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A practical method for regiocontrolled one-carbon ring contraction

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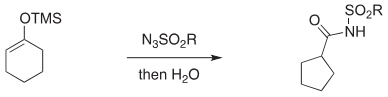
ABSTRACT

A practical and efficient method for the perfluorobutanesulfonyl azide-mediated one-carbon ring contraction of cyclic enoxysilanes is described. High-yielding procedures for the elaboration of the resulting *N*-acyl sulfonamide products are reported.

1. Introduction

One-carbon ring contractions—the six-to-five variant in particular—are mainstays of synthetic chemistry. Among the many available protocols,[1] ring contractions of α-diazo (Wolff rearrangement)[2,3] and α-halo (Favorskii rearrangement)[4,5] cycloalkanones are most commonly employed. Arenesulfonyl- and fluoroalkanesulfonyl azide-mediated one-carbon ring contractions of cyclic enoxysilanes have been known since 1973 (Eq. 1); however, such reactions frequently fail to give satisfactory yields, even with the simplest of substrates.[6] Furthermore, fluoroalkanesulfonyl azide-mediated ring contractions afford robust *N*-acyl fluoroalkanesulfonamides, the functionalization of which has not been reported, to our knowledge.



(1)

Enoxysilanes represent attractive starting materials for ring contractions because they can be formed using well-established regiocontrolled methods. For example, enoxysilanes may be generated regioselectively from simple ketones by hard or soft enolization techniques;[7] from α,β-unsaturated ketones by tandem Michael addition–enolate silylation;[8] from Birch reduction of aryl silyl ethers;[9] or from Diels–Alder cycloaddition reactions,[10] among other techniques. Realization of a practical method for ring contraction of enoxysilanes could exploit these synthetic methods and provide a handle for regiocontrol in the rearrangement step.

Herein we report an efficient and practical method for the perfluorobutanesulfonyl azide (nonaflyl azide, NfN_3)-mediated ring contraction of cyclic enoxysilanes. Nonaflyl azide is a nonvolatile liquid prepared in one-step by the reaction of the inexpensive commercial reagent nonaflyl fluoride with sodium azide.[11] Unlike trifluoromethanesulfonyl azide (triflyl azide, TfN_3),[12] NfN_3 may be stored and handled safely as a neat liquid at room temperature.[11] Moreover, we report an improved synthesis of NfN_3 that avoids the use of halogenated solvents, thereby minimizing the risks associated with the synthesis of fluoroalkanesulfonyl azides.[13,14] We also report high-yielding procedures for the transformation of the *N*-acyl sulfonamide functionality of the ring contraction product to alcohol, ester, and carboxamide products.

2. Results and discussion

The mechanism of this ring contraction is proposed by Xu et al. to proceed via aziridine intermediate **2**,[6b] formed upon loss of dinitrogen from either [3+2] cycloadduct **1a** or **1b**, depending on whether electronic or steric effects predominate in the formation of the triazoline (Scheme 1). While ring contraction is effected by alkyl migration to open the aziridine, a competing pathway involves aziridine opening without concomitant alkyl shift to afford α-aminated products **4**. Optimization experiments focused on maximizing the yield of ring-contracted product, utilizing the tetralone derivative **5g** as a model substrate (Table 1). We found that across a range of solvents tested, the dielectric constant of the solvent

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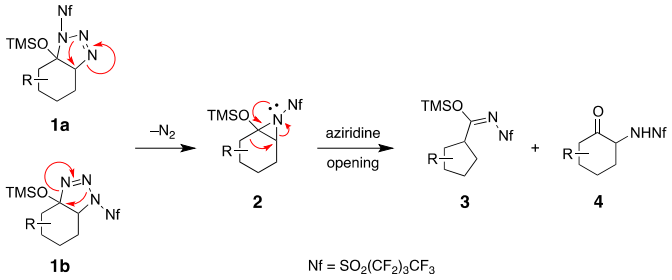
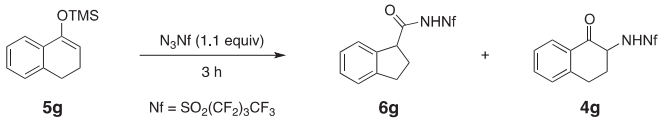


Scheme 1. Aziridine-mediated ring contraction mechanism as proposed by Xu et al.

Table 1
Optimization of ring contraction conditions



5g 6g 4g

Entry	Solvent[a]	Temperature	Yield **6g**[b,c]	Yield **4g**[b]
1	CH_3CN	60 °C	69%	7%
2	CH_3CN	40 °C	72%	8%
3	CH_3OH	40 °C	31%	N.O.
4	CH_2Cl_2	40 °C	70%	7%
5	$PhCH_3$	40 °C	61%	9%
6	THF	40 °C	71%	11%

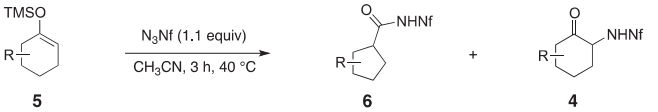
[a] [**5g**]=0.3 M.
[b] Yields determined by ^1H NMR analysis using anisole as an internal standard.
[c] Yield represented as the sum of trimethylsilyl imidate and *N*-acyl sulfonamide ring contraction products.

manifested little effect on the relative formation of ring contraction and α-amination products (**6g** and **4g**, respectively; ^1H NMR analysis). This finding supports the suggestion that the reaction proceeds via an aziridine intermediate, rather than through concerted migration–dinitrogen extrusion.[6b] While solvent polarity may be expected to influence dipolar orientation of the reactants and thus lead to differential formation of cycloadducts **1a** and **1b**, this information is lost upon extrusion of dinitrogen. The propensity of the alkyl substituent to undergo migration and the developing ring strain in the product thus govern the product distribution. For example, attempts to carry out ring contraction on 1-(trimethylsiloxy) cyclopentene gave the α-aminated product exclusively (70% yield). In the absence of exchangeable protons, the immediate product of ring contraction is the trimethylsilyl imidate **3**, which is isolable by direct concentration of the reaction mixture. Hydrolysis is observed upon purification by silica gel flash-column chromatography, yielding the *N*-acyl sulfonamide **6**.

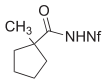
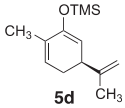
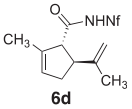
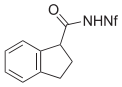
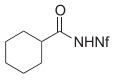
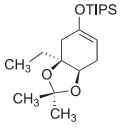
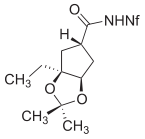
This ring contraction is relatively general in scope. The mild reaction conditions (1.10 equiv perfluorobutanesulfonyl azide, acetonitrile, 40 °C, 3 h) lead to broad functional group compatibility (Table 2). In the case of the simple cyclohexanone-derived substrate **5a**, the desired ring contraction product was isolated in near-quantitative yield. Excellent site-selectivity was observed with substrates bearing unfunctionalized alkenes (entries 3–6). The reaction was not limited to six-membered carbocycle starting materials, as the enoxysilane **5h**, derived from cycloheptanone, was converted to **6h** in 67% yield—a significant improvement over the analogous arenesulfonyl azide-induced transformation reported by Wohl (50%).[6a] Furthermore, more robust triisopropyl enoxysilanes may be employed (entry 9).

Acyclic enoxysilanes undergo an analogous rearrangement, provided the migratory group is electron-rich (Table 3). Thus, the trimethylenoxysilane derived from 3′,4′,5′-trimethoxyacetophenone

Table 2
Substrate scope of the ring contraction



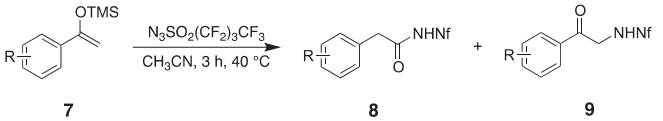
5 6 4

Entry	Enoxysilane	Ring-contracted product	Yield **6**[a]	Yield **4**[b]
1	 **5a**	 **6a**	97%	<1%
2	 **5b**	 **6b**	84%[c]	<1%
3	 **5c**	 **6c**	78%	<1%
4	 **5d**	 **6d**	74% >99:1 dr	25%
5	 **5e**	 **6e**	76% 2:1 dr	<1%
6[d]	 **5f**	 **6f**	75% 1.2:1 dr[e]	11%
7	 **5g**	 **6g**	87%	7%
8	 **5h**	 **6h**	67%	32%
9	 **5i**	 **6i**	65% >99:1 dr	8%

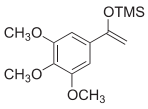
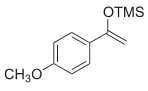
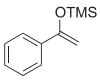
[a] Isolated yield after purification by flash-column chromatography.
[b] Yield of α-aminated product determined by ^1H NMR analysis of the unpurified product mixture.
[c] Theoretical yield 85%, based on isomeric purity of starting material.
[d] [**5f**]=1.0 M.
[e] Inseparable mixture of diastereomers, relative stereochemistry not assigned.

(**7a**) formed the rearranged product **8a** in 76% yield, with only 10% yield of the corresponding α-aminated ketone **9a**. As the electron density of the arene is decreased (**7b**, **7c**) the amount of α-amination product increases (29% of **9b** and 50% of **9c** for enoxysilanes **7b** and **7c**, respectively).

Table 3
Electronic influence on aryl migration versus α-amination

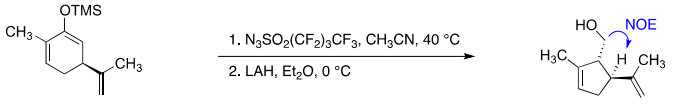


7 8 9

Entry	Starting material	Yield **8**[a]	Yield **9**[a]
1	 **7a**	76%	10%
2	 **7b**	51%	29%
3	 **7c**	22%	50%

[a] Yields calculated by ^{1}H NMR analysis using hexamethylbenzene as an internal standard.

As expected, ring contraction was amenable to substrate-based stereocontrol. Substrate **5d**, derived from (*S*)-carvone, undergoes rearrangement to provide the *trans* diastereomer, as established by NOE analysis of the corresponding primary alcohol (Scheme 2). Within the limits of detection (^{1}H NMR analysis) only a single diastereomeric product was formed. This stereochemical outcome is likely a reflection of preferential triazoline formation at the unhindered (α) face of **5d**, closure to the aziridine, and stereospecific vinyl migration. Diastereoselectivity decreased as steric differentiation at the allylic position of the enoxysilane diminished (compare entries 5 and 6, Table 2).



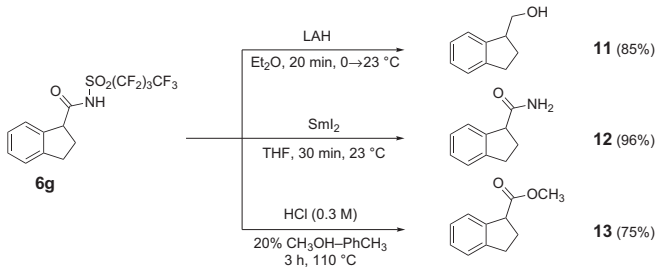
5d **10**

Scheme 2. Establishment of relative stereochemistry in the (*S*)-carvone system.

The synthetic utility of this transformation is enhanced by the development of methods to convert the ring-contracted *N*-acyl sulfonamide to common functional groups (Scheme 3). Reduction of the ring contraction product **6g** with lithium aluminum hydride provided the alcohol **11** in 85% yield. Alternatively, the carboxamide **12** was obtained in 96% yield by reduction with samarium diiodide.[15] Methanolysis could be effected by heating under acidic conditions to provide the methyl ester **13** in 75% yield.

3. Conclusions

In summary, we have developed a practical and versatile methodology for the ring contraction of cyclic enoxysilanes. The utility of this chemistry is twofold: First, the chemistry exploits the manifold methods for regiocontrolled enoxysilane formation to control selectivity in the bond-migration step. Second, our work



Scheme 3. Functionalization of the *N*-acyl sulfonamide. Isolated yields shown.

shows that the perfluoroalkanesulfonyl products can be converted to common functional groups (alcohol, amide, and ester) in one-step and in high yield. We envision that the predictability, selectivity, and mild, neutral character of the reaction make this a valuable addition to the synthetic repertoire.

4. Experimental

4.1. General

All reactions were performed in single-neck, flame-dried, round-bottomed borosilicate glass flasks fitted with a rubber septum under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via syringe or stainless steel cannula, or were handled in a nitrogen-filled drybox (working oxygen level <10 ppm). Organic solutions were concentrated by rotary evaporation at 30–33 °C. Flash-column chromatography was performed as described by Still et al.,[16] employing silica gel (60 Å, 40–63 μm particle size) purchased from Silicycle (Quebec, Canada). Specific elution parameters accompany each experimental. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel (250 μm, 60 Å pore size) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV) and/or submersion in aqueous potassium permanganate solution ($KMnO_4$) or ethanolic phosphomolybdic acid solution (PMA), followed by brief heating on a hot plate (120 °C, 10–15 s).

4.2. Materials

Commercial solvents and reagents were used as received with the following exceptions. Toluene was purified according to the method of Pangborn et al.[17] Methanol was distilled from magnesium methoxide under an atmosphere of nitrogen immediately before use. Acetonitrile was distilled from calcium hydride under an atmosphere of nitrogen immediately before use. Enoxysilanes **5a**–**i** and **7a**–**c** were prepared according to published procedures.[9c,18]

4.3. Instrumentation

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 400 or 500 MHz at 24 °C unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane, and are referenced to residual protium in the NMR solvent ($CHCl_3$, δ 7.26; CHD_2OD, δ 3.31; $CHD_2S(O)CD_3$, δ 2.50). Data are represented as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, quint=quintet, m=multiplet and/or multiple resonances, br=broad, app=apparent), coupling constant in Hertz, and integration. Proton-decoupled carbon nuclear magnetic resonance (^{13}C NMR) spectra

were recorded at 75, 100 or 125 MHz at 24 °C, unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane, and are referenced to the carbon resonances of the solvent ($CDCl_3$, δ 77.16; CD_3OD, δ 49.00; $(CD_3)_2SO$, δ 39.52). Distortionless enhancement by polarization transfer (DEPT-135) spectra were recorded at 100 or 125 MHz at 24 °C unless otherwise noted. ^{13}C NMR and DEPT-135 data are combined and represented as follows: chemical shift, carbon type (obtained from DEPT-135 experiments). Fluorine nuclear magnetic resonance (^{19}F NMR) spectra were recorded at 282 MHz at 24 °C unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from $CFCl_3$. Data are represented as follows: chemical shift, and integration. Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectra were obtained using a Thermo Electron Corporation Nicolet 6700 FTIR spectrometer referenced to a polystyrene standard. Data are represented as follows: frequency of absorption (cm^{-1}), and intensity of absorption (s=strong, m=medium, w=weak, br=broad). High-resolution mass spectrometry (HRMS) data were obtained on a Waters analytical ultra high-performance liquid chromatography–mass spectrometry (UPLC/HRMS) instrument equipped with an electrospray ionization (ESI) mass spectrometry detector and photodiode-array detector; otherwise, HRMS spectra were obtained by chemical ionization (CI) at the W. M. Keck Foundation Biotechnology Resource Laboratory at Yale University. In the first case, UPLC/HRMS samples were eluted over a reverse-phase C-18 column (1.7 μm particle size, 2.1×50 mm) with a linear gradient of 5% acetonitrile–water (v/v) to 95% acetonitrile–water (v/v) containing 0.1% formic acid over 3 min at a flow rate of 0.8 mL/min.

4.4. Procedure for the preparation of perfluoro-*n*-butanesulfonyl azide (nonaflyl azide, NfN_3)

A 50-mL round-bottomed flask was charged with a magnetic stir bar, sodium azide (880 mg, 13.6 mmol, 1.00 equiv) and anhydrous methanol (15 mL). To this mixture was added perfluorobutanesulfonyl fluoride (NfF, 4.10 g, 13.6 mmol, 1 equiv) and the mixture was stirred for 18 h at 23 °C behind a blast shield. The mixture was then passed over a fritted glass funnel to remove solid precipitate. The filtrate was collected in a 75-mL pear-shaped flask, and the filtrate was shaken with 20 mL of deionized water. The fluorous phase was collected and passed over a plug of sodium sulfate to afford neat nonaflyl azide as a colorless oil (2.16 g, 49%). ^{19}F NMR and IR spectral data were in agreement with those reported.[11]

4.5. General procedure for the ring contraction of enoxysilanes

A flame-dried 10-mL round-bottomed flask that had been fused to a Teflon-coated valve was charged with a solution of perfluorobutanesulfonyl azide (44.9 mg, 138 μmol, 1.10 equiv) in acetonitrile (420 μL). To this solution was added the enoxysilane (126 μmol, 1 equiv) at 23 °C. The reaction vessel was then sealed and heated for 3 h at 40 °C. The mixture was then cooled to 23 °C and the solvent was removed by evaporation under a stream of nitrogen gas. The residue obtained was purified by flash-column chromatography (eluting with dichloromethane initially, grading to 50% ethyl acetate–dichloromethane over two-steps). Fractions containing product were identified using TLC (50% ethyl acetate–dichloromethane, $KMnO_4$ stain). All *N*-acyl sulfonamide products thus afforded (**6a**–**i**; **8a**–**c**) featured R_f values of 0.10–0.20 in 50% ethyl acetate–dichloromethane.

*4.5.1. N-((Perfluorobutyl)sulfonyl)cyclopentanecarboxamide (**6a**).* White solid. ^1H NMR (500 MHz, CD_3OD), δ 2.69 (app quint, J = 8.0 Hz, 1H), 1.86–1.74 (m, 4H), 1.72–1.64 and 1.59–1.53 (m, 4H). ^{13}C NMR (125 MHz, CD_3OD), δ 186.0 (C), 50.0 (C), 31.4 (CH_2), 26.9 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.0 (2F), −122.3 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 3492.5 (br), 2959.4 (m), 2873.3 (w), 1652.0 (s), 1620.5 (m), 1290.0 (s), 1189.7 (s). LC/HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{10}H_{10}F_9NO_3S$, 396.0310; found 396.0311.

*4.5.2. 1-Methyl-N-((perfluorobutyl)sulfonyl)cyclopentanecarboxamide (**6b**).* White solid. ^1H NMR (400 MHz, CD_3OD), δ 2.21–2.14 (m, 2H), 1.68–1.61 (m, 4H), 1.40–1.35 (m, 2H). 1.20 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD), δ 189.2 (C), 54.0 (C), 39.0 (CH_2), 26.2 (CH_3), 26.0 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.5 (2F), −122.1 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 2961.7 (m), 2876.6 (w), 1641.7 (s), 1467.1 (w), 1195.1 (s), 1133.5 (s). LC/HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{11}H_{12}F_9NO_3S$, 410.0467; found 410.0465.

*4.5.3. N-((Perfluorobutyl)sulfonyl)cyclopent-2-enecarboxamide (**6c**).* White solid. ^1H NMR (400 MHz, CD_3OD), δ 5.80 (m, 1H), 5.76 (m, 1H), 3.48 (tdd, J=8.8, 4.9, 2.4 Hz, 1H), 2.47–2.38 and 2.34–2.25 (m, 2H), 2.16–1.99 (m, 2H). ^{13}C NMR (125 MHz, CD_3OD), δ 184.1 (C), 133.1 (CH), 131.9 (CH), 56.77 (CH), 33.20 (CH_2), 27.88 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.0 (2F), −122.4 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 3471.3 (br), 1605.3 (m), 1285.7 (s), 1194.5 (s), 1135.3 (s), 1010.1 (m). LC/HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{10}H_8F_9NO_3S$, 394.0154; found 394.0160.

*4.5.4. (1R,5S)-2-Methyl-N-((perfluorobutyl)sulfonyl)-5-(prop-1-en-2-yl)cyclopent-2-enecarboxamide (**6d**).* White Solid. ^1H NMR (400 MHz, CD_3OD), δ 5.42 (br, 1H), 4.76 (br, 1H), 4.68 (br, 1H), 3.27 (app t, J=6.5 Hz, 1H), 2.57–2.49 and 2.24–2.17 (m, 2H), 1.71 (s, 6H). ^{13}C NMR (75 MHz, CD_3OD), δ 184.4 (C), 148.8 (C), 140.5 (C), 126.9 (CH), 110.0 (CH_2), 64.6 (CH), 51.9 (CH), 37.9 (CH_2), 20.7 (CH_3), 15.4 (CH_3). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −113.9 (2F), −122.3 (2F), −127.3 (2F). FTIR (thin film), cm^{-1}: 3439.1 (br), 2979.1 (w), 1605.0 (s), 1299.7 (s), 1197.0 (s). LC/HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{14}H_{14}F_9NO_3S$, 470.0443; found 470.0439.

*4.5.5. trans-N-((Perfluorobutyl)sulfonyl)-2-vinylcyclopentanecarboxamide and cis-N-((perfluorobutyl)sulfonyl)-2-vinylcyclopentanecarboxamide (trans-**6e** and cis-**6e**, inseparable mixture). trans-**6e**:* ^1H NMR (500 MHz, CD_3OD), δ 5.81 (ddd, J=17.4, 10.3, 7.2 Hz, 1H), 5.01 (app d, J=17.2 Hz, 1H), 4.89 (dd, J=10.5, 2.0 Hz, 1H). 2.78 (m, 1H), 2.44 (app q, J=8.7 Hz, 1H), 1.99–1.39 (m, 6H). ^{13}C NMR (100 MHz, CD_3OD), δ 185.9 (C), 142.7 (CH), 113.8 (CH_2), 56.6 (CH), 49.61 (CH), 33.7 (CH_2), 32.1 (CH_2), 25.4 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.3 (2F), −122.2 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 3478.9 (br), 2956.0 (m), 1638.3 (s), 1351.4 (m), 1209.2 (s). LC/HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{12}F_9NO_3S$, 422.0467; found 422.0461. *cis-***6e**: ^1H NMR (500 MHz, CD_3OD), δ 5.90 (ddd, J=17.2, 10.2, 8.1 Hz, 1H), 5.01 (app d, J=17.2 Hz, 1H), 4.88 (app d, J=10.3 Hz, 1H), 2.84 (app q, J=7.6 Hz, 1H), 2.78 (m, 1H), 1.99–1.57 (m, 6H). ^{13}C NMR (100 MHz, CD_3OD), δ 184.4 (C), 140.6 (CH), 114.7 (CH_2), 54.6 (CH), 49.2 (CH), 33.0 (CH_2), 29.3 (CH_2), 24.9 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.3 (2F), −122.2 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 3478.9 (br), 2957.0 (m), 1638.3 (s), 1351.4 (m), 1209.2 (s). LC/HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{12}F_9NO_3S$, 422.0467; found 422.0461.

*4.5.6. 2-Methyl-N-((perfluorobutyl)sulfonyl)-2-vinylcyclopent-anecarboxamide (**6f**, inseparable mixture, stereochemistry not determined, * designates other diastereomer).* ^1H NMR (400 MHz, CD_3OD), δ 6.02 (dd, J=10.7, 17.5 Hz, 1H, 1H*), 4.99 (dd, J=1.2, 17.5 Hz, 1H*), 4.98 (dd, J=1.32, 17.5 Hz, 1H), 4.91 (dd, J=1.6, 10.8 Hz, 1H), 4.90 (dd, J=1.4, 10.7 Hz, 1H*), 2.59 (app t, J=8.1 Hz, 1H), 2.49 (app t, J=8.1 Hz, 1H*), 2.06–1.42 (m, 6H, 6H*), 1.22 (s, 3H*), 1.06 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD), δ 183.9 (C), 183.8 (C*), 149.1 (CH), 145.0 (CH*), 111.7 (CH_2), 110.6 (CH_2*), 60.8 (CH), 58.7 (CH*), 40.5 (CH_2), 40.0 (CH_2*), 29.8 (C),

29.6 (C), 29.1 (CH_2), 28.8 (CH_2*), 26.7 (CH_3), 23.3 (CH_2), 23.1 (CH_2*), 21.3 (CH_3*). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.2 (2F), −122.1 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 3554.8 (br), 2971.1 (w), 2159.4 (w), 2020.7 (s), 1637.9 (s), 1196.6 (s). LC/HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{13}H_{14}F_9NO_3S$, 436.0623; found 436.0629.

*4.5.7. N-((Perfluorobutyl)sulfonyl)-2,3-dihydro-1H-indene-1-carboxamide (**6g**).* White solid. ^{1}H NMR (400 MHz, CD_3OD), δ 7.38−7.36 (m, 1H), 7.18−7.17 (m, 1H), 7.13−7.07 (m, 2H), 3.95 (app t, *J*=7.4 Hz, 1H), 3.09−3.02 (m, 1H), 2.88−2.80 (m, 1H), 2.42−2.33 (m, 1H), 2.29−2.20 (m, 1H). ^{13}C NMR (100 MHz, CD_3OD), δ 183.8 (C), 145.6 (C), 144.2 (C), 127.9 (CH), 127.0 (CH), 125.8 (CH), 125.2 (CH), 56.3 (CH), 32.8 (CH_2), 30.6 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.1 (2F), −122.3 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 3464.1 (br), 2948.1 (w), 1609.3 (s), 1294.2 (s), 1135.3 (s). LC/HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{14}H_{10}F_9NO_3S$, 444.0310; found 444.0299.

*4.5.8. N-((Perfluorobutyl)sulfonyl)cyclohexanecarboxamide (**6h**).* White solid. ^{1}H NMR (400 MHz, CD_3OD) δ 2.17 (tt, *J*=11.4, 3.3 Hz, 1H), 1.85 (app d, *J*=12.8 Hz, 2H), 1.76−1.73 (m, 2H), 1.66−1.64 (m, 1H), 1.43−1.18 (m, 5H). ^{13}C NMR (75 MHz, CD_3OD), δ 186.3 (C), 49.5 (CH), 30.9 (CH_2), 27.2 (CH_2), 26.9 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −83.0 (3F), −114.5 (2F), −122.8 (2F), −127.7 (2F). FTIR (thin film), cm^{-1}: 3543.2 (br), 2936.1 (w), 2158.7 (m), 2020.9 (m), 1640.9 (m), 1159.8 (s). LC/HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{11}H_{12}F_9NO_3S$, 410.0467; found 410.0465.

*4.5.9. (3aS,5R,6aR)-3a-Ethyl-2,2-dimethyl-N-((perfluorobutyl) sulfonyl)tetrahydro-3aH-cyclopenta[d][1,3]dioxole-5-carboxamide (**6i**).* White solid. ^{1}H NMR (500 MHz, CD_3OD) δ 4.31 (d, *J*=4.3 Hz, 1H), 3.04 (app tt, *J*=12.1, 6.3 Hz, 1H), 2.02 (ddd, *J*=13.6, 5.7, 1.9 Hz, 1H), 1.95 (ddd, *J*=13.6, 6.9, 1.9 Hz, 1H), 1.83 (dq, *J*=14.7, 7.4 Hz, 1H), 1.77−1.71 (m, 1H), 1.70−1.60 (m, 2H), 1.40 (s, 3H), 1.31 (s, 3H), 0.99 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (125 MHz, CD_3OD), δ 184.2 (C), 86.5 (CH), 47.7 (CH), 42.6 (CH_2), 38.1 (CH_2), 33.6 (CH_2), 27.9 (CH_3), 27.0 (CH_3), 9.1 (CH_3). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.2 (2F), −122.3 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 3549.1 (m), 3496.5 (m), 2985.8 (w), 2160.4 (m), 2017.6 (s), 1619.4 (s), 1173.2 (s). LC/HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{18}F_9NO_5S$, 518.0654; found 518.0650.

*4.5.10. N-((Perfluorobutyl)sulfonyl)-2-(3,4,5-trimethoxyphenyl) acetamide (**8a**).* White solid. ^{1}H NMR (500 MHz, CD_3OD) δ 6.61 (s, 2H), 3.82 (s, 6H), 3.73 (s, 3H), 3.47 (s, 2H). ^{13}C NMR (125 MHz, CD_3OD), δ 180.9 (C), 154.1 (C), 137.6 (C), 133.9 (C), 107.8 (CH), 61.1 (CH_3), 56.4 (CH_3), 47.8 (CH_2). ^{19}F NMR (282 MHz, CD_3OD), δ −82.5 (3F), −114.1 (2F), −122.3 (2F), −127.2 (2F). FTIR (thin film), cm^{-1}: 1629.9 (s), 1593.2 (m), 1310.1 (s), 1195.0 (s), 1116.6 (s). LC/HRMS-ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{15}H_{14}F_9NO_6S$, 508.0471; found 508.0473.

4.6. Reduction of *N*-acyl sulfonamide 6g to afford alcohol 11

A solution of lithium aluminum hydride in tetrahydrofuran (1 M, 271 μL, 271 μmol, 4.00 equiv) was added to a stirred solution of *N*-acyl sulfonamide **6g** (30.0 mg, 67.7 μmol, 1 equiv) in ether (1.50 mL) at 0 °C. After the addition, the resulting mixture was warmed to 23 °C and stirred for 20 min, after which TLC analysis (50% ethyl acetate−dichloromethane, $KMnO_4$ stain) indicated full conversion of starting material. The reaction mixture was then cooled to 0 °C, and distilled water (14 μL), 15% aqueous sodium hydroxide solution (14 μL), and additional distilled water (30 μL) were sequentially added. The resulting mixture was diluted with ethyl acetate (5 mL) and was filtered over Celite, rinsing the reaction vessel and Celite pad with additional ethyl acetate (2×5 mL). The filtrate was dried over sodium sulfate and was concentrated to dryness; the residue obtained was purified by flash-column chromatography (eluting with 0%−10% ethyl acetate−dichloromethane) to afford 1-indanmethanol (**11**, 8.5 mg, 85%, colorless oil). ^{1}H and ^{13}C NMR spectra were in agreement with those reported.[19]

4.7. Reductive desulfonylation of *N*-acyl sulfonamide 6g to afford carboxamide 12

Adapted from Ankner and Hilmersson.[15] In a nitrogen-filled drybox, a flame-dried 10-mL round-bottomed glass flask fitted with a rubber septum and Teflon-coated magnetic stir bar was charged with a solution of samarium diiodide in tetrahydrofuran (0.1 M, 3.38 mL, 338 μmol, 6.00 equiv). To this solution was added a solution of *N*-acyl sulfonamide **6g** (25.0 mg, 56.4 μmol, 1 equiv) in tetrahydrofuran (300 μL). The resulting mixture was stirred for 30 min at 23 °C. The reaction mixture was then removed from the drybox, and 1 mL of saturated aqueous sodium bicarbonate solution was added with stirring. The resulting mixture was then concentrated to dryness under reduced pressure, was suspended in 5 mL of methanol, and was filtered over a Celite pad, rinsing the reaction vessel and Celite pad with additional methanol (2×5 mL). This filtrate was concentrated to dryness, and the residue obtained was purified by flash-column chromatography (eluting with ethyl acetate) to afford indan-1-carboxamide (**12**, 9.0 mg, 96%, white solid). R_f=0.70 (15% methanol−ethyl acetate; UV, PMA). ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ 7.56 (br s, 1H), 7.27−7.26 (m, 1H), 7.23−7.21 (m, 1H), 7.16−7.14 (m, 2H), 6.96 (br s, 1H), 3.84 (app t, *J*=7.6 Hz, 1H), 2.98 (app ddd, *J*=14.8, 8.8, 5.3 Hz, 1H), 2.82 (app dt, *J*=15.8, 7.8 Hz, 1H), 2.26−2.11 (m, 2H). ^{13}C NMR (125 MHz, $(CD_3)_2SO$), δ 174.85 (C), 143.9 (C), 142.9 (C), 126.8 (CH), 126.0 (CH), 124.3 (CH), 124.0 (CH), 50.4 (CH), 31.6 (CH_2), 28.47 (CH_2). FTIR (thin film), cm^{-1}: 3357.5 (s), 3174.5 (s), 2159.9 (s), 2022.3 (s), 1646.9 (s), 1425.9 (s). HRMS-CI (*m*/*z*): $[M+Na]^+$ calcd for $C_{10}H_{11}NO$, 184.0733; found 184.0732.

4.8. Methanolysis of *N*-acyl sulfonamide 6g to afford methyl ester 13

A flame-dried 10-mL round-bottomed flask that had been fused to a Teflon-coated valve was charged with *N*-acyl sulfonamide **6g** (30.0 mg, 67.7 μmol, 1 equiv), which was dissolved in methanol (135 μL) and toluene (540 μL). A solution of hydrogen chloride in diethyl ether (1 M, 203 μL) was added and the reaction vessel was sealed. The resulting mixture was heated to 110 °C for 3 h, and then was cooled to 23 °C. The solvent was removed under reduced pressure and the residue obtained was purified by flash-column chromatography (eluting with 15% ethyl acetate−hexanes) to afford methyl indane-1-carboxylate (**13**, 8.8 mg, 75%, white solid). ^{1}H and ^{13}C NMR spectral data were in agreement with those reported.[20]

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Supplementary data

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