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Amination of Aryl Iodides Using a Fluorous-Tagged Ammonia Equivalent

Simon Dalsgaard Nielsen,[a] Garrick Smith,[b] Mikael Begtrup,[a] and Jesper Langgaard Kristensen*[a]

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A fluorous-tagged ammonia equivalent for the Cu-catalyzed amination of aryl iodides is described in which *N*-Boc-protected anilines are produced in high overall yield and purity. All purification steps are performed using Fluorous Solid-Phase Extraction (F-SPE) greatly simplifying and speeding up the isolation of the desired products.

Introduction

Anilines have numerous applications in many areas of organic chemistry. They are used for the production of dyes and as intermediates in pharmaceutical and agrochemical research.[1] Various methods for the synthesis of anilines have been developed, but due to their importance new protocols are still being pursued. In particular transition-metal catalyzed procedures in which an aryl halide or pseudo halide is coupled with an amine have been very actively developed in recent years.[2] One of the most challenging transformation has been the coupling of the simplest of all amines: NH_3. This has led to the development of several different ammonia surrogates that can be used to prepareanilines indirectly, see Figure 1 for a list of different reagents.[3] Procedures for direct coupling of ammonia with aryl halides have been developed only recently.[4]

By-products from the catalyst or homo-couplings are often formed in transition metal catalyzed coupling reactions, which complicates the purification of the desired compounds. Trace amounts of residual catalyst is very undesirable in the products, especially within the pharmaceutical industry. Solid-phase organic synthesis alleviates many of these purification problems, but also has some serious drawbacks.[5]

Fluorous linker-facilitated chemical synthesis is an emerging technique in organic synthesis.[6] A fluorous tag is attached to the substrate by using a linker. After the reaction has been completed, very often with an excess of reagents to ensure complete conversion, the crude mixture is passed through a cartridge containing a perfluorinated bonded silica phase. In a simple two-step procedure, termed Fluorous Solid-Phase Extraction (F-SPE), fluorous compounds and non-fluorous compounds are split into two separate fractions.[7]

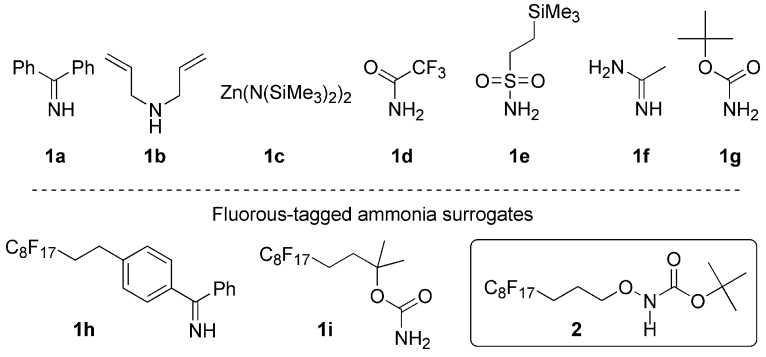

Figure 1. NH_3 surrogates for the synthesis of anilines.[3]

Using a fluorophobic eluent (such as methanol/water or acetonitrile/water), the non-fluorous material is washed off the cartridge. The fluorous-tagged compound is then eluted using a fluorophilic solvent (such as methanol, acetone or THF).

[a] Department of Medicinal Chemistry, University of Copenhagen, Pharma,
Universitetsparken 2, 2100 Copenhagen, Denmark
Fax: +45-35336040
E-mail: jekr@farma.ku.dk
[b] H. Lundbeck A/S,
Ottiliavej 9, 2650 Valby, Denmark

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Finally, the fluorous-tag is cleaved thereby releasing the product.

The use of fluorous-tags has several advantages compared to classic solid-phase organic synthesis; for example, favorable homogeneous solution phase reaction kinetics. This means that protocols developed in solution very often can be adapted to a fluorous procedure with very little optimization effort. Furthermore, reactions can be monitored by standard analytical methods (such as TLC, NMR and HPLC), and conventional methods for purification can also be used in addition to F-SPE.

The fluorous-tagged ammonia equivalents **1h** and **1i** have been developed as direct analogs of **1a** and **1g**, thereby taking advantage of the F-SPE purification technique, see Figure 1.[3] Subsequent removal of the fluorous tag under acidic conditions produced the anilines.

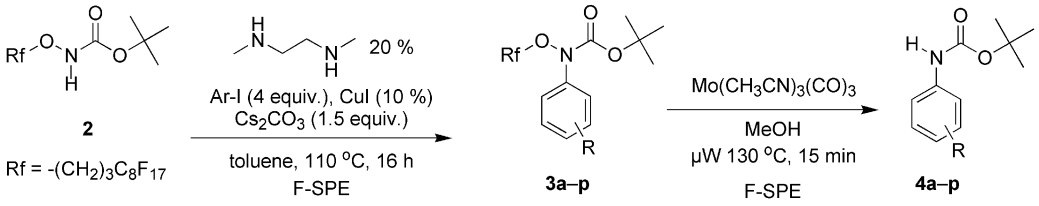
We recently described how **2** can be implemented in the synthesis of *N*-alkylated amides, ureas and sulfonamides, using a novel fluorous strategy.[8] The key starting material **2** is readily prepared in 91% isolated yield on multigram scale via alkylation of *N*-Boc-hydroxylamine with $I(CH_2)_3C_8F_{17}$.

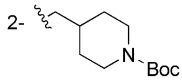
Herein we wish to report that **2** can be coupled very effectively with aryl iodides, and that *N*-Boc-anilines are released in high overall yield and purity upon chemoselective cleavage of the N–O linker with $Mo(CO)_3(CH_3CN)_3$.

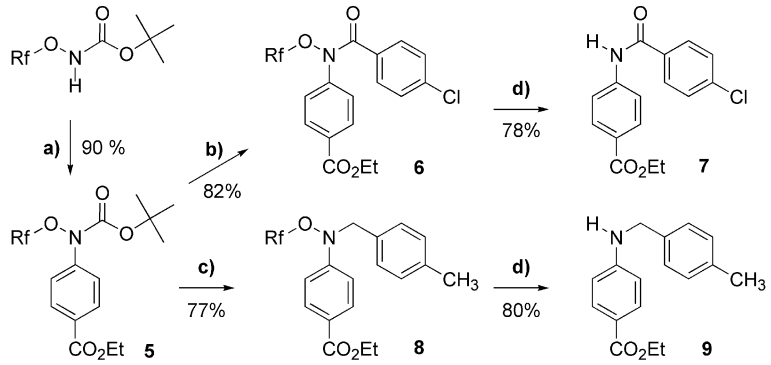
Results and Discussion

Jones et al.[9] reported the coupling of *N*-Boc-*O*-methylhydroxylamine with aryl iodides by using 0.1 equiv. of CuI in combination with 0.5 equiv. of 1,10-phenanthroline as catalyst system. When these conditions were applied to the coupling of **2** the desired products were obtained, but F-SPE purification gave very dark-colored products, presumably due to contamination from the catalyst, hence the search for an alternative protocol was initiated. After screening a series of different conditions, it was found that the use of CuI in combination with *N*,*N*′-dimethylethylenediamine was very efficient for the cross coupling of **2** with aryl iodides.[10] Under these optimized conditions **2** was treated with four equivalents of aryl iodides in the presence of 10 mol-% CuI, 20 mol-% *N*,*N*′-dimethylethylenediamine

Table 1. Synthesis of anilines via Cu-catalyzed amination of aryl iodides using a fluorous-tagged ammonia equivalent.



Entry	R	Product	Yield %	Purity (UV / ELS)	Product	Yield %	Purity (UV / ELS)
1	4-Br	**3a**	99	95 / 100	**4a**	71	99 / 100
2	4-F	**3b**	96	100 / 100	**4b**	49	100 / n.d.
3	4-CH_2OH	**3c**	92	80 / 96	**4c**	98	74 / 91
4	4-CN	**3d**	84	99 / 100	**4d**	92	91 / 100
5	4-CHO	**3e**	89	99 / 100	**4e**	94	81 / n.d.
6	4-CF_3	**3f**	93	99 / 100	**4f**	20	100 / n.d.
7	4-*i*Pr	**3g**	>99	99 / 100	**4g**	70	100 / n.d.
8	4-Ac	**3h**	89	92 / 100	**4h**	>99	100 / 100
9	3-OH	**3i**	86	73 / 96	**4i**	76	61 / 86
10	3-CO_2Et	**3j**	89	100 / 100	**4j**	88	100 / 100
11	3-OMe	**3k**	96	97 / 100	**4k**	74	100 / n.d.
12	3-Cl	**3l**	94	100 / 100	**4l**	73	99 / n.d.
13	3,4-ethylenedioxy	**3m**	96	98 / 99	**4m**	91	97 / 100
14	2-SMe	**3n**	68	97 / 99	**4n**	44	97 / n.d.
15		**3o**	74	100 / 100	**4o**	92	100 / 100
16		**3p**	51	100 / 100	**4p**	57	100 / 100



Scheme 1. *Reagents and conditions*: a) ethyl 4-iodobenzoate, CuI, *N*,*N*′-dimethylethanediamine, Cs_2CO_3, toluene, 110 °C, 16 h. b) i) HCl/EtOH, ii) 4-ClC_6H_4–COCl, Et_3N, MeCN. c[(i] HCl/EtOH (ii) 4-MeC_6H_4–CH_2Cl, Cs_2CO_3, MeCN. d) $Mo(CH_3CN)_3(CO)_3$, MeOH, μW, 130 °C, 15 min.

and 1.5 equiv. Cs_2CO_3 in toluene at 110 °C for 16 hours, which led to full conversion of **2**, see Table 1.[11] Furthermore, F-SPE was not hampered by coloration of the products, as observed above. After aqueous workup the crude mixtures were loaded onto F-SPE cartridges. Firstly, the non-fluorous material was eluted with methanol/water (4:1), acetonitrile/water (4:1) and acetone/water (2:1). Subsequently, the fluorous-tagged products were eluted with methanol and acetone. Evaporation of the fluorous fractions gave the products **3a**–**p** in high yield and purity, see Table 1.

A wide variety of functional groups were tolerated in the cross coupling, including bromine (entry 1), free alcohol (entry 3), nitrile (entry 4), aldehyde (entry 5), ketone (entry 8) and a free phenol (entry 9). Bulky *ortho* substituents were also allowed (entries 15 and 16). Aryl iodides were efficiently coupled, whereas aryl bromides did not react. This selectivity towards aryl iodides gives the option of having a bromo substituent on the product, as in **3a**, that subsequently can be used for further transition-metal-catalyzed transformations.

The fluorous tag was released by reductive cleavage of the N–O bond using $Mo(CH_3CN)_3(CO)_3$. This reagent has several advantages when compared to $Mo(CO)_6$.[12] It is more reactive and solvents other than CH_3CN can be used.[8] The substrates **3a**–**p** were heated using microwave irradiation at 130 °C for 15 min with 1.5 equiv. of $Mo(CH_3CN)_3(CO)_3$ in methanol. Prior to heating, the molybdenum complex was dissolved by ultrasonication of the vial for 10 min. Aqueous workup and F-SPE gave the *N*-Boc-protected anilines **4a**–**p** in moderate to excellent yield and high purity. The N–O cleavage procedure was very chemoselective being compatible with all the indicated functional groups present on the aromatic ring in the products.

It is also possible to remove the Boc group from some of the coupling products and further functionalize the resulting fluorous-tagged anilines. To demonstrate this, the sequence outlined in Scheme 1 was performed. Coupling of **2** with ethyl 4-iodobenzoate gave **5** in 90% yield after F-SPE. Deprotection of the Boc group in **5** with HCl in EtOH gave the best results. The reaction was slow at room temperature, and if the reaction was left to run overnight substantial decomposition was observed.

However, at 50 °C deprotection was complete after two hours. The resulting hydrochloride salt slowly decomposed upon storage, so it was used immediately after evaporation of the solvent. Acylation with 4-chlorobenzoyl chloride gave **6** in 82% yield and alkylation with 4-methylbenzyl bromide gave **8** in 77% yield after F-SPE. Subsequent cleavage of the N–O linker produced **7** and **9** in 78 and 80% yield after F-SPE.

It should be noted that the sequence shown in Scheme 1 is limited to compounds containing an electron-withdrawing group on the aromatic ring. Attempted *N*-Boc deprotection of a 4-tolyl derivative led to decomposition, presumably via a Bamberger-type rearrangement.[13]

Conclusions

In conclusion, the application of a new fluorous-tagged ammonia equivalent has been described, where substituted iodoarenes are transformed into *N*-Boc-anilines in high yields and purity after F-SPE. The procedure tolerates a wide range of functional groups, thus providing easy access to *N*-Boc-anilines suitably poised for further manipulations. The results described herein supplements our previously published application of **2**[8] making it a very versatile starting point fluorous linker-facilitated chemical synthesis of wide array of compound classes.

Experimental Section

General: Chemicals and solvents were obtained from commercial suppliers and used as received unless otherwise noted. THF and DMF were dried with molecular sieves (3 Å) prior to use. The molybdenum complex tris(acetonitrile)(tricarbonyl)molybdenum [CAS # 15038-48-9] used for reductive N–O cleavage in general procedure B was purchased from AcrosOrganics and used as received. The reagent appears as a dark brown powder, however if it turns black over time it is not reliable. Flash column chromatography was carried out using Scharlau 60 (230–400 mesh) silica gel (sorbil) and thin-layer chromatography (TLC) was performed on

Merck 60 F254 0.25-μm silica-gel plates. ^{1}H-NMR and ^{1}H-decoupled/^{13}C-NMR spectra were recorded at 500.13 MHz and 125.67 MHz, respectively, on a Bruker Avance DRX 500 instrument using deuterated chloroform (99.8%) unless otherwise noted. Chemical shifts for ^{1}H-NMR are reported in ppm with TMS as internal reference. Chemical shifts for ^{13}C-NMR are reported in ppm relative to chemical shifts of $CHCl_3$. Coupling constants (*J* values) are in Hertz. The following abbreviations are used for multiplicity of NMR signals: s = singlet, d = doublet, t = triplet, q = quartet, dd = double doublet, ddt = double doublet of triplets and m = multiplet. Elemental analyses were performed at H. Lundbeck A/S, with a Flash EA1112 from Thermo Fischer Scientific. HRMS were performed on an Agilent/Bruker Daltonics LC-SPE-MS at H. Lundbeck A/S. The vacuum centrifuges applied were either HT-4 or EZ2 from genevac®. Fluorous Solid Phase Extraction (F-SPE) was carried out using cartridges from Fluorous Technologies Inc. and a FlashVac-10 from Biotage designed to accommodate 10 collection tubes with 25 mm diameter vessels.

***tert*-Butyl (3-Perfluorooctyl)propoxycarbamate (2):**[8] A mixture of *tert*-butyl *N*-hydroxycarbamate (17.0 g, 0.13 mol) and DBU (13 mL, 80 mmol) in dry tetrahydrofuran (300 mL) was cooled to 0 °C. To it was added a solution of 3-(perfluorooctyl)propyl iodide (25.0 g, 42.5 mmol) in 100 mL of dry tetrahydrofuran dropwise over 1.5 h. After 1 h the mixture became milky-white, the ice bath was removed and it was stirred at room temperature overnight. The solvent was evaporated on a rotavapor and the crude was worked up with saturated aqueous hydrogen carbonate (300 mL) and ethyl acetate (3 × 200 mL). The combined organic phases were dried with magnesium sulfate, evaporated and purified by flash chromatography (heptane/ethyl acetate, 9:1) to yield 22.9 g (91%) of **2** as a colourless oil. The oil was dissolved in 100 mL of dioxane, cooled to –78 °C and freeze dried in vacuo to give a white solid (mp 33–34 °C). ^{1}H NMR: δ = 1.49 (s, 9 H), 1.91–1.97 (m, 2 H), 2.20–2.33 (m, 2 H), 3.93 (t, *J* = 6.0 Hz, 2 H), 7.10 (br. soad, 1 H) ppm. ^{13}C NMR: δ = 19.3, 27.8 (t, *J* = 22.2 Hz), 28.1, 75.0, 82.0, 156.9 ppm. HRMS calcd. for $C_{12}H_9F_{17}NO_3^+$, 538.0305 (– *t*Bu, + H^+); found 538.0302. $C_{16}H_{16}F_{17}NO_3$ (593.28): calcd. C 32.39, H 2.72, N 2.36; found C 32.50, H 2.70, N 2.31.

General Procedure for Fluorous Solid-Phase Extraction (F-SPE): A 5-g or 10-g F-SPE cartridge was charged with water corresponding to the volume of about half of the dissolved crude product. This was followed by addition of the crude oil or solid dissolved in a water-miscible solvent. Using vacuum, the non-fluorous fraction was eluted with approximately 15 mL of methanol/water (4:1), 15 mL of acetonitrile/water (4:1), and 15 mL of acetone/water (2:1). The fluorous fraction was eluted with approximately 25 mL of MeOH and 25 mL of acetone.

General Procedure A: Cross Coupling of 2 with Aryl Iodides: A vial was charged with **2** (0.4 mmol), cesium carbonate (0.6 mmol), copper(I) iodide (0.04 mmol), dry toluene (2.5 mL), N^1,N^2-dimethylethane-1,2-diamine (1.6 mmol) aryl iodide (1.6 mmol), flushed with argon and finally sealed with a septum. The mixture was stirred for 16 h at 110 °C and analysed by TLC (heptane/ethyl acetate, 3:1). In most cases 2 was fully consumed after this time and the reaction mixture was worked up with water (40 mL) and ethyl acetate (3 × 20 mL). The organic fractions were evaporated and purified by F-SPE. The fluorous fraction was evaporated on a rotavapor and dried in a vacuum centrifuge. The average yield was 87% ranging from 51–100%. The average purity by LC-UV was 96% ranging from 73–100%.

***tert*-Butyl 4-Bromophenyl(3-perfluorooctylpropoxy)carbamate (3a):** Prepared by general procedure A to give 312 mg (99%) of **3a** as a light brown solid. Purity by LC-UV(ELS): 95% (100%). ^{1}H and ^{13}C NMR showed impurities after F-SPE so an analytical sample was obtained by flash chromatography (heptane/ethyl acetate, 9:1), TLC R_f = 0.66 (heptane/ethyl acetate, 3:1). ^{1}H NMR: δ = 1.52 (s, 9 H), 1.92–1.99 (m, 2 H), 2.22–2.34 (m, 2 H), 3.95 (t, *J* = 5.9 Hz, 2 H), 7.30 (d, *J* = 8.8 Hz, 2 H), 7.46 (d, *J* = 8.8 Hz, 2 H) ppm. ^{13}C NMR: δ = 19.3, 28.0 (t, *J* = 22 Hz), 28.1, 73.1, 82.9, 118.6, 107–121 (8 fluorinated C), 123.3, 131.6, 139.6, 153.2 ppm. HRMS calcd. for $C_{17}H_{12}BrF_{17}NO^+$, 647.9825 (– Boc, + H^+); found 647.9812.

***tert*-Butyl 4-Fluorophenyl(3-perfluorooctylpropoxy)carbamate (3b):** Prepared by general procedure A to give 279 mg (96%) of **3b** as a brown oil. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.51 (s, 9 H), 1.91–1.97 (m, 2 H), 2.19–2.32 (m, 2 H), 3.96 (t, *J* = 5.9 Hz, 2 H), 7.01–7.06 (m, 2 H), 7.33–7.38 (m, 2 H) ppm. ^{13}C NMR: δ = 19.3, 28.0 (t, *J* = 22 Hz), 28.2, 73.0, 82.6, 107–121 (8 fluorinated C), 115.4 (d, *J* = 22 Hz), 124.6 (d, *J* = 8 Hz), 136.6, 153.9, 160.6 (d, *J* = 246 Hz) ppm. HRMS calcd. for $C_{17}H_{12}F_{18}NO+$, 588.0626 (+ H^+); found 588.0622.

***tert*-Butyl 4-(Hydroxymethyl)phenyl(3-perfluorooctylpropoxy)carbamate (3c):** Prepared by general procedure A to give 270 mg (92%) of **3c** as a yellow solid. Purity by LC-UV(ELS): 80% (96%). ^{1}H NMR: δ = 1.52 (s, 9 H), 1.92–1.98 (m, 2 H), 2.21–2.34 (m, 2 H), 3.96 (t, *J* = 5.9 Hz, 2 H), 4.68 (s, 2 H), 7.35 (d, *J* = 8.5 Hz, 2 H), 7.39 (d, *J* = 8.5 Hz, 2 H) ppm. ^{13}C NMR: δ = 19.3, 28.1 (t, *J* = Hz), 28.2, 64.8, 73.0, 82.5, 107–121 (8 fluorinated C), 122.3, 127.3, 138.3, 139.8, 153.6 ppm. HRMS calcd. for $C_{19}H_{15}F_{17}NO_4^+$, 644.0724 (– *t*Bu, + H^+); found 644.0710.

***tert*-Butyl 4-Cyanophenyl(3-perfluorooctylpropoxy)carbamate (3d):** Prepared by general procedure A to give 245 mg (84%) of **3d** as a white solid. Purity by LC-UV(ELS): 99% (100%). ^{1}H NMR: δ = 1.56 (s, 9 H), 1.96–2.03 (m, 2 H), 2.25–2.37 (m, 2 H), 3.98 (t, *J* = 6.0 Hz, 2 H), 7.58 (d, *J* = 6.9 Hz, 2 H), 7.63 (d, *J* = 6.9 Hz, 2 H) ppm. ^{13}C NMR: δ = 19.3, 28.0 (t, *J* = 23 Hz), 28.1, 73.4, 83.8, 107–121 (8 fluorinated C), 107.7, 118.7, 119.9, 132.7, 144.1, 152.3 ppm. HRMS calcd. for $C_{18}H_{12}F_{17}N_2O^+$, 595.0673 (+ H^+); found 595.0668.

***tert*-Butyl 4-Formylphenyl(3-perfluorooctylpropoxy)carbamate (3e):** Prepared by general procedure A to give 262 mg (89%) of **3e** as a green solid. Purity by LC-UV(ELS): 99% (100%). ^{1}H NMR: δ = 1.58 (s, 9 H), 1.98–2.04 (m, 2 H), 2.26–2.38 (m, 2 H), 4.00 (t, *J* = 5.9 Hz, 2 H), 7.63 (d, *J* = 8.7 Hz, 2 H), 7.86 (d, *J* = 8.7 Hz, 2 H), 9.95 (s, 1 H) ppm. ^{13}C NMR: δ = 19.4, 28.0 (t, *J* = 22 Hz), 28.2, 73.4, 83.6, 107–121 (8 fluorinated C), 119.8, 130.5, 132.6, 145.5, 152.4, 191.0 ppm. HRMS calcd. for $C_{18}H_{13}F_{17}NO2^+$, 598.0669 (– Boc, + H^+); found 598.0674.

***tert*-Butyl 4-(Trifluoromethyl)phenyl(3-perfluorooctylpropoxy)carbamate (3f):** Prepared by general procedure A to give 290 mg (93%) of **3f** as a light brown oil. Purity by LC-UV(ELS): 100% (99%). ^{1}H NMR: δ = 1.55 (s, 9 H), 1.95–2.02 (m, 2 H), 2.25–2.37 (m, 2 H), 3.99 (t, *J* = 5.9 Hz, 2 H), 7.57 (d, *J* = 9.0 Hz, 2 H), 7.60 (d, *J* = 9.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 19.4, 28.05 (t, *J* = 22 Hz), 28.13, 73.3, 83.3, 107–121 (8 fluorinated C), 120.5, 124.8 (q, *J* = 272 Hz) 125.8 (q br, *J* = 4 Hz) 126.8 (q, *J* = 33 Hz), 143.4, 152.9 ppm. HRMS calcd. for $C_{18}H_{12}F_{20}NO^+$, 638.0594 (– Boc, + H^+); found 638.0578.

***tert*-Butyl 4-Isopropylphenyl(3-perfluorooctylpropoxy)carbamate (3g):** Prepared by general procedure A to give 601 mg (100%) of **3g** as a light brown oil. Purity by LC-UV(ELS): 99% (100)%. ^{1}H NMR: δ = 1.24 (d, *J* = 6.9 Hz, 6 H), 1.52 (s, 9 H), 1.91–1.97 (m, 2 H), 2.21–2.34 (m, 2 H), 2.90 (hept, *J* = 6.9 Hz, 1 H), 3.97 (t, *J* = 5.8 Hz, 2 H), 7.20 (d, *J* = 8.5 Hz, 2 H), 7.31 (d, *J* = 8.5 Hz, 2 H)

ppm. ^{13}C NMR: δ = 19.4, 24.0, 28.2 (t, J = 22 Hz), 28.3, 33.7, 73.0, 82.3, 107–121 (8 fluorinated C), 122.7, 126.6, 138.2, 146.7, 154.0 ppm. HRMS calcd. for $C_{20}H_{19}F_{17}NO^+$, 612.1190 (– Boc, + H$^+$); found 612.1196.

***tert*-Butyl 4-Acetylphenyl(3-perfluorooctylpropoxy)carbamate (3h):** Prepared by general procedure A to give 265 mg (89%) of **3h** as a light brown solid. Purity by LC-UV(ELS): 92% (100%). ^{1}H NMR: δ = 1.56 (s, 9 H), 1.96–2.03 (m, 2 H), 2.25–2.38 (m, 2 H), 2.58 (s, 3 H), 3.99 (t, J = 5.9 Hz, 2 H), 7.55 (d, J = 8.7 Hz, 2 H), 7.95 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR: δ = 19.4, 26.4, 28.0 (t, J = 22 Hz), 28.2, 73.3, 83.4, 107–121 (8 fluorinated C), 119.7, 129.7, 129.1, 133.4, 144.4, 152.6, 196.9 ppm. HRMS calcd. for $C_{19}H_{15}F_{17}NO_2^+$, 612.0826 (– Boc, + H$^+$); found 612.0830.

***tert*-Butyl 3-Hydroxyphenyl(3-perfluorooctylpropoxy)carbamate (3i):** Prepared by general procedure A to give 251 mg (86%) of **3i** as a black oil. Purity by LC-UV(ELS): 73% (96%). ^{1}H NMR showed the presence of starting material 2 and other impurities after F-SPE so an analytical sample was obtained by flash chromatography (heptane/ethyla acetate, 9:1) TLC R_f = 0.39 (heptane/ethyl acetate, 3:1). ^{1}H NMR (600 MHz): δ = 1.52 (s, 9 H), 1.90–1.96 (m, 2 H), 2.21–2.31 (m, 2 H), 3.94 (t, J = Hz, 2 H), 6.03 (br. s, 1 H), 6.64–6.66 (m, 1 H), 6.92–6.96 (m, 2 H), 7.16–7.19 (m, 1 H) ppm. ^{13}C NMR (150 MHz): δ = 19.3, 28.0 (t, J = 22 Hz), 28.1, 72.9, 82.9, 109.5, 113.0, 114.4, 107–121 (8 fluorinated C), 129.5, 141.2, 153.8, 156.2 ppm. HRMS calcd. for $C_{17}H_{13}F_{17}NO_2^+$, 586.0669 (– Boc, + H$^+$); found 586.0671.

***tert*-Butyl 3-(Ethoxycarbonyl)phenyl(3-perfluorooctylpropoxy)carbamate (3j):** Prepared by general procedure A to give 277 mg (89%) of **3j** as a light brown oil. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.38 (t, J = 7.1 Hz, 3 H), 1.53 (s, 9 H), 1.93–2.00 (m, 2 H), 2.23–2.35 (m, 2 H), 3.98 (t, J = 5.9 Hz, 2 H), 4.37 (q, J = 7.1 Hz, 2 H), 7.39–7.43 (m, 1 H), 7.60–7.63 (m, 1 H), 7.84–7.86 (m, 1 H), 8.08 (s, 1 H) ppm. ^{13}C NMR: δ = 14.2, 19.3, 28.0 (t, J = 22 Hz), 28.1, 61.1, 73.2, 82.9, 107–121 (8 fluorinated C), 122.8, 126.0, 126.5, 128.6, 131.1, 140.8, 153.3, 166.0 ppm. HRMS calcd. for $C_{20}H_{17}F_{17}NO_3$+, 642.0931 (– Boc, + H$^+$); found 642.0933.

***tert*-Butyl 3-Methoxyphenyl(3-perfluorooctylpropoxy)carbamate (3k):** Prepared by general procedure A to give 284 mg (96%) of **3k** as a light brown oil. Purity by LC-UV(ELS): 97% (100%). ^{1}H NMR: δ = 1.53 (s, 9 H), 1.92–1.99 (m, 2 H), 2.23–2.35 (m, 2 H), 3.80 (s, 3 H), 3.97 (t, J = 5.9 Hz, 2 H), 6.71–6.74 (m, 1 H), 6.99–7.01 (m, 2 H), 7.22–7.27 (m, 1 H) ppm. ^{13}C NMR: δ = 19.3, 28.1 (t, J = 22 Hz), 28.2, 55.3, 73.0, 82.5, 107.8, 107–121 (8 fluorinated C), 111.2, 114.4, 129.2, 142.6, 153.5, 159.9 ppm. HRMS calcd. for $C_{18}H_{15}F_{17}NO_2^+$, 600.0826 (– Boc, + H$^+$); found 600.0830.

***tert*-Butyl 3-Chlorophenyl(3-perfluorooctylpropoxy)carbamate (3l):** Prepared by general procedure A to give 279 mg (94%) of **3l** as an orange oil. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.54 (s, 9 H), 1.94–2.00 (m, 2 H), 2.24–2.36 (m, 2 H), 3.97 (t, J = 5.9 Hz, 2 H), 7.12–7.15 (m, 1 H), 7.25–7.29 (m, 1 H), 7.31–7.34 (m, 1 H), 7.46–7.48 (m, 1 H) ppm. ^{13}C NMR: δ = 19.3, 28.0 (t, J = 22 Hz), 28.1, 73.2, 83.0, 105–121 (8 fluorinated C) 119.4, 121.5, 125.3, 129.5, 134.3, 141.6, 153.1 ppm. HRMS calcd. for $C_{18}H_{12}ClF_{17}NO_3^+$, 648.0229 (– *t*Bu, + H$^+$); found 648.0223.

***tert*-Butyl 2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl(3-perfluorooctylpropoxy)carbamate (3m):** Prepared by general procedure A to give 295 mg (96%) of **3m** as a white solid. Purity by LC-UV(ELS): 98% (99%). ^{1}H NMR: δ = 1.50 (s, 9 H), 1.89–1.95 (m, 2 H), 2.20–2.32 (m, 2 H), 3.94 (t, J = 5.9 Hz, 2 H), 4.24 (br. s, 4 H), 6.81–6.87 (m, 2 H), 6.90–6.92 (m, 1 H) ppm. ^{13}C NMR: δ = 19.3, 28.1 (t, J = 22 Hz), 28.2, 64.3, 72.8, 82.2, 107–121 (8 fluorinated C), 112.9, 116.9, 117.1, 134.0, 142.0, 143.2, 154.1 ppm. HRMS calcd. for $C_{19}H_{15}F_{17}NO_3^+$, 628.0775 (– Boc, + H$^+$); found 628.0770.

***tert*-Butyl 2-(Methylthio)phenyl(3-perfluorooctylpropoxy)carbamate (3n):** Prepared by general procedure A to give 204 mg (68%) of **3n** as a brown oil. Purity by LC-UV(ELS): 97% (99%). ^{1}H NMR: δ = 1.47 (s, 9 H), 1.91–1.98 (m, 2 H), 2.15–2.27 (m, 2 H), 2.44 (s, 3 H), 4.01 (t, J = 5.9 Hz, 2 H), 7.15–7.18 (m, 1 H), 7.24–7.27 (m, 1 H), 7.28–7.32 (m, 2 H) ppm. ^{13}C NMR: δ = 15.4, 19.4, 28.0 (t, J = 22 Hz), 28.1, 73.4, 82.2, 107–121 (8 fluorinated C), 125.2, 125.9, 127.5, 128.9, 138.47, 138.50, 154.5 ppm. HRMS calcd. for $C_{18}H_{15}F_{17}NOS^+$, 616.0597 (– Boc, + H$^+$); found 616.0582.

***tert*-Butyl {2-[*tert*-Butoxycarbonyl(methyl)amino]methyl}phenyl(3-perfluorooctylpropoxy)carbamate (3o):** Prepared by general procedure A to give 256 mg (74%) of **3o** as a brown oil. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.43 & 1.50 (two [s br], 9 H, *E*/*Z* isomers), 1.46 (s, 9 H), 1.86–1.93 (m, 2 H), 2.16–2.28 (m, 2 H), 2.77–2.84 (m, 3 H), 3.94 (t, J = 5.9 Hz, 2 H), 4.46 (br. s, 2 H), 7.20–7.34 (m, 4 H) ppm. ^{13}C NMR: δ = 19.4, 27.9 (t, J = 22 Hz), 28.1, 28.4, 34.2, 47.6, 48.4, 72.8, 79.8, 82.3, 107–121 (8 fluorinated C), 126.8, 127.5, 128.6, 135.5, 138.4, 154.6, 156.0 ppm. HRMS calcd. for $C_{20}H_{18}F_{17}N_2O_3^+$, 657.1040 (– Boc, – *t*Bu, + H$^+$); found 657.1044.

***tert*-Butyl-4-{2-[*tert*-butoxycarbonyl(3-perfluorooctylpropoxy)amino]-benzyl}piperi-dine-1-carboxylate (3p):** Prepared by general procedure A to give 187 mg (51%) of **3p** as a brown oil. Purity by LC-UV(ELS): 100% (100%); TLC R_f = 0.46 (heptane/ethyl acetate, 3:1) ^{1}H NMR & TLC showed the presence of starting material after F-SPE. The product was used in the next step without further purification. HRMS calcd. for $C_{23}H_{24}F_{17}N_2O^+$, 667.1312 (– Boc × 2, + H$^+$); found 667.1600.

General Procedure B: Release of the Fluorous Tag by Reductive Cleavage of the N–O Bond: A microwave vial was charged with the N–O substrate (1.0 equiv., 0.15 mmol), tris(acetonitrile)molybdenumtricarbonyl (1.5 equiv., 67 mg, 0.22 mmol), methanol (2.5 mL), flushed with argon and sealed with a cap. The mixture was sonicated with ultrasound for 15 min and then heated in a Biotage Initiator sixty microwave for 15 min at 130 °C. The mixture was then added 3 mL of sat. aq. hydrogen carbonate, 3 mL of water, 6 mL of ethyl acetate and stirred overnight with no lid on the tube (in a few instances the dark brown colour had not disappeared and the remaining molybdenum was oxidized by adding 2 equiv. KIO_3). It was then worked up with ethyl acetate (3 × 20 mL) and water (20 mL). The combined organic phases were evaporated and purified by F-SPE. The non-fluorous fraction was rotavaped and dried in a vacuum centrifuge. The average yield was 74% ranging from 20 to >99%. The average purity by LC-UV was 94% ranging from 61–100%.

***tert*-Butyl (4-Bromophenyl)carbamate (4a):** Prepared by general procedure B to give 26 mg (71%) of **4a** as a white solid. Purity by LC-UV(ELS): 99% (n.d.). ^{1}H NMR: δ = 1.51 (s, 9 H), 6.50 (s, 1 H), 7.25 (d, J = 8.6 Hz, 2 H), 7.38 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR: δ = 28.3, 80.9, 115.4, 120.0, 131.8, 137.4, 152.5 ppm. HRMS calcd. for $C_7H_7BrNO_2^+$, 215.9655 (– *t*Bu, + H$^+$); found 215.9661.

***tert*-Butyl (4-Fluorophenyl)carbamate (4b):** Prepared by general procedure B to give 16 mg (49%) of **4b** as a grey solid. Purity by LC-UV(ELS): 100% (n.d.). ^{1}H NMR: δ = 1.51 (s, 9 H), 6.46 (s, 1 H), 6.96–7.00 (m, 2 H), 7.29–7.33 (m, 2 H) ppm. ^{13}C NMR: δ = 28.3, 80.6, 115.4, 115.6, 120.3 (broad), 134.3, 152.9, 158.8, 159.7 ppm. HRMS calcd. for $C_7H_7FNO_2^+$, 156.0455 (– *t*Bu, + H$^+$); found 156.0463.

***tert*-Butyl (4-Hydroxyphenyl)carbamate (4c):** Using general procedure B this compound was obtained as a black oil, 27 mg (98%),

purity by LC-UV(ELS): 74% (91%). An analytically pure sample was obtained by FC (heptane/ethyl acetate, 6:1) TLC R_f = 0.39 (heptane/ethyl acetate, 1:1). HRMS calcd. for $C_8H_{10}NO_3^+$, 168.0655 (– *t*Bu, + H^+); found 168.0651. Spectral data (^{1}H NMR) matched those previously reported in the literature.[14]

***tert*-Butyl (4-Cyanophenyl)carbamate (4d):** Prepared by general procedure B to give 31 mg (92%) of **4d** as a grey solid. Purity by LC-UV(ELS): 91% (100%). ^{1}H NMR: δ = 1.52 (s, 9 H), 6.76 (s, 1 H), 7.48 (d, J = 8.6 Hz, 2 H), 7.57 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR: δ = 28.2, 81.7, 105.7, 118.1, 119.0, 133.3, 142.6, 151.9 ppm. HRMS calcd. for $C_8H_7N_2O_2^+$, 163.0502 (– *t*Bu, + H^+); found 163.0503.

***tert*-Butyl (4-Formylphenyl)carbamate (4e):** Prepared by general procedure B to give 32 mg (92%) of **4e** as a brown solid. Purity by LC-UV(ELS): 81% (81%). ^{1}H NMR: δ = 1.54 (s, 9 H), 6.92 (s, 1 H), 7.55 (d, J = 8.4 Hz, 2 H), 7.83 (d, J = 8.4 Hz, 2 H), 9.90 (s, 1 H) ppm. ^{13}C NMR: δ = 28.2, 81.5, 117.8, 131.2 (both *para*- and *meta*-carbons), 144.2, 152.0, 191.0 ppm. HRMS calcd. for $C_7H_8NO^+$, 122.0600 (– Boc, + H^+); found 122.0595.

***tert*-Butyl 4-(Trifluoromethyl)phenylcarbamate (4f):** Prepared by general procedure B to give 8 mg (20%) of **4f** as a brown solid. Purity by LC-UV(ELS): 100% (n.d.). ^{1}H NMR: δ = 1.53 (s, 9 H), 6.63 (s, 1 H), 7.47 (d, J = 8.5 Hz, 2 H), 7.54 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR: δ = 28.2, 117.8, 124.3 (q, J = 271 Hz), 124.8 (q, J = 33 Hz), 126.3 (q, J = 4 Hz), 141.5, 152.2 ppm. HRMS calcd. for $C_8H_7F_3NO2^+$, 206.0423 (– *t*Bu, + H^+); found 206.0420.

***tert*-Butyl (4-Isopropylphenyl)carbamate (4g):** Prepared by general procedure B to give 30 mg (70%) of **4g** as a yellow solid. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.22 (d, J = 6.9 Hz, 6 H), 1.51 (s, 9 H), 2.85 (hept, J = 6.9 Hz, 1 H), 6.42 (s, 1 H), 7.14 (d, J = 8.3 Hz, 2 H), 7.26 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR: δ = 24.0, 28.3, 33.5, 80.3, 118.8, 126.8, 135.9, 143.7, 152.9 ppm. HRMS calcd. for $C_{10}H_{14}NO_2^+$, 180.1019 (– *t*Bu, + H^+); found 180.1020.

***tert*-Butyl (4-Acetylphenyl)carbamate (4h):** Prepared by general procedure B to give 36 mg (100%) of **4h** as a white solid. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.52 (s, 9 H), 2.56 (s, 3 H), 6.77 (br. s, 1 H), 7.45 (d, J = 8.5 Hz, 2 H), 7.91 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR: δ = 26.3, 28.2, 81.3, 117.4, 129.8, 131.8, 142.9, 152.1, 196.9 ppm. HRMS calcd. for $C_{13}H_{18}NO_3^+$, 236.1281 (+H^+); found 236.1279.

***tert*-Butyl (3-Hydroxyphenyl)carbamate (4i):** Prepared by general procedure B to give 24 mg (86%) of **4i** as a brown oil. Purity by LC-UV(ELS): 61% (86%). HRMS calcd. for $C_{11}H_{15}NNaO_3^+$, 232.0944 (+Na^+); found 232.0948, An analytical sample was obtained by flash chromatography (heptane/ethyla acetate, 8:1) TLC R_f = 0.29 (heptane/ethyl acetate, 3:1). Spectral data (^{1}H NMR) was identical to an authentic sample.

***tert*-Butyl [3-(Ethoxycarbonyl)phenyl]carbamate (4j):** Prepared by general procedure B to give 38 mg (88%) of **4j** as a white solid. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.38 (t, J = 7.1 Hz, 3 H), 1.52 (s, 9 H), 4.37 (q, J = 7.1 Hz, 2 H), 6.61 (s, 1 H), 7.36 (m, 1 H), 7.71 (m, 1 H), 7.90 (s, 1 H) ppm. ^{13}C NMR: δ = 14.3, 28.3, 61.1, 80.9, 119.4, 122.8, 124.1, 129.0, 131.2, 138.6, 152.6, 166.3 ppm. HRMS calcd. for $C_{10}H_{12}NO_4^+$, 210.0761 (– *t*Bu, + H^+); found 210.0769.

***tert*-Butyl (3-Methoxyphenyl)carbamate (4k):** Prepared by general procedure B to give 29 mg (74%) of **4k** as a light brown oil. Purity by LC-UV(ELS): 100% (n.d.). ^{1}H NMR: δ = 1.52 (s, 9 H) 3.79 (s, 3 H), 6.55 (br. s, 1 H), 6.57–6.60 (m, 1 H), 6.82–6.86 (m, 1 H), 7.10 (br. s, 1 H), 7.14–7.19 (m, 1 H) ppm. ^{13}C NMR: δ = 28.3, 55.2, 80.5, 104.0, 108.9, 110.6, 129.6, 139.6, 152.6, 160.2 ppm. HRMS calcd. for $C_8H_{10}NO_3^+$, 168.0655 (– *t*Bu, + H^+); found 168.0654.

***tert*-Butyl (3-Chlorophenyl)carbamate (4l):** Prepared by general procedure B to give 27 mg (73%) of **4l** as a brown solid. Purity by LC-UV(ELS): 99% (n.d.). ^{1}H NMR: δ = 1.52 (s, 9 H), 6.49 (s, 1 H), 6.99–7.01 (m, 1 H), 7.13–7.21 (m, 2 H), 7.52 (s, 1 H) ppm. ^{13}C NMR: δ = 28.3, 81.0, 116.3, 118.5, 123.0, 129.9, 134.7, 134.7, 139.5, 152.4 ppm. HRMS calcd. for $C_7H_7ClNO_2^+$, 172.0160 (– *t*Bu, + H^+); found 172.0156.

***tert*-Butyl 2,3-Dihydrobenzo[*b*][1,4]dioxin-6-ylcarbamate (4m):** Prepared by general procedure B to give 36 mg (91%) of **4m** as a light brown solid. Purity by LC-UV(ELS): 97% (100%). ^{1}H NMR: δ = 1.49 (s, 9 H), 4.20 (d, J = 5.3 Hz, 1 H), 4.22 (d, J = 5.3 Hz, 1 H), 6.37 (s, 1 H), 6.76 (s, 2 H), 6.95 (s, 1 H) ppm. ^{13}C NMR: δ = 28.3, 64.2, 64.4, 80.2, 108.5, 112.3, 117.1, 132.1, 139.5, 143.5, 152.9 ppm. HRMS calcd. for $C_9H_{10}NO_4^+$, 196.0604 (– *t*Bu, + H^+); found 196.0603.

***tert*-Butyl [2-(Methylthio)phenyl]carbamate (4n):** Prepared by general procedure B to give 17 mg (44%) of **4n** as a brown oil. Purity by LC-UV(ELS): 97% (n.d.). ^{1}H NMR: δ = 1.54 (s, 9 H), 2.36 (s, 3 H), 6.97 (m, 1 H), 7.25–7.29 (m, 1 H), 7.44–7.47 (m, 1 H), 7.60 (br. s, 1 H), 8.08–8.12 (m, 1 H) ppm. ^{13}C NMR: δ = 19.0, 28.3, 80.6, 118.8, 123.0, 124.1, 128.9, 133.2, 139.0, 152.8 ppm. HRMS calcd. for $C_7H_{10}NS^+$, 140.0528 (– Boc, + H^+); found 140.0527.

***tert*-Butyl 2-(*tert*-Butoxycarbonylamino)benzyl(methyl)carbamate (4o):** Prepared by general procedure B to give 47 mg (92%) of **4o** as a brown oil. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.50 (s, 9 H), 1.52 (s, 9 H), 2.74 (s, 3 H), 4.36 (s, 2 H), 6.92–6.96 (m, 1 H), 7.08–7.11 (m, 1 H), 7.26–7.30 (m, 1 H), 8.24 (br. s, 1 H), 8.67 (br. s, 1 H) ppm. ^{13}C NMR: δ = 28.30, 28.34, 32.9, 49.6, 79.7, 80.6, 119.3, 121.7, 124.3, 129.0, 131.2, 138.3, 153.5, 156.5 ppm. HRMS calcd. for $C_{18}H_{29}N_2O_4^+$, 337.2122 (+ H^+); found 337.2115.

***tert*-Butyl 4-[2-(*tert*-Butoxycarbonylamino)benzyl]piperidine-1-carboxylate (4p):** Prepared by general procedure B to give 23 mg (57%) of **4p** as a light brown oil. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.11–1.22 (m, 2 H), 1.44 (s, 9 H), 1.51 (s, 9 H), 1.57–1.66 (m, 2 H), 2.15–2.17 (m, 2 H), 2.49 (d, J = 6.8 Hz, 2 H), 2.57–2.67 (m, 2 H), 4.07 (br. s, 2 H), 6.22 (s, 1 H), 7.01–7.06 (m, 1 H), 7.07–7.10 (m, 1 H), 7.17–7.21 (m, 1 H), 7.64–7.69 (m, 1 H) ppm. ^{13}C NMR: δ = 28.3, 28.4, 32.1, 37.0, 38.4, 43.8, 79.3, 80.4, 123.2, 124.3, 127.0, 130.4, 130.9, 135.8, 153.4, 154.8 ppm. HRMS calcd. for $C_{22}H_{35}N_2O_4^+$, 391.2591 (– Boc, – *t*Bu, +H^+); found 391.2608.

***tert*-Butyl 4-(Ethoxycarbonyl)phenyl(3-perfluorooctylpropoxy)carbamate (5):** Prepared by general procedure A to give 553 mg (90%) of **5** as a white solid. Purity by LC-UV(ELS): 100% (99%). ^{1}H NMR: δ = 1.37 (t, J = 7.1 Hz, 3 H), 1.55 (s, 9 H), 1.95–2.01 (m, 2 H), 2.25–2.36 (m, 2 H) 3.98 (t, J = 5.9 Hz, 2 H), 4.37 (q, J = 7.1 Hz, 2 H), 7.51 (d, J = 8.8 Hz, 2 H), 8.02 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR δ = 14.3, 19.4, 28.0 (t, J = 22 Hz), 28.2, 60.9, 73.2, 83.2, 107–121 (8 fluorinated C), 119.8, 126.6, 130.2, 144.2, 152.7, 166.0 ppm. HRMS calcd. for $C_{21}H_{17}F_{17}NO_5^+$, 686.0830 (– *t*Bu, + H^+); found 686.0827.

Ethyl 4-[4-Chloro-*N*-(3-perfluorooctyl)propoxybenzamido]benzoate (6): Water-free ethanol (3 mL) was slowly added acetyl chloride (720 μL, 10.1 mmol) and stirred for 5 min. To it was added **5** (250 mg, 0.34 mmol) and the mixture was heated on an oil bath for two hours at 50 °C under argon. TLC (heptane/ethyl acetate, 3:1) showed completion of the reaction. The solvent and excess HCl was removed in vacuo and the remaining solid was dissolved in dry acetonitrile (5 mL) and cooled to 0 °C in an ice bath under argon.

To it was added triethylamine (140 μL, 1.0 mmol) and 4-chlorobenzoyl chloride (86 μL, 0.67 mmol). The mixture was stirred overnight at room temperature and purified by F-SPE to give 248 mg (94%) of **6** as a white solid. Purity by LC-UV(ELS): 98% (100%). ^{1}H NMR: δ = 1.38 (t, J = 7.1 Hz, 3 H), 1.81–1.88 (m, 2 H), 1.90–2.03 (m, 2 H), 3.91 (t, J = 5.9 Hz, 2 H), 4.39 (q, J = 7.1 Hz, 2 H), 7.34 (d, J = 8.4 Hz, 2 H), 7.57–7.60 (m, 4 H), 8.07 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR: δ = 14.3, 19.1, 27.5 (t, J = 22 Hz), 61.2, 73.3, 107–121 (8 fluorinated C), 121.9, 128.5, 129.9, 130.6, 132.5, 137.5, 142.9, 165.7, 167.3 ppm. HRMS calcd. for $C_{27}H_{20}F_{17}NO_4^+$, 780.0804 ($+H^+$); found 780.0819.

Ethyl 4-(4-Chlorobenzamido)benzoate (7): Prepared by general procedure B to give 29 mg (78%) of **7** as a white solid. Purity by LC-UV(ELS): 100% (100%). ^{1}H NMR: δ = 1.39 (t, J = 7.1 Hz, 3 H), 4.36 (q, J = 7.1 Hz, 2 H), 7.45 (d, J = 8.6 Hz, 2 H), 7.72 (d, J = 8.6 Hz, 2 H), 7.81 (d, J = 8.6 Hz, 2 H), 8.04 (d, J = 8.6 Hz, 2 H), 8.08 (br. s, 1 H) ppm. ^{13}C NMR: δ = 14.3, 61.0, 119.3, 126.4, 128.5, 129.2, 130.8, 132.9, 138.5, 141.8, 164.8, 166.1 ppm. HRMS calcd. for $C_{16}H_{14}ClNO_3^+$, 304.0735 ($+H^+$); found 304.0729.

Ethyl 4-[(4-Methylbenzyl)(3-perfluorooctylpropoxy)amino]benzoate (8): Water-free ethanol (3 mL) was slowly added acetyl chloride (650 μL, 9.1 mmol) and stirred for 5 min. To it was added **5** (225 mg, 0.3 mmol) and the mix was heated on an oil bath for two hours at 50 °C under argon. TLC (heptane/ethyl acetate, 3:1) showed completion of the reaction. The solvent and excess HCl was removed in vacou and the remaining solid was dissolved in dry acetonitrile (5 mL) and cooled to 0 °C in an ice bath under argon. To it was added cesium carbonate (346 mg, 1.06 mmol) and 1-(bromomethyl)-4-methylbenzene (116 mg, 0.61 mmol). The mix was stirred overnight at room temperature and purified by F-SPE to give 175 mg (77%) of **8** as a light brown solid. Purity by LC-UV(ELS): 90 (100). ^{1}H NMR: δ = 1.38 (t, J = 7.1 Hz, 3 H), 1.74–1.80 (m, 2 H), 1.87–1.98 (m, 2 H), 2.33 (s, 3 H), 3.68 (t, J = 5.9 Hz, 2 H), 4.35 (q, J = 7.1 Hz, 2 H), 4.44 (s, 2 H), 7.08 (d, J = 8.8 Hz, 2 H), 7.13 (d, J = 7.8 Hz, 2 H), 7.25 (d, J = 7.8 Hz, 2 H), 7.98 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR: δ = 14.4, 19.4, 21.0, 27.9 (t, J = 22 Hz), 60.6, 62.0, 72.0, 115.3, 107–121 (8 fluorinated C), 123.9, 129.0, 130.8, 133.4, 137.5, 155.1, 166.4 ppm. HRMS calcd. for $C_{28}H_{25}F_{17}NO_3^+$, 746.1557 ($+H^+$); found 746.1552.

Ethyl 4-[(4-Methylbenzyl)amino]benzoate (9): Prepared by general procedure B to give 28 mg (80%) of **9** as a yellow solid. Purity by LC-UV(ELS): 96% (100%). ^{1}H NMR: δ = 1.35 (t, J = 7.2 Hz, 3 H), 2.35 (s, 3 H), 4.31 (q, J = 7.2 Hz, 2 H), 4.34 (s, 2 H), 4.43 (br. s, 1 H), 6.58 (d, J = 8.7 Hz, 2 H), 7.16 (d, J = 7.8 Hz, 2 H), 7.23 (d, J = 7.8 Hz, 2 H), 7.87 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR: δ = 14.4, 21.1, 47.5, 60.2, 111.6, 119.0, 127.4, 129.4, 131.5, 135.3, 137.2, 151.7, 166.8 ppm. HRMS calcd. for $C_{17}H_{20}NO_2^+$, 270.1489 ($+H^+$); found 270.1481.

Supporting Information (see also the footnote on the first page of this article): Copies of NMR spectra.

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