# Facile and Efficient Synthesis of 4-Azidotetrafluoroaniline: A New Photoaffinity Reagent†

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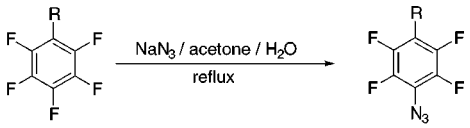
*p*-Azidotetrafluoroaniline (**1**) was synthesized in 65−73% yield by two different methods employing a stable carbamate intermediate. The first method trapped the intermediate isocyanate generated via a modified Curtius rearrangement with 2-methyl-2-propanol or 2-(trimethylsilyl)ethanol to form the stable carbamates **2d** and **2e**, respectively. Benzoic acid **2c** was first converted to its acid chloride with $PCl_5$. Displacement of the chloride by $NaN_3$ in acetone/water formed the acyl azide. Thermal rearrangement followed by the addition of the appropriate alcohols provided the carbamates. The acid labile carbamate **2d** was deprotected with HCl/AcOH to provide **1**, while trifluoroacetic acid was required to deprotect **2e** and afford **1**. In the second path, **1** was synthesized in five steps from pentafluoronitrobenzene (**3a**) in 65% overall yield. Compound **3a** was converted into 4-azidotetrafluoronitrobenzene (**3b**) with $NaN_3$ in 93% yield and was used without further purification to form 1,4-diaminotetrafluorobenzene (**3c**) by Sn/HCl reduction in 85% yield. The mono-9-fluorenylmethoxycarbonyl (FMOC) derivative **3d** was formed from **3c** with FMOC−Cl and pyridine in EtOAc in 92% yield. Diazotization of **3d** under anhydrous conditions with TFA/$NaNO_2$ and $NaN_3$ gave **3e** in 87% yield. The aryl azide was formed with concurrent nitration of the 2-position of the fluorenyl system. The protecting group was removed with piperidine to afford **1** in 93% yield. Irradiation of **1** with 254 nm light in cyclohexane gave cyclohexylamine **11**, diamine **3c**, and azobenzene **12** as the primary products. The formation of C−H insertion product **11** indicates that **1** forms a singlet nitrene upon photolysis. Two heterobifunctional photoaffinity reagents iodoacetamide **9** and dansyl derivative **10** were prepared.

## Introduction

Fluorinated aryl azides have been used extensively as photoaffinity probes to study protein structure and function.[1] Photolysis of fluorinated aryl azides yields singlet nitrenes that are capable of inserting into C−H bonds. Consequently, molecules containing fluorinated aryl azides are useful in probing reversible biochemical binding interactions involving nonpolar surfaces.[2] A variety of perfluorophenyl azides bearing functionality suitable for incorporation of the photoprobe into structures of interest have been synthesized.[2g,h] However, *p*-azidotetrafluoroaniline (**1**) is conspicuously absent among the described perfluorophenyl azides (Figure 1). In the course of developing a series of heterobifunctional cross-linking reagents, we required **1** as a synthon and have developed two routes for the preparation of **1**




**2a**. R = $CO_2Me$ **5a**. R = COMe **2b**. R = $CO_2Me$ **5b**. R = COMe
**3a**. R = $NO_2$ **6a**. R = $CONH_2$ **3b**. R = $NO_2$ **6b**. R = $CONH_2$
**4a**. R = CHO **7a**. R = CN **4b**. R = CHO **7b**. R = CN

**Figure 1.**

(Schemes 1 and 2), a new member to the functionalized perfluorophenyl azide family containing a chemically reactive electron-donating amino group *para* to the azido functionality.

## Results and Discussion

The first route to **1** employed a modified Curtius reaction, where the intermediate isocyanante was trapped with 2-methyl-2-propanol or 2-(trimethylsilyl)ethanol to form the stable carbamates **2d** and **2e**, respectively (Scheme 1). Methyl pentafluorobenzoate (**2a**) was first converted into methyl 4-azidotetrafluorobenzoate (**2b**) by nucleophilic aromatic substitution with $NaN_3$ in 96% yield.[2g] Saponification of **2b** with NaOH in aqueous methanol gave **2c** in nearly quantitative yield. Compound **2c** was transformed into the intermediate acid chloride,[3] followed by conversion to the acyl azide through $NaN_3$

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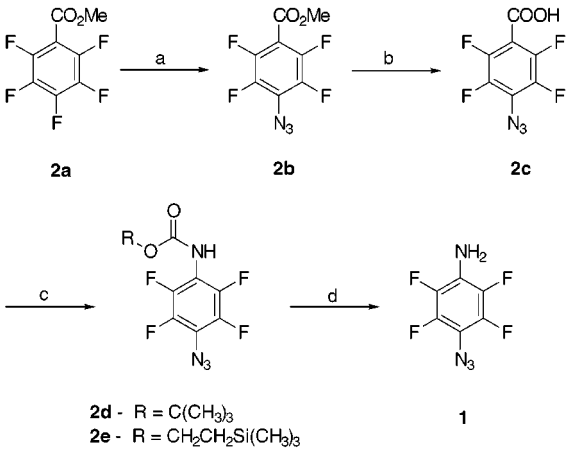
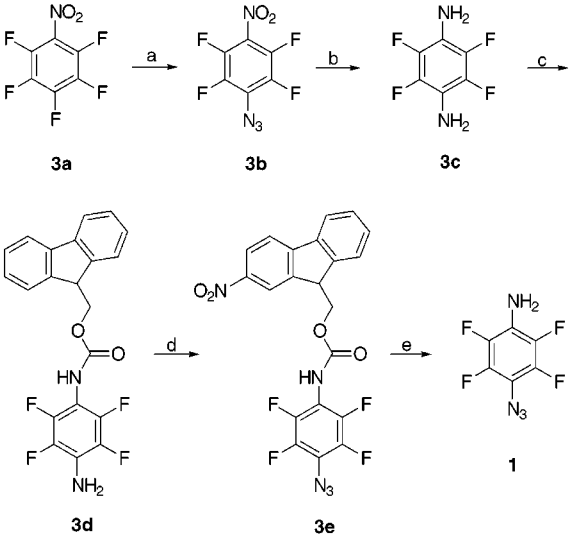
**Scheme 1**[a]




[a] Reaction conditions: (a) acetone, $H_2O$, $NaN_3$; (b) KOH, MeOH, $H_2O$; (c) (1) $PCl_5$, $Et_2O$; (2) $NaN_3$; (3) $C_6H_6$, $\Delta$; (4) $(CH_3)_3COH$ or $(CH_3)_3SiCH_2CH_2OH$; (d) **10d**—HCl, HOAc, $Et_2O$; **10e**—TFA, $CH_2Cl_2$.

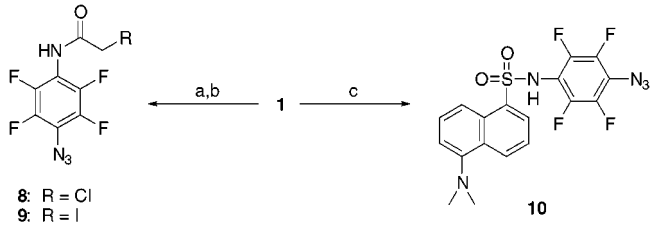
**Scheme 2**[a]




[a] Reaction conditions: (a) acetone, $H_2O$, $NaN_3$; (b) Sn, HCl, EtOH; (c) FMOC—Cl, pyridine, EtOAc; (d) $CF_3CO_2H$, $NaNO_2$; $NaN_3$; (e) piperidine.

displacement in acetone/water. The crude acyl azide was isolated, immediately converted into the isocyanate by thermal rearrangement in dry benzene, and trapped as the carbamates **2d** and **2e** by the subsequent addition of 2-methyl-2-propanol or 2-trimethylsilylethanol, respectively. Yields of the purified carbamates ranged between 76 and 88%. This appears to be the first example of a Curtius rearrangement of a perfluoroaryl compound. Azide **1** was liberated from the acid labile *tert*-butyl carbamate in 83% yield with hydrogen chloride in acetic acid. Deprotection of **2e** required trifluoroacetic acid in $CH_2Cl_2$ to liberate **1** in 86% yield. The normal route for deprotection of trimethylsilylethyl carbamates using $(n\text{-}Bu)_4NF$ in tetrahydrofuran (THF) was not employed because perfluorinated aryl azides are not compatible with this reagent.[4] Although **1** is stable up to several months if stored at −20 °C under argon, azide **1** forms deeply colored contaminants on standing at room temperature. Therefore, it is highly desirable to store the synthon as the stable carbamates **2d** or **2e** and liberate **1** immediately before use.

**Scheme 3**[a]




[a] Reaction conditions: (a) chloroacetyl chloride, pyridine, EtOAc; (b) acetone, NaI; (c) dansyl chloride, $LiN[Si(CH_3)_3]_2$, THF.

The second approach to **1** employed a five-step scheme via the base-labile 9-fluorenylmethoxycarbonyl (FMOC) carbamate in an overall yield of 65% from **3a** (Scheme 2). Commercially available pentafluoronitrobenzene **3a** was converted into 4-azidotetrafluoronitrobenzene **3b** by nucleophilic aromatic substitution with $NaN_3$ in 93% yield.[2g,5] No *ortho* isomer was detected in the crude reaction mixture, and azide **3b** was used without further purification to form the air and light sensitive diamine **3c** by Sn/HCl reduction in 85% yield. Previously reported methods to generate **3c** gave either poor yields or required expensive starting materials.[6] We benefited from the low reactivity of the parent tetrafluorophenylenediamine (**3c**) to successfully form the mono-FMOC protected derivative **3d** in 92% yield by reacting **3c** with FMOC—Cl and pyridine in EtOAc. Reaction of **3c** with $(Boc)_2O$ and Hünig's base gave no product. Diazotization of **3d** under anhydrous conditions with trifluoroacetic acid (TFA)/$NaNO_2$ and $NaN_3$ gave **3e** in 87% yield.[7] One- and two-dimensional and $^1H$ and $^{13}C$ NMR, IR, elemental analysis, and mass spectral data confirm that the aryl azide was formed with concurrent nitration of the 2-position of the fluorenyl system. This was not surprising, as TFA/$NaNO_2$ has been previously shown to nitrate fluorenes at the 2-position.[8] The 2-nitro-FMOC protecting group was removed with piperidine to afford **1** in 93% yield. As noted above, it is highly desirable to store azide **1** as the stable carbamate **3e** and liberate it with piperidine immediately before use.

Irradiation of tetrafluoroaryl azide **1** with 254 nm light in cyclohexane gave cyclohexylamine **11**, diamine **3c**, and azobenzene **12** as the primary products (Figure 2). The formation of C—H insertion product **11** indicates that azide **1** forms a singlet nitrene upon photolysis.[9] Formation of diamine **3c** is expected from hydrogen abstraction by the nitrene, and azobenzene **12** is expected because nitrenes couple with nitrenes to form diazo compounds much more efficiently than they C—H insert.[2d,10]

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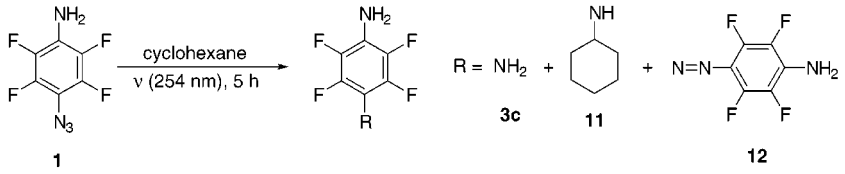


1 3c 11 12

**Figure 2.**

Two derivatives of azide **1** were prepared to demonstrate its potential utility in heterobifunctional photoaffinity reagents (Scheme 3). Azide **9** was synthesized by reacting aniline **1** with chloroacetyl chloride to provide chloroacetamide **8** followed by conversion to the corresponding iodide via the Finkelstein reaction in 73% overall yield. Attempts to synthesize azide **9** directly from iodoacetyl chloride were unsuccessful. The iodoacetamido azide **9** is attractive because the chemically reactive iodoacetamido group is connected to the perfluoroaryl azide, which can form a singlet nitrene upon UV irradiation. Dansyl derivative **10** is a photoreactive fluorophore suitable for labeling nonpolar residues and surfaces. Azide **10** was prepared in 67% yield by condensing dansyl chloride with aniline **1** in the presence of lithium bis(trimethylsilyl)amide in THF.

## Experimental Section

**General Procedures.**[11] *Caution! Organic azides should be considered explosive, and all manipulations should take place behind a blast shield! Aryl azides are light sensitive, and all reactions and flash chromatography procedures should be conducted under diminished light.* All reactions were conducted under dry argon and stirred magnetically except as noted. Analytical TLC was performed on precoated (0.25 mm) silica gel 60F-254 plates purchased from E. Merck, developed with 30% ethyl acetate in hexane, except where noted, and visualized under UV irradiation. Melting points are uncorrected. Chemical shifts are reported in parts per million downfield using the $CDCl_3$ peak (7.27 ppm, $^1$H; 77.4 ppm, $^{13}$C) or the DMSO-$d_6$ (2.54 ppm, $^1$H; 43 ppm, $^{13}$C) as an internal reference. Hexafluorobenzene ($C_6F_6$) was used as an internal reference (−162.9 ppm, $^{19}$F). Electron impact, FAB, and MALDI mass spectra were performed at the University of Kentucky Mass Spectra Facility. Combustion analyses were performed by Atlantic Microlabs, Inc., Norcross, GA.

**General Procedure for Carbamate Synthesis.** The carboxylic acid **2c** (2.00 g, 8.51 mmol) was dissolved in $Et_2O$ (30 mL) followed by the addition of $PCl_5$ (1.88 g, 9.02 mmol). The mixture was stirred under argon for 1 h at room temperature. The solvent was removed in vacuo to leave a yellow oil which was further evaporated for 1 h at 25 °C under vacuum affording 2.16 g (100%) of a yellow oil. The acid chloride was dissolved in 45 mL of dry acetone, and the resulting solution was added dropwise to a rapidly stirred solution of 2.03 g (31.2 mmol) sodium azide in 6.5 mL of water at 0 °C. After the final addition of the acid chloride, the mixture was stirred for an additional 15 min at 0 °C. The reaction mixture was poured into a separatory funnel containing 150 mL of hexane and 100 mL of $H_2O$ and shaken. The hexane layer was removed, and the aqueous layer was extracted with hexane again. The combined organic layers were dried over $MgSO_4$ ($R_f$ of acyl azide: 0.64), filtered, and concentrated. The crude acyl azide was then dissolved in 20 mL of anhydrous benzene and heated at 70 °C for 1 h ($R_f$ of isocyanate: 0.48) before the addition of either 5 mL (52.3 mmol) of anhydrous 2-methyl-2-propanol or 2.5 mL (17.4 mmol) of 2-(trimethylsilyl)ethanol. The solution was stirred at 70 °C for an additional 6 h ($R_f$'s: **2d**, 0.56; **2e**, 0.58). The red-violet reaction mixture was concentrated, loaded onto a silica column, and purified by flash chromatography (5% EtOAc in hexane).

**4-(*N*-(*tert*-Butoxycarbonyl)amino)tetrafluorophenyl Azide (2d).** A 2.29 g amount (88%) of a white crystalline solid. $^1$H NMR (400 MHz) $\delta$ 6.13 (bs, 1H), 1.51 (s, 9H). $^{13}$C NMR (100.7 MHz) $\delta$ 152.6, 144.3 (m), 142.4 (m), 141.9 (m), 139.9 (m), 117.9 (m), 113.4 (m), 82.7, 28.4. $^{19}$F NMR (376.7 MHz) $\delta$ −153.78 (m), −147.77 (m). IR: 3298, 2976, 2121, 1720, 1535, 1510, 1488, 1445, 1401, 1369, 1252, 1166, 1001, 985 cm$^{-1}$. Sublimation (70 °C/0.5 mm) followed by crystallization from hexane provided the analytical sample of **10d** as colorless prismatic needles, mp 80 °C. Anal. Calcd for $C_{11}H_{10}F_4N_4O_2$: C, 43.14; H, 3.29; N, 18.30. Found: C, 43.31; H, 3.30; N, 18.55. High-resolution EIMS calcd for $C_{11}H_{10}F_4N_4O_2$: 306.0740. Found: 306.0733.

**4-(*N*-((2-(Trimethylsilyl)ethoxy)carbonyl)amino)tetrafluorophenyl Azide (2e).** A 2.74 g amount of pale-yellow viscous oil (92%). $^1$H NMR (200 MHz) $\delta$ 6.08 (bs, 1H), 4.29 (m, 2H), 1.05 (m, 2H), 0.06 (s, 9H). $^{13}$C NMR (50.3 MHz) $\delta$ 153.9, 147.9 (m), 146.0 (m), 141.5 (m), 139.9 (m), 139.7 (m), 138.0 (m), 119.4 (m), 105.8 (m), 65.6, 18.0, 1.2. $^{19}$F NMR (376.7 MHz) $\delta$ −153.55 (m), −147.65 (m). IR: 3274, 2957, 2901, 2126, 1714, 1652, 1509, 1251, 1179, 1125, 1041, 1002, 932, 839, 770, 743, 696, 671 cm$^{-1}$. Anal. Calcd for $C_{12}H_{14}F_4N_4O_2Si$: C, 41.14; H, 4.03; N, 15.99. Found: C, 41.26; H, 4.16; N, 15.90. High-resolution EIMS calcd for $C_{12}H_{14}F_4N_4O_2Si$: 350.0822. Found: 350.0820.

**Deprotection of 4-(*N*-(*tert*-butoxycarbonyl)amino)tetrafluorophenyl Azide (2d) To Give 1.** The carbamate **2d** (1.31 g, 4.28 mmol) was dissolved in 5 mL of $CH_2Cl_2$ in a 50 mL pear-shaped flask at 0 °C. To the solution was added 15 mL of a 1 N HCl solution in HOAc (Aldrich). The solution was stirred at 0 °C for 2 h and then stirred at room temperature overnight. A 20 mL aliquot of $H_2O$ was added, and the mixture was transferred to a separatory funnel containing 150 mL of hexane/$Et_2O$ (1:1 (v/v)) and 20 mL of $H_2O$ and shaken. The aqueous layer was discarded, and the organics were then washed with 5% $NaHCO_3$ and water, dried ($MgSO_4$), filtered over a short pad of silica gel, and concentrated to afford 0.73 g (83%) of **1**.

**Deprotection of 4-(*N*-((2-(Trimethylsilyl)ethoxy)carbonyl)amino)tetrafluorophenyl Azide (2e) To Give 1.** The carbamate **2e** (1.50 g, 4.28 mmol) was dissolved in 25 mL of $CH_2Cl_2$ at 0 °C. To the solution was added 2.5 mL of TFA. The solution was allowed to stir at 0 °C for 3 h and then at room temperature overnight. The reaction was then slowly quenched by the addition of a saturated $NaHCO_3$ solution. The reaction mixture was transferred to a separatory funnel containing 100 mL of $Et_2O$ and 20 mL of $H_2O$ and shaken and the aqueous layer discarded. The organics were washed once more with water, dried ($MgSO_4$), filtered through a pad of silica gel, and concentrated to afford 0.76 g (86%) of **1**.

**1,4-Tetrafluorophenylenediamine (3c).** Pentafluoronitrobenzene (**3a**) was converted into 4-azidotetrafluoronitrobenzene (**3b**) with $NaN_3$ as described by Keana and Cai[2g] in 93% yield and used without further purification. Into a 1000 mL three neck round-bottom flask equipped with reflux condenser was added 200 mL of 95% EtOH, 60 g (0.51 mol) of powdered tin (325 mesh), and 26.41 g (0.11 mol) of crude **3b** dissolved in 50 mL of 95% EtOH with stirring. A 140 mL aliquot of concentrated HCl was then added dropwise to the heterogeneous mixture over a 30 min period. The mixture was refluxed for 4 h, cooled to room temperature, and placed into an ice bath. The mixture was made basic by slow addition of 160 g

(11) For additional information, see supporting information.

of NaOH dissolved in 250 mL of water. The mixture was warmed to room temperature, and 100 g of NaCl was added. The mixture was poured into a 2 L separatory funnel containing 600 mL of $Et_2O$ and extracted (3×) with $Et_2O$. The combined organic extracts were washed with water and brine and dried over $MgSO_4$. The solution was filtered and evaporated to yield 18.25 g of an off-white/pink solid. The solid was purified by sublimation (90 °C/0.5 mm) to yield 17.88 g (85% from **3a**) of **3c** as colorless crystals, mp 143−145 °C. These crystals were stored in a foil-wrapped container under argon at −20 °C. TLC: $R_f$ 0.42. $^1$H NMR (500 MHz) $\delta$ 3.49 (s). $^{13}$C NMR (125.7 MHz) $\delta$ 139.1 (m), 137.2 (m), 116.5 (m). $^{19}$F NMR (470.3 MHz) $\delta$ −162.15 (s). IR: 3430, 3330, 1627, 1516, 1178, 1000, 920 cm$^{-1}$. Crystallization (1 g of tetrafluorophenylenediamine/3 mL of toluene) of the sublimate gave the analytical sample of **3c** as colorless needles, mp 143−144 °C (lit.,[6a] 143.5−144 °C). Anal. Calcd for $C_6H_4F_4N_2$: C, 40.01; H, 2.24; N, 15.55. Found: C, 40.21; H, 2.35; N, 15.64. Low-resolution EIMS calcd for $C_6H_4F_4N_2$: 180. Found: 180.

**4-(*N*-((9-Fluorenylmethoxy)carbonyl)amino)tetrafluoroaniline (3d).** Into a 250 mL three-neck flask equipped with a 50 mL addition funnel was introduced 8.35 g (46.4 mmol) of freshly purified **3c**, 100 mL of dry EtOAc, and 3.75 mL (46.4 mmol) of anhydrous pyridine. After stirring to homogeneity at room temperature, the flask was immersed in an ice bath, and 10.0 g (38.7 mmol) of FMOC−Cl, dissolved in 35 mL of dry EtOAc, was added dropwise to the solution over a 30 min period. The mixture was stirred at 0 °C for 4 h and then at room temperature overnight (TLC of **3d**: $R_f$, 0.26). The reaction mixture was poured into a separatory funnel containing 500 mL of EtOAc, and the organic layer was washed with cold 1 N HCl, water, brine, and dried ($Na_2SO_4$) and concentrated to yield 14.75 g of crude off-white crystals. Recrystallization from $CHCl_3$/hexane afforded 14.30 g (92%, two crops) of **3d** as fine colorless needles, mp 189 °C. $^1$H NMR (500 MHz, 60 °C, DMSO-$d_6$) $\delta$ 8.90 (bs, 1H), 7.85 (m, 2H), 7.63 (bs, 2H), 7.41 (t, $J$ = 7.3 Hz, 2H), 7.32 (m, 2H), 5.80 (m, 1H), 4.68 (m, 0.5H), 4.42 (d, $J$ = 6.8 Hz, 1.5H), 4.25 (m, 1H), 3.16 (s, 1H). $^{13}$C NMR (125.7 MHz, 60 °C, DMSO-$d_6$) $\delta$ 157.8, 147.9 (m), 146.9, 146.00 (m), 144.1, 142.7, 141.5 (m), 140.8, 139.9 (m), 139.7 (m), 138.0 (m), 132.1, 130.8, 130.5, 130.3, 130.2, 128.2, 124.5, 123.2, 123.1, 119.4 (m), 112.5, 105.8 (m), 69.7, 49.9. $^{19}$F NMR (470.3 MHz, 60 °C, DMSO-$d_6$) $\delta$ −162.98 (m), −162.65 (m). IR: 3419, 1703, 1668, 1541, 1521, 1495, 1452, 1306, 1261, 981, 946, 738 cm$^{-1}$. Anal. Calcd for $C_{21}H_{14}F_4N_2O_2$: C, 62.69; H, 3.51; N, 6.96. Found: C, 62.56; H, 3.57; N, 7.00. Low-resolution EIMS calcd for $C_{21}H_{14}F_4N_2O_2$ 402.3. Found: 402.2. High-resolution MALDIMS calcd for $C_{21}H_{14}F_4N_2O_2Na$: 425.0889. Found: 425.0894.

**4-(*N*-(((2-Nitrofluorenyl)-9-methoxy)carbonyl)amino)-tetrafluorophenyl Azide (3e).** Aniline **3d** (6.00 g, 14.9 mmol) was dissolved in TFA (100 mL) and stirred at 0 °C for 10 min. Solid $NaNO_2$ (4.12 g, 59.7 mmol) was added in portions over 15 min with stirring, and the stirring was continued for an additional 15 min. Solid $NaN_3$ (3.27 g, 50.3 mmol) was then added to the red-violet solution over a 10 min period, and the mixture was allowed to stir at 0 °C for 80 min. The reaction was warmed to room temperature over 10 min and then poured onto 400 mL of ice water (ice is added to the 400 mL mark of the beaker, followed by addition of water to the same mark) and stirred for 5 min. The solid was filtered, washed with water (2×), and dried in vacuo at 40 °C. Two recrystallizations from $CH_2Cl_2$/pentane afforded 6.30 g (89%, two crops) of **3e** as an off-white solid, mp 151−152 °C (dec). TLC: $R_f$, 0.34. $^1$H NMR (500 MHz) $\delta$ 8.39 (bs, 1H), 8.35 (dd, $J$ = 2.0 Hz, 1H), 7.87 (m, 2H), 7.64 (d, $J$ = 7.3 Hz, 1H), 7.49 (m, 2H), 6.26 (bs, 1H, CON*H*), 4.82 (m, 1H), 4.39 (m, 2H). $^{13}$C NMR (125 MHz) $\delta$ 153.4, 148.1, 147.4, 145.1, 144.8, 144.4 (m), 142.4 (m), 142.1 (m), 140.1 (m), 139.5, 129.7, 129.0, 125.5, 124.6, 121.9, 120.9, 120.5, 119.2 (m), 112.2 (m), 67.6, 47.5. $^{19}$F NMR (470.3 MHz) $\delta$ −210.47 (m), −204.86 (m). IR: 3217, 2130, 1708, 1513, 1485, 1337, 1266, 995, 978, 747 cm$^{-1}$. An analytical sample was obtained by recrystallization from $CH_2Cl_2$/pentane yielding **3e** as a white solid. Anal. Calcd for $C_{21}H_{11}F_4N_5O_4$: C, 53.29; H, 2.34; N, 14.80. Found: C, 53.35; H, 2.37; N, 14.80. Low-resolution EIMS calcd for $C_{21}H_{11}F_4N_5O_4$: 473.3. Found: 473.1.

**4-Azidotetrafluoroaniline (1).** Into a 250 mL round-bottom flask was added 3.08 g (6.51 mmol) of **3e** and 100 mL of $Et_2O$. The mixture was then placed in an ice bath, and 10 mL (0.10 mol) of piperidine was added. The solution was stirred at 0 °C for 50 min and then at room temperature for 10 min. The mixture was then poured into a 1 L separatory funnel containing 200 mL of ice-cold 2 N HCl and 150 mL of $Et_2O$. The aqueous layer was discarded, and the organic solution was then washed with 1 N HCl, water, and brine. The solution was dried ($MgSO_4$), filtered, and concentrated. The crude orange-brown solid was purified by sublimation (38 °C/0.5 mm) to yield 1.25 g (93%) of **1** as golden crystals, mp 68−71 °C (dec). The resulting aniline azide is pure enough for most purposes. TLC: $R_f$, 0.48. $^1$H NMR (500 MHz) $\delta$ 3.909 (s). $^{13}$C NMR (125.7 MHz) $\delta$ 142.6 (m), 140.7 (m), 138.3 (m), 136.4 (m), 123.4 (m), 108.4 (m). $^{19}$F NMR (470.3 MHz) $\delta$ −162.68 (m), −155.10 (m). IR: 3383, 3316, 3284, 3205, 2127, 1510, 1246, 969, 931 cm$^{-1}$. UV: $\lambda_{max}$(MeOH), 262 nm; $\epsilon_{max}$(MeOH) 19 772; $\lambda_{max}$(cyclohexane), 256 nm; $\epsilon_{max}$(cyclohexane) 16 813. Low-resolution EIMS calcd for $C_6H_2F_4N_4$: 206. Found 206. Resublimation (33 °C/0.5 mm) gave the analytical sample of **1** as pale yellow crystals. Anal. Calcd for $C_6H_2F_4N_4$: C, 34.97; H, 0.98; N, 27.18. Found: C, 35.09; H, 0.94; N, 27.39.

**4-(*N*-(Chloroacetyl)amino)tetrafluorophenyl Azide (8).** A 50 mL round-bottom flask was charged with 0.53 g (2.57 mmol) of **1**, 0.50 mL (3.78 mmol) of collidine, and 25 mL of anhydrous EtOAc. After stirring to homogeneity at room temperature, 3.00 mL (37.7 mmol) of chloroacetyl chloride, dissolved in 5 mL of dry EtOAc, was added dropwise to the solution over a 30 min period. The reaction mixture was then stirred at room temperature for 6 h (TLC of **8**: $R_f$, 0.32). The mixture was poured into a separatory funnel containing 150 mL of EtOAc, and the organic layer was washed with water, 1 N HCl, water, and 5% $NaHCO_3$. The ethereal layer was then dried ($MgSO_4$) and concentrated. The residual solid was purified by flash chromatography (10% EtOAc in hexane) to yield 0.57 g (79%) of **12** as a white solid, mp 109−110 °C (dec). $^1$H NMR (500 MHz) $\delta$ 7.89 (bs, 1H), 4.28 (s, 2H). $^{13}$C NMR (125.7 MHz) $\delta$ 164.9, 144.4(m), 142.5 (m), 140.5 (m), 119.4 (m), 111.5 (m), 4.9. $^{19}$F NMR (470.3 MHz) $\delta$ −152.79 (m), −145.88 (m). IR: 3225, 2132, 1694, 1651, 1511, 1488, 1245, 1207, 1011, 964, 947 cm$^{-1}$. An analytical sample was obtained by recrystallization from cyclohexane, yielding **8** as a white fibrous solid. Anal. Calcd for $C_8H_3F_4ClN_4O$: C, 34.00; H, 1.07; N, 19.83. Found: C, 33.97; H, 1.20; N, 19.97. High-resolution EIMS calcd for $C_8H_3F_4N_4OCl$: 281.9932. Found: 281.9936.

**4-(*N*-(Iodoacetyl)amino)tetrafluorophenyl Azide (9).** Into a 50 mL round-bottom flask was added 0.36 g (1.27 mmol) of **8** followed by 20 mL of dry acetone and 1.91 g (12.7 mmol) of NaI. The solution was stirred at room temperature overnight. The mixture was poured into a separatory funnel containing 150 mL of $Et_2O$, washed once with water, and dried ($MgSO_4$). Recrystallization from cyclohexane afforded 0.44 g (93%) of **9** as fine colorless needles, mp 151−153 °C (dec). (TLC of **9**: $R_f$. 0.38). $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 10.43 (bs, 1H), 3.88 (s, 2H). $^{13}$C NMR (125.7 MHz, DMSO-$d_6$) $\delta$ 167.3, 143.3 (m), 141.3 (m), 139.3 (m), 117.8 (m), 112.3 (m), −1.7. $^{19}$F NMR (470.3 MHz, DMSO-$d_6$) $\delta$ −153.39 (m), −146.85 (m). IR: 3243, 3208, 2132, 1674, 1651, 1488, 1072, 1010, 962 cm$^{-1}$. Anal. Calcd for $C_8H_3F_4IN_4O$: C, 25.69; H, 0.81; N, 14.98. Found: C, 25.76; H, 0.83; N, 15.06. High-resolution EIMS calcd for $C_8H_3F_4N_4OI$: 373.9288. Found: 373.9292.

**4-(*N*-(5-(Dimethylamino)-1-naphthalenesulfonyl)amino)tetrafluorophenyl Azide (10).** To a solution of 0.206 g (1.00 mmol) of **1** in 10 mL of anhydrous THF at −78 °C was added 0.278 g (1.03 mmol) of dansyl chloride immediately followed by 1 mL (1.00 mmol) of lithium bis(trimethylsilyl) amide (1 M solution in THF). The solution was stirred at −78 °C for 2 h. The solution was slowly warmed to room temperature and stirred for an additional hour. The solution was concentrated and purified by flash chromatography (15% EtOAc in hexane). Fractions containing **10** (TLC: $R_f$, 0.32) were combined and concentrated in vacuo to leave a viscous

oil which was further evaporated at 25 °C under high vacuum affording 0.295 g (67%) of **10** as an orange glass, mp 42−48 °C. $^1$H NMR (400 MHz) $\delta$ 8.70 (bs, 1H), 8.36 (d, 1H, $J$ = 8.1 Hz), 8.20 (d, 1H, $J$ = 7.3 Hz), 7.62 (dd, 1H, $J$ = 8.6 Hz), 7.54 (t, 1H, $J$ = 8.6 Hz), 7.28 (bs, 1H), 6.60 (bs, 1H), 2.98 (s, 6H). $^{13}$C NMR (100.7 MHz) $\delta$ 145.3 (m), 142.8 (m), 142.0 (m), 139.6 (m), 134.7, 131.5, 130.4, 130.0, 129.8, 128.9, 123.9, 119.7 (m), 116.1, 111.8 (m), 46.1. $^{19}$F NMR (376.7 MHz) $\delta$ −152.74 (m), −146.58 (m). IR: 3252, 2129, 1499, 1343, 1242, 1165, 1147, 1102, 1000, 949, 789 cm$^{-1}$. Anal. Calcd for $C_{18}H_{13}F_4N_5O_2S$: C, 49.20; H, 2.98; N, 15.94; S, 7.30. Found: C, 49.24; H, 3.17; N, 15.67; S, 7.10. High-resolution EIMS calcd for $C_{18}H_{13}F_4N_5O_2S$: 439.0726. Found: 439.0722.

**Photolysis of Azide 1 in Cyclohexane.** Into a quartz round-bottom vial equipped with a ground glass stopper was added 6 mL of a 3.5 × 10$^{-2}$ M solution of azide **1** in cyclohexane. The vial was then placed approximately 2 cm from a 254 nm hand-held light source (UVP Model UVG-11) and photolyzed for 7 h at 25 °C. Analysis of the reaction mixture by GC-MS indicated amine **11** ($M^+$ 262, 19%), diamine **3c** ($M^+$ 180, 17%), and azobenzene **12** ($M^+$ 356, 29%).

**Supporting Information Available:** Figures showing $^1$H, $^{13}$C, $^{19}$F NMR, and MS spectra for compounds **1**, **2a**−**e**, **3a**−**e**, and **8**−**10** and text describing syntheses of compounds **2b** and **2c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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