

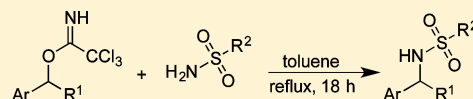
Alkylation of Sulfonamides with Trichloroacetimidates under Thermal Conditions

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S Supporting Information

ABSTRACT: An intermolecular alkylation of sulfonamides with trichloroacetimidates is reported. This transformation does not require an exogenous acid, base, or transition metal catalyst; instead the addition occurs in refluxing toluene without additives. The sulfonamide alkylation partner appears to be only limited by sterics, with unsubstituted sulfonamides providing better yields than more encumbered *N*-alkyl sulfonamides. The trichloroacetimidate alkylating agent must be a stable cation precursor for the substitution reaction to proceed under these conditions.



The sulfonamide functional group has played an important role in the development of numerous pharmaceuticals. While best known as antibiotics, sulfonamide scaffolds provide a diverse range of biological activity including antitumor, antiviral, diuretic, anti-inflammatory, and antihypertensive properties.¹ Summaries of the top selling pharmaceuticals clearly demonstrate that sulfonamides are well represented in these valuable structures.² Data on recently approved pharmaceuticals indicate that sulfonamides continue to be popular in drug discovery,³ with recent publications in the medicinal chemistry field corroborating that the investigation of sulfonamide-containing structures is ongoing.⁴ Sulfonamides also have proven useful in agricultural and insecticidal applications.⁵

In addition, sulfonamides serve an important function in synthetic organic chemistry, as they facilitate the introduction of nitrogen into organic molecules. The sulfonamide may then serve as a protecting group for the nitrogen atom during further synthetic manipulation. The use of sulfonamides as protecting groups in complex molecules was hindered by the harsh conditions⁶ needed to remove the sulfonamide. The development of 2-(trimethylsilyl)-ethanesulfonamide (SES-NH₂) by Weinreb⁷ and the implementation of 2- and 4-nitrobenzenesulfonamides by Fukuyama⁸ have resulted in a greatly increased use of sulfonamides in organic synthesis, primarily because these sulfonamides are readily and reliably removed under mild conditions. These developments have greatly popularized the use of sulfonamides in complex molecule synthesis.

With the obvious value of sulfonamides in chemical and pharmaceutical research, methods for their formation and elaboration have been heavily investigated. Classically substituted sulfonamides may be formed from amines and sulfonyl chlorides,⁹ by direct alkylation of sulfonamides with alkyl halides,¹⁰ or through reductive amination.¹¹ The Mitsunobu reaction has also been employed to convert an alcohol into a sulfonamide.^{7b,8a,12} Given the high level of interest in sulfonamides, it is perhaps unsurprising that new, more atom-economical catalytic methods for their formation have continued to evolve. Many of these methods employ transition

metal catalysts, including the hydroaminations of alkenes,¹³ C–H activation methods,¹⁴ metal catalyzed additions to *N*-sulfonyl imines,^{6b,15} alkylation via π -allyl metal complexes,¹⁶ and alkylation of alcohols via borrowing hydrogen methods.¹⁷ Direct alkylation of benzylic and allylic alcohols and ethers has also been explored,¹⁸ although these methods typically require the use of strong Brønsted or Lewis acids and elevated temperatures.

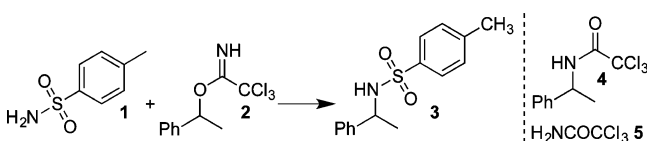
As part of our recent investigations into the use of trichloroacetimidates to alkylate carboxylic acids, alcohols, thiols, and anilines under mild conditions,¹⁹ we sought to determine if sulfonamides could be similarly elaborated. Lewis acid promoted alkylation with trichloroacetimidates has been widely utilized in the synthesis of ethers²⁰ and carbohydrates.²¹ Trichloroacetimidate displacements produce only trichloroacetamide as a byproduct, which is typically unreactive and may be removed by washing with aqueous NaOH solution.^{19d} More recently there have been several reports of additive-free trichloroacetimidate substitution reactions, with only heating being necessary to effect the displacement of some trichloroacetimidates with alcohols^{19c} and thiols.^{19d} Development of a new, catalyst-free method to access substituted sulfonamides would provide an inexpensive method to access these structures under mild conditions. Little is known about the reactivity of sulfonamides with trichloroacetimidates, although recently Kuroda and co-workers reported an intramolecular S_N2' substitution reaction of allylic imidates and sulfonamides catalyzed by a chiral phosphoric acid.²² To our knowledge this is the only example of a reaction between a trichloroacetimidate and a sulfonamide in the literature.

Initially, the reaction of *p*-toluenesulfonamide **1** with 1-phenethyl trichloroacetimidate **2** was studied (Table 1). Utilizing BF₃·OEt₂ as a catalyst in toluene, alkylation was rapid but only a 29% yield of the desired alkylation product **3** was realized. This poor yield was due to a significant portion of

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Table 1. Addition of Toluenesulfonamide 1 to Phenethyl Trichloroacetimidate 2



entry	equiv of 2	conditions	solvent	yield (%)
1	1.2	BF ₃ ·OEt ₂ (10 mol %), rt, 18 h	toluene	29
2	1.2	PPTS (10 mol %), rt, 18 h	toluene	50
3	1.2	DNBSA (10 mol %), rt, 18 h	toluene	71
4	1.2	reflux, 18 h	toluene	76
5	1.2	reflux, 4 h	toluene	24
6	1.2	reflux, 8 h	toluene	32
7	1.2	86 °C, 18 h	toluene	0
8	1.2	reflux, 18 h	THF	0
9	1.5	reflux ^a	toluene	86
10	1.5	reflux, 18 h	toluene	74

^aThe imidate added in six portions (one every 30 min) over 2.5 h, and then the reaction mixture was refluxed for another 16 h.

imidate 2 rearranging to the corresponding trichloroacetamide 4 during the alkylation. This rearrangement also complicated the isolation of the product 3, as the acetamide possessed similar chromatographic motility. Brønsted acid catalysis had proven superior in our study on the alkylation of anilines with trichloroacetimidates,^{19c} and so these catalysts were investigated next. Weak acids such as PPTS gave a slower reaction resulting in a 50% yield, while stronger acids such as dinitrobenzenesulfonic acid (DNBSA) gave a more rapid alkylation in 71% yield. While the reaction may be catalyzed with Brønsted or Lewis acids, given the acidity of the sulfonamide functional group the transformation in principle may also occur without a catalyst under thermal conditions as observed with alcohols and thiols.^{19c,d}

Heating a mixture of sulfonamide 1 and imidate 2 in toluene to reflux for 18 h (entry 4) resulted in a 76% yield of alkylated product. Shorter reaction times were not as effective, as the reaction was incomplete and therefore provided more moderate yields. Attempts to perform the alkylation at lower temperatures in toluene (entry 7) and in lower boiling solvents such as THF (entry 8) provided only unreacted starting materials, so a temperature near refluxing toluene was necessary for the alkylation to proceed. At this point it was noted that while *p*-toluenesulfonamide 1 was only slightly soluble in refluxing toluene, imidate 2 and the trichloroacetamide byproduct 5 were completely soluble, which led to the hypothesis that as trichloroacetamide 5 was formed it could compete with the sulfonamide 1 as a nucleophile, leading to the undesired product 4. To combat this problem the imidate 2 was added to the reaction mixture in portions which resulted in an increased yield of 86% (entry 9). Even though 1.5 equiv of imidate was used in this reaction, no increase in yield was noted with 1.5 equiv of imidate without the portionwise addition (entry 10). As entry 9 provided the best yield, this procedure was used henceforth.

The scope of the reaction of with respect to sulfonamide was then investigated (Table 2). A variety of different sulfonamides were found to undergo the alkylation reaction with imidate 2 in useful yields. Benzenesulfonamides substituted with electron-donating groups provided excellent yields of alkylated sulfonamide products (entries 1–3). 2-Nitrobenzenesulfon-

Table 2. Alkylation of Sulfonamides with Imidate 2

entry	sulfonamide	product	yield (%)
1			86
2			75
3			74
4			85
5			13 (70 ^a)
6			79
7			76
8			53
9			98
10			27
11			0 ^b

^aYield for a modified procedure using 10 mol % BF₃·OEt₂ in toluene at room temperature with the imidate being added as a refluxing solution of sulfonamide with a syringe pump over 1 h. ^bStarting sulfonamide 24 recovered unchanged.

amide 12 only provided a yield of 13% (entry 5), which was disappointing as Fukuyama has demonstrated the utility of this sulfonamide for installing amines.^{8a} This poor yield was attributed to the particular insolubility of this sulfonamide in toluene. Use of other solvents (α,α,α -trifluorotoluene, DCE, acetonitrile) did not improve the yield of the transformation. After some experimentation a solution was found, with a reaction catalyzed by BF₃·OEt₂ providing a 70% yield when the

imidate was added over the course of 1 h via syringe pump to the reaction mixture.

Alkyl sulfonamides were also well tolerated in the reaction with yields ranging from 70% to 79% (entries 6–8). The successful alkylation of 2-(trimethylsilyl)ethanesulfonamide **18** is particularly notable, as this sulfonamide can be removed to reveal the corresponding amine by treatment with fluoride. Sulfonamide **18** is often utilized to introduce a protected nitrogen into complex molecules.^{7c} The inexpensive carboxylic sulfonamide saccharin **20** reacted with trichloroacetimidate **2** with an excellent yield of 98% (entry 9). Saccharin has been used as a replacement for phthalimide in the Gabriel synthesis,²³ making this an inexpensive method to incorporate nitrogen in organic substrates. *N*-Alkyl sulfonamides gave lower yields, with *N*-methylbenzenesulfonamide **22** providing 27% of **23** (entry 10). *N*-Benzylbenzenesulfonamide **24** failed to react (entry 11). The decreased reactivity of *N*-substituted sulfonamides can be attributed to sterics and explains why no dialkylation products were observed.

To further probe the reaction scope, the reactivity of differentially substituted trichloroacetimidates with *p*-toluenesulfonamide **1** was investigated (Table 3). Secondary benzylic trichloroacetimidates were effective substrates, providing the *N*-alkyl sulfonamides in good yields. These reactions tolerated a sterically encumbering ortho-substituent on the aromatic ring next to the reactive center (as seen in the formation of **33** and **35**). The furanyl imidate **36** proved to be susceptible to hydrolysis and rearrangement to the corresponding acetamide, but still provided a 44% yield of substitution product **37**.

Diphenylmethyl imidate readily participated in the reaction to provide an 89% yield of sulfonamide **39**. This is notable, as diphenylmethyl groups have been utilized as protecting groups for sulfonamides.²⁴ Other diarylmethyl imidates also provided synthetically useful yields in the alkylation reaction, providing **41** in 67% yield. A number of primary benzylic trichloroacetimidates were also evaluated. Use of 4-methoxybenzyl trichloroacetimidate **42** or *o*-tolyl trichloroacetimidate **44** provided the alkylated products **43** and **45**, but the yields were lower than was observed for the secondary benzylic imidates. Benzyl trichloroacetimidate **46** was unreactive under these conditions. Secondary allylic trichloroacetimidates provided good yields of alkylated products, as seen in the case of compound **49**. Simple allyl trichloroacetimidate **50** provided a much lower yield of the product. Methyl and *tert*-butyl trichloroacetimidate were also evaluated, but product was only observed in the methyl case which gave low conversion.

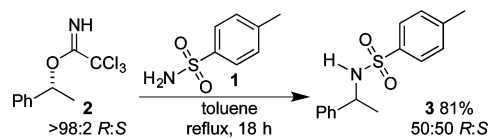
As defined in Table 3, imidates that are precursors to stable carbocations provide higher yields under these reaction conditions. This implies that the reaction proceeds through an S_N1 pathway, where the imidate ionizes and then is trapped with the sulfonamide. To further test this hypothesis the enantiopure imidate (*R*)-**2**^{19e} was subjected to the reaction conditions, providing the sulfonamide **3** in 81% yield (Scheme 1); however the product was racemic. This result is inconsistent with an S_N2 pathway and further supports an S_N1 pathway as is commonly invoked for trichloroacetimidate substitution reactions with benzylic substrates.

The new reaction was then applied to the synthesis of an interesting ketoprofen analog **58** (Scheme 2) discovered by Sakurai and co-workers.²⁵ Sulfonamide **58** showed a number of interesting pharmacological properties such as LTD₄ antagonistic activity, TXA₂ antagonistic activity, and TXA₂ synthase inhibitory activity.^{25,26} The synthetic scheme used by Sakurai to

Table 3. Addition of *p*-Toluenesulfonamide **1** to Different Trichloroacetimidates

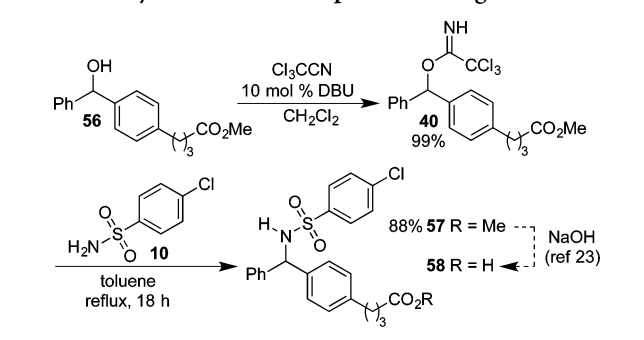
entry	imidate	product	yield (%)
1			86
2			89
3			79
4			79
5			94
6			88
7			44
8			89
9			67
10			68
11			55
12			0
13			60
14			28
15			5
16			0

Scheme 1. Substitution with a Chiral Trichloroacetimidate



synthesize **58** involved forming the azide, which was then reduced to the corresponding amine followed by transformation into the sulfonamide. Alternatively, sulfonamide **58** could be synthesized via imidate **40**, which avoids the use of the toxic sodium azide and eliminating the need for azide reduction. Initially, alcohol **56** was synthesized following the

Scheme 2. Synthesis of a Ketoprofen Analog



procedure of Sakurai and co-workers (Scheme 2).²⁵ Formation of the corresponding imidate **40** proceeded in near-quantitative yield. Imidate **40** was displaced with 4-chlorobenzenesulfonamide **10** to obtain sulfonamide **57** in 88% yield. Sulfonamide **57** may be transformed to ketoprofen analog **58** via saponification.²⁵

In summary, thermal conditions for the alkylation of sulfonamides with trichloroacetimidates have been developed. Unsubstituted sulfonamides were found to undergo alkylation well, but N-substituted sulfonamides were not effectively alkylated. The trichloroacetimidate alkylation partner must be a precursor to a stabilized carbocation, with the preponderance of evidence supporting an S_N1 reaction pathway in most cases. The formal synthesis of a biologically active ketoprofen analog was accomplished using this new substitution reaction.

EXPERIMENTAL SECTION

Representative Sulfonamide Substitution Procedure A.

To a flame-dried round-bottom flask under an atmosphere of argon was added *p*-toluene sulfonamide **1** (0.13 g, 0.77 mmol) and toluene (4 mL). Phenethyl imidate **2**^{19e} (51 mg, 0.19 mmol) was added, and the reaction mixture was heated to reflux. Phenethyl imidate **2** (0.05 g, 0.19 mmol) was added to the refluxing reaction mixture every 30 min until 1.14 mmol (1.5 equiv) of phenethyl imidate was added. After stirring at reflux overnight, the reaction mixture was allowed to cool to room temperature, preadsorbed on silica gel, and purified by silica gel chromatography (30% ethyl acetate/70% hexanes) to give 0.180 g (86%) of substituted sulfonamide **3** as a white solid.

4-Methyl-N-(1-phenylethyl)benzenesulfonamide (3).²⁷ Prepared using procedure A (0.180 g, 86%) using the known imidate^{19e} and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

3. White solid (0.18 g, 86%); mp = 74–78 °C; TLC R_f = 0.43 (20% ethyl acetate/80% hexanes); ¹H NMR (300 MHz, CDCl₃) δ 7.61 (dt, *J* = 8.7, 2.1 Hz, 2H), 7.21–7.17 (m, 5H), 7.11–7.08 (m, 2H), 4.76 (d, *J* = 6.8 Hz, 1H), 4.47 (p, *J* = 6.9 Hz, 1H), 2.39 (s, 3H), 1.42 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 143.1, 142.0, 137.7, 129.4, 128.5, 127.5, 127.1, 126.1, 53.6, 23.5, 21.5. Chiral HPLC analysis: Chiralcel OD (heptane/*i*-PrOH = 90/10, 1.0 mL/min, 254 nm, 25 °C): *t* = 10.6, 12.8 min.

4-Methoxy-N-(1-phenylethyl)benzenesulfonamide (7).²⁸ Prepared using procedure A (0.17 g, 75%) using the known imidate^{19e} and purified by silica gel chromatography (100% DCM).

7. Waxy off-white solid (0.17 g, 75%); mp = 94–96 °C; TLC R_f = 0.25 (100% DCM); ¹H NMR (400 MHz, CDCl₃) δ 7.65 (dt, *J* = 9.2, 2.8 Hz, 2H), 7.21–7.15 (m, 3H), 7.11–7.09 (m, 2H), 6.82 (dt, *J* = 9.6, 2.8 Hz, 2H), 5.35 (d, *J* = 7.2 Hz, 1H), 4.43 (p, *J* = 7.2 Hz, 1H), 3.82 (s, 3H), 1.40 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.6, 142.2, 132.2, 129.2, 128.5, 127.4, 126.2, 114.0, 55.6, 53.7, 23.6.

N-(1-Phenylethyl)benzenesulfonamide (9).²⁹ Prepared using procedure A (0.14 g, 72%) using the known imidate^{19e} and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

9. White solid (0.14 g, 85%); mp = 87–91 °C; TLC R_f = 0.44 (30% ethyl acetate/70% hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.74–7.71 (m, 2H), 7.44 (td, *J* = 6.4, 1.2 Hz, 1H), 7.36–7.31 (m, 2H), 7.14–7.07 (m, 5H), 5.65 (d, *J* = 7.2 Hz, 1H), 4.48 (p, *J* = 6.8 Hz, 1H), 1.40 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 142.0, 140.7, 132.3, 128.8, 128.5, 127.4, 127.0, 126.1, 53.8, 23.6.

4-Chloro-N-(1-phenylethyl)benzenesulfonamide (11).³⁰ Prepared using procedure A (0.19 g, 83%) using the known imidate^{19e} and purified using silica gel chromatography (10% ethyl acetate/90% hexanes).

11. White amorphous solid (0.15 g, 67%); mp = 71–75 °C; TLC R_f = 0.21 (10% ethyl acetate/90% hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 3H), 7.19–7.17 (m, 2H), 7.08–7.05 (m, 2H), 5.14 (d, *J* = 7.2 Hz, 1H), 4.50 (p, *J* = 6.8 Hz, 1H), 1.44 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 141.6, 139.2, 138.7, 129.0, 128.6, 128.5, 127.6, 126.1, 53.9, 23.6.

2-Nitro-N-(1-phenylethyl)benzenesulfonamide (13).³¹ 2-Nitrobenzenesulfonamide (0.18 g, 0.87 mmol) and BF₃·OEt₂ (0.02 g, 0.09 mmol) were suspended in DCM (4 mL). The suspension was heated to reflux. A 0.1 M solution of 1-phenethyl trichloroacetimidate **2**^{19e} (0.30 g, 1.13 mmol) in DCM was added to the suspension using a syringe pump over the course of 1 h. The reaction was refluxed for 18 h. After cooling to room temperature, the reaction was poured into saturated aq. NaHCO₃ and extracted with DCM (3×). The combined organic extracts were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The residue was purified via silica gel chromatography (100% DCM) providing **13** (0.18 g, 70%) as a white solid. The sulfonamide **13** was also prepared using procedure A (0.04 g, 13%).

13. White solid (0.18 g, 70%); mp = 89–91 °C; TLC R_f = 0.58 (100% DCM); ¹H NMR (400 MHz, CDCl₃) δ 7.71 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.67 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.54 (td, *J* = 7.6, 1.2 Hz, 1H), 7.40 (td, *J* = 8.0, 1.6 Hz, 1H), 7.12–7.06 (m, 5H), 5.77 (d, *J* = 8.4 Hz, 1H), 4.69 (p, *J* = 6.8 Hz, 1H), 1.52 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 147.3, 141.2, 134.5, 132.9, 132.5, 130.8, 128.5, 127.7, 126.1, 124.9, 55.0, 23.7.

N-(1-Phenylethyl)methanesulfonamide (15).³¹ Prepared using procedure A (0.12 g, 79%) using the known imidate^{19e} and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

15. Yellow oil (0.12 g, 79%); TLC R_f = 0.35 (30% ethyl acetate/70% hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.39–7.26 (m, 5H), 5.16 (d, *J* = 7.2 Hz, 1H); 4.64 (p, *J* = 7.2 Hz, 1H), 2.61 (s, 3H), 1.53 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 142.4, 129.0, 128.0, 126.2, 53.8, 41.8, 24.0.

N-(1-Phenylethyl)ethanesulfonamide (17).³² Prepared using procedure A (0.15 g, 76%) using the known imidate^{19e} and purified using silica gel chromatography (100% DCM flushed with 30% ethyl acetate/70% hexanes).

17. White solid (0.15 g, 76%); mp = 89–91 °C; TLC R_f = 0.34 (30% ethyl acetate/70% hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.26 (m, 5H), 5.17 (br d, *J* = 7.1 Hz, 1H), 4.62 (p, *J* = 7.1 Hz, 1H), 2.76 (hex, *J* = 7.4 Hz, 1H), 2.61 (hex, *J* = 7.4 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 3H), 1.17 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 142.8, 128.8, 127.9, 126.2, 53.7, 47.9, 24.2, 8.0.

N-(1-Phenylethyl)-2-(trimethylsilyl)ethanesulfonamide (19).³³ Prepared using procedure A (0.13 g, 70%) using the known imidate^{19e} and purified by silica gel chromatography (30% ethyl acetate/80% hexanes).

19. White crystals (0.13 g, 70%); mp = 61–64 °C; TLC R_f = 0.58 (20% ethyl acetate/80% hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.38–7.27 (m, 5H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.62 (p, *J* = 6.9 Hz, 1H), 2.61 (td, *J* = 14.0, 3.9 Hz, 1H), 2.47 (td, *J* = 13.9, 4.4 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 3H), 0.86 (td, *J* = 13.8, 4.0 Hz, 1H), 0.74 (td, *J* = 14.0, 4.3 Hz, 1H), -0.13 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 143.0, 129.1, 128.2, 126.4, 53.9, 50.0, 24.3, 10.5, -2.0.

3-Oxo-N-(1-phenylethyl)benzo[d]isothiazole-2(3H)-sulfonamide 1,1-Dioxide (21).³⁴ Prepared using procedure A using the known imidate^{19e} and purified by silica gel chromatography (20% ethyl acetate/80% hexanes). The crude product was then taken up in ethyl acetate (30 mL) and washed with 2 M NaOH (5 × 20 mL). The organic layers were combined, dried over sodium sulfate, and

concentrated *in vacuo* to provide **21** as a clear colorless oil (0.22 g, 98%).

21. Clear colorless oil (0.22 g, 98%); TLC R_f = 0.37 (20% ethyl acetate/80% hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.98–7.95 (m, 1H), 7.90–7.88 (m, 1H), 7.82 (td, J = 7.4, 1.2 Hz, 1H), 7.77 (td, J = 7.2, 1.4 Hz, 1H), 7.60–7.57 (m, 2H), 7.36 (tt, J = 6.8, 1.2 Hz, 2H), 7.29 (tt, J = 6.2, 1.3 Hz, 1H), 5.45 (q, J = 7.3 Hz, 1H), 2.03 (d, J = 7.3 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 158.5, 138.6, 137.8, 134.6, 134.2, 128.5, 128.2, 127.7, 127.3, 125.0, 120.7, 53.0, 17.7.

4-Methyl-N-(1-phenylethyl)benzenesulfonamide (23).³⁵ Prepared using procedure A (0.06 g, 27%) using the known imidate^{19e} and purified using silica gel chromatography (100% DCM).

23. White powder (0.06 g, 27%); mp = 60–62 °C; TLC R_f = 0.52 (100% DCM); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.74 (dt, J = 8.4, 1.8 Hz, 2H), 7.32–7.24 (m, 7H), 5.29 (q, J = 7.0 Hz, 1H), 2.57 (s, 3H), 2.43 (s, 3H), 1.29 (d, J = 7.0 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 143.1, 139.9, 137.3, 129.7, 128.4, 127.5, 127.3, 127.1, 54.8, 28.4, 21.5, 15.2.

1-(*p*-Tolyl)ethyl 2,2,2-Trichloroacetimidate (26). To a round-bottom flask under argon were added 1-(*p*-tolyl)ethanol (0.51 g, 3.74 mmol), trichloroacetonitrile (0.48 mL, 4.86 mmol), and DCM (7 mL). DBU (0.06 mL, 0.37 mmol) was added, and the reaction mixture was stirred at room temperature for 18 h. Triethylamine (1 mL) was added to the reaction mixture, and the solvent was removed *in vacuo*. Purification of the residue by silica gel chromatography (1% triethylamine/9% ethyl acetate/90% hexanes) provided imidate **26** as white crystals (0.81 g, 77%).

26. White crystals (0.81 g, 77%); mp = 41–42 °C; TLC R_f = 0.50 (10% ethyl acetate/90% hexanes); IR (KBr) 3344, 2982, 2931, 2868, 1663, 1285 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.27 (br s, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 5.94 (q, J = 6.6 Hz, 1H), 2.34 (s, 3H), 1.63 (d, J = 6.6 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 161.7, 138.4, 137.6, 129.2, 125.8, 91.8, 77.2, 22.2, 21.2. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{Cl}_3\text{NO}$: C, 47.09; H, 4.31; N, 4.99. Found: C, 46.75; H, 4.05; N, 4.80.

4-Methyl-N-(1-(*p*-tolyl)ethyl)benzenesulfonamide (27).³⁶ Prepared using procedure A (0.19 g, 89%) using imidate **26** and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

27. White powder (0.19 g, 89%); mp = 118–119 °C; TLC R_f = 0.65 (30% ethyl acetate/70% hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.62 (dt, J = 8.3, 1.0 Hz, 2H), 7.17 (dd, J = 8.5, 0.6 Hz, 2H), 6.98 (app s, 4H), 5.04 (d, J = 7.0 Hz, 1H), 4.40 (p, J = 6.9 Hz, 1H), 2.38 (s, 3H), 2.27 (s, 3H), 1.39 (d, J = 6.8 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 143.0, 139.1, 137.8, 137.1, 129.4, 129.2, 127.1, 126.1, 53.4, 23.5, 21.5, 21.0.

1,2,3,4-Tetrahydronaphthalen-1-yl 2,2,2-trichloroacetimidate (28). To a round-bottom flask under argon were added 1,2,3,4-tetrahydronaphthalen-1-ol (1.00 g, 6.75 mmol), DBU (0.10 mL, 0.67 mmol), and DCM (23 mL). The reaction mixture was stirred at room temperature for 15 min and then cooled to 0 °C in an ice/water bath. Trichloroacetonitrile (0.88 mL, 8.77 mmol) was added, and the reaction mixture was warmed to room temperature and stirred overnight. The solvent was then removed *in vacuo*. Triethylamine (1 mL) was added, and the residue was purified by silica gel chromatography (2% triethylamine/10% ethyl acetate/88% hexanes) to provide **28** as a clear colorless oil (1.68 g, 94%).

28. Clear colorless oil (1.68 g, 94%); TLC R_f = dec (10% ethyl acetate/90% hexanes); IR (thin film on KBr) 3341, 3064, 3024, 2940, 2869, 1657 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.39 (br s, 1H), 7.39–7.37 (m, 1H), 7.27–7.14 (m, 3H), 6.10 (t, J = 4.8 Hz, 1H), 2.93–2.74 (m, 2H), 2.22–1.96 (m, 3H), 1.89–1.81 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 162.5, 138.1, 134.2, 129.6, 129.1, 128.3, 126.1, 92.1, 75.5, 29.1, 27.9, 19.1. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{Cl}_3\text{NO}$: C, 49.26; H, 4.13; N, 4.75. Found: C, 48.92; H, 4.44; N, 4.92.

4-Methyl-N-(1,2,3,4-tetrahydronaphthalen-1-yl)benzenesulfonamide (29).³⁷ Prepared using procedure A (0.18 g, 79%) using imidate **28** and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

29. Beige solid (0.18 g, 79%); mp = 115–118 °C; TLC R_f = 0.62 (30% ethyl acetate/70% hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.75 (td, J = 8.4, 1.9 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 7.05 (td, J = 7.3, 1.2 Hz, 1H), 7.00–6.94 (m, 2H), 6.87 (d, J = 7.6 Hz, 1H), 4.67 (br d, J = 7.8 Hz, 1H), 4.37 (p, J = 5.2 Hz, 1H), 2.71–2.54 (m, 2H), 2.38 (s, 3H), 1.79–1.71 (m, 3H), 1.66–1.62 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 143.4, 138.2, 137.6, 135.6, 129.8, 129.2, 128.8, 127.6, 127.2, 126.3, 51.9, 30.8, 28.9, 21.6, 19.2.

1-(Naphthalen-1-yl)ethyl 2,2,2-trichloroacetimidate (30). To a round-bottom flask under argon was added 1-(naphthalen-1-yl)ethanol (0.85 g, 4.92 mmol), trichloroacetonitrile (0.59 mL, 5.90 mmol) and DCM (12 mL). DBU (0.08 mL, 0.49 mmol) was added to the reaction mixture and the reaction mixture was stirred at room temperature for 18h. Triethylamine (1 mL) was added to the reaction mixture and the reaction mixture was purified by silica gel chromatography (2% triethylamine/8% ethyl acetate/90% hexanes) to provide **30** as a clear colorless oil (1.32 g, 85%).

30. Clear colorless oil (1.32 g, 85%); TLC R_f = 0.80 (10% ethyl acetate/90% hexanes); IR (thin film on KBr) 3339, 3052, 2983, 2933, 2870, 1661, 1598 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.36 (br s, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.89–7.87 (m, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.71 (d, J = 7.1 Hz, 1H), 7.56–7.47 (m, 3H), 6.74 (q, J = 6.6 Hz, 1H), 1.81 (d, J = 6.6 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 161.7, 137.1, 133.8, 130.2, 128.9, 128.5, 126.3, 125.7, 125.4, 123.2, 123.0, 91.8, 74.6, 21.34. Anal. Calcd for $\text{C}_{14}\text{H}_{12}\text{Cl}_3\text{NO}$: C, 53.11; H, 3.82; N, 4.42. Found: C, 53.47; H, 3.62; N, 4.75.

4-Methyl-N-(1-(naphthalen-1-yl)ethyl)benzenesulfonamide (31).²⁸ Prepared using procedure A (0.20 g, 79%) using imidate **30** and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

31. Orange oil (0.20 g, 79%); TLC R_f = 0.43 (30% ethyl acetate/70% hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.89–7.87 (m, 1H), 7.80–7.78 (m, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.56 (dt, J = 8.3, 1.7 Hz, 2H), 7.47–7.40 (m, 2H), 7.36 (dd, J = 7.2, 1.0 Hz, 1H), 7.31–7.27 (m, 1H), 7.04 (d, J = 7.9 Hz, 2H), 5.28 (p, J = 6.8 Hz, 1H), 5.15 (d, J = 6.8 Hz, 1H), 2.31 (s, 3H), 1.58 (d, J = 6.8 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 143.1, 137.7, 137.5, 133.8, 130.1, 129.3, 128.8, 128.1, 127.1, 126.3, 125.6, 125.3, 123.4, 122.6, 49.8, 23.2, 21.4.

1-(*o*-Tolyl)ethyl 2,2,2-Trichloroacetimidate (32). To a round-bottom flask under argon was added 1-(*o*-tolyl)ethanol (1.08 g, 8.89 mmol), trichloroacetonitrile (1.16 mL, 11.56 mmol) and DCM (17 mL). DBU (0.13 mL, 0.89 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. The solvent was then removed *in vacuo*. Triethylamine (1 mL) was added, and the residue was purified by silica gel chromatography (1% triethylamine/9% ethyl acetate/90% hexanes) to provide **32** as white crystals (1.82 g, 73%).

32. Clear colorless oil (1.82 g, 73%); TLC R_f = 0.68 (10% ethyl acetate/90% hexanes); IR (KBr) 3342, 3025, 2980, 2931, 1662, 1288 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.27 (br s, 1H), 7.51–7.48 (m, 1H), 7.25–7.14 (m, 3H), 6.14 (q, J = 6.5 Hz, 1H), 2.42 (s, 3H), 1.61 (d, J = 6.6 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 161.5, 139.7, 134.7, 130.3, 127.7, 126.3, 125.1, 91.8, 74.3, 21.0, 19.0. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{Cl}_3\text{NO}$: C, 47.09; H, 4.31; N, 4.99. Found: C, 46.88; H, 4.06; N, 4.81.

4-Methyl-N-(1-(*o*-tolyl)ethyl)benzenesulfonamide (33).^{6b} Prepared using procedure A (0.21 g, 94%) using imidate **32** and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

33. Off-white solid (0.31 g, 94%); mp = 87–89 °C; TLC R_f = 0.56 (30% ethyl acetate/70% hexanes); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.50 (dt, J = 8.3, 1.7 Hz, 2H), 7.06–7.01 (m, 3H), 6.95–6.87 (m, 3H), 5.60 (d, J = 7.2 Hz, 1H), 4.62 (p, J = 6.9 Hz, 1H), 2.24 (s, 3H), 2.10 (s, 3H), 1.23 (d, J = 6.8 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 143.0, 140.5, 137.7, 134.3, 130.3, 129.4, 127.1, 127.0, 126.4, 125.5, 49.8, 23.1, 21.5, 19.0.

1-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)ethyl 2,2,2-Trichloroacetimidate (34). To a round-bottom flask under argon were added 1-(6-bromobenzo[*d*][1,3]dioxol-5-yl)ethanol³⁸ (2.90 g, 11.83 mmol), DBU (0.18 mL, 1.18 mmol), and DCM (39 mL). The reaction mixture was stirred at room temperature for 15 min and then

cooled to 0 °C in an ice/water bath. Trichloroacetonitrile (1.53 mL, 15.38 mmol) was added to the reaction mixture, and the reaction mixture was warmed to room temperature and stirred overnight. The solvent was then removed *in vacuo*. Triethylamine (1 mL) was added, and the residue was purified by silica gel chromatography (1% triethylamine/50% ethyl acetate/49% hexanes) to provide **34** as a clear colorless oil (3.80 g, 83%).

34. Clear colorless oil (3.80 g, 83%); TLC R_f = 0.69 (30% ethyl acetate/70% hexanes); IR (thin film on KBr) 3339, 3080, 2983, 2930, 2897, 1667 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.37 (br s, 1H), 7.03 (s, 1H), 6.98 (s, 1H), 6.17 (q, J = 6.4 Hz, 1H), 5.96 (q, J = 1.2 Hz, 2H), 1.58 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.1, 147.81, 147.80, 134.2, 112.6, 112.0, 106.2, 101.8, 91.5, 76.3, 21.0. Anal. Calcd for $\text{C}_{11}\text{H}_9\text{BrCl}_3\text{NO}_3$: C, 33.92; H, 2.33; N, 3.60. Found: C, 33.88; H, 2.49; N, 3.48.

N-(1-(6-Bromobenzo[d][1,3]dioxol-5-yl)ethyl)-4-methylbenzenesulfonamide (35). Prepared using procedure A (0.29 g, 88%) using imidate **34** and purified by silica gel chromatography (30% ethyl acetate/70% hexanes).

35. Yellow powder (0.29 g, 88%); mp = 106 °C (dec); TLC R_f = 0.53 (30% ethyl acetate/70% hexanes); IR (KBr) 3272, 2986, 1714, 1503, 1478, 1326 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.64 (dt, J = 8.5, 1.9 Hz, 2H), 7.18 (dd, J = 8.4, 0.5 Hz, 2H), 6.82 (s, 1H), 6.69 (s, 1H), 5.89 (dd, J = 6.9, 1.4 Hz, 2H), 5.46 (d, J = 6.6 Hz, 1H), 4.79 (p, J = 6.8 Hz, 1H), 2.38 (s, 3H), 1.32 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.6, 147.4, 143.2, 137.0, 134.6, 129.4, 127.2, 112.37, 112.36, 107.4, 101.8, 52.9, 22.9, 21.5. Anal. Calcd for $\text{C}_{16}\text{H}_{16}\text{BrNO}_4\text{S}$: C, 48.25; H, 4.05; N, 3.52. Found: C, 48.07; H, 4.06; N, 3.30.

1-(Furan-2-yl)pentyl 2,2,2-Trichloroacetimidate (36). To a round-bottom flask containing 1-(furan-2-yl)pentan-1-ol³⁹ (0.52 g, 3.37 mmol) dissolved in DCM (33 mL) were added trichloroacetonitrile (0.58 g, 4.04 mmol) and DBU (0.05 g, 0.34 mmol). The reaction mixture was stirred at room temperature for 1 h. The solvent was then removed *in vacuo*. Triethylamine (1 mL) was added, and the residue was purified by silica gel chromatography (1% triethylamine/19% ethyl acetate/80% hexanes) to provide **36** as a yellow oil (0.32 g, 33%).

36. Yellow oil (0.32 g, 33%); TLC R_f = 0.62 (20% ethyl acetate/80% hexanes); IR (KBr) 3346, 2960, 2873, 1656, 1501 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.35 (s, 1H), 7.40 (dd, J = 1.8, 0.8 Hz, 1H), 6.39 (d, J = 3.12 Hz, 1H), 6.34 (dd, J = 3.2, 1.8 Hz, 1H), 5.96 (t, J = 6.6 Hz, 1H), 2.18–2.08 (m, 1H), 2.07–1.98 (m, 1H), 1.47–1.26 (m, 4H), 0.91 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.0, 152.3, 142.4, 110.2, 108.5, 91.7, 73.9, 32.4, 27.4, 22.3, 13.9. Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{Cl}_3\text{NO}_2$: C, 44.25; H, 4.73; N, 4.69. Found: C, 44.49; H, 4.45; N, 4.79.

N-(1-(Furan-2-yl)pentyl)-4-methylbenzenesulfonamide (37).⁴⁰ Prepared using procedure A (0.09 g, 44%) with imidate **37** and purified using silica gel chromatography (20% ethyl acetate/80% hexanes).

37. Reddish solid (0.09 g, 44%); mp = 54–56 °C; TLC R_f = 0.38 (20% ethyl acetate/80% hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.61 (dt, J = 8.5, 1.9 Hz, 2H), 7.18 (dd, J = 8.5, 0.6 Hz, 2H), 7.12 (dd, J = 1.8, 0.8 Hz, 1H), 6.09 (dd, J = 3.2, 1.8 Hz, 1H), 5.89 (d, J = 3.2 Hz, 1H), 5.1 (d, J = 8.7 Hz, 1H), 4.38 (q, J = 7.3 Hz, 1H), 2.37 (s, 3H), 1.78–1.73 (m, 2H), 1.28–1.20 (m, 3H), 1.18–1.11 (m, 1H), 0.82 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 153.2, 142.9, 141.7, 137.8, 129.3, 127.0, 109.9, 106.7, 51.7, 34.7, 27.7, 22.1, 21.4, 13.8.

N-Benzhydryl-4-methylbenzenesulfonamide (39).⁴¹ Prepared using procedure A (0.23 g, 89%) using the known imidate⁴² and purified using silica gel chromatography (20% ethyl acetate/80% hexanes).

39. White powder (0.23 g, 89%); mp = 122–124 °C; TLC R_f = 0.42 (20% ethyl acetate/80% hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.56 (dt, J = 8.5, 2.0 Hz, 2H), 7.23–7.19 (m, 6H), 7.15–7.08 (m, 6H), 5.56 (d, J = 6.8 Hz, 1H), 5.01 (d, J = 6.8 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.2, 140.6, 137.4, 129.4, 128.5, 127.5, 127.4, 127.2, 61.4, 21.5.

Methyl 4-(4-(Phenyl(2,2,2-trichloro-1-iminoethoxy)methyl)phenyl)butanoate (40). To a round-bottom flask containing alcohol

56²⁵ (0.09 g, 0.31 mmol) was added DCM (1 mL) followed by trichloroacetonitrile (0.06 g, 0.38 mmol) and DBU (0.01 g, 0.03 mmol). The reaction mixture was stirred at room temperature for 4 h. The solvent was then removed *in vacuo*. Triethylamine (1 mL) was added to the residue, and the reaction mixture was purified by silica gel chromatography (1% triethylamine/29% ethyl acetate/70% hexanes) to provide **40** as a pale yellow oil (0.130 g, 99%).

40. Pale yellow oil (0.13 g, 99%); TLC R_f = 0.22 (30% ethyl acetate/70% hexanes); IR (KBr) 3651, 3279, 1731, 1495 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.40 (br s, 1H), 7.43–7.41 (m, 2H), 7.35–7.33 (m, 4H), 7.29–7.28 (m, 1H), 7.15 (d, J = 8.2 Hz, 2H), 6.92 (s, 1H), 3.63 (s, 3H), 2.62 (t, J = 7.4 Hz, 2H), 2.32 (t, J = 7.4 Hz, 2H), 1.93 (p, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.8, 161.4, 141.2, 139.9, 137.5, 128.6, 128.5, 128.0, 127.1, 126.9, 91.7, 81.3, 51.5, 34.8, 34.4, 26.3. Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{Cl}_3\text{NO}_3$: C, 56.03; H, 4.70; N, 3.27. Found: C, 56.28; H, 4.90; N, 3.28.

Methyl 4-(4-(4-Methylphenylsulfonamido)(phenyl)methyl)phenyl)butanoate (41). Prepared following procedure A (0.23 g, 67%) with imidate **40** and purified using silica gel chromatography (30% ethyl acetate/70% hexanes) followed by a second purification using silica gel chromatography (100% DCM).

41. Clear colorless oil (0.23 g, 67%); TLC R_f = 0.45 (30% ethyl acetate/70% hexanes); IR (thin film on KBr) 3328, 3227, 3062, 2950, 2864, 1731, 1599 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.55 (dt, J = 6.6, 1.6 Hz, 2H), 7.20–7.17 (m, 3H), 7.12–7.09 (m, 4H), 7.00 (d, J = 1.6 Hz, 4H), 5.53 (d, J = 6.9 Hz, 1H), 5.32 (d, J = 7.2 Hz, 1H), 3.65 (s, 3H), 2.56 (t, J = 7.4 Hz, 2H), 2.36 (s, 3H), 2.29 (t, J = 7.4 Hz, 2H), 1.88 (p, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 174.0, 143.0, 140.8, 140.7, 138.3, 137.4, 129.3, 128.6, 128.5, 127.44, 127.40, 127.3, 127.2, 61.1, 51.7, 34.6, 33.3, 26.4, 21.4. Anal. Calcd for $\text{C}_{25}\text{H}_{27}\text{NO}_4\text{S}$: C, 68.62; H, 6.22; N, 3.20. Found: C, 68.52; H, 6.44; N, 3.59.

N-(4-Methoxybenzyl)-4-methylbenzenesulfonamide (43).⁴³ Prepared using procedure A (0.17 g, 75%) using the commercially available imidate and purified using silica gel chromatography (100% DCM) followed by recrystallization from methanol.

43. White solid (0.17 g, 75%); mp = 122–123 °C; TLC R_f = 0.61 (40% acetone/60% hexanes); ^1H NMR (300 MHz, CDCl_3) δ 7.75 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 6.79 (d, J = 8.7 Hz, 2H), 4.59 (t, J = 5.8 Hz, 1H), 4.05 (d, J = 6.0 Hz, 2H), 3.78 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.3, 143.5, 136.9, 129.7, 128.3, 129.3, 127.2, 114.1, 55.3, 46.8, 21.5.

4-Methyl-N-(2-methylbenzyl)benzenesulfonamide (45).⁴⁴ Prepared using procedure A (0.12 g, 55%) using the known imidate⁴⁵ and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

45. White solid (0.12 g, 55%); mp = 107–109 °C; TLC R_f = 0.31 (30% ethyl acetate/70% hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.76 (dt, J = 8.5, 2.0 Hz, 2H), 7.31 (dd, J = 8.5, 0.6 Hz, 2H), 7.20–7.10 (m, 4H), 4.45 (t, J = 5.8 Hz, 1H), 4.09 (d, J = 6.0 Hz, 2H), 2.44 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.6, 136.7, 136.6, 133.9, 130.6, 129.7, 128.9, 128.3, 127.2, 126.2, 45.4, 21.6, 18.8.

N-(Cyclohex-2-en-1-yl)-4-methylbenzenesulfonamide (49).⁴⁶ Prepared using procedure A (0.12 g, 60%) using the known imidate⁴⁷ and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

49. Colorless crystals (0.12 g, 60%); mp = 99–100 °C; TLC R_f = 0.45 (30% ethyl acetate/70% hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.77 (dt, J = 8.5, 2.0 Hz, 2H), 7.30 (dd, J = 8.5, 0.6 Hz, 2H), 5.79–5.74 (m, 1H), 5.37–5.32 (m, 1H), 4.44 (d, J = 8.6 Hz, 1H), 3.84–3.79 (m, 1H), 2.43 (s, 3H), 2.00–1.87 (m, 2H), 1.79–1.73 (m, 1H), 1.64–1.50 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.2, 138.4, 131.5, 129.7, 127.1, 127.0, 49.0, 30.2, 24.5, 21.5, 19.3.

N-Allyl-4-methylbenzenesulfonamide (51).⁴⁸ Prepared using procedure A (0.05 g, 28%) using the commercially available imidate and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

51. Off-white solid (0.05 g, 28%); mp = 53–56 °C; TLC R_f = 0.42 (30% ethyl acetate/70% hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.76 (dt, J = 8.5, 2.0 Hz, 2H), 7.31 (dd, J = 8.5, 0.6 Hz, 2H), 5.77–5.68 (m, 1H), 5.19–5.08 (m, 2H), 4.51 (t, J = 4.50 Hz, 1H), 3.59 (t, J = 6.1,

1.5 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.5, 137.0, 133.0, 129.7, 127.2, 117.7, 45.8, 21.5.

N,4-Dimethylbenzenesulfonamide (53).⁴⁹ Prepared using procedure A (0.010 g, 5%) using the commercially available imidate and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

53. Off-white solid (0.010 g, 5%); mp = 69–71 °C; TLC R_f = 0.33 (30% ethyl acetate/70% hexanes); ^1H NMR (400 MHz CDCl_3) δ 7.68 (dt, J = 8.3 Hz, 2H), 7.25 (dd, J = 8.4, 0.5 Hz, 2H), 4.22 (d, J = 4.7 Hz, 1H), 2.58 (d, J = 5.4 Hz, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.5, 135.8, 129.7, 127.3, 29.4, 21.5.

Methyl-4-(4-(4-chlorophenylsulfonamido)(phenyl)methyl)butanoate (57).²⁵ Prepared using procedure A (0.08 g, 88%) and purified using silica gel chromatography (30% ethyl acetate/70% hexanes).

57. Clear colorless oil (0.08 g, 88%); TLC R_f = 0.40 (30% ethyl acetate/70% hexanes); IR (KBr) 3153, 2986, 2820, 1730, 1586 cm^{-1} ; ^1H NMR (400 MHz CDCl_3) δ 7.53 (dt, J = 9.2, 2.5 Hz, 2H), 7.25–7.18 (m, 5H), 7.12–7.09 (m, 2H), 7.00 (br s, 4H), 5.58 (d, J = 7.6 Hz, 1H), 5.53 (d, J = 7.6 Hz, 1H), 3.65 (s, 3H), 2.57 (t, J = 7.4 Hz, 2H), 2.30 (t, J = 7.4 Hz, 2H), 1.89 (p, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.9, 141.1, 140.2, 139.0, 138.7, 137.7, 128.9, 128.7, 128.59, 128.57, 127.7, 127.4, 127.3, 61.3, 51.6, 34.6, 33.4, 26.4. Anal. Calcd for $\text{C}_{24}\text{H}_{24}\text{ClNO}_4\text{S}$: C, 62.94; H, 5.28; N, 3.06. Found: C, 63.17; H, 5.35; N, 3.22.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01421.

Copies of ^1H and ^{13}C NMR spectra of new compounds and chiral HPLC data for compounds 2 and 3 (PDF)

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Notes

The authors declare no competing financial interest.

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