Electronic Supplementary Material (ESI) for ChemComm.

Table of Contents

1. General Information

All reagents and solvents used were obtained as analytical grade from commercial suppliers or purified with standard methods.[1] Sulfur dioxide (99.98%) was purchased from Linde AG in a 10 L pressure bottle. Electrochemical reactions were carried out at boron-doped diamond (BDD) electrodes. BDD electrodes (DIACHEM®, 15 µm boron-doped diamond layer on 3 mm silicon support/wafer) were purchased from CONDIAS GmbH, Itzhoe, Germany. The glass frits were purchased from ROBU® Glasfilter-Geräte GmbH (VitraPOR filter-disc; centred; porosity: P4; diameter: 10 mm; thickness standard: apx. 2.8 mm). Isostatic graphite Sigrafine® V2100 electrodes were purchased from SGL Carbon (Bonn-Bad Godesberg, Germany). Glassy carbon electrodes (SIGRADUR® G) were obtained from HTW Hochtemperatur-Werkstoffe GmbH (Thierhaupten, Germany).

Column chromatography was performed on silica gel 60 M (0.040–0.063 mm, Macherey-Nagel GmbH & Co, Düren, Germany). Therefore, a preparative chromatography system (Büchi, Flawil, Switzerland) was used with a Büchi Control Unit C-620, an UV detector Büchi UV photometer C-635, a Büchi fraction collector C-660 and two Pump Modules C-605 for adjusting the solvent mixtures. As eluent, mixtures of cyclohexane and ethyl acetate were employed. Silica gel 60 sheets on aluminium (F254, Merck KGaA, Darmstadt, Germany) were employed for thin layer chromatography.

Melting points were determined with a Melting Point Apparatus B-565 (Büchi, Flawil, Switzerland) and are uncorrected. Heating rate: 1°C/min.

NMR spectra of ^{1}H (300.13 MHz), ^{19}F (282.38 MHz) and $^{13}C\{1H\}$ (75.48 MHz) were recorded at 23 °C by Bruker Avance III HD spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to traces of $CHCl_3$ (7.26 ppm in ^{1}H, 77.16 ppm in $^{13}C\{1H\}$). For ^{19}F spectra $CFCl_3$ serves as reference compound.[2]

High-resolution mass spectra were obtained with QT of Ultima 3 (Waters, Milford, Massachusetts) using ESI^+ ionization mode.

X-ray analysis data were collected on a STOE IPDS-2T diffractometer (STOE & Cie GmbH, Darmstadt, Germany) using graphite monochromated Mo-K_α radiation (λ= 0.71073 Å).

Intensities were measured using fine-slicing ω and corrected for background, polarization and Lorentz effects. The structures were solved by direct methods and refined anisotropically by the least-squares procedure implemented in the SHELX program system. The supplementary crystallographic data for this paper can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif. Deposition numbers and further details are given with the individual characterization data.

Cyclic voltammetry was performed in a 10 mL snap-cap vial equipped with an Autolab PGSTAT101 potentiostat (Metrohm AG, Herisau, Switzerland). *WE*: platinum electrode tip, 2 mm diameter; *CE*: glassy carbon rod; *RE*: Ag/AgCl in saturated LiCl/EtOH. Solvent: MeCN. v = 100 mV/s, room temperature, c = 0.01 M, supporting electrolyte: NBu_4BF_4, c (NBu_4BF_4) = 0.1 M.

2. Experimental Procedures

Preparation of SO_2 stock solution:

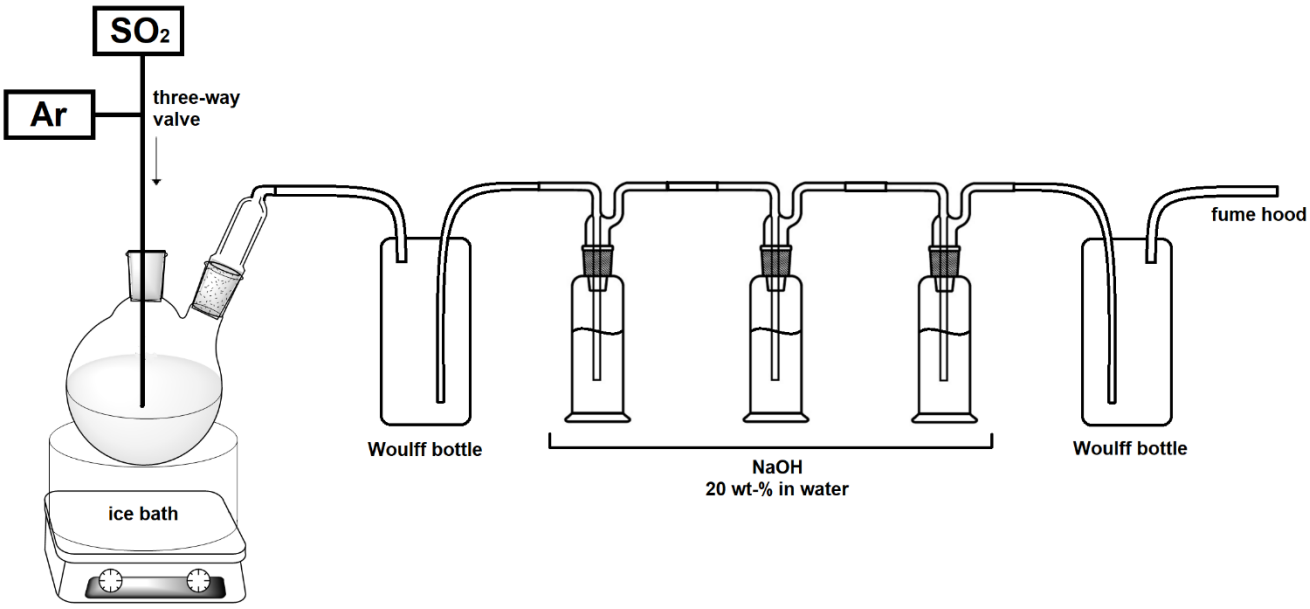


Figure 1. Gas-inlet apparatus for the preparation of SO_2 stock solutions**.**

According to Figure 1, 350 mL of MeCN was transferred into a dry two-neck round bottom flask. Sulfur dioxide was inserted for 60 minutes while constant stirring at 0 °C. After application, the gas-inlet apparatus was purged with argon. Excess SO_2 was quenched with aqueous NaOH (20 wt-%). The SO_2 stock solution was stored at +4 °C.

Determination of the SO_2 concentration of the stock solution:

The SO_2 molarity was determined according to the principles of iodometry.[3]

An aliquot of the SO_2 stock solution (0.5 mL) was slowly added under stirring to an aq. solution of I_2 (1.27 g, 5.00 mmol) and KI (2.20 g, 13.3 mmol) in distilled water (100 mL) (equation 1). (Please note: Low heat build-up was observed). The solution was then back titrated with a freshly prepared aq. $Na_2S_2O_3$ solution (0.2 M) as titrant (equation 2). (Optional: On the verge of the transition point (decolorization), a few drops of a freshly prepared starch solution can be added for better visualization). After full reduction of the iodine, the concentration of SO_2 was calculated according to the previously reduced amount of iodine by SO_2. The protocol was repeated twice. A SO_2 concentration not higher than 4.0 M in MeCN is highly recommended due

to saturation. If the concentration was too excessive, the stock-solution was diluted, and the titration was repeated. In case the stock solution was too diluted, SO_2 was again injected for several minutes and the titration was repeated.

$$SO_2 + 2\ H_2O + I_2 \rightarrow H_2SO_4 + 2\ HI \quad (1)$$

$$2\ Na_2S_2O_3 + I_2 \rightarrow Na_2S_4O_6 + 2\ NaI \quad (2)$$

Experimental set-up and general protocol for the synthesis of sulfonamides in divided cells:

The electrochemical conversion was conducted in divided cells made of Teflon™ according to Figure 2.[4] A porous glass frit (porosity: P4) was used as separator, sealed by an EPDM ring. As cathode and anode material, boron-doped diamond electrodes (BDD) were utilized, which can be fixed by Teflon screws. One round-shaped stirring bar is placed in each compartment of the cell. In total, six divided cells can be placed in a screening block, which can be located on a magnetic stirrer. This reaction set-up can be commercially obtained as IKA Screening System package (6 cells) from IKA®-Werke GmbH & Co. KG (Staufen, Germany).

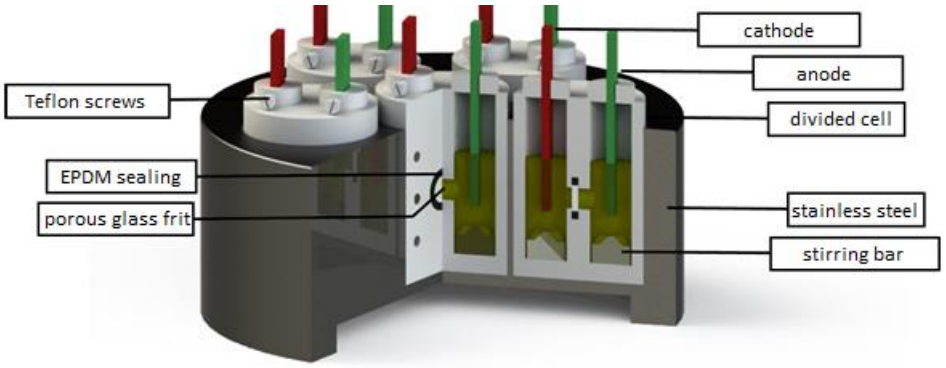


Figure 2. Screening system with 6 divided electrolysis cells fitting on a common magnetic stirrer; electrode gap: 2 cm; active surface of each planar electrode: 3.20 cm^2.

Scale-up Reaction:

The scale-up reaction was performed in an H-type glass cell, which is divided by a glass frit (Figure 3 and 4). Total volume was 160 mL (80.0 mL in each compartment). A star-shaped stirring bar was used on each side for efficient mixing. Platinum foils (dimensions: (4.00 x 2.00) cm) used for electrolysis were attached on a Teflon™ frame as depicted in Figure 3.

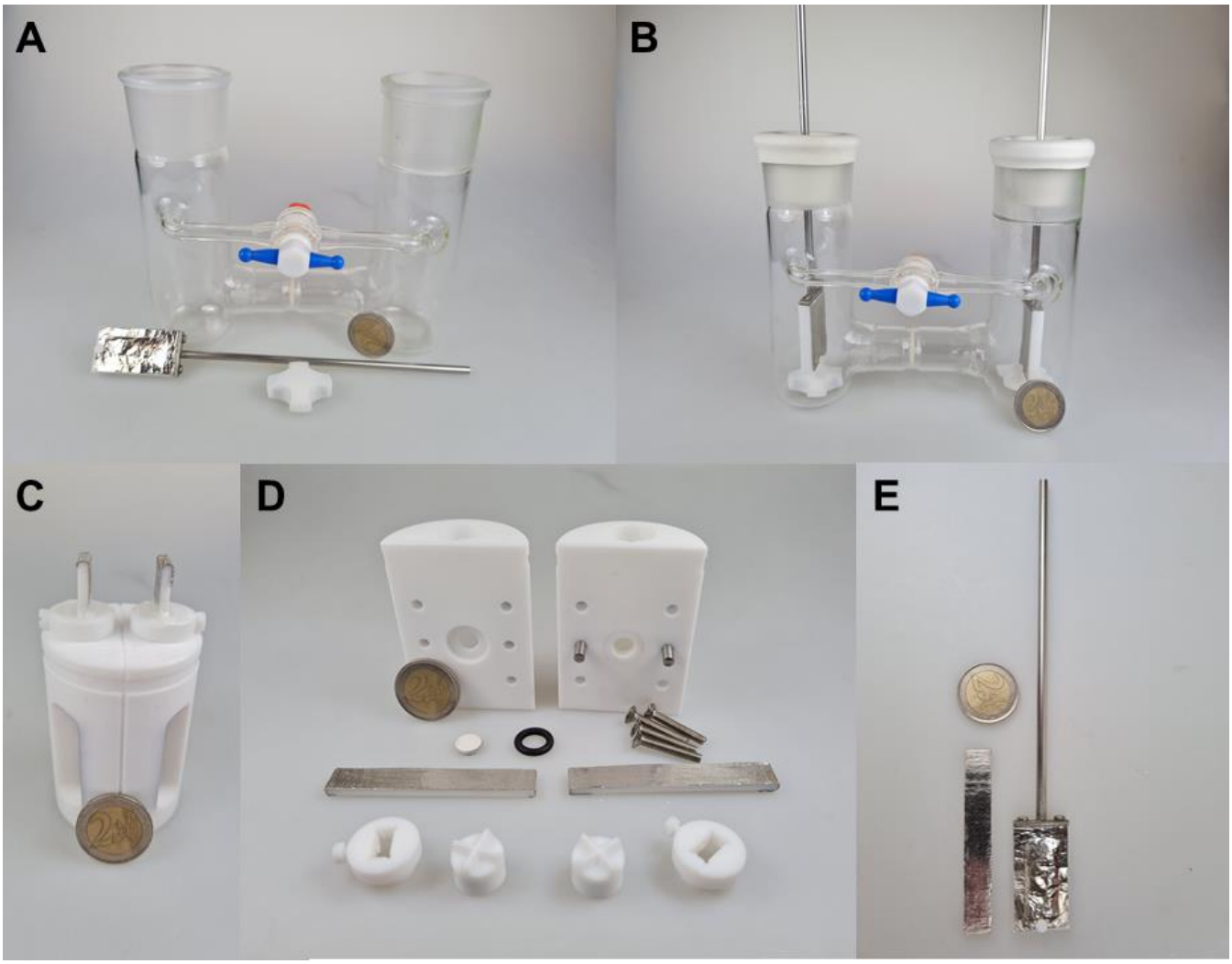


Figure 3. **A**: H-type divided glass cell (width: 16 cm, height: 14 cm, gap between electrodes: 12 cm) with star-shaped stirring bar (diameter: 3 cm) and platinum foil attached on a Teflon frame (2 x 4 cm); **B**: electrodes attached on the H-type divided glass cell with a septum (electrode gap: 12.5 cm); **C**: screening cell with platinum electrodes, which are sealed with Parafilm; **D**: components of the screening cell: two platinum electrodes (platinum plate attached on Teflon (1 x 7 cm)), 4 screws, glass frit (P4), EPDM ring, 2 round-shaped stirring bars, 2 Teflon™ holders to fix the electrodes with a Teflon™ srew; **E**: size comparison between platinum electrodes of screening cell (left) and H-type glass cell (right); a 2 € coin (diameter: 25.75 mm) has been placed next to each component for better size estimation.

Figure 4. H-type divided glass cell during electrolysis.

General protocol for optimization reactions (GP1):

The anodic compartment of a divided screening cell was charged with 4-*tert*-butylaniline (179 mg, 1.20 mmol, 1.00 eq.) and tetrabutylammonium iodide (44 mg, 0.12 mmol, 0.10 eq.). Preparation of the electrolyte: A ready-made solution of HFIP (605 mg, 3.60 mmol, 3.00 eq.), MeCN, DIPEA (414 mg, 3.20 mmol, 2.67 eq.), SO_2 in MeCN from a previously prepared stock solution, were added into a pre-dried pear-shaped flask with septum at 0 °C under stirring so that a total volume of 12.0 mL and the desired SO_2 concentration of 1.00 M was reached. The reaction mixture was then transferred into the two compartments of the divided cell (6.00 mL into each compartment). The electrodes were connected to a DC power device and the electrolysis was started under constant stirring (300 rpm, r.t.). The electrolysis was completed after 89 min. The reaction mixture was continued stirring overnight (total stirring time: 14 h). 1,3,5-Trimethoxybenzene from a stock solution (1.20 mL, 0.60 mmol, 0.50 M in MeOH) was transferred to the reaction mixture of the electrolytes of both cell compartments and mixed. An aliquot (1–2 mL) of the mixture was taken, diluted with ethyl acetate (3.00 mL), washed with distilled water (2 x 4.00 mL) and dried over $MgSO_4$. The organic solvent was removed under reduced pressure and the NMR yield of the desired product was calculated according to the ratio of the internal standard.

General protocol for the synthesis of symmetrical sulfamides (GP2):

The anodic compartment of a divided screening cell was charged with the aniline substrate (1.20 mmol, 1.00 eq.) and tetrabutylammonium iodide (44 mg, 0.12 mmol, 0.10 eq.). Preparation of the electrolyte: A ready-made solution of HFIP (605 mg, 3.60 mmol, 3.00 eq.), MeCN, DIPEA (414 mg, 3.20 mmol, 2.67 eq.), SO_2 in MeCN from a previously prepared stock solution, were added into a pre-dried pear-shaped flask with septum at 0 °C under stirring so that a total volume of 12.0 mL and the desired SO_2 concentration of 1.00 M was reached. The reaction mixture was then transferred into the two compartments of the divided cell (6.00 mL into each compartment). The platinum electrodes were connected to a DC power device and the electrolysis (7.50 mA/cm^2, 1.20 F) was started constant stirring (300 rpm, r.t.). The terminal voltage was around 13 V (±0.5 V). The electrolysis was completed after 89 min. The reaction mixture was continued stirring overnight (total stirring time: 14 h). Ethyl acetate (30.0 mL) was added to the crude reaction mixture (anolyte and catholyte), which was then washed with distilled water (2 x 30.0 mL). The aqueous fractions were backwashed with ethyl acetate (2 x 30.0 mL) and the combined organic fractions were washed with brine (30.0 mL) and dried over $MgSO_4$. The organic solvent was removed at reduced pressure and the crude product was

purified *via* column chromatography with an ethyl acetate/cyclohexane solvent gradient (1:49 to 2:3).

Important Considerations

MeCN, HFIP and DIPEA were dried with 3 Å MS. The Teflon cells were sealed with Parafilm, but were not pre-dried (also see Figure 3). All electrodes were cleaned with DMSO and acetone after usage. Platinum electrodes were glowed consistently.

3. Cyclic Voltammetry

CV investigations were performed for reaction mechanism elucidation. Unless otherwise noted, 0.10 M NBu_4BF_4 (165 mg, 0.50 mmol) was dissolved in MeCN (5.00 mL). The different substrates used can be retrieved from Table 1 and Graph 1. Ag/AgCl was used as internal reference.[5]

Table 1. Substrates used for CV studies (also see Graph 1).

Graph	Substrates	c [M]
black	Mediator (tetrabutylammonium iodide)	0.01
red	Base (DIPEA)	0.01
blue	Substrate (4-*tert*-butylaniline)	0.01

4. Mechanistic Proposal and Cyclic Voltammetry Results

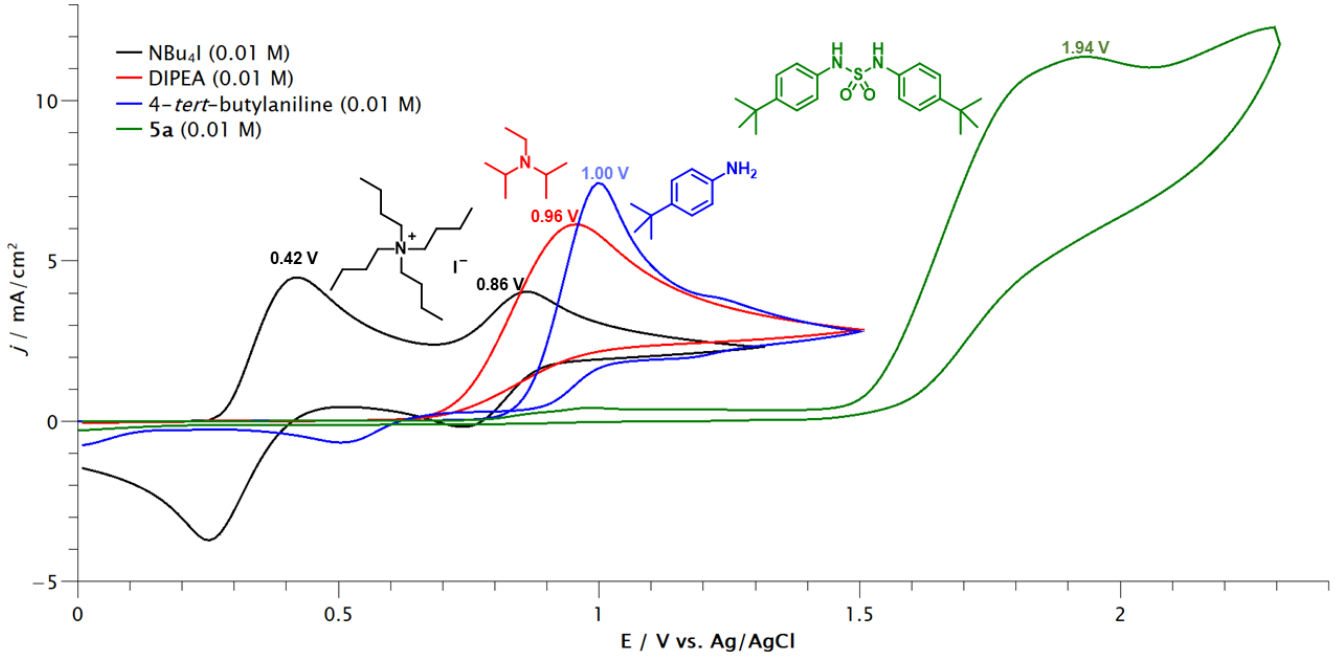
According to the cyclovoltammetry data obtained (Graph 1), the mechanism is proposed as follows:

The iodide species is supposed to undergo initial anodic oxidation to form I_2 at 0.42 V (black graph) as displayed in equation 3, followed by subsequent formation of I_3^- (equation 4). The second oxidation potential (0.86 V, black graph) can be assigned to the anodic oxidation of I_3^- to iodine (equation 5). In the literature, the electrochemical behavior of NBu_4I has been analyzed in dichloromethane at glassy carbon electrodes.[5] It is noteworthy, that iodide exhibits lower oxidation potentials in comparison to DIPEA (0.96 V, red graph) or 4-*tert*-butylaniline (1.00 V, blue graph), which confirms that no anodic oxidation of the anilines occurs and therefore polymerization can be avoided. Sulfamide **5a** exhibits an increased oxidation potential of 1.94 V (green graph), which proves that overoxidation is unlikely.

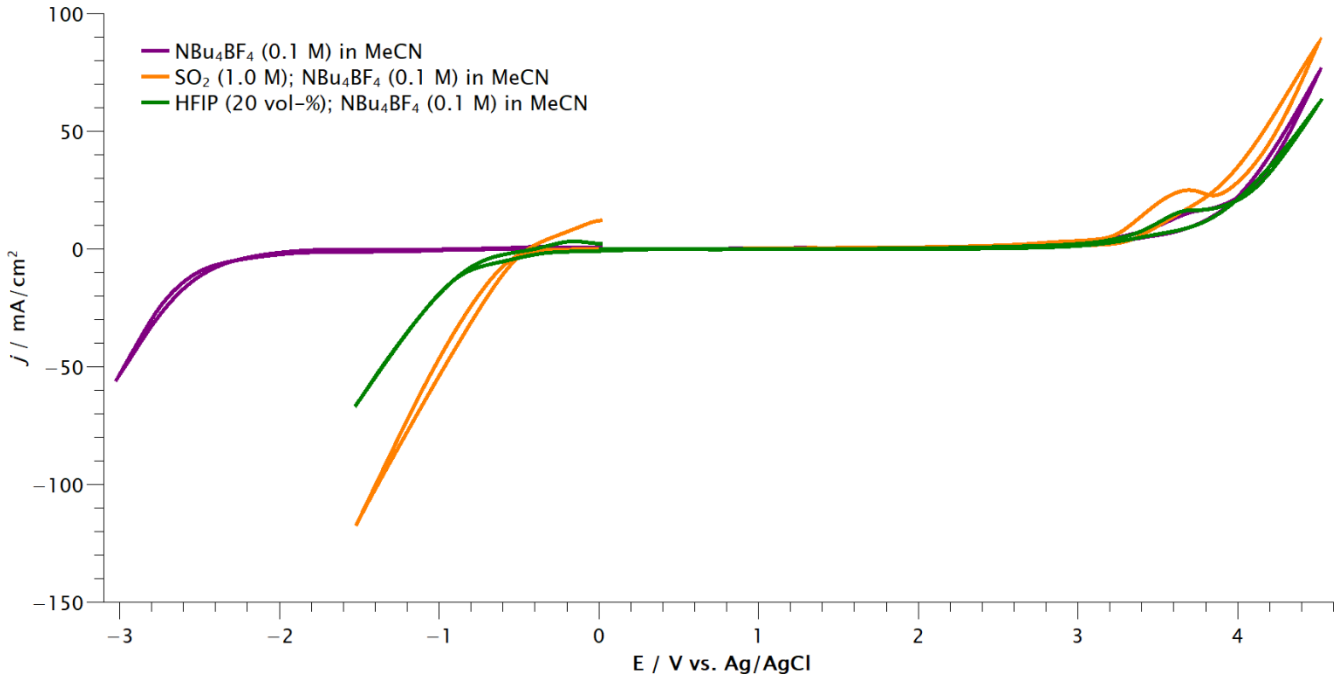
$$3\ I^- \rightarrow I_2 + 2\ e^- + I^- \quad (3)$$

$$I^- + I_2 \rightarrow I_3^- \quad (4)$$

$$2\ I_3^- \rightarrow 3\ I_2 + 2\ e^- \quad (5)$$



Graph 1. Cyclic Voltammetry measurements of NBu_4I (**black**), DIPEA (**red**), 4-*tert*-butylaniline (**blue**), and **5a** (**green**).



Graph 2. Cyclic Voltammetry measurements of NBu_4BF_4 (0.1 M) in MeCN (**purple**); SO_2 (1.0 M) and NBu_4BF_4 (0.1 M) in MeCN (**orange**); HFIP (20 vol-%) and NBu_4BF_4 (0.1 M) in MeCN (**green**).

The reaction mechanism proposal is depicted in Scheme 1. The addition of HFIP generates conductible species of the electrolytes,[6] which omits the use of additional supporting electrolytes leading to a lower overall atom economy. The electrochemically generated iodine is supposed to form extraordinarily strong Lewis acid–base adducts with DIPEA analogously to pyridine–I_2 or triethylamine–I_2 complexes reported in the literature, which to some extent have ionic character,[7,8,9] making them likely more reactive for subsequent reactions. Possibly, HFIP could further stabilize and activate these ionic species ($[R_3NI^+]I^-$ or even $[(R_3N)_2I^+]I^-$)[8,9] by hydrogen bonds. Additionally, HFIP is considered to disperse or alter the charge transfer complex (black color) between DIPEA and SO_2 in MeCN (Figure 5). Addition of HFIP changed the color of the solution from black to orange/yellow.

We consider the reaction to proceed via amidosulfinates generated from anilines, SO_2 and DIPEA, which could also be one of the conductible species in the electrolyte. The in-situ generated iodonium is considered to react with the amidosulfinate resulting in the formation of sulfamoyl iodide in an equilibrium reaction. This transformation could possibly be favored by hydrogen bond stabilization of the sulfamoyl iodide from stoichiometric amounts of HFIP. Subsequent nucleophilic displacement with another equivalent of aniline provides the symmetrical aromatic sulfamide.

As cathodic reaction, SO_2 reduction occurs (Graph 2). It is notable that the orange graph shows a narrower potential window, which is caused by cathodic reduction of sulfur dioxide in comparison to HFIP in MeCN (green graph; HFIP was added as proton source for H_2 generation).

The formation of the sulfur dioxide anion radical was also observed by formation of a dark/brown reaction mixture in the cathode compartment as can be seen during the scale-up reaction in Figure 4 (cathode compartment on the left side). No gas evolution was observed in both compartments.

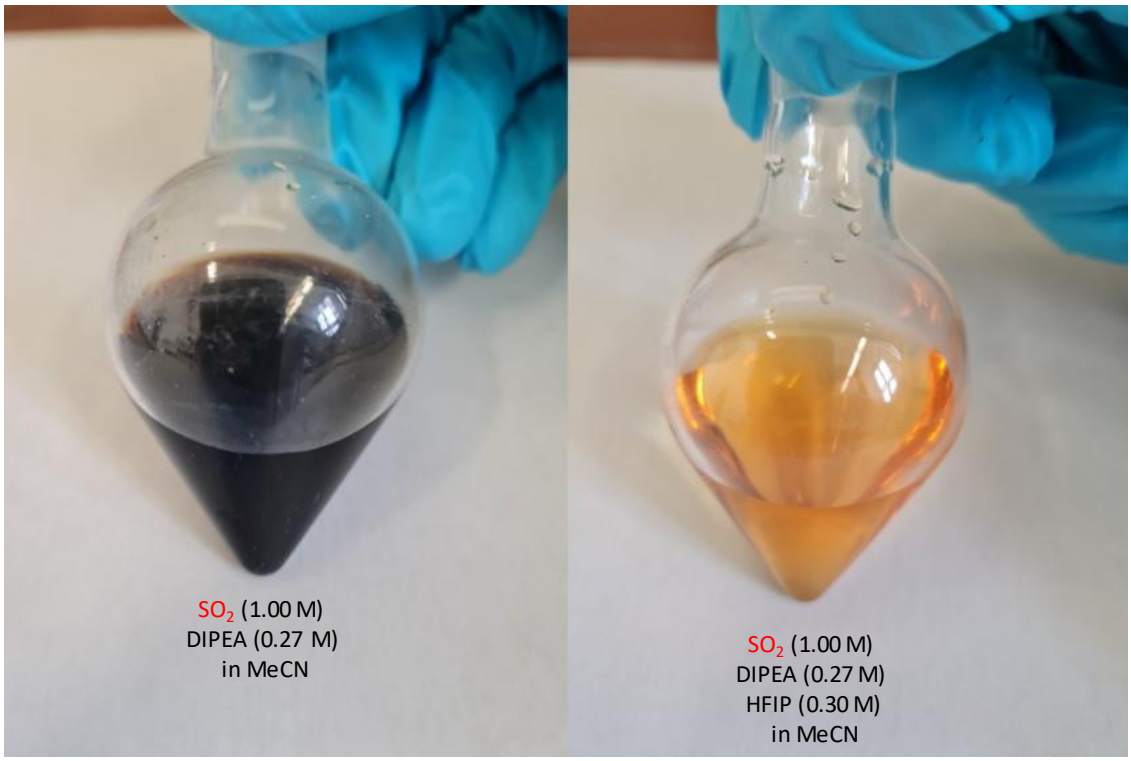
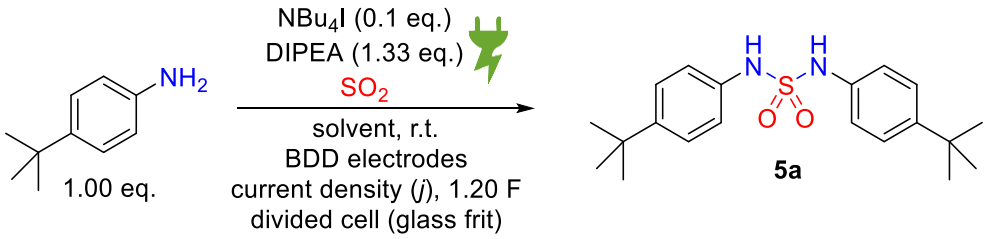


Figure 5. Comparison between a solution of SO_2 and DIPEA in MeCN (black solution, left) with a solution of SO_2, DIPEA and HFIP in MeCN (orange solution, right). The concentrations of SO_2, DIPEA and HFIP were chosen analogously to the reaction mixture with the optimized conditions (see next chapter).

5. Optimization of the Reaction Conditions

The reaction conditions were optimized in a step-by-step approach by using the general protocol GP1. The SO_2 concentration, aniline concentration, solvent ratio, current density, electrode material, the role of iodide and the cell type were investigated.



Scheme 1. Model reaction for optimization of reaction conditions; DIPEA = *N*,*N*-diisopropylethylamine.

According to Scheme 1 and Table 2, a series of reactions was executed by varying several parameters (Tab. 2). Initial experiments were carried out with BDD electrodes as can be seen in Scheme 2.

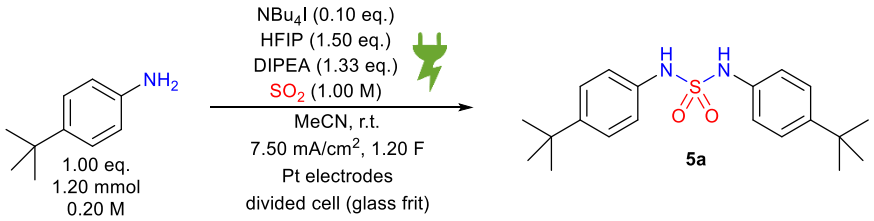
Table 2. Initial optimization reactions for the electrochemical sulfamide synthesis.

Entry	Solvent	Aniline [M]	SO_2 [M]	Iodide (0.1 eq.)	*j* [mA/cm^2]	NMR yield[a] [%]
1	MeCN	0.30	1.50	NBu_4I	12.0	0
2	HFIP/MeCN = 1 : 1	0.30	1.50	NaI	12.0	21
3	HFIP/MeCN = 1 : 1	0.30	1.50	–	12.0	0
4	HFIP/MeCN = 1 : 1	0.20	1.00	NBu_4I	7.50	72
5	HFIP/MeCN = 1 : 1	0.20	1.00	NBu_4I (0.20 eq.)	7.50	77
6	HFIP/MeCN = 1 : 1	0.40	1.50	NBu_4I	7.50	59
7	HFIP/MeCN = 1.5 : 10	0.20	1.00	NBu_4I	7.50	84
8	HFIP/MeCN = 10 : 1.5	0.20	1.00	NBu_4I	7.50	traces
9	HFIP/MeCN = 2.3 : 9.1	0.20	1.00	NBu_4I	7.50	84
10	HFIP/MeCN = 9.1 : 2.3	0.20	1.00	NBu_4I	7.50	traces

[a] Yield was determined by internal NMR standard (1,3,5-trimethoxybenzene).

Initial experiments revealed that no reaction occurred, when HFIP was omitted (Table 2, entry 1). The addition of HFIP in an HFIP/MeCN (1 : 1) solvent mixture with NaI gave 21% NMR yield (entry 2). No iodide present in the reaction mixture gave no conversion (entry 3). For further reactions, NBu_4I was preferred over NaI due to the excellent solubility of NBu_4I in MeCN and the preference of working metal-free. The conditions shown in entry 4 with only 0.20 M aniline concentration significantly improved the NMR yield to 72%, whereas slight increase of NBu_4I from 0.10 eq. to 0.20 eq. increased the conversion to 77%. Higher aniline concentration (0.40 M) lowered the NMR yield to only 59%. Lower HFIP ratios in the solvent mixture significantly

improved the yield to 84% (entry 7 and 9), while higher HFIP content (entry 8 and 10) only resulted in traces (possibly due to full protonation of DIPEA caused by the higher amount of HFIP). It is noteworthy, that lower conductivity was given when using higher amounts of HFIP resulting in a higher cell voltage (terminal voltage: entry 7: 10.3 V; entry 8: 23.2 V; entry 9: 10.4 V; entry 10: 18.9 V).



Scheme 2. Test reaction for optimization of reaction conditions.

Next, the different parameters were optimized in a step-by-step approach.

Table 3. Optimization table. Deviations from the standard conditions as displayed in Scheme 2.

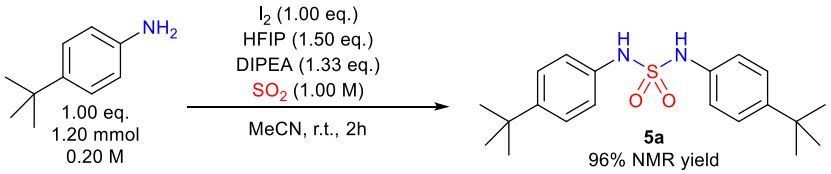
Entry	Deviations from the standard conditions	NMR yield[a] [%]
11	BDD electrodes, no HFIP, no DIPEA; instead: NBu_4BF_4 (0.10 M)	0
12	no DIPEA, instead: NBu_4BF_4 (0.10 M)	0
13	NBu_4Br instead of NBu_4I	0
14	glassy carbon electrodes, NBu_4Cl instead of NBu_4I	0
15	no iodide source	0
16	no electricity	0
17	addition of 100 µL water	0 (polymerization)
18	BDD electrodes, HFIP (3.00 eq.)	80
19	BDD electrodes	88
20	BDD electrodes, HFIP (1.00 eq.)	63
21	BDD electrodes, no HFIP	0
22	graphite electrodes	77
23	gassy carbon electrodes	89
24	none	96 (isolated: 89%)
25	5.00 mA/cm^2	80 (isolated: 75%)
26	10.0 mA/cm^2	94 (isolated: 87%)
27	12.0 mA/cm^2	86
28	pyridine instead of DIPEA	52
29	undivided cell	69

[a] Yield was determined by internal NMR standard (1,3,5-trimethoxybenzene).

At first, it was figured out that HFIP, DIPEA, and the addition of NBu_4I are crucial for the success of this reaction (entry 11 to 15 and 21). The application of a current is also indispensable (entry 16). Interestingly, the addition of low amounts of water resulted in polymerization and no sulfamide product was found (entry 17). Stoichiometric amounts of HFIP (entry 18 to 20

significantly improved the yield to 88% with only 1.50 eq. HFIP in entry 19. No HFIP resulted in no product formation (entry 21). The investigation of electrode materials revealed that platinum electrodes (entry 24) are superior to graphite (entry 22) or glassy carbon electrodes (entry 23). Variation of the current density (entry 25 to 27) confirmed that 7.50 mA/cm^2 is best (96% NMR yield and 89% isolated yield), whereas 10.0 mA/cm^2 gave similar results with 87% isolated yield. Pyridine as base instead of DIPEA resulted in lower yields (entry 28). Undivided cells are less preferred as the NMR yield was only 69%.

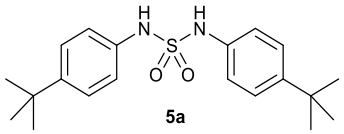
Additionally, the reaction was also performed with stoichiometric amounts of iodine instead of catalytic iodide without application of current (Scheme 3). Interestingly, the NMR yield was 96%, which is in the same range of yield compared to the electrochemical conditions depicted in Table 3 (entry 24). Morpholine as starting material instead of aniline resulted in no sulfamide formation.



Scheme 3. Synthesis of **5a** with stoichiometric amounts of iodine.

6. Product Characterization

6.1 *N*,*N*'-Bis(4-(2,2-dimethylethyl)phenyl)sulfamide (5a)



5a

According to GP2, 4-*tert*-butylaniline (179 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5a** (193 mg, 0.54 mmol, **89%**) was obtained as off-white solid.

Scale-up of electrolysis:

The anodic compartment of a divided H-type glass cell was charged with 4-*tert*-butylaniline (2.39 g, 16.0 mmol, 1.00 eq.) and tetrabutylammonium iodide (369 mg, 1.60 mmol, 0.10 eq.). Preparation of the electrolyte: A ready-made solution of HFIP (8.07 g, 48.0 mmol, 3.00 eq.), MeCN, DIPEA (5.51 g, 42.7 mmol, 2.67 eq.), SO_2 in MeCN from a previously prepared stock solution, were added into a pre-dried pear-shaped flask with septum at 0 °C under stirring so that a total volume of 160 mL and the desired SO_2 concentration of 1.00 M was reached. The reaction mixture was then transferred into the two compartments of the divided cell (80.0 mL into each compartment). The platinum electrodes were connected to a DC power device and the electrolysis (active surface of each electrode: 7.00 cm^2, j = 7.50 mA/cm^2, Q = 1.20 F) was started (applied terminal voltage: 18–23 V) under constant stirring (300 rpm, r.t.). The electrolysis was completed after 588 min. The reaction mixture was continued stirring overnight (total stirring time: 14 h). Ethyl acetate (300 mL) was added to the crude reaction mixture (anolyte and catholyte), which was then washed with distilled water (2 x 300 mL). The aqueous fractions were backwashed with ethyl acetate (2 x 300 mL) and the combined organic fractions were washed with brine (300 mL) and dried over $MgSO_4$. The organic solvent was removed at reduced pressure and the crude product was purified via column chromatography with an ethyl acetate/cyclohexane solvent gradient (1:49 to 2:3). The title compound (2506 mg, 6.96 mmol, **87%**) was obtained as off-white solid.

5a:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.34–7.28 (m, 4H), 7.06–7.01 (m, 4H), 6.59 (bs, 2H), 1.29 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 148.8, 133.7, 126.4, 121.8, 34.6, 31.5; m_R: 170–172 °C (decomposition); HRMS for $C_{20}H_{29}N_2O_2S^+$ (ESI+) $[M+H]^+$: calc.: 361.1944 g/mol, found: 361.1937 g/mol.

Crystallization was performed by dissolving **5a** (50 mg) in dichloromethane (2 mL) and cyclohexane (2 mL) at room temperature upon crystallization at 4 °C. Crystal structure

determination of **5a** (also see Figure 4): $C_{20}H_{28}N_2O_2S$, M = 360.52 g/mol; colorless needles (0.100 x 0.120 x 0.700 mm^3), T = 120 K, λ(Mo-K_α) = 0.71073 Å, space group P-1, a = 11.6468(5) Å, b = 12.4428(6) Å, c = 14.4199(7) Å, α = 105.247(4)°, ß = 103.876(3)°, γ = 92.488(4)°, V = 2004.85(17) $Å^3$, z = 4, ρ_{xray} = 1.194 mg/m^3, $2\theta_{max}$ = 55.8°, μ = 0.176 mm^{-1}, F(000) = 776, 17575 reflections, 9487 unique reflections (R_{int} = 0.0307), final R-values [I > 2σ(I)]: R_1 = 0.0507, *w*R_2 = 0.1169, R-values (all data): R_1 = 0.0663, *w*R_2 = 0.1279, CCDC-2070594.

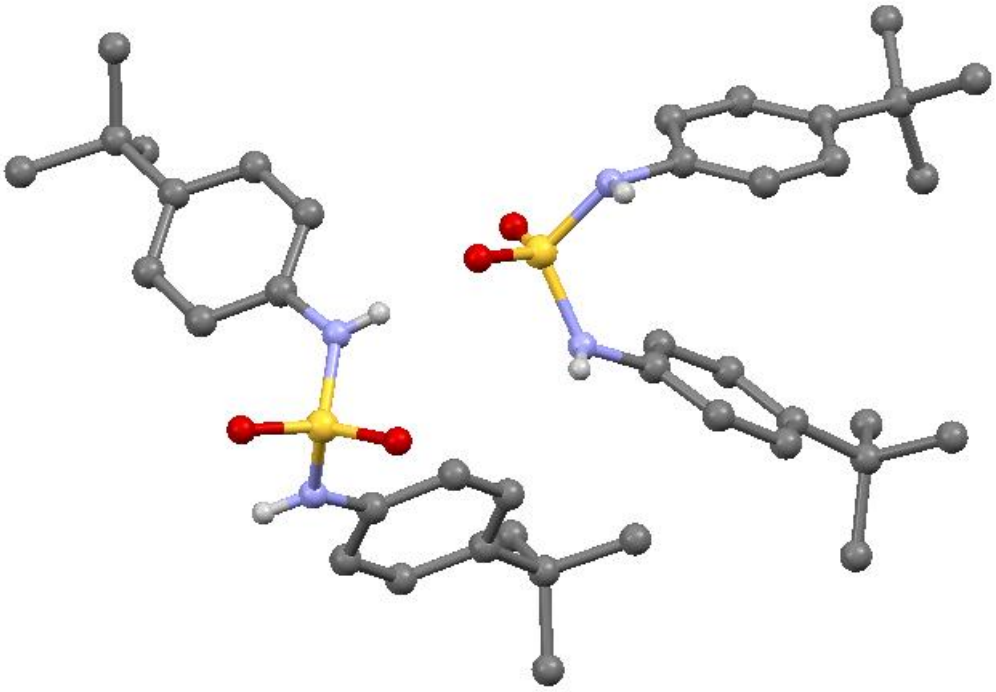
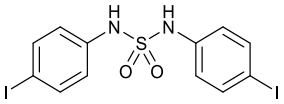


Figure 4. Molecular structure (**5a**) of the unit cell determined by X-ray analysis.

The structure (Fig. 4) contains two independent molecules, whose confirmation slightly differ: The *tert*-butyl groups are disordered (only main component shown). The N–H bond is localized and refined.

6.2 *N*,*N*'-Bis(4-iodophenyl)sulfamide (5b)



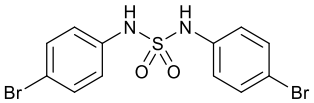
5b

According to GP2, 4-iodoaniline (263 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 0:1 → 1:4), the title compound (269 mg, 0.54 mmol, **90%**) was obtained as off-white solid.

5b:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.71–7.51 (m, 4H), 7.03–6.74 (m, 4H), 6.62 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 138.6, 135.8, 123.1, 89.7; m_R: 150–153 °C (decomposition); HRMS for $C_{12}H_{10}I_2N_2NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 522.8444 g/mol, found: 522.8438 g/mol.

6.3 *N*,*N*'-Bis(4-bromophenyl)sulfamide (5c)



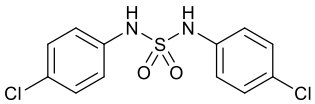
5c

According to GP2, 4-bromoaniline (206 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5c** (223 mg, 0.55 mmol, **92%**) was obtained as colorless solid.

5c:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.48–7.38 (m, 4H), 7.02–6.90 (m, 4H), 6.69 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 135.1, 132.8, 123.1, 119.1; m_R: 124–125 °C (decomposition); HRMS for $C_{12}H_{10}{}^{79}Br_2N_2NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 426.8722 g/mol, found: 426.8720 g/mol. Analytical data correspond to those reported in literature.[10,11]

6.4 *N*,*N*'-Bis(4-chlorophenyl)sulfamide (5d)



5d

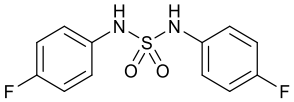
According to GP2, 4-chloroaniline (153 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5d** (162 mg, 0.51 mmol, **85%**) was obtained as off-white solid.

5d:

^{1}H NMR (300 MHz, DMSO-D_6) δ [ppm] = 10.46 (s, 2H), 7.42–7.26 (m, 4H), 7.17–7.05 (m, 4H); ^{13}C NMR (75 MHz, DMSO-D_6) δ [ppm] = 136.9, 129.0, 127.0, 119.9; m_R: 120–121 °C; HRMS for $C_{12}H_{10}{}^{35}Cl_2N_2NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 338.9732 g/mol, found: 338.9730 g/mol.

Analytical data correspond to those reported in literature.[11,12]

6.5 *N*,*N*'-Bis(4-fluorophenyl)sulfamide (5e)



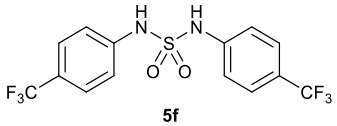
5e

According to GP2, 4-fluoroaniline (133 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5e** (116 mg, 0.41 mmol, **68%**) was obtained as off-white solid.

5e:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.10–6.96 (m, 8H), 6.60 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 160.7 (d, *J* = 245.9 Hz), 132.1 (d, *J* = 3.0 Hz), 124.1 (d, *J* = 8.2 Hz), 116.5 (d, *J* = 22.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ [ppm] = −117.01 (tt, *J* = 8.1, 4.8 Hz); m_R: 104–106 °C; HRMS for $C_{12}H_{10}F_2N_2NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 307.0323 g/mol, found: 307.0323 g/mol.

6.6 *N*,*N*'-Bis(4-trifluoromethylphenyl)sulfamide (5f)



5f

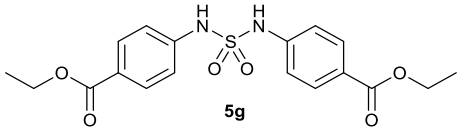
According to GP2, 4-(trifluoromethyl)aniline (193 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5f** (169 mg, 0.44 mmol, **73%**) was obtained as off-white solid.

5f:

^{1}H NMR (300 MHz, DMSO-D_6) δ [ppm] = 11.05 (s, 2H), 7.63 (d, *J* = 8.5 Hz, 4H), 7.31 (d, *J* = 8.5 Hz, 4H); ^{13}C NMR (75 MHz, DMSO-D_6) δ [ppm] = 141.5, 126.5 (d, *J* = 3.9 Hz), 124.4 (q, *J* = 271.3 Hz), 123.1 (q, *J* = 32.2 Hz), 117.5; ^{19}F NMR (282 MHz, DMSO-D_6) δ [ppm] = −61.60; m_R: 152–154 °C (decomposition); HRMS for $C_{14}H_{10}F_6N_2NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 407.0259 g/mol, found: 407.0258 g/mol.

Analytical data correspond to those reported in literature.[11]

6.7 *N*,*N*'-Bis(4-(ethoxycarbonyl)phenyl)sulfamide (5g)



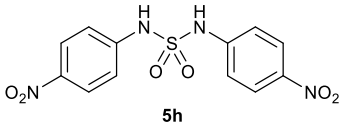
5g

According to GP2, Benzocaine (198 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5g** (203 mg, 0.52 mmol, **86%**) was obtained as colorless solid.

5g:

^{1}H NMR (300 MHz, DMSO-D_6) δ [ppm] = 11.04 (s, 2H), 7.84 (d, *J* = 8.5 Hz, 4H), 7.21 (d, *J* = 8.5 Hz, 4H), 4.24 (q, *J* = 7.1 Hz, 4H), 1.27 (td, *J* = 7.1, 1.4 Hz, 6H); ^{13}C NMR (75 MHz, DMSO-D_6) δ [ppm] = 165.2, 142.2, 130.5, 123.8, 116.8, 60.5, 14.2; m_R: 197–199 °C (decomposition); HRMS for $C_{18}H_{20}N_2NaO_6S^+$ (ESI+) $[M+Na]^+$: calc.: 415.0934 g/mol, found: 415.0941 g/mol.

6.8 *N*,*N*'-Bis(4-nitrophenyl)sulfamide (5h)



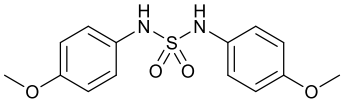
5h

According to GP2, 4-nitroaniline (166 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), the title compound (168 mg, 0.50 mmol, **83%**) was obtained as yellow solid.

5h:

^{1}H NMR (300 MHz, DMSO-D_6) δ [ppm] = 11.58 (s, 2H), 8.34–7.98 (m, 4H), 7.51–7.12 (m, 4H); ^{13}C NMR (75 MHz, DMSO-D_6) δ [ppm] = 143.9, 142.3, 125.4, 117.1; m_R: 194–196 °C (decomposition); HRMS for $C_{12}H_{10}N_4NaO_6S^+$ (ESI+) $[M+Na]^+$: calc.: 361.0213, found: 361.0217. Analytical data correspond to those reported in literature.[11,12]

6.19 *N*,*N*'-Bis(4-methoxyphenyl)sulfamide (5i)



5i

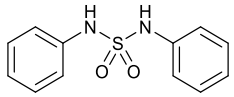
According to GP2, 4-methoxyaniline (148 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5i** (128 mg, 0.52 mmol, **86%**) were obtained as colorless waxy solid.

5i:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.09–6.98 (m, 4H), 6.85–6.78 (m, 4H), 6.56 (bs, 2H), 3.77 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 157.8, 129.1, 124.5, 114.7, 55.6; HRMS for $C_{14}H_{16}N_2NaO_4S^+$ (ESI+) $[M+Na]^+$: calc.: 331.0723 g/mol, found: 331.0727 g/mol.

Reported melting range: 98–101 °C.[11,13]

6.11 *N*,*N*'-Bis(phenyl)sulfamide (5j)



5j

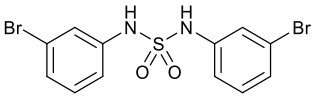
According to GP2, aniline (112 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **5j** (128 mg, 0.52 mmol, **86%**) were obtained as colorless solid.

5j:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.36–7.24 (m, 4H), 7.20–7.13 (m, 2H), 7.12–7.01 (m, 4H), 6.65 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 136.3, 129.6, 125.7, 121.5; m_R: 111–113 °C; HRMS for $C_{12}H_{13}N_2O_2S^+$ (ESI+) $[M+H]^+$: calc.: 249.0692 g/mol, found: 249.0697 g/mol.

Analytical data correspond to those reported in literature.[11,13]

6.12 *N*,*N*'-Bis(3-bromophenyl)sulfamide (6)



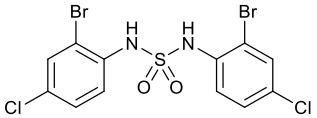
6

According to GP2, 3-bromoaniline (206 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **6** (226 mg, 0.56 mmol, **93%**) was obtained as off-white solid.

6:

^{1}H NMR (300 MHz, DMSO-D_6) δ [ppm] = 10.69 (s, 2H), 7.32 (t, *J* = 1.8 Hz, 2H), 7.27 – 7.15 (m, 4H), 7.09 (dt, *J* = 7.5, 1.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-D_6) δ [ppm] = 139.5, 131.1, 125.7, 122.0, 120.2, 117.0; m_R: 157–159 °C; HRMS for $C_{12}H_{10}{}^{79}Br_2N_2NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 426.8722 g/mol, found: 426.8722 g/mol.

6.13 *N*,*N*'-Bis(2-bromo-4-chlorophenyl)sulfamide (7)



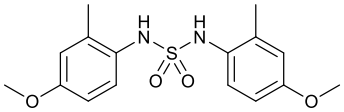
7

According to GP2, 2-bromo-4-chloroaniline (248 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **7** (246 mg, 0.52 mmol, **86%**) was obtained as an off-white solid.

7:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.64 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 2.3 Hz, 2H), 7.32 (dd, *J* = 8.8, 2.3 Hz, 2H), 6.95 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 133.0, 132.5, 131.4, 129.2, 122.3, 115.7; m_R: 154–156 °C (decomposition); HRMS for $C_{12}H_8{}^{79}Br_2{}^{35}Cl_2N_2NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 494.7942 g/mol, found: 494.7940 g/mol.

6.14 *N*,*N*'-Bis(4-methoxy-2-methylphenyl)sulfamide (8)



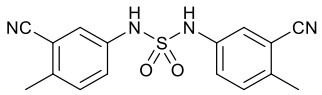
8

According to GP2, 4-methoxy-2-methylaniline (165 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **8** (147 mg, 0.44 mmol, **73%**) was obtained as colorless solid.

8:

^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 7.38 (d, *J* = 8.7 Hz, 2H), 6.77–6.67 (m, 4H), 6.12 (bs, 2H), 3.80 (s, 6H), 1.91 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 157.6, 132.8, 127.7, 124.2, 116.4, 111.9, 55.4, 17.5; m_R: 136–138 °C (decomposition); HRMS for $C_{16}H_{20}N_2NaO_4S^+$(ESI+) $[M+Na]^+$: calc.: 359.1036 g/mol, found: 359.1037 g/mol.

6.15 *N*,*N*'-Bis(3-cyano-4-methylphenyl)sulfamide (9)



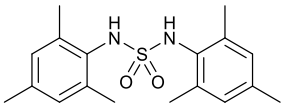
9

According to GP2, 5-amino-2-methylbenzonitril (159 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **9** (158 mg, 0.48 mmol, **81%**) was obtained as off-white solid.

9:

^{1}H NMR (300 MHz, DMSO-D_6) δ [ppm] = 10.73 (s, 2H), 7.43 (d, *J* = 2.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.21 (dd, *J* = 8.4, 2.4 Hz, 2H), 2.36 (s, 6H); ^{13}C NMR (75 MHz, DMSO-D_6) δ [ppm] = 136.2, 136.0, 131.4, 123.0, 120.7, 117.7, 112.2, 19.1; m_R: 224–226 °C (decomposition); HRMS for $C_{16}H_{14}N_4NaO_2S^+$ (ESI+) $[M+Na]^+$: calc.: 349.0729 g/mol, found: 349.0738 g/mol.

6.16 *N*,*N*'-Bis(2,4,6-trimethylphenyl)sulfamide (10)



10

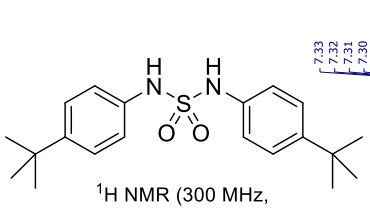
According to GP2, 2,4,6-trimethylaniline (162 mg, 1.20 mmol, 1.00 eq.) was used as substrate. After product purification *via* column chromatography (ethyl acetate:cyclohexane = 1:49 → 2:3), **10** (103 mg, 0.31 mmol, **52%**) was obtained as colorless solid.

10:

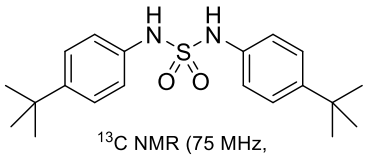
^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] = 6.88 (s, 4H), 5.74 (bs, 2H), 2.32 (s, 12H), 2.26 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ [ppm] = 137.8, 137.2, 130.7, 129.6, 21.0, 19.0; m_R: 159–161 °C (decomposition); HRMS for $C_{18}H_{25}N_2O_2S^+$ (ESI+) $[M+H]^+$: calc.: 333.1631 g/mol, found: 333.1637 g/mol.

Analytical data correspond to those reported in literature.[11,14]

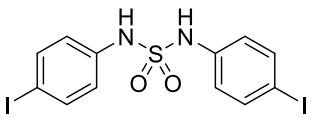
7. NMR Spectra of all Isolated Compounds



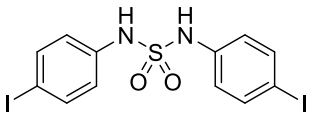
^{1}H NMR (300 MHz, $CDCl_3$/298 K): **5a**



^{13}C NMR (75 MHz, $CDCl_3$/298 K): **5a**

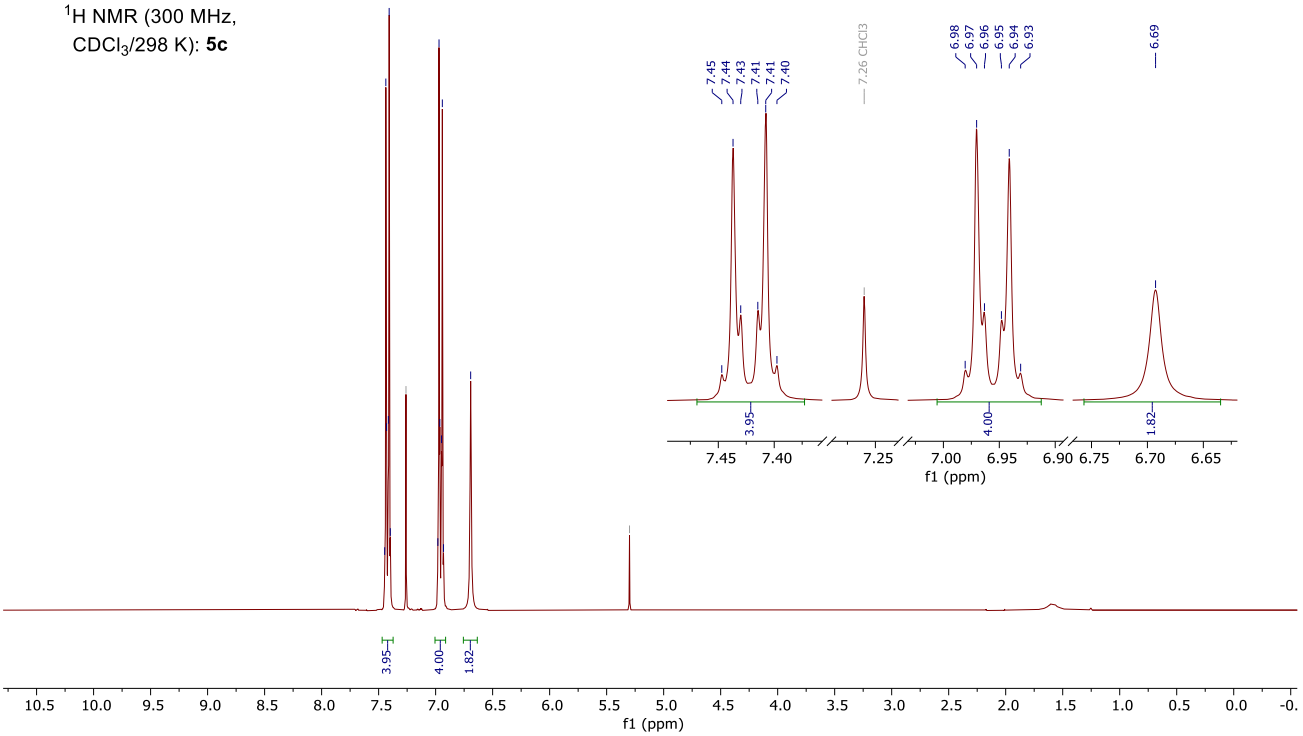


^{1}H NMR (300 MHz, $CDCl_3$/298 K): **5b**

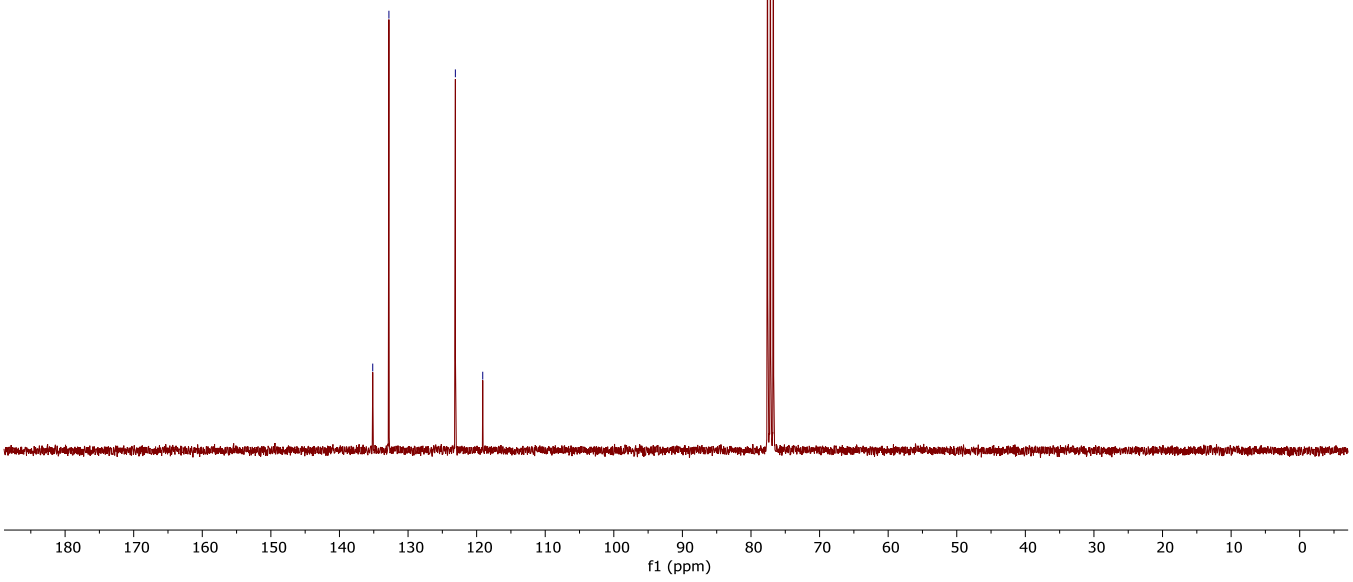


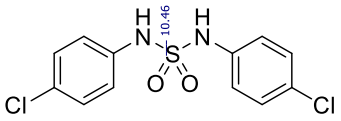
^{13}C NMR (75 MHz, $CDCl_3$/298 K): **5b**

^{1}H NMR (300 MHz, $CDCl_3$/298 K): **5c**

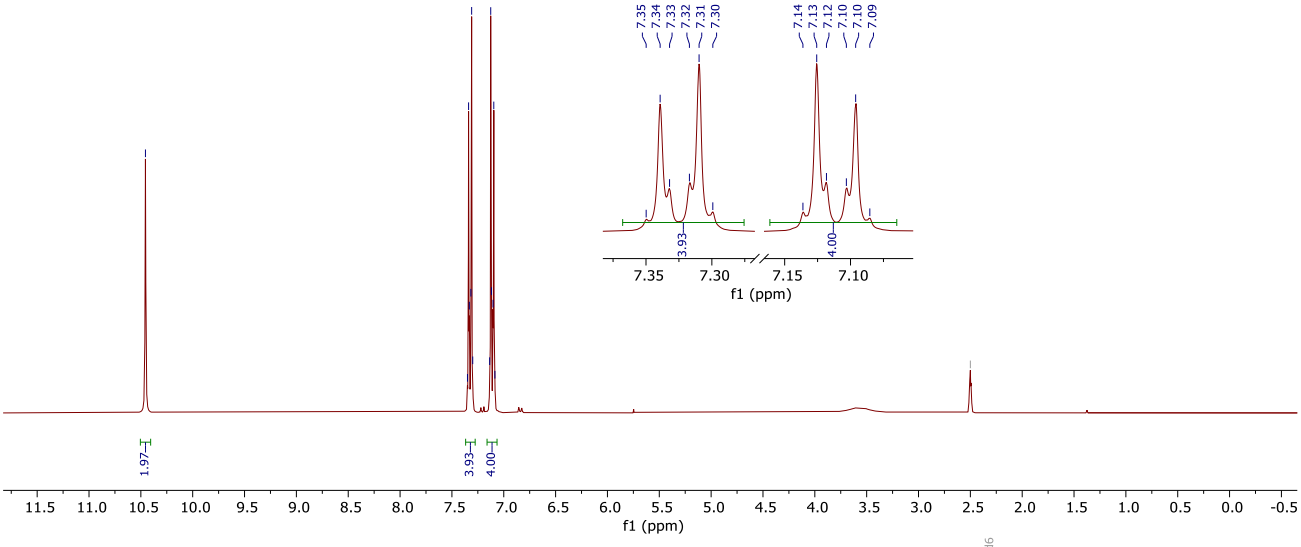


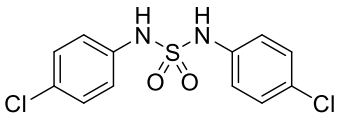
^{13}C NMR (75 MHz, $CDCl_3$/298 K): **5c**



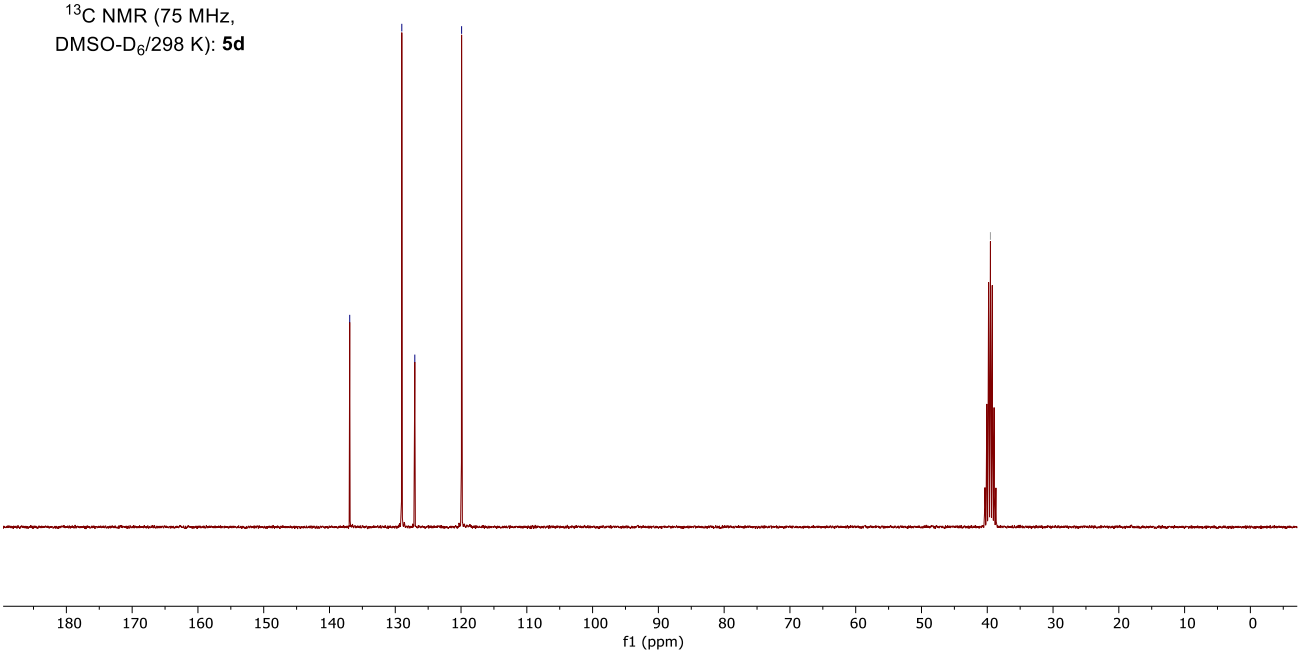


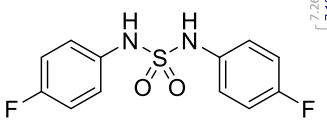
^{1}H NMR (300 MHz, DMSO-D_6/298 K): **5d**



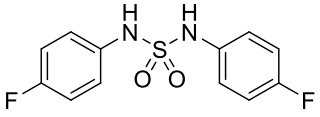


^{13}C NMR (75 MHz, DMSO-D_6/298 K): **5d**

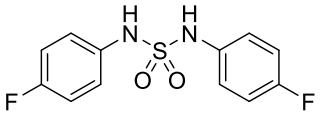




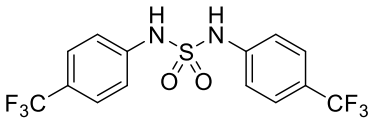
^{1}H NMR (300 MHz, $CDCl_3$/298 K): **5e**



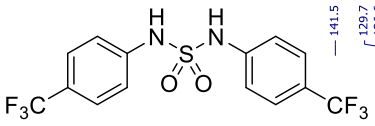
^{13}C NMR (75 MHz, $CDCl_3$/298 K): **5e**



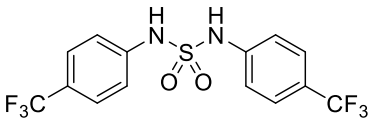
^{19}F NMR (282 MHz, $CDCl_3$/298 K): **5e**



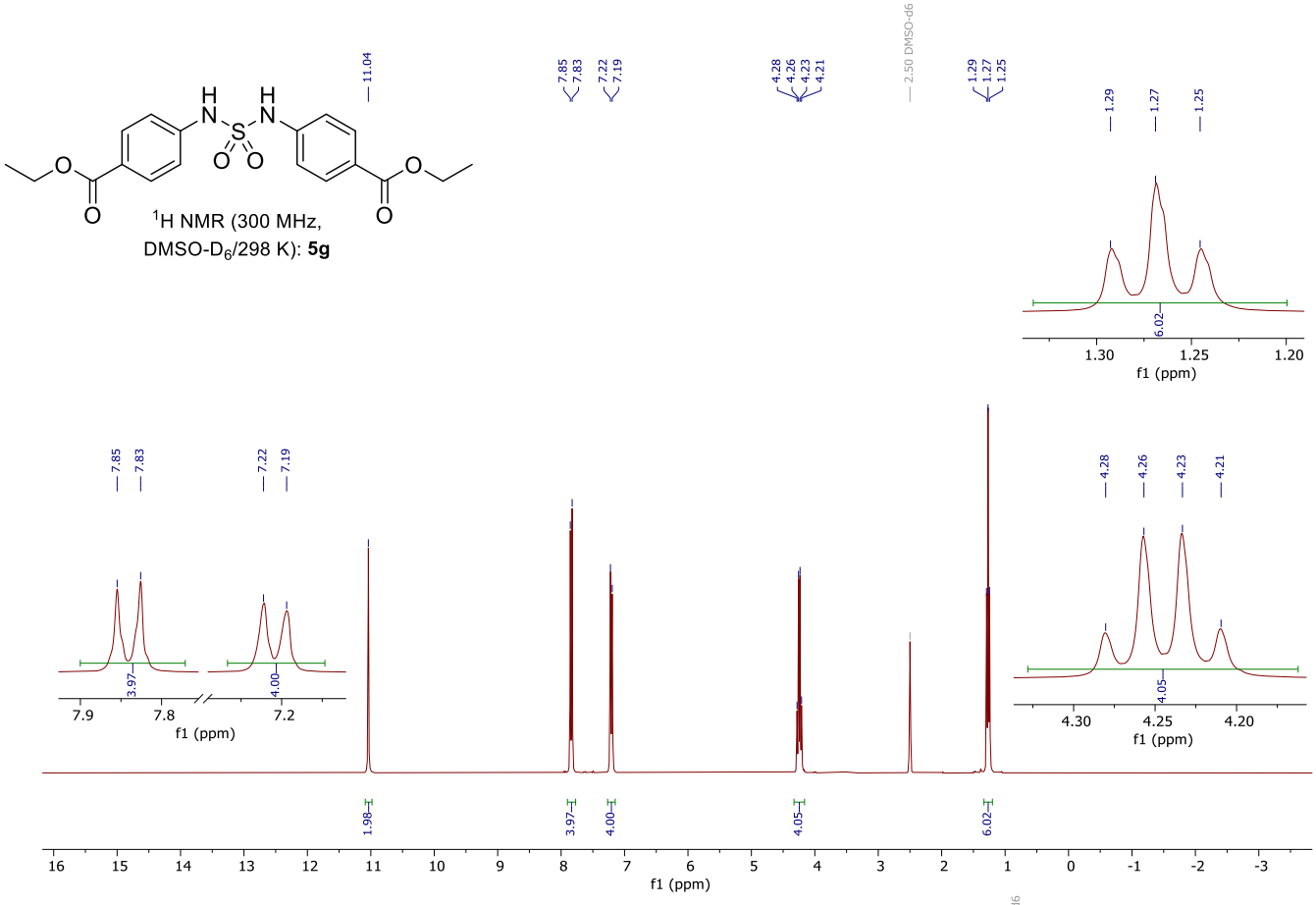
^{1}H NMR (300 MHz, DMSO-D_6/298 K): **5f**

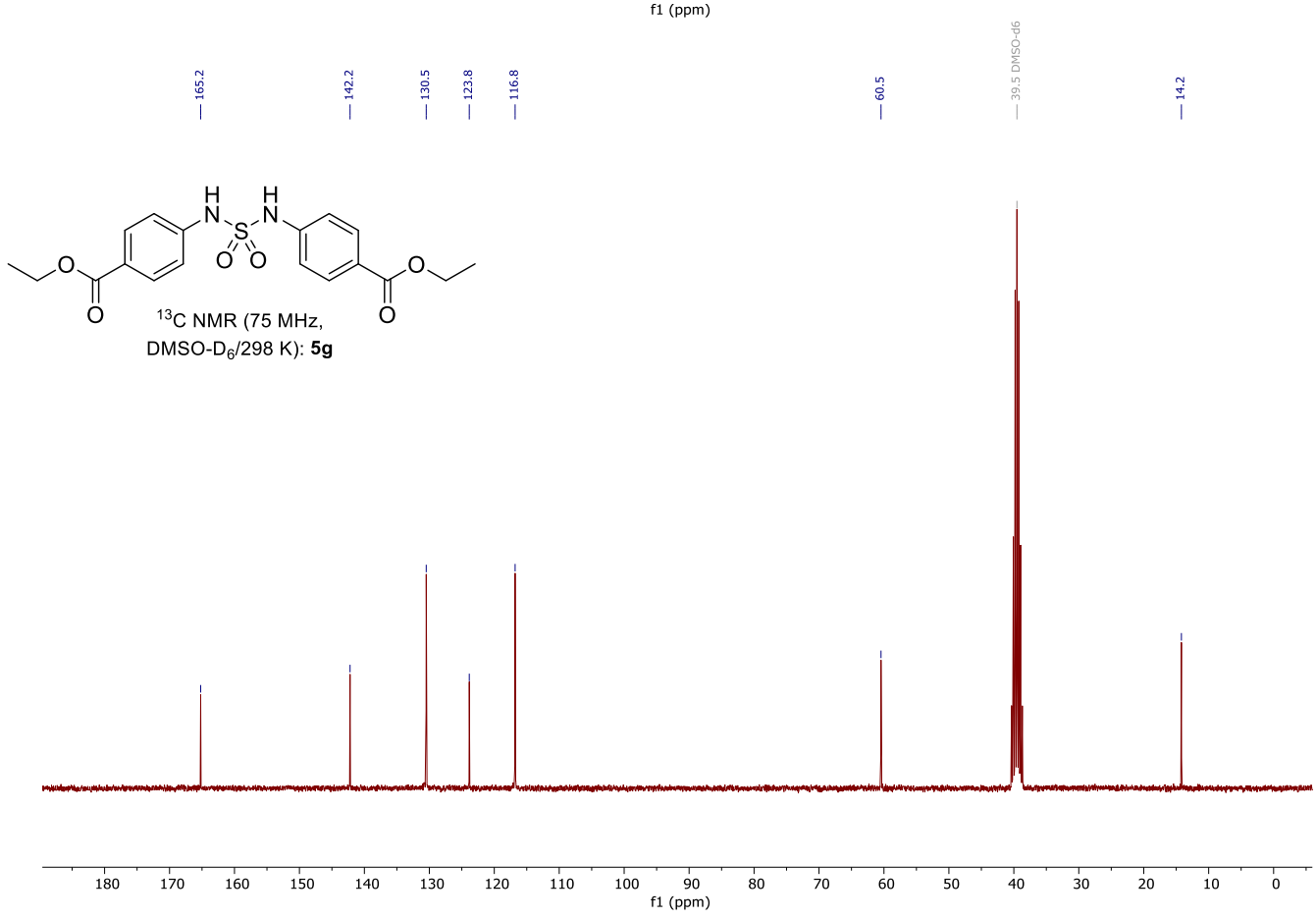


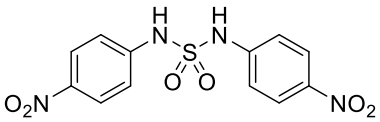
^{13}C NMR (75 MHz, DMSO-D_6/298 K): **5f**



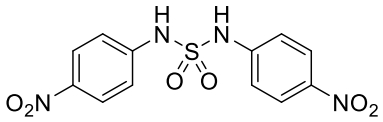
^{19}F NMR (282 MHz, DMSO-D_6/298 K): **5f**


^{1}H NMR (300 MHz, DMSO-D$_6$/298 K): **5g**
11.04
7.85
7.83
7.22
7.19
4.28
4.26
4.23
4.21
2.50 DMSO-d6
1.29
1.27
1.25
6.02
3.97
4.00
4.05
1.98
f1 (ppm)

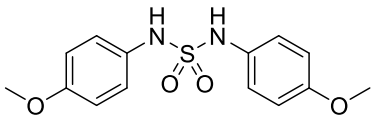

^{13}C NMR (75 MHz, DMSO-D$_6$/298 K): **5g**
165.2
142.2
130.5
123.8
116.8
60.5
39.5 DMSO-d6
14.2
f1 (ppm)



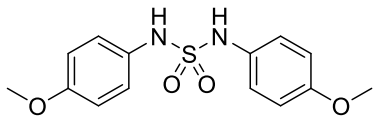
^{1}H NMR (300 MHz, DMSO-D_6/298 K): **5h**



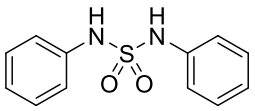
^{13}C NMR (75 MHz, DMSO-D_6/298 K): **5h**



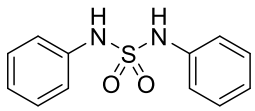
^{1}H NMR (300 MHz, $CDCl_3$/298 K): **5i**



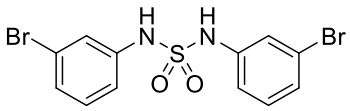
^{13}C NMR (75 MHz, $CDCl_3$/298 K): **5i**



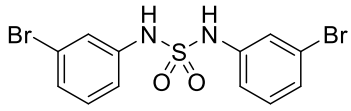
^{1}H NMR (300 MHz, $CDCl_3$/298 K): **5j**



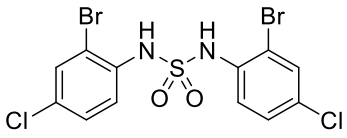
^{13}C NMR (75 MHz, $CDCl_3$/298 K): **5j**



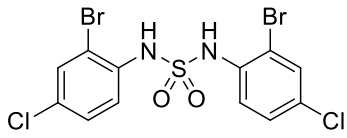
^{1}H NMR (300 MHz, DMSO-D_6/298 K): **6**



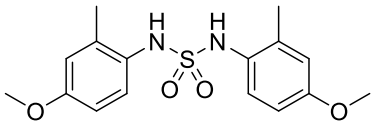
^{13}C NMR (75 MHz, DMSO-D_6/298 K): **6**



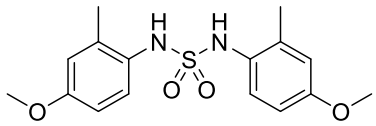
^{1}H NMR (300 MHz, $CDCl_3$/298 K): **7**



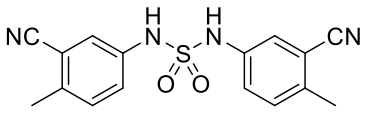
^{13}C NMR (75 MHz, $CDCl_3$/298 K): **7**



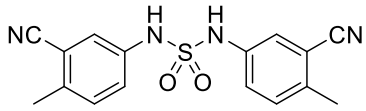
^{1}H NMR (300 MHz, $CDCl_3$/298 K): **8**



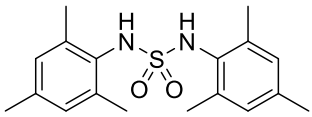
^{13}C NMR (75 MHz, $CDCl_3$/298 K): **8**



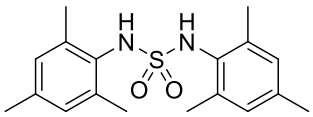
^{1}H NMR (300 MHz, DMSO-D_6/298 K): **9**



^{13}C NMR (75 MHz, DMSO-D_6/298 K): **9**



^{1}H NMR (300 MHz, $CDCl_3$/298 K): **10**



^{13}C NMR (75 MHz, $CDCl_3$/298 K): **10**

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