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Article

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Sulfonamide-Directed Chemo- and Site-Selective Oxidative Halogenation/Amination Using Halogenating Reagents Generated in situ from Cyclic Diacyl Peroxides

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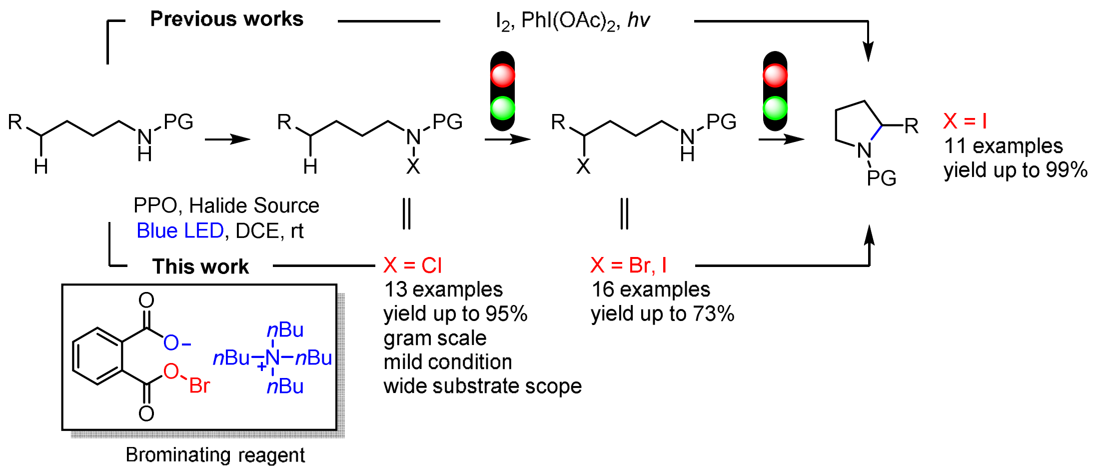


Abstract

The combination of cyclic diacyl peroxides with commercially available halide salts as a unique halogenating system is utilized in Hofmann-Löffler-Freytag-type reaction. This strategy allows for the formation of *N*–chloroamides, δ-brominated products and

even biologically relevant pyrrolidines under mild conditions in moderate to excellent yields. Meanwhile, the preliminary structure of the in situ formed brominating reagent is investigated by NMR and UV/Vis analysis.

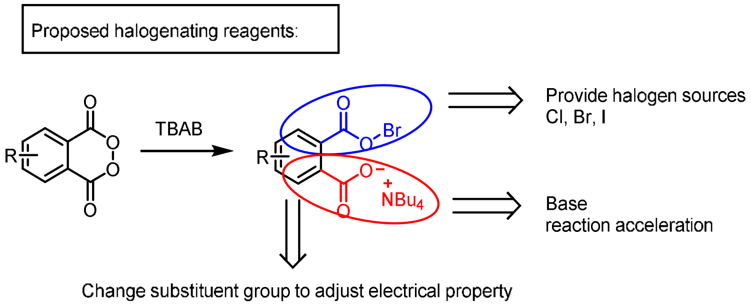
Introduction

Nitrogen-centered radical species including neutral *N*-centered radicals and radical ions as very attractive synthetic intermediates are usually used to effect intramolecular cyclization, rapid additions to olefin, and 1,5-H abstraction in the synthesis of nitrogen-containing compounds,[1] which can be traced back to the historical Hofmann-Löffler-Freytag (HLF) reaction in the early 1880s.[2] However, the generation of nitrogen-centered radical species seriously relies on pre-functionalization of the corresponding nitrogen-containing precursors.[1,3] These functional groups are then activated with a radical initiator, transition-metal catalyst at elevated temperature, UV light, or strong acid to generate the resulting radical intermediates through homolytic cleavage of various N–O, N–S, N–N, N–X, and N–H bonds. On the other hand, the subsequent reactions of nitrogen-centered radical species have yet to reach a satisfactory level of maturity of carbon counterparts,[4] in spite of their potential in the field of alkaloid and heterocyclic synthesis.

Gratifyingly, it was found that the electron-deficiency of the nitrogen-centered radical is increased by installing an electron-withdrawing group, such as a sulfonyl or carbonyl group, on the nitrogen and Suárez[5] discovered that for sulfonamides in situ formed IOAc can be used for HLF reaction. This approach allows the in situ formed nitrogen–halogen bond from a strong oxidant and a halogen source to be cleaved homolytically under mild conditions compatible with the stability of the protective groups most frequently used in synthetic organic chemistry. In this regard, Fan,[6] González and Herrera[7] independently reported an iodine-mediated Hofmann-Löffler-Freytag-type reaction of sulfonamides in the presence of a stoichiometric amount of $PhI(OAc)_2$. Yu[8] showed that a similar formation of pyrrolidine could be accompanied by the subsequent iodination through consecutive C−H homolysis. Recently, Muñiz developed iodine-catalyzed[9a,9b] (or *N*-iodosuccinimide-promoted[9c]) visible-light-initiated amination reactions of remote $C(sp^3)$–H bonds. Meanwhile, Tiefenbacher[10] extended the Suárez-modified HLF reaction through the in situ generation of the electron-deficient trifluoroethyl amidyl radicals. More recently, Nagib[11] employed a triiodide strategy that expanded the scope of the corresponding Suárez modification to enable the direct amination of secondary $C(sp^3)$–H bonds. Alternatively, the transition-metal catalysis[12-15] and visible-light photocatalysis[16,17] have also emerged as a useful and powerful complement for the remote $C(sp^3)$–H bond functionalization of amides, but still some drawbacks exist that limit practicability and large-scale applicability.

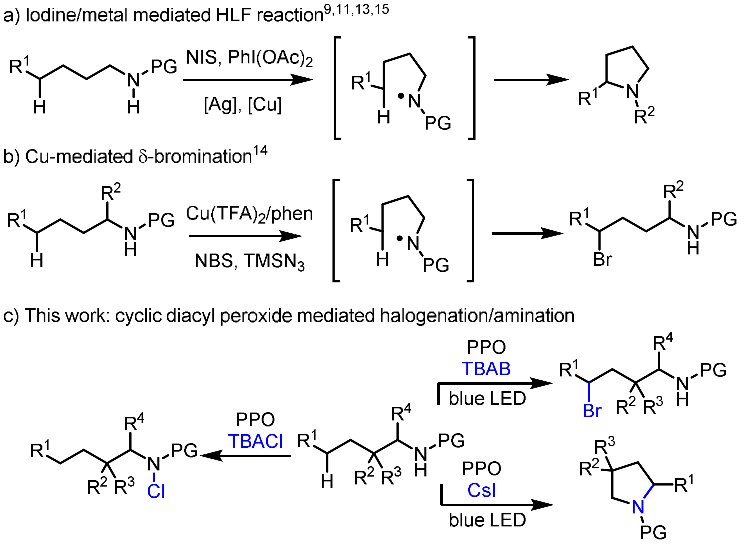
Organic peroxides have received attention as capable reagents for practical organic synthesis owing to their high reactivity, and generally low cost and low toxicity of reagents and byproducts.[18] Specifically, cyclic organic peroxides as a really interesting class of compounds are more thermal stable than acyclic peroxides sharing similarities in atom connectivity, which exhibited the dichotomy of ionic and radical mechanisms and constituted the key pharmacophore unit of some anti-malarial drugs (artemisinin, yingzhaosu A et al.).[18]

Figure 1. Proposed halogenating reagents.



Inspired by the enzyme-catalyzed oxidative halogenation in nature[19] and our continuing interest and efforts in the utilization of cyclic peroxides,[20] we are intrigued by the possibility of complementing the existing Hofmann-Löffler-Freytag-type processes by the combination of cyclic diacyl peroxides and diverse halide salts. We speculated that such proposed halogenating reagents (Figure 1) could increase the efficiency of Hofmann-Löffler-Freytag-type reactions by two potential pathways: increasing the reactivity of halogenating reagent by the existence of the intramolecular benzoates, or influencing the conformation of the substrates to favor reactivity and selectivity by intermolecular force. To our delight, our halide salts-enabled divergent oxidative halogenation/amination of a diverse array of easily available sulfonamides proceeded at room temperature in moderate to excellent yields to afford *N*–chloroamides, δ-brominated products and even biologically relevant pyrrolidines in a predictable and controllable fashion (Scheme 1). To the best of our knowledge, this is the first example of the cyclic diacyl peroxide-halide salt combinations as an efficient halogenating reagent system being exploited in the generation of *N*–haloamides and the subsequent application to facilitate remote C(sp^3)–H bromination and pyrrolidine synthesis.

Scheme 1. Direct remote C(sp^3)–H functionalization.

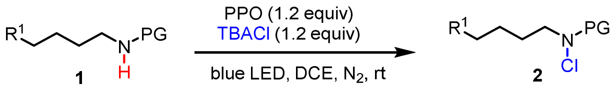


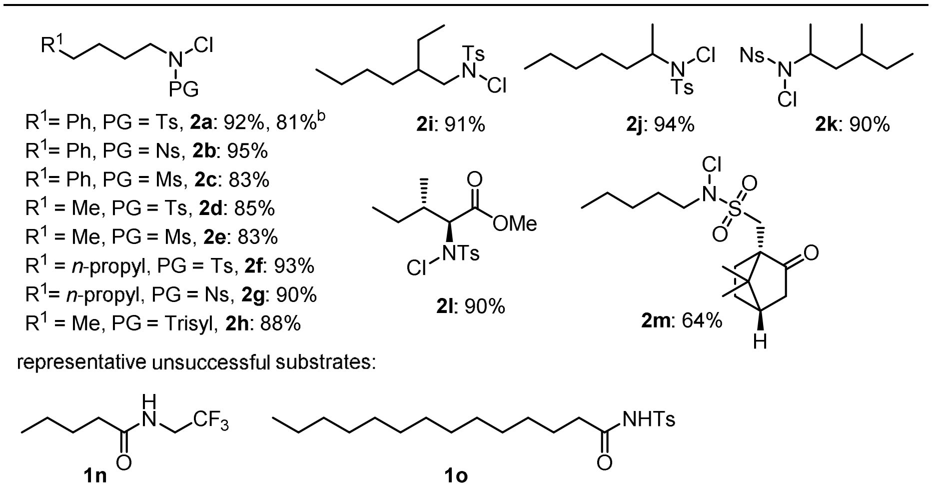
Results and Discussion

Our initial efforts to realize the Hofmann-Löffler-Freytag-type transformation commenced with the reaction of 4-methyl-*N*-(4-phenylbutyl)benzenesulfonamide **1a** with commercially available TBACl (Tetrabutyl ammonium chloride) as a halogen source. The choice of sulfonamidates as protecting groups were made for their certain application in amino and amino acid chemistry.[21] Moreover, they also played positive roles in avoiding over-oxidation of the amino group during the formation of the haloamide intermediate, and controlling the stability of the *N*-centered radical during the HAT process. Although the direct δ-C(sp^3)–H chlorination or pyrrolidine formation was not obtained even in the presence of blue light-emitting diodes (LEDs) irradiation, it is interesting to note that an in situ formation of **2a** was efficiently achieved in good yield (92%) using the combination of TBACl and PPO (phthaloyl peroxide).[22]

Encouraged by the above-mentioned results, we began to explore the generality of the *N*-chlorination in a variety of aliphatic amines containing different protecting groups with the results summarized in Table 1. Satisfyingly, in addition to the *N*-tosylated amines, mesyl-, 2,4,6-triisopropylbenzenesulfonyl and more easily removable nosyl-protected amines were perfectly compatible, with this reaction to provide the desired products in 83-95% yields (**2a-c**, **2h**). Various aliphatic sulfonamides (**1d-g**, **1i-k**) bearing an alkyl substituent in different position participated well in the *N*-chlorination reactions, affording a variety of useful *N*-chlorosulfonamide products. Notably, the optically active *N*-Ts-isoleucine (**1l**) and chiral camphorsulfonyl protected amine (**1m**) could also go through the transformation smoothly with complete retention at the stereogenic centers. Furthermore, trifluoroethyl carbamate (**1n**) and aliphatic amide (**1o**) were investigated, and no conversions could be observed (by TLC and NMR) probably due to their lower activity. In agreement with a previously reported literature,[23] the expected benzylic δ-amination of the corresponding chloramine **2a** can be further achieved in 80% yield with as little as 0.1 mol % of photocatalyst (Scheme 2).

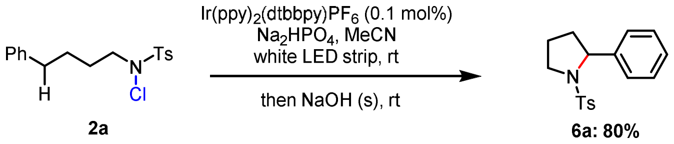
Table 1. Scope of N–H chlorination.[a]





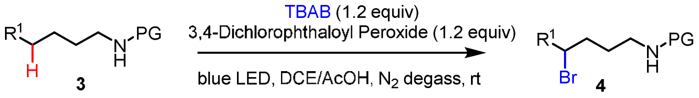
[a] Conditions: A solution of **1** (0.1 mmol), PPO (1.2 equiv) and TBACl (1.2 equiv) in DCE (2 mL) was stirred at room temperature under N_2 for 12 h; PPO = phthaloyl peroxide; TBACl = tetrabutyl ammonium chloride. [b] gram scale, 81% yield of **2a** (1.35 g) was obtained.

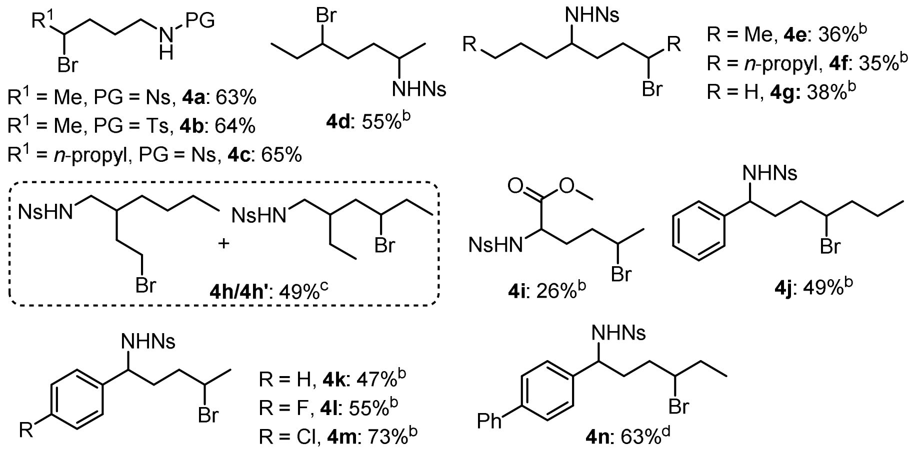
Scheme 2. Cyclization of N-Cl sulfonamide **2a**.



After an extensive survey of varying oxidants, bases, photocatalysts, bromine sources and other reaction parameters, it was found that the combination of 3,4-dichlorophthaloyl peroxide and TBAB (Tetrabutylammonium bromide) with visible light irradiation facilitated the desired bromination of remote C(sp^3)–H bonds to give the δ-brominated product **4a** in 63% yield.[22] With the optimized conditions in hand, substrates of this δ-brominated protocol were investigated and the results are presented in Table 2. Our metal-free and visible-light promoted approach is not limited to secondary C(sp^3)−H bonds (**3b-f**) but is also suitable for the bromination of primary nonactivated methyl groups (**3g**). Unlike previous work,[14] only δ-bromination of substrates containing both δ- and ε-methylene C(sp^3)−H bonds were observed. On the other hand, δ-brominated reaction mainly occurred at the δ-methylene C(sp^3)−H bond (**4h'**) rather than the δ-methyl one (**4h**) due to significant electronic effects. In addition, α-ester substituted substrates furnished the corresponding products in a slightly low yields. For example, δ-bromination of L-norleucine derivatives (**3i**) using this protocol afforded the expected product **4i** in 26% yield. More interestingly, a series of α-aryl, δ-bromo sulphonamides were obtained under the standard reaction conditions in moderate to good yields (**4j-n**), in which the potentially reactive arenes and benzylic C(sp^3)−H bonds remained intact. It is noteworthy that although δ-bromination of C(sp^3)−H bonds with alkyl amide substrates have been realized by using stoichiometric N–Br precursors[24] or transitional-metal catalyst,[14] our photo-induced δ-C(sp^3)–H bromination of sulfonamide substrates is operationally simple and does not require costly transition-metal or external radical initiators.

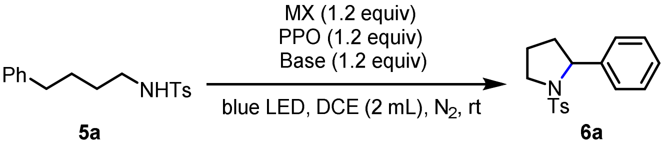
Table 2. Scope of δ-C(sp^3)–H bromination.[a]





[a] Conditions: A mixture of **3** (0.1 mmol), 3,4-dichlorophthaloyl peroxide (1.2 equiv), TBAB (1.2 equiv) and AcOH (0.2 mL) in DCE (2 mL) was irraditated by blue LED strips at room temperature under N_2 for 12 h; TBAB = tetrabutylammonium bromide. [b] obtained as a mixture of diastereomers (1:1). [c] product mixture (**4h**:**4h'** = 1:2) was obtained after purification. [d] obtained as a mixture of diastereomers (2:1).

Table 3. Optimization of δ-C(sp^3)-H cyclization.[a]



entry	MX	base	yield (%)
1	TBAB	---	20
2	TBAB	$NaHCO_3$	30
3	TBAI	---	0
4	NaI	---	30
5	KI	---	50
6	CsI	---	64
7[b]	CsI	K_2HPO_4	91

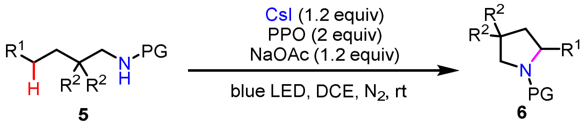
8[b]	CsI	Na_2HPO_4	63
9[b]	CsI	NaH_2PO_4	64
10[b]	CsI	NaOAc	99
11[b]	CsI	K_2CO_3	90
12[b]	CsI	NaOH	75
13[b]	CsI	K_3PO_4	92
14[b]	CsI	$NaHCO_3$	82
15[c]	CsI	---	13

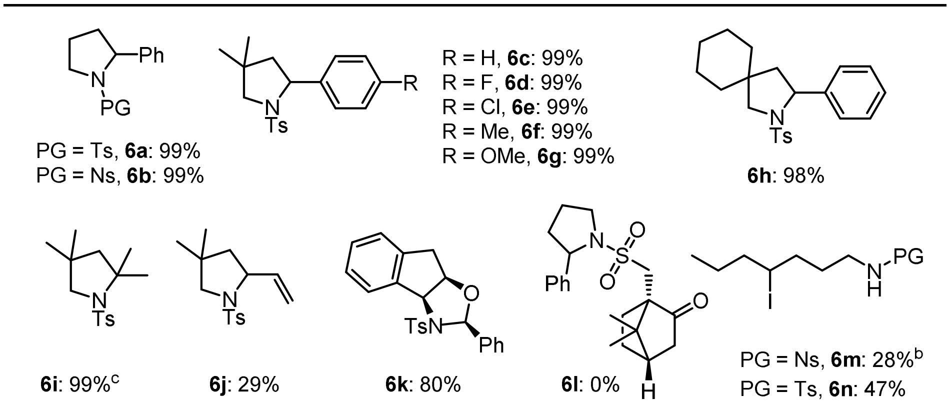
[a] Conditions: A mixture of **5a** (0.1 mmol), phthaloyl peroxide (1.2 equiv), MX (1.2 equiv) and base (1.2 equiv) in DCE (2 mL) was irraditated by blue LED strips at room temperature under N_2 for 24 h. [b] phthaloyl peroxide (2 equiv). [c] CsI (0.2 equiv).

Further attempts to arrive at the final pyrrolidine formation of **6a** using the combination of TBAI (Tetrabutylammonium iodide) and PPO as iodinating agent resulted in no conversion even under visible-light irradiation. Interestingly enough, by replacing the counterions from Bu_4N^+ to Na^+, K^+ and Cs^+ under blue-LED irradiation, a direct δ-amination product **6a** was obtained in 30%, 50% and 64% yields, respectively (Table 3, entries 4-6). It showed that the reaction efficiency was significantly affected by changing counter cations of the iodides, and CsI was the most effective reagent. This indicated that the base of the carboxylate of the in situ formed halide active intermediate had important effect on the reaction. To our delight, after screening of different bases, the employment of 1.2 equivalent NaOAc dramatically improved the yield of **6a** to

99% without a further over-oxidation or elimination (Table 3, entry 10). The reaction also worked well for *N*-nosylamidyl group (Table 4, **6b**, 99%). Substrates with β-alkyl substituted sulfonamides reacted with the combination of PPO and CsI to form pyrrolidines **6c** and **6h** in 99% and 98% yields. Meanwhile, different substituents in the *para*-substituted aryl group were well tolerated (**6d-g**), and either electron-withdrawing (F, Cl) or electron-donating (Me, OMe) substituents on the aromatic ring were all competent partners in this reaction showing that electronic factors played only a minor role. Gratifyingly, the formation of product **6i** demonstrated the applicability of our present amination conditions to the nonfunctionalized tertiary C(sp^3)–H bonds (99%). In parallel, this protocol could also be applied to an allylic amination reaction of **5j** without consumption of the free double bond, albeit in only 29% yield. Finally, amination of C(sp^3)–H bond adjacent to a heteroatom was carried out in presence of visible light irradiation at room temperature to provide the exclusive diastereoselective formation of **6k** (80%). To further reveal its synthetic potential, a camphorsulfonyl amide (**5l**) was investigated, however no desired product (**6l**) was detected. It is interesting to note that when linear sulfonamides (**5m** and **5n**) were employed as substrates, the reactions took place smoothly to deliver interrupted δ-iodination intermediates (**6m** and **6n**) as major products.

Table 4. Scope of δ-C(sp^3)–H Cyclization.[a]

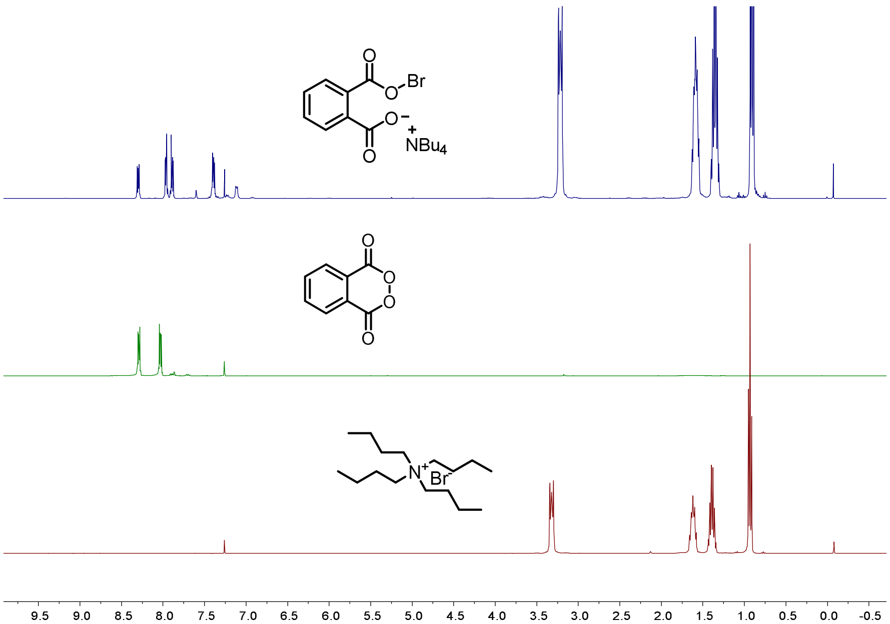




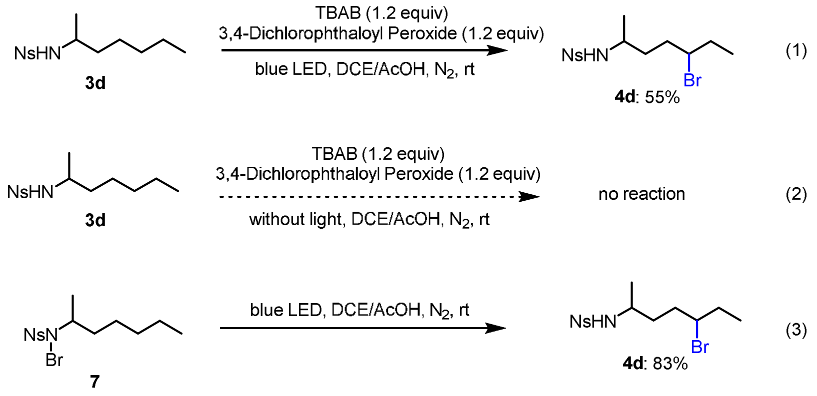
[a] Conditions: A solution of **3** (0.1 mmol), PPO (2 equiv), CsI (1.2 equiv) and NaOAc (1.2 equiv) in DCE (2 mL) was irradiated by blue LED strips at room temperature under N_2 for 24 h. [b] PPO (1.2 equiv) and without NaOAc.

To gain some insights into the reaction mechanism, a series of control reactions were conducted. NMR spectra of the combination of TBAB with phthaloyl peroxide definitely revealed an in situ formation of the corresponding brominated reagent (formed upon mixing PPO with 1 equiv of TBAB; Figure 2, blue line). Moreover, under the optimized conditions, **4a** and **6a** were not observed in the presence of TEMPO, BHT and other common radical scavengers, which revealed that the reaction might occur through a radical process.[22] Importantly, when TBAB or CsI was employed, the reactions did not proceed smoothly in the absence of light, which highlighted an essential role of photoirradiation in this 1,5-HAT process. Finally, we have also investigated a preformed stoichiometric N–Br precursor to this reaction conditions (Scheme 3) and the desired δ-brominated product was observed (**4d**, 85%).

Figure 2. ^{1}H NMR analysis of a proposed brominating reagent.

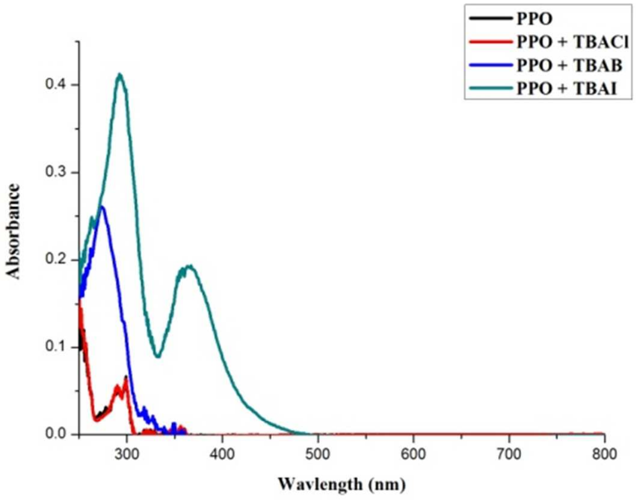


Scheme 3. δ-C(sp^3)-H bromination of Ns-sulfonamide **3d**.



As expected, the initial reaction between the halogen sources and the cyclic diacyl peroxides should lead to formation of the corresponding halogenating reagents. To confirm this hypothesis, UV/Vis and Cyclic Voltammetry (CV) measurements were performed with TBAX (Tetrabutylammonium halides) and cyclic diacyl peroxides (Figure 3).[22] It was observed that PPO did not absorb above λ = 310 nm (black line), and the resulting chlorinating reagent (formed upon mixing PPO with 1 equiv of TBACl) exhibited a similar absorption (red line). In contrast, addition of TBAB or TBAI induced an intense and a strong bathochromic shift up to λ = 340 nm (blue line) and 480 nm (green line) respectively, probably due to the formation of a more photosensitive molecule.

Figure 3. UV/Vis Experiment of PPO with TBAX (1 equiv) in DCE.

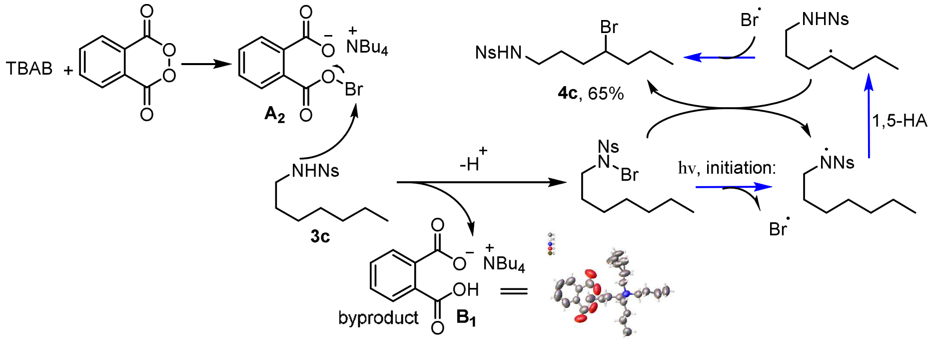


Meanwhile, tetrabutylammonium 2-carboxybenzoate was successfully isolated from our standard chlorination and bromination conditions as a byproduct. The corresponding structure of the byproduct was established unambiguously by single crystal X-ray diffraction analysis.[25]

On the basis of the above results, a prelimilary mechanism of δ-bromination was depicted in Scheme 4. With phthaloyl peroxide as oxidant, TBAB is converted to the proposed brominating reagent, followed by *N*-halogenation to afford the labile N–X specie. *N*-halosulfonamides, the parents of *N*-centered radicals, might strike a suitable balance between reactivity and stability to offer a controlled reactivity profile. Upon irradiation, the weak N–Br bond is broken and form a nitrogen-centered radical, which can undergo 1,5-H abstraction (BDE: N–Cl = 79.8 kcalmol^{-1}; N–Br = 67.1 kcalmol^{-1}; N–I = 38.0 kcalmol^{-1}).[26]

Then, the key radical recombination gives rise to δ-bromo amides (**4c**), reminiscent of the earlier reported transformations.[9a,9c,23]

Scheme 4. Plausible mechanism of δ-bromination.



Conclusion

In summary, we have developed a new strategy for the Hofmann-Löffler-Freytag-type chemistry using the combination of cyclic diacyl peroxides with halides as an in situ source of haloamines. Typical functional groups such as methyl, methoxy, fluoro, chloro, and ester were well tolerated under the reaction conditions. We viewed this transformation as particularly attractive due to the versatility of the *N*–chloroamides, δ-brominated products, as well as the construction of the valuable pyrrolidines motif. The other performance of this unique halogenating system is currently under investigation.

Experimental Section

Unless otherwise noted, all reagents were purchased from commercial sources and used without further purification. All reactions were monitored by TLC and visualized by UV lamp (254 nm)/or by staining with a solution of 10 g phosphomolybdic acid and 100 mL EtOH followed by heating. Flash column chromatography was performed using 230-400 mesh silica gel. ^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra were obtained on Bruker AV-400 or Bruker AV-600 instrument in $CDCl_3$. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. Data for ^{1}H NMR spectra are reported as follows: chemical shift (ppm, referenced to protium; s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, m = multiplet, coupling constant (Hz), and integration). The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet. HR-ESI-MS spectra were recorded on a Bruker Esquire LC mass spectrometer using electrospray ionization.

Representative Procedure for Phthaloyl Peroxide Synthesis.[20a] To a solution of phthaloyl chloride (0.40 g, 1.5 mmol, 1.0 equiv) in DCM (25 mL) was added solid sodium percarbonate (Aldrich available H_2O_2: 20-30%) (0.34 g, 2.2 mmol, 1.5 equiv) in one portion. The heterogeneous reaction mixture was stirred vigorously for 3 h (rapid stirring is required). The reaction mixture was filtered through Celite and concentrated to provide the phthaloyl peroxide as a white solid.

CAUTION: Peroxides are dangerous and the synthesis and handling of the cyclic peroxides should be conducted by experienced practitioners of organic synthesis using appropriate safety equipment.

General Protection Procedure.[9a,11,14] A DCM solution (25 mL) of free amine (5 mmol) in round bottom flask was cooled to 0 °C. Triethylamine (0.76 mL, 5.5 mmol, 1.1 equiv) and dimethylaminopyridine (61.1 mg, 0.5 mmol, 0.1 equiv) were added into the above mixture. A DCM solution (5 mL) of sulfonyl chloride (5.5 mmol, 1.1 equiv) was then added slowly. The solution was allowed to slowly warm to room temperature overnight. Once complete, the reaction was quenched with 1M HCl. The aqueous layer was washed with DCM. Combined organic phases were dried with anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by flash column chromatography (silica gel, petroleum ether/EtOAc 10:1 to 2:1).

4-Methyl-N-(4-phenylbutyl)benzenesulfonamide ***(1a, 5a)***.[9a] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 7.9 Hz, 2H), 7.46 – 7.06 (m, 7H), 4.95 (t, *J* = 6.2 Hz, 1H), 2.96 (q, *J* = 6.7 Hz, 2H), 2.57 (t, *J* = 7.5 Hz, 2H), 2.44 (s, 3H), 1.65 – 1.58 (m, 2H), 1.55 – 1.49 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.4, 141.9, 136.9, 129.7, 128.4, 128.3, 127.1, 125.8, 43.0, 35.3, 29.1, 28.2, 21.6.

4-Nitro-N-(4-phenylbutyl)benzenesulfonamide ***(1b, 5b)***.[11] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 7.31 – 7.25 (m, 2H), 7.23 – 7.16 (m, 1H), 7.15 – 7.07 (m, 2H), 4.60 (brs, 1H, NH), 3.06 (q, *J* = 6.7 Hz, 2H), 2.60 (t, *J* = 7.3 Hz, 2H), 1.73 – 1.39 (m, 4H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 150.0, 146.0, 141.4, 128.4, 128.3, 128.2, 126.0, 124.4, 43.3, 35.2, 29.2, 28.1.

N-(4-phenylbutyl)methanesulfonamide ***(1c)***.[11] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.28 (m, 2H), 7.24 – 7.20 (m, 3H), 4.92 (brs, 1H, NH), 3.17 – 3.11 (m, 2H), 2.92 (s, 3H), 2.67 (t, *J* = 7.5 Hz, 2H), 1.79 – 1.44 (m, 4H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 142.0, 128.5, 128.4, 125.9, 43.1, 40.0, 35.4, 29.6, 28.3.

4-Methyl-N-pentylbenzenesulfonamide ***(1d, 3b)***.[11] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 4.64 (brt, 1H, NH), 2.92 (q, J = 6.8 Hz, 2H), 2.43 (s, 3H), 1.45 (t, J = 7.1 Hz, 2H), 1.32 – 1.17 (m, 4H), 0.97 – 0.72 (m, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.4, 137.1, 129.8, 127.2, 43.3, 29.3, 28.8, 22.2, 21.6, 14.0.

N-pentylmethanesulfonamide ***(1e)***. ^1H NMR (600 MHz, Chloroform-*d*) δ 4.89 (brs, 1H, NH), 3.05 (q, J = 6.5 Hz, 2H), 2.90 (s, 3H), 1.56 –1.47 (m, 2H), 1.35 – 1.25 (m, 4H), 0.84 (t, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 43.3, 39.9, 29.7, 28.7, 22.2, 14.0. HRMS (ES+) Calculated for $C_6H_{15}NNaO_2S^+$ $[M+Na]^+$: 188.0716, found: 188.0726.

N-heptyl-4-methylbenzenesulfonamide ***(1f, 5n)***. ^1H NMR (600 MHz, Chloroform-*d*) δ 7.77 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 5.02 (t, J = 6.3 Hz, 1H), 2.92 – 2.89 (m, 2H), 2.42 (s, 3H), 1.46 – 1.41 (m, 2H), 1.30 – 1.11 (m, 8H), 0.84 (t, J = 7.2 Hz, 3H).

$^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.2, 137.0, 129.7, 127.1, 43.2, 31.6, 29.5, 28.7, 26.5, 22.5, 21.5, 14.0. HRMS (ES+) Calculated for $C_{14}H_{23}NNaO_2S^+$ $[M+Na]^+$: 292.1342, found: 292.1349.

N-heptyl-4-nitrobenzenesulfonamide ***(1g, 3c, 5m)***. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, J = 8.8 Hz, 2H), 8.08 (d, J = 8.9 Hz, 2H), 4.83 (t, J = 6.1 Hz, 1H), 3.03 (q, J = 6.8 Hz, 2H), 1.53 – 1.46 (m, 2H), 1.29 – 1.23 (m, 8H), 0.87 (t, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 150.0, 146.0, 128.3, 124.4, 43.4, 31.6, 29.7, 28.7, 26.4, 22.5, 14.0. HRMS (ES+) Calculated for $C_{13}H_{21}N_2O_4S^+$ $[M+H]^+$: 301.1217, found: 301.1219.

2,4,6-Triisopropyl-N-pentylbenzenesulfonamide ***(1h)****.* ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.16 (s, 2H), 4.38 (brs, 1H, NH), 4.17 (q, *J* = 6.8 Hz, 2H), 2.96 (m, 2H), 2.90 (q, *J* = 6.9 Hz, 1H), 1.26 (m, 24H), 0.83 (m, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 152.7, 150.4, 132.4, 123.9, 42.9, 34.3, 29.7, 29.5, 28.9, 25.0, 23.7, 22.3, 14.0. HRMS (ES+) Calculated for $C_{20}H_{36}NO_2S^+$ [M+H]$^+$: 354.2461, found: 354.2462.

N-(2-ethylhexyl)-4-methylbenzenesulfonamide ***(1i)****.* ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.13 (t, *J* = 6.3 Hz, 1H), 2.82 (t, *J* = 6.0 Hz, 2H), 2.41 (s, 3H), 1.42 – 1.02 (m, 9H), 0.84 – 0.75 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.2, 137.0, 129.6, 127.1, 45.7, 39.1, 30.6, 28.6, 23.8, 22.9, 21.5, 14.0, 10.7. HRMS (ES+) Calculated for $C_{15}H_{26}NO_2S^+$ [M+H]$^+$: 284.1679, found: 284.1678.

N-(heptan-2-yl)-4-methylbenzenesulfonamide ***(1j)****.* ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.52 (d, *J* = 8.0 Hz, 1H), 3.45 – 3.18 (m, 1H), 2.44 (s, 3H), 1.52 – 0.93 (m, 11H), 0.83 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.1, 138.3, 129.6, 127.0, 50.0, 37.4, 31.4, 25.2, 22.5, 21.8, 21.5, 14.0. HRMS (ES+) Calculated for $C_{14}H_{23}NNaO_2S^+$ [M+Na]$^+$: 292.1342, found: 292.1342.

N-(4-methylhexan-2-yl)-4-nitrobenzenesulfonamide ***(1k)****.* ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.34 (d, *J* = 8.5 Hz, 2H), 8.10 (d, *J* = 6.6 Hz, 2H), 5.39 – 5.33 (m, 1H), 3.45 – 3.40 (m, 1H), 1.48 – 0.88 (m, 8H), 0.83 – 0.56 (m, 6H). Major isomer in ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 149.8, 147.4, 128.2, 124.4, 48.7, 44.7, 30.9, 29.3, 22.5, 18.9, 11.0. HRMS (ES+) Calculated for $C_{13}H_{21}N_2O_4S^+$ $[M+H]^+$: 301.1217, found: 301.1217.

*Methyl tosyl-L-isoleucinate (**1l**).*[23] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.07 (d, *J* = 10.0 Hz, 1H), 3.80 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.45 (s, 3H), 2.44 (s, 3H), 1.84 – 1.68 (m, 1H), 1.49 – 1.39 (m, 1H), 1.24 – 1.05 (m, 1H), 0.98 – 0.82 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 171.8, 143.6, 136.6, 129.5, 127.3, 60.2, 52.1, 38.4, 24.6, 21.5, 15.3, 11.2.

*1-((1S,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-N-pentylmethanesulfonamide (**1m**).* ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.16 (t, *J* = 6.1 Hz, 1H), 3.41 (d, *J* = 15.1 Hz, 1H), 3.21 – 3.10 (m, 2H), 2.92 (d, *J* = 15.1 Hz, 1H), 2.41 (d, *J* = 18.6 Hz, 1H), 2.28 – 2.21 (m, 1H), 2.15 (t, *J* = 4.6 Hz, 1H), 2.06 – 1.91 (m, 3H), 1.60 (q, *J* = 7.2 Hz, 2H), 1.50 – 1.33 (m, 1H), 1.42 – 1.25 (m, 4H), 1.04 (s, 3H), 0.93 – 0.90 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 217.1, 59.2, 49.2, 48.8, 43.8, 43.0, 42.8, 29.7, 28.8, 27.0, 26.7, 22.3, 19.9, 19.5, 14.0. HRMS (ES+) Calculated for $C_{15}H_{27}NNaO_3S^+$ $[M+Na]^+$: 324.1604, found: 324.1607.

*N-(2,2,2-trifluoroethyl)pentanamide (**1n**).* ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.68 (brs, 1H, NH), 3.92 (m, 2H), 2.25 (t, *J* = 7.6 Hz, 2H), 1.64 (m, 2H), 1.36 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 173.8, 124.1 (q, *J* = 233.2 Hz), 40.4 (q, *J* = 34.9 Hz), 36.0, 27.5, 22.2, 13.7. HRMS (ES+) Calculated for $C_7H_{13}F_3NO^+$ $[M+H]^+$: 184.0944, found: 184.0939.

*N-tosyltetradecanamide (**1o**).* ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.79 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 2.46 (s, 3H), 2.26 (t, *J* = 7.5 Hz, 2H), 1.58 – 1.54 (m, 2H), 1.43 – 1.10 (m, 21H), 0.90 (t, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 171.2, 145.1, 135.6, 129.6, 128.3, 36.3, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.2, 28.8, 24.3, 22.7, 21.7, 14.2. HRMS (ES+) Calculated for $C_{21}H_{36}NO_3S^+$ $[M+H]^+$: 382.2411, found: 382.2413.

*4-Nitro-N-pentylbenzenesulfonamide (**3a**).* ^1H NMR (400 MHz, DMSO-d_6) δ 8.48 – 8.35 (m, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 7.95 (brt, 1H, NH), 2.79 (m, 2H), 1.45 – 1.28 (m, 2H), 1.27 – 1.13 (m, 4H), 0.89 – 0.71 (m, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ 149.4, 146.2, 128.0, 124.5, 42.5, 28.6, 28.1, 21.5, 13.7. HRMS (ES+) Calculated for $C_{11}H_{16}N_2NaO_4S^+$ $[M+Na]^+$: 295.0723, found: 295.0730.

*N-(heptan-2-yl)-4-nitrobenzenesulfonamide (**3d**).* ^1H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.8 Hz, 2H), 8.10 (d, *J* = 8.8 Hz, 2H), 4.94 (d, *J* = 8.3 Hz, 1H), 3.43 – 3.36 (m, 1H), 1.39 (q, *J* = 6.8 Hz, 2H), 1.30 – 1.11 (m, 6H), 1.08 (d, *J* = 6.5 Hz, 3H), 0.82 (t, *J* = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.9, 147.2, 128.2, 124.3, 50.7, 37.4, 31.3, 25.2, 22.5, 21.9, 13.9. HRMS (ES+) Calculated for $C_{13}H_{20}N_2NaO_4S^+$ $[M+Na]^+$: 323.1036, found: 323.1035.

*4-Nitro-N-(nonan-5-yl)benzenesulfonamide (**3e**).*[14] ^1H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 2H), 4.73 (d, *J* = 8.7 Hz, 1H), 3.31 (q, *J* = 7.0 Hz, 1H), 1.53 – 1.25 (m, 4H), 1.23 – 0.92 (m, 8H), 0.80 (t, *J* = 6.7 Hz, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.8, 147.4, 128.2, 124.2, 54.8, 34.8, 27.4, 22.4, 13.9.

*4-Nitro-N-(tridecan-7-yl)benzenesulfonamide (**3f**).* ^1H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 2H), 4.72 (d, *J* = 8.7 Hz, 1H), 3.30 (q, *J* = 7.0 Hz, 1H), 1.53 – 1.10 (m, 20H), 0.85 (t, *J* = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.8, 147.4, 128.2, 124.2, 54.9, 35.2, 31.6, 29.0, 25.3, 22.5, 14.0. HRMS (ES+) Calculated for $C_{19}H_{33}N_2O_4S^+$ $[M+H]^+$: 385.2156, found: 385.2159.

*N-(heptan-4-yl)-4-nitrobenzenesulfonamide (**3g**).* ^1H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 2H), 4.80 (d, *J* = 8.7 Hz, 1H), 3.37 – 3.30 (m, 1H), 1.58 – 1.10 (m, 8H), 0.80 (t, *J* = 7.3 Hz, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.8, 147.4, 128.2, 124.3, 54.4, 37.3, 18.5, 13.8. HRMS (ES+) Calculated for $C_{13}H_{21}N_2O_4S^+$ $[M+H]^+$: 301.1217, found: 301.1219.

*N-(2-ethylhexyl)-4-nitrobenzenesulfonamide (**3h**).* ^1H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 7.0 Hz, 2H), 8.08 (d, *J* = 7.0 Hz, 2H), 5.16 (t, *J* = 6.3 Hz, 1H), 2.92 (t, *J* = 6.2 Hz, 2H), 1.42 – 1.14 (m, 9H), 0.88 – 0.75 (m, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 150.0, 145.9, 128.3, 124.4, 46.0, 39.2, 30.5, 28.6, 23.7, 22.8, 14.0, 10.6. HRMS (ES+) Calculated for $C_{14}H_{23}N_2O_4S^+$ $[M+H]^+$: 315.1373, found: 315.1377.

*Methyl 2-((4-nitrophenyl)sulfonamido)hexanoate (**3i**).* ^1H NMR (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 8.4 Hz, 2H), 8.05 (d, *J* = 8.4 Hz, 2H), 5.44 (d, *J* = 9.3 Hz, 1H), 4.01 (q, *J* = 7.6 Hz, 1H), 3.56 (s, 3H), 1.92 – 1.60 (m, 2H), 1.35 – 1.27 (m, 4H), 0.89 – 0.86 (m, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 171.9, 150.1, 145.7, 128.5, 124.3, 55.9, 52.7, 33.0, 27.0, 22.0, 13.8. HRMS (ES+) Calculated for $C_{13}H_{19}N_2O_6S^+$ $[M+H]^+$: 331.0959, found: 331.0957.

*4-Nitro-N-(1-phenylheptyl)benzenesulfonamide (**3j**).* ^1H NMR (400 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 8.8 Hz, 2H), 7.73 (d, *J* = 8.9 Hz, 2H), 7.13 – 7.08 (m, 3H), 7.04 – 6.95 (m, 2H), 5.53 (d, *J* = 7.7 Hz, 1H), 4.40 (q, *J* = 7.5 Hz, 1H), 1.90 – 1.60 (m, 2H), 1.34 – 1.14 (m, 8H), 0.85 (t, *J* = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.4, 146.5, 140.0, 128.5, 128.1, 127.7, 126.6, 123.7, 58.9, 37.5, 31.6, 28.7, 25.9, 22.5, 14.0. HRMS (ES+) Calculated for $C_{19}H_{25}N_2O_4S^+$ $[M+H]^+$: 377.1530, found: 377.1540.

4-Nitro-N-(1-phenylpentyl)benzenesulfonamide ***(3k)***. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 8.9 Hz, 2H), 7.72 (d, *J* = 8.9 Hz, 2H), 7.17 – 7.06 (m, 3H), 7.00 – 6.94 (m, 2H), 5.34 (d, *J* = 7.6 Hz, 1H), 4.41 (q, *J* = 7.5 Hz, 1H), 1.89 – 1.65 (m, 2H), 1.36 – 1.10 (m, 4H), 0.85 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.4, 146.5, 140.0, 128.5, 128.1, 127.7, 126.6, 123.7, 58.9, 37.2, 28.0, 22.2, 13.8. HRMS (ES+) Calculated for $C_{17}H_{21}N_2O_4S^+$ $[M+H]^+$: 349.1217, found: 349.1219.

N-(1-(4-fluorophenyl)pentyl)-4-nitrobenzenesulfonamide ***(3l)***. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.9 Hz, 2H), 7.78 (d, *J* = 8.9 Hz, 2H), 7.00 (dd, *J* = 8.6, 5.3 Hz, 2H), 6.84 (t, *J* = 8.6 Hz, 2H), 5.46 (d, *J* = 7.3 Hz, 1H), 4.39 (q, *J* = 7.4 Hz, 1H), 1.85 – 1.62 (m, 2H), 1.35 – 1.03 (m, 4H), 0.83 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 162.0 (d, *J* = 246.6 Hz), 149.6, 146.5, 136.1, 128.2 (d, *J* = 8.0 Hz), 128.2, 123.8, 115.4 (d, *J* = 20.9 Hz), 58.1, 37.2, 28.0, 22.1, 13.8. ^{19}F NMR (376 MHz, Chloroform-*d*) *δ* -113.8. HRMS (ES+) Calculated for $C_{17}H_{20}FN_2O_4S^+$ $[M+H]^+$: 349.1217, found: 349.1219.

N-(1-(4-chlorophenyl)pentyl)-4-nitrobenzenesulfonamide ***(3m)***. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 6.96 (d, *J* = 8.5 Hz, 2H), 5.52 (d, *J* = 7.3 Hz, 1H), 4.37 (q, *J* = 7.4 Hz, 1H), 1.86 – 1.60 (m, 2H), 1.33 – 1.04 (m, 4H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 149.6, 146.4, 138.7, 133.7, 128.7, 128.2, 128.0, 123.9, 58.2, 37.0, 28.0, 22.1, 13.8. HRMS (ES+) Calculated for $C_{17}H_{20}ClN_2O_4S^+$ $[M+H]^+$: 383.0827, found: 383.0837.

N-(1-([1,1'-biphenyl]-4-yl)hexyl)-4-nitrobenzenesulfonamide ***(3n)***. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.8 Hz, 2H), 7.76 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 4.3 Hz, 4H), 7.42 – 7.32 (m, 3H), 7.06 (d, *J* = 8.2 Hz, 2H), 5.26 (t, *J* = 6.5 Hz, 1H), 4.46 (q, *J* = 7.4 Hz, 1H), 1.88 – 1.68 (m, 2H), 1.41 – 1.16 (m, 6H), 0.91 – 0.78 (m, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 149.5, 146.6, 140.9, 140.1, 138.9, 128.9, 128.2, 127.6, 127.2, 127.1, 126.9, 123.7, 58.6, 37.3, 31.2, 25.6, 22.4, 14.0. HRMS (ES+) Calculated for $C_{24}H_{27}N_2O_4S^+$ $[M+H]^+$: 439.1687, found: 439.1688.

N-(2,2-dimethyl-4-phenylbutyl)-4-methylbenzenesulfonamide ***(5c)***.[9a] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.70 (m, 2H), 7.38 – 7.05 (m, 7H), 4.73 (t, *J* = 6.9 Hz, 1H), 2.76 (d, *J* = 6.9 Hz, 2H), 2.62 – 2.46 (m, 2H), 2.44 (s, 3H), 1.59 – 1.47 (m, 2H), 0.95 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.3, 142.6, 136.9, 129.8, 128.4, 128.3, 127.1, 125.7, 52.8, 41.5, 34.0, 30.3, 25.0, 21.6.

N-(4-(4-fluorophenyl)-2,2-dimethylbutyl)-4-methylbenzenesulfonamide ***(5d)***. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.10 (dd, *J* = 8.2, 5.5 Hz, 2H), 6.93 (t, *J* = 8.5 Hz, 2H), 5.22 – 4.99 (brm, NH), 2.74 (d, *J* =

6.8 Hz, 2H), 2.54 – 2.45 (m, 2H), 2.43 (s, 3H), 1.65 – 1.41 (m, 2H), 0.93 (s, 6H). $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 161.1 (d, *J* = 251.6 Hz), 143.3, 138.2 (d, *J* =2.6 Hz), 136.9, 129.7, 129.6 (d, *J* = 7.6 Hz), 127.0, 115.0 (d, *J* = 20.0 Hz), 52.7, 41.5, 34.0, 29.4, 25.0, 21.5. HRMS (ES+) Calculated for $C_{19}H_{25}FNO_2S^+$ $[M+H]^+$: 350.1585, found: 350.1590.

N-(4-(4-chlorophenyl)-2,2-dimethylbutyl)-4-methylbenzenesulfonamide ***(5e)***.[9a] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.28 (m, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 4.85 (brt, *J* = 6.9 Hz, NH), 2.74 (d, *J* = 6.8 Hz, 2H), 2.52 – 2.46 (m, 2H), 2.44 (s, 3H), 1.57 – 1.42 (m, 2H), 0.93 (s, 6H). $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.4, 141.1, 136.9, 131.3, 129.8, 129.7, 128.4, 127.0, 52.7, 41.3, 34.0, 29.6, 25.0, 21.6.

N-(2,2-dimethyl-4-(p-tolyl)butyl)-4-methylbenzenesulfonamide ***(5f)***.[9a] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.39 – 7.25 (m, 2H), 7.18 – 6.95 (m, 4H), 4.64 (d, *J* = 6.7 Hz, 1H), 2.75 (d, *J* = 6.9 Hz, 2H), 2.51 – 2.38 (m, 5H), 2.34 (s, 3H), 1.55 – 1.41 (m, 2H), 0.94 (s, 6H). $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.3, 139.5, 137.0, 135.2, 129.7, 129.1, 128.2, 127.1, 52.8, 41.7, 34.0, 29.8, 25.0, 21.6, 21.0.

N-(4-(4-methoxyphenyl)-2,2-dimethylbutyl)-4-methylbenzenesulfonamide ***(5g)***.[9a] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.73 (t, *J* = 6.9 Hz, 1H), 3.80 (s, 3H), 2.75 (d, *J* = 6.9 Hz, 2H), 2.52 – 2.38 (m, 5H), 1.57 – 1.41 (m, 2H), 0.94 (s, 6H).

$^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 157.7, 143.3, 137.0, 134.6, 129.7, 129.2, 127.1, 113.8, 55.3, 52.8, 41.7, 34.0, 29.3, 25.0, 21.6.

4-Methyl-N-((1-phenethylcyclohexyl)methyl)benzenesulfonamide ***(5h)***.[9a] ^1H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.8 Hz, 2H), 7.40 – 7.03 (m, 7H), 4.79 – 4.63 (m, 1H), 2.85 (d, *J* = 6.8 Hz, 2H), 2.44 (s, 5H), 1.65 – 1.55 (m, 2H), 1.55 – 1.19 (m, 10H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.3, 142.8, 136.9, 129.8, 128.4, 128.4, 127.1, 125.7, 36.1, 33.5, 29.2, 26.1, 21.6, 21.2.

4-Methyl-N-(2,2,4-trimethylpentyl)benzenesulfonamide ***(5i)***.[9a] ^1H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.55 (t, *J* = 6.8 Hz, 1H), 2.69 (d, *J* = 6.8 Hz, 2H), 2.45 (s, 3H), 1.71 – 1.55 (m, 1H), 1.12 (d, *J* = 5.5 Hz, 2H), 0.89 (s, 6H), 0.88 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.3, 137.0, 129.7, 127.1, 53.9, 48.3, 34.4, 25.3, 25.3, 24.0, 21.5.

N-(2,2-dimethylhex-5-en-1-yl)-4-methylbenzenesulfonamide ***(5j)***. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 3H), 5.81 – 5.71 (m, 1H), 5.05 – 4.87 (m, 2H), 4.74 (t, *J* = 6.8 Hz, 1H), 2.70 (d, *J* = 6.8 Hz, 2H), 2.44 (s, 3H), 1.98 – 1.89 (m, 2H), 1.37 – 1.25 (m, 2H), 0.87 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.3, 138.9, 137.0, 129.7, 127.1, 114.3, 52.9, 38.5, 33.8, 28.1, 24.8, 21.5. HRMS (ES+) Calculated for $C_{15}H_{24}NO_2S^+$ $[M+H]^+$: 282.1522, found: 282.1522.

N-((1S,2R)-2-(benzyloxy)-2,3-dihydro-1H-inden-1-yl)-4-methylbenzenesulfonamide ***(5k)***. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.47 – 7.13 (m, 11H), 5.61 (d, *J* = 9.1 Hz, 1H), 4.90 – 4.86 (m, 1H), 4.48 (d, *J* = 11.6 Hz, 1H), 4.20 (d, *J* = 11.6 Hz, 1H), 4.02 – 3.99 (m, 1H), 3.08 (d, *J* = 16.6, 1H), 2.91 (dd, *J* = 16.6, 4.9

Hz, 1H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 142.3, 139.4, 137.9, 137.0, 136.4, 128.7, 127.4, 127.2, 126.8, 126.6, 126.0, 126.0, 123.9, 123.6, 78.0, 70.2, 59.0, 34.9, 20.5. HRMS (ES+) Calculated for $C_{23}H_{24}NO_3S^+$ $[M+H]^+$: 394.1471, found: 394.1478.

*1-((1S,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-N-(4-phenylbutyl)methanesulfonamide (**5l**).* ^1H NMR (600 MHz, Chloroform-*d*) δ 7.33 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 5.17 (d, *J* = 6.4 Hz, 1H), 3.37 (d, *J* = 15.1 Hz, 1H), 3.22 – 3.10 (m, 2H), 2.90 (d, *J* = 15.0 Hz, 1H), 2.65 (t, *J* = 7.7 Hz, 2H), 2.39 (d, *J* = 18.5 Hz, 1H), 2.24 – 2.18 (m, 1H), 2.17 – 1.86 (m, 4H), 1.74 – 1.69 (m, 2H), 1.66 – 1.62 (m, 2H), 1.45 (dt, *J* = 12.5, 6.2 Hz, 1H), 1.01 (s, 3H), 0.90 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 217.2, 142.0, 128.4, 128.4, 125.8, 59.3, 49.3, 48.9, 43.6, 43.0, 42.8, 35.4, 29.6, 28.4, 27.0, 26.7, 19.9, 19.5. HRMS (ES+) Calculated for $C_{20}H_{29}NNaO_3S^+$ $[M+Na]^+$: 386.1760, found: 386.1769.

General Procedure for Synthesis of N-Cl Sulfonamides. To a mixture of an appropriate sulfonamide (0.1 mmol) and PPO (19.7 mg, 0.12 mmol, 1.2 equiv) in a standard Schlenk tube, TBACl (33.3 mg, 0.12 mmol, 1.2 equiv) was added. The mixture was evacuated and backfilled with N_2 (3 times). Then, the solvent DCE (2 mL) was added via syringe, and the mixture was stirred for 12 h. Upon completion, the solvents were removed under reduced pressure and the resulting mixture was purified by preparative TLC using petroleum ether/EtOAc as the eluent.

*N-chloro-4-methyl-N-(4-phenylbutyl)benzenesulfonamide **(2a)**.*[23] Colorless oil (31.1 mg, 92% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.73 – 7.71 (m, 2H), 7.29 (d, *J*

= 7.9 Hz, 2H), 7.21 – 7.18 (m, 2H), 7.12 – 7.09 (m, 3H), 3.15 (t, *J* = 6.5 Hz, 2H), 2.56 (t, *J* = 6.3 Hz, 2H), 2.38 (s, 3H), 1.79 – 1.54 (m, 4H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 145.4, 141.8, 129.8, 129.7, 129.6, 128.4, 128.4, 125.9, 56.4, 35.2, 27.7, 26.5, 21.8. HRMS (ES+) Calculated for $C_{17}H_{21}ClNO_2S^+$ $[M+H]^+$: 338.0976, found: 338.0970.

N-chloro-4-nitro-N-(4-phenylbutyl)benzenesulfonamide ***(2b)***.[23] White solid (35.0 mg, 95% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 8.41 (d, *J* = 8.8 Hz, 2H), 8.10 (d, *J* = 8.8 Hz, 2H), 7.35 – 7.12 (m, 5H), 3.30 – 3.28 (m, 2H), 2.67 – 2.65 (m, 2H), 1.74 – 1.71 (m, 4H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 151.0, 141.5, 138.8, 130.7, 128.4, 128.4, 126.0, 124.2, 56.5, 35.1, 27.6, 26.4. HRMS (ES+) Calculated for $C_{16}H_{17}ClN_2NaO_4S^+$ $[M+Na]^+$: 391.0490, found: 391.0493.

N-chloro-N-(4-phenylbutyl)methanesulfonamide ***(2c)***. Colorless oil (21.7 mg, 83% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.22 – 7.19 (m, 2H), 7.12 – 7.10 (m, 3H), 3.36 (t, *J* = 6.6 Hz, 2H), 2.97 (s, 3H), 2.58 (t, *J* = 7.5 Hz, 2H), 1.78 – 1.57 (m, 4H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 141.7, 128.4, 126.0, 55.6, 35.2, 33.8, 27.7, 26.6.

HRMS (ES+) Calculated for $C_{11}H_{16}ClNNaO_2S^+$ $[M+Na]^+$: 284.0482, found: 284.0489.

N-chloro-4-methyl-N-pentylbenzenesulfonamide ***(2d)***.[23] Colorless oil (23.4 mg, 85% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.45 – 7.34 (d, *J* = 8.4 Hz, 2H), 3.22 (t, *J* = 6.9 Hz, 2H), 2.47 (s, 3H), 1.69– 1.65 (m, 2H), 1.42 – 1.28 (m, 4H), 0.90 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-*d*) δ 145.4, 130.1, 129.8, 129.7, 56.8, 28.3, 26.8, 22.3, 21.8, 14.1. HRMS (ES+) Calculated for $C_{12}H_{18}ClNNaO_2S^+$ $[M+Na]^+$: 298.0639, found: 298.0633.

*N-chloro-N-pentylmethanesulfonamide (**2e**).* Colorless oil (16.6 mg, 83% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 3.41 (t, *J* = 7.0 Hz, 2H), 3.06 (s, 3H), 1.75 – 1.73 (m, 2H), 1.36 – 1.34 (m, 4H), 0.90 (t, *J* = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 55.9, 33.8, 28.1, 26.8, 22.2, 13.9. HRMS (ES+) Calculated for $C_6H_{14}ClNNaO_2S^+$ $[M+Na]^+$: 222.0326, found: 222.0332.

*N-chloro-N-heptyl-4-methylbenzenesulfonamide (**2f**).* Colorless oil (28.2 mg, 93% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 3.21 (t, *J* = 6.9 Hz, 2H), 2.47 (s, 3H), 1.67 (p, *J* = 7.0 Hz, 2H), 1.39 – 1.10 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 145.3, 129.8, 129.7, 129.6, 56.7, 31.7, 28.8, 27.0, 26.0, 22.6, 21.7, 14.1. HRMS (ES+) Calculated for $C_{14}H_{22}ClNNaO_2S^+$ $[M+Na]^+$: 326.0952, found: 326.0947.

*N-chloro-N-heptyl-4-nitrobenzenesulfonamide (**2g**).* colorless oil (30.0 mg, 90% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 8.46 (d, *J* = 8.4 Hz, 2H), 8.16 (d, *J* = 8.4 Hz, 2H), 3.30 (t, *J* = 6.9 Hz, 2H), 1.71 (t, *J* = 7.1 Hz, 2H), 1.43 – 1.25 (m, 8H), 0.90 (t, *J* = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 151.0, 138.8, 130.7, 124.2, 56.7, 31.6, 28.7, 26.9, 25.9, 22.5, 14.1. HRMS (ES+) Calculated for $C_{13}H_{19}ClN_2NaO_4S^+$ $[M+Na]^+$: 357.0646, found: 357.0647.

*N-chloro-2,4,6-triisopropyl-N-pentylbenzenesulfonamide (**2h**).* Colorless oil (34.1 mg, 88% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.12 (s, 2H), 4.15 – 4.10 (m, 2H), 3.46 (t, *J* = 6.9 Hz, 2H), 2.87 – 2.82 (m, 1H), 1.72 – 1.68 (m, 2H), 1.34 – 1.24 (m, 4H), 1.19 (d, *J* = 7.2 Hz, 18H), 0.83 (t, *J* = 6.8, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 154.4, 152.8, 127.9, 124.1, 52.4, 34.3, 29.8, 28.3, 26.5, 24.8, 23.5, 22.2, 14.0. HRMS (ES+) Calculated for $C_{20}H_{34}ClNNaO_2S^+$ $[M+Na]^+$: 410.1891, found: 410.1890.

N-chloro-N-(2-ethylhexyl)-4-methylbenzenesulfonamide ***(2i)***. Colorless oil (28.9 mg, 91% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.06 – 2.94 (m, 2H), 2.40 (s, 3H), 1.69 – 1.65 (m, 1H), 1.35 – 1.13 (m, 8H), 0.82 – 0.78 (m, 6H). $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 144.2, 128.9, 128.7, 128.5, 59.2, 35.6, 29.0, 27.3, 22.3, 21.9, 20.7, 13.0, 9.2. HRMS (ES+) Calculated for $C_{15}H_{24}ClNNaO_2S^+$ $[M+Na]^+$: 340.1108, found: 340.1111.

N-chloro-N-(heptan-2-yl)-4-methylbenzenesulfonamide ***(2j)***. Colorless oil (28.6 mg, 94% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 4.32 – 4.27 (m, 1H), 2.47 (s, 3H), 1.73 – 1.51 (m, 2H), 1.40 – 1.25 (m, 6H), 1.05 (d, *J* = 6.3 Hz, 3H), 1.01 – 0.76 (m, 3H). $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 144.9, 133.8, 129.6, 128.9, 58.8, 34.4, 31.3, 25.7, 22.5, 21.7, 17.4, 14.0. HRMS (ES+) Calculated for $C_{14}H_{22}ClNNaO_2S^+$ $[M+Na]^+$: 326.0952, found: 326.0958.

N-chloro-N-(4-methylhexan-2-yl)-4-nitrobenzenesulfonamide ***(2k)***. Colorless oil (30.1 mg, 90% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 8.9, 1.4 Hz, 2H), 8.27 – 8.11 (m, 2H), 4.59 – 4.44 (m, 1H), 1.54 – 0.80 (m, 14H). One isomer in $^{13}C\{^{1}H\}$ NMR (150 MHz, Chloroform-*d*) δ 150.7, 142.6, 130.1, 124.2, 57.2, 41.2, 30.8, 29.8, 19.2, 18.0, 11.3. HRMS (ES+) Calculated for $C_{13}H_{19}ClN_2NaO_4S^+$ $[M+Na]^+$: 357.0646, found: 357.0650.

*Methyl N-chloro-N-tosyl-L-isoleucinate (**2l**).*[23] Colorless oil (30.0 mg, 90% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 4.43 (d, *J* = 9.9 Hz, 1H), 3.48 (s, 3H), 2.48 (s, 3H), 2.17 – 2.04 (m, 1H), 1.72 – 1.75 (m, 1H), 1.38 – 1.22 (m, 1H), 1.02 – 0.81 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 168.5, 145.1, 132.4, 129.4, 129.1, 66.2, 51.6, 34.2, 24.7, 21.7, 15.0, 10.0. HRMS (ES+) Calculated for $C_{14}H_{20}ClNNaO_4S^+$ $[M+Na]^+$: 356.0694, found: 356.0695.

*N-chloro-1-((1S,4S)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-N-pentylmethanesulfonamide (**2m**).* Colorless oil (21.5 mg, 64% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.68 (d, *J* = 14.6 Hz, 1H), 3.60 – 3.53 (m, 1H), 3.48 – 3.41 (m, 1H), 3.17 (d, *J* = 14.6 Hz, 1H), 2.61 – 2.35 (m, 2H), 2.20 – 1.95 (m, 3H), 1.81 – 1.68 (m, 3H), 1.55 – 1.32 (m, 6H), 1.18 (s, 3H), 0.94 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 214.4, 58.2, 56.0, 47.9, 43.1, 42.9, 42.5, 28.1, 27.0, 26.9, 25.2, 22.2, 20.1, 19.8, 13.9. HRMS (ES+) Calculated for $C_{16}H_{28}ClNNaO_3S^+$ $[M+Na]^+$: 372.1371, found: 372.1375.

General Procedure for δ-C(sp^3)-H Bromination of Sulfonamides. To a mixture of an appropriate sulfonamide (0.1 mmol) and 3,4-dichlorophthaloyl peroxide (28.0 mg, 0.12 mmol, 1.2 equiv) in a standard Schlenk tube, TBAB (38.7 mg, 0.12 mmol, 1.2 equiv) was added. The mixture was evacuated and backfilled with N_2 (3 times). Then, the solvent DCE (2 mL) and AcOH (0.2 mL) were added via syringe, and the mixture was irradiated by blue LED for 12 h. Upon completion, the reaction mixture was diluted with 10 mL ethyl acetate and filtered through a pad of celite. The solvents were removed under reduced pressure and the resulting mixture was purified by flash column chromatography using petroleum ether/EtOAc as the eluent.

*N-(4-bromopentyl)-4-nitrobenzenesulfonamide (**4a**).* Pale yellow oil (22.0 mg, 63% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 8.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 4.92 (t, *J* = 6.2 Hz, 1H), 4.12 – 4.02 (m, 1H), 3.07 (q, *J* = 6.5 Hz, 2H), 1.91 – 1.55 (m, 7H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 150.1, 145.8, 128.3, 124.5, 50.5, 42.7, 37.6, 28.0, 26.5. HRMS (ES+) Calculated for $C_{11}H_{16}BrN_2O_4S^+$ $[M+H]^+$: 351.0009, found: 351.0012.

*N-(4-bromopentyl)-4-methylbenzenesulfonamide (**4b**).* Pale yellow oil (20.5 mg, 64% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.66 (brt, 1H, NH), 4.13 – 3.96 (m, 1H), 2.96 (q, *J* = 6.6 Hz, 2H), 2.43 (s, 3H), 1.65 (m, 7H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.6, 136.9, 129.9, 127.2, 50.9, 42.6, 37.8, 28.0, 26.6, 21.7. HRMS (ES+) Calculated for $C_{12}H_{19}BrNO_2S^+$ $[M+H]^+$: 320.0314, found: 320.0314.

*N-(4-bromoheptyl)-4-nitrobenzenesulfonamide (**4c**).* Pale yellow oil in (24.6 mg, 65% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 8.3 Hz, 2H), 8.08 (d, *J* = 7.8 Hz, 2H), 4.76 (s, 1H), 4.02 – 3.95 (m, 1H), 3.09 (q, *J* = 6.6 Hz, 2H), 1.87 – 1.67 (m, 6H), 1.60 – 1.40 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 150.1, 145.8, 128.3, 124.5, 57.0, 42.8, 41.3, 35.7, 27.8, 20.8, 13.4.

HRMS (ES+) Calculated for $C_{13}H_{19}BrN_2NaO_4S^+$ $[M+Na]^+$: 401.0141, found: 401.0142.

N-(5-bromoheptan-2-yl)-4-nitrobenzenesulfonamide ***(4d)***. A mixture of diastereomers **4d** (1:1) was obtained as pale yellow oil (20.8 mg, 55% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 8.4 Hz, 2H), 8.10 (d, *J* = 8.4 Hz, 2H), 4.70 – 4.49 (m, 1H), 3.93 – 3.88 (m, 1H), 3.47 – 3.46 (m, 1H), 1.93 – 1.54 (m, 6H), 1.22 – 0.95 (m, 6H). One isomer in $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 150.0, 147.1, 128.2, 124.5, 59.4, 50.4, 35.5, 34.8, 32.2, 22.0, 12.1. HRMS (ES+) Calculated for $C_{13}H_{20}BrN_2O_4S^+$ $[M+H]^+$: 379.0322, found: 379.0328.

N-(2-bromononan-5-yl)-4-nitrobenzenesulfonamide ***(4e)***.[14] A mixture of diastereomers **4e** (1:1) was obtained as colorless oil (14.6 mg, 36% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 8.3 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 2H), 4.79 – 4.55 (m, 1H), 4.09 – 4.00 (m, 1H), 3.35 (q, *J* = 6.9 Hz, 1H), 1.86 – 1.04 (m, 13H), 0.79 (q, *J* = 6.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.9, 147.2, 128.2, 124.4, 54.5, 54.2, 51.0, 51.0, 36.9, 36.7, 35.2, 34.9, 33.5, 33.4, 27.6, 27.4, 26.6, 26.4, 22.3, 22.3, 13.8. HRMS (ES+) Calculated for $C_{15}H_{24}BrN_2O_4S^+$ $[M+H]^+$: 407.0635, found: 407.0636.

N-(4-bromotridecan-7-yl)-4-nitrobenzenesulfonamide ***(4f)***. A mixture of diastereomers **4f** (1:1) was obtained as colorless oil (16.2 mg, 35% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 8.3 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 2H), 4.61 (t, *J* = 9.9 Hz, 1H), 4.06 – 3.85 (m, 1H), 3.35 (q, *J* = 6.8 Hz, 1H), 1.89 – 1.04 (m, 18H), 0.92 (t, *J* = 7.5 Hz, 3H), 0.85 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.9, 147.2, 147.2, 128.2, 124.4, 57.5, 54.6, 54.3, 41.4, 41.2, 35.6, 35.2, 35.0, 34.8, 33.3, 33.3, 31.6, 28.9, 28.9, 25.4, 25.3, 22.5, 22.5, 20.8, 14.0, 13.4. HRMS (ES+) Calculated for $C_{19}H_{32}BrN_2O_4S^+$ $[M+H]^+$: 463.1261, found: 463.1258.

N-(1-bromoheptan-4-yl)-4-nitrobenzenesulfonamide ***(4g)***. A mixture of diastereomers **4g** (1:1) was obtained as colorless oil (14.4 mg, 38% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.5 Hz, 2H), 4.73 (d, *J* = 8.9 Hz, 1H), 3.36 (t, *J* = 6.5 Hz, 2H), 1.96 – 1.04 (m, 9H), 0.80 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 150.0, 147.1, 128.2, 124.4, 53.9, 37.4, 33.8, 33.2, 28.5, 18.6, 13.7. HRMS (ES+) Calculated for $C_{13}H_{20}BrN_2O_4S^+$ $[M+H]^+$: 379.0322, found: 379.0321.

N-(2-(2-bromoethyl)hexyl)-4-nitrobenzenesulfonamide ***(4h)*** *and* *N-(4-bromo-2-ethylhexyl)-4-nitrobenzenesulfonamide* ***(4h′)***. A product mixture **4h/4h′** (1:2) was obtained as pale yellow oil (19.2 mg, 49% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.7 Hz, 2H), 5.01 – 4.76 (m, 1H), 4.10 – 3.89 (m, 1H), 3.19 (t, *J* = 6.0 Hz, 1H), 3.07 – 2.92 (m, 1H), 2.44 – 2.21 (m, 1H), 2.00 – 1.13 (m, 8H), 1.07 – 1.02 (m, 2H), 0.94 – 0.79 (m, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 150.1, 145.8, 128.4, 128.3, 124.5, 58.0, 57.7, 51.2, 46.1, 45.9, 44.9, 44.8, 40.5, 40.0, 38.8, 37.7, 37.6, 32.9, 32.8, 25.7, 24.7, 23.0, 12.4, 12.1, 12.0, 10.9, 10.8, 10.2. HRMS (ES+) Calculated for $C_{14}H_{22}BrN_2O_4S^+$ $[M+H]^+$: 393.0478, found: 393.0480.

Methyl 5-bromo-2-((4-nitrophenyl)sulfonamido)hexanoate ***(4i)***.[14] A mixture of diastereomers **4i** (1:1) was obtained as white solid (10.6 mg，26% yield). ^{1}H NMR

(400 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 8.8 Hz, 2H), 8.05 (dd, *J* = 8.7, 1.7 Hz, 2H), 5.43 (t, *J* = 8.2 Hz, 1H), 4.18 – 3.96 (m, 2H), 3.59 (d, *J* = 3.9 Hz, 3H), 2.16 – 1.65 (m, 7H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 171.5, 171.4, 150.2, 145.4, 145.3, 128.5, 124.4, 55.5, 55.1, 53.0, 50.1, 49.9, 36.4, 36.0, 31.5, 31.6, 26.6, 26.4. HRMS (ES+) Calculated for $C_{13}H_{18}BrN_2O_6S^+$ $[M+H]^+$: 409.0063, found: 409.0064.

N-(4-bromo-1-phenylheptyl)-4-nitrobenzenesulfonamide ***(4j)***. A mixture of diastereomers **4j** (1:1) was obtained as pale yellow oil (22.3 mg, 49% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 8.19 – 8.01 (m, 2H), 7.75 – 7.72 (m, 2H), 7.21 – 7.07 (m, 3H), 7.06 – 6.90 (m, 2H), 5.21 (d, *J* = 7.9 Hz, 1H), 4.53 – 4.39 (m, 1H), 4.10 – 3.94 (m, 1H), 2.20 – 1.31 (m, 8H), 0.91 (q, *J* = 7.2 Hz, 3H). One isomer in $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.5, 146.4, 139.6, 128.7, 128.2, 128.1, 126.5, 123.8, 58.5, 57.0, 41.3, 35.6, 35.4, 20.8, 13.4. HRMS (ES+) Calculated for $C_{19}H_{24}BrN_2O_4S^+$ $[M+H]^+$: 455.0635, found: 455.0635.

N-(4-bromo-1-phenylpentyl)-4-nitrobenzenesulfonamide ***(4k)***. A mixture of diastereomers **4k** (1:1) was obtained as pale yellow oil (20.1 mg, 47% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dd, *J* = 8.8, 4.8 Hz, 2H), 7.73 (dd, *J* = 8.9, 2.5 Hz, 2H), 7.23 – 7.08 (m, 3H), 7.04 – 6.91 (m, 2H), 5.26 (d, *J* = 7.9 Hz, 1H), 4.50 – 4.35 (m, 1H), 4.13 – 4.06 (m, 1H), 2.20 – 1.53 (m, 7H). One isomer in $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.5, 146.3, 139.3, 128.7, 128.2, 128.1, 126.5, 123.8, 58.5, 50.5, 37.2, 35.5, 26.4. HRMS (ES+) Calculated for $C_{17}H_{20}BrN_2O_4S^+$ $[M+H]^+$: 427.0322, found: 427.0328.

*N-(4-bromo-1-(4-fluorophenyl)pentyl)- 4-nitrobenzenesulfonamide (**4l**).* A mixture of diastereomers **4l** (1:1) was obtained as pale yellow oil (24.5 mg, 55% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (dd, *J* = 8.8, 4.4 Hz, 2H), 7.79 (dd, *J* = 8.9, 2.8 Hz, 2H), 7.03 – 6.99 (m, 2H), 6.94 – 6.79 (m, 2H), 5.26 (d, *J* = 7.5 Hz, 1H), 4.52 – 4.38 (m, 1H), 4.11 – 4.04 (m, 1H), 2.09 – 1.52 (m, 7H). One isomer in ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 162.2 (d, *J* = 246.9 Hz), 149.7, 146.4, 135.4 (d, *J* = 49.5 Hz), 128.2 (d, *J* = 8.1 Hz), 128.2, 123.9, 115.7 (d, *J* = 7.0 Hz), 57.7, 50.4, 37.2, 35.8, 26.5. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.0, -113.1. HRMS (ES+) Calculated for $C_{17}H_{19}BrFN_2O_4S^+$ [M+H]$^+$: 445.0227, found: 445.0227.

*N-(4-bromo-1-(4-chlorophenyl)pentyl)- 4-nitrobenzenesulfonamide (**4m**).*[14] A mixture of diastereomers **4m** (1:1) was obtained as pale yellow oil (33.7 mg, 73% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (dd, *J* = 8.8, 4.0 Hz, 2H), 7.78 (dd, *J* = 8.9, 2.4 Hz, 2H), 7.15 (dd, *J* = 8.4, 4.5 Hz, 2H), 6.97 (dd, *J* = 8.4, 3.3 Hz, 2H), 5.26 (d, *J* = 7.5 Hz, 1H), 4.45 – 4.39 (m, 1H), 4.12 – 4.04 (m, 1H), 2.11 – 1.54 (m, 7H). One isomer in ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 149.7, 146.3, 138.2, 134.1, 128.9, 128.2, 128.0, 124.0, 57.7, 50.3, 37.1, 35.6, 26.5. HRMS (ES+) Calculated for $C_{17}H_{19}BrClN_2O_4S^+$ [M+H]$^+$: 460.9932, found: 460.9935.

*N-(1-([1,1'-biphenyl]-4-yl)-4-bromohexyl)-4-nitrobenzenesulfonamide (**4n**).* A mixture of diastereomers **4n** (2:1) was obtained as pale yellow oil (32.6 mg, 63% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 – 8.03 (m, 2H), 7.78 (dd, *J* = 8.9, 2.7 Hz, 2H), 7.52 – 7.31 (m, 7H), 7.07 (dd, *J* = 8.3, 2.8 Hz, 2H), 5.32 (d, *J* = 7.6 Hz, 1H), 4.56 – 4.41 (m, 1H), 3.99 – 3.93 (m, 1H), 2.27 – 1.65 (m, 6H), 1.05 – 0.98 (m, 3H). Major isomer in $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 149.6, 146.4, 141.2, 140.0, 138.5, 138.2, 129.0, 128.2, 127.7, 127.4, 127.0, 123.8, 59.1, 58.2, 35.1, 35.0, 32.2, 12.1. HRMS (ES+) Calculated for $C_{24}H_{26}BrN_2O_4S^+$ $[M+H]^+$: 517.0791, found: 517.0797.

General Procedure for δ-C(sp^3)-H Iodization and Cyclization of Sulfonamides. To a mixture of an appropriate sulfonamide (0.1 mmol), PPO (32.8 mg, 0.2 mmol, 2 equiv) and NaOAc (9.8 mg, 0.12 mmol, 1.2 equiv) in a standard Schlenk tube, CsI (31.2 mg, 0.12 mmol, 1.2 equiv) was added. The mixture was evacuated and backfilled with N_2 (3 times). Then, the solvent DCE (2 mL) was added via syringe, and the mixture was irradiated by blue LED for 24 h. Upon completion, the reaction mixture was diluted with 10 mL ethyl acetate and filtered through a pad of celite. The solvents were removed under reduced pressure and the resulting mixture was purified by flash column chromatography using petroleum ether/EtOAc as the eluent.

*2-Phenyl-1-tosylpyrrolidine (**6a**).*[11] Yellow solid (29.9 mg, 99% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.35 – 7.14 (m, 7H), 4.86 – 4.66 (m, 1H), 3.68 – 3.55(m, 1H), 3.47 – 3.36(m, 1H), 2.42 (s, 3H), 2.11 – 1.48 (m, 4H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-*d*) δ 143.4, 143.2, 135.2, 129.7, 128.4, 127.6, 127.1, 126.2, 63.4, 49.5, 35.9, 24.1, 21.6.

*1-((4-Nitrophenyl)sulfonyl)-2-phenylpyrrolidine (**6b**).*[11] Yellow solid (32.9 mg, 99% yield). ^1H NMR (600 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 8.8 Hz, 2H), 7.80 (d, *J* = 8.8 Hz, 2H), 7.29 – 7.20 (m, 3H), 7.19 – 7.12 (m, 2H), 4.93 – 4.82 (m, 1H), 3.70 – 3.54 (m, 2H), 2.22 – 2.10 (m, 1H), 2.03 –1.93 (m, 1H), 1.93 – 1.78 (m, 2H). $^{13}C\{^1H\}$ NMR

(150 MHz, Chloroform-*d*) δ 149.8, 144.7, 141.9, 128.5, 128.4, 127.6, 126.5, 124.1, 63.8, 49.6, 36.1, 24.4.

*4,4-Dimethyl-2-phenyl-1-tosylpyrrolidine (**6c**).*[9a] Pale yellow oil (32.5 mg, 99% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.9 Hz, 2H), 7.36 – 7.11 (m, 7H), 4.81 – 4.65 (m, 1H), 3.51 – 3.25 (m, 2H), 2.42 (s, 3H), 2.04 (dd, *J* = 12.8, 7.3 Hz, 1H), 1.75 (dd, *J* = 12.7, 9.4 Hz, 1H), 1.60 (s, 1H), 1.08 (s, 3H), 0.79 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.0, 142.9, 135.7, 129.3, 128.3, 127.4, 127.1, 126.5, 63.8, 61.9, 51.5, 38.1, 26.1, 25.7, 21.5.

*2-(4-Fluorophenyl)-4,4-dimethyl-1-tosylpyrrolidine (**6d**).*[9a] White solid (34.7 mg, 99% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.28 – 7.23 (m, 4H), 6.96 (t, *J* = 8.7 Hz, 2H), 4.77 – 4.66 (m, 1H), 3.53 – 3.25 (m, 2H), 2.43 (s, 3H), 2.03 (dd, *J* = 12.7, 7.0 Hz, 1H), 1.71 (dd, *J* = 12.8, 9.4 Hz, 1H), 1.08 (s, 3H), 0.78 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 161.9 (d, *J* = 253.6 Hz), 143.2, 138.6 (d, *J* = 2.8 Hz), 135.6, 129.4, 128.1 (d, *J* = 8.4 Hz), 127.3, 115.1 (d, *J* = 17.1 Hz), 63.2, 61.8, 51.5, 38.1, 26.1, 25.6, 21.5.

*2-(4-Chlorophenyl)-4,4-dimethyl-1-tosylpyrrolidine (**6e**).*[9a] White solid (36.1 mg, 99% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.46 – 7.14 (m, 7H), 4.75 – 4.61 (m, 1H), 3.55 – 3.19 (m, 2H), 2.43 (s, 3H), 2.02 (dd, *J* = 12.8, 7.2 Hz, 1H), 1.69 (dd, *J* = 12.8, 9.4 Hz, 1H), 1.07 (s, 3H), 0.77 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.3, 141.5, 135.4, 132.8, 129.4, 128.4, 127.8, 127.4, 63.2, 61.8, 51.4, 38.2, 26.1, 25.6, 21.5.

*4,4-Dimethyl-2-(p-tolyl)-1-tosylpyrrolidine (**6f**).*[9a] White solid (33.9 mg, 99% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 4.67 (dd, *J* = 9.4, 7.2 Hz, 1H), 3.60 – 3.26 (m, 2H), 2.42 (s, 3H), 2.34 (s, 3H), 2.04 – 1.99 (m, 1H), 1.77 – 1.71(m, 1H), 1.07 (s, 3H), 0.77 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 142.9, 139.9, 136.7, 135.7, 129.3, 129.0, 127.4, 126.4, 63.6, 61.9, 51.5, 38.0, 26.2, 25.7, 21.5, 21.1.

*2-(4-Methoxyphenyl)-4,4-dimethyl-1-tosylpyrrolidine (**6g**).*[9a] Pale yellow oil (35.7 mg, 99% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.21 (t, *J* = 8.6 Hz, 4H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.68 (dd, *J* = 9.4, 7.2 Hz, 1H), 3.81 (s, 3H), 3.54 – 3.23 (m, 2H), 2.41 (s, 3H), 2.03 – 1.98 (m, 1H), 1.73 (dd, *J* = 12.8, 9.4 Hz, 1H), 1.08 (s, 3H), 0.79 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 158.7, 142.9, 135.9, 134.8, 129.3, 127.7, 127.3, 113.6, 63.3, 61.8, 55.3, 51.5, 37.9, 26.2, 25.7, 21.5.

*3-Phenyl-2-tosyl-2-azaspiro[4.5]decane (**6h**).*[9a] White solid (36.1 mg, 98% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.18 (m, 7H), 4.64 (dd, *J* = 9.4, 7.3 Hz, 1H), 3.64 (d, *J* = 10.7 Hz, 1H), 3.32 (d, *J* = 10.8 Hz, 1H), 2.42 (s, 3H), 2.13 (dd, *J* = 12.9, 7.3 Hz, 1H), 1.67 (dd, *J* = 13.0, 9.4 Hz, 1H), 1.47 – 1.17 (m, 8H), 1.05 – 1.00 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.1, 143.0, 135.4, 129.3, 128.3, 127.4, 127.1, 126.4, 63.1, 42.0, 36.4, 33.9, 25.9, 23.8, 22.8, 21.5.

*2,2,4,4-Tetramethyl-1-tosylpyrrolidine (**6i**).*[9a] Colorless oil (28.0 mg, 99% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 7.9 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 2H), 3.09 (s, 2H), 2.43 (s, 3H), 1.71 (s, 2H), 1.51 (s, 6H), 1.05 (s, 6H). ^{13}C{^{1}H} NMR (150

MHz, Chloroform-*d*) δ 142.6, 138.2, 129.3, 127.4, 65.6, 61.2, 56.9, 36.2, 29.8, 27.4, 21.5.

4,4-Dimethyl-1-tosyl-2-vinylpyrrolidine ***(6j)***. Pale yellow oil (8.0 mg, 29% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.33 – 7.31 (d, *J* = 8.2 Hz, 2H), 5.93 – 5.85 (m, 1H), 5.33 – 4.95 (m, 2H), 4.05 (q, *J* = 7.8 Hz, 1H), 3.43 – 3.06 (m, 2H), 2.45 (s, 3H), 1.76 (dd, *J* = 12.6, 7.5 Hz, 1H), 1.62 – 1.57 (m, 1H), 1.08 (s, 3H), 0.72 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.2, 139.8, 135.3, 129.5, 127.6, 115.2, 62.5, 61.5, 47.5, 37.5, 26.5, 26.0, 21.6. HRMS (ES+) Calculated for $C_{15}H_{22}NO_2S^+$ $[M+H]^+$: 280.1366, found: 280.1366.

(2S,3aS,8aR)-2-phenyl-3-tosyl-3,3a,8,8a-tetrahydro-2H-indeno[1,2-d]oxazole ***(6k)***. Pale yellow oil (31.4 mg, 80% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.1 Hz, 2H), 7.56 – 7.47 (m, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.21 (m, 2H), 7.18 – 7.06 (m, 6H), 6.14 (s, 1H), 5.48 (d, *J* = 5.5 Hz, 1H), 4.51 (t, *J* = 5.1 Hz, 1H), 3.21 – 3.01 (m, 2H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 144.3, 140.0, 139.7, 138.4, 135.0, 130.0, 128.7, 128.6, 128.0, 127.9, 127.5, 127.0, 126.2, 125.1, 93.3, 81.9, 67.9, 37.5, 21.7. HRMS (ES+) Calculated for $C_{23}H_{22}NO_3S^+$ $[M+H]^+$: 392.1315, found: 392.1319.

N-(4-iodoheptyl)-4-nitrobenzenesulfonamide ***(6m)***. Yellow oil (11.9 mg, 28% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 7.4 Hz, 2H), 8.08 (d, *J* = 8.1 Hz, 2H), 4.71 (d, *J* = 6.6 Hz, 1H), 4.05 (s, 1H), 3.09 (q, *J* = 6.5 Hz, 2H), 1.91 – 1.40 (m, 8H), 1.00 – 0.82 (m, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 150.1, 145.9, 128.3, 124.5, 42.7, 42.6, 38.0, 37.2, 29.8, 22.7, 13.2. HRMS (ES+) Calculated for $C_{13}H_{20}IN_2O_4S^+$ $[M+H]^+$: 427.0183, found: 427.0188.

*N-(4-iodoheptyl)-4-methylbenzenesulfonamide **(6n)**.* Yellow oil (18.5 mg, 47% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 4.69 (t, *J* = 6.3 Hz, 1H), 4.08 – 3.94 (m, 1H), 3.04 – 2.91 (m, 2H), 2.43 (s, 3H), 1.91 – 1.18 (m, 8H), 0.90 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, Chloroform-*d*) δ 143.7, 129.9, 127.2, 42.8, 42.5, 38.8, 37.4, 29.8, 22.8, 21.7, 13.3. HRMS (ES+) Calculated for $C_{14}H_{23}INO_2S^+$ $[M+H]^+$: 396.0489, found: 396.0499.

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Supporting Information: ^{1}H and ^{13}C NMR spectra for all synthetic compounds. This material is available free of charge via the Internet at http://pubs.acs.org/.

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