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A New Synthesis of 3-(Sulfonamido)benzofurans through an Acid-Promoted Cascade Reaction of *N*-(2,2-Dichloro-2-phenylethylidene)arenesulfonamides with *para*-Substituted Phenols

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2-Phenyl-3-(sulfonamido)benzofurans are produced in a cascade reaction of *N*-(2,2-dichloro-2-phenylethylidene)arenesulfonamides with *para*-substituted phenols in the presence of the superacid H_2SO_4/P_4O_{10} system.

Introduction

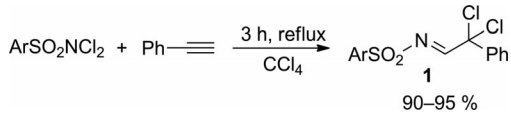
Benzofuran rings are important structural subunits in modern heterocyclic chemistry.[1] A wide range of natural compounds contain such moieties,[2] and numerous biologically active benzofurans are known to exert anti-inflammatory, anti-arrhythmic, haemostatic, anti-bacterial, fungicidal, anti-viral, anti-tumor, and anti-oxidant activities.[3] Some of them are promising drugs against Parkinson's[3e] and Alzheimer's disease.[3f]

Among various functionally substituted benzofuran derivatives, 3-amino- and 3-amido-substituted benzofurans are important due to their anti-tumor[4a] and anti-asthmatic[4b–4d] activities. 3-Aminobenzofurans are often used as key reagents in the synthesis of acyclic amino derivatives[4b–4d] or annulated heterocycles,[5] and are of interest for structural investigations.[6] Thus, these compounds are promising drugs and useful scaffolds for organic synthesis. Consequently, further development of known methods and elaboration of new protocols for 3-aminobenzofuran synthesis represent an urgent challenge.

Synthetic approaches to 3-amino- and 3-amido-substituted benzofurans are based on the reactions of *ortho*-hydroxybenzonitriles.[7] Three-component reactions of acetylenes with *ortho*-hydroxybenzaldehydes and amines in the presence of copper salts[8] or arylglyoxals, phenols and *para*-toluenesulfonamide, in the presence of $Hf(OTf)_4$, $TiCl_4$, or $InCl_3$ are also known.[9] In addition, the synthesis of 2,3-bis(arylamino)benzofurans by reaction of 2-[(arylimino)-methyl]phenols with aryl isocyanides catalyzed by BF_3 has been reported.[10] Among the disadvantages of these protocols are the application of moisture-sensitive reagents and catalysts (in some cases), or the use of expensive starting compounds. Furthermore, some of the methods are laborious and comprise multi-step procedures, and the target products are typically formed in only moderate yields.

Polyhaloaldimines exhibit high electrophilicity due to the strongly electron-withdrawing substituents. The ability of polyhalogenated *N*-sulfonylaldimines to react with various nucleophiles has been used for the design of a wide range of acyclic and heterocyclic sulfonamide derivatives.[11]

Sulfonylimines **1** are important representatives of activated imines containing electron-deficient azomethine groups. An effective synthetic protocol for obtaining these promising reagents has been developed on the basis of radical reactions of *N*,*N*-dichlorosulfonamides with phenylacetylene[12] (Scheme 1). Thus, sulfonylimines of type **1** are available for application in synthetic practice.



Scheme 1. Synthesis of imines **1** from *N*,*N*-dichlorosulfonamides and phenylacetylene.

Results and Discussion

Having studied *C*-amidoalkylation of aromatics with imines **1**, we found that the reaction with *para*-substituted phenols **2** in the presence of strong acids unexpectedly resulted in the formation of 2-phenyl-3-(sulfonamido)benzofurans **3**. Preliminarily, a range of Lewis and Brønsted acids were screened as catalysts in the model reaction of imine **1a** with *p*-chlorophenol (**2a**; Scheme 2).

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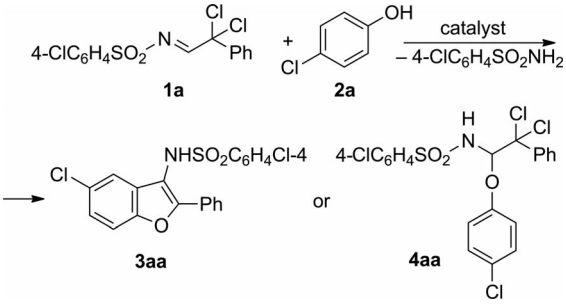
Table 1. Screening of Lewis and Brønsted acids in the reactions of imine **1a** with *p*-chlorophenol (**2a**).[a]

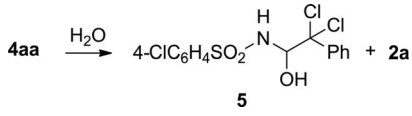
Entry	Catalyst	Amount	Time [h]	Product	Yield [%]
1	–	–	5	**4aa**	75[b]
2	$AlCl_3$	1 equiv.	5	**4aa**	83[b]
3	$BF_3{\cdot}Et_2O$	1 equiv.	10	**4aa**	67[b]
4	TsOH	1 equiv.	10	**4aa**	82[b]
5	3-NBSA[c]	1 equiv.	5	**4aa**	78[b]
6	$MeSO_3H$	1 equiv.	5	**4aa**	53[b]
7	H_2SO_4[d]	10 mol-%	5	**3aa**	37
8	H_2SO_4[d]	50 mol-%	5	**3aa**	41
9	H_2SO_4[d]	1 equiv.	5	**3aa**	47
10	H_2SO_4[d]	2 equiv.	5	**3aa**	43
11	oleum (20% free SO_3)	2 equiv. based on MW 98.08	5	**3aa**	50
12	H_2SO_4/P_4O_{10}[d]	10 mol-%/10 mol-%	5	**3aa**	32
13	H_2SO_4/P_4O_{10}[d]	50 mol-%/50 mol-%	5	**3aa**	46
14	H_2SO_4/P_4O_{10}[d]	1 equiv./1 equiv	5	**3aa**	59
15	P_4O_{10}	50 mol-%	5	**4aa**	77
16	P_4O_{10}	1 equiv.	5	**4aa**	75

[a] The reaction was carried out with *p*-chlorophenol (**2a**; 1 equiv.) by stirring in CCl_4 at room temp. [b] Semiaminal **5** and 4-chlorobenzenesulfonamide were formed as an admixture (identified by NMR spectroscopy). Compound **4aa** was quantitatively transformed into semiaminal **5** by addition of water or by standing in humid air (Scheme 3). [c] 3-Nitrobenzenesulfonic acid. [d] H_2SO_4 (96%) was used.



Scheme 2. Reaction of imine **1a** with *p*-chlorophenol **2a**.

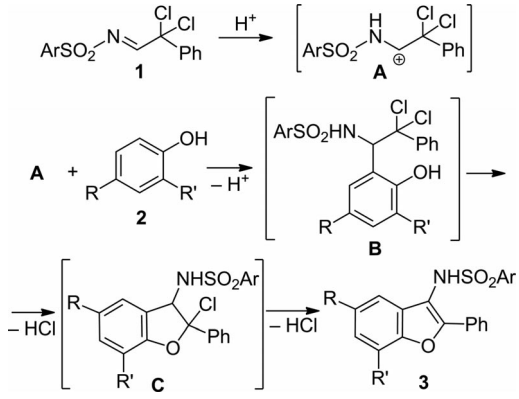
4-Chloro-*N*-(5-chloro-2-phenylbenzofuran-3-yl)benzenesulfonamide (**3aa**) was found to be formed in the presence of a strong Brønsted acid (Table 1). Maximal yield was achieved with an H_2SO_4/P_4O_{10} mixture (Table 1, Entry 14). Under these conditions, the process was accompanied by the formation of 4-chlorobenzenesulfonamide (ca. 15% yield). In the absence of a catalyst or in the presence of Lewis acids or sulfonic acids (Table 1, Entries 1–6), benzofuran **3aa** was not produced, and the reaction afforded a mixture of nucleophilic addition product **4aa**, semiaminal **5**, and 4-chlorobenzenesulfonamide (Schemes 2 and 3).



Scheme 3. Hydrolysis of **4a**.

The corresponding semiaminal, 4-chloro-*N*-(2,2-dichloro-1-hydroxy-2-phenylethyl)benzenesulfonamide (**5**), was produced by hydrolysis of compound **4aa** (Scheme 3).

The formation of substituted benzofurans **3** apparently proceeds through a reaction cascade (Scheme 4): *C*-Amidoalkylation by amidoalkyl cation **A** takes place *ortho* to the hydroxy group in phenol **2**, which is followed by spontaneous heterocyclization of the intermediate [2,2-dichloro-1-(2-hydroxyphenyl)-2-phenylethyl]amide **B** through the OH and CCl moieties. Subsequent aromatization of the bicyclic intermediate **C** as a result of HCl elimination gives **3**. The cyclization and dehydrochlorination steps occur easily, probably due to the effect of the benzene ring (benzylic position of the reaction centre), the intramolecular character of the substitution, and the formation of a thermodynamically stable heteroaromatic structure.



Scheme 4. Possible mechanism of the benzofuran **3** formation.

It is logical to suppose that the mixture of H_2SO_4 and P_4O_{10} can work as a superacid system that assists the generation of carbocation **A**. We did not find any literature data on the protonating ability and superacidic properties of H_2SO_4/P_4O_{10} mixtures, but the application of P_4O_{10} in the preparation of a binary superacid medium has been mentioned.[13] P_4O_{10} evidently plays the role of a conjugate base, similar to free SO_3 in oleum (Hammett's function[14] H_0 for H_2SO_4 = –12, H_0 for oleum ≤ –12.24), promoting the formation of a superacid medium. It can also be presumed that SO_3 is produced in situ in the equilibrium between H_2SO_4 and P_4O_{10}.

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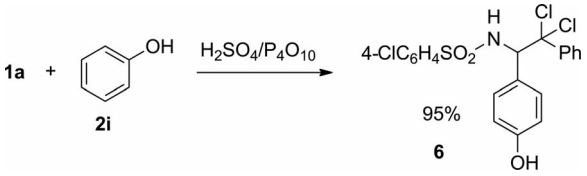
The application of phenol (**2i**) under the reaction conditions did not generate benzofurans, but selectively led to the formation of the *para*-substituted *C*-amidoalkylated derivative 4-chloro-*N*-[2,2-dichloro-1-(4-hydroxyphenyl)-2-phenylethyl]benzenesulfonamide (**6**; Scheme 5). However, *p*-halophenols **2a**–**c** as well as *p*-nitrophenol (**2d**), and 2,4-dichloro- and 2,4-dibromophenols (**2e** and **2f**) smoothly delivered the corresponding benzofurans **3** in moderate to good yields (Table 2). *p*-Cresol (**2g**) gave benzofuran **3ag** in poor yield, and no benzofuran was obtained from the *p*-*tert*-butylphenol **2h**, probably because of the tendency of alkylphenols to produce sulfonated and protonated species under the reaction conditions.



Scheme 5. Reaction between imine **1a** and phenol (**2i**).

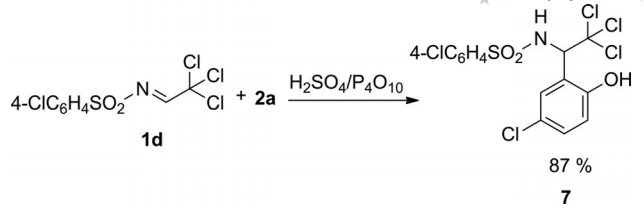
Table 2. Acid-promoted synthesis of benzofurans **3** from imines **1** and phenols **2** in the presence of an H_2SO_4/P_4O_{10} mixture.[a]

Entry	Imine	Ar	Phenol	R	R′	Benzofuran **3**	Yield [%]
1	**1a**	4-ClC_6H_4	**2a**	Cl	H	**3aa**	59
2	**1a**	4-ClC_6H_4	**2b**	Br	H	**3ab**	46
3	**1a**	4-ClC_6H_4	**2c**	F	H	**3ac**	67
4	**1a**	4-ClC_6H_4	**2d**	NO_2	H	**3ad**	58
5	**1a**	4-ClC_6H_4	**2e**	Cl	Cl	**3ae**	83
6	**1a**	4-ClC_6H_4	**2f**	Br	Br	**3af**	78
7	**1a**	4-ClC_6H_4	**2g**	Me	H	**3ag**	23
8	**1a**	4-ClC_6H_4	**2h**	*t*Bu	H	**3ah**	0
9	**1a**	4-ClC_6H_4	**2i**	H	H	**3ai**	0[b]
10	**1b**	Ph	**2a**	Cl	H	**3ba**	71
11	**1b**	Ph	**2b**	Br	H	**3bb**	30
12	**1b**	Ph	**2c**	F	H	**3bc**	44
13	**1b**	Ph	**2d**	NO_2	H	**3bd**	60
14	**1c**	4-MeC_6H_4	**2a**	Cl	H	**3ca**	68

[a] For reaction conditions, see the Experimental Section. [b] Compound **6** was isolated as the only product (see Scheme 5).

When chloralimines were used instead of imines **1a** and **1b** in the reaction with *para*-substituted phenols, the process stopped at the stage of the *C*-amidoalkylated product, and no benzofurans were formed. For instance, the reaction of 4-chloro-*N*-(2,2,2-trichloroethylidene)benzenesulfonamide (**1d**) with *p*-chlorophenol (**2a**) resulted in the formation of 4-chloro-*N*-[2,2,2-trichloro-1-(5-chloro-2-hydroxyphenyl)-ethyl]benzenesulfonamide (**7**) as a final product (Scheme 6).

It was shown[15] that saturation of a melt of *p*-cresol and chloral hydrate with hydrogen chloride led to the formation of 4-methyl-2-(2,2,2-trichloro-1-hydroxyethyl)phenol, which gave no heterocycles in the presence of H_2SO_4, similar to trichloroethylsulfonamide **7**. Heterocyclization[15] to the corresponding 2,3-dihydrobenzofuran-3-ol derivative was accomplished by treatment with aqueous potassium hydroxide. Clearly, the trichloromethyl group is less reactive than the dichloro(phenyl)methyl moiety. Therefore, heterocyclization of trichloroethylamides of type **7** to give benzofuran derivatives requires either more severe conditions or the assistance of a base; these approaches are the subject of our future investigations.



Scheme 6. Reaction between chloralimine **1d** and *p*-chlorophenol (**2a**).

The structures of the compounds obtained were deduced from their ^1H and ^{13}C NMR spectroscopic data. The ^1H and ^{13}C NMR signals of benzofurans **3** and sulfonamide **7** were assigned by using ^{13}C-HSQC, ^{13}C-HMBC, and NOESY experiments.

To establish the benzofuran structure HMBC ^1H–^{13}C techniques were used, which were optimized for ^{13}C–^1H spin–spin coupling constants of 10 Hz, which are typical for carbon and proton atoms separated by three bonds (Figure 1). In the HMBC ^1H–^{13}C spectra of benzofurans **3**, cross-peaks between the signals of the proton of the NH group and the carbon atom C-2 of the benzofuran ring were observed. The same C-2 atom has cross-peaks with the *ortho*-protons of the benzene ring. This can be observed only when the sulfonamide group and the benzene ring are bonded to different carbon atoms of the furan moiety. Moreover, cross-peaks between the C-3 atom and the 5-H proton can be seen in the HMBC spectra, which is in agreement with the proposed structure.

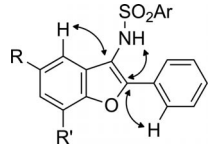


Figure 1. Main HMBC ^1H–^{13}C ($^3J_{CH}$) correlations for benzofurans **3**.

The structure of *C*-amidoalkylated chlorophenol derivative **7** was assigned by application of ^1H–^1H 2D homonuclear NOESY experiments (Figure 2). A cross-peak between the proton of the $CHCCl_3$ fragment and the 6-H proton of the phenol ring was observed in the spectrum of sulfonamide **7**, as were cross-peaks between the 3-H proton and both the 4-H and OH protons.

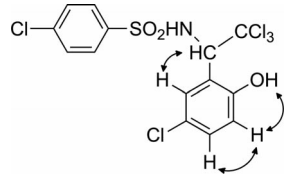


Figure 2. Main NOESY correlations for sulfonamide **7**.

The structure of sulfonamide **7** indirectly confirms the formation of the benzofuran ring through *C*-amidoalkylation *ortho* to the OH group of the phenol.

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Conclusions

An experimentally straightforward protocol for the synthesis of 2-phenyl-3-(sulfonamido)benzofuran by using an acid-assisted reaction of *N*-(2,2-dichloro-2-phenylethylidene)sulfonamides with *para*-substituted phenols was developed. The advantages of the above method are the availability of starting reagents (dichlorosulfonamides, phenylacetylene, and phenols), good yields of the target benzofuran derivatives, and the possibility of accessing benzofurans containing substituents in the annulated benzene ring. The reaction is likely to be applied with a range of polyhalogenated imines so that the substituent at position 2 of the annulated furan ring can be varied. The method presented herein and the known three-component approach[9] to benzofurans with similar structures, complement each other. The latter method[9] allows 2-aryl-3-(sulfonamido)benzofurans to be generated that are either unsubstituted or that include bulky substituents; however, these approaches require the use of more expensive reagents and catalysts (arylglyoxals, indium or hafnium salts).[9]

In addition, the synthesis of *C*-amidotrichloroethylated phenol **7** has been demonstrated. Compounds of the type **7** are promising reagents that can be used to obtain further 3-amino-2-chloro- and 3-amino-2-hydroxybenzofurans.

The structures of compounds **3**–**7** were established by NMR spectroscopy and confirmed by IR spectroscopy and elemental analysis (see Experimental Section).

Experimental Section

General Remarks: ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded with a Bruker DPX 400 MHz spectrometer (^{1}H, 400.13 MHz; ^{13}C, 100.61 MHz; ^{19}F, 376.50 MHz) in a 5 mm broadband probe at 25 °C in DMSO, with HMDS as an internal standard. Spectral assignments of the ^{1}H and ^{13}C NMR spectra of compounds **1**–**7** are based on the results of ^{13}C-HSQC, ^{13}C-HMBC, and NOESY experiments. Settings for the HMBC experiments were the following: pulse length 6 μs (^{1}H), 13 μs (^{13}C); spectral width 800 Hz (^{1}H), 7 kHz (^{13}C); acquisition time 1.3 s; relaxation delay 2 s; digital resolution 0.5 Hz; accumulation time 2 h. Settings for the HSQC experiments were the following: pulse length 6 μs (^{1}H), 13 μs (^{15}N); spectral width 800 Hz (^{1}H), 7 kHz (^{13}C); acquisition time 0.7 s; relaxation delay, 2.5 s; digital resolution 1 Hz; accumulation time 4 h. IR spectra were recorded with a Bruker IFS spectrophotometer. Elemental analyses were obtained with a Thermo Finnigan Flash series1112 EA analyzer.

General Procedure for the Synthesis of *N*-(2-Phenylbenzofuran-3-yl)-arenesulfonamides (3): *para*-Substituted phenol (10 mmol) was added to a stirred mixture of imine **1a**,**b** (10 mmol), P_4O_{10} (1 mmol, 0.28 g), and H_2SO_4 (96%, 0.55 mL, ca. 10 mmol) in CCl_4 (10 mL). The reaction mass was stirred for 5 h and mixed with water (100 mL). The precipitate was filtered off, dried, and recrystallized from $CHCl_3$ to give the final benzofuran **3**.

4-Chloro-*N*-(5-chloro-2-phenylbenzofuran-3-yl)benzenesulfonamide (3aa): Colorless needles; m.p. 194–196 °C; yield 2.47 g (59%). IR (KBr): $\tilde{\nu}$ = 1165, 1337 (SO_2), 3275 (NH) cm^{-1}. ^{1}H NMR ([D$_6$]-DMSO, 400.13 MHz): δ = 6.79 (d, ^4J = 2.2 Hz, 1 H, 4-H), 7.30 (dd, ^3J = 8.7, ^4J = 2.2 Hz, 1 H, 6-H), 7.41 (m, 2 H, H$_m$, C$_6$H$_5$), 7.42 (m, 1 H, H$_p$, C$_6$H$_5$), 7.47 (AA′BB′, 2 H, H$_m$, 4-ClC$_6$H$_4$), 7.63 (AA′BB′, 2 H, H$_o$, 4-ClC$_6$H$_4$), 7.61 (d, ^3J = 8.7 Hz, 1 H, 7-H), 7.91 (m, 2 H, H$_o$, C$_6$H$_5$), 10.25 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100.61 MHz): δ = 112.7 (C-3), 113.2 (C-7), 118.6 (C-4), 125.1 (C-6), 126.2 (C$_m$, C$_6$H$_5$), 127.8 (C-5), 128.0 (C$_i$, C$_6$H$_5$), 128.6 (C$_o$, C$_6$H$_5$), 128.6 (C-3a), 128.8 (C$_o$, 4-ClC$_6$H$_4$), 129.3 (C$_m$, 4-ClC$_6$H$_4$), 129.5 (C$_p$, C$_6$H$_5$), 138.3 (C$_p$, 4-ClC$_6$H$_4$), 138.7 (C$_i$, 4-ClC$_6$H$_4$), 150.6 (C-7a), 152.5 (C-2) ppm. $C_{20}H_{13}Cl_2NO_3S$ (418.29): calcd. C 57.43, H 3.13, Cl 16.95, N 3.35, S 7.66; found C 57.35, H 3.18, Cl 17.06, N 3.48, S 7.76.

***N*-(5-Bromo-2-phenylbenzofuran-3-yl)-4-chlorobenzenesulfonamide (3ab):** Colorless solid; m.p. 207–208 °C; yield 2.13 g (46%). IR (KBr): $\tilde{\nu}$ = 1164, 1337 (SO_2), 3227 (NH) cm^{-1}. ^{1}H NMR ([D$_6$]-DMSO, 400.13 MHz): δ = 6.86 (d, ^4J = 1.6 Hz, 1 H, 4-H), 7.43 (dd, ^3J = 8.6, ^4J = 1.6 Hz, 1 H, 6-H), 7.43 (m, 3 H, H$_m$, H$_p$, C$_6$H$_5$), 7.49 (AA′BB′, 2 H, H$_m$, 4-ClC$_6$H$_4$), 7.57 (d, ^3J = 8.6 Hz, 1 H, 7-H), 7.62 (AA′BB′, 2 H, H$_o$, 4-ClC$_6$H$_4$), 7.93 (m, 2 H, H$_o$, C$_6$H$_5$), 10.22 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 112.6 (C-3), 113.6 (C-7), 115.6 (C-4), 121.6 (C-6), 126.2 (C$_m$, C$_6$H$_5$), 127.7 (C-5), 128.0 (C$_i$, C$_6$H$_5$), 128.6 (C$_o$, C$_6$H$_5$), 128.8 (C$_p$, 4-ClC$_6$H$_4$), 129.0 (C-3a), 129.3 (C$_m$, 4-ClC$_6$H$_4$), 129.5 (C$_p$, C$_6$H$_5$), 138.3 (C$_p$, 4-ClC$_6$H$_4$), 138.8 (C$_i$, 4-ClC$_6$H$_4$), 150.9 (C-7a), 152.2 (C-2) ppm. $C_{20}H_{13}BrClNO_3S$ (462.74): calcd. C 51.91, H 2.83, N 3.03, S 6.93; found C 52.01, H 2.86, N 3.12, S 6.84.

4-Chloro-*N*-(5-fluoro-2-phenylbenzofuran-3-yl)benzenesulfonamide (3ac): Colorless needles; m.p. 175–176 °C; yield 2.69 g (67%). IR (KBr): $\tilde{\nu}$ = 1165, 1337 (SO_2), 3261 (NH) cm^{-1}. ^{1}H NMR ([D$_6$]-DMSO, 400.13 MHz): δ = 6.69 (dd, ^4J = 2.6, $^3J_{HF}$ = 8.7 Hz, 1 H, 4-H), 7.15 (m, ^3J = 9.0, ^4J = 2.6, $^3J_{H,F}$ = 9.2 Hz, 1 H, 6-H), 7.38 (m, 3 H, H$_m$, H$_p$, C$_6$H$_5$), 7.43 (AA′BB′, 2 H, H$_m$, 4-ClC$_6$H$_4$), 7.61 (AA′BB′, 2 H, H$_o$, 4-ClC$_6$H$_4$), 7.62 (d, ^3J = 9.0 Hz, 1 H, 7-H), 7.84 (m, 2 H, H$_o$, C$_6$H$_5$), 10.25 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100.61 MHz): δ = 104.7 (d, $^2J_{C,F}$ = 26.4 Hz, C-4), 112.8 (d, $^3J_{C,F}$ = 9.5 Hz, C-7), 112.8 (d, $^2J_{C,F}$ = 26.8 Hz, C-6), 113.4 (d, $^4J_{C,F}$ = 4.0 Hz, C-3), 126.1 (C$_m$, C$_6$H$_5$), 128.2 (C$_i$, C$_6$H$_5$), 128.2 (d, $^3J_{C,F}$ = 10.6 Hz, C-3a), 128.4 (C$_o$, C$_6$H$_5$), 128.7 (C$_o$, 4-ClC$_6$H$_4$), 129.2 (C$_m$, 4-ClC$_6$H$_4$), 129.3 (C$_p$, C$_6$H$_5$), 137.9 (C$_p$, 4-ClC$_6$H$_4$), 138.9 (C$_i$, 4-ClC$_6$H$_4$), 148.4 (C-7a), 152.5 (C-2), 158.5 (d, $^1J_{C,F}$ = 237.7 Hz, C-5) ppm. ^{19}F NMR ([D$_6$]DMSO, 376.50 MHz): δ = 119.93 ppm. $C_{20}H_{13}ClFNO_3S$ (401.84): calcd. C 59.78, H 3.26, N 3.49, S 7.98; found C 59.56, H 3.35, N 3.61, S 8.08.

4-Chloro-*N*-(5-nitro-2-phenylbenzofuran-3-yl)benzenesulfonamide (3ad): Colorless needles; m.p. 235–236 °C; yield 2.49 g (58%). IR (KBr): $\tilde{\nu}$ = 1171, 1338 (SO_2), 1357, 1515 (NO_2), 3262 (NH) cm^{-1}. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 7.46 (m, 3 H, H$_m$, H$_p$, C$_6$H$_5$), 7.46 (AA′BB′, 2 H, 4-ClC$_6$H$_4$), 7.94 (m, 2 H, H$_o$, C$_6$H$_5$), 7.64 (AA′BB′, 2 H, 4-ClC$_6$H$_4$), 7.69 (d, ^4J = 1.7 Hz, 1 H, 4-H), 8.18 (dd, ^3J = 8.8, ^4J = 1.7 Hz, 1 H, 6-H), 7.84 (d, ^3J = 8.8 Hz, 1 H, 7-H), 10.44 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 112.7 (C-7), 113.2 (C-3), 115.7 (C-4), 120.8 (C-6), 126.4 (C$_m$, C$_6$H$_5$), 127.5 (C-3a), 127.5 (C$_i$, C$_6$H$_5$), 128.7 (C$_o$, C$_6$H$_5$), 128.8 (C$_o$, 4-ClC$_6$H$_5$), 129.4 (C$_m$, 4-ClC$_6$H$_5$), 130.0 (C$_p$, C$_6$H$_5$), 138.5 (C$_p$, 4-ClC$_6$H$_5$), 138.5 (C$_i$, 4-ClC$_6$H$_5$), 143.7 (C-5), 154.0 (C-2), 154.8 (C-7a) ppm. $C_{20}H_{14}ClN_2O_5S$ (429.85): calcd. C 55.88, H 3.28, Cl 8.25, N 6.52, S 7.46; found C 55.95, H 3.31, Cl 8.36, N 6.39, S 7.35.

4-Chloro-*N*-(5,7-dichloro-2-phenylbenzofuran-3-yl)benzenesulfonamide (3ae): Colorless needles; m.p. 221–222 °C; yield 3.75 g (83%). IR (KBr): $\tilde{\nu}$ = 1169, 1379 (SO_2), 3296 (NH) cm^{-1}. ^{1}H NMR ([D$_6$]-DMSO, 400.13 MHz): δ = 6.76 (d, ^4J = 1.3 Hz, 1 H, 6-H), 7.45 (m, 3 H, H$_m$, H$_p$, C$_6$H$_5$), 7.46 (AA′BB′, 2 H, H$_m$, 4-ClC$_6$H$_4$), 7.56 (d, ^4J = 1.3 Hz, 1 H, 4-H), 7.62 (AA′BB′, 2 H, H$_o$, 4-ClC$_6$H$_4$), 7.90 (m, 2 H, H$_o$, C$_6$H$_5$), 10.36 (s, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]-

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DMSO, 100.61 MHz): δ = 113.3 (C-7), 116.7 (C-3), 117.9 (C-4), 124.7 (C-6), 126.4 (C_m, C_6H_5), 127.5 (C_i, C_6H_5), 128.3 (C-3a), 128.8 (C_o, 4-ClC_6H_4), 129.0 (C_o, C_6H_5), 129.4 (C_m, 4-ClC_6H_4), 129.9 (C-5), 130.0 (C_p, C_6H_5), 138.5 (C_p, 4-ClC_6H_4), 138.5 (C_i, 4-ClC_6H_4), 146.4 (C-7a), 153.4 (C-2) ppm. $C_{20}H_{11}Cl_3NO_3S$ (451.73): calcd. C 53.18, H 2.45, Cl 23.54, N 3.10, S 7.10; found C 53.25, H 2.50, Cl 23.45, N 3.06, S 7.02.

4-Chloro-*N*-(5,7-dibromo-2-phenylbenzofuran-3-yl)benzenesulfonamide (3af): Colorless needles; m.p. 235–236 °C; yield 4.23 g (78%). IR (KBr): $\tilde{\nu}$ = 1164, 1336 (SO_2), 3263 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 400.13 MHz): δ = 6.89 (d, ^4J = 1.3 Hz, 1 H, 6-H), 7.42 (m, 3 H, H_m, H_p, C_6H_5), 7.45 (AA′BB′, 2 H, H_m, 4-ClC_6H_4), 7.63 (AA′BB′, 2 H, H_o, 4-ClC_6H_4), 7.68 (d, ^4J = 1.3 Hz, 1 H, 4-H), 7.92 (m, 2 H, H_o, C_6H_5), 10.36 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 100.61 MHz): δ = 104.7 (C-7), 113.1 (C-4), 115.9 (C-3), 121.3 (C-6), 126.3 (C_m, C_6H_5), 127.5 (C_i, C_6H_5), 128.7 (C_o, 4-ClC_6H_4), 128.9 (C_o, C_6H_5), 129.4 (C_m, 4-ClC_6H_4), 129.5 (C-5), 129.9 (C-3a), 130.0 (C_p, C_6H_5), 138.5 (C_p, 4-ClC_6H_4), 138.5 (C_i, 4-ClC_6H_4), 148.1 (C-7a), 153.2 (C-2) ppm. $C_{20}H_{12}Br_2ClNO_3S$ (541.64): calcd. C 44.35, H 2.23, N 2.59, S 5.92; found C 44.48, H 2.29, N 2.54, S 6.01.

4-Chloro-*N*-(5-methyl-2-phenyl-1-benzofuran-3-yl)benzenesulfonamide (3ag): Colorless needles; m.p. 189–191 °C; yield 0.91 g (23%). IR (KBr): $\tilde{\nu}$ = 1170, 1380 (SO_2), 3300 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 400.13 MHz): δ = 2.24 (s, 3 H, CH_3), 6.54 (d, ^4J = 1.6 Hz, 1 H, 4-H), 7.10 (dd, ^3J = 8.4, ^4J = 1.6 Hz, 1 H, 6-H), 7.40 (m, 2 H, H_m, C_6H_5), 7.41 (m, 1 H, H_p, C_6H_5), 7.44 (d, ^3J = 8.4 Hz, 1 H, 7-H), 7.48 (AA′BB′, 2 H, H_m, 4-ClC_6H_4), 7.62 (AA′BB′, 2 H, H_o, 4-ClC_6H_4), 7.91 (m, 2 H, H_o, C_6H_5), 10.12 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 100.61 MHz): δ = 20.6 (CH_3), 110.9 (C-7), 112.8 (C-3), 118.9 (C-4), 125.9 (C_m, C_6H_5), 126.3 (C-6), 127.1 (C-5), 128.4 (C_o, C_6H_5), 128.6 (C-3a), 128.8 (C_o, 4-ClC_6H_4), 128.9 (C_i, C_6H_5), 129.2 (C_m, 4-ClC_6H_4), 132.0 (C_p, C_6H_5), 137.9 (C_p, 4-ClC_6H_4), 139.2 (C_i, 4-ClC_6H_4), 150.5 (C-7a), 151.0 (C-2) ppm. $C_{21}H_{16}ClNO_3S$ (397.88): calcd. C 63.39, H 4.05, N 3.52, Cl 8.91, S 8.06; found C 63.35, H 4.02, N 3.58, Cl 8.84, S 7.98.

***N*-(5-Chloro-2-phenylbenzofuran-3-yl)benzenesulfonamide (3ba):** Colorless needles; m.p. 191–192 °C; yield 2.73 g (71%). IR (KBr): $\tilde{\nu}$ = 1163, 1332 (SO_2), 3258 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 400.13 MHz): δ = 6.66 (d, ^4J = 1.5 Hz, 1 H, 4-H), 7.26 (dd, ^3J = 8.8, ^4J = 1.5 Hz, 1 H, 6-H), 7.42 (m, 2 H, H_m, C_6H_5), 7.44 (m, 1 H, H_p, C_6H_5), 7.47 (m, 2 H, H_m, $C_6H_5SO_2$), 7.59 (d, ^3J = 8.8 Hz, 1 H, 7-H), 7.59 (m, 1 H, H_p, $C_6H_5SO_2$), 7.69 (m, 2 H, H_o, $C_6H_5SO_2$), 7.96 (m, 2 H, H_o, C_6H_5), 10.28 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 100.61 MHz): δ = 113.6 (C-3), 113.6 (C-7), 119.3 (C-4), 125.6 (C-6), 126.7 (C_m, C_6H_5), 127.4 (C-5), 127.4 (C_m, $C_6H_5SO_2$), 128.2 (C_i, C_6H_5), 128.7 (C-3a), 129.1 (C_o, C_6H_5), 129.7 (C_o, $C_6H_5SO_2$), 130.1 (C_p, C_6H_5), 133.7 (C_p, $C_6H_5SO_2$), 140.9 (C_i, $C_6H_5SO_2$), 151.0 (C-7a), 152.8 (C-2) ppm. $C_{20}H_{14}ClNO_3S$ (383.85): calcd. C 62.58, H 3.68, Cl 9.24, N 3.65, S 8.35; found C 62.53, H 3.71, Cl 9.36, N 3.59, S 8.39.

***N*-(5-Bromo-2-phenylbenzofuran-3-yl)benzenesulfonamide (3bb):** Colorless needles; m.p. 197–198 °C; yield 1.28 g (30%). IR (KBr): $\tilde{\nu}$ = 1163, 1331 (SO_2), 3259 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 400.13 MHz): δ = 6.77 (d, ^4J = 1.7 Hz, 1 H, 4-H), 7.39 (dd, ^3J = 8.8, ^4J = 1.7 Hz, 1 H, 6-H), 7.45 (m, 3 H, H_m, H_p, C_6H_5), 7.45 (m, 2 H, H_m, $C_6H_5SO_2$), 7.55 (d, ^3J = 8.8 Hz, 1 H, 7-H), 7.62 (m, 1 H, H_p, $C_6H_5SO_2$), 7.69 (m, 2 H, H_o, $C_6H_5SO_2$), 7.97 (m, 2 H, H_o, C_6H_5), 10.12 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 100.61 MHz): δ = 112.7 (C-3), 113.5 (C-7), 115.6 (C-4), 121.7 (C-6), 126.1 (C_m, C_6H_5), 126.9 (C_m, $C_6H_5SO_2$), 127.7 (C-5), 128.1 (C_i, C_6H_5), 128.5 (C_o, C_6H_5), 129.0 (C-3a), 129.2 (C_p, C_6H_5), 129.2 (C_o, $C_6H_5SO_2$), 133.2 (C_p, $C_6H_5SO_2$), 140.2 (C_i, $C_6H_5SO_2$), 150.8 (C-7a), 152.1 (C-2) ppm. $C_{20}H_{14}BrNO_3S$ (428.30): calcd. C 56.09, H 3.29, N 3.27, S 7.49; found C 56.15, H 3.32, N 3.35, S 7.57.

***N*-(5-Fluoro-2-phenylbenzofuran-3-yl)benzenesulfonamide (3bc):** Colorless needles; m.p. 192–194 °C; yield 1.62 g (44%). IR (KBr): $\tilde{\nu}$ = 1165, 1337 (SO_2), 3265 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 400.13 MHz): δ = 6.74 (dd, ^4J = 2.7, $^3J_{H,F}$ = 8.7 Hz, 1 H, 4-H), 7.10 (m, ^3J = 9.1, ^4J = 2.7, $^3J_{H,F}$ = 9.3 Hz, 1 H, 6-H), 7.43 (m, 3 H, H_m, H_p, C_6H_5), 7.44 (m, 2 H, H_m, $C_6H_5SO_2$), 7.59 (d, ^3J = 9.1 Hz, 1 H, 7-H), 7.59 (m, 1 H, H_p, $C_6H_5SO_2$), 7.70 (m, 2 H, H_o, $C_6H_5SO_2$), 7.95 (m, 2 H, H_o, C_6H_5), 10.16 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 100.61 MHz): δ = 104.7 (d, $^2J_{C,F}$ = 26.5 Hz, C-4), 112.7 (d, $^3J_{C,F}$ = 9.6 Hz, C-7), 112.7 (d, $^2J_{C,F}$ = 26.2 Hz, C-6), 113.5 (d, $^4J_{C,F}$ = 4.1 Hz, C-3), 126.1 (C_m, C_6H_5), 126.8 (C_m, $C_6H_5SO_2$), 128.1 (d, $^3J_{C,F}$ = 10.7 Hz, C-3a), 128.3 (C_i, C_6H_5), 128.5 (C_o, C_6H_5), 129.1 (C_o, $C_6H_5SO_2$), 129.4 (C_p, C_6H_5), 133.0 (C_p, $C_6H_5SO_2$), 140.3 (C_i, $C_6H_5SO_2$), 148.5 (C-7a), 152.5 (C-2), 158.4 (d, $^1J_{C,F}$ = 237.7 Hz, C-5) ppm. ^{19}F NMR ([D_6]DMSO, 376.50 MHz): δ = 120.06 ppm. $C_{20}H_{14}FNO_3S$ (367.39): calcd. C 65.38, H 3.84, N 3.81, S 8.73; found C 65.31, H 3.88, N 3.90, S 9.02.

***N*-(5-Nitro-2-phenylbenzofuran-3-yl)benzenesulfonamide (3bd):** Colorless needles; m.p. 247–249 °C; yield 2.36 g (60%). IR (KBr): $\tilde{\nu}$ = 1169, 1341 (SO_2), 1355, 1514 (NO_2), 3259 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 400.13 MHz): δ = 7.48 (m, 3 H, H_m, H_p, C_6H_5), 7.48 (m, 2 H, H_m, $C_6H_5SO_2$), 7.57 (m, 1 H, H_p, $C_6H_5SO_2$), 7.69 (d, ^4J = 2.3 Hz, 1 H, 4-H), 7.72 (m, 2 H, H_o, $C_6H_5SO_2$), 7.85 (d, ^3J = 9.1 Hz, 1 H, 7-H), 8.03 (m, 2 H, H_o, C_6H_5), 8.18 (dd, ^3J = 9.1, ^4J = 2.3 Hz, 1 H, 6-H), 10.32 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 100.61 MHz): δ = 113.9 (C-7), 114.8 (C-3), 116.3 (C-4), 121.3 (C-6), 126.9 (C_m, C_6H_5), 127.4 (C_m, $C_6H_5SO_2$), 128.1 (C-3a), 128.3 (C_i, C_6H_5), 129.2 (C_o, C_6H_5), 129.8 (C_o, $C_6H_5SO_2$), 130.5 (C_p, C_6H_5), 133.8 (C_p, $C_6H_5SO_2$), 140.6 (C_i, $C_6H_5SO_2$), 144.2 (C-5), 154.2 (C-2), 155.3 (C-7a) ppm. $C_{20}H_{14}N_2O_5S$ (394.40): calcd. C 60.91, H 3.58, N 7.10, S 8.13; found C 60.87, H 3.53, N 7.15, S 8.19.

***N*-(5-Chloro-2-phenylbenzofuran-3-yl)-4-methylbenzenesulfonamide (3ca):** Colorless needles; m.p. 187–189 °C; yield 2.71 g (68%). IR (KBr): $\tilde{\nu}$ = 1161, 1333 (SO_2), 3265 (NH) cm^{-1}. ^1H NMR ([D_6]DMSO, 400.13 MHz): δ = 2.34 (s, 3 H, CH_3), 7.24 (AA′BB′, 2 H, H_m, 4-$CH_3C_6H_4$), 7.26 (dd, ^3J = 8.6, ^4J = 2.1 Hz, 1 H, 6-H), 7.44 (m, 3 H, H_m, H_p, C_6H_5), 7.54 (AA′BB′, 2 H, H_o, 4-$CH_3C_6H_4$), 7.60 (m, 2 H, H_o, C_6H_5), 6.55 (d, ^4J = 2.1 Hz, 1 H, 4-H), 7.60 (d, ^3J = 8.6 Hz, 1 H, 7-H), 9.93 (s, 1 H, NH) ppm. ^{13}C NMR ([D_6]DMSO, 100.61 MHz): δ = 20.9 (CH_3), 113.0 (C-7), 113.1 (C-3), 118.7 (C-4), 124.9 (C-6), 126.2 (C_m, C_6H_5), 127.0 (C_m, 4-$CH_3C_6H_4$), 127.6 (C-5), 128.2 (C_i, C_6H_5), 128.5 (C-3a), 128.5 (C_o, C_6H_5), 129.4 (C_p, C_6H_5), 129.6 (C_o, 4-$CH_3C_6H_4$), 137.2 (C_p, 4-$CH_3C_6H_4$), 143.7 (C_i, 4-$CH_3C_6H_4$), 150.4 (C-7a), 152.4 (C-2) ppm. $C_{21}H_{16}ClNO_3S$ (397.88): calcd. C 63.39, H 4.05, Cl 8.91, N 3.52, S 8.06; found C 63.31, H 4.08, Cl 9.01, N 3.61, S 8.14.

Synthesis of 4-Chloro-*N*-[2,2-dichloro-1-(4-chlorophenoxy)-2-phenylethyl]benzenesulfonamide (4aa) and 4-Chloro-*N*-(2,2-dichloro-1-hydroxy-2-phenylethyl)benzenesulfonamide (5): 4-Chloro-*N*-(2,2-dichloro-2-phenylethylidene)benzenesulfonamide (**1a**; 10 mmol, 3.63 g) and 4-chlorophenol (**2a**; 10 mmol, 1.29 g) were stirred in CCl_4 (10 mL) for 5 h at room temp., either in the absence of a catalyst or in the presence of Lewis or Brønsted acids (Table 1, Entries 1–6 and 15–16). The reaction mass was kept in the cold for 12 h, then the precipitate of compound **4aa** was filtered off and recrystallized from $CHCl_3$. Upon standing in humid air or in water, compound **4aa** was quantitatively converted into compound **5**.

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Compound **5** was also obtained in quantitative yield by exposing imine **1a** to humid air for 20 h.

4-Chloro-*N*-[2,2-dichloro-1-(4-chlorophenoxy)-2-phenylethyl]benzenesulfonamide (4aa): Colorless moisture-sensitive solid; m.p. 111–113 °C; yield without a catalyst (Table 1, Entry 1): 3.68 g (74%). IR (KBr): $\tilde{\nu}$ = 1170, 1340 (SO_2), 3290 (NH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 5.32 (d, ^3J = 10.1 Hz, 1 H, $CHCCl_2$), 7.18 (AA′BB′, 2 H, H_o, C_6H_4O), 7.04 (AA′BB′, 2 H, H_m, C_6H_4O), 7.30 (AA′BB′, 2 H, H_m, 4-ClC_6H_4), 7.42 (m, 3 H, H_o, H_p, C_6H_5), 7.49 (AA′BB′, 2 H, H_o, 4-ClC_6H_4), 7.81 (m, 2 H, H_m, C_6H_5), 8.52 (d, ^3J = 10.1 Hz, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 86.0 (*C*HCCl$_2$), 96.9 (CCl_2), 114.5 (C_o, C_6H_4O), 125.9 (C_m, C_6H_4O), 127.4 (C_m, C_6H_5), 127.8 (C_o, C_6H_5), 128.2 (C_o, 4-ClC_6H_4), 128.7 (C_m, 4-ClC_6H_4), 129.6 (C_p, C_6H_5), 136.9 (C_i, C_6H_5), 138.3 (C_p, 4-ClC_6H_4), 140.3 (C_i, 4-ClC_6H_4), 145.1 (C_p, C_6H_4O), 154.3 (C_i, C_6H_4O) ppm.

4-Chloro-*N*-(2,2-dichloro-1-hydroxy-2-phenylethyl)benzenesulfonamide (5): Colorless needles; m.p. 86–88 °C; yield 3.73 g (98%). IR (KBr): $\tilde{\nu}$ = 1170, 1340 (SO_2), 3270 (NH), 3460 (OH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 5.37 (d, ^3J = 9.3 Hz, 1 H, CH), 7.24 (br. s, 1 H, OH), 7.41 (m, 2 H, H_o, C_6H_5), 7.42 (m, 1 H, H_p, C_6H_5), 7.58, 7.80 (AA′BB′, 4 H, 4-ClC_6H_4), 7.91 (m, 2 H, H_m, C_6H_5), 8.58 (d, ^3J = 9.3 Hz, 1 H, NH) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 84.7 (*C*HCCl$_2$), 95.5 (CCl_2), 127.9 (C_o, C_6H_5), 128.6 (C_m, C_6H_5), 129.2 (C_o, 4-ClC_6H_4), 129.4 (C_m, 4-ClC_6H_4), 129.7 (C_p, C_6H_5), 137.5 (C_i, C_6H_5), 139.7 (C_i, 4-ClC_6H_4), 141.3 (C_p, 4-ClC_6H_4) ppm. $C_{14}H_{12}Cl_3NO_3S$ (380.67): calcd. C 44.17, H 3.18, Cl 27.94, N 3.68, S 8.42; found C 45.13, H 3.25, Cl 27.42, N 3.61, S 8.58.

Synthesis of 4-Chloro-*N*-[2,2-dichloro-1-(4-hydroxyphenyl)-2-phenylethyl]benzenesulfonamide (6): Compound **6** was obtained from imine **1a** and phenol (**2i**) under the conditions used for the synthesis of benzofurans **3**. Colorless solid; m.p. 157–159 °C; yield 4.34 g (95%). IR (KBr): $\tilde{\nu}$ = 1170, 1340 (SO_2), 3160 (NH), 3340 (OH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 5.06 (d, ^3J = 10.7 Hz, 1 H, $CHCCl_2$), 6.32 (AA′BB′, 2 H, H_m, C_6H_4OH), 6.78 (AA′BB′, 2 H, H_o, C_6H_4OH), 7.30 (AA′BB′, 2 H, H_m, 4-ClC_6H_4), 7.33 (m, 1 H, H_p, C_6H_5), 7.34 (m, 2 H, H_o, C_6H_5), 7.47 (AA′BB′, 2 H, H_o, 4-ClC_6H_4), 7.54 (m, 2 H, H_m, C_6H_5), 8.75 (d, ^3J = 10.7 Hz, 1 H, NH), 9.30 (s, 1 H, OH) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 63.4 (*C*HCCl$_2$), 95.8 (CCl_2), 113.7 (C_m, C_6H_4OH), 124.7 (C_i, C_6H_4OH), 127.3 (C_o, C_6H_5), 127.9 (C_m, C_6H_5), 128.3 (C_o, 4-ClC_6H_4), 128.4 (C_m, 4-ClC_6H_4), 129.2 (C_p, C_6H_5), 130.4 (C_o, C_6H_4OH), 136.7 (C_p, 4-ClC_6H_4), 139.7 (C_i, C_6H_5), 139.8 (C_i, 4-ClC_6H_4), 156.9 (C_p, C_6H_4OH) ppm. $C_{20}H_{16}Cl_3NO_3S$ (456.77): calcd. C 52.59, H 3.53, Cl 23.28, N 3.07, S 7.02; found C 52.53, H 3.05, Cl 23.48, N 3.00, S 7.68.

Synthesis of 4-Chloro-*N*-[2,2,2-trichloro-1-(5-chloro-2-hydroxyphenyl)ethyl]benzenesulfonamide (7): Compound **7** was obtained from chloralimine **1d** and 4-chlorophenol (**2a**) by the procedure described for benzofurans **3**. Colorless solid; m.p. 199–201 °C; yield 3.92 g (87%). IR (KBr): $\tilde{\nu}$ = 1173, 1343 (SO_2), 1583 (C=C_{Ar}), 3249 (NH), 3520 (OH) cm^{-1}. ^1H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 5.63 (d, ^3J = 10.7 Hz, 1 H, $CHCCl_3$), 6.63 (d, ^3J = 8.7 Hz, 1 H, 6-H), 7.02 (dd, ^3J = 8.7, ^4J = 2.5 Hz, 1 H, 4-H), 7.32 (AA′BB′, 2 H, H_m, 4-ClC_6H_4), 7.44 (d, ^4J = 2.5 Hz, 1 H, 6-H), 7.54 (AA′BB′, 2 H, H_o, 4-ClC_6H_4), 9.10 (d, ^3J = 10.7 Hz, 1 H, NH), 10.37 (s, 1 H, OH) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 63.8 (*C*HCCl$_3$), 101.6 (CCl_3), 116.9 (C-3), 122.7 (C-5), 122.8 (C-1), 128.5 (C-6), 128.5 (C_o, 4-ClC_6H_4), 129.0 (C_m, 4-ClC_6H_4), 129.9 (C-4), 137.5 (C_p, 4-ClC_6H_4), 139.2 (C_i, 4-ClC_6H_4), 154.7 (C-2) ppm. $C_{14}H_{10}Cl_5NO_3S$ (449.56): calcd. C 37.40, H 2.24, Cl 39.43, N 3.12, S 7.13; found C 37.31, H 2.20, Cl 39.48, N 3.06, S 7.26.

Supporting Information (see footnote on the first page of this article): NMR spectra of the products obtained.

[1] a) B. A. Keay, P. W. Dibble, *Comprehensive Heterocyclic Chemistry II*, Pergamon Press, Oxford, **1996**, p. 395–436; b) B. H. Lipshutz, *Chem. Rev.* **1986**, *86*, 795–819; c) D. M. X. Donelly, M. J. Meegan, *Comprehensive Heterocyclic Chemistry IV*, Pergamon Press, New York, **1984**, p. 657–712; d) C. W. Bird, G. W. H. Cheeseman, *Comprehensive Heterocyclic Chemistry IV*, Pergamon Press, New York, **1984**, p. 89–147.

[2] a) T. Yuan, S.-P. Yang, H.-Y. Zhang, S.-G. Liao, W. Wang, Y. Wu, X.-C. Tang, J.-M. Yue, *J. Asian Nat. Prod. Res.* **2009**, *11*, 243–249; b) C. C. Hughes, D. Trauner, *Angew. Chem.* **2002**, *41*, 1569–1572; c) D. E. Fuerst, B. M. Stoltz, J. L. Wood, *Org. Lett.* **2000**, *2*, 3521–3523; d) J. Boukouvalas, M. Pouliot, J. Robichaud, S. MacNeil, V. Snieckus, *Org. Lett.* **2006**, *8*, 3597–3599; e) F. Marion, D. E. Williams, B. O. Patrick, I. Hollander, R. Mallon, S. C. Kim, D. M. Roll, L. Feldberg, R. V. Soest, R. J. Andersen, *Org. Lett.* **2006**, *8*, 321–324; f) G. E. Schneiders, R. J. Stevenson, *J. Org. Chem.* **1979**, *44*, 4710–4711; g) K.-S. Huang, M. Lin, G.-F. Cheng, *Phytochemistry* **2001**, *58*, 357–362; h) O. Shirota, V. Pathak, S. Sekita, M. Stake, Y. Nagashima, Y. Hirayama, Y. Hakamata, T. Haysahi, *J. Nat. Prod.* **2003**, *66*, 1128–1133; i) Y. Okamoto, M. Ojika, Y. Sakagami, *Tetrahedron Lett.* **1999**, *40*, 507–510; j) Y. Okamoto, M. Ojika, S. Suzuki, M. Murakami, Y. Sakagami, *Bioorg. Med. Chem.* **2001**, *9*, 179–183; k) D. M. X. Donnelly, T. O'Cridain, M. O'Sullivan, *J. Chem. Soc., Chem. Commun.* **1981**, 1254–1255.

[3] a) R. E. Ziegert, J. Toräng, K. Knepper, S. Bräse, *J. Comb. Chem.* **2005**, *7*, 147–169; b) R. Fleischer, M. Wiese, *J. Med. Chem.* **2003**, *46*, 4988–5004; c) J. J. Marugán, C. Manthey, B. Anaclerio, L. Lafrance, T. Lu, T. Markotan, K. A. Leonard, C. Crysler, E. Eisennagel, M. Dasgupta, B. Tomczuk, *J. Med. Chem.* **2005**, *48*, 926–934; d) S. Butini, S. Gemma, G. Campiani, S. Franceschini, F. Trotta, M. Borriello, N. Ceres, S. Ros, S. S. Coccone, M. Bernetti, M. D. Angelis, M. Brindisi, V. Nacci, I. Fiorini, E. Novellino, A. Cagnotto, T. Mennini, K. Sandager-Nielsen, J. T. Andreasen, J. Scheel-Kruger, J. D. Mikkelsen, C. Fattorusso, *J. Med. Chem.* **2009**, *52*, 151–159; e) O. Saku, M. Saki, M. Kurokawa, K. Ikeda, T. Takizawa, N. Uesaka, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1090–1093; f) S. Rizzo, C. Riviare, L. Piazzi, A. Bisi, S. Gobbi, M. Bartolini, V. Andrisano, F. Morroni, A. Tarozzi, J.-P. Monti, A. Rampa, *J. Med. Chem.* **2008**, *51*, 2883–2886; g) S. Boyle, S. Guard, M. Higginbottom, D. C. Horwell, W. Howson, A. T. McKnight, K. Martin, M. C. Pritchard, J. O'Toole, J. Raphy, D. C. Rees, E. Roberts, K. J. Watling, G. N. Woodruff, J. Hughes, *Bioorg. Med. Chem.* **1994**, *2*, 357–370; h) R. Kiyama, T. Homna, K. Hayashi, M. Ogawa, M. Hara, M. Fujimoto, T. Fujishita, *J. Med. Chem.* **1995**, *38*, 2728–2741; i) S. Yoo, S.-H. Kim, S.-H. Lee, N.-J. Kim, D.-W. Lee, *Bioorg. Med. Chem.* **2000**, *8*, 2311–2316; j) J. Gubun, H. de Vogelaer, H. Inion, C. Houben, J. Lucchetti, J. Mahaux, G. Rosseels, M. Peiren, M. Clinat, P. Polster, P. Chatelain, *J. Med. Chem.* **1993**, *36*, 1425–1433; k) A. E. Kozikowsky, WO 010008, **2006** (*Chem. Abstr.* **2006**, *144*, 164278); l) K. A. Ohemeng, M. A. Apollina, V. N. Nguyen, C. F. Schwender, M. Singer, M. Steber, J. Araseli, D. Argentieri, W. Hageman, *J. Med. Chem.* **1994**, *37*, 3663–3667.

[4] a) R. Romagnoli, P. G. Baraldi, T. Sarkar, M. D. Carrion, O. Cruz-Lopez, C. L. Cara, M. Tolomeo, S. Grimaudo, A. D. Cristina, M. R. Pipitone, J. Balzarini, R. Gambari, L. Ilaria, R. Saletti, A. Brancale, E. Hamel, *Bioorg. Med. Chem.* **2008**, *16*, 8419–8426; b) K. Ando, Y. Kawamura, Y. Akai, J. Kunitomo, T. Yokomizo, M. Yamashita, S. Ohta, T. Ohishi, Y. Ohishi, *Org.*

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Biomol. Chem. **2008**, *6*, 296–307; c) K. Ando, E. Tsuji, Y. Ando, N. Kuwata, J. Kunitomo, M. Yamashita, S. Ohta, S. Kohno, Y. Ohishi, *Org. Biomol. Chem.* **2004**, *2*, 625–635; d) E. Tsuji, K. Ando, J. Kunitomo, M. Yamashita, S. Ohta, S. Kohno, Y. Ohishi, *Org. Biomol. Chem.* **2003**, *1*, 3139–3141.

[5] O. V. Il'chenko, O. V. Zaremba, S. M. Kovalenko, A. A. Sherakov, V. P. Chernykh, *Synth. Commun.* **2007**, *37*, 2559–2568.

[6] a) F. Bachechi, V. M. Coiro, M. Delfini, G. Settimj, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1988**, *44*, 1449–1451; b) N. O. Iskeleli, C. Kazak, C. Kirilmis, M. Koca, *Acta Cryst. Sect. E: Struct. Rep. Online* **2005**, *E61*, o1571–o1573; c) F. Bachechi, V. M. Coiro, F. Gatta, G. Settimj, M. Delfini, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1988**, *44*, 300–303.

[7] a) K. Gewald, H. J. Jaensch, *J. Prakt. Chem.* **1973**, *315*, 779–785; b) S. Radl, P. Hezky, P. Konvicka, I. Krejci, *Collect. Czech. Chem. Commun.* **2000**, *65*, 1093–1108; c) K. Ando, Y. Akai, J. Kunitomo, T. Yokomizo, H. Nakajima, T. Takeuchi, M. Yamashita, S. Ohta, T. Ohishi, Y. Ohishi, *Org. Biomol. Chem.* **2007**, *5*, 655–663; d) F. A. Trofimov, G. F. Lelyak, L. I. Shevchenko, A. N. Grinev, *Chem. Heterocycl. Compd.* **1974**, *10*, 1016–1018; e) F. A. Trofimov, G. F. Lelyak, L. I. Shevchenko, A. N. Grinev, *Chem. Heterocycl. Compd.* **1975**, *11*, 1129–1131.

[8] a) N. Sakai, N. Uchida, T. Konakahara, *Tetrahedron Lett.* **2008**, *49*, 3437–3440; b) H. Li, J. Liu, B. Yan, Y. Li, *Tetrahedron Lett.* **2009**, *50*, 2353–2357.

[9] C.-X. Chen, L. Liu, D.-P. Yang, D. Wang, Y.-J. Chen, *Synlett* **2005**, 2047–2051.

[10] K. Kobayashi, Y. Shirai, S. Fukamachi, H. Konishi, *Synthesis* **2010**, 666–670.

[11] G. G. Levkovskaya, T. I. Drozdova, I. B. Rozentsveig, A. N. Mirskova, *Russ. Chem. Rev.* **1999**, *68*, 581–604.

[12] a) L. B. Krivdin, K. A. Chernyshev, G. N. Rosentsveig, I. V. Ushakova, I. B. Rosentsveig, G. G. Levkovskaya, *Magn. Reson. Chem.* **2007**, *45*, 980–984; b) I. B. Rozentsveig, G. N. Rozentsveig, A. N. Mirskova, K. A. Chernyshev, L. B. Krivdin, G. G. Levkovskaya, *Russ. J. Gen. Chem.* **2008**, *78*, 1371–1379.

[13] a) P. E. Eaton, G. R. Carlson, J. T. Lee, *J. Org. Chem.* **1973**, *38*, 4071–4073; b) N. Yonezawa, T. Hino, K. Matsuda, T. Matsuki, D. Narushima, M. Kobayashi, T. Ikeda, *J. Org. Chem.* **2000**, *65*, 941–944; c) J.-B. Baek, L.-S. Tan, *Macromolecules* **2006**, *39*, 2794–2803.

[14] G. A. Olah, G. K. S. Prakash, Á. Molnár, J. Sommer in *Superacid Chemistry*, 2nd ed., John Wiley & Sons Inc., Hoboken, New Jersey, **2009**, pp. 47–49.

[15] M. P. Balfe, W. C. Webber, *J. Chem. Soc.* **1942**, 718–720.

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