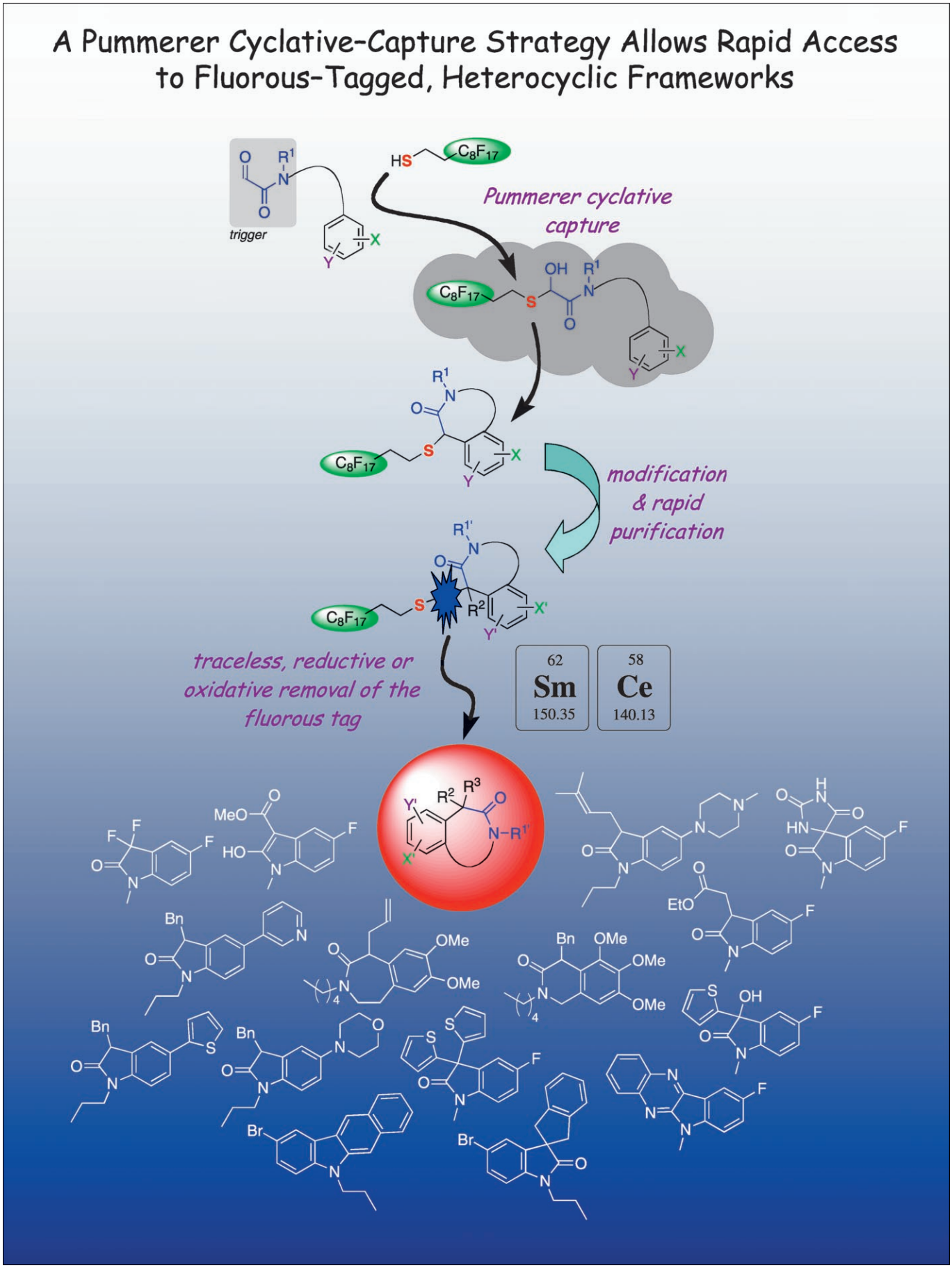
DOI: 10.1002/chem.200601429

A Pummerer Cyclative-Capture Strategy Allows Rapid Access to Fluorous-Tagged, Heterocyclic Frameworks



A Fluorous, Pummerer Cyclative-Capture Strategy for the Synthesis of N-Heterocycles

Laura A. McAllister,[a] Rosemary A. McCormick,[a] Karen M. James,[b] Stephen Brand,[c] Nigel Willetts,[d] and David J. Procter*[b]

Abstract: A fluorous, cyclative-capture strategy based on a new Pummerer cyclization process allows rapid access to tagged, heterocyclic frameworks. Convenient modification of the fluorous, heterocyclic scaffolds by using a variety of approaches including Pd-catalyzed cross-couplings is possible. Traceless, reductive cleavage of the fluorous-phase tag or oxidative cleavage and further elaboration, completes a strategy for the high-throughput, fluorous-phase synthesis of a diverse range of N-heterocycles.

Keywords: fluorous-phase synthesis · heterocycles · organic synthesis · Pummerer reaction · samarium

Introduction

Nitrogen-containing, heterocyclic organic compounds in the form of biologically active drugs or agents play an important role in the pharmaceutical and agrochemical industries.[1] The development of new strategies for the assembly of collections of heterocyclic compounds in a rapid and efficient high-throughput manner is therefore a key activity in synthetic chemistry.[2]

The use of phase tags to facilitate the purification of intermediates during multistep sequences is a common strategy in synthesis. Whereas solid-phase synthesis involves the use of insoluble polymers as phase tags, fluorous-phase synthesis uses a soluble perfluoroalkyl group in place of the polymer tag.[3] In recent years, thanks largely to the efforts of Curran and co-workers, fluorous-phase synthesis has emerged as an important tool for synthetic chemists.[4] Fluorous-phase synthesis has several advantages over solid-phase synthesis, but arguably the most important is the ability to monitor reactions by using conventional analytical methods, such as TLC, HPLC, IR, and NMR.[4] We envisaged that the combination of fluorous-phase techniques with versatile, sequential processes that achieve multiple synthetic objectives in a single operation could lead to efficient routes to important compound classes. Here we report in full our studies on the development and evaluation of a fluorous, Pummerer cyclative-capture strategy for the synthesis of N-heterocycles.[5]

Results and Discussion

The Pummerer reaction[6] has evolved into a useful tool for the synthesis of heterocyclic compounds.[7] We have recently reported a solid-phase approach to oxindoles utilising the Pummerer cyclization of substrates attached to resin via an "enabling" sulfur atom.[8] The approach is limited by the synthetic sequence required to access the immobilized heterocyclic framework (immobilization/oxidation/cyclization). A more general limitation, common to many solid-phase processes, arises from the considerable investment required to optimize solid-phase sequences due to difficulties monitoring transformations.[9] The work described here was borne from a need to address these issues and has led to the development of a sequential, fluorous process involving a Pummerer cyclative-capture step.

[a] Dr. L. A. McAllister, R. A. McCormick
Department of Chemistry, The Joseph Black Building
The University of Glasgow, Glasgow G12 8QQ (Scotland)

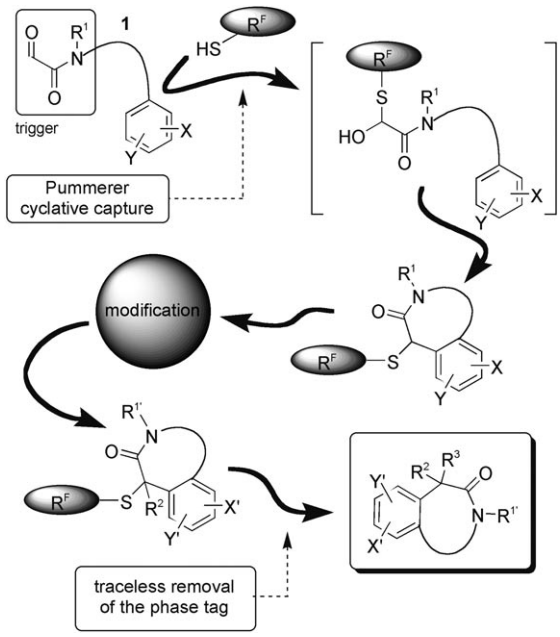
[b] K. M. James, Dr. D. J. Procter
The School of Chemistry, The University of Manchester
Oxford Road M13 9 PL (UK)
Fax: (+44) 161-275-4939
E-mail: David.J.Procter@manchester.ac.uk

[c] Dr. S. Brand
Celltech R&D, 216 Bath Road, Slough
Berkshire SL1 4EN (UK)

[d] N. Willetts
Syngenta, Jealott's Hill International Research Centre
Bracknell, Berkshire RG42 6EY (UK)

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

Pummerer cyclative capture: Our approach is based on the addition of thiols to glyoxamides **1**. The resultant hemithioacetals are at the correct oxidation level for activation and Pummerer cyclization. This constitutes a new, general strategy for generating thionium ions and triggering Pummerer cyclizations.[10] The use of a thiol containing a phase tag leads to cyclative capture of the substrate. The choice of a fluorous thiol[11] allows reactions to be monitored conveniently whilst allowing phase-tag assisted purification at each stage of the process.[3,4] Our approach constitutes the first example of fluorous, cyclative capture and utilises a fluorous-phase scavenging reagent in a novel manner. Upon completion of the sequence, the fluorous-phase tag can be removed in a traceless manner to give a potentially diverse collection of product heterocycles (Scheme 1).



Scheme 1. Fluorous, Pummerer cyclative-capture strategy (R^F = fluorous alkyl).

Treatment of readily accessible glyoxamide[12] starting materials with 1*H*,1*H*,2*H*,2*H*-perfluorodecane-1-thiol ($C_8F_{17}CH_2CH_2SH$) results in capture of the substrate through hemithioacetal formation. In the same reaction pot, activation (TFAA) and treatment with $BF_3{\cdot}OEt_2$ gave the product heterocycle in good isolated yield after rapid purification by using fluorous-solid-phase extraction (FSPE).[13] The fluorous-phase, Pummerer cyclative capture of a range of glyoxamides is shown in Table 1.

Oxindoles (entries 1–7), tetrahydroisoquinolinones (entries 8–10) and tetrahydrobenzazepinones (entries 11–17) can be prepared by straightforward variation of the glyoxamide substrate. For the formation of six and seven-membered heterocycles (entries 8–17), electronic activation of the aromatic ring leads to higher yields of product. In contrast, the formation of oxindoles (entries 1–7) proceeds efficiently with neutral, electron-deficient and -rich substrates. Several nitrogen protecting groups, for example, Bn, *p*-methoxybenzyl (PMB) and 2-phenylsulfonyl ethyl (PSE) have been shown to be compatible with the reaction conditions for cyclative capture, thus allowing access to heterocycles bearing free NH groups.

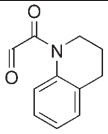
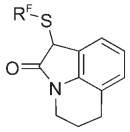
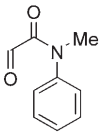
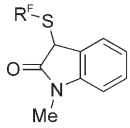
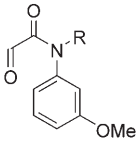
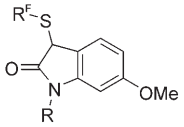
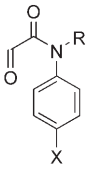
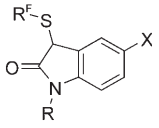
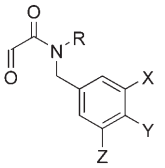
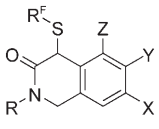
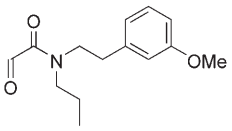
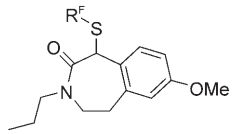
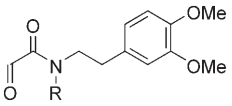
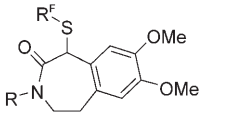
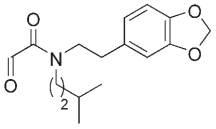
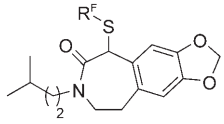
Developing conditions for the removal of the fluorous tag: Identifying effective conditions for the efficient removal of the fluorous tag is crucial to our approach. We decided to use simple, unmodified, tagged-heterocycles as model substrates to help develop and optimize methods for the removal of the fluorous tag. These conditions would then be used to access more complex systems in a library synthesis.

We began by examining reductive methods for the "traceless" removal of the fluorous tag. A number of electron-transfer reagents are known to reduce α-heteroatom-substituted carbonyl compounds to the parent carbonyl compound.[14] By using a range of model tagged substrates, it was found that reduction with SmI_2[15] resulted in the clean removal of the fluorous tag (Figure 1). We have previously utilised this process in the cleavage of oxygen and sulfur-linker systems for solid-phase synthesis.[8,16] No additives are required to activate SmI_2,[17] due to the reactive nature of the carbon–sulfur linkage to the fluorous tag present in our systems.

Alternative cleavage methods were investigated for use with the fluorous-phase approach. In particular, we wished to develop a complimentary oxidative method for the cleavage of the sulfur linker. Again, unmodified, tagged heterocycles were used as model substrates. We began by focusing on the removal of the fluorous tag from oxindole **7** by oxidative cleavage of the sulfur linker by using a Pummerer process.[18] Selective oxidation of **7** by using Bégué's H_2O_2-hexafluoroisopropanol (HFIP) system gave sulfoxide **19**, with no over oxidation.[19] Pummerer cleavage was then carried out by using TFAA to give indoline-1,2-dione **20** in moderate yield (Scheme 2). We subsequently found that the Pummerer, oxidative cleavage of **7** could be carried out in a single step with ceric(IV) ammonium nitrate ($Ce(NH_4)_2(NO_3)_6$, CAN), giving **20** in quantitative yield (Scheme 2).[20]

The oxidative removal of the fluorous tag worked well for a range of tagged oxindoles (Figure 1), giving the expected 1,2-dicarbonyl products in high yield after purification with FSPE. Interestingly, in the reaction of benzazepinone **15** with CAN, the fluorous tag can be removed in the presence of the PMB protecting group to give dihydrobenzazepine-1,2-dione **21** (Figure 1). The only side product from this reaction is the alternative benzylic oxidation product **22**; however, as this still contains a fluorous tag it is readily removed from the product mixture during FSPE. FSPE proved effective in removing the fluorous byproduct after both reductive and oxidative cleavage, the desired products eluting in the non-fluorous fraction.

Table 1. Fluorous, Pummerer cyclative-capture of glyoxamides.[a]

Entry	Glyoxamide	Tagged heterocycle[b]	Product	Isolated yield [%][c]
1			**2**	65[5]
2			**3**	54
3 R = *n*Pr			**4**	75[5][d]
4 R = PSE			**5**	55[d]
5 X = Cl, R = Me			**6**	79[5]
6 X = Br, R = *n*Pr			**7**	85[5]
7 X = F, R = Me			**8**	80[5]
8 X,Y,Z = H, R = Me			**9**	45[5]
9 X = OMe, X,Z = H, R = *n*Pr			**10**	51[5][e]
10 X,Y,Z = OMe, R = *n*-pentyl			**11**	60[5]
11			**12**	76[5][f]
12 R = *n*-pentyl			**13**	98[5]
13 R = Bn			**14**	80
14 R = PMB			**15**	77
15 R = PSE			**16**	100
16 R = allyl			**17**	60
17			**18**	82[5]

[a] Conditions: $C_8F_{17}CH_2CH_2SH$, CH_2Cl_2, 18 h then trifluoroacetic anhydride, 1 h then $BF_3{\cdot}OEt_2$, 1 h see Experimental Section for details. [b] $R^F = C_8F_{17}CH_2CH_2$. [c] Isolated yield for 2 steps. [d] 5:1 and [e] ≈1:1 mixture of isomers. [f] ≈2:1 mixture of isomers. Major isomers shown.

With efficient methods for the reductive and oxidative removal of the fluorous tag in place, we next examined the versatility of the fluorous-tagged heterocycles as frameworks for library synthesis.

Elaboration of tagged heterocycles: The Pummerer cyclative-capture process allows convenient access to fluorous-tagged heterocyclic frameworks. These tagged heterocycles are versatile scaffolds that can be modified in a variety of ways. In particular, the sulfur linkage to the fluorous tag can be used to facilitate elaboration, that is, in alkylation and acylation reactions, at either the sulfide or sulfone oxidation states. For example, adducts **23**[5] and **24** were prepared by Michael addition while the fluorous oxindole, tetrahydroisoquinolinone and tetrahydrobenzazepinone derivatives **25**, **26**, **28**[5] and **29**[5] were formed by alkylation. Ester **27**[5] was prepared by *O*-acylation followed by DMAP-catalysed rearrangement.[21] In all cases, excess reagent can be used to drive reactions to completion as purification after each modification step can be conveniently carried out by using FSPE (Scheme 3).

Palladium-catalysed couplings[22] are amongst the most powerful reactions for library synthesis and such processes must be accommodated in any new high-throughput synthetic strategy. The transformations illustrated in Scheme 4 show the compatibility of the linker system with palladium-catalysed cross-coupling technologies. For example, sequences to prepare alkynes **30**[5] and **31**[5] include sulfone-assisted alkylation and Sonagashira cross-coupling.[22,23] Tagged 5-bromooxindoles **32**[5] and **35**[5] readily undergo Suzuki–Miyaura cross-coupling[22,24] with aryl and heteroaryl boronic acids to give **33**,[5] **34**[5] and **36**.[5] Hartwig–Buchwald amination[22] of tagged substrates was also possible by using phosphine ligand **37**[25] and microwave (MW) assistance.[26] For example, coupling of **32** and **26** with different amines gave the expected adducts **38**–**40** in good yield. Again, purification after each modification step can be conveniently carried out by using FSPE (Scheme 4).

Removal of the fluorous tag: As already illustrated for unmodified systems (Figure 1), the fluorous tag can be reductively removed from elaborated heterocyclic systems by treatment with SmI_2. For the cleavage of the linker at the sulfone oxidation state, the fluorous component is lost to the aqueous layer during work up and no purification is required. Cleavage reactions at the sulfide oxidation state can

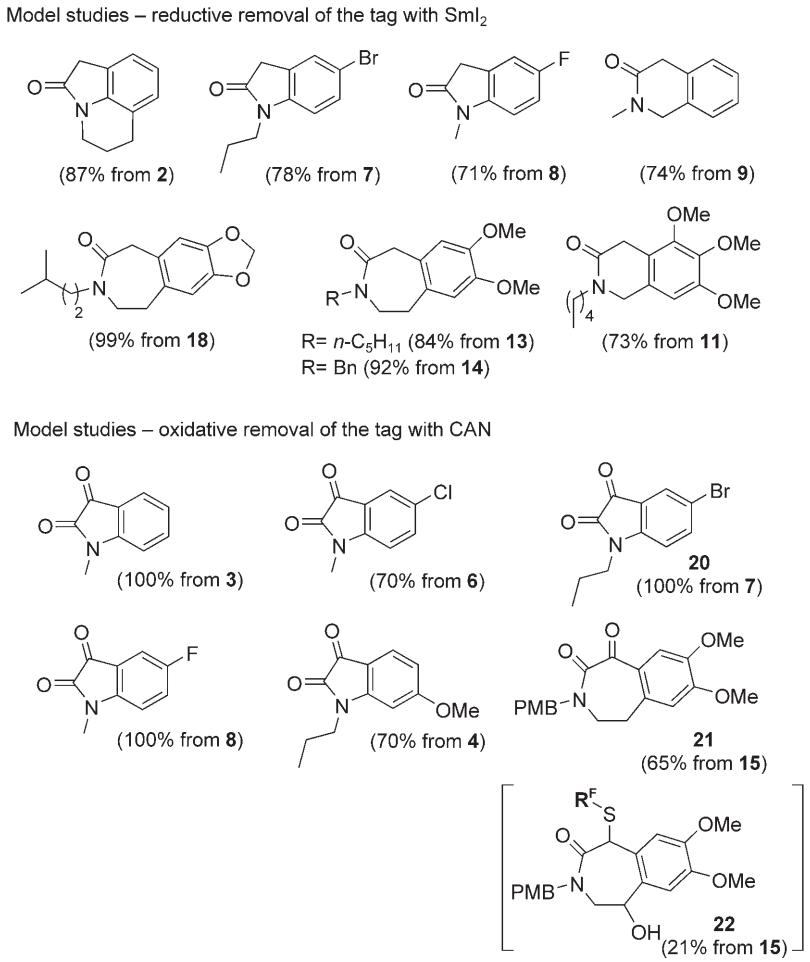
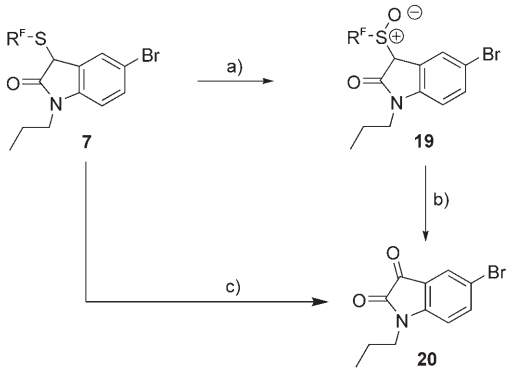


Figure 1. Products from the reductive and oxidative removal of the fluorous tag ($R^F = C_8F_{17}CH_2CH_2$).



Scheme 2. Optimizing an oxidative method for removal of the fluorous tag. a) 30% H_2O_2, H_2O, HFIP/CH_2Cl_2, 99%; b) TFAA, NEt_3, EtOH, THF, 55%; c) CAN, MeCN, H_2O, 100%. $R^F = C_8F_{17}CH_2CH_2$; HFIP = hexafluoroisopropanol; TFAA = trifluoroacetic anhydride; CAN = ceric ammonium nitrate.

be readily purified by using FSPE. Figure 2 shows the diverse range of products accessible from the cyclative-capture approach and modification, coupled with reductive cleavage of the fluorous tag.

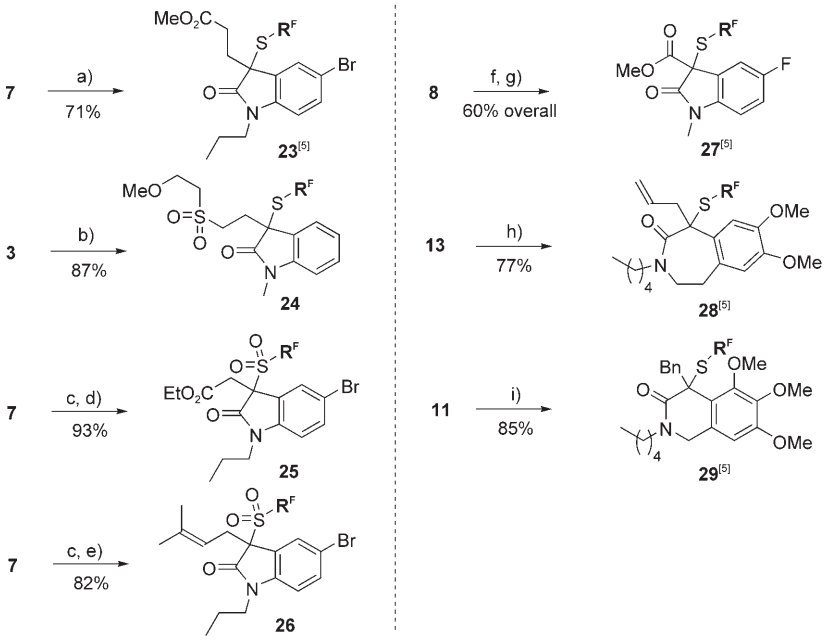
As previously discussed, oxidative cleavage of the sulfide linker releases heterocycles bearing a 1,2-dicarbonyl motif (Figure 1). These compounds are versatile substrates for the introduction of structural diversity. After cleavage and FSPE to remove the fluorous byproduct, modification of the released heterocycle can be carried out. For example, oxidative cleavage of tagged oxindoles **7** and **8**, FSPE and condensation with 1,2-phenyldiamine, gave **54** and **55**,[27] while fluorination with diethylaminosulfur trifluoride (DAST) gave difluorooxindoles[28] **56** and **57** (Scheme 5).

Similarly, after cleavage of the tag from **8** and FSPE, treatment of the crude indoline-1,2-dione with varying amounts of 2-thienyllithium led to the corresponding mono- and bisaddition products,[29] **58** and **59** (Scheme 6). Finally, a Bucherer–Bergs reaction[30] was used to convert the crude indoline-1,2-dione to spirohydantoin **60**.

Finally, we have carried out preliminary investigations into the development of sequential tag-cleavage/cyclization processes. For example, tagged oxindole **61** was prepared and the fluorous tag cleaved with SmI_2. We were pleased to find that the intermediate Sm^{III} enolate formed on cleavage of the tag underwent intramolecular alkylation to give the expected spirocycle **62** in good yield (Scheme 7). We were intrigued by the isolation of indolocarbazole **63** as the only byproduct from the reaction. On changing the order of addition, **63** was isolated as the major product. We believe **63** was formed after reductive cleavage of the tag by the intramolecular Barbier addition of a benzylic samarium to the oxindole carbonyl followed by dehydration and aromatization. Thus, by changing the order of addition of SmI_2, the mode of sequential tag-cleavage/cyclization can be controlled to access two very different heterocyclic systems (Scheme 7).

Conclusion

This report describes the development of a new strategy for the high-throughput, fluorous-phase synthesis of N-heterocycle libraries. The sequence involves several key features: 1) a new Pummerer process used in a fluorous, cyclative-



Scheme 3. Elaboration of fluorous-tagged heterocyclic frameworks—modification α to sulfur. a) NaOMe, MeOH, methylacrylate, 18 h, 71%; b) NaOMe, MeOH, divinylsulfone, RT, 18 h, 87%; c) *m*CPBA, CH_2Cl_2, 4 h, 90%; d) K_2CO_3, DMF, ethyl bromoacetate, 40°C, 93%; e) K_2CO_3, DMF, prenyl bromide, 40°C, 82%; f) methylchloroformate, CH_2Cl_2, NEt_3, RT, 3 h; g) 30 mol% DMAP, toluene, 70°C, 3 h, 60% for two steps; h) NaH, THF/DMF, 80°C, 18 h, allyl bromide, 77%; i) LHMDS, THF, −78°C, 7 h, BnBr, 85%. $R^F = C_8F_{17}CH_2CH_2$; *m*CPBA = *meta*-chloroperbenzoic acid; DMAP = 4-dimethylaminopyridine; LHMDS = lithium hexamethyl disilazide.

capture strategy for rapid access to tagged, heterocyclic frameworks, 2) modification of the fluorous, heterocyclic scaffolds by using a variety of approaches including Pd-catalyzed cross-couplings and 3) traceless reductive or oxidative removal of the fluorous-phase tag. The overall sequence allows a diverse range of pharmaceutically interesting N-heterocyclic systems to be accessed.

Experimental Section

General considerations: All experiments were performed under an atmosphere of Ar or N_2 and anhydrous solvents, unless stated otherwise. Oven-dried glassware was used in the reactions. THF was distilled from sodium/benzophenone, CH_2Cl_2 was distilled from CaH_2, Et_2O was distilled from CaH_2, and *i*$PrNH_2$ was distilled from CaH_2. Et_3N was distilled from CaH_2 and stored over KOH under Ar/N_2. DMSO was distilled from CaH_2 and stored over molecular sieves and under Ar/N_2.

^{1}H and ^{13}C NMR spectra were recorded on a Fourier transform spectrometer, with chemical shift values being reported in ppm relative to residual chloroform ($\delta_H = 7.27$ or $\delta_C = 77.2$ ppm) as an internal standard unless otherwise stated. NMR signals were assigned by using DEPT-135, HMQC and COSY spectra. All coupling constants (J) are reported in Hertz (Hz). $R^F = C_8F_{17}$. Perfluorinated carbon atoms are not observed in the ^{13}C NMR spectra. Mass spectra and microanalyses were recorded at the University of Glasgow and the University of Manchester. IR spectra were recorded by using a FTIR spectrometer. Column chromatography was carried out with silica gel 60 and fluorous silica. Aluminium-backed plates precoated with silica gel 60 (UV_{254}) were used for TLC and were visualised by UV or staining with alkali $KMnO_4$.

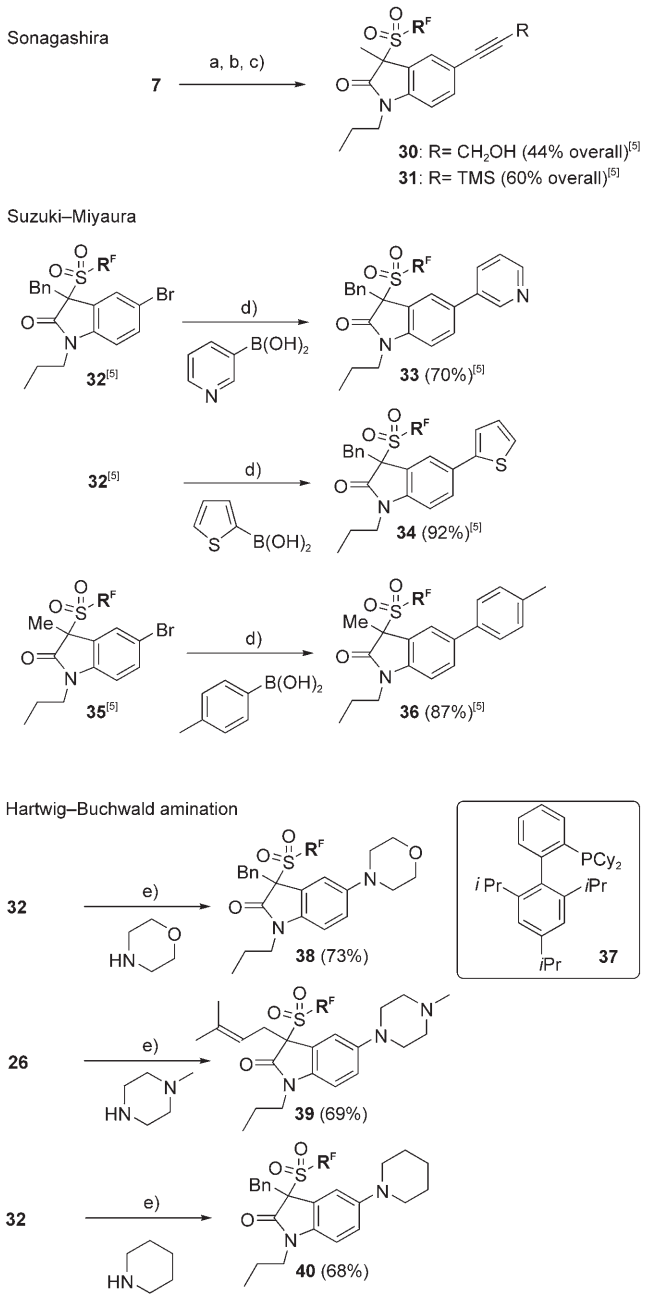
In a typical FSPE separation, a crude product mixture containing tagged and non-tagged organic compounds was loaded onto the fluorous silica by using a minimum amount of organic solvent (less than 20% of silica gel volume). Elution with a fluorophobic solvent mix, such as 80% MeCN/H_2O, removes non-fluorinated compounds from the column. The column was then eluted with a fluorophilic solvent, such as MeCN, which removes tagged compounds from the column. The fluorous silica gel could often be reused.

General procedure A for the cyclative capture of glyoxamide: Details for general procedure A can be found in reference [5].

3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecylsulfanyl)-1-methyl-1,3-dihydroindole-2-one (3): General procedure A was followed as described in reference [5]. Thus, treatment of crude *N*-methyl-2-oxo-*N*-phenylacetamide with $C_8F_{17}CH_2CH_2SH$ (0.15 mL, 0.5265 mmol, 0.7 equiv), TFAA (0.96 mL, 6.77 mmol, 9 equiv) and $BF_3{\cdot}OEt_2$ (0.46 mL, 3.76 mmol, 5 equiv) and purification by fluorous chromatography gave **3** (0.179 g, 0.286 mmol, 54%) as a light-brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.34$–7.43 (2H, m; 2×Ar*H*), 7.14 (1H, t, $J = 6.0$ Hz; Ar*H*), 6.87 (1H, d; $J = 6.0$ Hz; Ar*H*), 4.36 (1H, s; C*H*), 3.25 (3H, s; CH_3), 2.96–3.05 (1H, m; 1H of CH_2), 2.80–2.90 (1H, m; 1H of CH_2), 2.35–2.53 ppm (2H, m; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.1$ (*C*=O), 144.2 (Ar*C*), 129.6 (Ar*C*H), 125.3 (Ar*C*), 125.2 (Ar*C*H), 123.2 (Ar*C*H), 108.5 (Ar*C*H), 45.0 (*C*H), 32.1 (t, $J = 22.0$ Hz; CH_2), 26.4 (CH_3), 21.2 ppm (CH_2); IR (ATR): $\tilde{\nu} = 1705$ (C=O), 1611, 1470, 1348, 1199, 1134, 941 cm^{-1}; MS (ES$^+$ mode): *m*/*z* (%): 648 $[M+Na]^+$ (83), 643 (23), 381 (13); HRMS: *m*/*z*: calcd for $C_{19}H_{16}ON_2F_{17}S$: 643.0706; found: 643.0703 $[M+NH_4]^+$.

1-(2-Benzenesulfonylethyl)-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-6-methoxy-1,3-dihydroindol-2-one (5): General procedure A was followed as described in reference [5]. Thus, treatment of *N*-(2-benzenesulfonylethyl)-*N*-(3-methoxyphenyl)-2-oxoacetamide (0.47 g, 1.35 mmol, 1 equiv) with $C_8F_{17}CH_2CH_2SH$ (1.58 mL, 5.39 mmol, 4 equiv), TFAA (1.80 mL, 12.12 mmol, 9 equiv) and $BF_3{\cdot}OEt_2$ (0.85 mL, 6.74 mmol, 5 equiv) and purification by using fluorous silica (eluting with 80% MeCN/H_2O then MeCN) and then on silica (eluting with 30% EtOAc/petroleum ether (40–60°C)) gave **5** (0.60 g, 0.74 mmol, 55%) as a pale-yellow solid and as a 5:1 mixture of regioisomers.

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.84$–7.82 (2H, m; Ar*H*), 7.62–7.58 (1H, m; Ar*H*), 7.51–7.47 (2H, m; Ar*H*), 7.16 (1H, d, $J = 8.4$ Hz; Ar*H*), 6.54 (1H, dd, $J = 8.2$, 2.2 Hz; Ar*H*), 6.44 (1H, d, 2.2; Ar*H*), 4.05 (1H, s; C*H*S), 4.02 (2H, t; $J = 7.0$ Hz; NCH_2), 3.78 (3H, s; CH_3O), 3.50–3.43 (1H, m; 1H of NCH$_2$C*H*$_2$), 3.40–3.33 (1H, m; 1H of NCH$_2$C*H*$_2$), 2.92–2.85 (1H, m; 1H of C*H*$_2$CH$_2$R^F), 2.76–2.68 (1H, m; 1H of C*H*$_2$CH$_2$R^F), 2.38–2.23 ppm (2H, m; C*H*$_2$R^F); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 175.7$ (*C*=O), 161.3 (Ar*C*OMe), 143.3 (Ar*C*), 138.7 (Ar*C*), 134.2 (Ar*C*H), 129.5 (2×Ar*C*H), 127.9 (2×Ar*C*H), 126.2 (Ar*C*H), 116.3 (Ar*C*), 107.8 (Ar*C*H), 96.5 (Ar*C*H), 55.7 (CH_3O), 52.4 (NCH$_2$*C*H$_2$), 44.2 (*C*HS), 34.3 (N*C*H$_2$), 31.8 ppm (t, $J = 21.5$ Hz; *C*H$_2$R^F), 21.2 (*C*H$_2$CH$_2$R^F); IR (KBr): $\tilde{\nu} = 2966$, 1720, 1628 (C=O), 1504, 1450, 1377, 1315, 1219 cm^{-1}; MS (FAB mode, NOBA, NaI): *m*/*z* (%): 832 $[M+Na]^+$ (100), 71 (17), 330 (58); HRMS: *m*/*z*: calcd for $C_{27}H_{20}O_4NF_{17}S_2Na$: 832.0460; found: 832.0463 $[M+Na]^+$.



Scheme 4. Elaboration of fluorous-tagged heterocycles—Pd-catalyzed modifications. a) *m*CPBA, CH_2Cl_2, RT, 2 h; b) K_2CO_3, MeI, DMF, 40 °C, 2 h; c) $Pd(PPh_3)_4$ (20 mol %), NEt_3, 80 °C, 18 h, propargyl alcohol or trimethylsilylacetylene (CuI 20 mol %), 44 and 60 % overall, respectively; d) $Pd(PPh_3)_4$ (20 mol %), Na_2CO_3, H_2O, dioxane, 80 °C, 3.5 h, $ArB(OH)_2$; e) $Pd(OAc)_2$ (4 mol %), **37** (8 mol %), morpholine or *N*-methylpiperazine or piperidine, Cs_2CO_3, toluene, MW (120 °C), 2 h, 73 % (**38**), 69 % (**39**), 68 % (**40**). $R^F = C_8F_{17}CH_2CH_2$.

3-Benzyl-1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-7,8-dimethoxy-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (14): General procedure A was followed as described in reference [5]. Thus, treatment of *N*-benzyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-2-oxoacetamide (0.39 g, 1.20 mmol, 1 equiv) with $C_8F_{17}CH_2CH_2SH$ (0.25 mL, 0.84 mmol, 0.7 equiv), TFAA (1.60 mL, 10.8 mmol, 9 equiv) and $BF_3{\cdot}OEt_2$ (0.76 mL, 5.99 mmol, 5 equiv) and purification by using fluorous silica (eluting with 80 % MeCN/H_2O then MeCN) gave **14** (0.53 g, 0.67 mmol, 80 %) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.28$–7.19 (5H, s; Ar*H*), 6.59 (1H, s; Ar*H*), 6.41 (1H, s; Ar*H*), 4.82 (1H, d, $J = 14.8$ Hz; 1H of NCH_2), 4.79 (1H, s; C*H*S), 4.67–4.57 (1H, m; 1H of ring CH_2N), 4.40 (1H, d, $J = 14.8$; 1H of NCH_2), 3.80 (3H, s; CH_3O), 3.75 (3H, s; CH_3O), 3.28–3.23 (1H, m; 1H of ring CH_2N), 3.03–2.79 (4H, m; $CH_2CH_2R^F$ and ring CH_2CH_2N), 2.49–2.42 ppm (2H, m; CH_2R^F); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.9$ (*C*=O), 148.9 (Ar*C*OMe), 147.7 (Ar*C*OMe), 137.3 (Ar*C*), 131.3 (Ar*C*), 128.7 (2×Ar*C*H), 128.1 (2×Ar*C*H), 127.7 (Ar*C*H), 123.1 (Ar*C*), 114.6 (Ar*C*H), 112.9 (Ar*C*H), 56.0 (CH_3O), 55.9 (CH_3O), 55.9 (*C*HS), 51.4 (NCH_2), 44.8 (ring CH_2N), 32.9 (ring CH_2CH_2N), 31.6 (t, $J = 21.8$ Hz; CH_2R^F), 24.4 ppm ($CH_2CH_2R^F$); IR (KBr): $\tilde{\nu} = 2936$ (C–H), 1633 (C=O), 1519, 1438, 1365, 1243, 1196, 1146, 1118 cm^{-1}; MS (EI mode): *m*/*z* (%): 789 $[M]^+$ (12), 155 (11), 164 (12), 282 (100), 283 (20), 310 (24), 311 (27); HRMS: *m*/*z*: calcd for $C_{29}H_{24}O_3NF_{17}S$: 789.1205; found: 789.1208 $[M]^+$.

1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecylsulfanyl)-7,8-dimethoxy-3-(4-methoxybenzyl)-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (15): General procedure A was followed as described in reference [5]. Thus, treatment of *N*-[2-(3,4-dimethoxyphenyl)ethyl]-*N*-(4-methoxybenzyl)-2-oxoacetamide (0.56 g, 1.57 mmol, 1 equiv) with $C_8F_{17}CH_2CH_2SH$ (0.32 mL, 1.10 mmol, 0.7 equiv), TFAA (2.09 mL, 14.1 mmol, 9 equiv) and $BF_3{\cdot}OEt_2$ (0.99 mL, 7.84 mmol, 5 equiv) and purification by using fluorous silica (eluting with 80 % MeCN/H_2O then MeCN) gave **15** (0.69 g, 0.85 mmol, 77 %) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.17$ (2H, d; $J = 8.4$; Ar*H*), 6.79 (2H, d, $J = 8.8$; Ar*H*), 6.59 (1H, s; Ar*H*), 6.41 (1H, s; Ar*H*), 4.78 (1H, s; C*H*S), 4.70 (1H, d, $J = 14.4$; 1H of NCH_2), 4.62–4.55 (1H, m; 1H of ring CH_2N), 4.38 (1H, d, $J = 14.4$; 1H of NCH_2), 3.80 (3H, s; CH_3O), 3.76 (3H, s; CH_3O), 3.73 (3H, s; CH_3O), 3.29–3.23 (1H, m; 1H of ring CH_2N), 3.02–2.80 (4H, m; $CH_2CH_2R^F$ and ring CH_2CH_2N), 2.54–2.37 ppm (2H, m; CH_2R^F); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.7$ (*C*=O), 159.1 (Ar*C*OMe), 148.8 (Ar*C*OMe), 147.6 (Ar*C*OMe), 129.9 (Ar*C*), 129.5 (2×Ar*C*H), 129.3 (Ar*C*), 123.1 (Ar*C*), 114.6 (Ar*C*H), 114.1 (2×Ar*C*H), 112.9 (Ar*C*H), 56.0 (2×CH_3O and *C*HS), 55.2 (CH_3O), 50.8 (NCH_2), 44.5 (ring CH_2N), 33.0 (ring CH_2CH_2N), 31.6 (t, $J = 22.1$; CH_2R^F), 24.4 ppm ($CH_2CH_2R^F$); IR (KBr): $\tilde{\nu} = 2933$, 1635 (C=O), 1516, 1471, 1363, 1246, 1204, 1150, 1119, 1038 cm^{-1}; MS (FAB mode, NOBA, NaI): *m*/*z* (%): 842 (45) $[M+Na]^+$, 70 (17), 121 (100), 192 (13), 312 (74), 363 (12), 599 (10); HRMS: *m*/*z*: calcd for $C_{30}H_{26}O_4NF_{17}SNa$: 842.1209; found: 842.1207 $[M+Na]^+$.

3-(2-Benzenesulfonylethyl)-1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-7,8-dimethoxy-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (16): General procedure A was followed as described in reference [5]. Thus, treatment of *N*-(2-benzenesulfonylethyl)-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-2-oxoacetamide (0.39 g, 0.96 mmol, 1 equiv) with $C_8F_{17}CH_2CH_2SH$ (0.20 mL, 0.67 mmol, 0.7 equiv), TFAA (1.27 mL, 8.60 mmol, 9 equiv) and $BF_3{\cdot}OEt_2$ (0.61 mL, 4.78 mmol, 5 equiv) and purification by using fluorous silica (eluting with 80 % MeCN/H_2O then MeCN) gave **16** (0.58 g, 0.67 mmol, 100 %) as a cream solid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.94$–7.92 (2H, m; Ar*H*), 7.70–7.67 (1H, m; Ar*H*), 7.61–7.57 (2H, m; Ar*H*), 6.64 (1H, s; Ar*H*), 6.57 (1H, s; Ar*H*), 4.90–4.83 (1H, m; 1H of ring CH_2N), 4.75 (1H, s; C*H*S), 4.05–3.98 (1H, m; 1H of NCH_2), 3.87 (3H, s; CH_3O), 3.86 (3H, s; CH_3O), 3.80–3.73 (1H, m; 1H of NCH_2), 3.57–3.48 (2H, m; 1H of ring CH_2N and 1H of NCH_2CH_2), 3.40–3.33 (1H, m; 1H of NCH_2CH_2), 3.18–2.88 (4H, m; ring CH_2CH_2N and $CH_2CH_2R^F$), 2.64–2.40 ppm (2H, m; CH_2R^F); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.0$ (*C*=O), 149.0 (Ar*C*OMe), 147.8 (Ar*C*OMe), 139.3 (Ar*C*), 134.0 (Ar*C*H), 129.6 (Ar*C*), 129.4 (2×Ar*C*H), 127.8 (2×Ar*C*H), 122.7 (Ar*C*), 114.4 (Ar*C*H), 113.1 (Ar*C*H), 55.9 (CH_3O), 55.9 (CH_3O), 55.5 (*C*HS), 54.2 (NCH_2CH_2), 47.4 (ring CH_2N), 43.9 (NCH_2), 33.1 (ring CH_2CH_2N), 31.4 (t, $J = 21.9$; CH_2R^F), 24.2 ppm ($CH_2CH_2R^F$); IR (KBr): $\tilde{\nu} = 3074$, 3005, 2976, 2955, 2927, 2838, 1648 (C=O), 1611, 1521, 1482, 1469 cm^{-1}; MS (FAB mode, NOBA, NaI): *m*/*z* (%): 890 (97) $[M+Na]^+$, 199 (11), 218 (13), 360 (71); HRMS: *m*/*z*: calcd for $C_{30}H_{26}O_5NF_{17}S_2Na$: 890.0879; found: 890.0876 $[M+Na]^+$.

3-Allyl-1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-7,8-dimethoxy-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (17): General

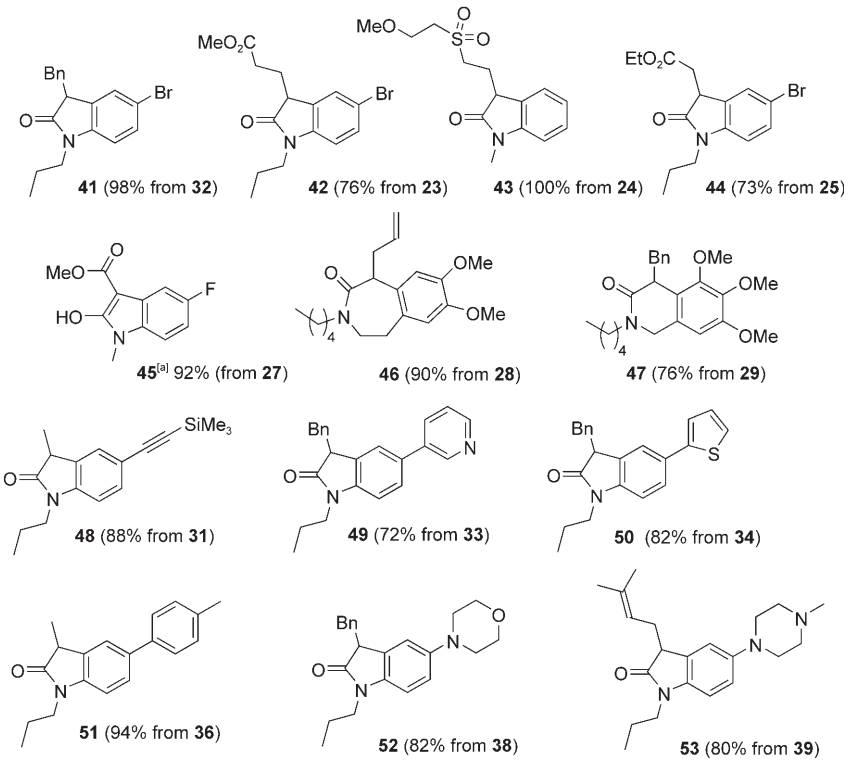
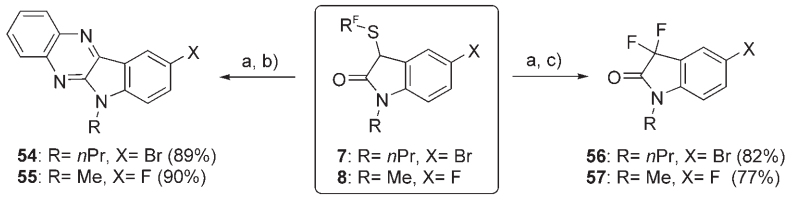
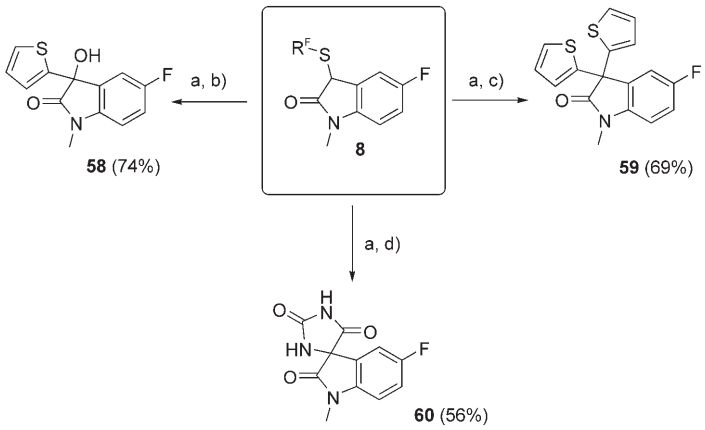


Figure 2. Products of the reductive removal of the fluorous tag from decorated heterocyclic scaffolds. [a] Obtained as a 1:1 mixture of tautomers by NMR spectroscopy.



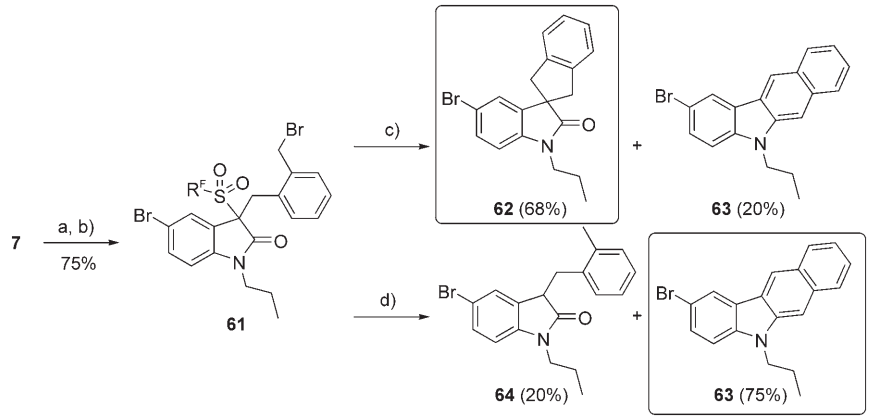
Scheme 5. Sequential-oxidative-cleavage modification. a) $Ce(NH_4)_2(NO_3)_6$, $MeCN/H_2O$, FSPE; b) 1,2-diaminobenzene, AcOH, Δ, 20 min, 89% for **54**, 90% for **55**; c) DAST, CH_2Cl_2, RT, 82% for **56**, 77% for **57**. $R^F = C_8F_{17}CH_2CH_2$; FSPE = fluorous solid-phase extraction; DAST = diethylaminosulfur trifluoride.



Scheme 6. Sequential-oxidative-cleavage modification. a) $Ce(NH_4)_2(NO_3)_6$, $MeCN/H_2O$, FSPE; b) 2-thienyllithium (1 equiv), THF, 0 °C to RT, 74%; c) 2-thienyllithium (3 equiv), THF, 0 °C to RT, 69%; d) KCN, $(NH_4)_2CO_3$, MeOH, RT to 70 °C, 56%. $R^F = C_8F_{17}CH_2CH_2$.

procedure A was followed as described in reference [5]. Thus, treatment of *N*-allyl-*N*-[2-(3,4-dimethoxyphenyl)ethyl]-2-oxoacetamide (0.21 g, 0.76 mmol, 1 equiv) with $C_8F_{17}CH_2CH_2SH$ (0.16 mL, 0.53 mmol, 0.7 equiv), TFAA (1.01 mL, 6.81 mmol, 9 equiv) and $BF_3{\cdot}OEt_2$ (0.48 mL, 3.79 mmol, 5 equiv) and purification by using fluorous silica (eluting with 80% MeCN/H_2O then MeCN) and then silica (eluting with 30% EtOAc/petroleum ether (40–60)) gave **17** (0.23 g, 0.32 mmol, 60%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.58$ (1H, s; Ar*H*), 6.46 (1H, s; Ar*H*), 5.80–5.70 (1H, m; C*H*=CH_2), 5.20–5.12 (2H, m; CH=CH_2), 4.72 (1H, s; C*H*S), 4.67–4.60 (1H, m; 1H of ring CH_2N), 4.21 (1H, dd, $J = 15.2$, 5.6 Hz; 1H of NCH_2), 3.84 (1H, dd; $J = 15.2$, 5.6 Hz; 1H of NCH_2), 3.80 (3H, s; CH_3O), 3.77 (3H, s; CH_3O), 3.28–3.22 (1H, m; 1H of ring CH_2N), 3.03–2.85 (4H, m; CH_2CH$_2$R^F and ring CH_2CH$_2$N), 2.53–2.38 ppm (2H, m; CH_2R^F); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 169.5$ (*C*=O), 148.9 (Ar*C*OMe), 147.7 (Ar*C*OMe), 133.0 (*C*H=CH_2), 129.9 (Ar*C*), 123.2 (Ar*C*), 117.6 (CH=*C*H_2), 114.7 (Ar*C*H), 113.0 (Ar*C*H), 56.0 (*C*HS), 55.9 (*C*H_3O), 55.9 (*C*H_3O), 50.7 (NCH_2), 44.7 (ring *C*H_2N), 33.1 (ring *C*H_2CH$_2$N), 31.7 (t, $J = 22.0$; *C*H_2R^F), 24.4 ppm (*C*H_2CH$_2$R^F); IR (KBr): $\tilde{\nu} = 3066$, 3010, 2965, 2936, 2911, 2853, 2835, 2255, 1649 (C=O), 1634, 1519 cm^{-1}; MS (FAB mode, NOBA, NaI): *m*/*z* (%): 762 (100) $[M+Na]^+$, 71 (11), 178 (10), 232 (88), 260 (65); HRMS: *m*/*z*: calcd for $C_{25}H_{22}O_3NF_{17}SNa$: 762.0947; found: 762.0945 $[M+Na]^+$.

3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecylsulfanyl)-3-[2-(2-methoxyethanesulfonyl)ethyl]-1-methyl-1,3-dihydroindol-2-one (24): NaOMe (0.04 mL, 25% wt solution in MeOH, 0.364 mmol, 2.5 equiv) and divinyl sulfone (0.02 mL, 0.189 mmol, 1.3 equiv) were added to a solution of **3** (0.091 g, 0.145 mmol, 1 equiv) in methanol (7 mL) at room temperature. The reaction was allowed to stir at room temperature for 19 h. The reaction was then quenched with saturated aqueous NH_4Cl (5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The organic layer was then dried ($MgSO_4$), filtered and concentrated in vacuo to give the crude product as a brown oil. Purification by fluorous chromatography gave **24** (0.098 g, 0.126 mmol, 87%) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.27$–7.35 (2H, m; 2×Ar*H*), 7.11 (1H, t, $J = 6.0$ Hz; Ar*H*), 6.85 (1H, d, $J = 6.0$ Hz; Ar*H*), 3.69 (2H, t, $J = 6.0$ Hz; CH_2), 3.25 (3H, s; CH_3), 3.20 (3H, s; CH_3), 3.09–3.12 (2H, m; CH_2), 2.90–3.01 (2H, m; CH_2), 2.75–2.42 (4H, m; 2×CH_2), 2.04–2.22 ppm (2H, m; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 175.4$ (*C*=O), 143.1 (Ar*C*), 130.2 (Ar*C*H), 127.7 (Ar*C*), 124.3 (Ar*C*H), 123.7 (Ar*C*H), 108.9 (Ar*C*H), 66.1 (*C*H_2), 59.1 (*C*H_3), 53.4 (*C*H_2), 52.8 (S*C*C=O), 50.5 (*C*H_2), 31.6 (t, $J = 21$ Hz; *C*H_2), 28.5 (*C*H_2), 26.6 (*C*H_3), 19.9 ppm (*C*H_2); IR (ATR): $\nu = 2924$, 1713, 1611, 1466, 1344, 1198 cm^{-1}; MS (ES$^+$ mode): *m*/*z* (%): 798 (100) $[M+Na]^+$, 653 (18), 574 (14), 374 (24); HRMS: *m*/*z*: calcd for $C_{24}H_{26}O_4N_2F_{17}S_2$: 793.1057; found: 793.1054 $[M+NH_4]^+$.



Scheme 7. Sequential tag-cleavage/cyclization. a) *m*CPBA, CH_2Cl_2, 4 h, 90%; b) K_2CO_3, α,α′-dibromo-*o*-xylene, DMF, 40°C, 4 h, 83%; c) SmI_2 (syringe pump addition of SmI_2 to substrate), THF, RT; d) SmI_2 (syringe pump addition of substrate to SmI_2), THF, RT; $R^F = C_8F_{17}CH_2CH_2$.

[5-Bromo-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfonyl)-2-oxo-1-propyl-2,3-dihydro-1*H*-indole-3-yl]acetic acid ethyl ester (25): Ethylbromoacetate (0.15 mL, 1.31 mmol, 5 equiv) and K_2CO_3 (0.181 g, 1.31 mmol, 5 equiv) were added to a solution of 5-bromo-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfonyl)-1-propyl-1,3-dihydroindole-2-one (**7**) (0.20 g, 0.263 mmol, 1 equiv) in DMF (6 mL) and the reaction was heated to 40°C. The reaction was left to stir for 2 h. Ethyl acetate (5 mL) was added to the reaction mixture and the organic layer washed with water (3×5 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to give a crude orange solid. The crude product was purified by fluorous chromatography to give **25** (0.208 g, 0.245 mmol, 93%) as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59–7.65 (2H, m; 2×Ar*H*), 6.87 (1H, d, J = 9.0 Hz; Ar*H*), 4.08–3.95 (2H, m; CH_2), 3.87–3.76 (2H, m; 1H of SCH_2 and 1H of NCH_2), 3.74–3.67 (1H, m; 1H of NCH_2), 3.49 (1H, app. d, J = 15.0 Hz; 1H of CH_2CO$_2$Et), 3.56 (1H, app. d, J = 15.0 Hz; 1H of CH_2CO$_2$Et), 3.38–3.28 (1H, m; 1H of SCH_2), 2.75–2.60 (2H, m; CH_2), 1.84–1.75 (2H, m; CH_2), 1.13 (3H, t, J = 6.0 Hz; CH_3), 1.04 ppm (3H, t, J = 9.0 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.0 (*C*=O), 167.0 (*C*=O), 144.5 (Ar*C*), 134.4 (Ar*C*H), 129.0 (Ar*C*H), 122.5 (Ar*C*), 116.0 (Ar*C*), 110.8 (Ar*C*H), 71.1 (*C*SO$_2$), 61.9 (OCH$_2$), 42.9 (NCH$_2$), 40.5 (SCH$_2$), 36.0 (*C*H$_2$), 23.8 (t, J = 21.7 Hz; *C*H$_2$), 20.7 (CH$_2$), 14.0 (*C*H$_3$), 11.4 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 1719 (C=O), 1605 (C=O), 1474, 1334, 1197, 1126, 957 cm^{-1}; MS (ES$^+$ mode): *m*/*z* (%): 872 (100) [*M*+Na]$^+$, 794 (37), 278 (23), 110 (22), 105 (26); HRMS: *m*/*z*: calcd for $C_{25}H_{25}O_5N_2BrF_{17}S$: 867.0391; found: 867.0392 [*M*+NH$_4$]$^+$.

5-Bromo-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfonyl)-3-(3-methylbut-2-enyl)-1-propyl-1,3-dihydroindol-2-one (26): K_2CO_3 (0.292 g, 2.11 mmol, 5 equiv) and prenyl bromide (0.240 mL, 2.11 mmol, 5 equiv) were added to a solution of **7** (0.323 g, 0.422 mmol, 1 equiv) in DMF (9 mL) at room temperature. The reaction was then heated to 40°C and allowed to stir for 2 h. Ethyl acetate (12 mL) was added to the reaction mixture and the organic layer was separated, washed with water (3×10 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to give a crude orange solid. The crude product was purified by fluorous chromatography to give **26** (0.288 g, 0.346 mmol, 82%) as a light-brown solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.75 (3H, t, J = 7.4 Hz; CH_3), 1.35 (3H, s; CH_3), 1.43 (3H, s; CH_3), 1.48–1.53 (2H, m; CH_2), 2.49–2.52 (2H, m; CH_2), 2.89–2.90 (1H, m; 1H from CH_2), 2.97–3.00 (1H, m; 1H from CH_2), 3.22–3.30 (1H, m; 1H from CH_2), 3.44–3.46 (1H, m; 1H from CH_2), 3.56–3.60 (1H, m; 1H from CH_2), 3.67–3.75 (1H, m; 1H from CH_2), 4.41–4.44 (1H, m; C*H*=), 6.62–6.64 (1H, m; Ar*H*), 7.36–7.37 (1H, m; Ar*H*), 7.54 ppm (1H, s; Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.3 (*C*H$_3$), 18.5 (*C*H$_3$), 20.8 (*C*H$_2$), 24.1 (*C*H$_2$), 26.0 (*C*H$_3$), 30.8 (*C*H$_2$), 40.8 (*C*H$_2$), 42.6 (*C*H$_2$), 74.1 (*C*CH$_2$CH=), 110.7 (Ar*C*H), 113.7 (*C*H=), 116.2 (Ar*C*H), 123.1 (*C*(CH$_3$)$_2$), 129.8 (Ar*C*H), 134.0 (Ar*C*H), 139.1 (Ar*C*), 143.7 (Ar*C*), 170.2 ppm (*C*=O); IR (ATR): $\tilde{\nu}$ = 2938, 1714 (C=O), 1466, 1342, 1137, 519 cm^{-1}; MS (ES$^+$ mode): *m*/*z* (%): 854 (91) [*M*+Na]$^+$, 851 (23), 813(15), 776 (20); HRMS: *m*/*z*: calcd for $C_{26}H_{23}O_3NBrF_{17}NaS$: 854.0205; found: 854.0203 [*M*+Na]$^+$.

General Procedure B—Pd-catalysed Hartwig–Buchwald aminations

3-Benzyl-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfonyl)-5-morpholin-4-yl-1-propyl-1,3-dihydroindol-2-one (38): 3-Benzyl-5-bromo-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-sulfonyl)-1-propyl-1,3-dihydroindol-2-one (**32**) (0.043 g, 0.050 mmol, 1 equiv), Pd(OAc)$_2$ (0.0004 g, 0.0019 mmol, 0.04 equiv), X-Phos (0.0019 g, 0.0039 mmol, 0.08 equiv), Cs_2CO_3 (0.078 g, 0.240 mmol, 4.8 equiv) and morpholine (0.010 mL, 0.10 mmol, 2 equiv) were added to a microwave vial equipped with a magnetic stirrer and sealed. Toluene (0.8 mL) was injected into the vial and the reaction underwent microwave irradiation for 2 h at 120°C. The reaction vessel was then allowed to cool to room temperature before diluting with ethyl acetate (6 mL). The solution was filtered through a plug of Celite and concentrated in vacuo to give the crude product. Purification by flash chromatography using 40% ethyl acetate in petroleum ether gave **38** (0.031 g, 0.036 mmol, 73%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (1H, d, J = 2.0 Hz; Ar*H*), 7.02–6.94 (3H, m; 3×Ar*H*), 6.82 (2H, dd, J = 2.0, 7.6 Hz; 2×Ar*H*), 6.78 (1H, d, J = 7.6 Hz; Ar*H*), 6.50 (1H, d, J = 8.4 Hz; Ar*H*), 3.83–3.79 (4H, m; 2×CH_2), 3.79–3.74 (1H, m; 1H from CH_2), 3.65 (1H, d, J = 12.6 Hz; 1H from CH_2), 3.54 (1H, d, J = 12.6 Hz; 1H from CH_2), 3.43–3.50 (1H, m; 1H from CH_2), 3.24–3.38 (2H, m; 2×1H from CH_2S), 3.09–3.02 (4H, m; 2×CH_2), 2.51–2.64 (2H, m; CH_2), 1.22–1.31 (2H, m; CH_2), 0.59 ppm (3H, t, J = 7.6 Hz; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4 (*C*=O), 132.3 (Ar*C*), 130.3 (2×Ar*C*H), 128.3 (2×Ar*C*H), 127.7 (2×Ar*C*), 121.5 (Ar*C*), 118.6 (Ar*C*H), 116.4 (Ar*C*H), 109.6 (2×Ar*C*H), 75.4 (*C*CH$_2$Ph), 67.0 (2×*C*H$_2$O), 50.7 (2×*C*H$_2$N), 42.3 (*C*H$_2$), 40.9 (*C*H$_2$), 37.4 (*C*H$_2$), 23.9 (*C*H$_2$), 20.5 (*C*H$_2$), 11.3 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 2920, 2337, 1706 (C=O), 1598, 1501, 1448, 1196, 941 cm^{-1}; MS (ES$^+$ mode): *m*/*z* (%): 883 (100) [*M*+Na]$^+$, 798 (40), 622 (17), 515 (59), 492 (22), 290 (9), 105 (19); HRMS: *m*/*z*: calcd for $C_{32}H_{29}O_4N_2F_{17}NaS$: 883.1469; found: 883.1480 [*M*+Na]$^+$.

3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecane-1-sulfonyl)-3-(3-methylbut-2-enyl)-5-(4-methylpiperazin-1-yl)-1-propyl-1,3-dihydroindol-2-one (39): General procedure B was followed. Thus, treatment of **26** (0.047 g, 0.057 mmol, 1 equiv) with Pd(OAc)$_2$ (0.0005 g, 0.0023 mmol, 0.04 equiv), X-Phos (0.0022 g, 0.0045 mmol, 0.08 equiv), Cs_2CO_3 (0.089 g, 0.27 mmol, 4.8 equiv) and *N*-methylpiperazine (0.010 mL, 0.11 mmol, 2 equiv) and purification by fluorous chromatography gave **39** (0.033 g, 0.039 mmol, 69%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (1H, d, J = 2.4 Hz; ArC*H*), 6.96 (1H, dd, J = 2.4, 8.4 Hz; ArC*H*), 6.80 (1H, d, J = 8.4 Hz; ArC*H*), 4.61 (1H, t, J = 6.4 Hz; C*H*), 3.81–3.71 (2H, m; 2×1H from 2×CH_2), 3.64–3.57 (1H, m; 1H from CH_2), 3.34–3.41 (1H, m; 1H from CH_2), 3.19 (4H, app. t, J = 5.0 Hz; 2×CH_2), 3.16–3.14 (1H, m; 1H from CH_2), 3.06–3.01 (1H, m; 1H from CH_2), 2.64 (4H, app. t, J = 5.0 Hz; 2×CH_2), 2.40 (3H, s; CH_3), 1.86 (2H, m; CH_2), 1.67 (2H, app. q, J = 7.2 Hz; CH_2), 1.60 (3H, s; CH_3), 1.52 (3H, s; CH_3), 0.93 ppm (3H, t; J = 7.2 Hz; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8 (*C*=O), 148.0 (Ar*C*H), 138.1 (Ar*C*H), 137.2 (Ar*C*H), 121.8 (=*C*(CH$_3$)$_2$), 118.2 (Ar*C*H), 116.2 (Ar*C*H), 114.1 (*C*H=), 109.3 (Ar*C*H), 74.0 (*C*CH$_2$CH=), 55.0 (2×*C*H$_2$), 50.0 (2×*C*H$_2$), 46.0 (*C*H$_3$), 42.2 (*C*H$_2$), 40.6 (*C*H$_2$), 30.4 (*C*H$_2$), 25.7 (*C*H$_3$), 23.9 (*C*H$_2$), 20.6 (*C*H$_2$), 18.3 (*C*H$_3$), 11.1 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 2938, 1710 (C=O), 1456, 1352, 1185 cm^{-1}; MS (ES$^+$ mode): *m*/*z* (%): 874 (17) [*M*+Na]$^+$, 852 (100) [*M*]$^+$, 510 (4), 129 (7), 105 ppm (15); HRMS: *m*/*z*: calcd for $C_{31}H_{35}O_3N_3F_{17}S$: 852.2122; found: 852.2116 [*M*+H]$^+$.

3-Benzyl-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfonyl)-5-piperidin-1-yl-1-propyl-1,3-dihydroindol-2-one (40): General procedure B was followed. Thus, treatment of **32** (0.042 g, 0.050 mmol; 1 equiv) with $Pd(OAc)_2$ (0.0004 g, 0.0019 mmol, 0.04 equiv), X-Phos (0.0019 g, 0.0039 mmol, 0.08 equiv), Cs_2CO_3 (0.078 g, 0.24 mmol, 4.8 equiv) and piperidine (0.010 mL, 0.10 mmol, 2 equiv) and purification by fluorous chromatography gave **40** (0.029 g, 0.034 mmol, 68%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (1H, s; ArC*H*), 7.09–7.05 (3H, m; 3×ArC*H*), 6.94–6.89 (3H, m; 3×ArC*H*), 6.57 (1H, d, J = 8.2 Hz; ArC*H*), 3.85–3.79 (1H, m; 1H of CH_2), 3.74 (1H, d, J = 12.7 Hz; 1H of CH_2), 3.64 (1H, d, J = 12.7 Hz; 1H of CH_2), 3.58–3.52 (1H, m; 1H of CH_2), 3.45–3.38 (1H, m; 1H of CH_2), 3.39–3.32 (1H, m; 1H of CH_2), 3.16–3.08 (4H, m; 2×CH_2), 2.76–2.56 (2H, m; CH_2), 1.78–1.74 (4H, m; 2×CH_2), 1.62–1.57 (2H, m; CH_2), 1.39–1.31 (2H, m; CH_2), 0.68 ppm (3H, t, J = 7.4 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3 (*C*=O), 149.5 (Ar*C*), 137.0 (Ar*C*), 132.4 (Ar*C*), 130.3 (2×Ar*C*H), 128.4 (Ar*C*H), 128.3 (Ar*C*H), 127.6 (Ar*C*H), 121.2 (Ar*C*), 119.4 (Ar*C*H), 117.1 (Ar*C*H), 109.5 (Ar*C*H), 75.3 (*C*–C=O), 52.2 (*C*H_2), 52.1 (*C*H_2), 42.3 (*C*H_2), 40.9 (*C*H_2), 37.3 (*C*H_2), 26.0 (*C*H_2), 26.0 (*C*H_2), 24.3 (*C*H_2), 24.2 (t, J = 15.0 Hz; *C*H_2), 20.5 (*C*H_2), 11.2 ppm (*C*H_3); IR (ATR): $\tilde{\nu}$ = 2936, 1708 (C=O), 1498, 1332, 1210 cm^{-1}; MS (ES$^+$ mode): m/z (%): 881 (100) [M+Na]$^+$, 798 (8), 512 (3), 393 (4), 349 (13), 305 (21), 261 (12), 217 ppm (8); HRMS: m/z: calcd for $C_{33}H_{31}O_3N_2F_{17}NaS$: 881.1676; found: 881.1677 [M+Na]$^+$.

General Procedure C—the reductive cleavage of the fluorous tag

5,6-Dihydro-1*H*-pyrrolo[3,2,1-*ij*]quinolin-2(4*H*)one:[31] SmI_2 (4.5 mL of a 0.1 M solution in THF, 0.45 mmol, 2.5 equiv) was added to a solution of 1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-5,6-dihydro-1*H*-pyrrolo[3,2,1-ij]quinolin-2(4*H*)-one (**2**) (118 mg, 0.18 mmol, 1 equiv) in THF (5 mL) and the reaction was allowed to stir at room temperature for 24 h. $NaHCO_3$ (10 mL) was added to the reaction and the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product mixture was purified by fluorous chromatography to give the title compound (27 mg, 0.16 mmol, 87%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.00–2.06 (2H, app. pentet, J = 5.9 Hz; CH_2), 2.79 (2H, t, J = 6.1 Hz; ArCH_2), 3.52 (2H, s; CH_2CO), 3.74 (2H, t, J = 5.9 Hz; CH_2N), 6.95 (1H, t, J = 7.8 Hz; Ar*H*), 7.05 (1H, d, J = 7.7 Hz; Ar*H*), 7.09 ppm (1H, d, J = 7.3 Hz; Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6 (*C*H_2), 24.8 (*C*H_2), 36.9 (*C*H_2), 39.9 (*C*H_2), 120.5 (Ar*C*), 122.1 (Ar*C*H), 122.5 (Ar*C*H), 123.6 (Ar*C*), 126.9 (Ar*C*H), 141.5 (Ar*C*), 174.5 ppm (*C*=O); IR (ATR): $\tilde{\nu}$ = 3041, 2924, 1691 (C=O), 1600, 1479, 1345 cm^{-1}; MS (EI$^+$ mode): m/z (%): 173 (100) [M]$^+$, 144 (67), 117 (15), 83 (65), 47 (13); HRMS: m/z: calcd for $C_{11}H_{11}NO$: 173.0841; found: 173.0840 [M]$^+$.

5-Bromo-1-propyl-1,3-dihydroindol-2-one: General procedure C was followed. Thus, treatment of **7** (292 mg, 0.40 mmol, 1 equiv) in THF (10 mL) with SmI_2 (10 mL of a 0.1 M solution in THF, 1.0 mmol, 2.5 equiv) and purification by using fluorous silica gave 5-bromo-1-propyl-1,3-dihydro-indol-2-one (57 mg, 0.22 mmol, 57%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (3H, t, J = 7.4 Hz; CH_3), 1.57–1.66 (2H, m; CH_2), 3.45 (2H, s; CH_2CO), 3.58 (2H, t, J = 7.4 Hz; CH_2N), 6.63 (1H, d, J = 8.2 Hz; Ar*H*), 7.30–7.33 ppm (2H, overlapping doublet and singlet; 2×Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.8 (*C*H_3), 21.1 (*C*H_2), 36.0 (*C*H_2CO), 42.1 (*C*H_2N), 110.1 (Ar*C*H), 115.1 (Ar*C*), 127.0 (Ar*C*), 128.0 (Ar*C*H), 131.0 (Ar*C*H), 144.2 (Ar*C*), 174.7 ppm (*C*=O); IR (ATR): $\tilde{\nu}$ = 2965, 2935, 2877, 1695 (C=O), 1606, 1484, 1342, 1105 cm^{-1}; MS (EI$^+$ mode): m/z (%): 253 (56) [M]$^+$, 224 (25), 196 (25), 117 (100), 84 (56), 47 (12); HRMS: m/z: calcd for $C_{11}H_{12}ONBr$: 253.0102; found: 253.0101 [M]$^+$.

5-Fluoro-1-methyl-1,3-dihydroindol-2-one:[32] General procedure C was followed. Thus, treatment of 5-fluoro-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-1-methyl-1,3-dihydroindol-2-one (**8**) (170 mg, 0.26 mmol, 1 equiv) in THF (3 mL) with SmI_2 (6.5 mL of a 0.1 M solution in THF, 0.65 mmol, 2.5 equiv) and purification by fluorous chromatography gave the title compound (31 mg, 0.19 mmol, 71%) as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.13 (3H, s; CH_3N), 3.45 (2H, s; CH_2CO), 6.65 (1H, dd, J = 8.4, 4.4 Hz; Ar*H*), 6.89–6.94 ppm (2H, m; 2×Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.7 (*C*H_3N), 36.4 (*C*H_2CO), 108.7 (d, J = 7.9 Hz; Ar*C*H), 112.9 (d, J = 24.8 Hz; Ar*C*H), 114.4 (d, J = 23.1 Hz; Ar*C*H), 126.4 (d, J = 9.1 Hz; Ar*C*), 138.5 (Ar*C*N), 159.5 (d, J = 238.6 Hz; Ar*C*F), 175.0 (C=O); IR (ATR): $\tilde{\nu}$ = 1695 (C=O), 1621, 1494, 1348, 1222, 1133 cm^{-1}; MS (EI$^+$ mode): m/z (%): 165 (100) [M]$^+$, 150 (10), 136 (99), 109 (20), 96 (10); HRMS: m/z: calcd for C_9H_8NOF: 165.1670; found: 165.1676 [M]$^+$.

2-Methyl-1,4-dihydro-2*H*-isoquinolin-3-one:[33] General procedure C was followed. Thus, treatment of 4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-2-methyl-1,2-dihydroisoquinolin-3(4*H*)one (**9**) (153 mg, 0.24 mmol, 1 equiv) in THF (5 mL) with SmI_2 (6.0 mL of a 0.1 M solution in THF, 0.60 mmol, 2.5 equiv) and purification by using fluorous silica gel gave the title compound (39 mg, 0.18 mmol, 74%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.05 (3H, s; NCH_3), 3.55 (2H, s; CH_2N), 4.43 (2H, s; CH_2CO), 7.08–7.10 (2H, m; 2×Ar*H*), 7.14–7.24 ppm (2H, m; 2×Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.8 (*C*H_3), 37.9 (*C*H_2N), 53.3 (*C*H_2CO), 125.4 (Ar*C*H), 126.9 (Ar*C*H), 127.7 (Ar*C*H), 127.9 (Ar*C*H), 131.3 (Ar*C*), 132.6 (Ar*C*), 169.2 (C=O); IR (ATR): $\tilde{\nu}$ = 3033, 2922, 1632 (C=O), 1493, 1457, 1401, 1088 cm^{-1}; MS (EI$^+$ mode): m/z (%): 161 (14) [M]$^+$, 118 (10), 104 (22), 85 (100), 83 (100), 47 (46); HRMS: m/z: calcd for $C_{10}H_{11}NO$: 161.0841; found: 161.0841 [M]$^+$.

3,4-Methylenedioxy-3-(3-methyl-butyl)-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one: General procedure C was followed. Thus, treatment of 1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decylsulfanyl)-3,4-methylenedioxy-3-(3-methyl-butyl)-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (**18**) (0.10 g, 0.13 mmol, 1 equiv) with SmI_2 (2.93 mL, 0.1 M in THF, 0.29 mmol, 2.2 equiv) and concentration in vacuo gave the title compound (0.04 g, 0.14 mmol, 99%) as a dark-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.62 (1H, s; Ar*H*), 6.57 (1H, s; Ar*H*), 5.92 (2H, s; OCH_2O), 3.78 (2H, s; CH_2C(O)), 3.69–3.66 (2H, t, J = 6.1 Hz; ring CH_2N), 3.45–3.42 (2H, t; J = 7.8 Hz; NCH_2), 3.06–3.03 (2H, t, J = 6.0 Hz; ring CH_2CH$_2$N), 1.63–1.53 (1H, m; C*H*(CH$_3$)$_2$), 1.48–1.42 (2H, m; NCH$_2$CH_2), 0.94–0.93 ppm (6H, d, J = 6.6 Hz; CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7 (*C*=O), 147.1 (Ar*C*O), 146.4 (Ar*C*O), 129.3 (Ar*C*), 125.2 (Ar*C*), 111.2 (Ar*C*H), 110.1 (Ar*C*H), 101.4 (O*C*H$_2$O), 46.8 (ring *C*H$_2$N), 45.9 (N*C*H$_2$), 43.3 (*C*H$_2$C(O)), 37.4 (NCH$_2$*C*H$_2$), 33.3 (ring *C*H$_2$CH$_2$N), 26.4 (*C*H(CH$_3$)$_2$), 23.0 ppm (2×CH$_3$ of CH(*C*H$_3$)$_2$); IR (ATR): $\tilde{\nu}$ = 2952, 2251, 2063, 1651 (C=O), 1505, 1484, 1224, 1038, 909, 858 cm^{-1}; MS (EI mode): m/z (%): 275 (88) [M]$^+$, 42 (10), 77 (10), 84 (35), 86 (22), 89 (13), 91 (11), 103 (15), 131 (13), 147 (23), 148 (99), 149 (58), 161 (21), 162 (44), 176 (15), 190 (58), 204 (18), 205 (44), 219 (60), 260 (22), 176 (17); HRMS: m/z: calcd for $C_{16}H_{21}O_3N$: 275.1521; found: 275.1520 [M]$^+$.

7,8-Dimethoxy-3-pentyl-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one: General procedure C was followed. Thus, treatment of 1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-7,8-dimethoxy-3-pentyl-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (**13**) (0.20 g, 0.26 mmol, 1 equiv) in THF (4 mL) with SmI_2 (5.72 mL, 0.1 M in THF, 0.57 mmol, 2.2 equiv) and concentration in vacuo gave the title compound (0.06 g, 0.22 mmol, 84%) as a cream solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (1H, s; Ar*H*), 6.49 (1H, s; Ar*H*), 3.77 (3H, s; CH_3O), 3.76 (3H, s; CH_3O), 3.73 (2H, s; CH_2C(O)), 3.65–3.62 (2H, t, J = 6.0 Hz; ring CH_2N), 3.35–3.31 (2H, t, J = 7.6 Hz; NCH_2), 2.98–2.95 (2H, t, J = 5.9 Hz; ring CH_2CH$_2$N), 1.52–1.45 (2H, m; NCH$_2$CH_2), 1.31–1.15 (4H, m; CH_2CH$_2$CH$_3$, CH$_2$CH_2CH$_3$), 0.83–0.79 ppm (3H, t, J = 7.0 Hz; CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9 (*C*=O), 146.8 (Ar*C*OMe), 146.1 (Ar*C*OMe), 126.5 (Ar*C*), 122.6 (Ar*C*), 113.0 (Ar*C*H), 112.1 (Ar*C*H), 54.9 (*C*H$_3$O), 54.9 (*C*H$_3$O), 45.9 (N*C*H$_2$), 45.3 (ring *C*H$_2$N), 41.7 (*C*H$_2$C(O)), 31.4 (ring *C*H$_2$CH$_2$N), 28.7 (*C*H$_2$CH$_2$CH$_3$), 27.0 (NCH$_2$*C*H$_2$), 21.5 (CH$_2$*C*H$_2$CH$_3$), 13.0 ppm (CH$_2$*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 3001, 2954, 2927, 2858, 2359, 2025, 1959, 1643 (C=O), 1606, 1522, 1485, 1458, 1421 cm^{-1}; MS (EI mode): m/z (%): 291 (98) [M]$^+$, 83 (33), 85 (22), 121 (13), 163 (12), 164 (81), 165 (48), 178 (53), 206 (58), 221 (55), 235 (11), 291 (98), 292 (18); HRMS: m/z: calcd for $C_{17}H_{25}O_3N$: 291.1834; found: 291.1837 [M]$^+$.

3-Benzyl-7,8-dimethoxy-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one:[34] General procedure C was followed. Thus, treatment of **14** (0.12 g, 0.14 mmol, 1 equiv) with SmI_2 (6.34 mL, 0.1 M solution in THF, 0.63 mmol, 4.4 equiv) and purification by using fluorous silica (eluting with 80% MeCN/H_2O

then MeCN) gave 3-benzyl-7,8-dimethoxy-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (41 mg, 0.13 mmol, 92%) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.18 (5H, m; Ar*H*), 6.58 (1H, s; Ar*H*), 6.44 (1H, s; Ar*H*), 4.58 (2H, s; NCH_2), 3.84 (2H, s; CH_2C(O)), 3.79 (3H, s; CH_3O), 3.75 (3H, s; CH_3O), 3.59 (2H, t, J = 6.0 Hz; ring CH_2N), 2.83 ppm (2H, t, J = 6.0 Hz; CH_2CH$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (*C*=O), 147.9 (Ar*C*OMe), 147.2 (Ar*C*OMe), 137.6 (Ar*C*), 128.7 (2×Ar*C*H), 128.2 (2×Ar*C*H), 127.6 (Ar*C*), 127.5 (Ar*C*H), 123.4 (Ar*C*), 113.9 (Ar*C*H), 113.0 (Ar*C*H), 55.9 (2×*C*H$_3$O), 49.7 (N*C*H$_2$), 45.7 (ring *C*H$_2$N), 42.6 (*C*H$_2$C(O)), 31.9 ppm (ring *C*H$_2$CH$_2$N); IR (neat): $\tilde{\nu}$ = 2935 (C–H), 1640 (C=O), 1517, 1486, 1448, 1420, 1355, 1257, 1243, 1218 cm^{-1}; MS (EI mode): *m*/*z* (%): 311 (99) $[M]^+$, 91 (38), 121 (13), 164 (57), 220 (50), 312 (22); HRMS: *m*/*z*: calcd for $C_{19}H_{21}O_3N$: 311.1521; found: 311.1523 $[M]^+$.

5,6,7-Trimethoxy-2-pentyl-1,4-dihydro-2*H*-isoquinolin-3-one: General procedure C was followed. Thus, treatment of 4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-5,6,7-trimethoxy-2-pentyl-1,4-dihydro-2*H*-isoquinolin-3-one (**11**) (0.10 g, 0.13 mmol, 1 equiv) with SmI_2 (8.37 mL, 0.1 M in THF, 0.84 mmol, 6.6 equiv) and purification by using flash chromatography on silica (eluting with CH_2Cl_2 then 50% EtOAc/petroleum ether (40–60 °C)) gave the title compound (0.03 g, 0.09 mmol, 73%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.40 (1H, s; Ar*H*), 4.36 (2H, s; ring CH_2N), 3.81 (3H, s; CH_3O), 3.79 (3H, s; CH_3O), 3.78 (3H, s; CH_3O), 3.46 (4H, br s; CH_2C(O), NCH_2), 1.54 (2H, br s; NCH$_2$CH_2), 1.26 (4H, br s; CH_2CH$_2$CH$_3$, CH$_2$CH_2CH$_3$), 0.85–0.82 ppm (3H, t, J = 6.6 Hz; CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8 (*C*=O), 152.8 (Ar*C*OMe), 150.7 (Ar*C*OMe), 141.6 (Ar*C*OMe), 126.9 (Ar*C*), 118.7 (Ar*C*), 104.5 (Ar*C*H), 61.3 (*C*H$_3$O), 61.2 (*C*H$_3$O), 56.6 (*C*H$_3$O), 51.4 (ring *C*H$_2$N), 47.4 (*C*H$_2$C(O)), 31.7 (N*C*H$_2$), 29.5 (*C*H$_2$CH$_2$CH$_3$), 27.4 (NCH$_2$*C*H$_2$), 22.9 (*C*H$_2$CH$_3$), 14.4 ppm (CH$_2$*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 2932, 2859, 2235, 2035, 1647 (C=O), 1491, 1465, 1415, 1353, 1311, 1270 cm^{-1}; MS (EI mode): *m*/*z* (%): 307 (99) $[M]^+$, 84 (55), 86 (35), 179 (25), 181 (12), 194 (42), 195 (17), 206 (14), 221 (14), 222 (31), 236 (14), 237 (25), 251 (13), 276 (13), 292 (13), 306 (37), 308 (20); HRMS: *m*/*z*: calcd for $C_{17}H_{25}O_4N$: 307.1784; found: 307.1781 $[M]^+$.

3-[2-(2-Methoxyethanesulfonyl)ethyl]-1-methyl-1,3-dihydroindol-2-one (43): General procedure C was followed. Thus, treatment of **24** (0.115 g, 0.148 mmol, 1 equiv) in THF (4.5 mL) with SmI_2 (3.7 mL, 0.1 M solution in THF, 0.371 mmol, 3.7 mL) and purification by fluorous chromatography gave **43** (0.044 g, 0.148 mmol, 100%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.31 (2H, m; 2×Ar*H*), 7.19–7.10 (1H, m; Ar*H*), 6.90 (1H, t, J = 6.0 Hz; Ar*H*), 3.83 (2H, t, J = 6.0 Hz; CH_2), 3.65–3.57 (1H, m; C*H*), 3.38 (3H, s; CH_3), 3.22–2.32 (7H, m; CH_3, 2×CH_2), 2.62–2.52 (1H, m; 1H of CH_2), 2.43–2.28 ppm (1H, m; 1H of CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 176.6 (*C*=O), 144.4 (Ar*C*), 128.7 (Ar*C*H), 127.4 (Ar*C*), 124.1 (Ar*C*H), 122.9 (Ar*C*H), 108.4 (Ar*C*H), 66.1 (*C*H$_2$), 59.1 (*C*H$_3$), 53.5 (*C*H$_2$), 51.3 (*C*H$_2$), 43.7 (*C*H), 26.4 (*C*H$_3$), 23.3 ppm (*C*H$_2$). IR (ATR): $\tilde{\nu}$ = 1707 (C=O), 1613, 1470, 1296, 1111 cm^{-1}; MS (CI$^+$ mode): *m*/*z* (%): 298 (100) $[M]^+$, 173 (26), 160 (8); HRMS: *m*/*z*: calcd for $C_{14}H_{20}O_4NS$: 298.1108; found: 298.1108 $[M+H]^+$.

(5-Bromo-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-3-yl)acetic acid ethyl ester (44): General procedure C was followed. Thus, treatment of **25** (0.23 g, 0.28 mmol, 1 equiv) in THF (7 mL) with SmI_2 (6.1 mL, 0.1 M solution in THF, 0.61 mmol, 2.2 equiv) and purification by flash chromatography using 30% ethyl acetate in petroleum ether gave **44** (0.058 g, 0.17 mmol, 73% (based on recovered starting material)) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (3H, t, J = 9.0 Hz; CH_3), 1.22 (3H, t, J = 6.0 Hz; CH_3), 1.64–1.76 (2H, m; CH_2), 2.80 (1H, dd, J = 9.0, 18.0 Hz; 1H of CH_2), 3.07 (1H, dd, J = 6.0, 18.0 Hz; 1H of CH_2), 3.66 (2H, t, J = 9.0 Hz; CH_2), 3.75 (1H, dd, J = 6.0, 18.0 Hz; C*H*), 4.09–4.20 (2H, m; CH_2), 6.73 (1H, d, J = 9.0 Hz; Ar*H*), 7.38–7.41 ppm (2H, m; 2×Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.5 (*C*H$_3$), 14.2 (*C*H$_3$), 20.7 (*C*H$_2$), 34.9 (*C*H$_2$), 41.9 (*C*H), 41.9 (*C*H$_2$), 61.2 (*C*H$_2$), 109.8 (Ar*C*H), 115.0 (Ar*C*), 127.4 (Ar*C*H), 130.5 (Ar*C*), 131.1 (Ar*C*H), 143.1 (Ar*C*H), 170.9 (*C*=O), 176.2 ppm (*C*=O); IR (ATR): $\tilde{\nu}$ = 2972, 1720 (C=O), 1605, 1474, 1348, 1199 cm^{-1}; MS (CI$^+$ mode): *m*/*z* (%): 340 (100) $[M]^+$, 262 (33), 207 (10), 88 (15), 74 (38); HRMS: *m*/*z*: calcd for $C_{15}H_{19}O_3NBr$: 340.0543; found: 340.0545 $[M]^+$.

3-Benzyl-5-morpholin-4-yl-1-propyl-1,3-dihydroindol-2-one (52): General procedure C was followed. Thus, treatment of **38** (0.072 g, 0.084 mmol, 1 equiv) in THF (2.5 mL) with SmI_2 (2.1 mL, 0.1 M solution in THF, 0.21 mmol, 2.5 equiv) and purification by flash chromatography (50% ethyl acetate in petroleum ether) gave **52** (0.024 g, 0.069 mmol, 82%) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23–7.16 (3H, m; 3×Ar*H*), 7.13–7.10 (2H, m; 2×Ar*H*), 6.72 (1H, dd, J = 3.0, 9.0 Hz; Ar*H*), 6.62 (1H, d, J = 9.0 Hz; Ar*H*), 6.31 (1H, d, J = 3.0 Hz; Ar*H*), 3.77 (4H, t, J = 6.0 Hz; 2×CH_2), 3.67–3.57 (2H, m; 2×1H of CH_2), 3.51–3.42 (2H, m; 1H of CH_2 + C*H*), 2.90–2.87 (4H, m; 2×CH_2), 2.85–2.78 (1H, m; 1H of CH_2), 1.54 (2H, app. q, J = 6.0 Hz; CH_2), 0.82 (3H, t, J = 6.0 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.8 (*C*=O), 147.2 (Ar*C*), 138.2 (Ar*C*), 137.6 (Ar*C*), 129.9 (Ar*C*H), 129.8 (Ar*C*H), 129.7 (Ar*C*), 128.5 (Ar*C*H), 128.4 (Ar*C*H), 126.8 (Ar*C*H), 115.7 (Ar*C*H), 114.9 (Ar*C*H), 108.6 (Ar*C*H), 67.2 (*C*H$_2$), 67.1 (*C*H$_2$), 50.9 (*C*H$_2$), 50.8 (*C*H$_2$), 47.5 (*C*H), 41.7 (*C*H$_2$), 37.1 (*C*H$_2$), 20.9 (*C*H$_2$), 11.5 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 1694 (C=O), 1596, 1481, 1359, 1211, 1111, 934 cm^{-1}; MS (CI$^+$ mode): *m*/*z* (%): 351 (100) $[M]^+$, 166 (23), 108 (17), 91 (27), 79 (12), 69 (9), 58 (16); HRMS: *m*/*z*: calcd for $C_{22}H_{26}O_2N_2$: 350.1989; found: 350.1992 $[M]^+$.

3-(3-Methylbut-2-enyl)-5-(4-methylpiperazin-1-yl)-1-propyl-1,3-dihydroindol-2-one (53): General procedure C was followed. Thus, treatment of **39** (0.068 g, 0.079 mmol, 1 equiv) in THF (3 mL) with SmI_2 (1.7 mL, 0.1 M solution in THF, 0.17 mmol, 2.2 equiv) and purification by column chromatography using (20% ethyl acetate in petroleum ether) gave **53** (0.022 g, 0.064 mmol, 80%) as a light-brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.82 (1H, d, J = 2.0 Hz; Ar*H*), 6.69 (1H, dd, J = 2.0, 8.4 Hz; Ar*H*), 6.58 (1H, d, J = 8.4 Hz; Ar*H*), 4.92 (1H, t, J = 7.3 Hz; C*H*), 3.58–3.54 (1H, m; 1H of CH_2), 3.44–3.40 (1H, m; 1H of CH_2), 3.27–3.25 (1H, m; 1H of C*H*), 3.00 (4H, app. t, J = 4.8 Hz; 2×CH_2), 2.51 (4H, app. t, J = 4.8 Hz; 2×CH_2), 2.47–2.43 (2H, m; 1H of CH_2CH=), 2.26 (3H, s; CH_3N), 1.53 (2H, app. q, J = 7.4 Hz; CH_2), 1.50 (3H, s; CH_3), 1.43 (3H, s; CH_3), 0.78 ppm (3H, t, J = 7.4 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.4 (*C*=O), 147.4 (Ar*C*), 137.8 (Ar*C*), 134.7 (Ar*C*), 130.4 (=*C*), 119.9 (CH=), 116.1 (Ar*C*H), 114.8 (Ar*C*H), 108.4 (Ar*C*H), 55.4 (*C*H$_2$), 55.3 (*C*H$_2$), 50.8 (*C*H$_2$), 50.7 (*C*H$_2$), 46.2 (*C*H$_3$), 46.1 (*C*H$_2$), 41.6 (*C*H$_2$), 29.6 (*C*H), 26.0 (*C*H$_3$), 21.0 (*C*H$_2$), 18.3 (*C*H$_3$), 11.4 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 2931, 2798, 1697 (C=O), 1449, 1359, 1212 cm^{-1}; MS (CI$^+$ mode): *m*/*z* (%): 342 (100) $[M]^+$, 274 (22), 152 (8), 101 (37), 97 (17), 74 (15), 70 (26), 58 (43); HRMS: *m*/*z*: calcd for $C_{21}H_{32}ON_3$: 342.2545; found 342.2540.

5-Bromo-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfinyl)-1-propyl-1,3-dihydroindol-2-one (19): H_2O_2 (0.050 mL, 0.435 mmol, 4 equiv) was added to a solution of **7** (0.080 g, 0.109 mmol, 1 equiv) in HFIP (1 mL) and CH_2Cl_2 (0.5 mL) was added at room temperature. The reaction was allowed to stir at room temperature for 2 h before quenching with aqueous saturated Na_2SO_3 (1 mL) and the aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The organic layer was then dried ($MgSO_4$), filtered and concentrated in vacuo to give **19** (0.081 g, 0.108 mmol, 99%) as an orange solid which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66–7.63 (1H, m; Ar*H*), 7.49 (1H, s; Ar*H*), 6.66 (1H, d, J = 8.4 Hz; Ar*H*), 4.69 (1H, s; C*H*), 3.67–3.57 (2H, m; CH_2), 2.95–2.66 (2H, m; CH_2), 2.49–2.28 (2H, m; CH_2), 1.66–1.60 (2H, m; CH_2), 0.93–0.86 ppm (3H, m; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.3 (*C*=O), 142.5 (Ar*C*), 132.3 (Ar*C*H), 128.5 (Ar*C*H), 127.3 (Ar*C*), 115.4 (Ar*C*), 110.1 (Ar*C*H), 44.6 (*C*H), 42.0 (*C*H$_2$), 31.0 (*C*H$_2$), 29.7 (*C*H$_2$), 20.6 (*C*H$_2$), 11.3 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$ = 3071, 2955, 1721 (C=O), 1589, 1430, 1329, 1177, 1103 cm^{-1}; MS (ES$^-$ mode) *m*/*z* (%): 748 (100) $[M]^+$, 746 (85), 559 (50), 527 (53), 479 (30), 304 (29), 269 (37), 248 (49), 212 (41), 203 (28), 127 (37); HRMS: *m*/*z*: calcd for $C_{21}H_{16}O_2NBrF_{17}S$: 747.9808; found: 747.9813 $[M+H]^+$.

5-Bromo-1-propyl-1*H*-indol-2,3-dione (20)[35] from 19: TFAA (0.030 mL, 0.216 mmol, 2 equiv) was added to a solution of **19** (0.081 g, 0.108 mmol, 1 equiv) in THF (2 mL) at 0 °C and the reaction was stirred at 0 °C for 2.5 h. NEt_3 (1.5 μL, 0.011 mmol, 0.1 equiv) and ethanol (0.010 mL, 0.238 mmol, 2.2 equiv) were then added to the reaction at 0 °C and the reaction was stirred at room temperature for 4.5 h. After this time, the

reaction mixture was quenched with aqueous saturated $NaHCO_3$ (10 mL) and the aqueous layer extracted with CH_2Cl_2 (3×15 mL). The organic layer was then washed with aqueous saturated $NaHCO_3$ (2×10 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to give the crude product. Purification by fluorous chromatography gave **20** (0.016 g, 0.060 mmol, 55%) as a dark-orange solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.87 (3H, t, J=7.4 Hz; CH_3), 1.57–1.65 (2H, m; CH_2), 3.58 (2H, t, J=7.3 Hz; CH_2N), 6.75 (1H, d, J=8.4 Hz; ArH), 7.52 (1H, d, J=2.0 Hz; ArH), 7.58 ppm (1H, dd, J=2.0, 8.4 Hz; ArH); ^{13}C NMR (300 MHz, $CDCl_3$): δ=11.6 (*C*H$_3$), 20.8 (*C*H$_2$), 42.2 (*C*H$_2$N), 112.3 (Ar*C*H), 116.6 (Ar*C*), 118.9 (Ar*C*), 128.3 (Ar*C*H), 140.8 (Ar*C*H), 150.1 (Ar*C*), 157.7 (*C*=O), 182.8 ppm (*C*=O); IR (ATR): $\tilde{\nu}$=3456, 2966, 2931, 1733, 1601, 1462, 1432, 1329, 1179, 698, 581 cm^{-1}; MS (EI$^+$ mode): m/z (%): 267 (48) [M]$^+$, 209 (28), 102 (21), 74 (100), 69 (20), 62 (86), 56 (72), 49 (62), 41 (92); HRMS: m/z: calcd for $C_{11}H_{14}O_2N_2Br$: 285.0238; found: 285.1233 [M]$^+$.

General Procedure D—CAN oxidative cleavage of the fluorous tag

1-Methyl-1*H*-indole-2,3-dione:[36] CAN (0.377 g, 0.666 mmol, 3 eq) was added to a solution of **3** (0.139 g, 0.222 mmol, 1 equiv) in MeCN (5 mL) and water (0.6 mL) at room temperature. The reaction was allowed to stir at room temperature for 15 h. The reaction mixture was then washed with H_2O (10 mL) and brine (10 mL) and the aqueous layer was extracted with ethyl acetate (3×10 mL). The organic layer was then dried ($MgSO_4$), filtered and concentrated in vacuo to give the crude product as an orange solid which was purified by fluorous chromatography to give the title compound (0.036 g, 0.223 mmol, 100%) as an orange solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.56–7.52 (2H, m; 2×ArH), 7.06 (1H, t, J=6.9 Hz; ArH), 6.83 (1H, d, J=7.9 Hz; ArH), 3.19 ppm (3H, s; NCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=183.5 (*C*=O), 158.4 (*C*=O), 151.6 (Ar*C*), 138.6 (Ar*C*H), 125.5 (Ar*C*H), 124.0 (Ar*C*H), 117.6 (Ar*C*), 110.1 (Ar*C*H), 26.4 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$=1713 (C=O), 1589 (C=O), 1450, 1324, 1087, 847, 754 cm^{-1}; MS (EI$^+$ mode): m/z (%): 179 (49) [M+NH$_4$]$^+$, 164 (70), 162 (40), 148 (69), 136 (30), 121 (30), 108 (35), 94 (72), 78 (51), 69 (30), 60 (100), 58 (51), 44 (50); HRMS: m/z: calcd for $C_{33}H_{11}O_2N_2$: 179.0815; found: 179.0811 [M+NH$_4$]$^+$.

5-Chloro-1-methyl-1*H*-indole-2,3-dione:[37] General procedure D was followed. Thus, treatment of 5-chloro-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-1-methyl-1,3-dihydro-indol-2-one (**6**) (0.15 g, 0.24 mmol, 1 equiv) with CAN (0.40 g, 0.72 mmol, 3 equiv) and purification by using fluorous silica (eluting with 80% MeCN/H_2O then MeCN) gave the title compound (33 mg, 0.17 mmol, 70%) as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.52–7.48 (2H, m; ArH), 6.81 (1H, d, J=8.4 Hz; ArH), 3.19 ppm (3H, s; NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=182.4 (*C*=O), 157.7 (*C*=O), 149.7 (Ar*C*), 137.8 (Ar*C*H), 129.7 (Ar*C*), 125.2 (Ar*C*H), 118.2 (Ar*C*), 111.3 (Ar*C*H), 26.4 ppm (N*C*H$_3$); IR (KBr): $\tilde{\nu}$=2359, 1749 (C=O), 1734 (C=O), 1608, 1456, 1354, 1327, 1263, 1175, 1109 cm^{-1}; MS (CI mode, isobutane): m/z (%): 196 (99) [M+H]$^+$, 71 (18), 79 (10), 81 (17), 83 (11), 85 (11), 197 (14), 198 (64); HRMS: m/z: calcd for $C_9H_7O_2NCl$: 196.0165; found: 196.0164 [M+H]$^+$.

5-Bromo-1-propyl-1*H*-indole-2,3-dione (20): General procedure D was followed. Thus, treatment of **7** (0.123 g, 0.168 mmol, 1 equiv) in MeCN (9 mL) and water (1 mL) with CAN (0.276 g, 0.504 mmol, 3 equiv) and purification by fluorous chromatography gave **20** (0.045 g, 0.168 mmol, 100%) as a red solid. Data given earlier.

5-Fluoro-1-methyl-1*H*-indole-2,3-dione:[38] General procedure D was followed. Thus, treatment of **8** (0.15 g, 0.23 mmol, 1 equiv) with CAN (0.38 g, 0.70 mmol, 3 equiv) and purification by using fluorous silica (eluting with 80% MeCN/H_2O then MeCN) gave the title compound (42 mg, 0.23 mmol, 100%) as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.29–7.20 (2H, m; ArH), 6.82–6.79 (1H, m; ArH), 3.19 ppm (3H, s; NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=182.8 (*C*=O), 159.4 (d, J=244.3 Hz; ArCF), 158.0 (*C*=O), 147.5 (Ar*C*), 124.7 (d, J=24.2 Hz; Ar*C*H), 118.0 (d, J=6.7; Ar*C*), 112.5 (d, J=24.1 Hz; Ar*C*H), 111.1 (d, J=7.4 Hz; Ar*C*H), 26.4 (N*C*H$_3$); IR (KBr): $\tilde{\nu}$=2359, 1748 (C=O), 1731 (C=O), 1683, 1652, 1622, 1557, 1540, 1488, 1359 cm^{-1}; MS (EI mode): m/z (%): 179 (20) [M]$^+$, 47 (23), 48 (11), 83 (100), 85 (65), 87 (11), 96 (12), 122 (26), 123 (16), 151 (10); HRMS: m/z: calcd for $C_9H_6O_2NF$: 179.0383; found: 179.0384 [M]$^+$.

6-Methoxy-1-propyl-1*H*-indole-2,3-dione: General procedure D was followed. Thus, treatment of 3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-6-methoxy-1-propyl-1,3-dihydroindole-2-one (**4**) (0.281 g, 0.411 mmol, 1 equiv) in MeCN (10 mL) and water (1.2 mL) with CAN (0.686 g, 1.232 mmol, 3 equiv) and purification by fluorous chromatography gave the title compound (0.062 g, 0.283 mmol, 70%) as an orange solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.46 (1H, d, J=8.4 Hz; ArH), 6.41 (1H, dd, J=2.1, 8.4 Hz; ArH), 6.24 (1H, d, J=2.1 Hz; ArH), 3.80 (3H, s; OCH_3), 3.52 (2H, t, J=7.4 Hz; CH_2), 1.62–1.56 (2H, m; CH_2), 0.86 ppm (3H, t, J=7.4 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=181.2 (*C*=O), 168.4 (*C*=O), 159.8 (Ar*C*), 153.7 (Ar*C*), 128.2 (Ar*C*H), 111.5 (Ar*C*H), 107.6 (Ar*C*H), 97.7 (Ar*C*H), 56.3 (O*C*H$_3$), 41.9 (*C*H$_2$), 20.9 (*C*H$_2$), 11.5 ppm (*C*H$_3$); IR (ATR): $\tilde{\nu}$=2940, 1721 (C=O), 1597 (C=O), 1358, 1211, 1096 cm^{-1}; MS (CI$^+$ mode): m/z (%): 237 (50) [M+NH$_4$]$^+$, 220 (42), 206 (100), 190 (17), 176 (5), 96 (13), 58 (12); HRMS: m/z: calcd for $C_{12}H_{17}O_3N_2$: 237.1234; found: 237.1238 [M+NH$_4$]$^+$.

7,8-Dimethoxy-3-(4-methoxybenzyl)-4,5-dihydro-3*H*-benzo[*d*]azepine-1,2-dione (21) and 1-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-5-hydroxy-7,8-dimethoxy-3-(4-methoxy-benzyl)-1,3,4,5-tetrahydrobenzo[*d*]azepin-2-one (22): General procedure D was followed. Thus, treatment of **15** (0.15 g, 0.18 mmol, 1 equiv) in MeCN (9 mL) and H_2O (1 mL) with CAN (0.30 g, 0.55 mmol, 3 equiv) and purification by using fluorous silica (eluting with 80% MeCN/H_2O then MeCN) gave **21** (42 mg, 0.12 mmol, 65%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23–7.19 (3H, m; ArH), 6.82 (2H, d, J=8.8 Hz; ArH), 6.51 (1H, s; ArH), 4.59 (2H, s; NCH_2), 3.84 (3H, s; CH_3O), 3.83 (3H, s; CH_3O), 3.75 (3H, s; CH_3O), 3.56–3.54 (2H, m; ring CH_2N), 2.88–2.86 ppm (2H, m; CH_2CH$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.2 (*C*=O), 167.1 (*C*=O), 159.4 (Ar*C*OMe), 153.3 (Ar*C*OMe), 148.0 (Ar*C*OMe), 135.6 (Ar*C*), 130.0 (2×Ar*C*H), 128.3 (Ar*C*), 126.7 (Ar*C*), 114.3 (2×Ar*C*H), 111.9 (Ar*C*H), 111.9 (Ar*C*H), 56.1 (*C*H$_3$O), 56.1 (*C*H$_3$O), 55.3 (*C*H$_3$O), 48.7 (N*C*H$_2$), 45.2 (ring *C*H$_2$N), 33.8 ppm (ring *C*H$_2$CH$_2$N); IR (neat): $\tilde{\nu}$=2935 (C–H), 2837, 1657 (C=O), 1599, 1514, 1463, 1442, 1418, 1402 cm^{-1}; MS (EI mode): m/z (%): 355 (55) [M]$^+$, 121 (100), 122 (10), 190 (18), 191 (10), 234 (25), 356 (12); HRMS: m/z: calcd for $C_{20}H_{21}O_5N$: 355.1420; found: 355.1419 [M]$^+$. Byproduct **22** (32.4 mg, 0. 038 mmol, 21%) was isolated from the fluorous wash. ^{1}H NMR (400 MHz, CDCl3): δ=7.19 (2H, d, J=8.8 Hz; ArH), 6.80 (2H, d, J=8.4 Hz; ArH), 6.78 (1H, s; ArH), 6.56 (1H, s; ArH), 5.11 (1H, d, J=14.4 Hz; 1H of NCH_2), 4.79 (1H, s; C*H*S), 4.75 (1H, d, J=15.6 Hz; 1H of ring CH_2N), 4.65 (1H, m; ring C*H*CH$_2$N), 4.12 (1H, d, J=14.4; 1H of NCH_2), 3.81 (3H, s; CH_3O), 3.81 (3H, s; CH_3O), 3.72 (3H, s; CH_3O), 3.52 (1H, dd, J=15.6, 4.8 Hz; 1H of ring CH_2N), 2.97–2.78 (2H, m; CH_2CH$_2$R^F), 2.51–2.33 (2H, m; CH_2R^F), 2.00 ppm (1H, br d, J=8.8 Hz; OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=169.6 (*C*=O), 159.3 (Ar*C*OMe), 149.5 (Ar*C*OMe), 149.2 (Ar*C*OMe), 131.4 (Ar*C*), 129.6 (2×Ar*C*H), 129.2 (Ar*C*), 123.1 (Ar*C*), 114.2 (2×Ar*C*H), 114.1 (Ar*C*H), 113.9 (Ar*C*H), 70.0 (ring *C*HCH$_2$N), 56.0 (*C*H$_3$O), 56.0 (*C*H$_3$O), 55.5 (*C*HS), 55.2 (*C*H$_3$O), 52.8 (N*C*H$_2$), 49.7 (ring *C*H$_2$N), 31.2 (t, J=21.9 Hz; *C*H$_2$R^F), 24.1 ppm (*C*H$_2$CH$_2$R^F); IR (thin film): $\tilde{\nu}$=3384 (OH), 3004, 2934 (C–H), 2842, 1643 (C=O), 1516, 1467, 1442 cm^{-1}; MS (FAB mode, NOBA, NaI): m/z (%): 858 (57) [M+Na]$^+$, 122 (100), 218 (16), 328 (32); HRMS: m/z: calcd for $C_{30}H_{26}O_5NF_{17}SNa$: 858.1158; found: 858.1161 [M+Na]$^+$.

9-Bromo-6-propyl-6*H*-indolo[2,3-*b*]quinoxaline (54): 1,2-Phenylenediamine (0.029 g, 0.269 mmol, 1.4 equiv) was added to a solution of **20** (0.052 g, 0.192 mmol, 1 equiv) in acetic acid (2 mL) and the mixture was heated under reflux for 1 h. The reaction mixture was then allowed to cool to room temperature before being placed in an ice bath. The resulting solid was concentrated in vacuo to give the crude product as a brown solid which was purified by flash chromatography using 60% ethyl acetate in petroleum ether to give **54** (0.058 g, 0.17 mmol, 89%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.55 (1H, s; ArH), 8.23 (1H, d, J=8.6 Hz; ArH), 8.07 (1H, d, J=8.6 Hz; ArH), 7.73–7.63 (3H, m; 3×ArH), 7.32 (1H, d, J=8.6 Hz; ArH), 4.39 (2H, t, J=7.4 Hz; CH_2), 1.92 (2H, app. q, J=7.4 Hz; CH_2), 0.95 ppm (3H, t, J=7.4 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=139.7 (Ar*C*), 133.6 (2×Ar*C*H), 129.7 (2×Ar*C*), 129.4 (Ar*C*H), 128.2 (2×Ar*C*), 126.5 (2×Ar*C*), 125.7 (2×Ar*C*H), 111.3 (2×Ar*C*H), 43.4 (*C*H$_2$), 22.1 (*C*H$_2$), 11.8 ppm (*C*H$_3$); MS (EI$^+$

mode): *m/z* (%): 341 (5) $[M]^+$, 310 (9), 297 (20), 231 (41), 218 (25), 204 (11), 177 (13), 164 (12), 129 (24), 102 (35), 90 (67), 75 (27), 63 (32), 50 (15); HRMS: *m/z*: calcd for $C_{17}H_{15}N_3Br$: 340.0442; found: 340.0444 $[M]^+$.

9-Fluoro-6-methyl-6,11-dihydro-5*H*-indolo[2,3-*b*]quinoxaline (55): A solution of 5-fluoro-1-methyl-1*H*-indole-2,3-dione (50 mg, 0.28 mmol, 1 equiv) and 1,2-phenylenediamine (42 mg, 0.39 mmol, 1.4 equiv) in AcOH (2 mL) was heated under reflux. After 18 h, the reaction mixture was cooled to room temperature then placed in an ice bath. The resulting solid was then concentrated in vacuo. The crude product was purified by flash chromatography on silica (eluting with 30% EtOAc/petroleum ether (40–60°C)) to give **55** (63 mg, 0.25 mmol, 90%) as a bright-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33–8.31 (1H, m; Ar*H*), 8.19–8.15 (2H, m; Ar*H*), 7.83–7.79 (1H, m; Ar*H*), 7.74–7.70 (1H, m; Ar*H*), 7.50–7.40 (2H, m; Ar*H*), 4.00 ppm (3H, s; NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1 (d, *J* = 237.7 Hz, ArCF), 146.3 (Ar*C*), 141.2 (Ar*C*), 140.8 (Ar*C*), 139.5 (d, *J* = 3.8 Hz, Ar*C*), 139.2 (Ar*C*H), 129.5 (Ar*C*H), 129.3 (Ar*C*H), 127.7 (Ar*C*H), 126.2 (Ar*C*H), 120.0 (d, *J* = 8.8 Hz; Ar*C*), 118.5 (d, *J* = 25.1 Hz; Ar*C*H), 110.0 (d, *J* = 8.0 Hz; Ar*C*H), 108.8 (d, *J* = 24.3 Hz; Ar*C*H), 27.7 ppm (NCH_3); IR (KBr): $\tilde{\nu}$ = 2926, 1615, 1585, 1482, 1482, 1391, 1350 cm^{-1}; MS (EI mode): *m/z* (%): 250 (35) $[M]^+$, 47 (20), 83 (100), 85 (65), 251 (53), 252 (10); HRMS: *m/z*: calcd for $C_{15}H_{10}N_3F$: 251.0859; found: 251.0860 $[M]^+$.

5-Bromo-3,3-difluoro-1-propyl-1,3-dihydroindol-2-one (56): DAST (0.07 mL) was added to a solution of 5-bromo-1-propyl-1*H*-indol-2,3-dione (0.055 g, 0.204 mmol, 1 equiv) in CH_2Cl_2 (1.8 mL) at room temperature and the reaction was stirred for 4 d. The reaction mixture was then quenched with MeOH (3 mL) and washed with water (2×5 mL). The aqueous layer was extracted with CH_2Cl_2 (2×5 mL) and the organic layer dried ($MgSO_4$), filtered and concentrated in vacuo to give the crude product as a brown solid. Purification by flash chromatography using 10% ethyl acetate in petroleum ether gave **56** (0.052 g, 0.167 mmol, 82%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 (1H, s; Ar*H*), 7.54 (1H, d, *J* = 8.4 Hz; Ar*H*), 6.73 (1H, d, *J* = 8.4 Hz; Ar*H*), 3.58 (2H, t, *J* = 7.4 Hz; CH_2), 1.64 (2H, app. q, *J* = 7.4 Hz; CH_2), 0.90 ppm (3H, t, *J* = 7.4 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.6 (*C*=O), 136.4 (Ar*C*H), 128.3 (Ar*C*H), 122.1 (Ar*C*), 116.4 (Ar*C*), 113.6 (Ar*C*), 111.5 (Ar*C*H), 42.1 (CH_2), 20.5 (CH_2), 11.3 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$): δ = −113 (s; 2×*F*); IR (neat): ν = 2929, 1743, 1614, 1476, 1271, 1074, 715 cm^{-1}; MS (CI$^+$ mode): *m/z* (%): 289 (18) $[M]^+$, 229 (67), 135 (18), 58 (22); HRMS: *m/z*: calcd for $C_{11}H_{11}ONBrF_2$: 289.9987; found: 289.9990 $[M]^+$.

3,3,5-Trifluoro-1-methyl-1,3-dihydroindol-2-one (57): DAST (46 μL, 0.35 mmol, 2.5 equiv) was added to a solution of 5-fluoro-1-methyl-1*H*-indole-2,3-dione (25 mg, 0.14 mmol, 1 equiv) in CH_2Cl_2 (1 mL) at room temperature. After 72 h, the reaction mixture was carefully quenched with MeOH and then washed with H_2O. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica (eluting with 40% EtOAc/petroleum ether (40–60°C)) to give **57** (22 mg, 0.11 mmol, 77%) as a pale-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.12 (2H, m; Ar*H*), 6.80–6.77 (1H, m; Ar*H*), 3.15 ppm (3H, s; NCH_3); ^{19}F NMR (367 MHz, $CDCl_3$): δ = −112.4 (2F, s), −117.5 ppm (1F, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0 (t, *J* = 29.8 Hz; *C*=O), 159.5 (d, *J* = 243.5 Hz; ArCF), 139.9 (Ar*C*F), 121.3 (m; CF_2), 120.0 (d, *J* = 23.3 Hz; Ar*C*H), 112.9 (d, *J* = 25.7 Hz; Ar*C*H), 110.5 (d, *J* = 7.7 Hz; Ar*C*H), 107.9 (ArC), 26.4 ppm (NCH_3); IR (KBr): $\tilde{\nu}$ = 3075, 2927, 1747 (C=O), 1651, 1626, 1503, 1425, 1370 cm^{-1}; MS (EI mode): *m/z* (%): 201 (100) $[M]^+$, 47 (21), 63 (30), 78 (23), 83 (89), 85 (57), 145 (26), 153 (38), 154 (22), 172 (51), 173 (36); HRMS: *m/z*: calcd for $C_9H_6NF_3$: 201.0401; found: 201.0403 $[M]^+$.

5-Fluoro-3-hydroxy-1-methyl-3-thiophen-2-yl-1,3-dihydroindol-2-one (58): 2-Thienyllithium (0.14 mL, 1.0 M in THF, 0.14 mmol, 1 equiv) was added to a solution of 5-fluoro-1-methyl-1*H*-indole-2,3-dione (25 mg, 0.14 mmol, 1 equiv) in THF (1 mL) at 0°C and the reaction was warmed to room temperature. After 18 h, the reaction mixture was quenched with aqueous saturated NH_4Cl (5 mL). The layers were then separated and the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica (eluting with 50% EtOAc/petroleum ether (40–60°C)) to give **58** (63 mg, 0.09 mmol, 74% by conversion) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.35 (1H, m; Ar*H*), 7.32–7.29 (1H, m; Ar*H*), 7.13–7.08 (1H, m; Ar*H*), 7.01–6.96 (2H, m; Ar*H*), 6.86–6.83 (1H, m; Ar*H*), 3.91 (1H, brs; O*H*), 3.24 ppm (3H, s; NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0 (*C*=O), 159.6 (d, *J* = 240.9 Hz; Ar*C*F), 142.8 (Ar*C*), 139.0 (d, *J* 1.8, Ar*C*), 132.0 (d, *J* = 7.7 Hz; Ar*C*), 126.9 (d, *J* = 6.6 Hz; 2×thiophene Ar*C*H), 126.0 (thiophene Ar*C*H), 116.5 (d, *J* = 23.4 Hz; Ar*C*H), 113.2 (d, *J* = 25.1; Ar*C*H), 109.5 (d, *J* = 7.9 Hz; Ar*C*H), 75.6 (d, *J* = 1.5 Hz; *C*), 26.8 ppm (N−CH_3); IR (KBr): $\tilde{\nu}$ = 3287 (OH), 3113, 3078, 2968, 2939, 1857, 1701 (C=O), 1619, 1496, 1470 cm^{-1}; MS (EI mode): *m/z* (%): 263 (99) $[M]^+$, 84 (24), 111 (75), 122 (20), 202 (88), 218 (49), 230 (66), 234 (72), 235 (39); HRMS: *m/z*: calcd for $C_{13}H_{10}O_2NFS$: 263.0416; found: 263.0415 $[M]^+$.

5-Fluoro-1-methyl-3,3-di-thiophen-2-yl-1,3-dihydroindol-2-one (59): 2-Thienyllithium (0.8 mL, 1.0 M in THF, 0.84 mmol, 3 equiv) was added to a solution of crude 5-fluoro-1-methyl-1*H*-indole-2,3-dione (50 mg, 0.28 mmol, 1 equiv) in THF (2 mL) at 0°C and the reaction was warmed to room temperature. After 18 h, the reaction mixture was quenched with aqueous saturated NH_4Cl (5 mL). The layers were then separated and the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica (eluting with 10% EtOAc/petroleum ether (40–60°C)) to give **59** (63 mg, 0.19 mmol, 69%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.22 (1H, m; Ar*H*), 7.18–7.16 (2H, m; Ar*H*), 7.03–6.98 (3H, m; Ar*H*), 6.87–6.85 (2H, m; Ar*H*), 6.79–6.76 (1H, m; Ar*H*), 3.19 ppm (3H, s; NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1 (*C*=O), 159.2 (d, *J* = 240.5 Hz; Ar*C*F), 143.4 (2×Ar*C*), 138.8 (d, *J* = 1.8 Hz; Ar*C*), 134.0 (d, *J* = 7.8 Hz; Ar*C*), 126.7 (d, *J* = 7.8 Hz; 4×thiophene Ar*C*H), 126.0 (2×thiophene Ar*C*H), 115.6 (d, *J* = 23.3 Hz; Ar*C*H), 113.9 (d, *J* = 25.1; Ar*C*H), 109.3 (d, *J* = 7.9 Hz; Ar*C*H), 56.1 (*C*), 27.1 ppm (N−CH_3); IR (KBr): $\tilde{\nu}$ = 1719 (C=O), 1608, 1496, 1466, 1348, 1263 cm^{-1}; MS (EI mode): *m/z* (%): 329 (100) $[M]^+$, 83 (73), 85 (48), 284 (95), 285 (23), 296 (27), 300 (47), 330 (22); HRMS: *m/z*: calcd for $C_{17}H_{12}ONFS_2$: 329.0344; found: 329.0342 $[M]^+$.

6′-Fluoro-1′-methyl-1′*H*-spiro[imidazolidine-4,3′-indole]-2,5,2′-trione (60): KCN (36 mg, 0.56 mmol, 2 equiv) was added to a solution of 5-fluoro-1-methyl-1*H*-indole-2,3-dione (50 mg, 0.28 mmol, 1 equiv) in MeOH (3 mL) at room temperature. After 15 min, $(NH_4)_2CO_3$ (0.27 g, 2.79 mmol, 10 equiv) and H_2O (5 mL) were added. The reaction mixture was then heated to 70°C. After 18 h, the reaction mixture was cooled, MeOH removed in vacuo and H_2O (10 mL) was added. The reaction mixture was acidified with 6 M HCl (10 mL) and extracted with Et_2O (2×10 mL). The organic layers were combined and washed with aqueous saturated NaCl (15 mL). The organic layer was then dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica (eluting with 80% EtOAc/petroleum ether (40–60°C) then EtOAc) to give **60** (39 mg, 0.16 mmol, 56%) as a cream solid. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 11.42 (1H, brs; N*H*), 8.60 (1H, brs; N*H*), 7.52–7.49 (1H, m; Ar*H*), 7.34–7.29 (1H, m; Ar*H*), 7.18–7.15 (1H, m; Ar*H*), 3.18 ppm (3H, s; NCH_3); ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 170.8 (*C*=O), 170.1 (*C*=O), 158.8 (d, *J* = 237.9 Hz; ArCF), 157.5 (*C*=O), 140.5 (Ar*C*), 126.3 (Ar*C*), 116.9 (d, *J* = 23.2 Hz; Ar*C*H), 112.4 (d, *J* = 25.8 Hz; Ar*C*H), 110.5 (d, *J* = 8.0 Hz; Ar*C*H), 69.1 (C), 26.9 ppm (NCH_3); IR (KBr): $\tilde{\nu}$ = 3433, 3194, 1747 (C=O), 1705 (C=O), 1620 (C=O), 1489, 1362, 1265, 1219 cm^{-1}; MS (EI mode): *m/z* (%): 249 $[M]^+$, 28 (20), 44 (21), 95 (12), 108 (15), 122 (24), 149 (60), 150 (78), 178 (50), 179 (17), 206 (60), 250 (13); HRMS: *m/z*: calcd for $C_{11}H_8O_3N_3F$: 249.0550; found: 249.0551 $[M]^+$.

5-Bromo-3-(2-bromomethylbenzyl)-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfonyl)-1-propyl-1,3-dihydroindol-2-one (61): K_2CO_3 (0.099 g, 0.713 mmol, 5 equiv) and α,α′-dibromo-*o*-xylene (0.188 g, 0.713 mmol, 5 equiv) were added to a solution of 5-bromo-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecane-1-sulfonyl)-1-propyl-1,3-dihydroindol-2-one (0.109 g, 0.143 mmol, 1 equiv) in DMF (12 mL) and the reaction mixture was heated to 40°C. The reaction was left to stir for 1.5 h. After this time, ethyl acetate (10 mL) was added to

the reaction mixture and the organic layer washed with water (5× 10 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to give a crude brown oil. The crude product was purified by fluorous chromatography to give **61** (0.112 g, 0.118 mmol, 83%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.85 (1H, d, J=3.0 Hz; Ar*H*), 7.48 (1H, dd, J=3.0, 9.0 Hz; Ar*H*), 7.20 (1H, dd, J=3.0, 9.0 Hz; Ar*H*), 7.07 (1H, dt, J=3.0, 9.0 Hz; Ar*H*), 6.93 (1H, dt, J=3.0, 9.0 Hz; Ar*H*), 6.60 (2H, d, J=9.0 Hz; 2×Ar*H*), 4.82 (1H, d, J=9.0 Hz; 1H of CH_2), 4.38 (1H, d, J=9.0 Hz; 1H of CH_2), 4.01 (1H, d, J=15.0 Hz; 1H of CH_2), 3.92–3.82 (1H, m; 1H of CH_2), 3.67 (1H, d, J=15.0 Hz; 1H of CH_2), 3.60–3.49 (2H, m; CH_2), 3.38–3.29 (1H, m; 1H of CH_2), 2.78–2.62 (2H, m; CH_2), 1.32–1.25 (2H, m; CH_2), 0.57 ppm (3H, t, J=9.0 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=169.8 (*C*=O), 143.6 (Ar*C*), 137.2 (Ar*C*H), 134.4 (Ar*C*), 131.3 (Ar*C*), 131.2 (Ar*C*H), 130.7 (Ar*C*H), 129.9 (Ar*C*H), 128.8 (Ar*C*H), 128.6 (Ar*C*H), 122.8 (Ar*C*), 116.2 (Ar*C*), 110.8 (Ar*C*H), 74.9 (*C*SO_2), 42.4 (*C*H_2), 40.9 (*C*H_2), 32.8 (*C*H_2), 31.8 (*C*H_2), 23.4 (t, J=33.8 Hz; *C*H_2), 20.3 (*C*H_2), 11.0 ppm (*C*H_3); IR (ATR): $\tilde{\nu}$=1706 (C=O), 1601, 1477, 1313, 1201, 1133, 953 cm^{-1}; MS (ES$^+$ mode): m/z (%): 970 (100), 968 (32) $[M+Na]^+$, 934 (20), 927 (12), 892 (30); HRMS: m/z: calcd for $C_{29}H_{22}O_3NBr_2F_{17}NaS$: 967.9308; found: 967.9320 $[M+Na]^+$.

Spirocycle 62 and 2-bromo-5-propyl-5*H*-benzo[*b*]carbazole (63): SmI_2 (2.4 mL, 0.1 M solution in THF, 0.24 mmol, 2.2 equiv) was added to a solution of **61** (0.102 g, 0.12 mmol, 1 equiv) in THF (5 mL) by using a syringe pump over 0.5 h. The reaction was then stirred at room temperature for 1.5 h. Aqueous saturated $NaHCO_3$ (5 mL) was added to the reaction mixture and the aqueous layer was extracted with EtOAc (3×5 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product mixture was purified by flash chromatography using 10% ethyl acetate in petroleum ether to give **62** (0.026 g, 0.073 mmol, 68%) as a yellow solid and **63** (0.007 g, 0.021 mmol, 20%) as a yellow solid.

Product ***62***: ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.36 (1H, dd, J=2.0, 8.4 Hz; Ar*H*), 7.27 (4H, brs; 4×Ar*H*), 6.93 (1H, d, J=2.0 Hz; Ar*H*), 6.75 (1H, d, J=8.4 Hz; Ar*H*), 3.72 (2H, t, J=7.2 Hz; CH_2), 3.63 (2H, d, J=15.4 Hz; 2×1H from two CH_2), 3.06 (2H, d, J=15.4 Hz; 2×1H from two CH_2), 1.79–1.70 (2H, m; CH_2), 0.98 ppm (3H, t, J=7.2 Hz; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=179.3 (*C*=O), 141.1 (Ar*C*), 140.8 (Ar*C*), 140.7 (Ar*C*), 138.5 (Ar*C*), 130.7 (Ar*C*H), 127.3 (Ar*C*H), 127.2 (Ar*C*H), 124.8 (Ar*C*H), 124.7 (Ar*C*H), 124.6 (Ar*C*H), 115.0 (Ar*C*), 109.7 (Ar*C*H), 54.1 (*C*), 44.1 (*C*H_2), 44.0 (*C*H_2), 41.7 (*C*H_2), 20.7 (*C*H_2), 11.3 ppm (*C*H_3); IR (ATR): $\tilde{\nu}$=2925, 2854, 1695 (C=O), 1597, 1474, 1349, 1204, 1102 cm^{-1}; MS (CI$^+$ mode): m/z (%): 356 (100) $[M]^+$, 295 (20), 278 (50), 120 (19), 58 (21); HRMS: m/z: calcd for $C_{19}H_{19}ONBr$: 356.0648; found: 356.0645 $[M]^+$. *Product* ***63***: ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.53 (1H, s; Ar*H*), 8.32 (1H, d, J=2.0 Hz; Ar*H*), 8.05 (1H, dd, J=8.4, 0.4 Hz; Ar*H*), 7.97 (1H, dd, J=8.4, 0.4 Hz; Ar*H*), 7.69 (1H, s; Ar*H*), 7.61 (1H, dd, J=8.4, 2.0 Hz; Ar*H*), 7.51 (1H, td, J=8.4, 1.6 Hz; Ar*H*), 7.42 (1H, td, J=8.4, 1.6 Hz; Ar*H*), 7.27 (1H, d, J=8.4 Hz; Ar*H*), 4.30 (2H, t, J=7.3 Hz; CH_2), 1.97 (2H, app. q, J=7.3 Hz; CH_2), 1.02 ppm (3H, t, J=7.3 Hz; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=171.9 (*C*=O), 141.8 (Ar*C*), 140.6 (Ar*C*), 132.8 (Ar*C*), 129.7 (Ar*C*H), 128.5 (Ar*C*), 128.0 (Ar*C*H), 127.0 (Ar*C*H), 125.5 (Ar*C*H), 124.5 (Ar*C*H), 124.0 (Ar*C*), 123.8 (Ar*C*), 122.8 (Ar*C*H), 119.1 (Ar*C*H), 111.3 (Ar*C*), 109.6 (Ar*C*H), 103.6 (Ar*C*H), 44.9 (*C*H_2), 21.8 (*C*H_2), 11.8 ppm (*C*H_3); IR (ATR): $\tilde{\nu}$=2929, 1461, 1137, 848 cm^{-1}; MS (CI$^+$ mode): m/z (%): 338 (100) $[M]^+$, 260 (17), 74 (25), 63 (18); HRMS: m/z: calcd for $C_{19}H_{17}NBr$: 338.054; found: 338.0539 $[M]^+$.

2-Bromo-5-propyl-5*H*-benzo[*b*]carbazole (63) and 5-bromo-3-(2-methylbenzyl)-1-propyl-1,3-dihydroindol-2-one (64): A solution of **61** (0.091 g, 0.096 mmol, 1 equiv) in THF (4.5 mL) was added to a flask containing SmI_2 (4 mL, 0.1 M solution in THF, 0.40 mmol, 4.2 equiv) by using a syringe pump over 0.5 h. The reaction was stirred at room temperature for 2 h. Aqueous saturated $NaHCO_3$ (5 mL) was added to the reaction mixture and the aqueous layer was extracted with EtOAc (3×8 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by flash chromatography using 10% ethyl acetate in petroleum ether to give **63** (0.024 g, 0.072 mmol, 75%) as a yellow solid and **64** (0.007 g, 0.020 mmol, 20%) as a yellow oil. Data for **63** given earlier.

Product ***64***: ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.37 (1H, dd, J=3.0, 9.0 Hz; Ar*H*), 7.24–7.13 (4H, m; 4×Ar*H*), 6.72 (2H, d, J=9.0 Hz; 2×Ar*H*), 3.77–3.62 (3H, m; CH_2N, C*H*), 3.52 (1H, dd, J=3.0, 15.0 Hz; 1H of CH_2Ar), 2.79 (1H, dd, J=9.0, 15.0 Hz; 1H of CH_2), 2.33 (3H, s; CH_3), 1.69 (2H, app. q, J=9.0 Hz; CH_2), 0.96 ppm (3H, t, J=9.0 Hz; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=176.8 (*C*=O), 143.0 (Ar*C*), 136.9 (Ar*C*), 136.3 (Ar*C*), 131.0 (Ar*C*H), 130.9 (Ar*C*H), 130.8 (Ar*C*H), 130.3 (Ar*C*H), 128.3 (Ar*C*), 127.4 (Ar*C*H), 126.2 (Ar*C*H), 114.7 (Ar*C*), 109.8 (Ar*C*H), 45.9 (*C*H), 41.9 (*C*H_2), 34.6 (*C*H_2), 20.9 (*C*H_2), 19.8 (*C*H_3),11.6 ppm (*C*H_3); IR (ATR): ν=2924, 2852, 1705 (C=O), 1597, 1474, 1349, 1202, 1110 cm^{-1}; MS (CI$^+$ mode): m/z (%): 358 (85) $[M]^+$, 297 (19), 280 (100), 207 (9), 122 (11); HRMS: m/z: calcd for $C_{19}H_{21}ONBr$: 358.0801; found: 358.0801 $[M]^+$.

Acknowledgements

We thank the Carnegie Trust for the Universities of Scotland (Scholarship to L.A.M.), Celltech R&D (CASE award, L.A.M.), The University of Glasgow (University Scholarship to R.A.M), The University of Manchester (K.M.J.), and Syngenta (CASE award K.M.J.). Additional, unrestricted support was provided by AstraZeneca and Pfizer.

[1] a) J. K. Landquist in *Comprehensive Heterocyclic Chemistry* (Eds.: A. R. Katritzky, C. W. Rees), Pergamon, New York, **1984**; b) P. J. Crowley in *Comprehensive Heterocyclic Chemistry* (Eds.: A. R. Katritzky, C. W. Rees), Pergamon, New York, **1984**.

[2] a) V. Krchnak, M. W. Holladay, *Chem. Rev.* **2002**, *102*, 61; b) for a review of fluorous-phase approaches in heterocycle synthesis see: W. Zhang, *Chem. Rev.* **2004**, *104*, 2531.

[3] For a discussion of fluorous tagging see A. Studer, S. Hadida, R. Ferritto, S.-Y. Kim, P. Jeger, P. Wipf, D. P. Curran, *Science* **1997**, *275*, 823.

[4] For recent reviews see: a) D. P. Curran in *The Handbook of Fluorous Chemistry* (Eds.: J. A. Gladysz, D. P. Curran, I. T. Horváth), Wiley-VCH, Weinheim, **2004**; b) W. Zhang, *Tetrahedron* **2003**, *59*, 4475.

[5] For a preliminary account of this work see: L. A. McAllister, R. A. McCormick, S. Brand, D. J. Procter, *Angew. Chem.* **2005**, *117*, 456; *Angew. Chem. Int. Ed.* **2005**, *44*, 452.

[6] R. Pummerer, *Chem. Ber.* **1909**, *42*, 2282.

[7] For recent reviews on the Pummerer reaction see: a) K. S. Feldman, *Tetrahedron* **2006**, *62*, 5003; b) S. K. Bur, A. Padwa, *Chem. Rev.* **2004**, *104*, 2401; c) A. Padwa, D. M. Danca, J. D. Ginn, S. M. Lynch, *J. Braz. Chem. Soc.* **2001**, *12*, 571; d) A. Padwa, A. G. Waterson, *Curr. Org. Chem.* **2000**, *4*, 175; e) A. Padwa, D. E. Gunn Jr, M. H. Osterhout, *Synthesis* **1997**, 1353.

[8] a) L. A. McAllister, S. Brand, R. de Gentile, D. J. Procter, *Chem. Commun.* **2003**, 2380; b) L. A. McAllister, K. L. Turner, S. Brand, M. Stefaniak, D. J. Procter, *J. Org. Chem.* **2006**, *71*, 6497.

[9] F. Z. Dörwald, *Organic Synthesis on Solid Phase*, Wiley-VCH, Weinheim, **2000**.

[10] For thiol additions to glyoxalates see: J. Milton, S. Brand, M. F. Jones, C. M. Rayner, *Tetrahedron Lett.* **1995**, *36*, 6961.

[11] Fluorous thiols as nucleophilic scavenging reagents see: a) C. W. Lindsley, Z. Zhao, W. H. Leister, *Tetrahedron Lett.* **2002**, *43*, 4225; b) W. Zhang, D. P. Curran, C. H-T. Chen, *Tetrahedron* **2002**, *58*, 3871. Fluorous thiols to introduce tags for multistep synthesis see: c) W. Zhang, *Org. Lett.* **2003**, *5*, 1011; d) Y. Jing, X. Huang, *Tetrahedron Lett.* **2004**, *45*, 4615.

[12] Glyoxamide substrates were prepared from secondary amines in three steps see: M. A. Marx, A-L. Grillot, C. T. Louer, K. A. Beaver, P. A. Bartlett, *J. Am. Chem. Soc.* **1997**, *119*, 6153.

[13] D. P. Curran, Z. Luo, *J. Am. Chem. Soc.* **1999**, *121*, 9069.

[14] Similar reductions using other electron-transfer reagents have been reported: a) J. M. Manthorpe, J. L. Gleason, *J. Am. Chem. Soc.* **2001**, *123*, 2091; b) J. M. Manthorpe, J. L. Gleason, *Angew. Chem.*

2002, *114*, 2444; *Angew. Chem. Int. Ed.* **2002**, *41*, 2338; c) E. D. Burke, J. L. Gleason, *Org. Lett.* **2004**, *6*, 405.
[15] G. A. Molander, *Org. React.* **1994**, *46*, 211.
[16] a) F. McKerlie, D. J. Procter, G. Wynne, *Chem. Commun.* **2002**, 584; b) F. McKerlie, I. M. Rudkin, G. Wynne, D. J. Procter, *Org. Biomol. Chem.* **2005**, *3*, 2805; c) K. L. Turner, T. M. Baker, S. Islam, D. J. Procter, M. Stefaniak, *Org. Lett.* **2006**, *8*, 329; d) L. A. McAllister, K. L. Turner, S. Brand, M. Stefaniak, D. J. Procter, *J. Org. Chem.* **2006**, *71*, 6497.
[17] a) H. B. Kagan, J. L. Namy in *Lanthanides: Chemistry and Use in Organic Synthesis* (Ed.: S. Kobayashi), Springer, New York, **1999**; b) A. Dahlén, G. Hilmersson, *Eur. J. Inorg. Chem.* **2004**, 3393.
[18] The oxidation of sulfide linkers to the corresponding sulfoxide, followed by Pummerer rearrangement has been used in cleavage strategies to release alcohols and aldehydes from solid supports: a) C. Rolland, G. Hanquet, J. B. Ducep, G. Solladié, *Tetrahedron Lett.* **2001**, *42*, 7563; b) C. H. Tai, H. Wu, W. R. Li, *Org. Lett.* **2004**, *6*, 2905. For a review of the use of sulfur linkers see: L. A. McAllister, R. A. McCormick, D. J. Procter, *Tetrahedron* **2005**, *61*, 11527.
[19] K. S. Ravikumar, J-P. Bégué, D. Bonnet-Delpon, *Tetrahedron Lett.* **1998**, *39*, 3141.
[20] R. A. McCormick, K. M. James, N. Willetts, D. J. Procter, *QSAR Comb. Sci.* **2006**, *25*, 709.
[21] Rearrangements to benzofuranones see: a) T. H. Black, S. M. Arrivo, J. S. Schumm, J. M. Knobeloch, *J. Chem. Soc. Chem. Commun.* **1986**, 1524; b) T. H. Black, S. M. Arrivo, J. S. Schumm, J. M. Knobeloch, *J. Org. Chem.* **1987**, *52*, 5425; for the first studies on rearrangements to oxindoles see: I. D. Hills, G. C. Fu, *Angew. Chem.* **2003**, *115*, 3969; *Angew. Chem. Int. Ed.* **2003**, *42*, 3921.
[22] *Handbook of organopalladium chemistry for organic synthesis* (Ed.: E. Negishi), Wiley-Interscience, New York, **2002**.
[23] E. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979.
[24] N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457.
[25] X. Huang, K. W. Anderson, D. Zim, L. Jiang, A. Klapars, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 6653.
[26] R. R. Poondra, N. J. Turner, *Org. Lett.* **2005**, *7*, 863.
[27] V. Q. Yen, N. P. Buu-Hoï, N. D. Xuong, *J. Org. Chem.* **1958**, *23*, 1858.
[28] J. C. Torres, S. J. Garden, A. C. Pinto, F. S. Q. da Silva, N. Boechat, *Tetrahedron* **1999**, *55*, 1881.
[29] G. V. Tormos, K. A. Belmore, M. P. Cava, *J. Am. Chem. Soc.* **1993**, *115*, 11512.
[30] H. Otomasu, K. Natori, H. Takahashi, *Chem. Pharm. Bull.* **1975**, *7*, 1431.
[31] K. Nagarajan, M. D. Nair, P. M. Pillai, *Tetrahedron* **1967**, *23*, 1683.
[32] E. H. Wiseman, J. Chiaini, J. M. McManus, *J. Med. Chem.* **1973**, *16*, 131.
[33] Y. Tamura, J. Uneshi, H. Maeda, H. D. Choi, H. Ishibashi, *Synthesis* **1981**, 534.
[34] B. Pecherer, R. C. Sunbury, A. Brossi, *J. Heterocycl. Chem.* **1972**, *9*, 609.
[35] V. Nair, S. Vellalath, M. Poonoth, R. Mohan, E. Suresh, *Org. Lett.* **2006**, *8*, 507.
[36] A. A. Esmaili, A. Bodaghi, *Tetrahedron* **2003**, *59*, 1169.
[37] S. E. Webber, J. Tikhe, S. T. Worland, S. A. Fuhrman, T. F. Hendrickson, D. A. Matthews, R. A. Love, A. K. Patick, J. W. Meador, R. A. Ferre, E. L. Brown, D. M. DeLisle, C. E. Ford, S. L. Binford, *J. Med. Chem.* **1996**, *39*, 5072.
[38] F. Da Settimo, G. Primofiore, A. Da Settimo, C. La Motta, F. Simorini, E. Novellino, G. Greco, A. Lavecchia, E. Boldrini, *J. Med. Chem.* **2003**, *46*, 1419.

Received: October 6, 2006
Published online: January 3, 2007

