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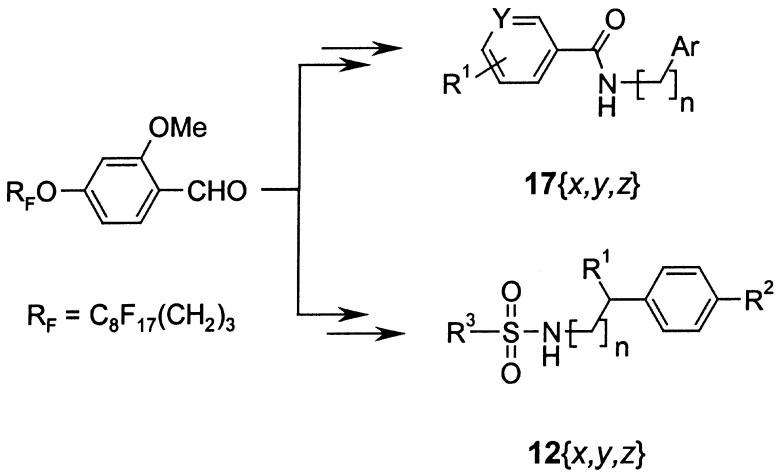

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A Fluorous-Tagged, Acid-Labile Protecting Group for the Synthesis of Carboxamides and Sulfonamides

Anne-Laure Villard, Brian H. Warrington, and Mark Ladlow*

GlaxoSmithKline Cambridge Technology Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, U.K.

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A new acid-labile, fluorous-tagged protecting group that facilitates the preparation of carboxamides and sulfonamides by parallel solution-phase synthesis is introduced. Its use is exemplified by the preparation of a 27-member library of biaryl sulfonamides and an 18-member library of biaryl carboxamides. Intermediates were purified by solid-phase extraction over reversed-phase fluorous silica gel to afford library members in high yields and purities (>95%) without the need for column chromatographic purification.

Introduction

The high-throughput synthesis of carboxamides and sulfonamides represents an important objective within the pharmaceutical industry in the search for lead compounds to initiate drug discovery research programs.[1] Some recent examples are the integrin $\alpha_4\beta_7$ antagonist **1**,[2] the AMPA potentiator **2**,[3] and the Kv1.5 channel blocker **3**[4] (Figure 1).

To exploit the efficiencies inherent in combinatorial strategies, a popular approach to such compounds utilizes solid-phase organic synthesis (SPOS) in combination with an acid-labile backbone amide linker (BAL).[5] However, the attachment of intermediates to insoluble polymer beads can lead to difficulties in monitoring reactions and prolonged reaction development and optimization times, and the inability to effect compound purification prior to final cleavage from the resin may introduce cumulative purity problems. Therefore, particularly for smaller focused arrays, attention has increasingly turned to the identification of alternative solution-phase approaches that do not suffer from these limitations.

One such strategy is fluorous-assisted synthesis in which a soluble "light" perfluoroalkyl affinity tag is attached to either the reagents or the substrate.[6] In this way, all synthetic transformations are carried out in homogeneous solution and thereby benefit from the associated favorable kinetics. Moreover, large excesses of reagents are typically not required to drive reactions to completion, and reaction progress may be readily monitored by TLC, LC/MS and NMR. Most significantly, however, all intermediates can be conveniently purified "in-line" by solid-phase extraction (SPE)[7] over reversed-phase fluorous silica gel (RPFSG)[8] without resorting to time-consuming column chromatography.

Results and Discussion

Herein, we describe the preparation and use of an acid-labile perfluoro-tagged protecting group **5** that facilitates the parallel solution-phase synthesis of carboxamide and sulfonamide compound arrays. The aldehyde **5** is readily prepared by O-alkylation of 4-hydroxy-2-methoxybenzaldehyde **4** with 3-(perfluorooctyl)propyl iodide in the presence of cesium carbonate and can be isolated in both high yield and purity by a simple aqueous workup (Scheme 1).

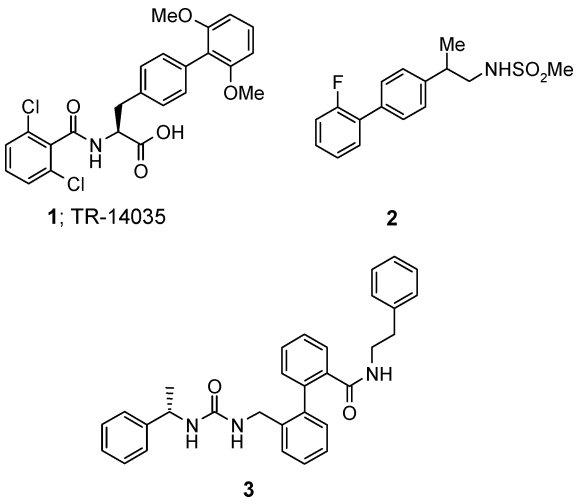
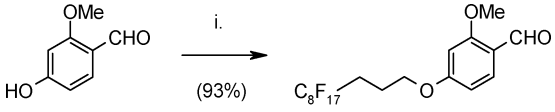


Figure 1.

Scheme 1[a]



[a] Reagents and conditions: (i) $C_8F_{17}(CH_2)_3I$, Cs_2CO_3, DMF, rt, 24 h.

To demonstrate its use in facilitating parallel solution-phase synthesis in combination with reversed-phase fluorous SPE purification, the fluorous-tagged protecting group **5** was used to prepare a 27-member 3D array of biaryl sulfonamides based upon the reported AMPA potentiator lead **2**, and an 18-member array of biaryl carboxamides.

Preparation of Sulfonamide Array 12{*x,y,z*}. A sulfonamide array based upon the AMPA potentiator lead **2** was prepared as outlined in Scheme 2. The initial reductive

* To whom correspondence should be addressed. Mark.2.Ladlow@gsk.com.

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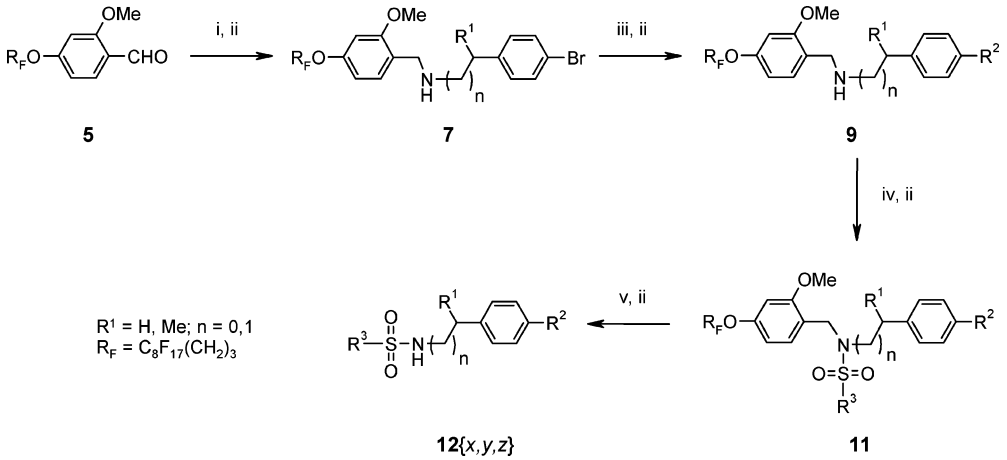
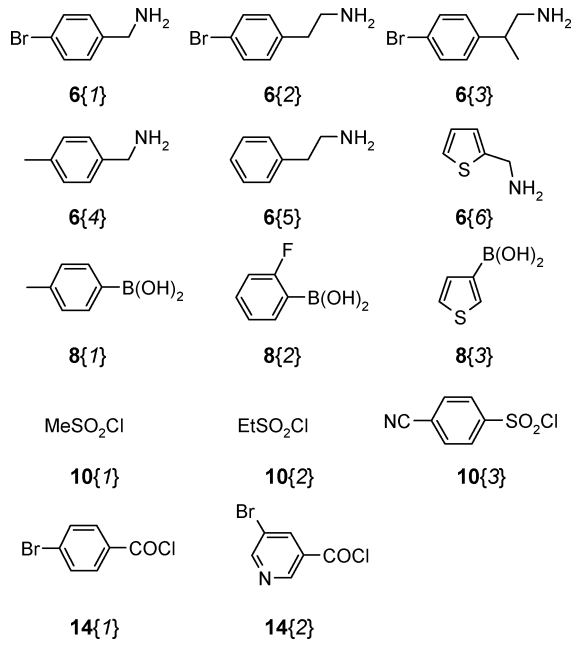
Scheme 2[a]

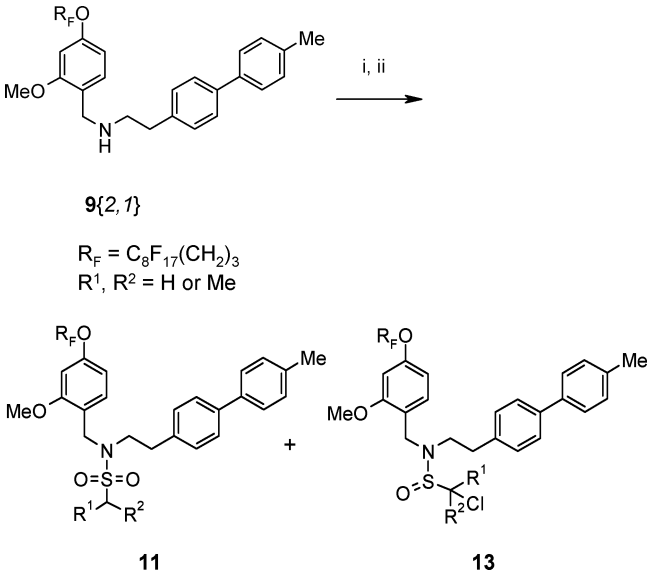


[a] Reagents and conditions: (i) amine **6**{*x*}, $NaBH(OAc)_3$, CH_2Cl_2, rt, 3 h; (ii) R_F-SPE; (iii) $R^2B(OH)_2$ **8**{*y*}, $Pd(Ph_3P)_4$, K_3PO_4, PhMe, H_2O, MW, 120 °C, 20 min; (iv) R^3SO_2Cl **10**{*z*}, MTDA, CH_2Cl_2, rt, 18 h; (v) TFA, TES, H_2O, CH_2Cl_2, [5:5:0.5:89.5], rt, 3 h.

Chart 1



Scheme 3[a]



[a] Reagents and conditions: (i) $R^1R^2CHSO_2Cl$, DMAP, CH_2Cl_2, rt, or $R^1R^2CHSO_2Cl$, MTDA, CH_2Cl_2, rt; (ii) R_F-SPE.

amination of **5** with each of the amines **6**{*1*−*3*} (Chart 1) was investigated using both sodium triacetoxyborohydride and its more organic soluble tetramethylammonium salt. Although in our hands, both of these reagents gave similar isolated yields, sodium triacetoxyborohydride afforded the intermediate fluorous-tagged secondary amines **7**{*1*−*3*} in higher purities and was, therefore, selected as the reagent of choice in this case.

The reaction mixtures were each preabsorbed onto an inert support and applied to fluorous SPE cartridges.[9] The cartridges were first eluted with a fluorophobic solvent mixture ([80:20] MeOH/H_2O) to remove all nonfluorous material and then with a fluorophilic solvent (MeOH) to elute the fluorous-tagged amines **7**{*1*−*3*} in high purities. Subsequently, the amines were each split into three parts and then subjected to a Suzuki−Miyaura coupling[10] with the boronic acids **8**{*1*−*3*} in the presence of palladium tetrakistriphenylphosphine to afford the tagged biarylamines **9**{*1*−*3,1*−*3*}. This transformation was most conveniently performed under microwave irradiation (external vessel temperature, 120 °C; 20 min) using an automated microwave batch reactor.[11] Again, all products were purified by parallel fluorous SPE; however, in this case, we found that either a second fluorous SPE purification or, alternatively, elution through an aminopropyl SPE cartridge[9] was required to rigorously remove all arylphosphine-derived contaminants. The biaryls **9**{*1*−*3,1*−*3*} were converted to the sulfonamides **11**{*1*−*3,1*−*3,1*−*3*} following treatment with the sulfonyl chlorides **10**{*1*−*3*}. Critically, to cleanly effect this transformation, we found it necessary to avoid the use of bases such as diisopropylethylamine or 4-(dimethylamino)pyridine (DMAP) and, instead, to replace these with the proton scavenger methyl trimethylsilyl dimethylketene acetal (MTDA). In this way, the competing formation of an α-chlorosulfoxide byproduct **13** arising from the instability of sulfonyl chlorides under basic conditions was prevented (Scheme 3).[12] Interestingly, it was noted that this side reaction became more prevalent with increasing steric hindrance at the sulfonyl chloride (^{i}Pr > Et > Me), presumably because under these circumstances, the rate of the desired sulfona-

Table 1. Yields and Purities for the Sulfonamide Array **12**{*x,y,z*}

12{*x,y,z*}	**6**{*x*}	**8**{*y*}	**10**{*z*}	yield (%)[a]	purity (%)[b]	$[M - H]^-$ [c]
{***1,1,1***}	***1***	***1***	***1***	**80**	>**95**	**274.0**
{*1,1,2*}	*1*	*1*	*2*	81	>95	288.1
{*1,1,3*}	*1*	*1*	*3*	73	>95	361.1
{***1,2,1***}	***1***	***2***	***1***	**96**	>**95**	**278.0**
{*1,2,2*}	*1*	*2*	*2*	95	>95	292.0
{*1,2,3*}	*1*	*2*	*3*	69	>95	365.0
{***1,3,1***}	***1***	***3***	***1***	**64**	>**95**	**266.0**
{*1,3,2*}	*1*	*3*	*2*	51	>95	279.9
{*1,3,3*}	*1*	*3*	*3*	42	>95	353.0
{*2,1,1*}	*2*	*1*	*1*	89	>95	288.1
{***2,1,2***}	***2***	***1***	***2***	**78**	>**95**	**302.1**
{*2,1,3*}	*2*	*1*	*3*	74	>95	375.1
{*2,2,1*}	*2*	*2*	*1*	95	>95	292.1
{***2,2,2***}	***2***	***2***	***2***	**87**	>**95**	**306.1**
{*2,2,3*}	*2*	*2*	*3*	75	>95	379.1
{*2,3,1*}	*2*	*3*	*1*	65	>95	280.0
{***2,3,2***}	***2***	***3***	***2***	**61**	>**95**	**294.1**
{*2,3,3*}	*2*	*3*	*3*	65	>95	367.0
{*3,1,1*}	*3*	*1*	*1*	96	>95	302.1
{*3,1,2*}	*3*	*1*	*2*	81	>95	316.2
{***3,1,3***}	***3***	***1***	***3***	**86**	>**95**	**389.0**
{***3,2,1***}	***3***	***2***	***1***	**76**	>**95**	**306.1**
{*3,2,2*}	*3*	*2*	*2*	95	>95	320.1
{***3,2,3***}	***3***	***2***	***3***	**71**	>**95**	**393.0**
{*3,3,1*}	*3*	*3*	*1*	64	>95	294.0
{*3,3,2*}	*3*	*3*	*2*	74	>95	308.1
{***3,3,3***}	***3***	***3***	***3***	**48**	>**95**	**381.0**

[a] Percentage yields were measured gravimetrically. [b] Purities were determined by LC/MS with UV detection at 220−330 nm. In addition, compounds highlighted in bold were analyzed by ^{1}H and ^{13}C NMR. [c] Molecular ions observed by electrospray (ES − ve) ionization as $[M - H]^-$.

midation process was slower. Thus, for example, using isopropyl sulfonyl chloride under standard sulfonamidation conditions (^{i}PrSO$_2$Cl, DMAP, CH_2Cl_2, rt, 18 h) the α-chlorosulfoxide **13** ($R^1 = R^2 =$ Me) was isolated as the only product in 73% yield.[13] However, in the presence of methyl trimethylsilyl dimethylketene acetal (^{i}PrSO$_2$Cl, MTDA, CH_2Cl_2, rt, 24 h), only the desired sulfonamide **11** ($R^1 = R^2 =$ Me) was obtained (28%), although this reaction was still incomplete after 24 h. In the case of ethanesulfonyl chloride, a mixture of the two possible products **11** ($R^1 =$ H, $R^2 =$ Me) and **13** ($R^1 =$ H, $R^2 =$ Me) was obtained under standard conditions (in a ratio of 4:6), but complete conversion to the desired ethanesulfonamide **11** ($R^1 =$ H, $R^2 =$ Me) was obtained using MTDA (95%). Methanesulfonyl chloride gave only the desired methanesulfonamide **11** ($R^1 = R^2 =$ H) under both sets of conditions (97%).

The sulfonamides **11**{*1−3,1−3,1−3*} were each treated with a mixture of trifluoroacetic acid, triethylsilane (TES), and water in dichloromethane [5:5:0.5:89.5] to afford the desired biaryl sulfonamides **12**{*1−3,1−3,1−3*}, which were isolated in good yields and excellent purities following a final fluorous SPE purification (Table 1). The ^{1}H NMR spectrum of a representative compound **12**{*3,2,1*} is shown in Figure 2, and the purity profile of the intermediates leading to this compound as monitored by UV−HPLC is reproduced in Figure 3, where the effectiveness of fluorous SPE purification can be clearly seen.

Preparation of Carboxamide Array 17{***x,y,z***}**.** To further demonstrate the utility of the fluorous-tagged aldehyde **5**, an 18-member 3D array of biaryl carboxamides was prepared as outlined in Scheme 4. In this case, to demonstrate some flexibility in the order in which the monomers are assembled into final library products, the biaryl moiety was incorporated in the penultimate synthesis step following acylation of the intermediate secondary amine with a bromoaryl acid chloride. Thus, again using sodium triacetoxyborohydride as the reagent of choice, **5** was subjected to reductive amination with the amine set **6**{*4−6*} to afford, after fluorous SPE, the secondary amines **7**{*4−6*} in high purities and excellent isolated yields. The amines were acylated with the acid chlorides **14**{*1−2*} in the presence of 4-(dimethylamino)-pyridine, and the products were purified by fluorous SPE. The resulting aryl bromides **15**{*4−6,1−2*} were homologated by palladium-mediated Suzuki−Miyaura coupling with the boronic acid set **8**{*1−3*} under microwave irradiation to give

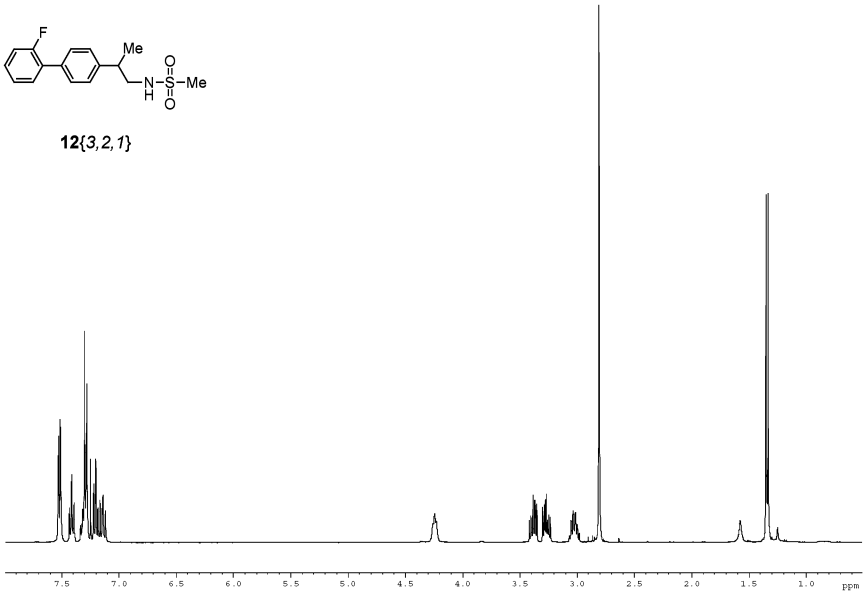


Figure 2. ^{1}H NMR spectrum of representative library member **12**{*3,2,1*}.

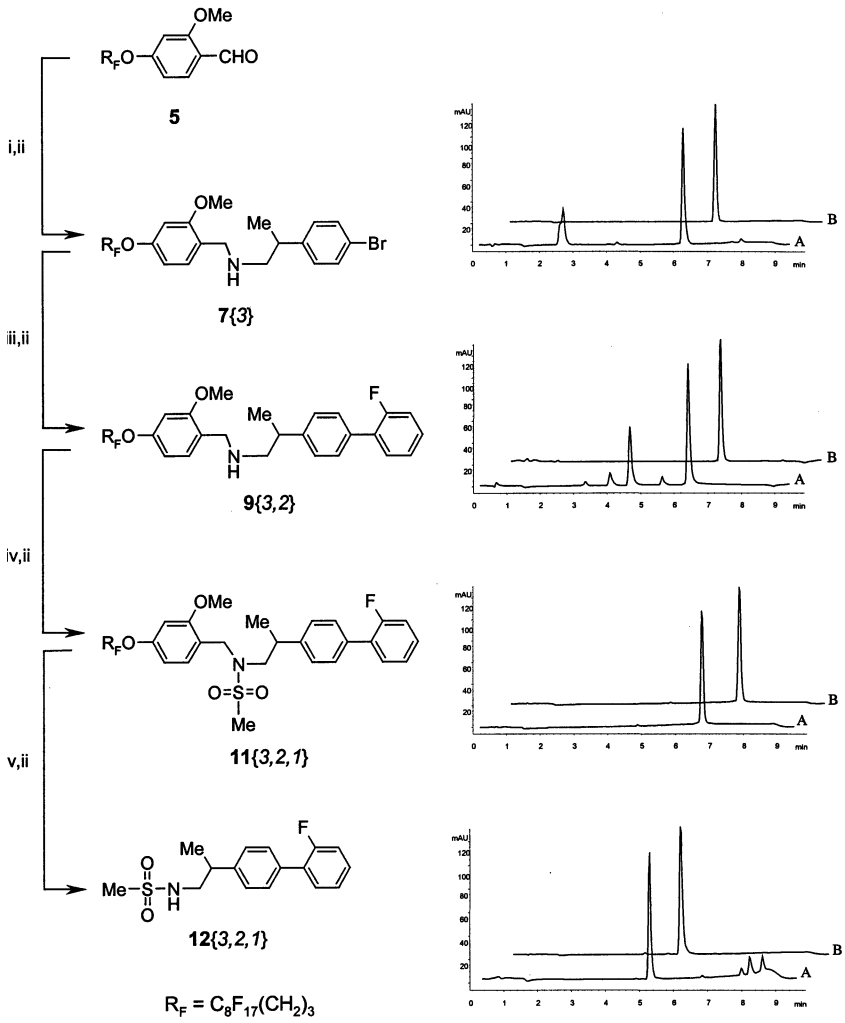


Figure 3. HPLC traces before and after fluorous SPE purification for the synthesis of a representative library member **12**{*3,2,1*}. A: crude reaction product. B: R_F-SPE purified material. (Note: in all cases, this is the fluorous fraction following elution with MeOH or [50:50] MeOH/CH_2Cl_2, except for the detagged final product **12**{*3,2,1*}, which is isolated from the nonfluorous fraction following elution with [80:20] MeOH/H_2O). Reagents and conditions as given for Scheme 2.

the corresponding biaryl carboxamides **16**{*4−6,1−2,1−3*}. In this case, in contrast to the preparation of the biaryl sulfonamides, microwave irradiation (external vessel temperature, 120 °C) for only 10 min was observed to routinely lead to complete reaction. Again, purification by either sequential fluorous and aminopropyl silica SPE or by repeating fluorous SPE twice proved most effective to afford the desired biaryl carboxamides **16**{*4−6,1−2,1−3*} in excellent purities (>95%) free of any residual arylphosphine-derived material. Finally, removal of the perfluoroalkyl tag was achieved under more forcing conditions[14] than those required for the corresponding sulfonamides **11** by exposure to a mixture of trifluoroacetic acid, triethylsilane, and water [90:5:5] at ambient temperature for 18 h. Subsequent fluorous SPE purification afforded the desired biaryl carboxamide array **17**{*4−6,1−2,1−3*} in good yields and excellent purities (> 95%) (Table 2).

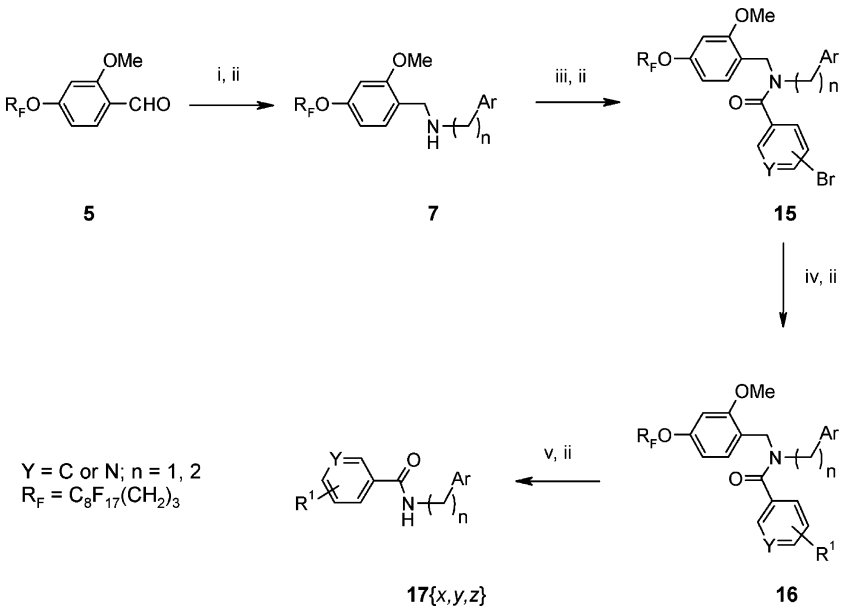
Conclusion

In summary, we have demonstrated the use of the new acid-labile fluorous protecting group **5** to facilitate the rapid parallel solution-phase multistep synthesis of a 27-member array of sulfonamides **12** and an 18-member array of carboxamides **17**. The fluorous tag was found to be compatible with microwave accelerated Suzuki−Miyaura coupling and greatly facilitated the routine purification of all intermediates by reversed-phase fluorous SPE to afford compounds in good yields and excellent purities without the need for subsequent column chromatography (Figure 2). The ability to combine the attributes of solution-phase parallel synthesis with "in-line" fluorous SPE purification in this way represents an attractive paradigm for the rapid synthesis of focused compound arrays that has potential for automated sample processing.

Experimental Section

General Methods. All starting materials, solvents, and reagents were commercially available and used without further purification, except the racemic amine **6**{*3*}, which was prepared as described in the literature.[3] Analytical high-pressure liquid chromatography (HPLC) was performed under the following conditions. Column: Supelcosil ABZ$^+$Plus, 3.3 cm × 4.6 mm, 3 μm. Eluent A: water, TFA 0.1%; B: acetonitrile 95%, water 5%, TFA 0.05%. Flow rate: 1 mL/min. Detection: UV (diode array, 215, 230, 254 nm). Method 1: gradient 10−95% B in A over 7 min. Method

Scheme 4[a]



[a] Reagents and conditions: (i) amine **6**{*x*}, $NaBH(OAc)_3$, CH_2Cl_2, rt, 3 h; (ii) R_F-SPE; (iii) acid chloride **14**{*y*}, DMAP, CH_2Cl_2, rt, 20 h; (iv) $R^1B(OH)_2$ **8**{*z*}, $Pd(Ph_3P)_4$, K_3PO_4, PhMe, H_2O, MW, 120 °C, 10 min; (v) TFA/TES/H_2O, [90:5:5], rt, 18 h.

Table 2. Yields and Purities for the Carboxamide Array **17**{*x*,*y*,*z*}

17{*x*,*y*,*z*}	**6**{*x*}	**14**{*y*}	**8**{*z*}	yield (%)[a]	purity (%)[b]	$[M + H]^{+c}$
{***4,1,1***}	***4***	***1***	***1***	**85**	>**95**	**316.2**
{*4,1,2*}	*4*	*1*	*2*	76	>95	320.2
{***4,1,3***}	***4***	***1***	***3***	**72**	>**95**	**308.1**
{*4,2,1*}	*4*	*2*	*1*	72	>95	317.2
{***4,2,2***}	***4***	***2***	***2***	**77**	>**95**	**321.2**
{*4,2,3*}	*4*	*2*	*3*	62	>95	309.1
{*5,1,1*}	*5*	*1*	*1*	80	>95	316.1
{***5,1,2***}	***5***	***1***	***2***	**68**	>**95**	**320.2**
{*5,1,3*}	*5*	*1*	*3*	64	>95	308.0
{***5,2,1***}	***5***	***2***	***1***	**95**	>**95**	**317.2**
{*5,2,2*}	*5*	*2*	*2*	82	>95	321.2
{***5,2,3***}	***5***	***2***	***3***	**97**	>**95**	**309.1**
{***6,1,1***}	***6***	***1***	***1***	**69**	>**95**	**308.1**
{***6,1,2***}	***6***	***1***	***2***	**75**	>**95**	**312.0**
{*6,1,3*}	*6*	*1*	*3*	50	>95	300.0
{*6,2,1*}	*6*	*2*	*1*	98	>95	309.1
{***6,2,2***}	***6***	***2***	***2***	**87**	>**95**	**313.1**
{***6,2,3***}	***6***	***2***	***3***	**70**	>**95**	**301.1**

[a] Percentage yields were measured gravimetrically. [b] Purities were determined by LC/MS with UV detection at 220−330 nm. In addition, compounds highlighted in bold were analyzed by ^1H and ^{13}C NMR. [c] Molecular ions observed by electrospray (ES + ve) ionization as $[M + H]^+$.

2: stepwise gradient 10−50% B in A from 0 to 1.00 min, then 50−95% B in A from 1.00 to 5.50 min. Infrared spectra were recorded on an FTIR spectrometer by attenuated total reflectance (ATR). Liquid chromatography/mass spectra (LC/MS) were recorded under electrospray positive and negative ionization following HPLC. Column: Supelcosil ABZ$^+$PLUS 3.3 cm × 4.6 mm, 3 μm. Eluent A: 10 mM solution of ammonium acetate in water, 0.1% formic acid, B: acetonitrile 95%, water 5%, formic acid 0.05%. Flow rate: 1 mL/min. Detection: UV (diode array: 220−330 nm). Gradient: 0−100% B in A over 7 min. High-resolution mass spectra were obtained in either positive or negative electrospray (ES) ionization mode using a time-of-flight spectrometer. ^1H and proton decoupled ^{13}C NMR spectra were recorded at 400 and 125 MHz, respectively, in the indicated solvent. Chemical shifts are in parts per million relative to TMS ($\delta = 0$). Multiplicities are indicated as s, singlet; d, doublet; t, triplet; m, multiplet; dd, doublet of doublet; brs, broad singlet; q, quartet; and coupling constant *J* values are quoted in hertz.

2-Methoxy-4-[3-(perfluorooctyl)propyl-1-oxy]benzaldehyde 5. A suspension of 3-(perfluorooctyl)propyl iodide (3.03 g, 5.16 mmol), 4-hydroxy-2-methoxybenzaldehyde **4** (1.02 g, 6.70 mmol) and cesium carbonate (5.00 g, 15.4 mmol) in dry DMF (20 mL) was stirred at room temperature for 24 h under nitrogen. The reaction mixture was concentrated in vacuo, and the residue was partitioned between 2 M aqueous sodium carbonate solution (200 mL) and diethyl ether (200 mL). The organic layer was separated, washed with 2 M aqueous sodium carbonate solution (3 × 50 mL) and saturated brine, and dried ($MgSO_4$). The solvent was evaporated in vacuo to afford **5** as a pale yellow powder (2.95 g, 93%). mp 72.3−72.4 °C. HPLC (method 1, 230 nm): $t_R = 7.91$ min (100%). IR: υ_{max}/cm^{-1} 1674, 1606. ^1H NMR (400 MHz, $CDCl_3$): δ_H 2.13 (2H, m), 2.32 (2H, m), 3.90 (3H, s), 4.11 (2H, t, $J_{H,F} = 6.0$), 6.45 (1H, d, $J = 2.4$), 6.53 (1H, dd, $J = 8.4, 2.4$), 7.80 (1H, d, $J = 8.4$), 10.29 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.4 (1C, d, $J_{C-F} = 3.8$), 27.8 (1C, t, $J_{C-F} = 22.3$), 55.6 (1C), 66.6 (1C), 98.4 (1C), 105.9 (1C), 105−120.7 (m, C_8F_{17}), 119.3 (1C), 130.8 (1C), 163.6 (1C), 165.0 (1C), 188.3 (1C). LC/MS (ESI): $t_R = 5.25$ min (*m*/*z* 613.1 $[M + H]^+$). HRMS (ESI): *m*/*z* calcd ($C_{19}H_{14}O_3F_{17}$) 613.0671, found 613.0682 $[M + H]^+$.

Representative Procedure for Reductive Amination. Preparation of 7{*3*}. To a stirring suspension of the amine **6**{*3*} (736 mg, 2.94 mmol) and triethylamine (410 μL, 2.94 mmol) in dry CH_2Cl_2 (14 mL) was added the aldehyde **5** (900 mg, 1.47 mmol). Stirring was continued at room temperature for 10 min, when sodium triacetoxyborohydride (1.25 g, 5.88 mmol) was added. After an additional 3 h, the

reaction mixture was quenched by adding saturated aqueous sodium bicarbonate solution (5 mL). The resulting mixture was diluted with CH_2Cl_2 (100 mL) and washed with 5 M aqueous potassium carbonate solution (50 mL). The organic layer was separated, preabsorbed onto ISOLUTE HM-N (5 g) and applied to the top of a Fluoro*Flash* silica gel SPE cartridge (12 g) which had been preconditioned with [80:20] MeOH/H_2O. The cartridge was eluted with [80:20] MeOH/H_2O (3 × 20 mL), followed by MeOH (3 × 20 mL). The MeOH fractions were combined and evaporated in vacuo to afford the amine **7**{*3*} as a colorless gum (1.10 g, 92.5%). HPLC (method 1, 230 nm): $t_R = 6.40$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.21 (3H, d, $J = 6.8$), 2.09 (2H, m), 2.32 (2H, m), 2.69 (3H, m), 2.92 (1H, m), 3.61 (1H, d, $J = 13.2$), 3.66 (3 H, s), 3.72 (1H, d, $J = 13.2$), 4.02 (2H, t, $J_{H,F} = 6.0$), 6.37 (1H, d, $J = 2.4$), 6.39 (1H, s), 7.04 (3H, m), 7.39 (2H, m).^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.0 (1C), 20.6 (1C, d, $J_{C,F} = 3.6$), 28.0 (1C, t, $J_{C,F} = 22.3$), 39.5 (1C), 49.0 (1C), 55.0 (1C), 55.8 (1C), 66.4 (1C), 98.8 (1C), 104.0 (1 C), 107−120.7 (m, C_8F_{17}), 119.8 (1C), 121.0 (1C), 129.0 (1C), 129.1 (1C), 130.3 (1C), 131.4 (1C), 131.6 (1C), 144.5 (1C), 158.6 (1C), 159.0 (1C). LC/MS (ESI): $t_R = 4.37$ min (*m*/*z* 810.2, 812.2 $[M + H]^+$).

7{***1***}**.** White solid (1.09 g, 95%). HPLC (method 1, 230 nm): $t_R = 6.23$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.10 (2H, m), 2.32 (2H, m), 3.71 (2H, s), 3.72 (2H, s), 3.81 (3H, s), 4.04 (2H, t, $J_{H,F} = 6.0$), 6.42 (1H, dd, $J = 8.4$, 2.4), 6.46 (1H, d, $J = 2.4$), 7.10 (1H, d, $J = 8.0$), 7.22 (1H, d, $J = 8.4$), 7.43 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 28.0 (1C, t, $J_{C,F} = 22.2$), 48.2 (1C), 52.1 (1C), 55.3 (1C), 66.4 (1C), 99.0 (1C), 104.1 (1 C), 107−120.7 (m, C_8F_{17}), 120.5 (1C), 121.0 (1C), 129.9 (2C), 130.5 (1C), 131.3 (2C), 139.6 (1C), 158.7 (1C), 159.1 (1C). LC/MS (ESI): $t_R = 4.29$ min (*m*/*z* 782.1, 784.1 $[M + H]^+$).

7{***2***}**.** White solid (1.10 g, 95%). HPLC (method 1, 230 nm): $t_R = 6.39$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.09 (2H, m), 2.31 (2H, m), 2.79 (4H, m), 3.72 (5H, s), 4.02 (2H, t, $J_{H,F} = 6.0$), 6.39 (1H, dd, $J = 8.0$, 2.4), 6.42 (1H, d, $J = 2.4$), 7.06 (3H, m), 7.39 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 28.0 (1C, t, $J_{C,F} = 22.2$), 35.6 (1C), 48.8 (1C), 49.9 (1C), 55.1 (1C), 66.4 (1C), 98.9 (1C), 104.1 (1 C), 107.0−121.2 (m, C_8F_{17}), 119.8 (1C), 120.9 (1C), 130.4 (2C), 130.5 (1C), 131.4 (2C), 139.2 (1C), 158.6 (1C), 159.0 (1C). LC/MS (ESI): $t_R = 4.32$ min (*m*/*z* 796.1, 798.1 $[M + H]^+$).

7{***4***}**.** Pale yellow gum (1.02 g, 97%). HPLC (method 1, 230 nm): $t_R = 6.15$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.10 (2H, m), 2.33 (2H, m), 2.34 (3H, s), 3.73 (2H, s), 3.75 (2H, s), 3.81 (3H, s), 4.04 (2H, t, $J_{H,F} = 6.0$), 6.42 (1H, dd, $J = 8.0$, 2.4), 6.46 (1H, d, $J = 2.4$), 7.13 (2H, d, $J = 8.4$), 7.23 (2H, d, $J = 8.0$). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 21.1 (1C), 28.0 (1C, t, $J_{C,F} = 22.3$), 48.3 (1C), 52.6 (1C), 55.3 (1C), 66.4 (1C), 99.0 (1C), 104.1 (1 C), 107.0−120.7 (m, C_8F_{17}), 121.3 (1C), 128.1 (2C), 128.8 (2C), 130.5 (1C), 136.3 (1C), 137.5 (1C), 158.7 (1C), 159.0 (1C). LC/MS (ESI): $t_R = 4.25$ min (*m*/*z* 718.2 $[M + H]^+$).

7{***5***}**.** Pale yellow gum (961 mg, 91%). HPLC (method 1, 230 nm): $t_R = 6.17$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_C 2.09 (2H, m), 2.31 (2H, m), 2.84 (4H, m), 3.71 (3H, s), 3.74 (2H, s), 4.02 (2H, t, $J_{H,F} = 6.0$), 6.39 (1H, dd, $J = 8.0$, 2.4), 6.42 (1H, d, $J = 2.4$), 7.09 (1H, d, $J = 8.0$), 7.20 (3H, m), 7.29 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C, d, $J_{C,F} = 3.6$), 28.0 (1C, t, $J_{C,F} = 22.2$), 36.3 (1C), 48.9 (1C), 50.2 (1C), 55.5 (1C), 66.4 (1C), 98.9 (1C), 104.1 (1C), 105.5−120.7 (m, C_8F_{17}), 121.3 (1C), 126.0 (1C), 128.4 (2C), 128.7 (2C), 130.4 (1C), 140.2 (1C), 158.6 (1C), 158.9 (1C). LC/MS (ESI): $t_R = 4.22$ min (*m*/*z* 718.3 $[M + H]^+$).

7{***6***}**.** Pale yellow gum (976 mg, 94%). HPLC (method 1, 230 nm): $t_R = 6.05$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.10 (2H, m), 2.33 (2H, m), 3.78 (2H, s), 3.81 (3H, s), 3.94 (2H, s), 4.04 (2H, t, $J_{H,F} = 6.0$), 6.42 (1H, dd, $J = 8.4$, 2.4), 6.46 (1H, d, $J = 2.4$), 6.94 (2H, m), 7.12 (1H, d, $J = 8.4$), 7.21 (1H, dd, $J = 4.8$, 1.2). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 28.0 (1C, t, $J_{C,F} = 22.2$), 47.4 (1C), 48.0 (1C), 55.3 (1C), 66.4 (1C), 99.0 (1C), 104.1 (1 C), 105.5−120.7 (m, C_8F_{17}), 120.9 (1C), 124.3 (1C), 124.7 (1C), 126.5 (1C), 130.6 (1C), 144.5 (1C), 158.8 (1C), 159.1 (1C). LC/MS (ESI): $t_R = 4.18$ min (*m*/*z* 710.2 $[M + H]^+$).

Representative Microwave Mediated Suzuki−Miyaura Coupling Procedure. Preparation of 9{***3,2***}**.** 2-Fluorobenzene boronic acid **8**{*2*} (242 mg, 1.73 mmol), aqueous potassium phosphate solution (0.5 mL × 4 M, 2.08 mmol), and palladium tetrakistriphenylphosphine (40.0 mg, 0.03 mmol) were added to a solution of the bromide **7**{*3*} (280 mg, 0.35 mmol) in degassed toluene (1.5 mL) contained in a 10-mL glass microwave reactor under nitrogen. The tube was sealed with a septum and inserted into the microwave cavity. The mixture was irradiated with stirring and simultaneous gas cooling (300 W, 120 °C) for 20 min before being allowed to cool to room temperature. The reaction mixture was diluted with water (30 mL) and ethyl acetate (30 mL), and the organic phase was separated and preabsorbed onto ISOLUTE HM-N (2 g). The preabsorbed material was applied to the top of a Fluoro*Flash* silica gel cartridge (5 g) which had been preconditioned with [80:20] MeOH/H_2O. The cartridge was eluted with [80:20] MeOH/H_2O (3 × 10 mL), then [50:50] MeOH/CH_2Cl_2 (3 × 10 mL). The MeOH/CH_2Cl_2 fractions were combined, evaporated in vacuo, and then redissolved in CH_2Cl_2 and eluted through an aminopropyl silica gel cartridge (5 g) with CH_2Cl_2 (2 × 10 mL) [alternatively, repeating the fluorous SPE purification twice gave similar results]. The filtrate was evaporated in vacuo to afford **9**{*3,2*} as a pale yellow gum (239 mg, 83%). HPLC (method 2, 254 nm): $t_R = 6.72$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.28 (3H, d, $J = 7.0$), 2.09 (2H, m), 2.30 (2H, m), 2.77 (1H, d, $J = 7.0$), 3.02 (1H, m), 3.63 (3 H, s), 3.64 (1H, d, $J = 13.2$), 3.77 (1H, d, $J = 13.2$), 4.02 (2H, t, $J_{H,F} = 6.0$), 6.38 (2H, m), 7.09 (1H, m), 7.24 (5H, m), 7.45 (3H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.2 (1C), 20.6 (1C), 28.0 (1C, t, $J_{C,F} = 22.1$), 30.7 (1C), 49.1 (1C), 55.0 (1C), 55.9 (1C), 66.3 (1C), 98.8 (1C), 104.0 (1 C), 107.0−120.7 (m, C_8F_{17}), 116.1 (1C, d, $J_{C,F} = 22.6$), 121.0 (1C), 124.3 (1C, d, $J_{C,F} = 3.6$), 127.3 (2C), 128.7 (1C, d, $J_{C,F} = 8.2$), 128.9 (2C, d, $J_{C,F} = 13.4$), 129.0 (1C, d, $J_{C,F} = 2.8$), 130.4 (1C), 130.6 (1C, d, $J_{C,F} = 3.5$), 133.7 (1C), 144.9 (1C), 158.6 (1C), 159.0 (1C), 159.8 (1C, d, $J_{C,F} = 246$). LC/MS (ESI): $t_R = 4.48$ min (*m*/*z* 826.3 $[M + H]^+$).

9{***1,1***}**.** White solid (253 mg, 91%). HPLC (method 2, 254 nm): t_R = 6.76 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.09 (2H, m), 2.33 (2H, m), 2.40 (3H, s), 3.79 (2H, s), 3.81 (2H, s), 3.82 (3H, s), 4.04 (2H, t, $J_{H,F}$ = 6.0), 6.43 (1H, dd, J = 8.0, 2.4), 6.46 (1H, d, J = 2.4), 7.16 (1H, d, J = 8.0), 7.24 (2H, d, J = 8.0), 7.40 (2H, d, J = 8.0), 7.49 (2H, dd, J = 6.8, 1.6), 7.54 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 21.1 (1C), 28.0 (1C, t, $J_{C,F}$ = 22.2), 48.1 (1C), 52.3 (1C), 55.3 (1C), 66.4 (1C), 99.0 (1C), 104.2 (1C), 107.0−120.7 (m, C_8F_{17}), 120.6 (1C), 126.8 (2C), 126.9 (2C), 128.7 (2C), 129.4 (2C), 130.7 (1C), 136.9 (1C), 138.1 (1C), 138.7 (1C), 139.8 (1C), 158.7 (1C), 159.2 (1C). LC/MS (ESI): t_R = 4.51 min (*m*/*z* 794.3 [M + H]$^+$).

9{***1,2***}**.** Pale yellow gum (265 mg, 95%). HPLC (method 2, 254 nm): t_R = 6.58 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.11 (2H, m), 2.33 (2H, m), 3.79 (2H, s), 3.80 (2H, s), 3.82 (3H, s), 4.04 (2H, t, $J_{H,F}$ = 6.0), 6.43 (1H, dd, J = 8.0, 2.4), 6.47 (1H, d, J = 2.4), 7.17 (2H, m), 7.30 (1H, m), 7.46 (5H, m). LC/MS (ESI): t_R = 4.42 min (*m*/*z* 798.3 [M + H]$^+$).

9{***1,3***}**.** Pale yellow gum (228 mg, 83%). HPLC (method 2, 254 nm): t_R = 6.51 min (98.5%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.10 (2H, m), 2.32 (2H, m), 3.77 (2H, s), 3.79 (2H, s), 3.82 (3H, s), 4.04 (2H, t, $J_{H,F}$ = 6.0), 6.43 (1H, dd, J = 8.0, 2.4), 6.47 (1H, d, J = 2.4), 7.14 (1H, d, J = 8.4), 7.37 (3H, m), 7.46 (2H, m), 7.54 (2H, m). LC/MS (ESI): t_R = 4.39 min (*m*/*z* 786.2 [M + H]$^+$).

9{***2,1***}**.** White solid (240 mg, 85%). HPLC (method 2, 254 nm): t_R = 6.84 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.08 (2H, m), 2.32 (2H, m), 2.39 (3H, s), 2.88 (4H, m), 3.69 (3H, s), 3.77 (2H, s), 4.01 (2H, t, $J_{H,F}$ = 6.0), 6.38 (1H, d, J = 2.4), 6.40 (1H, s), 7.11 (1H, d, J = 8.0), 7.24 (2H, d, J = 8.0), 7.40 (2H, d, J = 8.0), 7.49 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 21.1 (1C), 28.0 (1C, t, $J_{C,F}$ = 22.2), 35.5 (1C), 48.7 (1C), 49.9 (1C), 55.2 (1C), 66.4 (1C), 98.9 (1C), 104.2 (1 C), 107.0−120.7 (m, C_8F_{17}), 120.2 (1C), 126.7 (2C), 126.9 (2C), 129.1 (2C), 129.4 (2C), 130.6 (1C), 136.9 (1C), 138.1 (1C), 138.6 (1C), 139.0 (1C), 158.4 (1C), 159.2 (1C). LC/MS (ESI): t_R = 4.58 min (*m*/*z* 808.3 [M + H]$^+$).

9{***2,2***}**.** Pale yellow gum (230 mg, 81%). HPLC (method 2, 254 nm): t_R = 6.64 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.10 (2H, m), 2.32 (2H, m), 2.89 (4H, m), 3.70 (3H, s), 3.77 (2H, s), 4.02 (2H, t, $J_{H,F}$ = 6.0), 6.40 (2H, m), 7.16 (3H, m), 7.29 (3H, m), 7.42 (1H, dt, J = 8.0, 1.6), 7.47 (2H, dd, J = 8.0, 1.6). LC/MS (ESI): t_R = 4.45 min (*m*/*z* 812.3 [M + H]$^+$).

9{***2,3***}**.** Pale yellow gum (238 mg, 85%). HPLC (method 2, 254 nm): t_R = 6.58 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.10 (2H, m), 2.32 (2H, m), 2.86 (4H, m), 3.71 (3H, s), 3.75 (2H, s), 4.02 (2H, t, $J_{H,F}$ = 6.0), 6.40 (2H, m), 7.10 (1H, d, J = 8.4), 7.22 (2H, d, J = 8.0), 7.39 (3H, m), 7.52 (2H, m). LC/MS (ESI): t_R = 4.43 min (*m*/*z* 800.3 [M + H]$^+$).

9{***3,1***}**.** White solid (262 mg, 91%). HPLC (method 2, 254 nm): t_R = 6.91 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.27 (3H, d, J = 6.8), 2.09 (2H, m), 2.32 (2H, m), 2.40 (3H, s), 2.78 (2H, d, J = 7.6), 3.02 (1H, m), 3.62 (3H, s), 3.65 (1H, d, J = 13.4), 3.76 (1H, d, J = 13.4), 4.02 (2H, t, $J_{H,F}$ = 6.0), 6.39 (2H, m), 7.07 (1H, d, J = 8.4), 7.24 (4H, m), 7.49 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.2 (1C), 20.6 (1C), 21.1 (1C), 28.0 (1C, t, $J_{C,F}$ = 22.2), 39.5 (1C), 49.0 (1C), 55.0 (1C), 55.9 (1C), 66.4 (1C), 98.9 (1C), 104.0 (1C), 107.0−120.7 (m, C_8F_{17}), 120.6 (1C), 126.8 (2C), 127.0 (2C), 127.6 (2C), 129.5 (2C), 130.4 (1C), 136.9 (1C), 138.1 (1C), 139.1 (1C), 144.0 (1C), 158.6 (1C), 159.0 (1C). LC/MS (ESI): t_R = 4.62 min (*m*/*z* 822.3 [M + H]$^+$).

9{***3,3***}**.** Pale yellow gum (222 mg, 78%). HPLC (method 2, 254 nm): t_R = 6.65 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.25 (3H, d, J = 6.4), 2.10 (2H, m), 2.32 (2H, m), 2.75 (2H, d, J = 7.6), 2.99 (1H, m), 3.64 (3H, s), 3.65 (1H, d, J = 13.2), 3.75 (1H, d, J = 13.2), 4.02 (2H, t, $J_{H,F}$ = 6.0), 6.38 (2H, m), 7.06 (1H, d, J = 8.8), 7.21 (2H, m), 7.42 (3H, m), 7.53 (2H, m). LC/MS (ESI): t_R = 4.46 min (*m*/*z* 814.3 [M + H]$^+$).

Representative Sulfonamidation Procedure. Preparation of 11{***3,2,1***}**.** To a solution of the amine **9**{*3,2*} (86 mg, 104 μmol) in dry CH_2Cl_2 (800 μL) at room temperature was added methyl trimethylsilyl dimethylketene acetal (MTDA, 85 μL, 0.42 mmol) and methanesulfonyl chloride (12 μL, 156 μmol) with stirring. After 24 h, the reaction mixture was quenched by adding 5% aqueous potassium carbonate solution (1 mL). The organic phase was separated using a hydrophobic fritted SPE cartridge and preabsorbed onto ISOLUTE HM-N (0.5 g). The preabsorbed material was applied to the top of a Fluoro*Flash* silica gel SPE cartridge (1 g) which had been preconditioned with [80:20] MeOH/H_2O. The cartridge was eluted with [80:20] MeOH/H_2O (3 × 5 mL), followed by [50:50] MeOH/CH_2Cl_2 (3 × 5 mL). The MeOH/CH_2Cl_2 fractions were combined and evaporated in vacuo to afford the methanesulfonamide **11**{*3,2,1*} as a pale yellow gum (80 mg, 84%). HPLC (method 2, 254 nm): t_R = 7.23 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.26 (3H, d, J = 6.8), 2.11 (2H, m), 2.32 (2H, m), 2.50 (3H, s), 3.11 (1H, m), 3.29 (1H, m), 3.41 (1H, m), 3.83 (3H, s), 4.03 (2H, t, $J_{H,F}$ = 6.0), 4.24 (1H, d, J = 14.8), 4.43 (1H, d, J = 14.8), 6.45 (2H, m), 7.17 (m, 2H), 7.29 (4H, m), 7.42 (1H, dt, J = 8.0, 2.0), 7.49 (2H, dd, J = 8.0, 2.0). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 18.7 (1C), 20.5 (1C), 28.0 (1C, t, $J_{C,F}$ = 22.2), 38.5 (1C), 38.8 (1C), 45.6 (1C), 54.2 (1C), 55.2 (1C), 66.4 (1C), 98.9 (1C), 104.7 (1C), 107.0−120.7 (m, C_8F_{17}), 116.1 (1C, d, $J_{C,F}$ = 22.6), 116.7 (1C), 124.3 (1C, d, $J_{C,F}$ = 3.6), 127.6 (2C), 128.7 (1C, d, $J_{C,F}$ = 13.3), 128.9 (1C, d, $J_{C,F}$ = 8.1), 129.1 (1C, d, $J_{C,F}$ = 2.9), 130.6 (1C, d, $J_{C,F}$ = 3.5), 132.1 (1C), 134.1 (1C), 143.9 (1C), 158.6 (1C), 159.7 (1C, d, $J_{C,F}$ = 246), 159.8 (1C). LC/MS (ESI): t_R = 5.59 min (*m*/*z* 948.6 [M + HCOO$^-$]).

Representative Acylation Procedure. Preparation of 15-{***4,1***}**.** To a stirring solution of the amine **7**{*4*} (198 mg, 0.28 mmol) in dry CH_2Cl_2 (1.5 mL) at room temperature was added DMAP (202 mg, 1.65 mmol) and 4-bromobenzoyl chloride **14**{*1*} (181 mg, 0.82 mmol). After 20 h, the reaction mixture was quenched by adding 5% aqueous potassium carbonate solution (1 mL). The organic phase was separated by percolation through a hydrophobic frit and preabsorbed onto ISOLUTE HM-N (1.5 g). The preabsorbed material was applied to the top of a Fluoro*Flash* silica gel SPE cartridge (5 g) which had been preconditioned with [80:20] MeOH/

Table 3. Yields and Purities for the Fluorous-Tagged Sulfonamides **11**{*x,y,z*}

11{*x,y,z*}	**6**{*x*}	**8**{*y*}	**10**{*z*}	yield (%)[a]	purity (%)[b]	$[M + HCOO]^-$ [c]
{*1,1,1*}	*1*	*1*	*1*	96	>95	916.5
{*1,1,2*}	*1*	*1*	*2*	97	>95	930.5
{*1,1,3*}	*1*	*1*	*3*	97	>95	1003.6
{*1,2,1*}	*1*	*2*	*1*	94	>95	920.4
{*1,2,2*}	*1*	*2*	*2*	85	>95	934.9
{*1,2,3*}	*1*	*2*	*3*	90	>95	1007.5
{*1,3,1*}	*1*	*3*	*1*	94	>95	908.4
{*1,3,2*}	*1*	*3*	*2*	92	>95	922.4
{*1,3,3*}	*1*	*3*	*3*	96	>95	995.5
{*2,1,1*}	*2*	*1*	*1*	97	>95	930.5
{*2,1,2*}	*2*	*1*	*2*	97	>95	944.7
{*2,1,3*}	*2*	*1*	*3*	95	>95	1017.6
{*2,2,1*}	*2*	*2*	*1*	89	>95	934.4
{*2,2,2*}	*2*	*2*	*2*	93	>95	948.5
{*2,2,3*}	*2*	*2*	*3*	91	>95	1021.6
{*2,3,1*}	*2*	*3*	*1*	92	>95	922.5
{*2,3,2*}	*2*	*3*	*2*	95	>95	936.5
{*2,3,3*}	*2*	*3*	*3*	97	>95	1009.5
{*3,1,1*}	*3*	*1*	*1*	97	>95	944.5
{*3,1,2*}	*3*	*1*	*2*	97	>95	958.6
{*3,1,3*}	*3*	*1*	*3*	99	>95	1031.4
{*3,2,1*}	*3*	*2*	*1*	84	>95	948.6
{*3,2,2*}	*3*	*2*	*2*	91	>95	962.5
{*3,2,3*}	*3*	*2*	*3*	85	>95	1035.6
{*3,3,1*}	*3*	*3*	*1*	99	>95	936.5
{*3,3,2*}	*3*	*3*	*2*	89	>95	950.5
{*3,3,3*}	*3*	*3*	*3*	93	>95	1023.6

[a] Percentage yields were measured gravimetrically. [b] Purities were determined by LC/MS with UV detection at 220−330 nm. [c] Molecular ions observed by electrospray (ES − ve) ionization as $[M + HCOO]^-$.

H_2O. The cartridge was eluted with [80:20] MeOH/H_2O (3 × 10 mL), followed by [50:50] MeOH/CH_2Cl_2 (3 × 10 mL). The MeOH/CH_2Cl_2 fractions were combined and evaporated in vacuo to afford the carboxamide **15**{*4,1*} as a pale yellow gum (237 mg, 96%). HPLC (method 2, 230 nm): $t_R = 7.64$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.12 (2H, m), 2.33 (2H, m), 2.36 (3H, s), 3.69 (1.5H, brs), 3.76 (1.5H, brs), 4.05 (2H, t, $J_{H,F} = 6.0$), 4.32 (1H, brs), 4.37 (1H, brs), 4.62 (1H, brs), 4.65 (1H, brs), 6.44 (2H, m), 6.98 (2H, m), 7.20 (4H, m), 7.35 (2H, m), 7.50 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 21.1 (1C), 28.0 (1C, t, $J_{C,F} =$ 22.3), 29.7 (1C), 46.8 {42.2} (1C, rotamers), 47.2 {51.7} (1C, rotamers), 55.1 {55.2} (1C, rotamers), 66.4 (1C), 99.0 {98.9} (1C, rotamers), 104.3 {104.6} (1C, rotamers), 105−120.7 (m, C_8F_{17}), 116.0 (1C), 117.8 (1C), 123.7 (1C), 126.7, 129.0, 128.2, 128.4, 128.6, 129.3, 129.4, 131.0, 131.4, 131.6 (9C, rotamers), 134.1 {133.8} (1C, rotamers), 135.5 (1C), 137.0 {137.1} (1C, rotamers), 158.5 {158.8} (1C, rotamers), 159.6 {159.4} (1C, rotamers), 171.3 {171.1} (1C, rotamers). LC/MS (ESI): $t_R = 5.83$ min (*m/z* 900.6, 902.6 $[M + H]^+$).

15{***4,2***}**.** Pale yellow oil (235 mg, 93%). HPLC (method 2, 230 nm): $t_R = 7.08$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.12 (2H, m), 2.34 (2H, m), 2.36 (3H, s), 3.70 (1.3H, brs), 3.78 (0.7H, brs), 4.05 (2H, t, $J_{H,F} = 6.0$), 4.32 (1.3H, brs), 4.39 (0.7H, brs), 4.63 (1.3H, brs), 4.69 (0.7H, brs), 6.44 (2H, m), 6.97 (2H, m), 7.18 (4H, m), 7.86 (0.35H, brs), 7.94 (0.65H, brs), 8.58 (0.35H, brs), 8.63 (0.65 H, brs), 8.69 (1H, brs). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.5 (1C), 21.0 (1C), 21.5 (1C), 27.9 (1C, t, $J_{C,F} = 22.2$), 46.8 {42.8} (1C, rotamers), 47.6 {51.8} (1C, rotamers), 55.0 {55.2} (1C, rotamers), 66.4 (1C), 99.2 {98.9} (1C, rotamers), 104.4 {104.6} (1C, rotamers), 105.0−120.7 (m, C_8F_{17}), 116.2 (1C), 120.4 (1C), 126.2, 128.2, 129.4, 129.5, 129.8, 131.4 (5C, rotamers), 133.6 {133.3} (1C, rotamers), 134.0 {133.9} (1C, rotamers), 137.3 {137.2} (1C, rotamers), 137.3 {137.5} (1C, rotamers), 145.7 {145.4} (1C, rotamers), 151.5 (1C), 158.6 {158.9} (1C, rotamers), 159.9 {159.6} (1C, rotamers), 168.0 {167.9} (1C, rotamers). LC/MS (ESI): $t_R = 5.83$ min (*m/z* 901.6, 903.6 $[M + H]^+$).

15{***5,1***}**.** White powder (232 mg, 92%). HPLC (method 2, 230 nm): $t_R = 7.39$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.11 (2H, m), 2.33 (2H, m), 2.76 (0.72H, brs), 2.94 (1.28H, m), 3.36 (0.72 H, brs), 3.63 (1.72H, m), 3.72 (1.92H, brs), 3.87 (1.08H, brs), 4.04 (2H, brs), 4.27 (1.28H, brs), 4.81 (0.72H, m), 6.46 (2H, m), 6.96 (2H, m), 7.26 (6H, m), 7.49 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 27.9 (1C, t, $J_{C,F} = 22.3$), 33.4 {34.7} (1C, rotamers), 48.6 {41.5} (1C, rotamers), 46.4 {49.7} (1C, rotamers), 55.1 {55.4} (1C, rotamers), 66.4 (1C), 99.0 {98.9} (1C, rotamers), 104.4 {104.9} (1C, rotamers), 105.0−120.7 (m, C_8F_{17}), 117.3 (1C), 126.3 {126.5} (1C, rotamers), 128.1, 128.4, 128.5, 128.8, 128.9, 129.0, 131.1, 131.4 (8C, rotamers), 135.7 (1C), 139.2 {138.1} (1C, rotamers), 158.4 {158.8} (1C, rotamers), 159.6 {159.4} (1C, rotamers), 171.0 (1C). LC/MS (ESI): $t_R = 5.71$ min (*m/z* 900.5, 902.5 $[M + H]^+$).

15{***5,2***}**.** Pale yellow oil (240 mg, 95%). HPLC (method 2, 230 nm): $t_R = 6.89$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.11 (2H, m), 2.32 (2H, m), 2.79 (0.76H, brs), 2.92 (1.24H, m), 3.41 (0.76H, brs), 3.66 (1.24H, m), 3.72 (1.86H, brs), 3.88 (1.14H, brs), 4.04 (2H, m), 4.23 (1.24H, brs), 4.84 (0.76H, brs), 6.47 (2H, m), 6.95 (1H, m), 7.27 (5.38H, m), 7.82 (0.62H, brs), 8.21 (0.38H, brs), 8.50 (0.62H, brs), 8.61 (0.38H, brs), 8.68 (0.62H, brs). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.5 (1C), 21.4 (1C), 27.9 (1C, t, $J_{C,F} =$ 22.2), 33.4 {34.3} (1C, rotamers), 46.2 {49.7} (1C, rotamers), 49.0 {41.6} (1C, rotamers), 55.1 {55.4} (1C, rotamers), 66.4 (1C), 99.2 {99.0} (1C, rotamers), 104.4 {104.9} (1C, rotamers), 105.0−120.7 (m, C_8F_{17}), 116.5 {117.5} (1C, rotamers), 120.4 {120.5} (1C, rotamers), 126.5 {126.9} (1C, rotamers), 128.5, 128.8, 128.9, 129.8, 131.3 (5C, rotamers), 133.8 {134.2} (1C, rotamers), 137.3 {136.8} (1C, rotamers), 138.9 {137.7} (1C, rotamers), 145.7 {145.0} (1C, rotamers), 151.3 {151.1} (1C, rotamers), 158.6 {158.6} (1C, rotamers), 160.0 {159.6} (1C, rotamers), 167.7 (1C). LC/MS (ESI): $t_R = 5.54$ min (*m/z* 901.6, 903.6 $[M + H]^+$).

15{***6,1***}**.** White powder (250 mg, 91%). HPLC (method 2, 230 nm): $t_R = 7.29$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.12 (2H, m), 2.33 (2H, m), 3.71 (1.89H, brs), 3.80 (1.11H, m), 4.05 (2H, t, $J_{H,F} = 6.0$), 4.39 (1.26H, brs), 4.52 (0.74H, brs), 4.74 (2H, m), 6.46 (2H, m), 7.11 (3H, m), 7.25 (1H, m), 7.35 (2H, m), 7.51 (2H, d, $J = 8.0$). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 27.9 (1C, t, $J_{C,F} =$ 22.2), 42.4 {41.9} (1C, rotamers), 47.4 {47.2} (1C, rotamers), 55.1 (1C), 66.4 (1C), 99.1 (1C), 104.4 {104.7} (1C, rotamers), 105.0−120.7 (m, C_8F_{17}), 116.8 (1C), 123.9 (1C), 125.2, 125.5, 126.0, 126.4, 126.9, 129.1 (4C, rotamers), 128.6 (2C), 131.4 {131.7} (2C, rotamers), 135.1 (1C), 139.8 (1C), 158.5 {158.9} (1C, rotamers), 159.7 (1C), 171.0 {170.7} (1C,

rotamers). LC/MS (ESI): t_R = 5.68 min (*m*/*z* 892.5, 894.5 $[M + H]^+$).

15{***6,2***}**.** White powder (250 mg, 91%). HPLC (method 2, 230 nm): t_R = 6.78 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.12 (2H, m), 2.32 (2H, m), 3.72 (2.16H, brs), 3.82 (0.84H, m), 4.05 (2H, t, $J_{H,F}$ = 6.0), 4.38 (1.44H, brs), 4.52 (0.56H, brs), 4.78 (2H, brs), 6.45 (2H, m), 6.90 (3H, m), 7.27 (1H, m), 7.92 (1H, brs), 8.61 (1H, d, J = 1.6), 8.70 (1H, d, J = 2.4). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.5 (1C), 27.9 (1C, t, $J_{C,F}$ = 22.2), 42.3 {42.5} (1C, rotamers), 47.8 {47.3} (1C, rotamers), 55.1 (1C), 66.4 (1C), 99.2 {99.0} (1C, rotamers), 104.5 {104.8} (1C, rotamers), 105.0−120.7 (m, C_8F_{17}), 116.1 (1C), 120.4 (1C), 125.7 {125.5} (1C, rotamers), 126.5 {126.1} (1C, rotamers), 127.1 {126.9} (1C, rotamers), 129.9 {131.7} (1C, rotamers), 133.6 (1C), 137.4 {137.1} (1C, rotamers), 139.3 (1C), 151.6 (1C), 158.7 (1C), 160.0 {159.8} (1C, rotamers), 167.7 {167.4} (1C, rotamers). LC/MS (ESI): t_R = 5.49 min (*m*/*z* 893.5, 895.5 $[M + H]^+$).

Representative Microwave-Mediated Suzuki−Miyaura Coupling Procedure. Preparation of 16{***6,2,2***}**.** 2-Fluorobenzene boronic acid **8**{*2*} (78.0 mg, 0.56 mmol), aqueous potassium phosphate solution (0.33 mL × 2 M, 0.67 mmol), and palladium tetrakistriphenylphosphine (13.3 mg, 11.5 μmol) were added to a solution of the bromide **15**{*6,2*} (99.6 mg, 111.5 μmol) in degassed toluene (1 mL) contained in a 10-mL glass microwave reactor under nitrogen. The tube was sealed with a septum and inserted into the microwave cavity. The mixture was irradiated with stirring and simultaneous gas cooling (300 W, 120 °C) for 10 min before being allowed to cool to room temperature. The reaction mixture was diluted with water (10 mL) and ethyl acetate (10 mL), and the organic phase was separated and preabsorbed onto ISOLUTE HM-N (0.5 g). The preabsorbed material was applied to the top of a Fluoro*Flash* silica gel cartridge (1 g), which had been preconditioned with [80:20] MeOH/H_2O. The cartridge was eluted with [80:20] MeOH/H_2O (3 × 5 mL), then [50:50] MeOH/CH_2Cl_2 (3 × 5 mL). The MeOH/CH_2Cl_2 fractions were combined, evaporated in vacuo and then redissolved in CH_2Cl_2 and eluted through an aminopropyl silica gel cartridge (1 g) with CH_2Cl_2 (2 × 5 mL) [alteratively, repeating the fluorous SPE purification twice gave similar results]. The filtrate was evaporated in vacuo to afford **16**{*6,2,2*} as a colorless oil (96 mg, 95%). HPLC (method 2, 254 nm): t_R = 6.46 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): 2.12 (2H, m), 2.32 (2H, m), 3.72 (2H, brs), 3.82 (1H, m), 4.05 (2H, t, $J_{H,F}$ = 6.0), 4.46 (1.25H, brs), 4.59 (0.75H, brs), 4.78 (2H, m), 6.45 (2H, m), 6.78−7.42 (8H, m), 7.95 (1H, brs), 8.70 (1H, brs), 8.82 (1H, brs). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 27.9 (1C, t, $J_{C,F}$ = 22.2), 42.4 (1C), 47.8 {47.3} (1C, rotamers), 55.1 {55.3} (1C, rotamers), 66.4 (1C), 99.2 (1C), 104.4 {104.7} (1C, rotamers), 105.0−120.7 (m, C_8F_{17}), 116.3 (1C, d, $J_{C,F}$ = 22.0), 116.5 (1C), 124.8 (1C, d, $J_{C,F}$ = 3.6), 125.7 {125.3} (1C, rotamers), 126.5 {126.1} (1C, rotamers), 127.0 {126.9} (1C, rotamers), 129.7 (1C), 130.3 (1C, d, $J_{C,F}$ = 8.1), 130.4 (1C, d, $J_{C,F}$ = 2.9), 131.2 (1C), 131.5 (1C), 131.6 (1C), 134.9 {134.7} (1C, rotamers), 139.6 (1C), 146.7 {146.4} (1C, rotamers), 150.4 (1C, d, $J_{C,F}$ = 3.3), 158.7 {158.8} (1C, rotamers), 159.8 (1C, d, $J_{C,F}$ = 248), 159.9 {159.7} (1C, rotamers), 169.2 {168.9} (1C, rotamers). LC/MS (ESI): t_R = 5.65 min (*m*/*z* 909.3 $[M + H]^+$).

Table 4. Yields and Purities for the Fluorous-Tagged Carboxamides **16**{*x,y,z*}

16{*x,y,z*}	**6**{*x*}	**14**{*y*}	**8**{*z*}	yield (%)[a]	purity (%)[b]	$[M + H]^{+c}$
{*4,1,1*}	*4*	*1*	*1*	99	89	912.4
{*4,1,2*}	*4*	*1*	*2*	95	95	916.3
{*4,1,3*}	*4*	*1*	*3*	89	96	904.3
{*4,2,1*}	*4*	*2*	*1*	91	>95	913.4
{*4,2,2*}	*4*	*2*	*2*	91	>95	917.4
{*4,2,3*}	*4*	*2*	*3*	91	>95	905.3
{*5,1,1*}	*5*	*1*	*1*	95	>95	912.4
{*5,1,2*}	*5*	*1*	*2*	92	93	916.4
{*5,1,3*}	*5*	*1*	*3*	89	95	904.3
{*5,2,1*}	*5*	*2*	*1*	93	>95	913.4
{*5,2,2*}	*5*	*2*	*2*	93	>95	917.3
{*5,2,3*}	*5*	*2*	*3*	92	>95	905.3
{*6,1,1*}	*6*	*1*	*1*	96	97	904.3
{*6,1,2*}	*6*	*1*	*2*	92	>95	908.2
{*6,1,3*}	*6*	*1*	*3*	91	>95	896.2
{*6,2,1*}	*6*	*2*	*1*	96	>95	905.3
{*6,2,2*}	*6*	*2*	*2*	95	>95	909.3
{*6,2,3*}	*6*	*2*	*3*	91	>95	897.3

[a] Percentage yields were measured gravimetrically. [b] Purities were determined by LC/MS with UV detection at 220−330 nm. [c] Molecular ions observed by electrospray (ES + ve) ionization as $[M + H]^+$.

General Procedure for Cleavage of the Fluorous Tag. Preparation of Sulfonamides 12{***x,y,z***} **and Carboxamides 17**{***x,y,z***}.** The sulfonamides **11**{*x,y,z*} were treated with a mixture of 5% trifluoroacetic acid, 5% triethylsilane and 0.5% water in CH_2Cl_2 (1 mL) at room temperature for 3 h. The carboxamides **16**{*x,y,z*} were treated with a mixture of 90% trifluoroacetic acid, 5% triethylsilane, and 5% water (1 mL) at room temperature for 18 h.

In all cases, the resulting solutions were evaporated in vacuo, and the residues were redissolved with CH_2Cl_2 and preabsorbed onto ISOLUTE HM-N (0.5 g). These preabsorbed samples were applied to the top of Fluoro*Flash* silica gel SPE cartridges (1 g) which had been preconditioned with [80:20] MeOH/H_2O. The cartridges were eluted with [80:20] MeOH/H_2O (3 × 10 mL), and the filtrates were evaporated in vacuo to afford the desired sulfonamide **12**{*1−3,1−3,1−3*} or carboxamide **17**{*4−6,1−2,1−3*} products (Tables 1 and 2).

Note: in those cases in which the products **12** or **17** contained a thiophene moiety, it was observed that washing with [80:20] MeOH/H_2O did not efficiently remove all the desired product from the fluorous SPE cartridge. In these instances, to maximize yields, the cartridges were washed with [50:50] MeOH/CH_2Cl_2 (3 × 10 mL) to remove all the remaining material from the support, and this material was then subjected to a second fluorous SPE purification eluting with [80:20] MeOH/H_2O (3 × 10 mL) as above.

Characterization for 10 representative sulfonamides **12** and 10 representative carboxamides **17** follows:

12{***1,1,1***}**.** White solid (22.0 mg, 80%). HPLC (method 1, 254 nm): t_R = 5.31 min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (3H, s), 2.90 (3H, s), 4.35 (2H, d, J = 6.0), 4.79 (1H, m), 7.25 (2H, d, J = 8.0), 7.40 (2H, d, J = 8.4), 7.48 (2H, m), 7.58 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$):

δ 23.6 (1C), 42.9 (1C), 48.4 (1C), 125.3 (2C), 125.8 (2C), 126.7 (2C), 127.9 (2C), 133.4 (1C), 135.4 (1C), 135.5 (1C), 138.9 (1C). LC/MS (ESI): $t_R = 4.12$ min (*m*/*z* 274.0 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{15}H_{17}NO_2SNa$) 298.0878, found 298.0878 [M + Na]$^+$.

12{***1,2,1***}**.** White solid (26.2 mg, 96%). HPLC (method 1, 254 nm): $t_R = 4.88$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.92 (3H, s), 4.38 (2H, d, $J = 6.0$), 4.74 (1H, m), 7.18 (2H, m), 7.33 (1H, m), 7.42 (3H, m), 7.56 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 42.9 (1C), 48.4 (1C), 115.0 (1C, d, $J_{C,F} = 21.6$), 123.0 (1C, d, $J_{C,F} = 3.5$), 126.4 (2C), 126.7 (1C, d, $J_{C,F} = 12.8$), 127.6 (1C, d, $J_{C,F} = 8.0$), 127.9 (2C, d, $J_{C,F} = 2.9$), 128.9 (1C, d, $J_{C,F} = 3.3$), 133.8 (1C, d, $J_{C,F} = 0.6$), 134.1 (1C), 156.9 (1C, d, $J_{C,F} = 237$). LC/MS (ESI): $t_R = 3.93$ min (*m*/*z* 278.0 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{14}H_{14}NO_2SNaF$) 302.0627, found 302.0616 [M + Na]$^+$.

12{***1,3,1***}**.** Pale yellow solid (16.7 mg, 64%). HPLC (method 1, 254 nm): $t_R = 4.65$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.90 (3H, s), 4.35 (2H, d, $J = 6.0$), 4.61 (1H, m), 7.39 (4H, m), 7.47 (1H, m), 7.60 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.6 (1C), 47.3 (1C), 121.0 (1C), 126.5 (1C), 126.8 (1C), 127.2 (2C), 128.8 (2C), 135.7 (1C), 136.1 (1C), 141.9 (1C). LC/MS (ESI): $t_R = 3.83$ min (*m*/*z* 266.0 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{12}H_{13}NO_2S_2$-Na) 290.0285, found 290.0280 [M + Na]$^+$.

12{***3,2,1***}**.** Pale yellow gum (20.4 mg, 76%). HPLC (method 1, 254 nm): $t_R = 5.30$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (3H, d, $J = 6.8$), 2.82 (3H, s), 3.04 (1H, m), 3.28 (1H, m), 3.40 (1H, m), 4.26 (1H, m), 7.18 (2H, m), 7.32 (3H, m), 7.43 (1H, m), 7.53 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.3 (1C), 40.5 (1C), 40.7 (1C), 50.2 (1C), 116.5 (1C, d, $J_{C,F} = 22.6$), 124.7 (1C, d, $J_{C,F} = 3.6$), 127.7 (2C), 128.8 (1C, d, $J_{C,F} = 13.2$), 129.4 (1C, d, $J_{C,F} = 8.1$), 129.9 (2C, d, $J_{C,F} = 2.9$), 130.9 (1C, d, $J_{C,F} = 3.5$), 135.0 (1C), 142.8 (1C), 160.1 (1C, d, $J_{C,F} = 246$). LC/MS (ESI): $t_R = 4.12$ min (*m*/*z* 306.1 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{16}H_{18}NO_2SFNa$) 330.0940, found 330.0938 [M + Na]$^+$.

12{***2,1,2***}**.** White solid (23.9 mg, 78%). HPLC (method 1, 254 nm): $t_R = 5.70$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (3H, t, $J = 7.0$), 2.40 (3H, s), 2.95 (4H, m), 3.42 (2H, q, $J = 7.0$), 4.20 (1H, m), 7.26 (4H, m), 7.48 (2H, m), 7.54 (2H, m). ^{13}C NMR (120 MHz, $CDCl_3$): δ 8.6 (1C), 21.4 (1C), 36.7 (1C), 44.8 (1C), 47.4 (1C), 127.2 (2C), 127.7 (2C), 129.6 (2C), 129.9 (2C), 136.8 (1C), 137.5 (1C), 138.1 (1C), 140.2 (1C). LC/MS (ESI): $t_R = 4.32$ min (*m*/*z* 302.1 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{17}H_{21}NO_2SNa$) 326.1191, found 326.1191 [M + Na]$^+$.

12{***2,2,2***}**.** Colorless oil (25.9 mg, 87%). HPLC (method 1, 254 nm): $t_R = 5.79$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (3H, t, $J = 7.0$), 2.95 (4H, m), 3.43 (2H, q, $J = 7.0$), 4.28 (1H, m), 7.18 (2H, m), 7.31 (3H, m), 7.42 (1H, m), 7.48 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.6 (1C), 36.8 (1C), 44.7 (1C), 47.4 (1C), 116.5 (1C, d, $J_{C,F} = 22.6$), 122.8 (1C, d, $J_{C,F} = 3.8$), 128.9 (1C, d, $J_{C,F} = 13.4$), 129.3 (2C), 129.4 (1C, d, $J_{C,F} = 12.4$), 129.8 (2C, d, $J_{C,F} = 2.9$), 131.0 (1C, d, $J_{C,F} = 3.5$), 134.8 (1C), 137.7 (1C), 160.1 (1C, d, $J_{C,F} = 246$). LC/MS (ESI): $t_R = 4.13$ min (*m*/*z* 306.1 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{16}H_{18}NO_2SFNa$) 330.0940, found 330.0932 [M + Na]$^+$.

12{***2,3,2***}**.** Pale yellow solid (17.8 mg, 61%). HPLC (method 1, 254 nm): $t_R = 5.12$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (3H, t, $J = 7.0$), 2.95 (4H, m), 3.41 (2H, q, $J = 7.0$), 4.11 (1H, m), 7.24 (5H, m), 7.38 (2H, m), 7.44 (1H, m), 7.56 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.7 (1C), 36.8 (1C), 44.8 (1C), 47.5 (1C), 120.6 (1C), 126.6 (1C), 126.7 (1C), 127.2 (2C), 129.7 (2C), 135.0 (1C), 137.0 (1C), 142.2 (1C). LC/MS (ESI): $t_R = 4.05$ min (*m*/*z* 294.1 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{14}H_{17}NO_2S_2Na$) 318.0598, found 318.0599 [M + Na]$^+$.

12{***3,1,3***}**.** Pale yellow gum (34.6 mg, 86%). HPLC (method 1, 254 nm): $t_R = 6.42$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (3H, d, $J = 7.2$), 2.40 (3H, s), 2.92 (1H, m), 3.08 (1H, m), 3.30 (1H, m), 4.44 (1H, m), 7.12 (2H, m), 7.26 (2H, m), 7.49 (4H, m), 7.75 (2H, m), 7.86 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.7 (1C), 23.6 (1C), 41.4 (1C), 51.1 (1C), 115.1 (1C), 116.1 (1C), 125.2 (2C), 125.8 (2C), 125.9 (2C), 126.0 (2C), 128.0 (2C), 131.1 (2C), 135.4 (1C), 135.5 (1C), 138.1 (1C), 138.9 (1C), 142.1 (1C). LC/MS (ESI): $t_R = 4.63$ min (*m*/*z* 389.0 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{23}H_{23}N_2O_2S$) 391.1480, found 391.1499 [M + H]$^+$.

12{***3,2,3***}**.** Pale yellow oil (24.8 mg, 71%). HPLC (method 1, 254 nm): $t_R = 6.10$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (3H, d, $J = 6.8$), 2.94 (1H, m), 3.10 (1H, m), 3.31 (1H, m), 4.41 (1H, m), 7.19 (4H, m), 7.33 (2H, m), 7.42 (1H, m), 7.48 (2H, m), 7.76 (2H, m), 7.83 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.4 (1C), 40.1 (1C), 50.1 (1C), 116.6 (1C, d, $J_{C,F} = 22.6$), 116.7 (1C), 117.6 (1C), 124.9 (1C, d, $J_{C,F} = 3.6$), 127.6 (2C), 127.9 (2C), 128.6 (1C, d, $J_{C,F} = 13.3$), 129.6 (1C, d, $J_{C,F} = 8.1$), 129.9 (1C, d, $J_{C,F} = 2.9$), 130.9 (2C, d, $J_{C,F} = 3.4$), 133.3 (2C), 135.2 (1C), 142.1 (1C), 144.7 (1C), 160.1 (1C, d, $J_{C,F} = 246$). LC/MS (ESI): $t_R = 4.47$ min (*m*/*z* 393.0 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{22}H_{19}N_2O_2SFNa$) 417.1049, found 417.1060 [M + Na]$^+$.

12{***3,3,3***}**.** Pale yellow gum (17.8 mg, 48%). HPLC (method 1, 254 nm): $t_R = 5.96$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (3H, d, $J = 7.2$), 2.91 (1H, m), 3.07 (1H, m), 3.29 (1H, m), 4.45 (1H, m), 7.09 (2H, m), 7.40 (3H, m), 7.50 (2H, m), 7.74 (2H, m), 7.84 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.6 (1C), 41.4 (1C), 51.1 (1C), 115.1 (1C), 116.1 (1C), 119. 0 (1C), 124.6 (1C), 125.0 (1C), 125.4 (2C), 125.9 (2C), 126.0 (2C), 131.1 (2C), 133.1 (1C), 139.1 (1C), 139.4 (1C), 142.1 (1C). LC/MS (ESI): $t_R = 4.42$ min (*m*/*z* 381.0 [M − H]$^-$). HRMS (ESI): *m*/*z* calcd ($C_{20}H_{18}N_2O_2S_2$-Na) 405.0707, found 405.0721 [M + Na]$^+$.

17{***4,1,1***}**.** White solid (29.6 mg, 85%). HPLC (method 1, 254 nm): $t_R = 6.32$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (3H, s), 2.41 (3H, s), 4.63 (2H, d, $J = 5.6$), 6.44 (1H, m), 7.17 (2H, d, $J = 8.0$), 7.27 (4H, d, $J = 8.0$), 7.51 (2H, m), 7.63 (2H, m), 7.84 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (2C), 44.3 (1C), 127.3 (2C), 127.4 (2C), 127.8 (2C), 128.3 (2C), 129.8 (2C), 130.0 (2C), 133.1 (1C), 135.5 (1C), 137.4 (1C), 137.7 (1C), 138.3 (1C), 144.6 (1C), 167.4 (1C). (LC/MS (ESI): $t_R = 4.61$ min (*m*/*z* 316.2

$[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{22}H_{12}NO$) 316.1701, found 316.1702 $[M + H]^+$.

17{***4,1,3***}**.** Pale yellow solid (22.0 mg, 72%). HPLC (method 1, 254 nm): $t_R = 5.80$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (3H, s), 4.62 (2H, d, $J = 5.6$), 6.36 (1H, m), 7.18 (2H, d, $J = 8.0$), 7.27 (4H, m), 7.41 (2H, d, $J = 2.0$), 7.53 (1H, t, $J = 2.0$), 7.65 (2H, m), 7.82 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (1C), 44.3 (1C), 121.9 (1C), 126.5 (1C), 126.8 (2C), 127.0 (1C), 127.9 (2C), 128.3 (2C), 129.8 (2C), 133.1 (1C), 135.5 (1C), 137.8 (1C), 139.2 (1C), 141.5 (1C), 167.2 (1C). LC/MS (ESI): $t_R = 4.37$ min (*m/z* 308.1 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{19}H_{18}NOS$) 308.1109, found 308.1106 $[M + H]^+$.

17{***4,2,2***}**.** White solid (33.9 mg, 77%). HPLC (method 1, 254 nm): $t_R = 4.70$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (3H, s), 4.59 (2H, d, $J = 5.6$), 7.11 (2H, m), 7.24 (4H, m), 7.38 (1H, m), 7.44 (2H, m), 8.49 (1H, m), 8.84 (1H, m), 9.02 (1H, d, $J = 2.0$), 10.7 (1H, brs). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.4 (1C), 44.4 (1C), 116.8 (1C, d, $J_{C,F} = 22.0$), 124.4 (1C, d, $J_{C,F} = 13.3$), 125.3 (1C, d, $J_{C,F} = 3.8$), 128.4 (2C), 128.9 (1C, d, $J_{C,F} = 12.1$), 129.8 (2C), 130.8 (1C, d, $J_{C,F} = 2.6$), 130.9 (1C), 131.2 (1C, d, $J_{C,F} = 8.4$), 132.6 (1C), 134.9 (1C), 136.9 (1C), 137.9 (1C, d, $J_{C,F} = 2.1$), 145.9 (1C), 150.9 (1C), 160.1 (1C, d, $J_{C,F} = 248$), 165.1 (1C). LC/MS (ESI): $t_R = 4.10$ min (*m/z* 321.2 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{20}H_{18}N_2OF$) 321.1403, found 321.1401 $[M + H]^+$.

17{***5,1,2***}**.** White solid (22.5 mg, 68%). HPLC (method 1, 254 nm): $t_R = 5.78$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.96 (2H, *t*, $J = 6.8$), 3.75 (2H, m), 6.23 (1H, m), 7.21 (4H, m), 7.35 (3H, m), 7.44 (1H, m). 7.58 (2H, m), 7.75 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 36.0 (1C), 41.5 (1C), 116.6 (1C, d, $J_{C,F} = 22.4$), 124.8 (1C, d, $J_{C,F} = 3.6$), 127.0 (1C), 127.3 (2C), 128.3 (1C, d, $J_{C,F} = 13.1$), 129.1 (2C), 129.2 (3C), 129.5 (2C, d, $J_{C,F} = 3.1$), 130.0 (1C, d, $J_{C,F} = 8.3$), 130.9 (1C, d, $J_{C,F} = 3.3$), 134.0 (1C), 139.2 (1C, d, $J_{C,F} = 3.4$), 160.0 (1C, d, $J_{C,F} = 247$), 167.5 (1C). (LC/MS (ESI): $t_R = 4.37$ min (*m/z* 320.2 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{21}H_{19}NOF$) 320.1451, found 320.1455 $[M + H]^+$.

17{***5,2,1***}**.** Pale yellow solid (42.4 mg, 95%). HPLC (method 1, 254 nm): $t_R = 4.46$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (3H, s), 2.96 (2H, t, $J = 7.2$), 3.74 (2H, m), 7.27 (8H, m), 7.47 (2H, d, $J = 8.0$), 8.51 (1H, s), 8.85 and 8.90 (2H, 2brs), 14.21 (1H, brs). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (1C), 35.8 (1C), 41.8 (1C), 127.0 (1C), 127.3 (2C), 129.0 (4C), 130.5 (2C), 131.8 (1C), 132.9 (1C), 135.9 (1C), 138.0 (1C), 138.9 (1C), 139.7 (1C), 143.9 (1C), 147.8 (1C), 165.0 (1C). LC/MS (ESI): $t_R = 4.17$ min (*m/z* 317.2 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{21}H_{21}N_2O$) 317.1654, found 317.1660 $[M + H]^+$.

17{***5,2,3***}**.** Pale yellow solid (42.0 mg, 97%). HPLC (method 1, 254 nm): $t_R = 4.01$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.96 (2H, t, $J = 7.2$), 3.74 (2H, m), 7.26 (5H, m), 7.38 (1H, d, $J = 3.6$), 7.47 (1H, m), 7.62 (1H, m), 8.50 (1H, s), 8.84 and 8.86 (2H, 2 brs), 10.14 (1H, brs). ^{13}C NMR (125 MHz, $CDCl_3$): δ 35.8 (1C), 41.8 (1C), 123.5 (1C), 125.8 (1C), 127.0 (1C), 128.1 (1C), 129.0 (2C), 129.1 (2C), 131.9 (1C), 133.0 (1C), 135.4 (1C), 136.8 (1C), 138.9 (1C), 143.6 (1C), 147.1 (1C), 164.8 (1C). LC/MS (ESI): $t_R = 3.95$ min (*m/z* 309.1 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{18}H_{17}N_2OS$) 309.1062, found 309.1060 $[M + H]^+$.

17{***6,1,1***}**.** Pale yellow solid (22.7 mg, 69%). HPLC (method 1, 254 nm): $t_R = 6.02$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (3H, s), 4.84 (2H, d, $J = 5.6$), 6.54 (1H, m), 6.98 (1H, m), 7.06 (1H, m), 7.26 (3H, m), 7.50 (2H, m), 7.63 (2H, m), 7.84 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.5 (1C), 39.2 (1C), 125.7 (1C), 126.6 (1C), 127.3 (3C), 127.4 (2C), 127.8 (2C), 130.0 (2C), 132.8 (1C), 137.4 (1C), 138.3 (1C), 141.1 (1C), 144.8 (1C), 167.2 (1C). LC/MS (ESI): $t_R = 4.47$ min (*m/z* 308.1 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{19}H_{18}NOS$) 308.1109, found 308.1103 $[M + H]^+$.

17{***6,1,2***}**.** White solid (24.0 mg, 75%). HPLC (method 1, 254 nm): $t_R = 5.59$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.83 (2H, m), 6.52 (1H, m), 6.98 (1H, m), 7.06 (1H, m), 7.20 (3H, m), 7.35 (1H, m), 7.44 (1H, m), 7.62 (2H, m), 7.86 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 39.2 (1C), 116.6 (1C, d, $J_{C,F} = 22.5$), 124.9 (1C, d, $J_{C,F} = 3.6$), 125.8 (1C), 126.6 (1C), 127.3 (2C), 127.5 (2C), 128.3 (1C, d, $J_{C,F} = 13.1$), 129.6 (1C, d, $J_{C,F} = 3.1$), 130.1 (1C, d, $J_{C,F} = 8.3$), 130.9 (1C, d, $J_{C,F} = 3.3$), 133.5 (1C), 139.5 (1C), 141.0 (1C), 159.5 (1C, d, $J = 247$), 167.1 (1C). LC/MS (ESI): $t_R = 4.25$ min (*m/z* 312.0 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{18}H_{15}NOSF$) 312.0858, found 312.0857 $[M + H]^+$.

17{***6,2,2***}**.** Pale yellow oil (39.3 mg, 87%). HPLC (method 1, 254 nm): $t_R = 4.24$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.86 (d, 2H, $J = 5.2$), 6.59 (1H, brs), 6.98 (1H, m), 7.07 (1H, m), 7.20 (1H, m), 7.27 (2H, m), 7.43 (2H, m), 8.29 (1H, m), 8.90 (1H, m), 8.95 (1H, d, $J = 2.4$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 39.2 (1C), 116.6 (1C, d, $J_{C,F} = 22.0$), 124.1 (1C, d, $J_{C,F} = 13.1$), 125.4 (1C, $J_{C,F} = 3.8$), 125.9 (1C), 126.9 (1C), 127.4 (1C), 129.0 (1C, d, $J_{C,F} = 12.1$), 130.8 (1C, d, $J_{C,F} = 2.6$), 131.0 (1C), 131.4 (1C, d, $J_{C,F} = 12.1$), 133.0 (1C), 137.6 (1C), 145.4 (1C), 150.4 (1C), 160.1 (1C, d, $J_{C,F} = 248$), 164.7 (1C). LC/MS (ESI): $t_R = 3.89$ min (*m/z* 313.1 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{17}H_{14}N_2OSF$) 313.0811, found 313.0817 $[M + H]^+$.

17{***6,2,3***}**.** Pale yellow solid (29.4 mg, 70%). HPLC (method 1, 254 nm): $t_R = 3.73$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.84 (2H, d, $J = 5.6$), 6.96 (2H, m), 7.05 (1H, d, $J = 2.8$), 7.25 (1H, m), 7.39 (1H, m), 7.44 (1H, m), 7.56 (1H, m), 8.33 (1H, m), 8.82 (1H, d, $J = 2.0$), 8.90 (1H, d, $J = 2.0$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 39.2 (1C), 122.7 (1C), 125.9 (1C), 126.1 (1C), 126.9 (1C), 127.4 (1C), 127.7 (1C), 130.3 (1C), 132.0 (1C), 133.2 (1C), 137.9 (1C), 140.5 (1C), 146.1 (1C), 150.3 (1C), 165.6 (1C). LC/MS (ESI): $t_R = 3.82$ min (*m/z* 301.1 $[M + H]^+$). HRMS (ESI): *m/z* calcd ($C_{15}H_{13}N_2OS_2$) 301.0469, found 301.0470 $[M + H]^+$.

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Supporting Information Available. Copies of ^{1}H and ^{13}C NMR spectra for 20 representative library members. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) **13** ($R^1 = R^2 =$ Me). HPLC (method 2, 254 nm): $t_R = 8.56$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.73 (3H, s), 1.74 (3H, s), 2.11 (2H, m), 2.32 (2H, m), 2.37 (3H, s), 2.87 (2H, m), 3.07 (1H, m), 3.44 (1H, m), 3.84 (3H, s), 4.03 (2H, t, $J_{H,F} = 6.0$), 4.33 (1H, d, $J = 15.0$), 4.44 (1H, d, $J = 15.0$), 6.45 (2H, m), 7.11 (2H, d, $J = 8.0$), 7.21 (2H, d, $J = 8.0$), 7.28 (1H, d, $J = 8.8$), 7.44 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.6 (1C), 21.0 (1C), 25.6 (1C), 27.2 (1C), 28.0 (1C, t, $J_{C,F} = 22.3$), 34.5 (1C), 45.0 (1C, brs), 47.5 (1C, brs), 55.3 (1C), 66.4 (1C), 88.1 (1C), 98.8 (1C), 104.6 (1 C), 107.0−120.7 (m, C_8F_{17}), 117.3 (1C), 126.8 (2C), 127.0 (2C), 129.0 (2C), 129.4 (2C), 131.2 (1C), 136.9 (1C), 137.7 (1C), 138.0 (1C), 139.2 (1C), 159.0 (1C), 159.6 (1C). LC/MS (ESI): $t_R = 6.10$ min (*m*/*z* 976.5, 978.5 [M + HCOO$^-$]). **11** ($R^1 = R^2 =$ Me): HPLC (method 2, 254 nm): $t_R = 8.00$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.27 (6H, d, $J = 7.0$), 2.11 (2H, m), 2.32 (2H, m), 2.37 (3H, s), 2.85 (2H, m), 2.95 (1H, m), 3.41 (2H, m), 3.83 (3H, s), 4.03 (2H, t, $J_{H,F} = 6.0$), 4.44 (2H, s), 6.45 (2H, m), 7.16 (2H, d, $J =$ 8.0), 7.21 (2H, d, $J = 8.0$), 7.32 (1H, d, $J = 8.8$), 7.44 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 16.6 (1C), 20.6 (1C), 21.0 (1C), 28.0 (1C, t, $J_{C,F} = 22.1$), 35.4 (2C), 45.6 (1C), 49.7 (1C), 53.9 (1C), 55.3 (1C), 66.4 (1C), 98.8 (1C), 104.7 (1 C), 107.0−120.7 (m, C_8F_{17}), 117.4 (1C), 126.8 (2C), 127.0 (2C), 129.2 (2C), 129.4 (2C), 131.7 (1C), 136.9 (1C), 137.6 (1C), 137.9 (1C), 139.3 (1C), 158.6 (1C), 159.7 (1C). LC/MS (ESI): $t_R = 6.08$ min (*m*/*z* 958.3 [M + HCOO$^-$]).

13 ($R^1 =$ H, $R^2 =$ Me): HPLC (method 2, 254 nm): $t_R =$ 7.92 (44%) and 8.36 min (56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.47 (1.32H, d, $J = 7.0$), 1.79 (1.68H, d, $J =$ 7.0), 2.11 (2H, m), 2.32 (2H, m), 2.38 (3H, s), 2.85 (2H, m), 3.21 (1H, m), 3.41 (1H, m), 3.82 (3H, m), 4.03 (2H, m), 4.17 (1H, m), 4.47 (2H, m), 6.45 (2H, m), 7.13 (2H, m), 7.23 (3H, m), 7.45 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 19.4 and 20.2 (1C), 20.6 (1C), 21.0 (1C), 28.0 (1C, t, $J_{C,F} = 22.2$), 34.8 and 35.1 (1C), 45.3 and 46.1 (1C), 48.4 and 49.1 (1C), 55.2 and 55.3 (1C), 66.3 and 66.4 (1C), 69.4 and 72.4 (1C), 98.9 and 99.0 (1C), 104.5 and 104.6 (1C), 107.0−120.7 (m, C_8F_{17}), 117.1 and 117.3 (1C), 126.7 and 126.8 (2C), 126.9 and 127.0 (2C), 129.0 and 129.1 (2C), 129.4 and 129.5 (2C), 131.2 and 131.8 (1C), 136.9 and 137.0 (1C), 137.6 and 137.7 (1C), 137.9 and 138.0 (1C), 139.2 and 139.4 (1C), 158.8 and 158.9 (1C), 159.7 and 159.9 (1C). LC/MS (ESI): $t_R = 5.88$ (44%) and 6.03 (56%) min (*m*/*z* 962.2, 964.1 [M + HCOO$^-$]). **11** ($R^1 =$ H, $R^2 =$ Me): HPLC (method 2, 254 nm): $t_R = 7.76$ min (100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.25 (3H, t, $J = 7.5$), 2.11 (2H, m), 2.32 (2H, m), 2.35 (3H, s), 2.84 (4H, m), 3.42 (2H, m), 3.83 (3H, s), 4.04 (2H, t, $J_{H,F} = 6.0$), 4.42 (2H, s), 6.46 (2H, m), 7.18 (2H, d, $J = 8.0$), 7.22 (2H, d, $J = 8.0$), 7.31 (1H, d, $J =$ 8.8), 7.46 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 8.1 (1C), 20.6 (1C), 21.0 (1C), 28.0 (1C, t, $J_{C,F} = 22.2$), 35.2 (1C), 45.3 (1C), 47.0 (1C), 55.3 (1C), 66.4 (1C), 98.9 (1C), 104.7 (1C), 107.0−120.7 (m, C_8F_{17}), 117.2 (1C), 126.8 (2C), 127.0 (2C), 129.2 (2C), 129.5 (2C), 131.7 (1C), 137.0 (1C), 137.5 (1C), 137.9 (1C), 139.3 (1C), 1158.6 (1C), 159.8 (1C). LC/MS (ESI): $t_R = 5.79$ min (*m*/*z* 944.7 [M + HCOO$^-$]).

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