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Tetrahedron
Tetrahedron 62 (2006) 1699–1707

Efficient sulfonation of 1-phenylsulfonyl-1*H*-pyrroles and 1-phenylsulfonyl-1*H*-indoles using chlorosulfonic acid in acetonitrile

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Received 1 September 2005; revised 3 November 2005; accepted 24 November 2005

Available online 20 December 2005

Abstract—The sulfonation of various 1-phenylsulfonyl-1*H*-pyrroles and 1-phenylsulfonyl-1*H*-indoles using chlorosulfonic acid in acetonitrile has been studied, leading to the development of a clean and operationally simple protocol allowing direct synthesis of the corresponding 1-phenylsulfonyl-1*H*-pyrrole-3-sulfonyl chlorides and 1-phenylsulfonyl-1*H*-indole-3-sulfonyl chlorides, respectively, both of which may be easily converted to various sulfonamide derivatives by treatment with nitrogen nucleophiles. Efficient and selective removal of the phenylsulfonyl- or tosyl groups in the sulfonamide series may be achieved under mild conditions.

1. Introduction

Sulfonation of aromatic compounds is a process of great industrial importance due to the availability and low cost of the reagents (i.e., H_2SO_4, $HOSO_2Cl$, SO_3, or its pyridine complex), the relatively simple technology required for these types of transformations, and perhaps most importantly, the broad applicability of the resulting products, for instance sulfonic acids and sulfonyl chlorides. Consequently, sulfonation reactions have been studied extensively over the years, leading to the syntheses of a multitude of various aromatic sulfonyl derivatives.[1,2] The mechanistic aspects of sulfonation and related reactions have also been investigated in considerable detail.[2] Despite the fact that efficient procedures for the sulfonation of a number of different heterocycles are known,[3] only a few examples of sulfonation reactions involving pyrroles or indoles have been described. Both indole and pyrrole are electron rich heterocyles, which dimerize or polymerize readily under acidic conditions, thereby severely limiting the choice of reagents and substrates. For example, treatment of various indoles possessing alkyl substituents with pyridinium-1-sulfonate in refluxing pyridine gave the expected pyridinium indole-3-sulfonates in good yields.[4] Moreover, four different indole-3-sulfonyl chlorides (**1**) have been obtained by sulfonation of the corresponding nitroindoles with chlorosulfonic acid in anhydrous chloroform in the presence of sodium sulfate.[5] The latter example demonstrates that the presence of strong electron-withdrawing substituents is necessary in order to access the desired products if the process is performed in acidic media. Similar structural requirements are valid for pyrroles, as a series of ethyl pyrrole-2-carboxylates having various substituents at the pyrrole nitrogen, for example, **2**, were prepared by sulfonation in neat chlorosulfonic acid.[6] In contrast to previous claims that pyrrole undergoes sulfonation with sulfur trioxide pyridine complex to afford pyridinium 1*H*-pyrrole-2-sulfonate,[7] it was recently shown that this reaction gives instead the corresponding C-3-sulfonated product. Thus, sulfonation of pyrrole with sulfur trioxide pyridine complex followed by treatment with Na_2CO_3 gave the salt **3**, which could in turn be converted to the sulfonyl chloride **4** upon treatment with PCl_5. The position of the substitution in **3** was elucidated from NOESY data, and further corroborated by an X-ray crystallographic study of a bicyclic sulfonamide derived from **4** (Fig. 1).[8]

Keywords: Pyrroles; Indoles; Sulfonation; Chlorosulfonic acid.
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0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.11.062

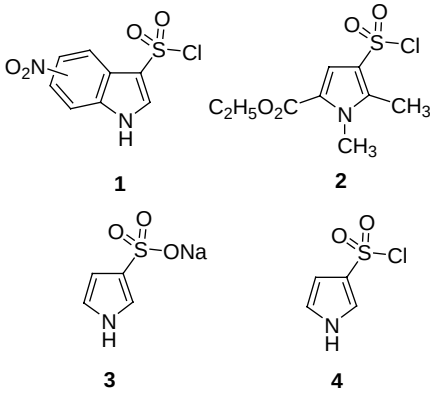


Figure 1.

Indoles possessing sulfone- or sulfonamide functionalities at C-3 have attracted considerable interest in medicinal chemistry. Thus, for example, L-737,126 (**5**) has been investigated as a inhibitor of HIV-1 reverse trancriptase,[9] while a series of closely related sulfones have been shown to possess activity against resistant HIV-1 mutants.[10] Very recently, short peptide derivatives of L-737,126 (**5**) have been demonstrated to exhibit in vitro activity against HIV-1 wild type and mutants possessing non-nucleoside reverse transcriptase inhibitor resistance.[11] The platelet-activating factor antagonist **6** was prepared via an indole-3-sulfonyl chloride, which was obtained from the corresponding *N*-protected indole involving bromination at C-3, followed by halogen–lithium exchange, treatment of the organometallic intermediate with SO_2, and subsequent chlorination with NCS (Fig. 2).[12]

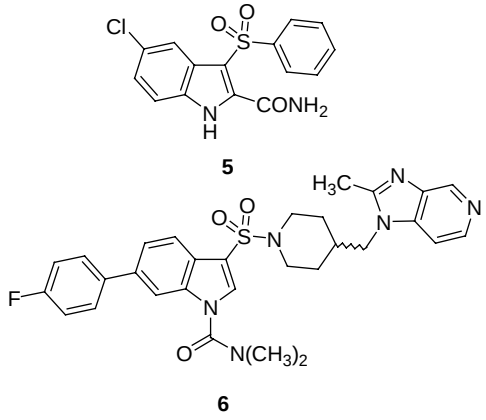
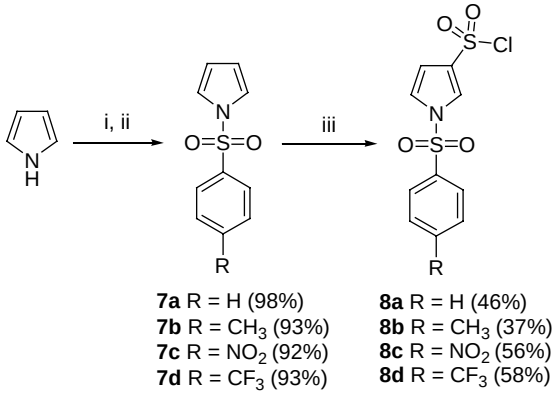


Figure 2.

2. Results and discussion

In order to evaluate the scope and limitations of chlorosulfonation of electron deficient indoles and pyrroles, a series of phenylsulfonyl-protected substrates were selected. Both 1-phenylsulfonyl-1*H*-indoles and 1-phenylsulfonyl-1*H*-pyrroles can be readily prepared, are stable towards acidic media, and the N-protecting group can be removed conveniently under various conditions.[13] Surprisingly enough, the reactivity of 1-phenylsulfonyl-1*H*-indoles and 1-phenylsulfonyl-1*H*-pyrroles towards sulfonating agents has never been studied. Since our initial experiments performed on the 1-phenylsulfonyl-1*H*-pyrroles **7a–b**[14a] in neat chlorosulfonic acid employing a procedure previously used for chlorosulfonation of some related electron deficient pyrroles[6] led to severe decomposition of the starting materials, the reactions were instead conducted in the presence of acetonitrile as the solvent. Using this reagent–solvent combination, clean conversion of **7a–b** to the desired 1-phenylsulfonyl-1*H*-pyrrole-3-sulfonyl chlorides **8a–b** took place (Scheme 1). Although the yields of **8a** and **8b** (46 and 37%, respectively) were only moderate, this route is very attractive because of the operational simplicity and the high purity even of the crude products. All side products are conveniently removed during aqueous workup. An excess of chorosulfonic acid must be used in order to effect efficient conversion to the desired sulfonyl chlorides, since it is known that treatment of, for example, benzene with equimolar amounts of chlorosulfonic acid gives benzenesulfonic acid, which is then in turn converted to benzenesulfonyl chloride upon treatment with an excess of the sulfonating agent in an equilibrium process.[15] Next, we turned our attention to even more electron deficient pyrroles such as **7c–d**. The standard procedures for the N-protection of pyrrole using phenylsulfonyl chlorides, which are usually conducted in the presence of strong inorganic bases such as NaOH[16] or KOH,[17] did not prove to be applicable for the synthesis of **7c–d** due to rapid decomposition of the products upon exposure to the strongly basic conditions (complex tarry mixtures were obtained). The alternative methods relying on treatment of pyrrole with potassium in refluxing THF, and subsequent introduction of 4-nitrobenzenesulfonyl chloride,[14a] or the reaction of 4-nitrobenzenesulfonamide with 2,5-dimethoxytetrahydrofuran,[14b] have been reported to give 1-(4-nitrophenyl)sulfonyl-1*H*-pyrrole (**7c**) in yields of only 26 and 46%, respectively. On the other hand, treatment of pyrrole with butyllithium in THF, followed by introduction of the appropriate sulfonyl chlorides, enabled clean and high-yielding syntheses of the known pyrroles **7a–c**,[14a] as well as the new compound **7d**. As anticipated, the pyrroles **7c–d** gave even better results during sulfonation, affording the corresponding sulfonyl chlorides **8c–d** in 56 and 58% yield, respectively, thus also supporting our expectation that the presence of strongly electron-withdrawing groups in the phenylsulfonyl part of the pyrroles **7** would provide higher yields of the sulfonyl chlorides **8**. In an additional experiment, the sulfonyl



Scheme 1. Reagents and conditions: (i) BuLi, THF, −78 °C to rt, 1 h; (ii) $RC_6H_4SO_2Cl$, −78 °C to rt, 15–20 h; (iii) $HOSO_2Cl$, CH_3CN, rt, 70–75.5 h.

chloride **8c** could also be obtained in comparable yield when **7c** and chlorosulfonic acid were heated at reflux in acetonitrile for 1.5 h, but the product contained a few percent of impurities (not identified), and the procedure performed at rt is therefore the method of choice. An X-ray crystallographic study of **8a** confirmed the expected functionalization at C-3 (Fig. 3),[18] which is in analogy with, for example, the regioselective C-3 acylation of 1-phenylsulfonyl-1*H*-pyrroles mediated by $AlCl_3$.[16b,19] Thus, the position of sulfonation is the same when using our procedure, as during sulfonation of pyrrole itself with sulfur trioxide pyridine complex in pyridine.[8] It is also interesting to note that the crystal structure of **8a** displays very similar geometry around the *N*-phenylsulfonyl unit as noted previously in several 1-phenylsulfonyl-1*H*-pyrroles and -indoles.[20]

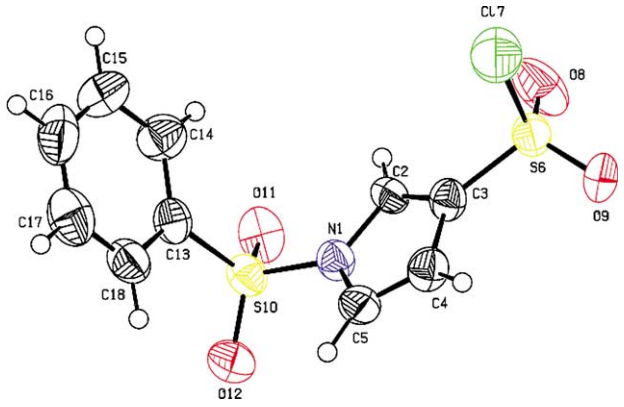
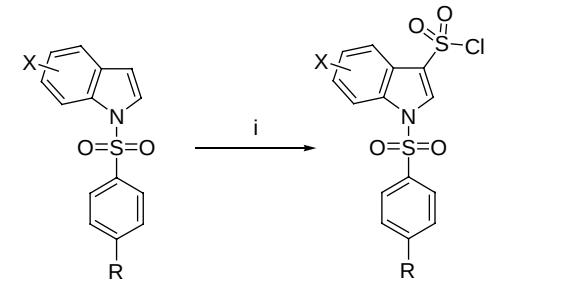


Figure 3. The molecular structure of compound **8a**, showing the atom labelling used in the crystal structure refinement.[18]



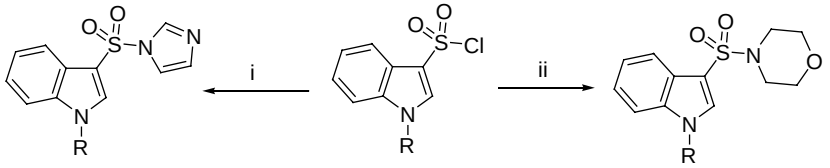
9a R = H, X = H
9b R = CH_3, X = H
9c R = H, X = 6-Br
9d R = H, X = 6-Cl
9e R = H, X = 5-F

10a R = H, X = H (79%)
10b R = CH_3, X = H (72%)
10c R = H, X = 6-Br (88%)
10d R = H, X = 6-Cl (89%)
10e R = H, X = 5-F (100%)

Scheme 2. Reagents and conditions: (i) $HOSO_2Cl$, CH_3CN, 0 °C to rt (for **10a–b**) or rt (for **10c–e**), 66–75.5 h.

Based on the observations made during the studies on the reactivity of 1-phenylsulfonyl-1*H*-pyrroles towards chlorosulfonic acid in acetonitrile, we wished to extend the scope of our method to indoles. A series of 1-phenylsulfonyl-1*H*-indoles was therefore subjected to similar reaction conditions. For instance, the readily available 1-phenylsulfonyl-1*H*-indole (**9a**)[16a,21] and 1-(*p*-toluenesulfonyl)-1*H*-indole (**9b**)[16a] underwent clean conversion to the sulfonyl chlorides **10a** and **10b**, respectively, upon treatment with 3 equiv of chlorosulfonic acid in acetonitrile (Scheme 2). The yields of these transformations were, just as expected, considerably higher than in the pyrrole series because the indoles **9a–b** are less electron rich heterocycles than the corresponding pyrroles, and are therefore also less likely to participate in side-reactions. Acceptable results can also be obtained by performing the reactions for shorter periods of time (48 h), which generally only leads to somewhat lower yields. Further deactivation of the indole nucleus leads, in similarity to the reactivity trend observed in the pyrrole series, to even more efficient chlorosulfonation, as illustrated by the syntheses of the halogenated indole-3-sulfonyl chlorides **10c–e** upon exposure of the indoles **9c**,[22] **9e**,[23] and 6-chloro-1-phenylsulfonyl-1*H*-indole (**9d**) to approximately 4 equiv of chlorosulfonic acid. On the other hand, the considerably more electron rich 5-methoxy-1-phenylsulfonyl-1*H*-indole[24] gave only a very low yield (~5%) of 5-methoxy-1-phenylsulfonyl-1*H*-indole-3-sulfonyl chloride in impure form under similar conditions, even when the reaction was initially performed at 0 °C, followed by slow warming to rt overnight. Attempted sulfonation of the somewhat more deactivated 5-methoxy-1-(4-nitrophenyl)sulfonyl-1*H*-indole[25] gave similar results. Obviously, the presence of electron releasing groups on the six-membered ring of the indole leads to extensive side reactions, and very little of the desired 3-sulfonated products are formed.

With substantial amounts of sulfonyl chlorides **8a–d** and **10a–e** in hand, studies of the reactivity and synthetic applicability of these compounds were initiated. For that purpose, indole-3-sulfonyl chlorides **10a–b** were chosen as the substrates and subjected to reactions with selected nitrogen nucleophiles (Scheme 3). Both compounds **10a–b** were cleanly converted to the imidazole derivatives **11a–b** upon treatment with imidazole in CH_2Cl_2. Likewise, exposure of **10a** to an excess of morpholine gave the sulfonamide **12** in excellent yield. As anticipated, cleavage of the phenylsulfonyl group of **12** was carried out conveniently and selectively employing potassium carbonate in aqueous methanol, providing the sulfonamide **13**.

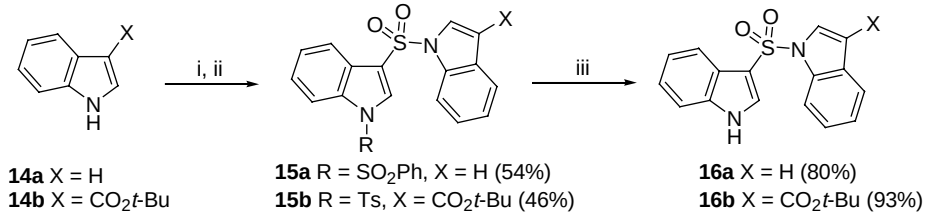


11a R = SO_2Ph (91%)
11b R = Ts (74%)

10a R = SO_2Ph
10b R = Ts

12 R = SO_2Ph (93%)
13 R = H (92%)

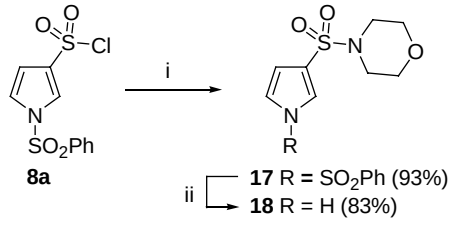
Scheme 3. Reagents and conditions: (i) imidazole, CH_2Cl_2, rt; (ii) morpholine, CH_2Cl_2, rt; (iii) K_2CO_3, MeOH, H_2O, rt.



Scheme 4. Reagents and conditions: (i) LDA, THF, −78 °C; (ii) **10a** (for **14a**), or **10b** (for **14b**), −78 °C to rt; (iii) K_2CO_3, MeOH, H_2O, rt (for **15a**), or K_2CO_3, MeOH, THF, H_2O, rt (for **15b**).

The sulfonyl chlorides **10a–b** were also used in reactions with *N*-metalated derivatives of the indoles **14a** and **14b**[26] (readily available by treatment of indole-3-carboxylic acid with oxalyl chloride, followed by exposure of the intermediate acid chloride to potassium *tert*-butoxide in *t*-BuOH), affording the new sulfur-containing systems **15a** and **15b**, respectively (Scheme 4). The use of LDA proved to be crucial in this application, as attempts involving indole and potassium *tert*-butoxide or BuLi gave inferior yields of the desired product **15a**, along with compound **16a**, resulting from base-induced cleavage of the protecting group. Again, selective cleavage of the phenylsulfonyl- or *p*-toluenesulfonyl protecting groups was achieved by treatment with potassium carbonate rendering compounds **16a–b**. Under these mild conditions, the sulfonyl linkage between the indole units remained untouched, presumably as a result of the different steric and electronic properties of the two sulfone functionalities. A member belonging to this class, namely 3-(1*H*-indole-1-sulfonyl)-7-nitro-1*H*-indole, has been prepared recently by treatment of indole with sodium hydride, followed by introduction of 7-nitro-1*H*-indole-3-sulfonyl chloride,[5] as an intermediate en route to new compounds displaying affinity for the 5-HT_6-receptor.[27] Attempts to use the sulfonyl chlorides **10a–b** in reactions with indolyl magnesium halides or *C*-metalated indoles under a variety of different conditions failed to produce the corresponding diindolyl sulfones.

In analogy to the indole-3-sulfonyl chlorides, the pyrrole-3-sulfonyl chloride **8a** could be efficiently converted to the sulfonamide **17**, which was in turn deprotected rendering **18** (Scheme 5), thus demonstrating the applicability of this chemistry to the pyrrole series.



Scheme 5. Reagents and conditions: (i) morpholine, CH_2Cl_2, rt; (ii) K_2CO_3, MeOH, H_2O, rt.

In conclusion, a practical procedure for sulfonation of 1-arylsulfonyl-1*H*-pyrroles and 1-arylsulfonyl-1*H*-indoles with chlorosulfonic acid in acetonitrile has been developed. Initial experiments probing the reactivity of the 1-arylsulfonyl-1*H*-indole-3-sulfonyl chlorides and the corresponding pyrrole derivatives clearly indicate that a wide variety of sulfonamides may be generated by reactions with suitable nitrogen nucleophiles, providing practical routes to new heterocyclic systems with potential for pharmacological applications, and that selective cleavage of the phenylsulfonyl or *p*-toluenesulfonyl protecting groups takes place under mild conditions, which tolerate the presence of sensitive functional groups.

3. Experimental

3.1. General experimental procedures

NMR data were recorded at 300.1 MHz for ^1H, and 75.5 MHz for ^{13}C, respectively. IR spectra were acquired on a FT-IR instrument. High-resolution mass spectra were recorded by Nilsson, University of Lund, Sweden. The elemental analyses were performed by Kolbe Mikroanalytisches Laboratorium, Mülheim an der Ruhr, Germany. Melting points were taken on a capillary apparatus in open capillary tubes. All reactions were performed under nitrogen atmosphere. Acetonitrile (analytical grade) was stored over activated molecular sieves (4 Å). Pyrrole was freshly distilled prior to use. THF was distilled from sodium and benzophenone.

3.1.1. 1-Phenylsulfonyl-1*H*-pyrrole (7a). BuLi (1.6 M in hexanes, 32.6 mL, 52.2 mmol) was added to a solution pyrrole (3.48 mL, 50 mmol) in anhydrous THF (100 mL) at −78 °C during 20 min. After complete addition, the mixture was stirred at −78 °C for 10 min, and was thereafter allowed to reach rt over 1 h. After cooling to −78 °C, a solution of benzenesulfonyl chloride (6.41 mL, 50 mmol) in anhydrous THF (12 mL) was added over 20 min at −78 °C. The resulting mixture was allowed to slowly reach rt overnight (~18.5 h), was thereafter poured into water (~200 mL) containing brine (~20 mL), and extracted with CH_2Cl_2 (100 mL) and (3×50 mL). The combined organic extracts were washed with water (100 mL), followed by a mixture of water (50 mL) and brine (50 mL), and dried over $MgSO_4$. Removal of the solvents in vacuo gave pure 1-phenylsulfonyl-1*H*-pyrrole (**7a**) (10.17 g, 98%) as an off-white solid. If necessary, this material can be crystallized from *i*-PrOH. Colourless plates, mp (*i*-PrOH) 88–89 °C [lit.[14a] mp (MeOH) 89–89.5 °C].

3.1.2. 1-(4-Methyl-phenylsulfonyl)-1*H*-pyrrole (7b). This compound was prepared according to the procedure above using *p*-toluenesulfonyl chloride (9.53 g, 50 mmol) dissolved in anhydrous THF (15 mL). Yield: 10.25 g (93%). If necessary, this compound can be crystallized

from *i*-PrOH. Colourless plates, mp (*i*-PrOH) 103–103.5 °C [lit.[14a] mp (MeOH) 104.5 °C].

3.1.3. 1-(4-Nitro-phenylsulfonyl)-1*H*-pyrrole (7c). BuLi (1.6 M in hexanes, 16.3 mL, 26.1 mmol) was added to a solution pyrrole (1.74 mL, 25 mmol) in anhydrous THF (50 mL) at −78 °C during 20 min. After complete addition, the mixture was stirred at −78 °C for 10 min, and was thereafter allowed to reach rt over 1 h. It was thereafter cooled to −78 °C, and a solution of 4-nitrobenzenesulfonyl chloride (5.54 g, 50 mmol) in anhydrous THF (15 mL) was added over 20 min at −78 °C. The resulting mixture was allowed to slowly reach rt overnight (∼15 h), was thereafter poured into water (∼200 mL) containing brine (∼20 mL), and extracted with CH_2Cl_2 (4×50 mL). The combined organic extracts were washed with water (50 mL), followed by a mixture of water (50 mL) and brine (50 mL), and dried over $MgSO_4$. Evaporation of the solvents gave a brownish crystalline residue, which was dissolved in CH_2Cl_2 (∼50 mL) and the solution was passed through a plug of silica gel, which was washed with several small portions of CH_2Cl_2. The combined filtrate and washings were concentrated in vacuo to give pure **7c** (5.80 g, 92%) as a yellowish/orange crystalline solid. Crystallization of this product from *i*-PrOH gave analytically pure material as golden plates, mp (*i*-PrOH) 140.5–141.5 °C [lit.[14a] mp (MeOH) 142–142.5 °C]; IR (neat) 1525, 1375, 1346, 1191, 1169, 1061, 865, 855, 740, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33 (d, J=8.7 Hz, 2H), 8.02 (d, J=8.7 Hz, 2H), 7.16 (dd, J=2.0, 2.0 Hz, 2H), 6.35 (dd, J=2.0, 2.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 150.8, 144.6, 128.3, 124.8, 121.2, 115.1.

3.1.4. 1-(4-Trifluoromethyl-phenylsulfonyl)-1*H*-pyrrole (7d). A solution of BuLi (1.6 M in hexanes, 8.2 mL, 13.1 mmol) was added to a solution pyrrole (0.87 mL, 12.5 mmol) in anhydrous THF (25 mL) at −78 °C during 10 min. After complete addition, the mixture was stirred at −78 °C for 10 min, and was thereafter allowed to reach rt over 1 h. It was thereafter cooled to −78 °C, and a solution of 4-(trifluoromethyl)benzenesulfonyl chloride (3.04 g, 12.4 mmol) in anhydrous THF (6 mL) was added over 15 min at −78 °C. The resulting mixture was allowed to slowly reach rt overnight (∼20 h), was thereafter poured into water (∼100 mL) containing brine (∼20 mL), and extracted with CH_2Cl_2 (4×30 mL). The combined organic extracts were washed with water (50 mL), followed by a mixture of water (50 mL) and brine (50 mL), and dried over $MgSO_4$. Evaporation of the solvents in vacuo gave pure **7d** (3.19 g, 93%) as an off-white crystalline solid. Crystallization from *i*-PrOH gave an analytically pure sample as colourless crystals, mp (*i*-PrOH) 92–93.5 °C; IR (neat) 1376, 1317, 1170, 1146, 1109, 1058, 1031, 1018, 731, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98 (d, J=8.6 Hz, 2H), 7.76 (d, J=8.6 Hz, 2H), 7.17 (dd, J=2.1, 2.1 Hz, 2H), 6.34 (dd, J=2.1, 2.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 142.7, 135.6 (q, J_{C-F}=33.2 Hz), 127.5, 126.8 (q, J_{C-F}=3.7 Hz), 123.1 (q, J_{C-F}=273.1 Hz), 121.1, 114.6. Anal. Calcd for $C_{11}H_8NO_2SF_3$: C, 48.00; H, 2.93; N, 5.09. Found: C, 47.98; H, 2.84; N, 5.02.

3.1.5. 6-Bromo-1-phenylsulfonyl-1*H*-indole (9c).[22] This compound was prepared using a modification[21,24a] of the procedure described by Illi.[16a] To a suspension of finely powdered NaOH (3.13 g, 78 mmol) in CH_2Cl_2 (50 mL) cooled to 0 °C were added 6-bromoindole (4.90 g, 25 mmol) in one portion, followed by tetrabutylammonium hydrogensulfate (220 mg, 0.65 mmol). To this mixture was thereafter added benzenesulfonyl chloride (4.0 mL, 31 mmol) dropwise at 0 °C during ∼25 min. The resulting mixture was stirred at 0 °C for 1 h, the cooling bath was then removed, and stirring was continued for another 2 h at rt. The mixture was filtered through Celite, the pad was washed with several small portions of CH_2Cl_2, and the combined filtrate and washings were concentrated in vacuo. The residue was crystallized from MeOH, which gave **9c** (5.47 g) as colourless crystals. A second crop (1.66 g) was obtained after slow concentration of the mother liquor. The residual mother liquors were concentrated and subjected to column chromatography [CH_2Cl_2–*n*-hexane (2/3)] to give more **9c** (1.04 g) as a colourless crystalline solid. Overall, 8.17 g (97%) of **9c** was obtained. Mp (MeOH) 100–101 °C; IR (neat) 1367, 1174, 1134, 1125, 1093, 991, 890, 804, 753, 723, 711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.19 (br, 1H), 7.89–7.87 (m, 2H), 7.59–7.32 (m, 6H), 6.62 (d, J=3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 138.2, 135.7, 134.3, 129.8, 129.6, 127.0, 127.0, 126.9, 122.7, 118.5, 116.8, 109.2.

3.1.6. 6-Chloro-1-phenylsulfonyl-1*H*-indole (9d). This material was prepared using a modification[21,24a] of the procedure described by Illi.[16a] To a suspension of finely powdered NaOH (1.25 g, 31 mmol) in CH_2Cl_2 (20 mL) cooled to 0 °C was added 6-chloroindole (1.52 g, 10 mmol) in one portion, followed by tetrabutylammonium hydrogensulfate (88 mg, 0.26 mmol). To this mixture was thereafter added benzenesulfonyl chloride (1.4 mL, 11 mmol) dropwise at 0 °C during ∼20 min. The resulting mixture was stirred at 0 °C for 1 h, the cooling bath was then removed, and stirring was continued for another 2 h at rt. The mixture was filtered through Celite, the pad was washed with several small portions of CH_2Cl_2, and the combined filtrate and washings were concentrated in vacuo. The residue was crystallized from MeOH, which gave **9d** (2.10 g) as colourless crystals. The mother liquor was concentrated and subjected to column chromatography [CH_2Cl_2–*n*-hexane (2/3)] to give more **9d** (0.70 g) as a colourless crystalline solid. Overall, 2.80 g (96%) of **9d** was obtained. Mp (MeOH) 98–99.5 °C; IR (neat) 1363, 1170, 1129, 1093, 897, 865, 806, 752, 723 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.03 (br, 1H), 7.90–7.87 (m, 2H), 7.59–7.41 (m, 5H), 7.22–7.19 (m, 1H), 6.63 (d, J=3.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 138.2, 135.4, 134.3, 130.9, 129.6, 129.4, 127.1, 127.0, 124.3, 122.4, 113.9, 109.1. Anal. Calcd for $C_{14}H_{10}NO_2SCl$: C, 57.63; H, 3.45; N, 4.80. Found: C, 57.60; H, 3.42; N, 4.75.

3.1.7. 1-Phenylsulfonyl-1*H*-pyrrole-3-sulfonyl chloride (8a). To a solution of 1-phenylsulfonyl-1*H*-pyrrole (**7a**) (2.07 g, 10 mmol) in dry CH_3CN (12.5 mL) was carefully added chlorosulfonic acid (4.0 mL, 60 mmol) at rt. An exothermic reaction ensued, and the resulting solution was stirred at rt for 72 h. The mixture was thereafter poured on ice/water (∼100 g), and extracted with $CHCl_3$ (3×50 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (3×50 mL) [addition of small amounts of brine (∼20 mL) was sometimes necessary to prevent formation of emulsions], brine (50 mL), and dried over

$MgSO_4$. Removal of the solvents in vacuo gave pure **9a** (1.41 g, 46%) as a colourless crystalline solid. An analytically pure sample was obtained as colourless crystals by crystallization from CH_3CN, mp (CH_3CN) 131.5–132.5 °C; IR (neat) 1378, 1363, 1188, 1176, 1149, 1084, 1050, 816, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98–7.95 (m, 2H), 7.89–7.88 (m, 1H), 7.77–7.71 (m, 1H), 7.64–7.59 (m, 2H), 7.26 (dd, $J=3.4$, 2.3 Hz, 1H), 6.73 (dd, $J=3.4$, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 137.2, 135.7, 132.2, 130.3, 127.8, 124.4, 122.5, 111.1. HRMS (EI) *m/z* calcd for $C_{10}H_8NO_4S_2^{35}Cl$: 304.9583 [M^+], found 304.9580. Anal. Calcd for $C_{10}H_8NO_4S_2Cl$: C, 39.28; H, 2.64; N, 4.58. Found: C, 39.27; H, 2.57; N, 4.49.

3.1.8. 1-(4-Methyl-phenylsulfonyl)-1*H*-pyrrole-3-sulfonyl chloride (8b). This compound was prepared according to the procedure above, using 1-(4-methylphenyl)sulfonyl-1*H*-pyrrole (2.21 g, 10 mmol). Yield: 1.17 g (37%). Colourless crystals, mp (CH_3CN) 146.5–148 °C; IR (neat) 1382, 1367, 1191, 1171, 1155, 1084, 1081, 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.87–7.83 (m, 3H), 7.40 (d, $J=8.1$ Hz, 2H), 7.23 (dd, $J=3.5$, 2.4 Hz, 1H), 6.71 (dd, $J=3.5$, 1.7 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 147.3, 134.2, 132.0, 131.0, 127.9, 124.3, 122.4, 111.0, 22.0. HRMS (EI) *m/z* calcd for $C_{11}H_{10}NO_4S_2^{35}Cl$: 318.9740 [$M^+$], found 318.9729. Anal. Calcd for $C_{11}H_{10}NO_4S_2Cl$: C, 41.31; H, 3.15; N, 4.38. Found: C, 41.43; H, 3.11; N, 4.36.

3.1.9. 1-(4-Nitro-phenylsulfonyl)-1*H*-pyrrole-3-sulfonyl chloride (8c). To a suspension of 1-(4-nitrophenyl)sulfonyl-1*H*-pyrrole (**7c**) (0.63 g, 2.5 mmol) in anhydrous CH_3CN (5 mL) was added chorosulfonic acid (2.0 mL, 30 mmol) carefully at rt. An exothermic reaction ensued. The mixture was stirred at rt for 70 h, was thereafter poured on ice/water (~50 g), and was extracted with $CHCl_3$ (3×30 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (3×25 mL) [addition of small amounts of brine (~20 mL) was sometimes necessary to prevent formation of emulsions], brine (50 mL), and dried over $MgSO_4$. Removal of the solvents in vacuo gave pure **8c** (0.49 g, 56%) as a colourless crystalline solid. An analytically pure sample was obtained as fine crystals with a yellowish tinge by crystallization from CH_3CN, mp (CH_3CN) 169.5–171 °C; IR (neat) 1525, 1396, 1367, 1347, 1185, 1150, 1050, 854, 740, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.46 (d, $J=9.0$ Hz, 2H), 8.17 (d, $J=9.0$ Hz, 2H), 7.90–7.89 (m, 1H), 7.28 (dd, $J=3.5$, 2.4 Hz, 1H), 6.79 (dd, $J=3.5$, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 151.7, 142.6, 133.3, 129.3, 125.6, 124.3, 122.6, 112.0. HRMS (EI) *m/z* calcd for $C_{10}H_7N_2O_6S_2^{35}Cl$: 349.9434 [$M^+$], found 349.9438. Anal. Calcd for $C_{10}H_7N_2O_6S_2Cl$: C, 34.24; H, 2.01; N, 7.99. Found: C, 34.30; H, 1.98; N, 8.00.

3.1.10. 1-(4-Trifluoromethyl-phenylsulfonyl)-1*H*-pyrrole-3-sulfonyl chloride (8d). This compound was prepared according to the procedure above, using 1-(4-trifluoromethylphenyl)sulfonyl-1*H*-pyrrole (**7d**) (0.69 g, 2.5 mmol). Reaction time: 75.5 h. Yield: 0.54 g (58%). Colourless crystals, mp (CH_3CN) 144–145 °C; IR (neat) 1389, 1374, 1322, 1182, 1163, 1153, 1133, 1110, 1051, 1011, 713 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10 (d, $J=8.3$ Hz, 2H), 7.89 (dd, $J=2.4$, 1.7 Hz, 1H), 7.89 (d, $J=8.3$ Hz, 2H), 7.27 (dd, $J=3.5$, 2.4 Hz, 1H), 6.77 (dd, $J=3.5$, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 140.7, 137.3 (q, $J_{C-F}=33.6$ Hz), 132.9, 128.4, 127.6 (q, $J_{C-F}=3.6$ Hz), 124.3, 123.1 (q, $J_{C-F}=273.5$ Hz), 122.6, 111.7. HRMS (EI) *m/z* calcd for $C_{11}H_7NO_4S_2^{35}ClF_3$: 372.9457 [$M^+$], found 372.9463. Anal. Calcd for $C_{11}H_7NO_4S_2ClF_3$: C, 35.35; H, 1.89; N, 3.75. Found: C, 35.49; H, 1.98; N, 3.71.

3.1.11. 1-Phenylsulfonyl-1*H*-indole-3-sulfonyl chloride (10a). To a solution of 1-phenylsulfonyl-1*H*-indole (**9a**)[21] (5.14 g, 20 mmol) in dry CH_3CN (25 mL) was carefully added chorosulfonic acid (4.0 mL, 60 mmol) at 0 °C. The solution was allowed to reach rt over ~4 h, and was thereafter stirred at rt for 68 h. The resulting mixture was poured into ice/water (~100 g), and extracted with $CHCl_3$ (100 mL and 2×50 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (2×50 mL) [addition of small amounts of brine (~20 mL) was sometimes necessary to prevent formation of emulsions], brine (50 mL), and dried over $MgSO_4$. Removal of the solvents in vacuo gave pure **10a** (5.65 g, 79%) as a pinkish crystalline solid. An analytically pure sample was obtained as colourless crystals by crystallization from CH_3CN, mp (CH_3CN) 144–145 °C; IR (neat) 1366, 1185, 1171, 1152, 1142, 1112, 1089, 942, 756, 729, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.40 (s, 1H), 8.05–7.96 (m, 4H), 7.70–7.65 (m, 1H), 7.60–7.44 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 136.9, 135.5, 134.5, 131.2, 130.2, 127.6, 127.3, 125.8, 125.2, 123.9, 120.6, 114.0. HRMS (EI) *m/z* calcd for $C_{14}H_{10}NO_4S_2^{35}Cl$: 354.9740 [$M^+$], found 354.9734. Anal. Calcd for $C_{14}H_{10}NO_4S_2Cl$: C, 47.26; H, 2.83; N, 3.94. Found: C, 47.26; H, 2.86; N, 3.99.

3.1.12. 1-(4-Methyl-phenylsulfonyl)-1*H*-indole-3-sulfonyl chloride (10b). This material was prepared as above, starting from 1-(4-methylphenyl)sulfonyl-1*H*-indole (**9b**)[16a] (5.42 g, 20 mmol). Reaction time: 66 h. Yield: 5.34 g (72%). Pinkish crystals, mp (CH_3CN) 160–161 °C; IR (neat) 1376, 1367, 1174, 1149, 1136, 1107, 1087, 939, 765, 758, 709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.38 (s, 1H), 8.04–8.01 (m, 1H), 7.98–7.95 (m, 1H), 7.89 (d, $J=8.5$ Hz, 2H), 7.54–7.43 (m, 2H), 7.35 (d, $J=8.5$ Hz, 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 147.1, 134.5, 133.9, 131.2, 130.8, 127.7, 127.2, 125.7, 125.0, 123.9, 120.5, 114.0, 21.9. HRMS (EI) *m/z* calcd for $C_{15}H_{12}NO_4S_2^{35}Cl$: 368.9896 [$M^+$], found 368.9897. Anal. Calcd for $C_{15}H_{12}NO_4S_2Cl$: C, 48.71; H, 3.27; N, 3.79. Found: C, 48.57; H, 3.21; N, 3.91.

3.1.13. 6-Bromo-1-phenylsulfonyl-1*H*-indole-3-sulfonyl chloride (10c). To a solution of 6-bromo-1-phenylsulfonyl-1*H*-indole (**9c**) (1.04 g, 3.1 mmol) in dry CH_3CN (8 mL) was carefully added chlorosulfonic acid (0.83 mL, 12.5 mmol) at rt. An exothermic reaction ensued, and the resulting solution was stirred at rt for 75.5 h. The mixture was thereafter poured on ice/water (~100 g), and extracted with $CHCl_3$ (50 mL, and 2×50 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (3×50 mL), brine (50 mL), and dried over $MgSO_4$. Removal of the solvents in vacuo gave pure **10c** (1.18 g, 88%) as a crystalline solid with a pinkish tinge. An analytically pure sample was obtained as pinkish crystals by crystallization from CH_3CN, mp (CH_3CN) 187.5–189 °C; IR (neat) 1379, 1166, 1142, 1119, 1086, 942, 740, 721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.33 (s, 1H), 8.22

(d, J=1.3 Hz, 1H), 8.02–7.99 (m, 2H), 7.83 (d, J=8.6 Hz, 1H), 7.75–7.70 (m, 1H), 7.64–7.58 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 136.8, 135.8, 135.2, 131.4, 130.4, 129.4, 127.7, 125.3, 122.8, 121.8, 121.3, 117.1. HRMS (EI) m/z calcd for $C_{14}H_9NO_4S_2^{79}Br^{35}Cl$: 432.8845 [$M^+$], found 432.8832. Anal. Calcd for $C_{14}H_9NO_4S_2BrCl$: C, 38.68; H, 2.09; N, 3.22. Found: C, 38.66; H, 1.95; N, 3.26.

3.1.14. 6-Chloro-1-phenylsulfonyl-1*H*-indole-3-sulfonyl chloride (10d). This compound was prepared according to the procedure above, starting from 6-chloro-1-phenylsulfonyl-1*H*-indole (**9d**) (904 mg, 3.1 mmol). Reaction time: 68 h. Yield: 1.08 g (89%). Colourless crystals, mp (CH_3CN) 180–181 °C; IR (neat) 1390, 1379, 1186, 1166, 1144, 1122, 1087, 953, 945, 814, 749, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.35 (s, 1H), 8.05–8.00 (m, 3H), 7.88 (d, J=8.6 Hz, 1H), 7.75–7.70 (m, 1H), 7.64–7.58 (m, 2H), 7.45 (dd, J=8.6, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 136.7, 135.8, 134.9, 133.7, 131.5, 130.4, 127.7, 126.7, 125.3, 122.4, 121.5, 114.2. HRMS (EI) m/z calcd for $C_{14}H_9NO_4S_2^{35}Cl_2$: 388.9350 [$M^+$], found 388.9338. Anal. Calcd for $C_{14}H_9NO_4S_2Cl_2$: C, 43.09; H, 2.32; N, 3.59. Found: C, 43.17; H, 2.27; N, 3.62.

3.1.15. 5-Fluoro-1-phenylsulfonyl-1*H*-indole-3-sulfonyl chloride (10e). This compound was prepared according to the procedure above, starting from 5-fluoro-1-phenylsulfonyl-1*H*-indole (**9e**)[23] (0.853 g, 3.1 mmol). Reaction time: 72 h. Yield: 1.16 g (100%). Colourless crystals, mp (CH_3CN) 171–172 °C; IR (neat) 1386, 1174, 1167, 1159, 1108, 1086, 972, 862, 857, 849, 816, 723 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.40 (s, 1H), 8.01–7.97 (m, 3H), 7.73–7.68 (m, 1H), 7.64–7.56 (m, 3H), 7.28–7.21 (m, 1H). HRMS (EI) m/z calcd for $C_{14}H_9NO_4S_2^{35}ClF$: 372.9646 [M^+], found 372.9626. Anal. Calcd for $C_{14}H_9NO_4S_2ClF$: C, 44.98; H, 2.43; N, 3.75. Found: C, 44.90; H, 2.38; N, 3.71.

3.1.16. 3-(Imidazole-1-sulfonyl)-1-phenylsulfonyl-1*H*-indole (11a). To a solution of **10a** (1.78 g, 5.0 mmol) in CH_2Cl_2 (50 mL) was added imidazole (0.73 g, 10.7 mmol). The resulting mixture was stirred at rt for 21 h, and was thereafter diluted with CH_2Cl_2 (50 mL), washed with water (3×50 mL), followed by brine (25 mL), and dried over $MgSO_4$. Removal of the solvent in vacuo gave a colourless residue, which was triturated with warm *i*-PrOH. The precipitate was collected by filtration (while warm), washed with *i*-PrOH, and dried to provide **11a** (1.76 g, 91%) as a white crystalline solid, mp (*i*-PrOH) 187–188 °C; IR (neat) 1376, 1149, 1140, 1089, 1035, 942, 727 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.39 (s, 1H), 8.11 (s, 1H), 7.99–7.96 (m, 3H), 7.82–7.80 (m, 1H), 7.67–7.57 (m, 1H), 7.58–7.53 (m, 2H), 7.48–7.35 (m, 3H), 7.07 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 137.0, 136.6, 135.5, 134.9, 132.1, 131.5, 130.2, 127.6, 127.2, 125.8, 124.3, 120.0, 119.0, 117.5, 114.2. MS (ESI+) m/z 388 [$M+H]^+$. Anal. Calcd for $C_{17}H_{13}N_3O_4S_2$: C, 52.70; H, 3.38; N, 10.85. Found: C, 52.68; H, 3.50; N, 10.86.

3.1.17. 3-(Imidazole-1-sulfonyl)-1-(4-methyl-phenylsulfonyl)-1*H*-indole (11b). This material was prepared according to the same procedure as for **11a**, using **10b** (0.93 g, 2.5 mmol), and imidazole (0.37 g, 5.4 mmol) in CH_2Cl_2 (25 mL). Workup as above, followed by trituration of the crude product with warm *i*-PrOH gave pure **11b** (0.74 g, 74%) as a white crystalline solid, mp (*i*-PrOH) 206.5–208 °C; IR (neat) 1383, 1166, 1152, 1136, 1090, 1053, 942, 735, 715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.39 (s, 1H), 8.11 (s, 1H), 7.98 (d, J=7.9 Hz, 1H), 7.88–7.80 (m, 3H), 7.49–7.33 (m, 5H), 7.08 (s, 1H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 147.1, 136.6, 134.8, 133.9, 132.1, 131.5, 130.8, 127.6, 127.0, 125.7, 124.3, 120.0, 118.7, 117.5, 114.2, 21.9. MS (ESI+) m/z 402 [$M+H]^+$. Anal. Calcd for $C_{18}H_{15}N_3O_4S_2$: C, 53.85; H, 3.77; N, 10.47. Found: C, 53.76; H, 3.77; N, 10.36.

3.1.18. 3-(Morpholine-4-sulfonyl)-1-phenylsulfonyl-1*H*-indole (12). To a solution of **10a** (1.78 g, 5.0 mmol) in CH_2Cl_2 (50 mL) was added morpholine (0.92 mL, 10.5 mmol) at rt. The resulting mixture was stirred at rt for 24 h, and was thereafter washed with a mixture of water (25 mL) and brine (25 mL). The aqueous layer was extracted with CH_2Cl_2 (25 mL), and the combined organic layers were washed sequentially with 1 M aqueous HCl (25 mL), water (25 mL), brine (25 mL), followed by drying over $MgSO_4$. Removal of the solvent in vacuo gave pure **12** (1.89 g, 93%) as colourless foam. Crystallization from ethanol gave an analytically pure sample as colourless crystals, mp (EtOH) 150–151 °C; IR (neat) 1355, 1158, 1138, 1071, 935, 765, 727 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.13 (s, 1H), 8.04–8.00 (m, 1H), 7.98–7.94 (m, 2H), 7.90–7.86 (m, 1H), 7.66–7.61 (m, 1H), 7.55–7.50 (m, 2H), 7.47–7.42 (m, 1H), 7.39–7.33 (m, 1H), 3.76–3.73 (m, 4H), 3.12–3.09 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 137.3, 135.1, 135.0, 130.7, 130.0, 127.3, 126.5, 126.2, 125.1, 121.3, 117.5, 113.9, 66.2, 46.0. HRMS (FAB+) m/z calcd for $C_{18}H_{19}N_2O_5S_2$: 407.0735 [$M+H]^+$, found 407.0734.

3.1.19. 3-(Morpholine-4-sulfonyl)-1*H*-indole (13). A mixture of **12** (0.81 g, 2.0 mmol) and K_2CO_3 (1.11 g, 8.0 mmol) in methanol (16 mL) and water (4 mL) was stirred at rt for 19 h. The pH was adjusted to ~5 by addition of acetic acid, and the mixture was thereafter concentrated at reduced pressure. The residue was partitioned between EtOAc (50 mL) and water (50 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (2×25 mL), brine (25 mL), and dried over $MgSO_4$. Evaporation of the solvents in vacuo gave pure **13** (490 mg, 92%) as a colourless foam. Crystallization from benzene gave an analytically pure sample as colourless crystals, mp (benzene) 177.5–178.5 °C; IR (neat) 3302, 1314, 1257, 1140, 1129, 1110, 1066, 936, 924, 753, 711 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.04 (br s, 1H), 7.97–7.94 (m, 1H), 7.71 (d, J=3.0 Hz, 1H), 7.49–7.46 (m, 1H), 7.35–7.25 (m, 2H), 3.77–3.74 (m, 4H), 3.10–3.07 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 136.2, 130.0, 124.5, 124.3, 122.7, 120.4, 112.3, 110.7, 66.3, 46.1. HRMS (FAB+) m/z calcd for $C_{12}H_{15}N_2O_3S$: 267.0803 [$M+H]^+$, found 267.0797.

3.1.20. *tert*-Butyl 1*H*-indole-3-carboxylate (14b).[26] Oxalyl chloride (4.87 mL, 55.8 mmol) was added to a suspension of indole-3-carboxylic acid (3.0 g, 18.6 mmol) in anhydrous CH_2Cl_2 (150 mL), followed by a catalytic amount of anhydrous DMF (four drops). The suspension was stirred at rt for 3 h. Removal of the solvent in vacuo gave the crude acid chloride a yellow solid. To this material was added slightly warmed anhydrous *t*-BuOH (25 mL), followed by potassium *tert*-butoxide (3.40 g, 30.3 mmol).

The resulting viscous mixture was stirred for 90 min, and was thereafter partitioned between Et_2O (200 mL), saturated aqueous NH_4Cl (100 mL), and brine (50 mL). The layers were separated, and the aqueous phase was extracted with additional Et_2O (100 mL). The combined organic extracts were washed with 2 M NaOH (100 mL), water (100 mL), and brine (100 mL), followed by drying over Na_2SO_4. Removal of the solvents in vacuo gave an oily residue, which was subjected to column chromatography [EtOAc–CH_2Cl_2 (4/1)] to provide **14b** (3.10 g, 77%) as a light tan viscous oil, IR (neat) 3287, 2971, 1663, 1530, 1365, 1148, 1120, 1044, 1026, 776, 741 cm^{-1}; ^1H NMR (DMSO-d_6) δ 11.83 (s, 1H), 7.99–7.97 (m, 2H), 7.48–7.44 (m, 1H), 7.21–7.13 (m, 2H), 1.56 (s, 9H); ^{13}C NMR (DMSO-d_6) δ 164.0, 136.4, 125.5, 122.1, 121.0, 120.5, 112.2, 108.2, 78.8, 28.2.

3.1.21. 3-(1*H*-Indole-1-sulfonyl)-1-phenylsulfonyl-1*H*-indole (15a). BuLi (2.5 M in hexanes, 3.8 mL, 10.6 mmol) was added at −78 °C to a solution of diisopropylamine (1.33 mL, 9.5 mmol) in THF (50 mL). After stirring at −78 °C for 20 min, indole (0.91 g, mmol) in THF (11 mL) was added at −78 °C during ~15 min. The mixture was stirred at −78 °C for 35 min, followed by addition of a solution of **10a** (2.89 g, 8.1 mmol) in THF (20 mL) during ~10 min at −78 °C. The resulting solution was allowed to slowly reach rt during 15 h. Saturated aqueous NH_4Cl (10 mL) was added, followed by water (50 mL). The resulting mixture was extracted with EtOAc (2×50 mL), and the combined organic layers were washed with water (2×50 mL), brine (50 mL), and dried over $MgSO_4$. Removal of the solvents in vacuo gave a residue, which was triturated with methanol (~30 mL). The precipitate was collected by filtration, washed with methanol, and dried to provide pure **15a** (1.83 g, 54%) as a slightly pinkish solid. An analytically pure sample was obtained by crystallization from toluene as colourless crystals, mp (toluene) 182–183.5 °C; IR (neat) 1444, 1385, 1374, 1174, 1155, 1134, 1111, 1088, 942, 745, 726 cm^{-1}; ^1H NMR (DMSO-d_6) δ 9.02 (s, 1H), 8.12–8.09 (m, 2H), 8.04 (d, J=8.3 Hz, 1H), 7.99 (d, J=3.7 Hz, 1H), 7.94 (d, J=8.2 Hz, 1H), 7.80 (d, J=7.4 Hz, 1H), 7.72–7.67 (m, 1H), 7.58–7.51 (m, 3H), 7.46–7.33 (m, 3H), 7.26–7.21 (m, 1H), 6.75 (d, J=3.7 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 135.6, 135.5, 133.7, 133.5, 132.6, 130.3, 130.1, 127.3, 127.0, 126.8, 125.2, 124.7, 123.5, 123.4, 121.5, 119.8, 117.8, 113.6, 113.1, 109.0. HRMS (FAB+) m/z calcd for $C_{22}H_{16}N_2O_4S_2$: 436.0551 [M^+], found 436.0543.

3.1.22. *tert*-Butyl 1-[1-(4-methyl-sulfonyl)-1*H*-indole-3-sulfonyl]-1*H*-indole-3-carboxylate (15b). The procedure above was used, employing *tert*-butyl indole-3-carboxylate (**14b**) (1.68 g, 7.7 mmol), and **10b** (3.0 g, 8.1 mmol) dissolved in THF (25 mL). After workup, removal of the solvents in vacuo gave a residue, which was triturated with EtOAc (~25 mL). The precipitate was collected by filtration, washed with EtOAc, and dried to provide **15b** (1.95 g, 46%) as a white crystalline solid, mp (EtOAc) 210–212 °C; IR (neat) 1700, 1378, 1169, 1141, 1129, 1110, 1066, 741 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.44 (s, 1H), 8.29 (s, 1H), 8.11–8.08 (m, 1H), 7.95–7.87 (m, 2H), 7.83–7.80 (m, 1H), 7.75–7.71 (m, 2H), 7.42–7.31 (m, 4H), 7.24–7.21 (m, 2H), 2.36 (s, 3H), 1.63 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 163.1, 146.8, 134.7, 134.6, 133.8, 131.9, 131.8, 130.6, 128.1, 127.4, 126.8, 125.5, 125.4, 124.5, 124.5, 122.6, 120.3, 118.6, 115.6, 114.0, 113.2, 81.6, 28.6, 21.9. Anal. Calcd for $C_{28}H_{26}N_2O_6S_2$: C, 61.07; H, 4.76; N, 5.09. Found: C, 61.16; H, 4.58; N, 4.81.

3.1.23. 3-(1*H*-Indole-1-sulfonyl)-1*H*-indole (16a). To a suspension of **15a** (0.48 g, 1.1 mmol) in MeOH (12 mL) and water (3 mL), was added K_2CO_3 (0.60 g, 4.3 mmol), and the resulting mixture was stirred at rt for 22 h. Acidification to pH ~5 with AcOH, followed by concentration at reduced pressure gave a residue, which was diluted with water (25 mL), and extracted with EtOAc (3×25 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (2×25 mL), brine (25 mL), and dried over $MgSO_4$. Removal of the solvent in vacuo gave a solid residue, which was subjected to column chromatography [EtOAc–*n*-heptane (3/7)] to provide **16a** (0.26 g, 80%) as a white crystalline solid, mp (*i*-PrOH) 193.5–195 °C; IR (neat) 3371, 1352, 1146, 1130, 1120, 1100, 742 cm^{-1}; ^1H NMR (DMSO-d_6) δ 12.39 (br s, 1H), 8.49 (s, 1H), 7.97–7.93 (m, 2H), 7.81–7.78 (m, 1H), 7.56–7.54 (m, 1H), 7.48–7.44 (m, 1H), 7.32–7.16 (m, 4H), 6.72 (dd, J=3.7, 0.7 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 136.2, 133.7, 132.7, 130.2, 127.0, 124.0, 123.5, 122.7, 122.5, 122.1, 121.3, 118.5, 113.0, 112.9, 110.5, 107.5. HRMS (FAB+) m/z calcd for $C_{16}H_{12}N_2O_2S$: 296.0619 [M^+], found 296.0625.

3.1.24. *tert*-Butyl 1-(1*H*-indole-3-sulfonyl)-1*H*-indole-3-carboxylate (16b). To a suspension of **15b** (0.60 g, 1.09 mmol) in a mixture of THF (12 mL), MeOH (12 mL), and water (3 mL), was added K_2CO_3 (1.80 g, 13.0 mmol), and the resulting mixture was stirred at rt for 30 min. It was thereafter acidified to pH ~5 with AcOH, and concentrated at reduced pressure. Workup as above for **15a** gave a residue, which was subjected to column chromatography [EtOAc–*n*-heptane (3/7)] to afford **16b** (0.40 g, 93%) as a white crystalline solid, mp (*i*-Pr_2O) 226 °C (dec); IR (neat) 3348, 1699, 1360, 1149, 1125, 1101, 1097, 965, 743 cm^{-1}; ^1H NMR (DMSO-d_6) δ 12.61 (br s, 1H), 8.68 (s, 1H), 8.39 (s, 1H), 8.04–7.96 (m, 2H), 7.83–7.78 (m, 1H), 7.52–7.49 (m, 1H), 7.39–7.23 (m, 4H), 1.55 (s, 9H); ^{13}C NMR (DMSO-d_6) δ 162.3, 136.2, 134.1, 133.8, 131.7, 126.9, 125.0, 124.0, 123.8, 122.6, 122.5, 121.5, 118.1, 113.3, 113.2, 113.0, 109.2, 80.8, 27.9. HRMS (FAB+) m/z calcd for $C_{21}H_{20}N_2O_4S$: 396.1144 [M^+], found 396.1126.

3.1.25. 4-(1-Phenylsulfonyl-1*H*-pyrrole-3-sulfonyl)-morpholine (17). The same procedure as for **12** was used, employing 1-phenylsulfonyl-1*H*-pyrrole-3-sulfonyl chloride (**8a**) (1.53 g, 5.0 mmol), to give pure **17** (1.66 g, 93%) as a white foamy solid. This material softens gradually at temperatures over ~80 °C, and a definite mp could not be determined. IR (neat) 1374, 1344, 1173, 1148, 1115, 1071, 1054, 946, 932, 723 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.95–7.91 (m, 2H), 7.74–7.68 (m, 1H), 7.63 (dd, J=2.4, 1.7 Hz, 1H), 7.62–7.56 (m, 2H), 7.25 (dd, J=3.3, 2.4 Hz, 1H), 6.48 (dd, J=3.3, 1.7 Hz, 1H), 3.76–3.73 (m, 4H), 3.01–2.98 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 137.7, 135.2, 130.1, 127.5, 123.8, 123.4, 122.3, 112.2, 66.1, 46.0. HRMS (FAB+) m/z calcd for $C_{14}H_{18}N_2O_5S_2$: 357.0579 [$M+H]^+$, found 357.0578.

3.1.26. 4-(1*H*-Pyrrole-3-sulfonyl)-morpholine (18). The same procedure was used as for **13** was used, employing compound **17** (0.71 g, 2 mmol), to afford pure **18** (0.36 g, 83%) as colourless crystals, mp (*i*-PrOH/*i*-Pr_2O) 102.5–104 °C; IR (neat) 3321, 1313, 1258, 1134, 1105, 1066, 939, 924, 750, 724 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.31 (br s, 1H), 7.25–7.23 (m, 1H), 6.86–6.84 (m, 1H), 6.44–6.41 (m, 1H), 3.77–3.74 (m, 4H), 2.99–2.96 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 122.6, 120.3, 116.7, 108.5, 66.1, 46.1. Anal. Calcd for $C_8H_{12}N_2O_3S$: C, 44.43; H, 5.59; N, 12.95. Found: C, 44.55; H, 5.65; N, 12.95.

3.1.27. Crystal data for 1-phenylsulfonyl-1*H*-pyrrole-3-sulfonyl chloride (8a). $C_{10}H_8NO_4Cl$, $M_r=305.76$, space group: monoclinic, $P2_1/c$ (No. 14). Unit-cell parameters: $a=13.597(1)$, $b=8.322(1)$, $c=11.496(1)$ Å, $\alpha=90$, $\beta=105.34(1)$, $\gamma=90°$, $V=1254.5(2)$ $Å^3$, $Z=4$. $D_x=1.619(1)$ g/cm^3, $F(000)=624$. μ(Mo Kα)=6.41 cm^{-1}. Crystal dimensions 0.06×0.29×0.29 mm. A total of 1054 independent reflections [$F^2>3\sigma(F^2)$] was refined on F^2 to give $R=0.0479$, $R_w=0.0934$ for 165 parameters $w=1/[\sigma^2F_o^2+(0.1000)F_o^2]$. $(\Delta/\sigma)_{max}=0.0002$, $(\Delta/\sigma)_{mean}=0.0000$, $\Delta\rho_{max}=1.16$ e $Å^{-3}$, $\Delta\rho_{min}=-1.73$ e $Å^{-3}$, $\Delta\rho_{mean}=0.32$ e $Å^{-3}$. The data was corrected for extinction effects.

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