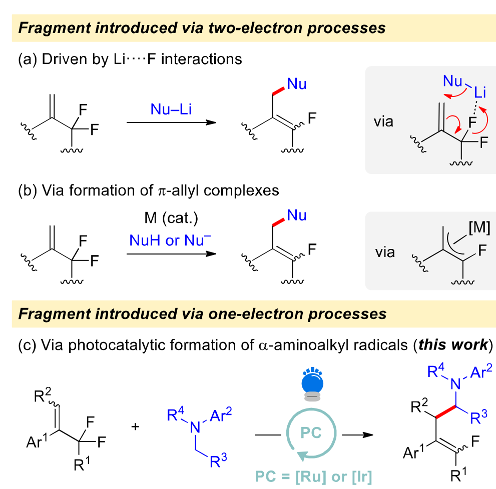
ABSTRACT: A photocatalytic process was devised to synthesize monofluoroalkenes via the defluorinative functionalization of allylic difluorides. *N*-Alkylanilines are used as precursors to α-aminoalkyl radicals, which undergo regioselective addition to allylic difluorides, and subsequent SET and fluoride elimination produce monofluoroalkenes. C–C bond formation on the aniline is site-selective for the least substituted carbon α to nitrogen.

INTRODUCTION

The increasing applications of fluorinated organic molecules as pharmaceuticals,[1] agrochemicals[2] and materials[3] result from the properties fluorine can impart and the stability of the C–F bond. Indeed, fluorine forms the strongest single bond to carbon, with C–F bond strength increasing with the number of geminal fluorine atoms.[4] In parallel, the selective cleavage of C–F bonds[5] is also highly desirable, but partial defluorination is challenging as the product is often more prone to subsequent defluorinative functionalization than the starting material.[5] Typically, this can be accomplished if: (1) the combined electron-withdrawing effect of all initial fluorine atoms is mandatory;[6] (2) functionalization installs a bulky group that prevents additional functionalization;[7] or (3) the carbon bearing the fluorine atoms changes hybridization.[8] The latter applies to the preparation of monofluoroalkenes from allylic difluorides, for example through direct substitution with organolithium reagents (**Scheme 1a**)[8c,d] or substitutions catalyzed by group 10 metals via π-allyl intermediates (Pd, Pt; **Scheme 1b**).[8a,b,f,h,i]

Similarly, structurally-related (trifluoromethyl)alkenes are susceptible to catalytic processes terminated by β-fluoride elimination[9] and to direct nucleophilic substitution with anionic nucleophiles via a carbanion intermediate that expels a fluoride.[10] Additionally, (trifluoromethyl)alkenes are amenable to defluorinative allylic functionalization under photocatalytic conditions.[8g,j,k,l] Inspired by this, we sought to establish a photocatalytic protocol for the preparation of monofluoroalkenes from allylic difluorides, exploiting *N*-alkylanilines[8g] as radical precursors (**Scheme 1c**). The system relies on the addition of an α-aminoalkyl radical to the alkene moiety, SET to generate a carbanion α to the CF_2 group, and fluoride elimination.

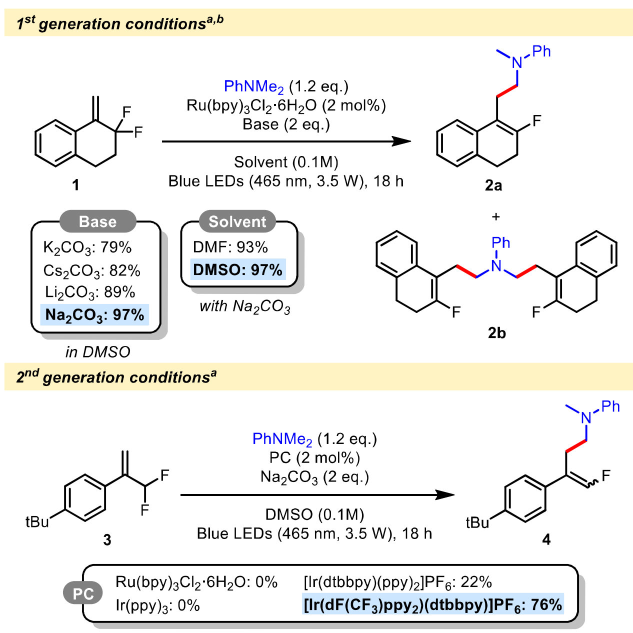
Scheme 1. Defluorinative substitution of allylic difluorides to monofluoroalkenes.



RESULTS AND DISCUSSION

Two key challenges had to be addressed: (1) allylic difluorides have a higher-lying LUMO than (trifluoromethyl)alkenes[11] which may hamper the radical addition step, and (2) exhaustive defluorination had to be avoided. Optimization started with cyclic allylic difluoride **1** and $PhNMe_2$ (**Scheme 2**). Two products of defluorinative α-aminoalkylation were consistently observed, resulting from monoalkylation (**2a**) or competitive dialkylation (**2b**) of $PhNMe_2$. Salient points of the optimization are that $Ru(bpy)_3Cl_2{\cdot}6H_2O$ was a suitable photocatalyst, DMSO was a somewhat better solvent than DMF, and the use of an inorganic base was preferable, with Na_2CO_3 being optimal. However, the catalytic system proved ineffective when applied to acyclic allylic difluoride **3**. Swapping out the photocatalyst for $[Ir(dF(CF_3)ppy_2)(dtbbpy)]PF_6$ unlocked formation of **4** as an mixture of isomers in 76% NMR yield, presumably through more facile reduction of the intermediate benzylic radical. This second-generation system is applicable to both cyclic and acyclic allylic difluorides, and accelerates rates when reactions performed with the Ru photocatalyst are slow or stall at partial conversion.

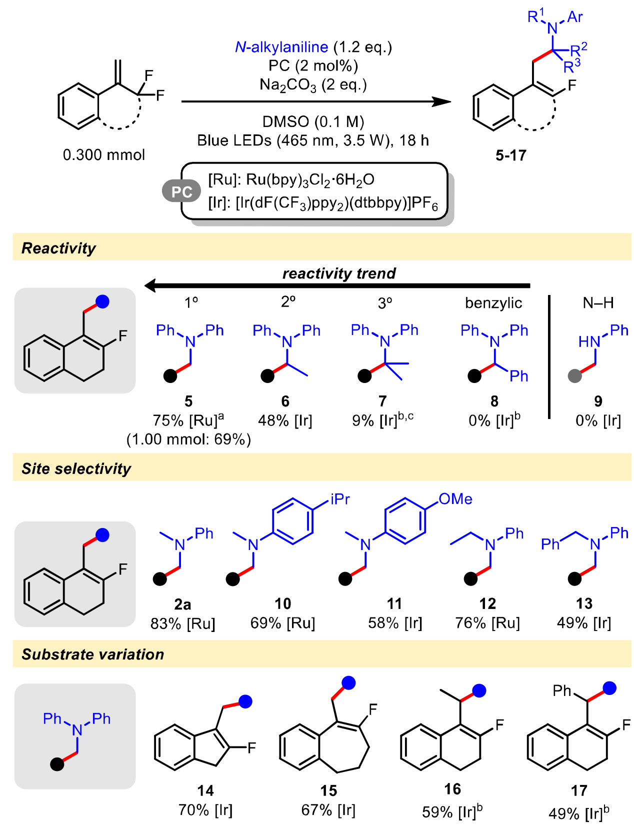
Scheme 2. Key optimization data.



[a] Yields estimated by ^{19}F NMR spectroscopy (internal standard: 2-fluoro-4-nitrotoluene)
[b] Reported yields are a sum of **2a+2b**; ratios reported in the Supporting Information

We first looked at the range of *N*-alkylanilines compatible with the α-aminoalkylation of cyclic allylic difluorides (**Scheme 3**). Diphenylamines provided a single site for functionalization, and the extent of substitution at the site of radical formation dramatically influenced the reaction outcome. With Ph_2NMe (1° site) and the Ru photocatalyst, a 75% yield of **5** was isolated (69% at a 1.00 mmol scale). However, with Ph_2NEt (2° site), an acceptable yield of **6** (48%) was only obtained upon opting for the Ir photocatalyst. Increasing substitution further to a 3° site resulted in very slow formation of **7** (9% after 72 hours), whereas formation of the radical at a benzylic site or in the presence of an N–H bond prevented formation of **8** and **9**, respectively. Overall, the transformation is more facile when a less stable radical is produced (1° > 2° >> 3°). Products of dialkylation can arise when two α-aminoalkyl radicals of equal aptitude can form (see **2a**, **10**, and **11**), and employing a more electron-rich aniline for the formation of **11** benefited from switching to the Ir photocatalyst. The transformation was consistently site-selective for alkylation via the least substituted α-aminoalkyl radical, such as in the formation of monofluoroalkenes **12** (1° vs 2°) and **13** (1° vs benzylic), but the Ir photocatalyst was necessary to achieve high conversion in the latter case.

Scheme 3. α-Aminoalkylation of cyclic allylic difluorides.

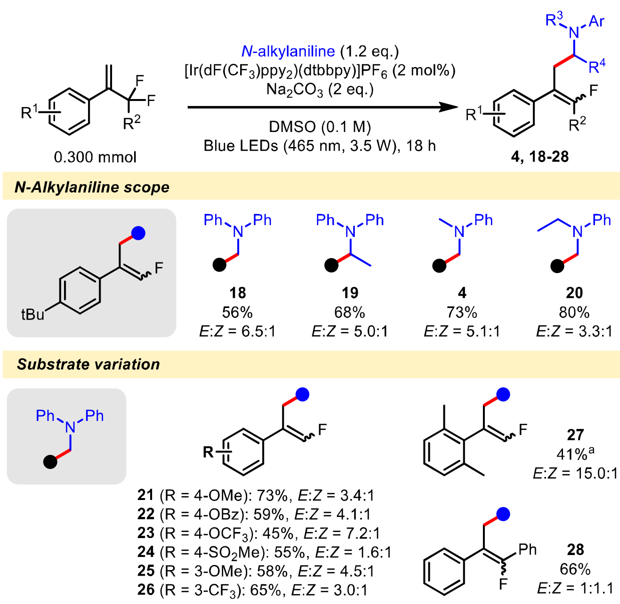


[a] Reaction performed at a 0.400 mmol scale
[b] 72 h instead of 18 h
[c] Yield estimated by ^{19}F NMR spectroscopy (internal standard: 2-fluoro-4-nitrotoluene)

Next, we altered the structure of the cyclic allylic difluoride. With a 5-membered aliphatic ring, the Ru photocatalyst led to slow reaction progress as determined by ^{19}F NMR analysis (62% conversion and 43% yield of **14**); this was resolved upon resorting to the Ir photocatalyst, achieving full conversion and an isolated yield of 70%. Increasing size to a 7-membered ring led to no conversion of the allylic difluoride when using the Ru photocatalyst. Opting for the Ir photocatalyst reinstated the desired reactivity and full conversion, with 67% of **15** being isolated. When 6-membered cyclic allylic difluorides with a substituent on the alkene (Me, Ph) were used, the Ir photocatalyst and prolonged reaction times were required, leading to the isolation of **16** and **17** in 59% and 49% yields, respectively.

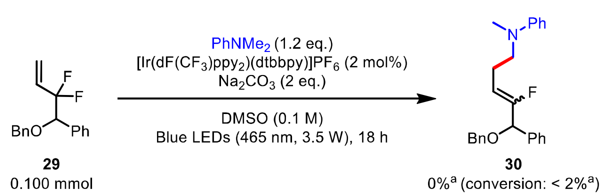
The Ir-catalyzed α-aminoalkylation reaction was further extended to a series of acyclic allylic difluorides (**Scheme 4**). In most cases, mixtures of *E* and *Z* monofluoroalkenes were isolated with the *E* isomer predominating,[12] but some isomers were fully separable (see SI for more information). When different *N*-alkylanilines were reacted with **3**, product formation was achieved in good to high yields when the α-aminoalkyl radical formed at a 1° or 2° site (**18** and **19**) and was site-selective towards 1° sites when multiple sites were available (**4** and **20**). Noteworthy, unlike for cyclic substrates, no dialkylation was concurrent to the formation of **4**. The impact of electronic and steric effects onto the reaction outcome was assessed next. Introduction of *para*-substituents on the 2-aryl group indicated high tolerance of both electron-donating (ether, ester; **21** and **22**) and electron-withdrawing groups (trifluoromethoxy and methylsulfonyl; **23** and **24**), with somewhat higher yields for more electron-rich arenes. Substituents at the *meta* position, whether electron-donating (**25**) or electron-withdrawing (**26**), led to comparably good yields. Steric hindrance from methyl substituents at both *ortho* positions slowed the transformation considerably (about 50% conversion after 72 hours), and 41% of **27** was isolated. To the contrary, positioning a substituent onto the difluoromethyl group (–CF_2Ph) did not considerably slow the reaction, and **28** was isolated in 66% yield. This is the only instance of preferential formation of the *Z* isomer. Finally, the 2-aryl group seems to be essential as no formation of **30** was detected despite using the Ir photocatalyst when the reaction was performed with allylic difluoride[13] **29** (**Scheme 5**).

Scheme 4. α-Aminoalkylation of acyclic allylic difluorides.



[a] Reaction performed for 72 h instead of 18 h

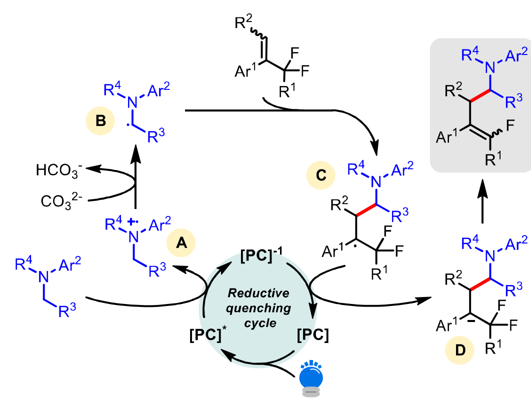
Scheme 5. Failed α-aminoalkylation of allylic difluoride 29.



[a] Estimated by ^{19}F NMR spectroscopy (internal standard: 2-fluoro-4-nitrotoluene)

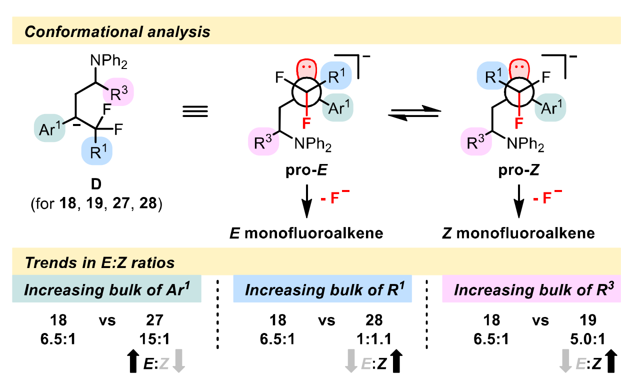
We sought to rationalize the effect the choice of photocatalyst has on the success of the reaction and its correlation with the structure of the allylic difluoride through the mechanism of the reaction (**Scheme 6**). We conjecture that it mirrors the mechanism proposed for reactions of (trifluoromethyl)alkenes under similar conditions,[8g] but that monofluoroalkenes are not susceptible to a subsequent defluorinative event, unlike difluoroalkenes. First, the excited photocatalyst oxidizes the aniline to radical cation **A**, and deprotonation by Na_2CO_3 generates α-aminoalkyl radical **B**. Its regioselective addition onto the allylic difluoride affords intermediate radical **C**, which is reduced to carbanion **D** upon SET from the reduced photocatalyst. Finally, loss of fluoride yields the monofluoroalkene. The exclusive step involving species derived from both the photocatalyst and the allylic difluoride is the reduction of **C** to **D**. This process would be influenced by the extent of resonance stabilization of **C**, itself dependent on planarization of the carbon atom for efficient conjugation with Ar^1. Acyclic substrates would benefit further from this stabilization due to minimization of geometric constraints hampering planarization, and may therefore require a more reducing species[14] for rapid conversion of **C** to **D**.

Scheme 6. Proposed mechanism.



A deeper understanding of the mechanism could also explain the vast range of diastereoselectivities observed for the formation of acyclic monofluoroalkenes, knowing that fluorine must be positioned antiperiplanar to the lone pair of carbanion **D** for elimination (**Scheme 7**). Conformers **pro-*E*** and **pro-*Z*** show that exact arrangement. The sterics of the substituents would affect the relative energies of both conformers, thereby influencing their proportion at equilibrium. In turn, this would impact the relative amounts of *E* and *Z* monofluoroalkenes formed upon loss of fluoride. This correlates with the differences in ratios for the formation of **18** (*E*:*Z* = 6.5:1) compared to those of monofluoroalkenes significantly bulkier at Ar^1 (**27**), R^1 (**28**) or R^3 (**19**). Increasing the bulk of Ar^1 to a 2,6-Me_2-Ph group would further skew the equilibrium towards the **pro-*E*** conformer, increasing the *E*:*Z* ratio to 15:1 for **27**. To the contrary, increasing the bulk of R^1 to a phenyl group (**28**: *E*:*Z* = 1:1.1) or R^3 to a methyl group (**19**: *E*:*Z* = 5.0:1) would shift the equilibrium towards a higher proportion of the **pro-*Z*** conformer, thus producing more *Z* isomer than for **18**. The larger influence of a change to R^1 relative to a change to R^3 correlates with their proximity to the site of C=C bond formation.

Scheme 7. Model for conformational bias directing the *E*:*Z* ratio of acyclic monofluoroalkenes.



The observed *E*:*Z* ratios could also arise from alkene isomerization. A mixture of Ir photocatalyst and **(*E*)-25** in DMSO was irradiated with blue light, but the *E*:*Z* ratio evolved towards a dominance of the Z isomer, ruling out photoisomerization[15] via energy transfer from the excited photocatalyst to the monofluoroalkene as the main influence. In another experiment, using ***(E)*-25** as a stoichiometric additive in the reaction of **1→5** caused its partial isomerization (E:Z = 10.3:1), possibly via reversible addition of a radical to the monofluoroalkene, but the extent of isomerization is insufficient to solely account for the diastereoselectivities. Thus, while photoisomerization must affect the E:Z ratio, conformational bias appears to be the main factor.

CONCLUSION

In summary, the photocatalytic defluorinative α-aminoalkylation of allylic difluorides with *N*-alkylanilines was achieved. This reaction affords monofluoroalkenes, which are isosteres of both amides and enols for medicinal chemistry[16] purposes and beyond, and valuable motifs for further transformations.[17] Mild reaction conditions provide good functional group tolerance. Reactions producing acyclic monofluoroalkenes display a wide range of E:Z ratios mainly accounted for by conformational bias in the fluoride elimination step. Further studies into the diastereoselectivities and ways to rectify diastereomeric ratios towards higher proportions of either E or Z isomers are in progress.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a nitrogen atmosphere. THF, DCM, toluene, MeCN, and benzene were purified using an MBraun solvent purification system (SPS). All other commercially available compounds were used as received. Vials (4-mL and 20-mL, Fisher Scientific) used to perform reactions were capped with Qorpak thermoset PTFE caps. Photoirradiation was carried out with a Lumidox® II LumLamp (3.5 W, 465 nm; commercially sold as 470-Blue LEDs with a 15-degree narrow spot beam reflector and a quartz lens). Thin layer chromatography (TLC) analysis of reaction mixtures was performed using Silicycle silica gel 60 Å F254 TLC plates, and the plates were visualized under UV light or by staining with potassium permanganate. Flash column chromatography was carried out on Silicycle silica gel 60 Å, 230-400 mesh. ^{1}H, ^{13}C{^{1}H} and ^{19}F NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 at room temperature using a Bruker Avance II (300 MHz for ^{1}H, 282 MHz for ^{19}F) or Avance III (700 MHz for ^{1}H, 659 MHz for ^{19}F, 176 MHz for ^{13}C{^{1}H}) NMR spectrometer. ^{1}H and ^{13}C{^{1}H} NMR chemical shifts are reported downfield of tetramethylsilane and are respectfully referenced to tetramethylsilane (δ = 0.00 ppm) and solvent ($CDCl_3$: δ = 77.16 ppm; DMSO-d_6: δ = 39.52). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, sept. = septet, m = multiplet. Infrared spectra were recorded using an Agilent Cary 630 FT-IR spectrometer. High-resolution mass spectra were obtained on a Thermo Scientific Orbitrap Fusion mass spectrometer using electrospray ionization (ESI).

General Procedure for the α-Aminoalkylation of Allylic Difluorides. A vial was charged with an allylic difluoride (1 eq.; 0.3-1.0 mmol), followed by the photocatalyst (2 mol%) and Na_2CO_3 (eq.). The *N*-alkylaniline (1.2 eq.) was dissolved in dry DMSO (0.1 M), and this solution was added to the vial. The vial was capped and the reaction mixture was irradiated with LED light (465 nm, 3.5 W) for 18-72 hours. The reaction was quenched with 0.1 M NaOH and extracted with ethyl acetate (x2). The combined organic layers were washed with water (x3) and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure. Product was purified by flash chromatography.

*N-(2-(2-Fluoro-3,4-dihydronaphthalen-1-yl)ethyl)-N-methylaniline **(2a)***. On a 0.300 mmol scale, the product (70.0 mg, 83%) was isolated as a colourless oil by flash chromatography using 15% DCM, 15% toluene and 70% hexanes. IR (ATR, diamond) v = 3060, 3019, 2937, 2885, 1677, 1599, 1505, 1330, 1125, 651 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.25-7.20 (m, 4H), 7.13-7.09 (m, 2H), 6.73 (d, 2H, J = 8.0 Hz), 6.68 (t, 1H, J = 7.3 Hz), 3.48 (m, 2H), 2.97 (s, 3H), 2.88 (td, 2H, J = 8.2, 2.6 Hz), 2.76 (m, 2H), 2.50 (dt, 2H, J = 4.8, 8.3 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -102.8 (s, 1F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 159.8 (d, J_{CF} = 266 Hz), 149.1, 134.3 (d, J_{CF} = 7.0 Hz), 133.3, 129.3, 127.6, 126.7, 126.2 (d, J_{CF} = 2.1 Hz), 122.4 (d, J_{CF} = 6.6 Hz), 116.2, 112.2, 111.9 (d, J_{CF} = 14.1 Hz), 51.3 (d, J_{CF} = 2.0 Hz), 38.1, 28.9 (d, J_{CF} = 7.3 Hz), 24.9 (d, J_{CF} = 24.9 Hz), 20.9 (d, J_{CF} = 3.9 Hz); HRMS calcd for $C_{19}H_{21}FN$ $[M+H]^+$ 282.1653, found 282.1663.

*N-(3-(4-(tert-Butyl)phenyl)-4-fluorobut-3-en-1-yl)-N-methylaniline **(4)***. On a 0.300 mmol scale, the product (68.2 mg, 73%, E:Z = 5.1:1) was isolated as a white solid by flash chromatography using 15% DCM, 15% toluene and 70% hexanes. The crude reaction mixture presented an E:Z ratio of 3.8:1. IR (ATR, diamond) v = 3026, 2959, 2866, 1654, 1599, 1505, 1360, 1099, 749, 680 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.37 (dt, 2H, J = 8.7, 2.2 Hz), 7.24-7.19 (m, 4H), 6.85 (d, 1H, E isomer, J = 84.9 Hz), 6.70-6.66 (m, 3H), 6.61 (d, 1H, Z isomer, J = 85.4 Hz), 3.41 (m, 2H, E isomer), 3.36 (m, 2H, Z isomer), 2.93 (s, 3H, E isomer), 2.89 (s, 3H, Z isomer), 2.78 (td, 2H, E isomer, J = 8.2, 2.9 Hz), 2.54 (td, 2H, Z isomer, J = 8.3, 3.9 Hz), 1.35 (s, 9H, Z isomer), 1.34 (s, 9H, E isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -129.3 (dt, 1F, Z isomer, J = 84.2, 3.6 Hz), -130.2 (dt, 1F, E isomer, J = 85.2, 3.0 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 150.9, 150.7, 149.0, 148.8, 146.7 (d, E isomer, J_{CF} = 260 Hz), 144.9 (d, Z isomer, J_{CF} = 264 Hz), 133.2 (d, J_{CF} = 9.0 Hz), 131.3, 129.33 (d, J_{CF} = 7.6 Hz), 129.31, 127.9 (d, J_{CF} = 4.4 Hz), 126.3 (d, J_{CF} = 2.0 Hz), 125.8, 125.5, 122.4 (d, J_{CF} = 9.2 Hz), 119.8, 116.27, 116.25, 112.3, 112.2, 51.8 (d, Z isomer, J_{CF} = 3.8 Hz), 51.1 (d, E isomer, J_{CF} = 2.5 Hz), 38.7 (Z isomer), 38.2 (E isomer), 34.73 (Z isomer), 34.68 (E isomer), 31.4 (E isomer), 29.9 (Z isomer), 27.6 (d, Z isomer, J_{CF} = 5.4 Hz), 24.2 (d, E isomer, J_{CF} = 3.3 Hz); HRMS calcd for $C_{21}H_{27}FN$ $[M+H]^+$ 312.2122, found 312.2122.

*N-(2-(2-Fluoro-3,4-dihydronaphthalen-1-yl)ethyl)-N-phenylaniline **(5)***. On a 0.400 mmol scale, the desired product (103 mg, 75%) was isolated as a pale yellow oil by flash chromatography using 10% DCM in hexanes. IR (ATR, diamond) v = 3019, 2937, 2836, 1677, 1587, 1490, 1364, 1165, 1110, 751 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.28-7.26 (m, 4H), 7.13 (td, 1H, J = 7.2, 2.4 Hz), 7.10-7.07 (m, 2H), 7.05 (d, 4H, J = 7.7 Hz), 7.03 (d, 1H, J = 7.6 Hz), 6.95 (t, 2H, J = 7.3 Hz), 3.85 (m, 2H), 2.91-2.86 (m, 4H), 2.52 (dt, 2H, J = 4.6, 8.5 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -102.2 (s, 1F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 159.9 (d, J_{CF} = 267 Hz), 147.9, 134.1 (d, J_{CF} = 6.9 Hz), 133.3, 129.4, 127.7, 126.9, 126.2 (d, J_{CF} = 2.1 Hz), 122.5 (d, J_{CF} = 6.5 Hz), 121.4, 121.0, 111.8 (d, J_{CF} = 14.0 Hz), 50.8 (d, J_{CF} = 2.1 Hz), 28.9 (d, J_{CF} = 7.3 Hz), 24.9 (d, J_{CF} = 24.9 Hz), 22.1 (d, J_{CF} = 2.8 Hz); HRMS calcd for $C_{24}H_{23}FN$ $[M+H]^+$ 344.1804, found 344.1812.

*N-(1-(2-Fluoro-3,4-dihydronaphthalen-1-yl)propan-2-yl)-N-phenylaniline **(6)***. On a 0.300 mmol scale, the desired product

(51.5 mg, 48%) was isolated as a white solid by flash chromatography using 20% DCM in hexanes. IR (ATR, diamond) v = 3030, 2974, 2937, 1677, 1587, 1490, 1449, 1210, 751, 692 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.29-7.26 (m, 4H), 7.22 (m, 1H), 7.18 (td, 1H, J = 6.6, 2.0 Hz), 7.13-7.10 (m, 2H), 6.99 (tt, 2H, J = 7.4, 1.1 Hz), 6.91 (dt, 4H, J = 7.5, 1.1 Hz), 4.40 (m, 1H), 2.95 (m, 1H), 2.89-2.84 (m, 2H), 2.64 (m, 1H), 2.56-2.45 (m, 2H), 1.15 (d, 3H, J = 7.0 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -105.7 (s, 1F); $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) δ 159.9 (d, J_{CF} = 267 Hz), 146.5, 134.3 (d, J_{CF} = 7.2 Hz), 133.5, 129.4, 127.7, 126.8, 126.2 (d, J_{CF} = 1.9 Hz), 123.1, 123.0 (d, J_{CF} = 6.6 Hz), 121.8, 112.0 (d, J_{CF} = 13.8 Hz), 51.5 (d, J_{CF} = 1.8 Hz), 29.8 (d, J_{CF} = 3.3 Hz), 29.0 (d, J_{CF} = 7.2 Hz), 25.0 (d, J_{CF} = 25.3 Hz), 18.4; HRMS calcd for $C_{25}H_{25}FN$ $[M+H]^+$ 358.1966, found 358.1972.

*N-(2-(2-Fluoro-3,4-dihydronaphthalen-1-yl)ethyl)-4-isopropyl-N-methylaniline **(10)***. On a 0.300 mmol scale, the desired product (67.0 mg, 69%) was isolated as a yellow oil by flash chromatography using 15% DCM, 15% toluene and 70% hexanes. IR (ATR, diamond) v = 2922, 2855, 1613, 1520, 1461, 1364, 1160, 821, 750, 712 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.25 (m, 1H), 7.23-7.21 (m, 1H), 7.12 (d, 2H, J = 3.9 Hz), 7.09 (dt, 2H, J = 8.6, 1,9 Hz), 6.70 (dt, 2H, J = 8.8, 2.2 Hz), 3.45 (m, 2H), 2.97 (s, 3H), 2.89 (td, 2H, J = 8.5, 2.9 Hz), 2.82 (sept., 1H, J = 6.8 Hz), 2.76 (t, 2H, J = 7.8 Hz), 2.50 (dt, 2H, J = 5.1, 8.4 Hz), 1.22 (d, 6H, J = 7.1 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -102.9 (s, 1F); $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) δ 159.7 (d, J_{CF} = 266 Hz), 147.4, 136.7, 134.3 (d, J_{CF} = 7.1 Hz), 133.4, 127.7, 127.2, 126.9, 126.1 (d, J_{CF} = 2.0 Hz), 122.5 (d, J_{CF} = 6.6 Hz), 112.5, 112.0 (d, J_{CF} = 14.4 Hz), 51.6 (d, J_{CF} = 2.0 Hz), 38.2, 33.2, 28.9 (d, J_{CF} = 7.3 Hz), 24.9 (d, J_{CF} = 24.9 Hz), 24.4, 21.0 (d, J_{CF} = 4.2 Hz); HRMS calcd for $C_{22}H_{27}FN$ $[M+H]^+$ 324.2122, found 324.2133.

*N-(2-(2-Fluoro-3,4-dihydronaphthalen-1-yl)ethyl)-4-methoxy-N-methylaniline **(11)***. On a 0.300 mmol scale, the desired product (54.4 mg, 58%) was isolated as a white solid by flash chromatography using 7.5% ethyl acetate in hexanes. IR (ATR, diamond) v = 3056, 2899, 2829, 1677, 1505, 1449, 1244, 1036, 816, 765 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.21 (d, 2H, J = 3.0 Hz), 7.11 (d, 2H, J = 3.0 Hz), 6.83 (dt, 2H, J = 10.6, 3.8 Hz), 6.72 (dt, 2H, J = 10.6, 3.8 Hz), 3.77 (s, 3H), 3.41 (m, 2H), 2.93 (s, 3H), 2.90 (td, 2H, J = 8.4, 2.8 Hz), 2.76 (t, 2H, J = 8.0 Hz), 2.51 (dt, 2H, J = 4.8, 8.4 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ 103.0 (ttt, 1F, J = 5.0, 2.5, 2.5 Hz); $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) δ 159.6 (d, J_{CF} = 266 Hz), 151.6, 144.1, 134.3 (d, J_{CF} = 7.1 Hz), 133.3, 127.7, 126.9, 126.1 (d, J_{CF} = 2.1 Hz), 122.5 (d, J_{CF} = 6.7 Hz), 114.9, 114.4, 112.0 (d, J_{CF} = 14.2 Hz), 56.0, 52.3 (d, J_{CF} = 2.1 Hz), 38.8, 28.9 (d, J_{CF} = 7.2 Hz), 24.9 (d, J_{CF} = 24.9 Hz), 20.7 (d, J_{CF} = 3.9 Hz); HRMS calcd for $C_{20}H_{23}FNO$ $[M+H]^+$ 312.1758, found 312.1754.

*N-Ethyl-N-(2-(2-fluoro-3,4-dihydronaphthalen-1-yl)ethyl)aniline **(12)***. On a 0.300 mmol scale, the desired product (67.3 mg, 76%) was isolated as a colourless oil by flash chromatography using 5% ethyl acetate in hexanes. IR (ATR, diamond) v = 3060, 3019, 2926, 1677, 1595, 1505, 1449, 1340, 1148, 739 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.26 (d, 1H, J = 7.6 Hz), 7.24-7.22 (m, 3H), 7.13 (m, 2H), 6.75 (d, 2H, J = 8.1 Hz), 6.66 (t, 1H, J = 7.2 Hz), 3.42 (dd, 2H, J = 7.8, 6.5 Hz), 3.41 (q, 2H, J = 7.2 Hz), 2.94 (td, 2H, J = 8.4, 2.7 Hz), 2.78 (td, 2H, J = 8.2, 2.2 Hz), 2.26 (dt, 2H, J = 5.0, 8.4 Hz), 1.19 (t, 3H, J = 7.1 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -102.6 (s, 1F); $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) δ 159.7 (d, J_{CF} = 267 Hz), 147.8, 134.3 (d, J_{CF} = 6.6 Hz), 133.3, 129.5, 127.7, 126.9, 126.2 (d, J_{CF} = 2.3 Hz), 122.5 (d, J_{CF} = 5.9 Hz), 115.7, 112.1 (d, J_{CF} = 14.4 Hz), 112.0, 49.2 (d, J_{CF} = 2.2 Hz), 44.9, 29.0 (d, J_{CF} = 7.6 Hz), 24.9 (d, J_{CF} = 24.9 Hz), 22.0 (d, J_{CF} = 3.8 Hz), 12.6; HRMS calcd for $C_{20}H_{23}FN$ $[M+H]^+$ 296.1809, found 296.1811.

*N-Benzyl-N-(2-(2-fluoro-3,4-dihydronaphthalen-1-yl)ethyl)aniline **(13)***. On a 0.300 mmol scale, the desired product (52.5 mg, 49%) was isolated as a yellow oil by flash chromatography using 20% DCM in hexanes. IR (ATR, diamond) v = 3026, 2940, 2885, 1677, 1595, 1502, 1356, 1131, 721, 694 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.30 (t, 2H, J = 7.3 Hz), 7.26-7.21 (m, 3H), 7.20 (t, 2H, J = 8.0 Hz), 7.16 (td, 1H, J = 6.6, 2.9 Hz), 7.10 – 7.08 (m, 3H), 6.77 (d, 2H, J = 8.4 Hz), 6.69 (t, 1H, J = 7.5 Hz), 4.58 (s, 2H), 3.55 (dd, 2H, J = 9.0, 6.8 Hz), 2.90 (dt, 2H, J = 8.5, 2.7 Hz), 2.84 (t, 2H, J = 8.10 Hz), 2.51 (dt, 2H, J = 4.8, 8.4 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -102.5 (s, 1F); $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) δ 159.8 (d, J_{CF} = 267 Hz), 148.5, 139.1, 134.2 (d, J_{CF} = 6.8 Hz), 133.3, 129.4, 128.7, 127.7, 127.0, 126.90, 126.87, 126.2 (d, J_{CF} = 2.0 Hz), 122.5 (d, J_{CF} = 6.7 Hz), 116.4, 112.3, 111.9 (d, J_{CF} = 14.0 Hz), 54.4, 49.9 (d, J_{CF} = 2.0 Hz), 28.9 (d, J_{CF} = 7.2 Hz), 24.9 (d, J_{CF} = 24.9 Hz), 21.7 (d, J_{CF} = 3.9 Hz); HRMS calcd for $C_{25}H_{25}FN$ $[M+H]^+$ 358.1966, found 358.1965.

*N-(2-(2-Fluoro-1H-inden-3-yl)ethyl)-N-phenylaniline **(14)***. On a 0.300 mmol scale, the desired product (69.2 mg, 70%) was isolated as a pale yellow oil by flash chromatography using 15% DCM, 15% toluene and 70% hexanes. IR (ATR, diamond) v = 3022, 2922, 1666, 1587, 1490, 1364, 1237, 1181, 745, 693 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.30 (d, 1H, J = 7.4 Hz), 7.27 (t, 4H, J = 7.8 Hz), 7.24 (d, 1H, J = 7.8 Hz), 7.15 (t, 1H, J = 7.6 Hz), 7.11 (d, 1H, J = 7.5 Hz), 7.04 (d, 4H, J = 7.9 Hz), 6.96 (t, 2H, J = 7.4 Hz), 3.98 (t, 2H, J = 8.3 Hz), 3.42 (s, 2H), 2.85 (t, 2H, J = 7.8 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -126.1 (s, 1F); $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) δ 163.8 (d, J_{CF} = 280 Hz), 147.67 143.1 (d, J_{CF} = 7.5 Hz), 135.2 (d, J_{CF} = 8.1 Hz), 129.5, 126.9, 124.5 (d, J_{CF} = 4.5 Hz), 123.8, 121.5, 120.9, 118.8 (d, J_{CF} = 6.9 Hz), 115.8 (d, J_{CF} = 11.1 Hz), 50.3 (d, J_{CF} = 3.0 Hz), 35.0 (d, J_{CF} = 21.3 Hz), 21.4. HRMS calcd for $C_{23}H_{21}FN$ $[M+H]^+$ 330.1653, found 330.1646.

N-(2-(8-Fluoro-6,7-dihydro-5H-benzo[7]annulen-9-yl)ethyl)-N-phenylaniline **(15)**. On a 0.300 mmol scale, the desired product (72.1 mg, 67%) was isolated as a pale yellow oil by flash chromatography using 5% DCM, 5% toluene and 90% hexanes. IR (ATR, diamond) v = 3022, 2929, 2858, 1673, 1587, 1490, 1356, 1140, 745, 693 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.24-7.22 (m, 6H), 7.18-7.15 (m, 2H), 6.96 (d, 4H, J = 7.8 Hz), 6.93 (t, 2H, J = 7.3 Hz), 3.73 (t, 2H, J = 7.9 Hz), 2.89 (m, 2H), 2.60 (t, 2H, J = 6.1 Hz), 2.20-2.16 (m, 4H); ^{19}F NMR (659 MHz, $CDCl_3$) δ -96.9 (m, 1F); $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$) δ 159.7 (d, J_{CF} = 262 Hz), 147.8, 140.9, 138.0 (d, J_{CF} = 9.5 Hz), 129.4, 126.9 (d, J_{CF} = 4.8 Hz), 126.8, 126.5, 122.9, 121.3, 120.9, 114.2 (d, J_{CF} = 17.1 Hz), 50.2 (d, J_{CF} = 2.4 Hz), 33.2, 32.4, 27.5 (d, J_{CF} = 27.8 Hz), 26.8 (d, J_{CF} = 3.8 Hz); HRMS calcd for $C_{25}H_{25}FN$ $[M+H]^+$ 358.1966, found 358.1960.

*N-(2-(2-Fluoro-3,4-dihydronaphthalen-1-yl)propyl)-N-phenylaniline **(16)***. The title compound was synthesized following general procedure D using allylic difluoride **S27** and *N*-methyl-*N*-phenylaniline, except the reaction was run for 72 hours. On a 0.300 mmol scale, the desired product (63.2 mg, 59%) was isolated as a yellow oil by flash chromatography using 2.5% DCM, 2.5% toluene and 95% hexanes. IR (ATR, diamond) v = *3022, 2937, 2877, 1669, 1587, 1490, 1218, 1148,* *728, 692 cm^{-1};* ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.24-7.19 (m, 4H), 7.10-7.05 (m, 4H), 6.97 (d, 4H, *J* = 8.2 Hz), 6.91 (t, 2H, *J* = 7.3 Hz), 4.11 (dd, 1H, *J* = 14.8, 6.6 Hz), 4.02 (dd, 1H, *J* = 14.8, 7.8 Hz), 3.27 (m, 1H), 2.82 (m, 2H), 2.42 (m, 1H), 2.34 (m, 1H), 1.35 (d, 3H, *J* = 7.1 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -98.5 (s, 1F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 160.6 (d, J_{CF} = 268 Hz), 148.5, 135.0 (d, J_{CF} = 9.1 Hz), 133.4, 129.3, 127.5, 126.8, 126.0, 123.0 (d, J_{CF} = 6.3 Hz), 121.21, 121.15, 117.2 (d, J_{CF} = 11.3 Hz), 56.5 (d, J_{CF} = 5.1 Hz), 31.0, 29.1 (d, J_{CF} = 6.9 Hz), 25.6 (d, J_{CF} = 25.2 Hz), 17.4 (d, J_{CF} = 3.6 Hz); HRMS calcd for $C_{25}H_{25}FN$ $[M+H]^+$ 358.1966, found 358.1961.

*N-(2-(2-Fluoro-3,4-dihydronaphthalen-1-yl)-2-phenylethyl)-N-phenylaniline **(17)***. On a 0.300 mmol scale, the desired product (61.7 mg, 49%) was isolated as a yellow solid by flash chromatography using 10% DCM, 10% toluene and 80% hexanes. IR (ATR, diamond) *v* = 3060, 2944, 2892, 1669, 1587, 1490, 1207, 1148, 731, 695 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.36 (d, 2H, *J* = 7.6 Hz), 7.29 (t, 2H, *J* = 7.9 Hz), 7.21 (tt, 1H, *J* = 7.4, 1.1 Hz), 7.17-7.13 (m, 4H), 7.07-6.97 (m, 4H), 6.88 (tt, 2H, *J* = 7.3, 1.0 Hz), 6.79 (dd, 4H, *J* = 8.6, 1.0 Hz), 4.61 (dd, 1H, *J* = 14.0, 5.7 Hz), 4.43-4.36 (m, 2H), 2.91 (m, 1H), 2.82 (m, 1H), 2.56 (m, 1H), 2.45 (m, 1H); ^{19}F NMR (659 MHz, $CDCl_3$) δ -96.5 (s, 1F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 160.9 (d, J_{CF} = 269 Hz), 148.4, 142.1 (d, J_{CF} = 2.2 Hz), 134.9 (d, J_{CF} = 8.7 Hz), 133.5, 129.2, 128.7, 128.3 (d, J_{CF} = 1.6 Hz), 127.4, 126.8 (d, J_{CF} = 1.9 Hz), 126.1 (d, J_{CF} = 1.5 Hz), 123.6 (d, J_{CF} = 6.3 Hz), 121.3, 115.0 (d, J_{CF} = 11.6 Hz), 56.8 (d, J_{CF} = 8.7 Hz), 42.2, 29.0 (d, J_{CF} = 6.9 Hz), 25.7 (d, J_{CF} = 25.7 Hz); HRMS calcd for $C_{30}H_{27}FN$ $[M+H]^+$ 420.2122, found 420.2117.

*N-(3-(4-(tert-Butyl)phenyl)-4-fluorobut-3-en-1-yl)-N-phenylaniline **(18).*** On a 0.300 mmol scale, the desired product (62.8 mg, 56% *E*:*Z* = 6.5:1) was isolated as a colourless oil by flash chromatography using 20% DCM in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 4.3:1. IR (ATR, diamond) *v* = 3034, 2959, 1654, 1587, 1490, 1255, 1102, 817, 749, 696 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.38-6.91 (m, 17H), 6.84 (d, 1H, *E* isomer, *J* = 85.1 Hz), 6.69 (d, 1H, *Z* isomer, *J* = 85.2 Hz), 3.78 (t, 2H, *E* isomer, *J* = 8.0 Hz), 3.72 (t, 2H, *Z* isomer, *J* = 7.7 Hz), 2.89 (td, 2H, *E* isomer, *J* = 7.5, 2.8 Hz), 2.62 (m, 2H, *Z* isomer), 1.33 (s, 9H, *Z* isomer), 1.32 (s, 9H, *E* isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -129.4 (dt, 1F, *Z* isomer, *J* = 85.1, 2.4 Hz), -129.8 (dt, 1F, *E* isomer, *J* = 84.9, 2.8 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 150.8, 150.7, 149.2, 147.7, 146.8 (d, *E* isomer, J_{CF} = 260 Hz), 146.4 (d, *Z* isomer, J_{CF} = 261 Hz), 133.1 (d, J_{CF} = 9.1 Hz), 132.6 (d, J_{CF} = 8.8 Hz), 129.4, 129.3, 129.0, 128.9, 127.9 (d, J_{CF} = 4.3 Hz), 126.3 (d, J_{CF} = 2.9 Hz), 125.8, 125.4, 123.2 (d, J_{CF} = 9.1 Hz), 122.2 (d, J_{CF} = 9.2 Hz), 121.4, 121.0, 51.2 (d, *Z* isomer, J_{CF} = 4.2 Hz), 50.6 (d, *E* isomer, J_{CF} = 2.5 Hz), 34.70 (d, *Z* isomer, J_{CF} = 9.3 Hz), 34.65 (d, *E* isomer, J_{CF} = 6.6 Hz), 31.5 (*Z* isomer), 31.4 (*E* isomer), 28.5 (d, *Z* isomer, J_{CF} = 5.5 Hz), 25.4 (d, *E* isomer, J_{CF} = 3.2 Hz); HRMS calcd for $C_{26}H_{29}FN$ $[M+H]^+$ 374.2279, found 374.2278.

*N-(4-(4-(tert-Butyl)phenyl)-5-fluoropent-4-en-2-yl)-N-phenylaniline **(19)***. On a 0.300 mmol scale, the desired product (79.2 mg, 68%, *E*:*Z* = 5.0:1) was isolated as a white solid by flash chromatography using 5% DCM, 5% toluene and 90% hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 5.9:1. IR (ATR, diamond) *v* = 3056, 2959, 2862, 1666, 1587, 1494, 1274, 1103, 733, 688 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.38 (dt, 2H, *J* = 9.1, 2.6 Hz), 7.24-7.21 (m, 6H), 6.98 (dt, 2H, *J* = 7.4, 1.0 Hz), 6.79 (dd, 4H, *J* = 8.6, 1.0 Hz), 6.77 (d, 1H, *E* isomer, *J* = 85.4 Hz), 6.50 (d, 1H, *Z* isomer, *J* = 84.7 Hz), 4.14 (m, 1H, *E* isomer), 4.08 (m, 1H, *Z* isomer), 2.91 (dt, 1H, *E* isomer, *J* = 13.5, 3.6 Hz), 2.86 (dt, 1H, *Z* isomer, *J* = 13.2, 4.4 Hz), 2.67 (m, 1H, *E* isomer), 2.08 (dd, 1H, *Z* isomer, *J* = 14.4, 9.8 Hz), 1.36 (s, 9H, *Z* isomer), 1.34 (s, 9H, *E* isomer), 1.10 (d, 3H, *Z* isomer, *J* = 6.6 Hz), 1.08 (d, 3H, *E* isomer, *J* = 6.6 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -129.0 (d, 1F, *E* isomer, *J* = 85.4 Hz), -130.2 (dd, 1F, *Z* isomer, *J* = 84.7, 6.0 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 151.0, 150.8, 146.7 (d, *E* isomer, J_{CF} = 261 Hz), 146.25, 146.24, 144.9 (d, *Z* isomer, J_{CF} = 263 Hz), 132.0 (d, J_{CF} = 9.2 Hz), 131.4, 129.31, 129.30, 128.1 (d, J_{CF} = 3.5 Hz), 127.0 (d, J_{CF} = 2.8 Hz), 125.7, 125.5, 123.01, 122.95, 122.7 (d, J_{CF} = 8.6 Hz), 121.9, 121.8, 120.2 (d, J_{CF} = 2.2 Hz), 50.9 (d, *E* isomer, J_{CF} = 2.8 Hz), 50.5 (d, *Z* isomer, J_{CF} = 3.7 Hz), 36.3 (d, *Z* isomer, J_{CF} = 4.7 Hz), 34.8 (*Z* isomer), 34.7 (*E* isomer), 32.6 (d, *E* isomer, J_{CF} = 2.3 Hz), 31.5 (*E* isomer), 29.9 (*Z* isomer), 18.5 (*E* isomer), 18.4 (*Z* isomer); HRMS calcd for $C_{27}H_{31}FN$ $[M+H]^+$ 388.2435, found 388.2435.

*N-(3-(4-(tert-Butyl)phenyl)-4-fluorobut-3-en-1-yl)-N-ethylaniline **(20)***. On a 0.300 mmol scale, the desired product (77.8 mg, 80%, *E*:*Z* = 3.3:1) was isolated by flash chromatography using 15% DCM, 15% toluene and 70% hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 3.0:1. **(*E*)-20**: Colourless oil; IR (ATR, diamond) *v* = 3030, 2963, 2870, 1654, 1595, 1505, 1360, 1105, 741, 681 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.38 (dt, 2H, *J* = 8.4, 1.8 Hz), 7.26-7.23 (m, 2H), 7.20 (m, 2H), 6.86 (d, 1H, *J* = 85.1 Hz), 6.66 (d, 2H, *J* = 8.8 Hz), 6.65 (t, 1H, *J* = 7.2 Hz), 3.36 (q, 2H, *J* = 7.1 Hz), 3.34 (m, 2H), 2.80 (td, 2H, *J* = 8.3, 2.9 Hz), 1.34 (s, 3H), 1.14 (t, 3H, *J* = 7.0 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -130.2 (dt, 1F, *J* = 85.4, 2.9 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 150.9, 147.7, 146.8 (d, J_{CF} = 260 Hz), 133.3 (d, J_{CF} = 9.2 Hz), 129.4, 126.3 (d, J_{CF} = 2.7 Hz), 125.8, 122.5 (d, J_{CF} = 9.4 Hz), 115.7, 111.9, 49.0 (d, J_{CF} = 2.1 Hz), 44.9, 34.7, 31.5, 25.3 (d, J_{CF} = 2.5 Hz), 12.6; HRMS calcd for $C_{22}H_{29}FN$ $[M+H]^+$ 326.2279, found 326.2280. **(*Z*)-20**: Colourless oil; IR (ATR, diamond) *v* = 3030, 2959, 2866, 1658, 1595, 1505, 1360, 1099, 740, 694 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.43-7.38 (m, 4H), 7.20 (m, 2H), 6.65 (t, 1H, *J* = 7.4 Hz), 6.64 (d, 1H, *J* = 84.3 Hz), 6.61 (d, 2H, *J* = 7.9 Hz), 3.31 (q, 2H, *J* = 7.1 Hz), 3.29 (m, 2H), 2.54 (m, 2H), 1.35 (s, 9H), 1.10 (t, 3H, *J* = 7.0 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -129.9 (dt, 1F, *J* = 84.2, 3.4 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 150.7, 147.5, 144.8 (d, J_{CF} = 264 Hz), 131.4, 129.4, 127.9 (d, J_{CF} = 4.4 Hz), 125.5, 119.9, 115.8, 112.0, 49.8 (d, J_{CF} = 4.0 Hz), 45.3, 34.7, 31.4, 28.4 (d, J_{CF} = 5.2 Hz), 12.6; HRMS calcd for $C_{22}H_{29}FN$ $[M+H]^+$ 326.2279, found 326.2281.

*N-(4-Fluoro-3-(4-methoxyphenyl)but-3-en-1-yl)-N-phenylaniline **(21)***. On a 0.300 mmol scale, the desired product (76.1 mg, 73%, *E*:*Z* = 3.4:1) was isolated as a colourless oil by flash chromatography using 2.5% ethyl acetate in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 3.5:1. IR (ATR, diamond) *v* = 3034, 2955, 1654, 1587, 1490, 1239, 1095, 1020, 749, 685 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.30-6.84 (m, 14H), 6.77 (d, 1H, *E* isomer, *J* = 85.4 Hz), 6.58 (d, 1H, *Z* isomer, *J* = 84.2 Hz), 3.82 (s, 3H, *Z* isomer), 3.81 (s, 3H, *E* isomer), 3.75 (t, 2H, *E* isomer, *J* = 8.1 Hz), 3.71 (t, 2H, *Z* isomer, *J* = 7.5 Hz), 2.87 (td, 2H, *E* isomer, *J* = 8.0, 2.8 Hz), 2.60 (m, 2H, *Z* isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -130.57 (d, 1F, *E* isomer, *J* = 84.9 Hz), -130.59 (d, 1F, *Z* isomer, *J* = 84.5 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 159.4, 159.0, 147.7, 146.2 (d, *E* isomer, J_{CF} = 259 Hz), 144.6 (d, *Z* isomer, J_{CF} = 263 Hz), 143.2, 129.48, 129.46, 129.39, 128.3 (d, J_{CF} = 9.0 Hz), 127.8 (d, J_{CF} = 2.9 Hz), 122.0 (d, J_{CF} = 9.3 Hz), 121.5, 121.4, 121.1, 121.04, 120.95, 117.9, 114.3, 113.9, 55.44 (*E* isomer), 55.40 (*Z* isomer), 51.2 (d, *Z* isomer, J_{CF} = 4.1 Hz), 50.5 (d, *E* isomer, J_{CF} = 2.5 Hz), 28.6 (d, *Z* isomer, J_{CF} = 5.3 Hz), 25.5 (d, *E* isomer, J_{CF} = 3.2 Hz); HRMS calcd for $C_{23}H_{23}FNO$ $[M+H]^+$ 348.1758, found 348.1763.

4-(4-(Diphenylamino)-1-fluorobut-1-en-2-yl)phenyl benzoate ***(22)***. On a 0.300 mmol scale, the desired product (77.4 mg, 59%, *E*:*Z* = 4.1:1) was isolated as a yellow solid by flash chromatography using 10% ethyl acetate in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 4.8:1. IR (ATR, diamond) ν = 3037, 2922, 1733, 1654, 1587, 1490, 1200, 1058, 749, 690 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.21 (d, 2H, *J* = 7.3 Hz), 7.65 (t, 1H, *J* = 7.5 Hz), 7.52 (t, 2H, *J* = 7.0 Hz), 7.41-6.91 (m, 14H), 6.84 (d, 1H, *E* isomer, *J* = 84.4 Hz), 6.63 (d, 1H, *Z* isomer, *J* = 83.6 Hz), 3.80 (m, 2H, *E* isomer), 3.75 (m, 2H, *Z* isomer), 2.91 (td, 2H, *E* isomer, *J* = 8.1, 2.6 Hz), 2.65 (m, 2H, *Z* isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -128.2 (dt, 1F, *E* isomer, *J* = 84.4, 2.8 Hz), -128.6 (dt, 1F, *Z* isomer, *J* = 84.0, 4.0 Hz); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 165.3 (*E* isomer), 165.2 (*Z* isomer), 150.6, 150.3, 147.7, 147.1 (d, *E* isomer, J_{CF} = 261 Hz), 145.3 (d, *Z* isomer, J_{CF} = 266 Hz), 143.2, 133.88, 133.85, 133.81 (d, J_{CF} = 4.5 Hz), 131.9, 130.3, 129.47, 129.44, 128.76, 128.75, 127.8 (d, J_{CF} = 2.8 Hz), 122.1, 122.0, 121.9, 121.8, 121.54, 121.45, 121.2, 121.12, 121.07, 120.97, 119.1, 117.9, 51.0 (d, *Z* isomer, J_{CF} = 4.8 Hz), 50.4 (d, *E* isomer, J_{CF} = 2.5 Hz), 28.6 (d, *Z* isomer, J_{CF} = 5.5 Hz), 25.6 (d, *E* isomer, J_{CF} = 2.9 Hz); HRMS calcd for $C_{29}H_{25}FNO_2$ $[M+H]^+$ 438.1864, found 438.1862.

N-(4-Fluoro-3-(4-(trifluoromethoxy)phenyl)but-3-en-1-yl)-N-phenylaniline ***(23)***. On a 0.300 mmol scale, the desired product (54.2 mg, 45%, *E*:*Z* = 7.2:1) was isolated as a yellow oil by flash chromatography using 2.5% ethyl acetate in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 6.8:1. IR (ATR, diamond) ν = 3037, 2933, 1658, 1587, 1494, 1261, 1203, 1161, 750, 688 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.34-6.88 (m, 14H), 6.81 (d, 1H, *E* isomer, *J* = 84.1 Hz), 6.61 (d, 1H, *Z* isomer, *J* = 83.8 Hz), 3.78 (m, 2H, *E* isomer), 3.71 (m, 2H, *Z* isomer), 2.89 (dt, 2H, *E* isomer, *J* = 8.2, 2.9 Hz), 2.64 (m, 2H, *Z* isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -57.77 (s, 3F, *Z* isomer), -57.85 (s, 3F, *E* isomer), -127.4 (dt, 1F, *E* isomer, *J* = 84.3, 2.8 Hz), -128.3, (dt, 1F, *Z* isomer, *J* = 83.6, 3.5 Hz); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 148.8, 147.6, 147.3 (d, *E* isomer, J_{CF} = 262 Hz), 145.5 (d, *Z* isomer, J_{CF} = 266 Hz), 134.9 (d, J_{CF} = 9.4 Hz), 132.9, 129.7 (d, J_{CF} = 4.3 Hz), 129.47, 129.43, 129.1, 128.6 (d, J_{CF} = 2.2 Hz), 128.1 (d, J_{CF} = 3.1 Hz), 121.7 (d, J_{CF} = 9.8 Hz), 121.6, 121.5, 121.3, 121.2, 121.03, 120.95, 120.6, 120.5 (q, 2C, J_{CF} = 258 Hz), 50.9 (d, *Z* isomer, J_{CF} = 3.3 Hz), 50.4 (d, *E* isomer, J_{CF} = 2.6 Hz), 28.6 (d, *Z* isomer, J_{CF} = 5.4 Hz), 25.6 (d, *E* isomer, J_{CF} = 3.1 Hz); HRMS calcd for $C_{23}H_{20}F_4NO$ $[M+H]^+$ 402.1476, found 402.1472.

N-(4-Fluoro-3-(4-(methylsulfonyl)phenyl)but-3-en-1-yl)-N-phenylaniline ***(24)***. On a 0.300 mmol scale, the desired product (65.3 mg, 55%, *E*:*Z* = 1.6:1) was isolated as a brown oil by flash chromatography using 2.5% ethyl acetate in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 1.7:1. IR (ATR, diamond) ν = 3026, 2926, 2855, 1654, 1587, 1490, 1308, 1148, 1092, 848 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.90 (dt, 2H, *Z* isomer, *J* = 8.4, 1.9 Hz), 7.85 (dt, 2H, *E* isomer, *J* = 8.4, 1.8 Hz), 7.48 (d, 2H, *Z* isomer, *J* = 8.4 Hz), 7.35 (d, 2H, *E* isomer, *J* = 8.4 Hz), 7.26-7.24 (m, 4H), 6.98-6.93 (m, 6H), 6.92 (d, 1H, *E* isomer, *J* = 83.3 Hz), 6.70 (d, 1H, *Z* isomer, *J* = 82.9 Hz), 3.80 (m, 2H, *E* isomer), 3.72 (m, 2H, *Z* isomer), 3.07 (s, 3H, *Z* isomer), 3.06 (s, 3H, *E* isomer), 2.95 (td, 2H, *E* isomer, *J* = 8.3, 2.7 Hz), 2.70 (m, 2H, *Z* isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -123.8 (dt, 1F, *E* isomer, *J* = 82.9, 2.7 Hz), -125.5 (dt, 1F, *Z* isomer, *J* = 83.1, 3.5 Hz); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 148.6 (d, *E* isomer, J_{CF} = 265 Hz), 147.57, 147.55, 146.6 (d, *Z* isomer, J_{CF} = 269 Hz), 142.1 (d, J_{CF} = 9.7 Hz), 140.1, 139.6, 139.5, 129.53, 129.48, 129.1 (d, J_{CF} = 4.3 Hz), 128.0, 127.6, 127.3 (d, J_{CF} = 3.0 Hz), 121.9, 121.8, 121.7, 121.1, 121.03, 120.95, 50.9 (d, *Z* isomer, J_{CF} = 3.5 Hz), 50.4 (d, *E* isomer, J_{CF} = 2.5 Hz), 44.7 (*E* isomer), 29.8 (*Z* isomer), 28.5 (d, *Z* isomer, J_{CF} = 4.7 Hz), 25.3 (d, *E* isomer, J_{CF} = 3.0 Hz); HRMS calcd for $C_{23}H_{23}FNO_2S$ $[M+H]^+$ 396.1428, found 396.1424.

N-(4-Fluoro-3-(3-methoxyphenyl)but-3-en-1-yl)-N-phenylaniline ***(25)***. On a 0.300 mmol scale, the desired product (60.5 mg, 58%, *E*:*Z* = 4.5:1) was isolated by flash chromatography using 20% DCM in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 4.2:1. **(*E*)-25**: Colourless oil; IR (ATR, diamond) ν = 3056, 2937, 1654, 1584, 1490, 1360, 1095, 1016, 731, 692 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.24-7.22 (m, 5H), 6.98 (d, 4H, *J* = 8.2 Hz), 6.94 (t, 2H, *J* = 7.4 Hz), 6.84 (d, 1H, *J* = 84.7 Hz), 6.83 (dd, 1H, *J* = 8.2, 2.2 Hz), 6.81 (d, 1H, *J* = 7.6 Hz), 6.73 (m, 1H), 3.77 (m, 2H), 3.76 (s, 3H), 2.90 (td, 2H, *J* = 7.9, 2.5 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -128.8 (dt, 1F, *J* = 84.6, 2.7 Hz); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 160.0, 147.8, 147.1 (d, J_{CF} = 260 Hz), 137.6 (d, J_{CF} = 9.3 Hz), 129.8, 129.4, 122.5 (d, J_{CF} = 9.5 Hz), 121.4, 121.0, 119.1 (d, J_{CF} = 2.7 Hz), 113.4, 112.2 (d, J_{CF} = 2.9 Hz), 55.3, 50.5 (d, J_{CF} = 2.6 Hz), 25.4 (d, J_{CF} = 3.2 Hz); HRMS calcd for $C_{23}H_{23}FNO$ $[M+H]^+$ 348.1758, found 348.1767. **(*Z*)-25**: Colourless oil; IR (ATR, diamond) ν = 3060, 2929, 1658, 1587, 1490, 1364, 1099, 1020, 740, 684 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.28 (t, 1H, *J* = 7.9 Hz), 7.25-7.22 (m, 4H), 6.95-6.90 (m, 7H), 6.89 (t, 1H, *J* = 2.0 Hz), 6.84 (dd, 1H, *J* = 8.0, 2.2 Hz), 6.61 (d, 1H, *J* = 84.0 Hz), 3.78 (s, 3H), 3.72 (m, 2H), 2.62 (m, 2H); ^{19}F NMR (659 MHz, $CDCl_3$) δ -128.6 (dt, 1F, *J* = 83.9, 3.1 Hz); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 159.7, 147.7, 145.1 (d, J_{CF} = 265 Hz), 135.6, 129.5, 129.4, 121.5, 121.0, 120.6 (d, J_{CF} = 3.9 Hz), 129.9, 113.8 (d, J_{CF} = 4.3 Hz), 113.5, 55.3, 51.1 (d, J_{CF} = 4.1 Hz), 28.7 (d, J_{CF} = 5.2 Hz); HRMS calcd for $C_{23}H_{23}FNO$ $[M+H]^+$ 348.1758, found 348.1763.

N-(4-Fluoro-3-(3-(trifluoromethyl)phenyl)but-3-en-1-yl)-*N*-phenylaniline (**26**). On a 0.300 mmol scale, the desired product (75.2 mg, 65%, *E*:*Z* = 3.0:1) was isolated as a colourless oil by flash chromatography using 8% DCM in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 3.0:1. IR (ATR, diamond) ν = 3060, 2929, 1654, 1587, 1490, 1326, 1259, 1118, 745, 693 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.60-6.90 (m, 14H), 6.85 (d, 1H, *E* isomer, *J* = 83.6 Hz), 6.66 (d, 1H, *Z* isomer, *J* = 83.3 Hz), 3.78 (m, 2H, *E* isomer), 3.70 (m, 2H, *Z* isomer), 2.93 (td, 2H, *E* isomer, *J* = 8.1, 2.7 Hz), 2.67 (m, 2H, *Z* isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -62.6 (s, 3F, *Z* isomer), -62.7 (s, 3F, *E* isomer), -126.4 (dt, 1F, *E* isomer, *J* = 83.8, 2.9 Hz), -127.5 (dt, 1F, *Z* isomer, *J* = 83.2, 3.6 Hz); $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$) δ 147.8 (d, *E* isomer, J_{CF} = 263 Hz), 147.58, 147.59, 146.0 (d, *Z* isomer, J_{CF} = 267 Hz), 137.0 (d, J_{CF} = 9.5 Hz), 135.1, 131.7, 131.3 (q, J_{CF} = 32.4 Hz), 131.0 (q, J_{CF} = 31.9 Hz), 129.9, 129.50, 129.45, 129.36, 129.0, 124.9 (m), 124.6 (m, 2C), 123.4 (m), 124.0 (q, 2C, J_{CF} = 273 Hz), 121.9 (d, J_{CF} = 10.3 Hz), 121.65, 121.56, 121.0, 120.9, 118.9, 50.9 (d, *Z* isomer, J_{CF} = 4.0 Hz), 50.3 (d, *E* isomer, J_{CF} = 2.6 Hz), 28.5 (d, *Z* isomer, J_{CF} =

4.8 Hz), 25.4 (d, *E* isomer, J_{CF} = 3.1 Hz); HRMS calcd for $C_{23}H_{20}F_4N$ $[M+H]^+$ 386.1526, found 386.1517.

N-(3-(2,6-Dimethylphenyl)-4-fluorobut-3-en-1-yl)-N-phenylaniline ***(27)***. On a 0.300 mmol scale, the desired product (42.5 mg, 41%, *E*:*Z* = 15.0:1) was isolated as a yellow solid by flash chromatography using 5% DCM in hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 14.1:1. IR (ATR, diamond) *ν* = 3060, 2922, 1662, 1587, 1490, 1367, 1241, 1110, 745, 681 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.23-7.20 (m, 4H), 7.13 (m, 1H), 7.09-7.05 (m, 2H), 6.95-6.84 (m, 6H), 6.46 (d, 1H, *E* isomer, *J* = 86.2 Hz), 6.45 (d, 1H, *Z* isomer, *J* = 85.1 Hz), 3.78 (m, 2H, *E* isomer), 3.72 (m, 2H, *Z* isomer), 2.76 (td, 2H, *E* isomer, *J* = 7.8, 1.8 Hz), 2.54 (m, 2H, *Z* isomer), 2.24 (s, 6H, *E* isomer), 2.20 (s, 6H, *Z* isomer); ^{19}F NMR (659 MHz, $CDCl_3$) δ -126.8 (d, 1F, *Z* isomer, *J* = 85.5 Hz), -127.5 (d, 1F, *E* isomer, *J* = 86.2 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 147.6, 147.5, 147.3 (d, *E* isomer, J_{CF} = 263 Hz), 147.0 (d, *Z* isomer, J_{CF} = 265 Hz), 137.4 (d, J_{CF} = 2.8 Hz), 134.9 (d, J_{CF} = 10.0 Hz), 129.5 (d, J_{CF} = 1.6 Hz), 129.45, 129.40, 121.9, 127.7, 121.6 (d, J_{CF} = 6.5 Hz), 121.5, 121.4, 121.1, 120.9, 120.86, 120.82, 119.3 (d, J_{CF} = 7.5 Hz), 117.9, 49.8 (d, *E* isomer, J_{CF} = 3.3 Hz), 49.7 (d, *E* isomer, J_{CF} = 9.9 Hz), 29.9 (d, *Z* isomer, J_{CF} = 4.9 Hz), 27.1 (d, *E* isomer, J_{CF} = 1.6 Hz), 20.6 (*E* isomer), 20.0 (*Z* isomer); HRMS calcd for $C_{24}H_{25}FN$ $[M+H]^+$ 346.1966, found 346.1952.

N-(4-Fluoro-3,4-diphenylbut-3-en-1-yl)-N-phenylaniline ***(28)***. On a 0.300 mmol scale, the desired product (72.8 mg, 66%, *E*:*Z* = 1:1.1) was isolated by flash chromatography using 5% DCM, 5% toluene and 90% hexanes. The crude reaction mixture presented an *E*:*Z* ratio of 1:1.1. **(*E*)-28**: Yellow solid; IR (ATR, diamond) *ν* = 3060, 3022, 2920, 1578, 1490, 1224, 1180, 1045, 758, 691 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.42 (d, 2H, *J* = 7.9 Hz), 7.40-7.38 (m, 4H), 7.37 (d, 1H, *J* = 7.0 Hz), 7.33-7.30 (m, 3H), 7.20-7.15 (m, 4H), 6.91 (t, 2H, *J* = 7.2 Hz), 6.80 (d, 4H, *J* = 7.8 Hz), 3.72 (m, 2H), 2.85 (m, 2H); ^{19}F NMR (659 MHz, $CDCl_3$) δ -98.0 (s, 1F); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 154.4 (d, J_{CF} = 249 Hz), 147.6, 136.6 (d, J_{CF} = 1.1 Hz), 132.7 (d, J_{CF} = 29.4 Hz), 129.4, 129.3 (d, J_{CF} = 1.6 Hz), 128.7 (d, J_{CF} = 3.2 Hz), 128.52, 128.50, 127.6, 121.4, 120.9, 117.9, 117.5 (d, J_{CF} = 15.9 Hz), 51.1 (d, J_{CF} = 4.5 Hz), 29.7 (d, J_{CF} = 1.9 Hz); HRMS calcd for $C_{28}H_{25}FN$ $[M+H]^+$ 394.1966, found 394.1956. **(*Z*):** Yellow solid; IR (ATR, diamond) *ν* = 3060, 3022, 2922, 1584, 1490, 1233, 1181, 1062, 749, 693 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.25-7.21 (m, 7H), 7.18 (m, 1H), 7.16-7.11 (m, 4H), 7.08 (dd, 2H, *J* = 7.2, 3.6 Hz), 6.96 (d, 4H, *J* = 7.7 Hz), 6.92 (t, 2H, *J* = 7.2 Hz), 3.82 (m, 2H), 2.99 (td, 2H, *J* = 8.1, 3.2 Hz); ^{19}F NMR (659 MHz, $CDCl_3$) δ -104.8 (t, 1F, *J* = 2.9 Hz); ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$) δ 154.8 (d, J_{CF} = 246 Hz), 147.7, 138.4 (d, J_{CF} = 8.1 Hz), 132.4 (d, J_{CF} = 29.3 Hz), 129.44 (d, J_{CF} = 2.9 Hz), 129.37, 128.8, 128.5, 128.3 (d, J_{CF} = 5.9 Hz), 127.9, 127.5, 121.3, 120.9, 118.8 (d, J_{CF} = 21.8 Hz), 50.3 (d, J_{CF} = 2.1 Hz), 30.2 (d, J_{CF} = 5.6 Hz); HRMS calcd for $C_{28}H_{25}FN$ $[M+H]^+$ 394.1966, found 394.1958.

ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Detailed experimental procedures and full spectroscopic data for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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