Syntheses of Ring-Fluorinated Isoquinolines and Quinolines via Intramolecular Substitution: Cyclization of 1,1-Difluoro-1-alkenes Bearing a Sulfonamide Moiety

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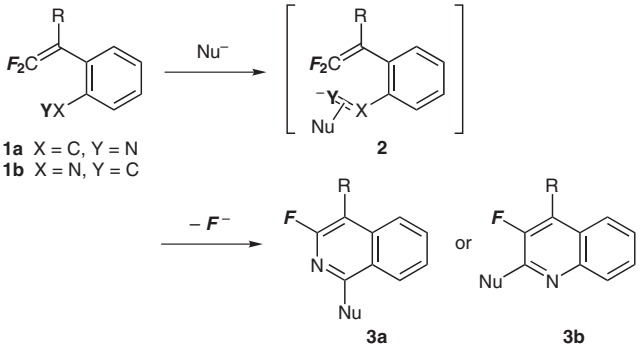
Abstract: On treatment of a base such as NaH, KH, or Et_3N, *N*-[*o*-(2,2-difluorovinyl)benzyl]- and *N*-[*o*-(3,3-difluoroallyl)phenyl]-substituted *p*-toluenesulfonamides readily undergo intramolecular substitution of sulfonamide nitrogens for vinylic fluorines in a 6-*endo-trig* fashion, leading to 3-fluoroisoquinoline and 2-fluoroquinoline derivatives, respectively, in high yields.

Key words: fluoroisoquinoline, fluoroquinoline, fluoroalkene, intramolecular substitution, desulfonylation

Quinolines and isoquinolines are widespread in the alkaloid family and constitute an important class of compounds in medicinal and agricultural chemistry, and also in material science.[1] Due to their substantial applicability, the syntheses of quinolines and isoquinolines are extensively studied topics.[2–4] Despite their common properties and much research on their preparation, little attention has hitherto been paid to synthetic methodology based on a single concept that can be applied to both ring systems.[5]

As an example embodying such a concept, we have developed a method for the construction of isoquinoline and quinoline frameworks on the basis of nucleophilic substitution of vinylic fluorines via addition–elimination processes (S_NV: nucleophilic vinylic substitution, Scheme 1):[5b] *o*-Cyano-substituted β,β-difluorostyrenes **1a** react with organolithiums selectively at the cyano carbon to generate the corresponding sp^2 nitrogen anions **2a**, which in turn undergo intramolecular replacement of the vinylic fluorine to afford 3-fluoroisoquinolines **3a**. Similarly, the reaction of *o*-isocyano-substituted β,β-difluorostyrenes **1b** with organomagnesiums or organolithiums proceeds via the corresponding sp^2 carbanions **2b**, which substitute the intramolecular fluorine to afford 3-fluoroquinolines **3b**. In these reactions, the choice of a cyano or an isocyano group at the *ortho* position is the key to isoquinoline or quinoline synthesis.

Previously, we reported the nucleophilic 5-*endo-trig* cyclization of 1,1-difluoro-1-alkenes bearing a sulfonamide moiety **4**.[6] The intramolecular substitution of nitrogen nucleophiles for the vinylic fluorines successfully afforded 2-fluoroindoles and 2-fluoropyrrolines **5** (Scheme 2).

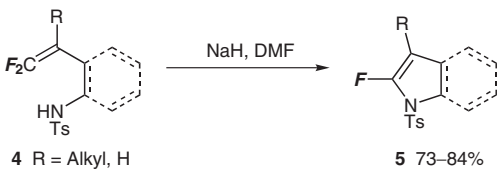


Scheme 1 Syntheses of 3-fluorinated isoquinolines **3a** and quinolines **3b** from β,β-difluorostyrenes **1**

During the study, we found that both *N*-aryl and *N*-alkyl tosylamides were good nucleophiles for the cyclization.

These facts prompted us to investigate both isoquinoline and quinoline syntheses via similar ring-forming reactions by just changing the position of the benzene ring in the substrates. Thus, *N*-[*o*-(2,2-difluorovinyl)benzyl]- and *N*-[*o*-(3,3-difluoroallyl)phenyl]-substituted *p*-toluenesulfonamides **6** and **7** were designed as starting materials for 6-*endo-trig* cyclization to provide 3-fluoroisoquinolines **8**, **9** and 2-fluoroquinolines **10**, **11**, respectively (Scheme 3).

These selectively ring-fluorinated heterocycles have significant potential as components[7] and synthetic intermediates[8] of biologically active substances and advanced materials.[9] However, their synthetic methods are still quite limited and remain to be developed.[4e,5b,10–12] Herein we report a facile, common method for the syntheses of ring-fluorinated isoquinolines and quinolines starting from *ortho*-functionalized (2,2-difluorovinyl)benzenes and (3,3-difluoroallyl)benzenes.



Scheme 2 Syntheses of 2-fluorinated indoles and pyrrolines via intramolecular substitution of tosylamide nitrogens

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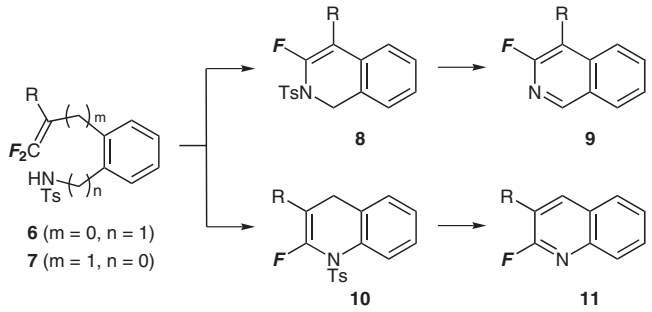
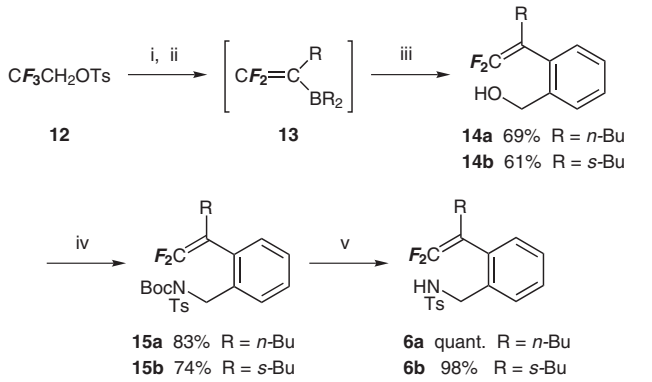


Scheme 3 Construction of isoquinoline and quinoline frameworks from (2,2-difluorovinyl)benzenes **6** and (3,3-difluoroallyl)benzenes **7**

Synthesis of 3-Fluorinated Isoquinoline Derivatives

The starting materials for isoquinolines, *o*-substituted (2,2-difluorovinyl)benzenes **6** were easily prepared from 2,2,2-trifluoroethyl *p*-toluenesulfonate (**12**) by the method which we have previously established: (i) the in situ generation of (2,2-difluorovinyl)boranes **13** and (ii) their palladium-catalyzed cross-coupling reaction with aryl iodides (Scheme 4).[13]

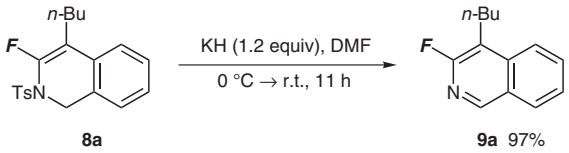


Scheme 4 Preparation of *o*-substituted (2,2-difluorovinyl)benzenes **6**. *Reagents and conditions*: (i) *n*-BuLi (2.1 equiv), THF, –78 °C, 0.5 h; (ii) BR_3 (1.1 equiv), THF, –78 °C → r.t., 4 h; (iii) *o*-I-$C_6H_4CH_2OMgBu$ (0.9 equiv), CuI (1.0 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.02 equiv), Ph_3P (0.08 equiv), THF–HMPA (4:1), r.t., 17 h; (iv) BocNHTs (1.5 equiv), Ph_3P (3.0 equiv), DEAD (2.5 equiv), THF, r.t., 1 or 10 h; (v) CF_3CO_2H (10 or 15 equiv), CH_2Cl_2, r.t., 11 h.

Difluorovinylbenzenes **14** bearing a hydroxymethyl group at the *ortho* position were obtained by the coupling of vinylboranes **13** with the corresponding aryl iodide.[14] *o*-Iodobenzyl alcohol was pretreated with equimolecular amounts of dibutylmagnesium to generate the metal alkoxide, which in turn coupled with **13** in the presence of a palladium catalyst to afford **14**. Thus, alcohols **14** were prepared in good yield from **12** in a one-pot operation. The Mitsunobu reaction[15] of **14** with BocNHTs allowed the introduction of a nitrogen atom to give carbamates **15**, whose deprotection of the Boc group led to the desired sulfonamides **6** (Scheme 4).

We examined the cyclization of difluorovinylbenzene substrates **6** via deprotonation on the sulfonamide nitrogen. When **6a** (R = *n*-Bu) was treated with 1.1 equivalents of NaH in DMF, intramolecular cyclization readily proceeded at room temperature to afford 3-fluoro-1,2-dihydroisoquinoline **8a** in 89% yield (Table 1, entry 1).

When an excess amount (1.2 equiv) of a base was used, aromatized 3-fluoroisoquinoline **9a** was formed along with **8a** (entries 2 and 3). KH was more suitable for the formation of **9a**, which seemed to be effected via the cyclization followed by elimination of a sulfinic acid.[12c,16] This route to **9a** via **8a** was supported by the following experiment: Treatment of **8a** with 1.2 equivalents of KH in DMF readily promoted the elimination of *p*-toluenesulfinic acid to give isoquinoline **9a** in almost quantitative yield (Scheme 5). The desulfonylative aromatization of **8** proceeded at room temperature, under mild conditions compared to the reported ones.[16]



Scheme 5 Desulfonylative aromatization of dihydroisoquinoline **8a** with KH

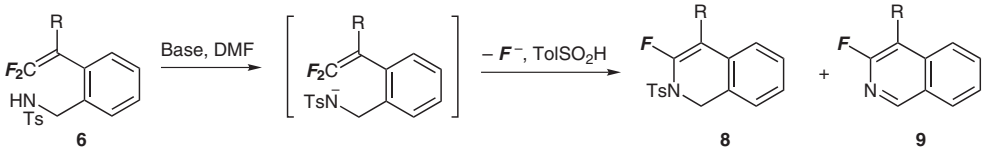
These results suggested that employing more than two equivalents of a base should promote the cyclization and the successive elimination of the sulfinic acid in a one-pot operation, leading to a direct synthesis of isoquinolines **9** from **6**. Thus, **6a** was treated with 2.1 equivalents of KH to afford **9a** in 81% yield without detectable formation of **8a** as expected. The use of 2.5 equivalents of KH improved the yields of **9a** up to 95% (Table 1, entry 4).

Ring closure of **6b** (R = *s*-Bu) successfully proceeded similarly to **6a** to give dihydroisoquinoline **8b** or isoquinoline **9b** with a secondary alkyl group at the 4-position, depending on the basic conditions: NaH (1.1 equiv) or KH (2.6 equiv) (entries 5 and 6).

Synthesis of 2-Fluorinated Quinoline Derivatives

For quinoline synthesis, *o*-substituted (3,3-difluoroallyl)benzenes **7** were adopted as precursors.[17] Their difluoroallylbenzene structure could be constructed by S_N2' reaction of 1-(trifluoromethyl)vinyl compounds[18] with *o*-functionalized aryllithiums, which were readily available via directed *ortho*-lithiation.[19] N-Protected anilines **16** were treated with more than 2 equivalents of butyllithium to generate dilithiated species **17**, whose reaction with 1-(trifluoromethyl)vinyl compounds **18** proceeded with accompanying elimination of an allylic fluorine. The S_N2' adducts, difluoroallyl compounds **19**, thus obtained were subjected to deprotection followed by tosylation of the

Table 1 Synthesis of 3-Fluoro-1,2-dihydroisoquinolines **8** and 3-Fluoroisoquinolines **9**

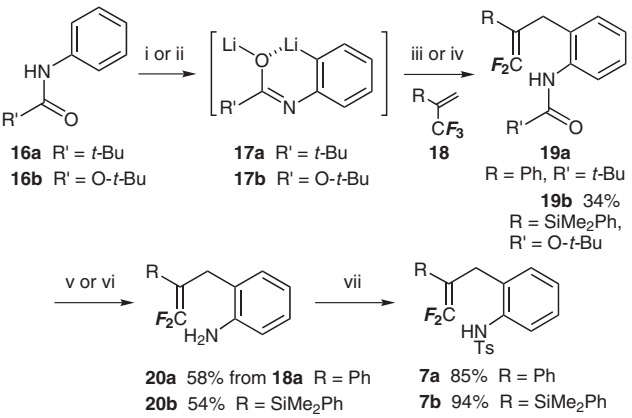


Entry	R	Base (equiv)	Conditions	Yield (%)[a] of **8**	Yield (%)[a] of **9**
1	**a**: *n*-Bu	NaH (1.1)	0 °C → r.t., 5 h	89 (94)	–
2	**a**: *n*-Bu	NaH (1.2)	0 °C → r.t., 4 h	80 (89)	10
3	**a**: *n*-Bu	KH (1.2)	0 °C → r.t., 4 h	33	45
4	**a**: *n*-Bu	KH (2.5)	0 °C → r.t., 4 h	–	95
5	**b**: *s*-Bu	NaH (1.1)	0 °C → r.t., 9 h	89	–
6	**b**: *s*-Bu	KH (2.6)	0 °C → r.t., 9 h	–	90

[a] Isolated yield. ^{19}F NMR yield relative to internal $C_6H_5CF_3$ standard is given in parentheses.

aniline nitrogen to afford the desired sulfonamides **7** (Scheme 6).

Intramolecular substitution of the amide nitrogen in difluoroallylbenzene substrates **7** was attempted to provide 2-fluorinated quinoline derivatives. When **7a** (R = Ph) was treated with 1.1 equivalents of NaH in DMF, the expected cyclization proceeded at 80 °C, leading not to 2-fluoro-1,4-dihydroquinoline **10a** but directly to the corresponding aromatized 2-fluoroquinoline **11a** in 47% yield (Table 2, entry 1). Then, we conducted the reaction with 2.2 equivalents of NaH, which afforded 2-fluoroquinoline **11a** in 79% yield via cyclization followed by elimination of a sulfinic acid (entry 2). While KH also gave compound



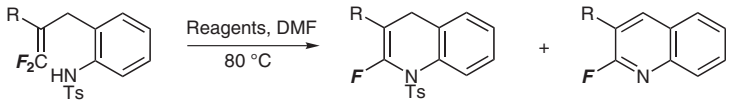
Scheme 6 Preparation of *o*-substituted (3,3-difluoroallyl)benzenes **7**. *Reagents and conditions*: (i) (for **16a**) *n*-BuLi (2.5 equiv), THF, 0 °C, 2 h → r.t., 20 h; (ii) (for **16b**) *t*-BuLi (2.5 equiv), tetrahydropyran, 0 °C → r.t., 1 h; (iii) (for **17a**) **18a** (R = Ph, 0.8 equiv), TMEDA (1.0 equiv), –78 °C → reflux, 5 h; (iv) (for **17b**) **18b** (R = $SiMe_2Ph$, 1.5 equiv), 0 °C → r.t., 20 h; (v) (for **19a**) HCl (20 equiv), H_2O–EtOH (1:1), reflux, 16 h; (vi) (for **19b**) Me_3SiI (2.0 equiv), $CHCl_3$, 0 °C, 2 h → r.t., 1 h; (vii) TsCl (1.5 equiv), pyridine, 0 °C → r.t., 10–16 h.

11a, the yield was quite low (11% yield) in contrast to the cyclization of **6**.

The cyclization of **7b** (R = $SiMe_2Ph$) was examined under similar reaction conditions as above. Treatment with 2.2 equivalents of NaH in DMF at 80 °C gave no cyclized products but a desilylated product, *N*-[*o*-(3,3-difluoroallyl)phenyl]-*p*-toluenesulfonamide **7c** (R = H) in 81% yield. After screening different bases, we found that the cyclization was effected by triethylamine (Et_3N, 3.0 equiv) to afford the desired 2-fluoro-1-tosyl-1,4-dihydroquinoline (**10b**) in 75% yield with accompanying formation of the desilylated product **7c** (R = H) in 19% yield (Table 2, entry 3). Addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 2.0 equiv) after the cyclization with Et_3N (3.0 equiv) gave an aromatized product, 2-fluoroquinoline **11b**, in 53% yield along with **7c** (R = H, 20% yield) and the desilylated dihydroquinoline **10c** (R = H, 14% yield) (entry 4).[20] Since desilylation giving rise to **7c** (R = H) and **10c** (R = H) seemed to be caused by a fluoride ion generated during the cyclization, we tried to capture the fluoride ion with trimethyl borate [$B(OMe)_3$]. On treatment of **7b** with Et_3N (6.0 equiv) and $B(OMe)_3$ (2.0 equiv), **10b** was successfully obtained in 85% yield (entry 5).[21]

For conversion of **10b** into 2-fluoroquinoline **11b**, we examined several conditions. While a base such as NaH or DBU in DMF gave a complex mixture of products, oxidative treatment with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) was quite effective. The reaction conducted in refluxing benzene gave rise to aromatization via cleavage of the tosyl group[22] to provide 2-fluoroquinoline **11b** in 92% yield without affecting the silyl group (Scheme 7).[21] The aromatization via desulfonylation normally requires harsh conditions with a base or an acid, such as KOH in DMSO at 140 °C for 30 minutes or 6 M aqueous HCl in refluxing dioxane for 24 hours,[12c,16] with

Table 2 Synthesis of 2-Fluoro-1,4-dihydroquinoline **10** and 2-Fluoroquinolines **11**



7a R = Ph
7b R = $SiMe_2Ph$

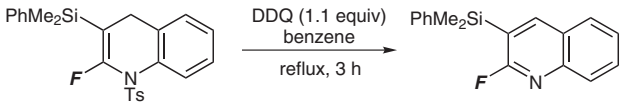
10a R = Ph
10b R = $SiMe_2Ph$

11a R = Ph
11b R = $SiMe_2Ph$

Entry	R	Reagents (equiv)	Time (h)	Yield (%) of **10**	Yield (%) of **11**
1	**a**: Ph	NaH (1.1)	2	–	47
2	**a**: Ph	NaH (2.2)	3	–	79
3[a]	**b**: $SiMe_2Ph$	Et_3N (3.0)	5	75	0
4[b]	**b**: $SiMe_2Ph$	i) Et_3N (3.0) ii) DBU (2.0)	i) 5 ii) 1	9	53
5	**b**: $SiMe_2Ph$	i) Et_3N (3.0), $B(OMe)_3$ (2.0) ii) Et_3N (3.0)	i) 5 ii) 3	85	0

[a] Anilide **7c** (R = H) was obtained in 19% yield.
[b] Anilide **7c** (R = H) and dihydroquinoline **10c** (R = H) were obtained in 20 and 14% yield, respectively.

one exception: reductive desulfonylation of a benzylsulfonamido group with Raney nickel.[16b] We have found that DDQ *oxidation* readily promotes the desulfonylative aromatization process under mild and neutral conditions, which offers a complementary method to Raney nickel *reduction*.



10b **11b** 92%

Scheme 7 Desulfonylative aromatization of dihydroquinoline **10b** via DDQ oxidation

Thus, 2-fluoroquinoline synthesis has been accomplished by combining two processes: (i) S_N2' reaction of trifluoromethylalkenes for the preparation of cyclization precursors and (ii) S_NV reaction of difluoroalkenes for the ring formation.

In conclusion, we have demonstrated the construction of both isoquinoline and quinoline frameworks by a common strategy: the intramolecular substitution of tosylamide nitrogens for vinylic fluorines in 1,1-difluoro-1-alkenes. The scope of this intramolecular substitution methodology has been expanded to the synthesis of 2-fluorinated quinolines starting from (3,3-difluoroallyl)benzene substrates, as well as 3-fluorinated quinolines from (2,2-difluorovinyl)benzene substrates.[23]

IR spectra were recorded on a JEOL JIR-WINSPEC50 or a Horiba FT-300S spectrometer. NMR spectra were obtained on a JEOL JNM-A-500 or a Bruker DRX500 spectrometer. Chemical shifts were given in ppm relative to internal Me_4Si (for ^1H and ^{13}C NMR) or internal C_6F_6 (for ^{19}F NMR). Mass spectra were taken with a JEOL JMS-DX-300 or a JEOL JMS-SX-102A spectrometer. Elemental analyses were performed with a YANAKO MT-3 CHN Corder apparatus. THF was distilled from sodium benzophenone ketyl prior to use. Tetrahydropyran was distilled from CaH_2 prior to use. HMPA and pyridine were distilled from CaH_2 and stored over molecular sieves (4 Å). CH_2Cl_2 was distilled from P_2O_5 and then from CaH_2, and stored over molecular sieves (4 Å). DMF was dried over P_2O_5, then distilled under reduced pressure from CaH_2, and stored over molecular sieves (4 Å). Benzene was dried over $CaCl_2$, then distilled, and stored over molecular sieves (4 Å). $CHCl_3$ (special grade, Kokusan Chemical Co., Ltd.) was passed through an alumina column prior to use. Commercial NaH and KH were used without further purification. Column chromatography and preparative thin-layer chromatography (PTLC) were performed on silica gel (Kanto Chemical Co., Inc., Silica Gel 60 and Wako Pure Chemical Industries, Ltd., B5-F, respectively).

***N-tert*-Butoxycarbonyl-*N*-[*o*-(1,1-difluorohex-1-en-2-yl)benzyl]-*p*-toluenesulfonamide (15a)**

To a solution of *N-tert*-butoxycarbonyl-*p*-toluenesulfonamide (314 mg, 1.16 mmol) in THF (5 mL) were added Ph_3P (624 mg, 2.32 mmol), alcohol **14a** (175 mg, 0.77 mmol)[13] in THF (2 mL), and diethyl azodicarboxylate (0.30 mL, 1.65 mmol) at r.t. under N_2. After stirring for 1 h, the mixture was concentrated under reduced pressure. The residue was purified by PTLC on silica gel (hexane–EtOAc, 3:1) to give **15a** (306 mg, 83%) as a pale-yellow liquid.

IR (neat): 2958, 1739, 1367, 1286, 1236, 1155, 1089, 790, 765, 676, 592, 545 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (3 H, t, *J* = 7.0 Hz), 1.36–1.40 (13 H, m), 2.30 (2 H, br s), 2.43 (3 H, s), 5.04 (2 H, s), 7.15 (1 H, d, *J* = 7.0 Hz), 7.24–7.35 (5 H, m), 7.70 (2 H, d, *J* = 8.2 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.8, 21.6, 22.4, 27.8, 28.7, 29.6 (dd, $J_{C,F}$ = 3, 3 Hz), 47.9 (d, $J_{C,F}$ = 2 Hz), 84.5, 90.3 (dd, $J_{C,F}$ = 22, 17 Hz), 126.2, 127.0, 128.1, 128.3, 129.2, 130.0 (d, $J_{C,F}$ = 2 Hz), 131.8 (d, $J_{C,F}$ = 5 Hz), 136.0, 137.0, 144.3, 151.1, 152.6 (dd, $J_{C,F}$ = 287, 287 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 68.5 (1 F, d, $J_{F,F}$ = 44 Hz), 73.0 (1 F, d, $J_{F,F}$ = 44 Hz).

HRMS: *m/z* calcd for $C_{25}H_{31}F_2NO_4S$: 479.1942 (M^+); found: 479.1972.

***N*-*tert*-Butoxycarbonyl-*N*-[*o*-(1,1-difluoro-3-methylpent-1-en-2-yl)benzyl]-*p*-toluenesulfonamide (15b)**

Compound **15b** was prepared by the method described for **15a** using *N*-*tert*-butoxycarbonyl-*p*-toluenesulfonamide (173 mg, 0.64 mmol), THF (3 mL), Ph_3P (343 mg, 1.28 mmol), alcohol **14b** (96 mg, 0.43 mmol)[13] in THF (2 mL), and diethyl azodicarboxylate (0.17 mL, 0.94 mmol). The mixture was stirred at r.t. for 10 h. Purification by PTLC on silica gel ($CHCl_3$–EtOAc, 20:1) gave **15b** (151 mg, 74%) as a pale-yellow liquid.

IR (neat): 2969, 1727, 1367, 1286, 1249, 1232, 1187, 1170, 1089, 676 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6, 90 °C): δ = 0.89–1.68 (8 H, m), 1.25 (9 H, s), 2.42 (3 H, s), 2.38–2.44 (1 H, m), 5.00 (2 H, s), 7.18 (1 H, br s), 7.25 (1 H, d, *J* = 7.4 Hz), 7.30 (1 H, dd, *J* = 7.4, 7.4 Hz), 7.35 (1 H, dd, *J* = 7.4, 7.4 Hz), 7.42 (2 H, d, *J* = 8.2 Hz), 7.77 (2 H, d, *J* = 8.2 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 12.3, 14.0, 18.1, 21.9, 27.6, 39.8, 48.4, 84.7, 91.9 (dd, $J_{C,F}$ = 20, 14 Hz), 124.6, 126.6, 128.2, 129.0 (d, $J_{C,F}$ = 5 Hz), 129.2, 129.3, 130.1, 135.6 (d, $J_{C,F}$ = 5 Hz), 136.1, 144.7, 150.8, 151.8 (dd, $J_{C,F}$ = 290, 290 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 70.1 (1 F, d, $J_{F,F}$ = 44 Hz), 74.2 (1 F, d, $J_{F,F}$ = 44 Hz).

HRMS: *m*/*z* calcd for $C_{25}H_{31}F_2NO_4S$: 479.1942 (M^+); found: 479.1905.

***N*-[*o*-(1,1-Difluorohex-1-en-2-yl)benzyl]-*p*-toluenesulfonamide (6a)**

To a solution of **15a** (69 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL) was added trifluoroacetic acid (0.17 mL, 2.2 mmol) at r.t. The mixture was stirred at r.t. for 11 h, and then aq $NaHCO_3$ was added. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 3:1) to give **6a** (55 mg, ca. 100%) as a pale-yellow liquid.

IR (neat): 3280, 2958, 2929, 1739, 1328, 1236, 1162, 1093, 813, 765 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.83 (3 H, t, *J* = 7.2 Hz), 1.14–1.28 (4 H, m), 2.13 (2 H, br s), 2.43 (3 H, s), 4.05 (2 H, d, *J* = 5.9 Hz), 4.79 (1 H, t, *J* = 5.9 Hz), 7.07–7.15 (1 H, m), 7.23–7.27 (2 H, m), 7.31 (2 H, d, *J* = 8.1 Hz), 7.33–7.37 (1 H, m), 7.76 (2 H, d, *J* = 8.1 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.7, 21.5, 22.3, 28.9, 29.4 (dd, $J_{C,F}$ = 3, 3 Hz), 44.5, 90.3 (dd, $J_{C,F}$ = 22, 17 Hz), 127.2, 128.0, 128.4, 129.1, 129.8, 130.1 (d, $J_{C,F}$ = 2 Hz), 133.0 (d, $J_{C,F}$ = 5 Hz), 134.8 (d, $J_{C,F}$ = 2 Hz), 136.6, 143.6, 152.5 (dd, $J_{C,F}$ = 287, 287 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 68.3 (1 F, d, $J_{F,F}$ = 46 Hz), 72.7 (1 F, d, $J_{F,F}$ = 46 Hz).

HRMS: *m*/*z* calcd for $C_{20}H_{23}F_2NO_2S$: 379.1418 (M^+); found: 379.1413.

***N*-[*o*-(1,1-Difluoro-3-methylpent-1-en-2-yl)benzyl]-*p*-toluenesulfonamide (6b)**

Compound **6b** was prepared by the method described for **6a** using **15b** (103 mg, 0.22 mmol), CH_2Cl_2 (2 mL), and trifluoroacetic acid (0.17 mL, 2.2 mmol). Purification by PTLC on silica gel (hexane–EtOAc, 3:1) gave **6b** (76 mg, 98%) as a pale-yellow liquid.

IR (neat): 3282, 2966, 1729, 1450, 1328, 1288, 1232, 1160, 1093, 1060 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.78 (3 H, d, *J* = 7.2 Hz), 0.93 (3 H, t, *J* = 7.1 Hz), 1.27–1.38 (2 H, m), 2.28–2.46 (1 H, m), 2.44 (3 H, s), 3.97–4.18 (2 H, m), 4.70 (1 H, br s), 7.04 (1 H, d, *J* = 7.0 Hz), 7.24 (1 H, ddd, *J* = 7.0, 7.0, 1.1 Hz), 7.28 (1 H, dd, *J* = 7.0, 7.0 Hz), 7.32 (2 H, d, *J* = 8.1 Hz), 7.39 (1 H, dd, *J* = 7.0, 1.1 Hz), 7.77 (2 H, d, *J* = 8.1 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 12.0, 17.9, 21.5, 28.0, 35.2, 44.5, 93.1 (dd, $J_{C,F}$ = 20, 14 Hz), 127.1, 127.7, 128.4, 129.0, 129.7, 130.6, 131.3, 135.4, 136.4, 143.6, 152.4 (dd, $J_{C,F}$ = 291, 280 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 69.6 (1 F, d, $J_{F,F}$ = 44 Hz), 74.6 (1 F, d, $J_{F,F}$ = 44 Hz).

HRMS: *m*/*z* calcd for $C_{20}H_{23}F_2NO_2S$: 379.1418 (M^+); found: 379.1421.

4-Butyl-3-fluoro-2-*p*-toluensulfonyl-1,2-dihydroisoquinoline (8a)

To a suspension of NaH (9 mg, 60% dispersion in mineral oil, 0.22 mmol) in DMF (0.5 mL) was added **6a** (75 mg, 0.20 mmol) in DMF (1.5 mL) at 0 °C under N_2. The reaction mixture was stirred at r.t. for 4.5 h, and then phosphate buffer (pH 7) was added to quench the reaction. Organic materials were extracted with Et_2O (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (pentane–Et_2O, 5:1 containing 1% Et_3N) to give **8a** (63 mg, 89%) as a pale-yellow liquid.

IR (neat): 2964, 1670, 1359, 1243, 1168, 1085, 1054, 817, 759, 680, 566, 545 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.91 (3 H, t, *J* = 7.5 Hz), 1.29–1.43 (4 H, m), 2.23 (3 H, s), 2.45 (2 H, td, *J* = 7.5 Hz, $J_{H,F}$ = 2.5 Hz), 4.79 (2 H, d, $J_{H,F}$ = 3.7 Hz), 6.88 (1 H, dd, *J* = 7.3, 1.5 Hz), 6.91–6.95 (1 H, m), 6.92 (2 H, dd, *J* = 7.9, 0.6 Hz), 7.00–7.07 (2 H, m), 7.42–7.46 (2 H, m).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.8, 21.4, 22.5, 23.9, 30.6 (d, $J_{C,F}$ = 2 Hz), 51.6, 109.8 (d, $J_{C,F}$ = 23 Hz), 122.5 (d, $J_{C,F}$ = 6 Hz), 125.1, 126.7 (d, $J_{C,F}$ = 2 Hz), 127.4, 127.6, 128.7, 128.9, 131.6 (d, $J_{C,F}$ = 4 Hz), 133.9, 144.1, 147.7 (d, $J_{C,F}$ = 267 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 65.0 (t, $J_{F,H}$ = 3 Hz).

HRMS: *m*/*z* calcd for $C_{20}H_{22}FNO_2S$: 359.1355 (M^+); found: 359.1367.

4-(*sec*-Butyl)-3-fluoro-2-*p*-toluenesulfonyl-1,2-dihydroisoquinoline (8b)

Compound **8b** was prepared by the method described for **8a** using NaH (10 mg, 60% dispersion in mineral oil, 0.24 mmol) in DMF (1 mL) and **6b** (82 mg, 0.22 mmol) in DMF (1.5 mL). The mixture was stirred at r.t. for 9 h. Purification by column chromatography on silica gel (pentane–Et_2O, 10:1 containing 1% Et_3N) gave **8b** (69 mg, 89%) as a pale-yellow solid.

IR (neat): 2969, 1654, 1452, 1357, 1234, 1164, 927, 765, 678, 578 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.84 (3 H, t, *J* = 7.3 Hz), 1.23 (3 H, dd, *J* = 7.3 Hz, $J_{H,F}$ = 1.1 Hz), 1.56–1.74 (2 H, m), 2.22 (3 H, s), 2.61 (1 H, tq, *J* = 7.3, 7.3 Hz), 4.74 (1 H, dd, *J* = 16.5 Hz, $J_{H,F}$ = 3.6 Hz), 4.80 (1 H, dd, *J* = 16.5 Hz, $J_{H,F}$ = 3.6 Hz), 6.90 (2 H, d, *J* = 8.2 Hz), 6.93–6.98 (2 H, m), 6.99–7.05 (2 H, m), 7.40 (2 H, d, *J* = 8.2 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 12.6, 18.9 (d, $J_{C,F}$ = 3 Hz), 21.3, 27.9 (d, $J_{C,F}$ = 4 Hz), 34.0 (d, $J_{C,F}$ = 3 Hz), 51.7, 114.2 (d, $J_{C,F}$ = 20 Hz), 122.8 (d, $J_{C,F}$ = 7 Hz), 125.2, 126.5 (d, $J_{C,F}$ = 2 Hz), 127.2, 127.5, 128.6, 129.0, 132.2 (d, $J_{C,F}$ = 5 Hz), 133.7, 144.0, 147.9 (d, $J_{C,F}$ = 271 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 69.3 (s).

HRMS: *m*/*z* calcd for $C_{20}H_{22}FNO_2S$: 359.1355 (M^+); found: 359.1347.

4-Butyl-3-fluoroisoquinoline (9a)

To a suspension of KH (85 mg, 33% dispersion in mineral oil, 0.70 mmol) in DMF (1 mL) was added **6a** (104 mg, 0.27 mmol) in DMF (2 mL) at 0 °C under N_2. The mixture was stirred at r.t. for 4 h, and then phosphate buffer (pH 7) was added to quench the reaction. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 3:1) to give **9a** (53 mg, 95%) as a pale-yellow liquid.

IR (neat): 2960, 2930, 2870, 1620, 1590, 1440, 1425, 1250, 1220, 750 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.97 (3 H, t, *J* = 7.5 Hz), 1.46 (2 H, tq, *J* = 7.5, 7.5 Hz), 1.63–1.71 (2 H, m), 3.03 (2 H, td, *J* = 7.5 Hz, $J_{H,F}$ = 0.9 Hz), 7.52 (1 H, ddd, *J* = 7.9, 7.9, 0.8 Hz), 7.71 (1 H, dd, *J* = 7.9, 7.9 Hz), 7.97 (1 H, d, *J* = 7.9 Hz), 7.99 (1 H, d, *J* = 7.9 Hz), 8.80 (1 H, s).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.9, 22.8, 24.1, 32.1, 115.0 (d, $J_{C,F}$ = 30 Hz), 122.9 (d, $J_{C,F}$ = 7 Hz), 125.6 (d, $J_{C,F}$ = 2 Hz), 127.6 (d, $J_{C,F}$ = 2 Hz), 128.4, 130.7, 138.4 (d, $J_{C,F}$ = 6 Hz), 148.6 (d, $J_{C,F}$ = 16 Hz), 159.1 (d, $J_{C,F}$ = 232 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 79.3 (s).

Anal. Calcd for $C_{13}H_{14}FN$: C, 76.82; H, 6.94; N, 6.89. Found: C, 76.54; H, 6.95; N, 6.76.

4-(*sec*-Butyl)-3-fluoroisoquinoline (9b)

Compound **9b** was prepared by the method described for **9a** using KH (70 mg, 33% dispersion in mineral oil, 0.57 mmol) in DMF (1 mL) and **6b** (83 mg, 0.22 mmol) in DMF (2.5 mL). The mixture was stirred at r.t. for 9 h. Purification by PTLC on silica gel (hexane–EtOAc, 5:1) gave **9b** (40 mg, 90%) as a pale-yellow solid.

IR (neat): 2969, 2873, 1623, 1585, 1567, 1500, 1442, 1423, 1380, 1268, 1247, 1153, 933, 752 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.86 (3 H, t, *J* = 7.3 Hz), 1.46 (3 H, d, *J* = 7.2 Hz, $J_{H,F}$ = 1.5 Hz), 1.82–2.01 (2 H, m), 3.49 (1 H, tq, *J* = 7.3, 7.3 Hz), 7.52 (1 H, dd, *J* = 7.9, 7.9 Hz), 7.70 (1 H, dd, *J* = 7.9, 7.9 Hz), 7.98 (1 H, d, *J* = 7.9 Hz), 8.14 (1 H, d, *J* = 7.9 Hz), 8.81 (1 H, s).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 12.8, 19.3 (d, $J_{C,F}$ = 3 Hz), 28.5 (d, $J_{C,F}$ = 3 Hz), 33.0 (d, $J_{C,F}$ = 4 Hz), 119.1 (d, $J_{C,F}$ = 26 Hz), 123.1 (d, $J_{C,F}$ = 6 Hz), 125.5 (d, $J_{C,F}$ = 2 Hz), 127.6 (d, $J_{C,F}$ = 2 Hz), 128.5, 130.6, 138.5, (d, $J_{C,F}$ = 7 Hz), 148.8 (d, $J_{C,F}$ = 17 Hz), 159.3 (d, $J_{C,F}$ = 235 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = 86.1 (br s).

Anal. Calcd for $C_{13}H_{14}FN$: C, 76.82; H, 6.94; N, 6.89. Found: C, 76.58; H, 7.00; N, 6.80.

***o*-(3,3-Difluoro-2-phenylprop-2-en-1-yl)aniline (20a)**

To a solution of amide **16a** (165 mg, 1.00 mmol) in THF (2.5 mL) was added dropwise *n*-BuLi (1.6 mL, 1.6 M in hexane, 2.5 mmol) at 0 °C under argon. After stirring at 0 °C for 2 h and at r.t. for 20 h, (3,3,3-trifluoroprop-1-en-2-yl)benzene (**18a**; 121 mg, 0.70 mmol) and *N*,*N*,*N*,*N*-tetramethylethylenediamine (116 mg, 1.0 mmol) were added, and the mixture was refluxed for 5 h. The reaction was quenched with phosphate buffer (pH 7) at r.t. The mixture was filtered through a pad of Celite, and then organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine. After removal of the solvent under reduced pressure, the residue was treated with aq HCl (2.5 mL, 12 M, 30 mmol) in EtOH (2.5 mL) and the mixture was refluxed for 16 h. The reaction was quenched with $CaCO_3$ (2.5 g, 25 mmol) and then phosphate buffer (pH 7) at 0 °C. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 3:1) to give **20a** (100 mg, 58%) as a pale-yellow oil.

IR (neat): 1716, 1622, 1495, 1456, 1234, 1101, 985, 744, 694, 603, 576 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.46 (2 H, br s), 3.51 (2 H, dd, $J_{H,F}$ = 2.0, 2.0 Hz), 6.57 (1 H, dd, *J* = 7.6, 0.9 Hz), 6.62 (1 H, ddd, *J* = 7.6, 7.6, 0.9 Hz), 6.93 (1 H, d, *J* = 7.6 Hz), 6.98 (1 H, ddd, *J* = 7.6, 7.6, 0.9 Hz), 7.16–7.20 (2 H, m), 7.22–7.25 (3 H, m).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 29.6, 90.4 (dd, $J_{C,F}$ = 21, 14 Hz), 115.6, 118.6, 122.2 (dd, $J_{C,F}$ = 3, 3 Hz), 127.4, 127.4, 128.1 (dd, $J_{C,F}$ = 3, 3 Hz), 128.3, 129.3, 133.3 (dd, $J_{C,F}$ = 3, 3 Hz), 144.2, 154.0 (dd, $J_{C,F}$ = 292, 287 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 71.4 (1 F, d, $J_{F,F}$ = 41 Hz), 72.2 (1 F, d, $J_{F,F}$ = 41 Hz).

Anal. Calcd for $C_{15}H_{13}F_2N$: C, 73.45; H, 5.34; N, 5.71. Found: C, 73.64; H, 5.50; N, 5.67.

***tert*-Butyl *N*-{*o*-[3,3-Difluoro-2-(dimethylphenylsilyl)prop-2-en-1-yl]phenyl}carbamate (19b)**

To a solution of carbamate **16b** (196 mg, 1.01 mmol) in tetrahydropyran (0.50 mL) was added dropwise *t*-BuLi (1.76 mL, 1.4 M in pentane, 2.5 mmol) at 0 °C under argon. After stirring at r.t. for 1 h, dimethylphenyl(3,3,3-trifluoroprop-1-en-2-yl)silane (**18b**; 350 mg, 1.52 mmol) was added at 0 °C. After stirring at r.t. for 20 h, the reaction was quenched with phosphate buffer (pH 7). The mixture was filtered through a pad of Celite, and then organic materials were extracted with EtOAc (3 ×). The combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 3:1) to give **19b** (139 mg, 34%) as a pale-yellow oil.

IR (neat): 2978, 1732, 1687, 1518, 1452, 1367, 1225, 1153, 1111, 1047, 1024, 835, 814, 779, 733, 700 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.32 (6 H, d, *J* = 1.3 Hz), 1.48 (9 H, s), 3.22 (2 H, s), 5.90 (1 H, br s), 6.93 (1 H, d, *J* = 7.5 Hz), 6.98 (1 H, dd, *J* = 7.5, 7.5 Hz), 7.17 (1 H, dd, *J* = 7.5, 7.5 Hz), 7.31 (2 H, dd, *J* = 7.2, 7.2 Hz), 7.34–7.39 (3 H, m), 7.54 (1 H, br s).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –2.6, 27.4 (dd, $J_{C,F}$ = 6, 6 Hz), 28.3, 68.7, 79.7 (dd, $J_{C,F}$ = 28, 5 Hz), 123.0 (dd, $J_{C,F}$ = 20, 13 Hz), 124.2, 127.1, 127.8, 129.3, 129.4, 133.8, 135.8, 136.4, 138.7 (dd, $J_{C,F}$ = 15, 4 Hz), 153.2, 156.9 (dd, $J_{C,F}$ = 305, 283 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 86.7 (1 F, d, $J_{F,F}$ = 31 Hz), 90.1 (1 F, d, $J_{F,F}$ = 31 Hz).

Anal. Calcd for $C_{22}H_{27}F_2NO_2Si$: C, 65.48; H, 6.74; N, 3.47. Found: C, 65.57; H, 6.89; N, 3.29.

3,3-Difluoro-[*o*-(2-dimethylphenylsilyl)]prop-2-en-1-yl]aniline (20b)

To a solution of carbamate **19b** (261 mg, 0.65 mmol) in $CHCl_3$ (8 mL) was added trimethylsilyl iodide (184 μL, 1.3 mmol) at 0 °C under argon. The mixture was stirred at 0 °C for 2 h and then at r.t. for an additional 1 h. The reaction was quenched with sat. aq $NaHCO_3$ at 0 °C. Organic materials were extracted with CH_2Cl_2 (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 2:1) to give **20b** (105 mg, 54%) as a pale-yellow oil.

IR (neat): 3381, 3068, 1684, 1622, 1495, 1456, 1427, 1250, 1215, 1111, 835, 812, 783, 733, 698 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.32 (6 H, s), 3.14 (2 H, s), 3.41 (2 H, br s), 6.58 (1 H, d, *J* = 7.8 Hz), 6.66 (1 H, dd, *J* = 7.5, 7.5 Hz),

6.84 (1 H, d, J = 7.5 Hz), 7.01 (1 H, dd, J = 7.8, 7.5 Hz), 7.30–7.39 (3 H, m), 7.42 (2 H, d, J = 7.4 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –2.6, 27.1 (dd, $J_{C,F}$ = 6, 6 Hz), 79.2 (dd, $J_{C,F}$ = 27, 5 Hz), 115.5, 118.5, 123.2 (dd, $J_{C,F}$ = 2, 2 Hz), 127.3, 127.8, 129.1, 129.3, 133.8, 136.8, 144.3, 159.1 (dd, $J_{C,F}$ = 282, 282 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 86.8 (1 F, d, $J_{F,F}$ = 33 Hz), 90.0 (1 F, d, $J_{F,F}$ = 33 Hz).

Anal. Calcd for $C_{17}H_{19}F_2NSi$: C, 67.29; H, 6.31; N, 4.62. Found: C, 67.32; H, 6.49; N, 4.40.

N-[*o*-(3,3-Difluoro-2-phenylprop-2-en-1-yl)phenyl]-*p*-toluenesulfonamide (7a)

To a solution of aniline **20a** (0.41 mg, 1.7 mmol) in pyridine (8 mL) was added *p*-toluenesulfonyl chloride (0.47 g, 2.5 mmol) at 0 °C. The mixture was stirred at r.t. for 16 h and then treated with H_2O. Organic materials were extracted with Et_2O (3 ×), and the combined extracts were washed with 2 M aq HCl (5 ×) and brine, and then dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (benzene–CH_2Cl_2, 2:1) to give **7a** (0.56 g, 85%) as a white solid.

IR (neat): 3253, 1728, 1489, 1404, 1333, 1248, 1163, 906, 729, 654 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.37 (3 H, s), 3.51 (2 H, dd, $J_{H,F}$ = 2.1, 2.1 Hz), 6.54 (1 H, s), 7.05–7.12 (5 H, m), 7.13–7.17 (1 H, m), 7.18–7.27 (5 H, m), 7.59 (2 H, d, J = 8.3, 1.4 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.4, 29.5, 90.5 (dd, $J_{C,F}$ = 21, 15 Hz), 126.0, 126.9, 127.1, 127.4, 127.5, 128.1 (dd, $J_{C,F}$ = 3, 3 Hz), 128.5, 129.4, 129.6, 132.8 (dd, $J_{C,F}$ = 3, 3 Hz), 133.4 (dd, $J_{C,F}$ = 2, 2 Hz), 134.0, 136.7, 143.8, 154.1 (dd, $J_{C,F}$ = 293, 288 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 72.3 (1 F, d, $J_{F,F}$ = 38 Hz), 72.6 (1 F, d, $J_{F,F}$ = 38 Hz).

HRMS: *m*/*z* calcd for $C_{22}H_{19}F_2NO_2S$: 399.1106 (M^+); found 399.1123.

N-{*o*-[3,3-Difluoro-2-(dimethylphenylsilyl)prop-2-en-1-yl]phenyl}-*p*-toluenesulfonamide (7b)

To a solution of aniline **20b** (105 mg, 0.35 mmol) in pyridine (5 mL) was added *p*-toluenesulfonyl chloride (99 mg, 0.54 mmol) at 0 °C. The mixture was stirred at r.t. for 10 h, and then treated with H_2O. Organic materials were extracted with Et_2O (3 ×), and the combined extracts were washed with 0.5 M aq HCl (5 ×) and brine, and then dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (benzene–CH_2Cl_2, 2:1) to give **7b** (149 mg, 94%) as a pale-yellow solid.

IR (neat): 3268, 1738, 1689, 1333, 1219, 1159, 1111, 1092, 1045, 811, 702, 660, 542 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.23 (6 H, s), 2.37 (3 H, s), 2.98 (2 H, s), 5.71 (1 H, s), 6.94 (1 H, dd, J = 4.6, 4.6 Hz), 7.04 (1 H, dd, J = 4.6, 4.6 Hz), 7.08 (1 H, d, J = 4.6 Hz), 7.09 (1 H, d, J = 4.6 Hz), 7.17 (2 H, d, J = 8.1 Hz), 7.28–7.33 (4 H, m), 7.38–7.41 (1 H, m), 7.49 (2 H, d, J = 8.1 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –2.7, 21.5, 26.8 (dd, $J_{C,F}$ = 6, 5 Hz), 79.7 (dd, $J_{C,F}$ = 28, 5 Hz), 126.2, 126.8, 127.1, 127.2, 127.9, 129.5, 129.5, 129.6, 133.8, 133.8, 134.6 (dd, $J_{C,F}$ = 3, 2 Hz), 136.2 (d, $J_{C,F}$ = 2 Hz), 136.5, 143.7, 157.1 (dd, $J_{C,F}$ = 307, 285 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 86.9 (1 F, d, $J_{F,F}$ = 32 Hz), 90.0 (1 F, d, $J_{F,F}$ = 32 Hz).

Anal. Calcd for $C_{24}H_{25}F_2NO_2SSi$: C, 62.99; H, 5.51; N, 3.06. Found: C, 62.76; H, 5.69; N, 2.83.

2-Fluoro-3-phenylquinoline (11a)

To a suspension of NaH (23 mg, 60% dispersion in mineral oil, 0.57 mmol) in DMF (2 mL) was added **7a** (103 mg, 0.46 mmol) in DMF (2 mL) at 0 °C under argon. The mixture was heated at 80 °C for 3 h. The reaction was quenched with phosphate buffer (pH 7) at r.t. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 5:1) to give **11a** (45 mg, 79%) as a white solid.

IR (neat): 3057, 1570, 1496, 1414, 1377, 1252, 1205, 777, 746, 696, 586, 515 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44 (1 H, tt, J = 7.4, 1.7 Hz), 7.50 (2 H, dd, J = 7.4, 7.4 Hz), 7.55 (1 H, dd, J = 8.0, 8.0 Hz), 7.66 (2 H, dd, J = 7.4, 1.7 Hz), 7.73 (1 H, ddd, J = 8.0, 8.0, 1.8 Hz), 7.88 (1 H, d, J = 8.0 Hz), 7.98 (1 H, d, J = 8.0 Hz), 8.27 (1 H, d, $J_{H,F}$ = 9.8 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 124.2, 124.4, 126.4 (d, $J_{C,F}$ = 2 Hz), 127.5, 127.8, 128.5, 128.7, 129.0 (d, $J_{C,F}$ = 3 Hz), 130.4, 134.1 (d, $J_{C,F}$ = 5 Hz), 140.5 (d, $J_{C,F}$ = 6 Hz), 144.9 (d, $J_{C,F}$ = 17 Hz), 158.4 (d, $J_{C,F}$ = 244 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 96.8 (d, $J_{F,H}$ = 10 Hz).

HRMS: *m*/*z* calcd for $C_{15}H_{10}FN$: 223.0798 (M^+); found: 223.0787.

N-[2-(3,3-Difluoroallyl)phenyl]-*p*-toluenesulfonamide (7c)

To a suspension of NaH (6.7 mg, 60% dispersion in mineral oil, 0.17 mmol) in DMF (2 mL) was added **7b** (35 mg, 0.076 mmol) in DMF (2 mL) at 0 °C under argon. The mixture was heated at 80 °C for 2 h. The reaction was quenched with phosphate buffer (pH 7) at r.t. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 2:1) to give **7c** (20 mg, 81%) as a colorless oil.

IR (neat): 1689, 1331, 1215, 1157, 1111, 1090, 908, 810, 729, 698, 656, 552 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.44 (3 H, s), 3.12 (2 H, ddd, J = 7.9 Hz, $J_{H,F}$ = 1.6, 1.6 Hz), 4.13 (1 H, dtd, $J_{H,F}$ = 24.9 Hz, J = 7.9 Hz, $J_{H,F}$ = 2.0 Hz), 6.42 (1 H, s), 7.13–7.21 (4 H, m), 7.24 (2 H, d, J = 8.7 Hz), 7.59 (2 H, d, J = 8.7 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.5, 24.0 (d, $J_{C,F}$ = 5 Hz), 76.4 (dd, $J_{C,F}$ = 23, 20 Hz), 126.2, 127.2, 127.2, 127.6, 129.6, 129.6, 133.8, 134.5, 136.4, 144.0, 156.5 (dd, $J_{C,F}$ = 287, 287 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 71.5 (1 F, dd, $J_{F,F}$ = 43 Hz, $J_{F,H}$ = 25 Hz), 74.4 (1 F, d, $J_{F,F}$ = 43 Hz).

HRMS: *m*/*z* calcd for $C_{16}H_{15}F_2NO_2S$: 323.0792 (M^+); found 323.0821.

2-Fluoro-3-(dimethylphenylsilyl)-1-(*p*-toluenesulfonyl)-1,4-dihydroquinoline (10b)

To a solution of sulfonamide **7b** (18.9 mg, 0.041 mmol) in DMF (3 mL) were added Et_3N (0.017 mL, 0.13 mmol) and $B(OMe)_3$ (9.3 μL, 0.083 mmol) under argon. The mixture was heated at 80 °C for 5 h. Another portion of Et_3N (0.017 mL, 0.13 mmol) was added, and the mixture was heated at 80 °C for an additional 3 h. The reaction was quenched with phosphate buffer (pH 7) at r.t. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 3:1) to give **10b** (15 mg, 85%) as a colorless oil.

IR (neat): 1653, 1371, 1244, 1205, 1165, 1111, 1088, 816, 768, 727, 700, 652, 571 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.44 (6 H, s), 2.16 (2 H, d, $J_{H,F}$ = 6.4 Hz), 2.37 (3 H, s), 6.82 (1 H, d, J = 7.5 Hz), 7.04 (2 H, d, J = 8.4 Hz), 7.16 (1 H, ddd, J = 7.7, 7.5, 1.2 Hz), 7.29 (1 H, dd, J = 7.9, 7.7 Hz), 7.29 (2 H, d, J = 8.4 Hz), 7.34–7.42 (3 H, m), 7.43 (2 H, ddd, J = 7.7, 1.6, 1.6 Hz), 7.65 (1 H, d, J = 7.9 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –3.0 (d, $J_{C,F}$ = 3 Hz), 21.6, 28.6 (d, $J_{C,F}$ = 7 Hz), 103.6 (d, $J_{C,F}$ = 34 Hz), 126.7, 126.8, 127.1, 127.3, 127.9, 128.0, 129.3, 129.4, 133.1, 133.7, 133.9, 136.6, 136.9, 144.8, 153.0 (d, $J_{C,F}$ = 261 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ_F = 83.2 (d, $J_{F,H}$ = 6 Hz).

HRMS: *m/z* calcd for $C_{24}H_{24}FNO_2SSi$: 437.1281 (M^+); found 437.1288.

3-(Dimethylphenylsilyl)-2-fluoroquinoline (11b)

Dihydroquinoline **10b** (20 mg, 0.045 mmol) and DDQ (11 mg, 0.049 mmol) were dissolved in benzene (3 mL) and refluxed for 3 h under argon. The reaction was quenched with phosphate buffer (pH 7) at r.t. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 5:1) to give **11b** (12 mg, 92%) as a colorless oil.

IR (neat): 3070, 2960, 1593, 1493, 1392, 1369, 1225, 1043, 912, 822, 785, 756, 702 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.70 (6 H, s), 7.39–7.47 (3 H, m), 7.50 (1 H, dd, J = 7.8, 7.6 Hz), 7.61 (2 H, dd, J = 7.6, 1.5 Hz), 7.71 (1 H, ddd, J = 8.1, 7.6, 1.5 Hz), 7.76 (1 H, d, J = 7.8 Hz), 7.92 (1 H, d, J = 8.1 Hz), 8.16 (1 H, d, $J_{H,F}$ = 8.2 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –2.7, 120.8 (d, $J_{C,F}$ = 51 Hz), 125.9 (d, $J_{C,F}$ = 3 Hz), 126.8, 127.6, 127.8, 128.1, 129.7, 130.9, 134.1, 135.9, 146.7 (d, $J_{C,F}$ = 17 Hz), 149.6 (d, $J_{C,F}$ = 12 Hz), 164.4 (d, $J_{C,F}$ = 239 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 111.3 (d, $J_{F,H}$ = 8 Hz).

HRMS: *m/z* calcd for $C_{17}H_{16}NFSi$ (M^+): 281.1036; found: 281.1030.

2-Fluoro-1-(*p*-toluenesulfonyl)-1,4-dihydroquinoline (10c) (And A One-Pot Procedure for 11b)

To a solution of sulfonamide **7b** (34 mg, 0.073 mmol) in DMF (3 mL) was added Et_3N (0.031 mL, 0.22 mmol), and the mixture was heated at 80 °C for 5 h under argon. After DBU (0.022 mL, 0.15 mmol) was added, the mixture was heated at 80 °C for an additional 1 h. The reaction was quenched with phosphate buffer (pH 7) at r.t. Organic materials were extracted with EtOAc (3 ×), and the combined extracts were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by PTLC on silica gel (hexane–EtOAc, 3:1) to give quinoline **11b** (11 mg, 53%) along with **10c** (4.4 mg, 20%) as a colorless oil.

10c

IR (neat): 1699, 1369, 1309, 1205, 1174, 1088, 1043, 787, 764, 696, 652, 600 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.36 (2 H, dd, J = 5.0 Hz, $J_{H,F}$ = 6.7 Hz), 2.41 (3 H, s), 5.24 (1 H, td, J = 5.0 Hz, $J_{H,F}$ = 1.7 Hz), 6.91 (1 H, d, J = 7.5 Hz), 7.15 (2 H, d, J = 8.3 Hz), 7.20 (1 H, ddd, J = 7.7, 7.4, 1.1 Hz), 7.31 (1 H, ddd, J = 7.5, 7.4, 1.1 Hz), 7.35 (2 H, d, J = 8.3 Hz), 7.70 (1 H, d, J = 7.7 Hz).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.7, 25.5 (d, $J_{C,F}$ = 4 Hz), 77.7 (d, $J_{C,F}$ = 34 Hz), 96.5 (d, $J_{C,F}$ = 27 Hz), 126.9, 127.4, 127.4, 128.3, 129.4, 132.6, 133.6, 136.8, 145.0, 150.3 (d, $J_{C,F}$ = 266 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = 69.2 (t, $J_{F,H}$ = 7 Hz).

HRMS: *m/z* calcd for $C_{16}H_{14}FNO_2S$ (M^+): 303.0729; found: 303.0723.

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