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Preparation of Unsymmetrical Sulfonylureas from *N*,*N*′-Sulfuryldiimidazoles

Serge Beaudoin,* Kenneth E. Kinsey, and James F. Burns

Department of Chemistry, Icagen Inc., P.O. Box 14487, Research Triangle Park, North Carolina 27709

sbeaudoin@icagen.com

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The synthetic methods reported in the literature for the preparation of sulfonylureas tend to be restricted in scope or unsuitable for use in parallel synthesis. We have developed a method for preparing sterically congested sulfonylureas based on *N*,*N*′-sulfuryldiimidazole that is both convenient and amenable to parallel synthesis. Sequential activation by way of alkylation of the imidazole group using methyl triflate followed by nucleophilic displacement with a variety of amines and anilines afford the unsymmetrical sulfonylurea. Sulfonylureas prepared from anilines were obtained in high yields using *N*,*N*′-sulfuryldiimidazole, while the somewhat more sterically congested analogue, *N*,*N*′-sulfurylbis-2-methylimidazole, proved to be superior for alkylamines.

Introduction

To attenuate toxicity and/or improve the pharmacokinetic profile of biologically active molecules, the medicinal chemist frequently utilizes a variety of bioisoteric replacements.[1] One such bioisostere, the sulfonylurea group, has been used as a surrogate for amides, ureas, thioureas, nitrosoureas, carbamates, and sulfonamides.[2] However, the limitations of the chemical methods available for the preparation of this pharmacophore have probably contributed to its limited use in medicinal chemistry. Our interest in the use of this functional group in our own research programs prompted us to search for a convenient method for the preparation of substituted sulfonylureas.

Primary sulfonylureas ($R^1R^2NSO_2NH_2$) are commonly prepared from the reaction of an amine with sulfamide.[3] Alternatively, they can be obtained in modest to moderate yields using sulfamoyl chloride.[4] Furthermore, secondary sulfonylureas ($R^1R^2NSO_2NHR^3$) can be synthesized by alkylation of a primary sulfonylurea derivatized as the *tert*-butyloxycarbonyl carbamate.[2d] Here, alkylation occurs at the most acidic nitrogen between the carbonyl of the carbamate and the sulfuryl group. Removal of the carbamate group then provides the desired sulfonylurea. Substituted sulfonylureas are also prepared from the reaction of an amine with a sulfamoyl chloride; however, only a very small number of sulfamoyl chlorides are commercially available.[5] In turn, sulfamoyl chlorides are obtained from the conversion of a sulfamic acid to the corresponding chloride using phosphorus pentachloride.[6] These conditions are usually not compatible with sensitive molecules and afford product with low to moderate overall yields. Sulfamoyl chlorides can alternatively be prepared from the reaction of an amine with sulfuryl chloride.[2b,5] This method can be problematic in the case of reactive amines, which sometimes leads to the formation of a symmetrical sulfonylurea.

Yet another synthetic method entails the displacement of the *N*-oxazolidinone group from a sulfamoyl *N*-oxazolidinone[7] by an amine.[6c] Since this method uses mild conditions, it seems amenable for use in parallel synthesis. In the course of one of our medicinal chemistry projects, we became interested in preparing a series of sulfonylureas from cyclic amines. When attached to a cyclic amine such as 1,2,3,4-tetrahydroisoquinalone, we found that the oxazolidin-2-one group was not displaced by a primary amine. Instead, the reaction occurred at the oxazolidinone ring to form the carbamate (Scheme 1).[8] Furthermore, we found that anilines failed to react

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(5) (a) Wheeler, K. W.; Degering, E. D. *J. Am. Chem. Soc.* **1944**, *66*, 1242−1243.
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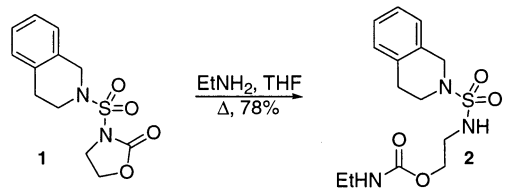
with the sulfamoyl oxazolidinone **1** under the usual reaction conditions.

SCHEME 1



In light of these results, we became interested in finding a better leaving group without the chemoselectivity liabilities of the oxazolidin-2-one moiety. A review of the literature showed imidazolinium salts to be superior leaving groups for the preparation of amides and esters[9] and sulfonamides and sulfonates.[10] Additionally, it is known that alkylation of the imidazole nitrogen increases its ability to act as a leaving group.[11] Accordingly, we decided to explore the use of *N*,*N*′-sulfuryldiimidazole[12] as a convenient reagent for the preparation of sulfonylureas. We anticipated that sequential activation of each of the imidazole moieties followed by displacement with an amine or an aniline would lead to the formation of unsymmetrical sulfonylureas (Figure 1). The key to the success of this synthetic strategy was selective monoalkylation of *N*,*N*′-sulfuryldiimidazole. We wish to report here the successful application of this methodology to the preparation of a variety of sulfonylureas, including both sterically crowded and electronically deactivated amines.

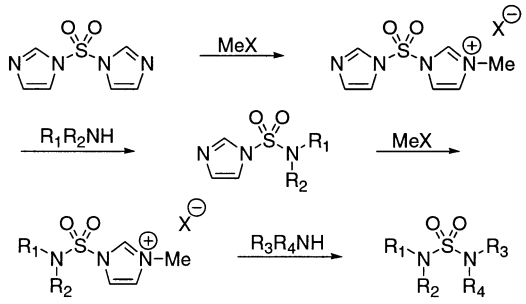
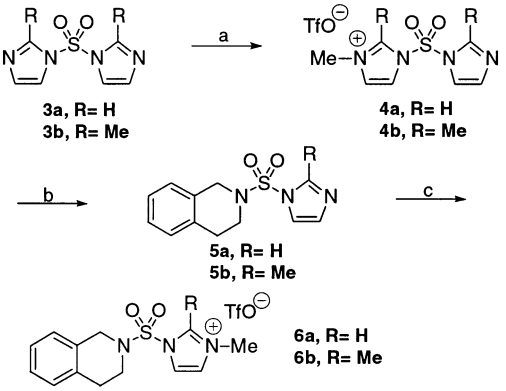


FIGURE 1.

Results and Discussion

In our hands, *N*,*N*′-sulfuryldiimidazole (**3a**) was conveniently prepared by reacting an excess of imidazole with sulfuryl chloride.[12] Alkylation of **3a** was readily achieved by treatment with methyl triflate in an ice-cooled methylene chloride solution. The resulting triflate salt **4a** spontaneously precipitated from the reaction mixture and was isolated by simple filtration. No dialkylation product was observed, presumably because precipitation of the monoalkylated salt **4a** occurred rapidly enough to prevent the alkylation of both imidazole groups of **3a**. The imidazolium group of salt **4a** was then displaced with an amine to afford the corresponding imidazoylsulfonylurea. As an example, reaction of **4a** with 1,2,3,4-tetrahydroisoquinoline resulted in the imidazolyl sulfonylurea **5a**. A second activation with methyl triflate then afforded the desired triflate salt **6a** quantitatively. This model system was used to study the preparation of sulfonylureas with various anilines and amines. Triflate salt **6b** was prepared following the same reaction sequence from **3b** (Scheme 2).

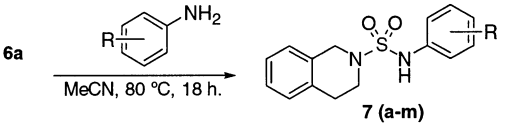
SCHEME 2[a]



[a] Key: (a) MeOTf, CH_2Cl_2, 0 °C; (b) 1,2,3,4-tetrahydroisoquinoline, MeCN, rt; (c) MeOTf, CH_2Cl_2, 0 °C.

We found that triflate salt **6a** failed to react with anilines at ambient temperature to give the desired sulfonylurea. However, when heated to 80 °C in acetonitrile, the reaction proceeded as expected to afford the desired products in moderate to excellent yields (Table 1). Use of other solvents such as DMF, toluene, *n*-BuOH, 1,4-dioxane, NMP, and chlorobenzene were found to be not as efficient for this transformation as judged by LC/MS analysis. The reactions in acetonitrile were typically

TABLE 1. Sulfonylureas from 6a and Primary Anilines



entry	R	product	yield[a] (%)
1	H	**7a**	94
2	4-Me	**7b**	92
3	4-OMe	**7c**	96
4	4-NMe_2	**7d**	58
5	4-F	**7e**	91
6	4-Cl	**7f**	89[b]
7	4-CO_2Et	**7g**	66
8	4-NO_2		trace
9	4-CN		trace
10	2-*i*-Pr	**7h**	83
11	2-OMe	**7i**	86
12	2-F	**7j**	74
13	2-Cl	**7k**	71[b]
14	2,6-(*i*-Pr)$_2$-	**7l**	48
15	2-CO_2Me	**7m**	69
16	2-NO_2		trace

[a] Isolated yields. [b] Reaction time of 48 h.

(9) Kamijo, T.; Yamamoto, R.; Harada, H.; Iizuka, K. *Chem. Pharm. Bull.* **1982**, *30*, 4242−4244.
(10) (a) Vilkas, E. *Bull. Soc. Ch. Fr.* **1978**, II, 37−38. (b) Monjoint, P.; Ruasse, M.-J. *Tetrahedron Lett.* **1984**, *25*, 3183−3186. (c) O'Connell, J. F.; Rapoport, H. *J. Org. Chem.* **1992**, *57*, 4775−4777.
(11) (a) Saha, A. K.; Schultz, P.; Rapoport, H. *J. Am. Chem. Soc.* **1989**, *111*, 4856−4859. (b) Watkins, B. E.; Kiely, J. S.; Rapoport, H. *J. Am. Chem. Soc.* **1982**, *104*, 5702−5708.
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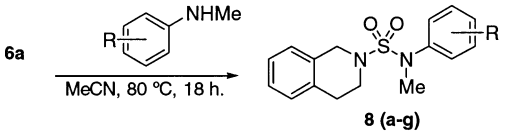
completed in a few hours to overnight. Since, in our hands, these reactions were typically run in a parallel fashion a convenient reaction time of 18 h was used for most cases. The reaction of **6a** with a variety of substituted anilines was explored and, in general, ready conversion to the desired product was observed. For example, treatment of **6a** with aniline or the moderately electron-donating analogue 4-methylaniline proceeded as expected to give the corresponding sulfonylurea in excellent yield (Table 1, entries 1 and 2). Anilines having moderate electron withdrawing substituents also reacted facilely to afford the desired products in good to excellent yield (Table 1, entries 5−7). Unfortunately, anilines substituted with stronger electron withdrawing groups such as nitro and cyano only afforded the desired sulfonylureas in trace amounts as determined by LC/MS (Table 1, entries 8 and 9). Surprisingly, while 4-chloroaniline (Table 1, entry 6) did react to give high yields of **7f**, a longer reaction time (48 h) was required. A variety of 2-substituted anilines (Table 1, entries 10−16) were also found to react smoothly with **6a**. Most notably, analogues having sterically bulky substituents in the 2-position also appeared to be well tolerated as exemplified by the reactions of 2-isopropylaniline and 2,6-diisopropylaniline to afford **7h** and **7l**, respectively (Table 1, entries 10 and 14).

Secondary anilines were also found to react with **6a** to give the corresponding sulfonylurea in moderate to excellent yields (Table 2). Similar steric and electronic effects were observed when compared to primary anilines (Table 1).

TABLE 2. Sulfonylureas from 6a and Secondary Anilines



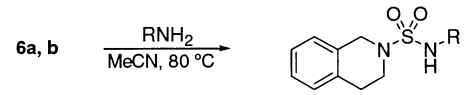
8 (a-g)

entry	R	product	yield[a] (%)
1	H	**8a**	90
2	4-Me	**8b**	95
3	4-OMe	**8c**	91
4	4-F	**8d**	93
5	4-CO_2Me	**8e**	70
6	2-Me	**8f**	87
7	2-CO_2Me	**8g**	50

[a] Isolated yields.

In contrast to anilines, alkylamines were found to react with **6a** at room temperature. As might be expected, reaction times varied with steric bulk, with sterically encumbered amines requiring longer reaction times. To ensure complete reaction, a reaction time of 20 h was selected when parallel syntheses were performed. Using these conditions, the reaction of alkylamines with **6a** was found to afford the expected sulfonylureas (Table 3). However, the yields tended to be variable, and significant amounts of side products could be observed in the reaction mixture. For example, low yields of the desired product were found when **6a** was reacted with butylamine, benzylamine, cyclopentylamine, and *tert*-butylamine (Table 3; entries 1, 3, 6, and 8). Examination of

TABLE 3. Sulfonylureas from 6a,b and Primary Amines



9 (a-e)

entry	R	reagent	product	yield[a] (%)
1	Bu	**6a**	**9a**	32
2	Bu	**6b**	**9a**	89
3	Bn	**6a**	**9b**	50
4	Bn	**6b**	**9b**	93
5	*i*-Pr	**6b**	**9c**	89
6	c-C_5H_9	**6a**	**9d**	34
7	c-C_5H_9	**6b**	**9d**	90
8	*t*-Bu	**6a**	**9e**	50
9	*t*-Bu	**6b**	**9e**	87

[a] Isolated yields.

the putative reaction mechanism offered some insights into the likely cause of these poor yields.

In contrast to the results reported by Monjoint[13] for the aminolysis of tosylimidazolinium salts, we observed the pentahedric intermediate **10a** by LC/MS analysis of the reaction mixture while monitoring the progression of the reaction with primary alkylamines (Table 3, entries 1, 3, 6, and 8) (Scheme 3). No attempts were made to isolate **10a**. Collapse of intermediate **10a** would be expected to afford the desired product (**11**) via elimination of the imidazolium group. A similar addition−elimination mechanism has been postulated for the nucleophilic substitutions of acetylimidazolinium chlorides.[14] However, kinetic studies were not able to support the formation of a discrete intermediate analogous to **10a** in the nucleophilic substitution of tosylimidazolinium salts.[15] For some amines (e.g., *N*-methyl-*tert*-butylamine), the symmetrical sulfonylurea **14**[16] was also observed in the reaction mixture.[17] Apparently, elimination of the tetrahydroisoquinoline moiety from intermediate **10a** afforded a second reactive intermediate **12** as well as **13**. Further reaction of **6a** with **13** would provide the observed side product **14**. Interestingly, the other possible symmetric sulfonylurea (**15**) that would be anticipated from reaction of **12** with the starting amine was not observed by LC/MS. With bulky secondary amines (e.g., *N*-methyl-*tert*-butylamine), **10a** could not be found in the reaction mixture. This may suggest that increased steric bulk accelerated the collapse of this pentahedric intermediate. Alternatively reaction of **6a** or **6b** with an amine via a concerted mechanism cannot be ruled out.[13]

It seemed reasonable to us that increasing the steric bulk around **10a** would improve its ability to collapse to give the desired products. For this reason, *N*,*N*′-sulfuryldi(2-methylimidazole) (**3b**) was synthesized. Reacting 2-methylimidazole and sulfuryl chloride in a

(13) Monjoint, P.; Ruasse, M.-J. *Bull. Soc. Ch. Fr.* **1988**, *2*, 356−360.

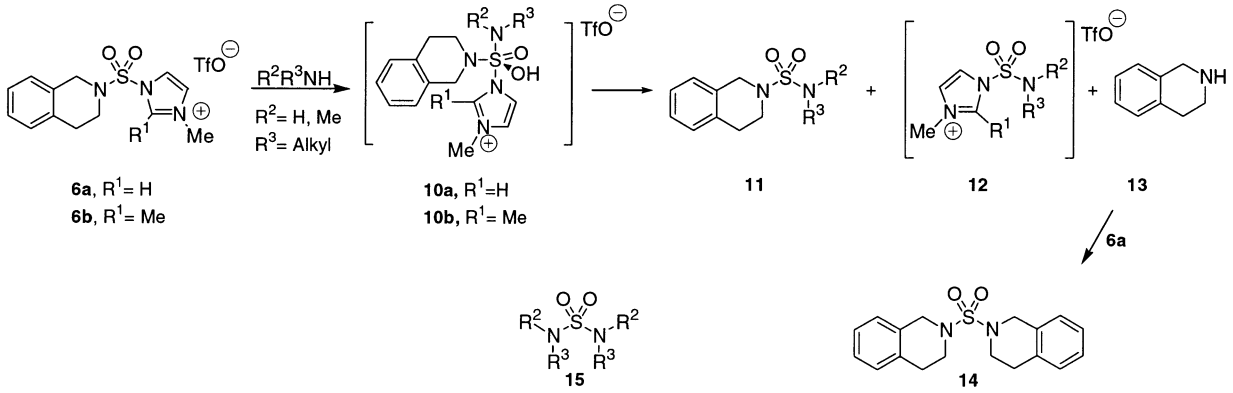
(14) (a) Oakenfull, D. G.; Jencks, W. P. *J. Am. Chem. Soc.* ***1971***, 93, 178. (b) Oakenfull, D. G.; Salvesen, K.; Jencks, W. P. *J. Am. Chem. Soc.* **1971**, *93*, 188.

(15) Monjoint, P.; Ruasse, M.-J. *Tetrahedron Lett.* **1984**, *25*, 3183−3186.

(16) Lee, C.-H.; Kohn, H. *J. Org. Chem.* **1990**, *55*, 6098.

(17) The LC/MS trace for the reaction of **6a** and *N*-methyl-*tert*-butylamine and the contaminated ^{1}H NMR spectra of **16d** with **14** are included in the Supporting Information.

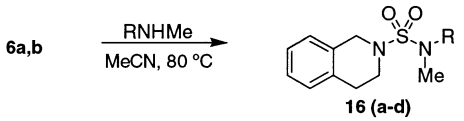
SCHEME 3



manner analogous to that described above for the synthesis of **3a** produced **3b**. In turn, **3b** reacted readily with 1,2,3,4-tetrahydroisoquinoline and methyl triflate to afford the triflate salt **6b** (Scheme 2). By using this bulkier reagent, reaction with primary amines proceeded readily and in high yield (Table 3). The pentahedric intermediate **10b** was not observed by LC/MS analysis of the reaction mixtures. In two direct comparisons, reaction of **6b** with butylamine or benzylamine products **9a** and **9b**, respectively, were synthesized in significantly higher yields than were observed for the corresponding reactions with **6a**. We speculate that the methyl group in the 2-position of the 2-methylimidazolium salt **6b** increases the steric interactions around the sulfur atom of intermediate **10b**. Clearly, elimination of the 1,2-dimethyl-1*H*-imidazole would release the steric crowding and so favor the formation of the unsymmetrical sulfonylureas **11**.

The results with secondary amines are shown in Table 4. As in the case with primary amines, higher yields of the sulfonylurea were obtained with **6b** (Table 4, entries 2 and 3). Good yields were obtained even for more sterically demanding amines such as *N*-methyl-*tert*-butylamine (Table 4, entry 6).

TABLE 4. Reaction of 6a,b with Secondary Amines



entry	R	reagent	product	yield[a] (%)
1	Bn	**6a**	**16a**	60
2	Bn	**6b**	**16a**	94
3	Bu	**6b**	**16b**	96
4	*i*-Pr	**6b**	**16c**	90
5	*t*-Bu	**6b**	**16d**	65

[a] Isolated yields.

Conclusion

In conclusion, we have developed a convenient method for the synthesis of unsymmetrical sulfonylureas that can be easily employed in parallel synthesis. The reaction conditions do not require the use of strongly acidic or basic reagents or anhydrous conditions. Anilines react with triflate salt **6a** to give the corresponding sulfonylurea in good to excellent yields. In the case of reaction with alkylamines, the added steric bulk of triflate **6b** gave the best results. We are currently expanding this methodology to encompass a broader combination of amines and anilines for the preparation of sulfonylureas. Additionally, several methods are being explored to adapt this methodology for use in solid-phase organic synthesis. The results of this work will be reported separately.

Experimental Section

General Methods. Melting points are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz. The signals of the deuterated solvent were employed as the reference. Coupling constants (*J*) are reported in Hz. Infrared spectra were obtained as KBr pellets or film onto NaCl plates. Commercially obtained anhydrous organic solvents and reagents were used without further purification. All reactions were monitored by LC/MS. Flash column chromatography (FC) was carried out using 32−63 μm silica gel.

3-(3,4-Dihydro-1*H*-isoquinoline-2-sulfonyl)oxazolidin-2-one (1). To a solution of chlorosulfonyl isocyanate (1.42 g, 10 mmol) in CH_2Cl_2 (100 mL) cooled to 0 °C was added 2-chloroethanol (0.81 g, 10 mmol) dropwise. After the mixture was stirred for 1.5 h at 0 °C, a solution of 1,2,3,4-tetrahydroisoquinoline (1.33 g, 10 mmol) and Et_3N (3.04 g, 30 mmol) in CH_2Cl_2 (60 mL) was added dropwise. When the addition was completed, the solution was stirred at room temperature for 12 h. The reaction was quenched with 2 N HCl saturated with NaCl (2 × 250 mL), the organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined extracts were dried (Na_2SO_4) and then filtered. Purification by FC on silica gel (1:1; hexanes−EtOAc) gave oxazolidinone **1** (2.20 g, 78%) as a white solid. Mp: 103−105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.98 (2 H, t, J = 5.9 Hz), 3.77 (2 H, t, J = 5.9 Hz), 4.09 (2 H, t, J = 8.3 Hz), 4.43 (2 H, t, J = 8.4), 4.65 (2 H, s), 7.07−7.22 (4 H, m). IR (KBr): 3004, 2994, 2942, 1764, 1476, 1379, 1150, 1078, 1026 cm^{-1}. Anal. Calcd for $C_{12}H_{14}N_2O_4S$: C, 51.05; H, 5.00; N, 9.92. Found: C, 50.79; H, 5.21; N, 9.77.

Ethylcarbamic Acid 2-(3,4-Dihydro-1*H*-isoquinoline-2-sulfonylamino)ethyl Ester (2). Oxazolidinone **1** (600 mg, (2.13 mmol) was dissolved in 2 M $EtNH_2$ in THF (1.5 mL) and heated at 70 °C for 10 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by FC on silica gel (1:1, hexanes−EtOAc) to give carbamate **2** (545 mg, 78%) as a beige solid. Mp: 62−64 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 (3 H, t, J = 7.3 Hz), 2.96 (2 H, t, J = 5.9 Hz), 3.17−3.29 (4 H, m), 3.53 (2 H, t, J = 5.9 Hz), 4.16 (2 H, bs), 4.42 (2 H, s), 4.68 (1 H, bs), 4.85 (1 H, bs), 7.06−7.20 (4 H, m). IR (KBr): 3364, 3350, 2979, 2839, 1686, 1534, 1452, 1430, 1323, 1259, 1151, 1094, 1066, 1038 cm^{-1}. Anal. Calcd for $C_{14}H_{21}N_3O_4S$: C, 51.36; H, 6.47; N, 12.83. Found: C, 51.35; H, 6.55; N, 12.73.

***N,N′*-Sulfuryl Bis-2-methylimidazole (3b).** To a solution of 2-methylimidazole (40 g, 487 mmol) in CH_2Cl_2 (200 mL)

cooled at 0 °C was slowly added a solution of sulfuryl chloride (8.2 mL, 102 mmol) in CH_2Cl_2 (45 mL). The reaction was warmed to room temperature and stirred overnight. The mixture was concentrated, and the resulting solid was recrystallized from isopropyl alcohol. The crystals were filtered and washed with cold isopropyl alcohol and dried under high vacuum to give **3b** (9.8 g, 42%) as a white crystalline solid. Mp: 90−91 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.53 (6 H, s), 6.96 (2 H, d, J = 1.7 Hz), 7.38 (2 H, d, J = 1.7 Hz). IR (KBr): 3145, 3118, 3005, 1756, 1555, 1422, 1378, 1354, 1267, 1056 cm^{-1}. Anal. Calcd for $C_8H_{10}N_4O_2S$: C, 42.47; H, 4.45; N, 24.76. Found: C, 42.56; H, 4.54; N, 24.89.

3-(Imidazole-1-sulfonyl)-1-methyl-3*H*-imidazol-1-ium Triflate (4a). To a solution of *N*,*N*′-sulfuryldiimidazole[12] **3a** (5.95 g, 30.0 mmol) in CH_2Cl_2 (120 mL) at 0 °C was added dropwise 4 mL (30.0 mmol) of methyl triflate over a period of 10 min. After 3 h at 0 °C, the solid was filtered and dried under high vacuum to give triflate salt **4a** (10.19 g, 94%) as a white solid. Mp: 85 °C dec. ^{1}H NMR (300 MHz, CD_3OD): δ 4.01 (3 H, s), 7.21 (1 H, s), 7.85−7.88 (2 H, m), 8.38 (1 H, t, J = 2.1 Hz), 8.51 (1 H, s), 10.05 (1 H, s). IR (KBr): 3144, 3120, 3081, 1538, 1528, 1457, 1416, 1281, 1197, 1161, 1122, 1094, 1077, 1033 cm^{-1}. Anal. Calcd for $C_8H_9F_3N_4O_5S_2$: C, 26.52; H, 2.50; N, 15.46. Found: C, 26.23; H, 2.62; N, 15.18.

2-(Imidazole-1-sulfonyl)-1,2,3,4-tetrahydroisoquinoline (5a). To a solution of triflate salt **(4a)** (2.5 g, 6.9 mmol) in MeCN (27 mL) was added 1,2,3,4-tetrahydroisoquinoline (576 μL, 4.6 mmol). After being stirred at room temperature overnight, the reaction mixture was concentrated and the residue purified using FC on silica gel (1:1 hexane/ethyl acetate) to give **5a** (675 mg, 56%) as a tan solid. Mp: 118−119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.93 (2 H, t, J = 6.1 Hz), 3.55 (2 H, t, J = 6.1 Hz), 4.43 (2 H, s), 7.04−7.21 (6 H, m), 7.99 (1 H, s). IR (KBr): 3145, 3121, 3081, 1583, 1528, 1416, 1281, 1224, 1197, 1161, 1123, 1094, 1078, 1033 cm^{-1}. Anal. Calcd for $C_{12}H_{13}N_3O_2S$: C, 54.74; H, 4.98; N, 15.96. Found: C, 54.79; H, 5.02; N, 16.17.

2-(3-Methyl-imidazole-1-sulfonyl)-1,2,3,4-tetrahydroisoquinoline Triflate (6a). To a solution of isoquinoline **5a** (1.11 g, 4.22 mmol) in CH_2Cl_2 (14 mL) cooled at 0 °C was added 0.52 mL (4.63 mmol) of methyl triflate. After being stirred for 2 h at 0 °C, the reaction mixture was concentrated under reduced pressure to give **6a** (1.80 g, 100%) as a beige solid. Mp: 111−113 °C. ^{1}H NMR (300 MHz, CD_3OD): δ 3.00 (2 H, t, J = 6.2 Hz), 3.83 (2 H, t, J = 6.2 Hz), 4.70 (3 H, s), 4.88 (2 H, s), 7.15−7.24 (4 H, m), 7.70 (1 H, s), 8.06 (1 H, s), 9.62 (1 H, s). IR (KBr): 3144, 3120, 3081, 1644, 1583, 1528, 1457, 1416, 1281, 1197, 1161, 1122, 1094, 1077, 1033 cm^{-1}. Anal. Calcd for $C_{14}H_{16}F_3N_3O_5S_2$: C, 39.34; H, 3.77; N, 9.83. Found: C, 39.15; H, 3.57; N, 9.56.

Typical Procedure for the Preparation of Sulfonylureas Exemplified by 3,4-Dihydro-1*H*-isoquinoline-2-sulfonic Acid Phenylamide (7a). A solution of triflate salt **6a** (175 mg, 0.41 mmol) and aniline (38 mg, 0.41 mmol) in MeCN (2 mL) was stirred at 80 °C for 18 h. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (20 mL), washed with 1 N HCl, 1 N NaOH, H_2O, and saturated NaCl, and dried over Na_2SO_4. Purification by silica gel chromatography (hexanes/EtOAc 9:1) gave **7a** (110 mg, 94%) as a white solid. Mp: 104−105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.82 (2 H, t, J = 5.9 Hz), 3.57 (2 H, t, J = 5.9 Hz), 4.51 (2 H, s), 7.02−7.29 (9 H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.83, 44.25, 47.65, 120.40, 124.69, 126.35, 126.42, 126.82, 128.93, 129.38, 131.85, 133.33, 137.15. IR (KBr): 3271, 2896, 2836, 1603, 1487, 1423, 1353, 1320, 1147, 1073, 1024 cm^{-1}. Anal. Calcd for $C_{15}H_{16}N_2O_2S$: C, 62.48; H, 5.59; N, 9.71. Found: C, 62.42; H, 5.63; N, 9.65.

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Note Added after ASAP Posting. The table of contents graphic had an incorrect structure in the version posted November 23, 2002; the correct version was posted December 4, 2002.

Supporting Information Available: Full characterization for compounds **4b**, **5b**, **6b**, **7b**−**m**, **8a**−**g**, **9a**−**e**, **16a**−**d**, ^{1}H NMR spectra for compounds **1**−**9e** and **16a**−**d**, and LC/MS traces of the crude reaction for the preparation of **9a**,**d**,**x** and **16d** using **6a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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