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Metal- and solvent-free synthesis of *N*-sulfonylformamidines†

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Nisha Chandna,[a,b] Navneet Chandak,[a] Pawan Kumar,[a] Jitander K. Kapoor[b] and Pawan K. Sharma*[a]

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A solvent-free green synthesis of *N*-sulfonylformamidines is reported *via* the direct condensation of *N*,*N*-dimethylformamide dimethyl acetal (DMF-DMA) and sulfonamide derivatives at room temperature. The described method avoids the use of metal catalysts as well as hazardous solvents, which are not permitted for pharmaceutical manufacture, for the reactions or isolation of products. Hence, the current work presents a fast and efficient alternative to earlier reported methods. The mild nature of the procedure is demonstrated by varied functional group tolerance.

Introduction

N-Sulfonylamidines present a versatile class of compounds as they widely serve as useful synthetic intermediates for compounds of immense biological importance.[1–3] In addition, the sulfonamide group itself is a unique pharmacophore and forms an integral part of various drugs or drug-like molecules.[4,5] Within the field of antisense technology, we have shown that the efficient stacking of sulfonamide substituted phenyltriazoles attached to the 5-position of the 2′-deoxyuridine leads to the formation of a very stable DNA : RNA hybrid duplexes.[6] However, the sulfonamide group often requires protection during the synthesis of drugs/drug-ike molecules, and *N*-sulfonylformamidines present a valuable choice for chemists due to the ease of their removal under mild conditions.[6,7]

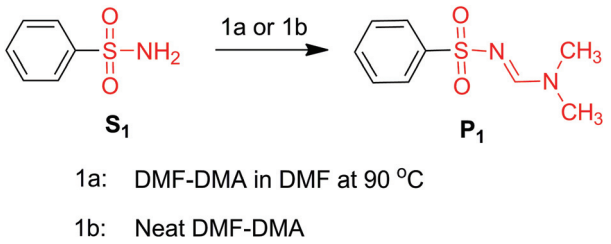
A variety of methods are known for the synthesis of *N*-sulfonylamidines. However, they suffer with one or more major drawbacks in terms of generality or reaction conditions. For instance, metal catalyzed reactions are often used to synthesize *N*-sulfonylamidine derivatives involving the use of transition metal catalysts.[8] In this field, Cu-catalyzed reactions[9–11] have received a lot of attention due to the tolerance of various functionalities. Another approach to synthesize this class of compounds requires the use of sulfonyl azide, which is known to be explosive in nature.[12] $POCl_3$ and DMF are used for the preparation of amidines but suffer from the serious limitations of using harsh and corrosive reagent $POCl_3$ and requiring anhydrous conditions.[6,13] A more direct method has been recently reported by Chen *et al.*, which involves the direct condensation of the sulfonamide group with DMF in the presence of NaI/TBHP.[7] Although it is a convenient approach and free from a transition-metal catalyst, this method requires an elevated temperature, an oxidant, longer reaction times (of the order of several hours), and the use of column chromatography to isolate pure products. Thus, a fast, efficient, and greener procedure which avoids the use of column chromatography, is desirable. This motivated us to develop a solvent-free green and spontaneous synthesis of *N*-sulfonylamidines. In continuation of our interest in sulfonamide derivatives of potential pharmacological interests,[6,13b,14] we now wish to report a green and general method for the synthesis of *N*-sulfonylformamidines by the direct condensation of sulfonamide derivatives and *N*,*N*-dimethylformamide dimethyl acetal (DMF-DMA). The use of DMF-DMA for the formation of *N*-sulfonylamidines has received very little attention even though it was initially introduced by Vandenheuvel and Gruber over 37 years ago at the submicrogram level for analytical purposes.[15] Our newly developed procedure does not involve any transition metal catalyst/oxidants or potentially explosive materials, and can be carried out at room temperature under solvent-free conditions. Moreover, the aqueous work-up of the reaction mixture and isolation of products without column chromatography make our procedure highly practical.

Results and discussion

Initially we treated benzenesulfonamide ($\mathbf{S_1}$) with 2 equivalents of DMF-DMA in DMF at 90 °C to obtain *N*-[(dimethylamino)-methylidene]benzenesulfonamide ($\mathbf{P_1}$) (Scheme 1), albeit in moderate yield (70%). Next, we took up the challenge to avoid

[a]*Department of Chemistry, Kurukshetra University, Kurukshetra-136 119, India. E-mail: pksharma@kuk.ac.in; Fax: +91 1744 238277; Tel: +91 94164 57355*
[b]*Department of Chemistry, National Institute of Technology, Kurukshetra-136119, India*

†Electronic supplementary information (ESI) available. See DOI: 10.1039/c3gc40797g



Scheme 1 Synthesis of *N*-[(dimethylamino)methylidene]benzenesulfonamide ($\mathbf{P_1}$) from benzenesulfonamide ($\mathbf{S_1}$).

the use of a solvent and treated $\mathbf{S_1}$ with neat DMF-DMA. A clean and instantaneous reaction was observed at elevated temperatures. It was intriguing to run the reaction at room temperature with 1 equivalent of DMF-DMA in order to see the effect of temperature as well as quantifying the optimum equivalents of the reagent required for this reaction. To our surprise, the reaction was found to be complete in no time with 1 equivalent of DMF-DMA and afforded the desired product in 98% yield without the use of column chromatography. The purity of the product was determined by the ^{1}H NMR spectrum as well as by comparing the melting point and mixed melting point with an authentic sample purified by column chromatography.

Next, we investigated the generality and scope of this reaction, by reacting a range of benzenesulfonamide derivatives under the optimized conditions and it is interesting to note that the instantaneous completion of the reaction was observed in most of the cases (Table 1). Moreover, the work-up simply amounted to adding water after the reaction reached completion and filtering the pure product, which was free from any associated impurities. In few cases ($\mathbf{P_{11}}$, $\mathbf{P_{12}}$, $\mathbf{P_{17}}$ and $\mathbf{P_{18}}$), the product had to be extracted with ethyl acetate due to the partial solubility of the product in water. To our satisfaction, the reaction was found to be independent of the substituents on the phenyl group and an instant reaction was observed in the case of electron-donating as well as electron-withdrawing groups (entries 1–4, Table 1). Other functional groups such as azides, esters, as well as heterocyclic moieties were found to be well tolerated under the developed conditions (entries

Table 1 Examples studied for *N*-sulfonylformamidine protection by DMF-DMA

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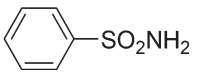
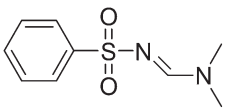
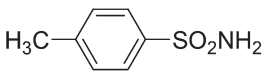
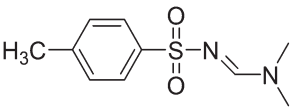
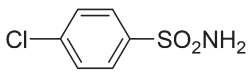
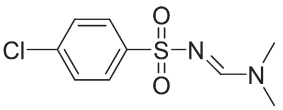
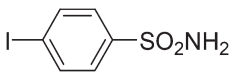
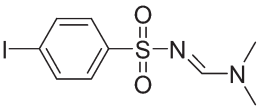
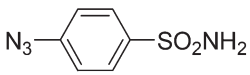
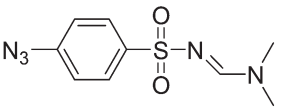
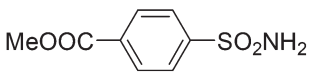
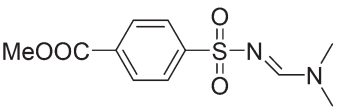
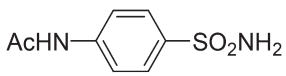
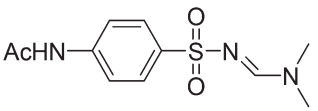
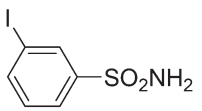
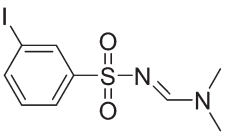
1		1		98
2		1		97
3		1.1		98
4		1		98
5		1		97
6		1		98
7		1		97
8		1		98

Table 1 *(Contd.)*

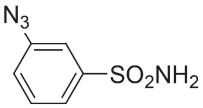
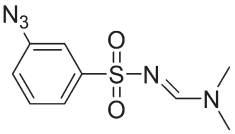
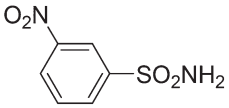
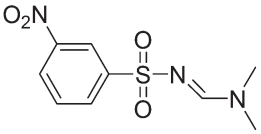
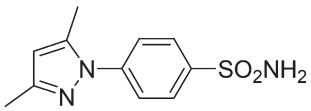
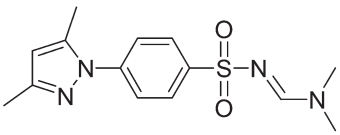
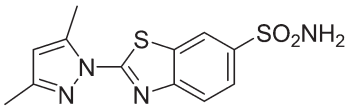
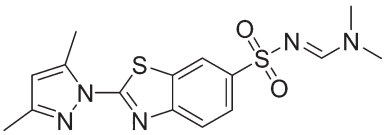
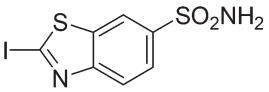
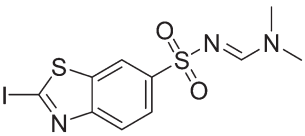
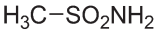
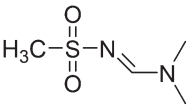
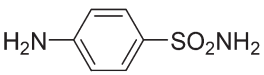
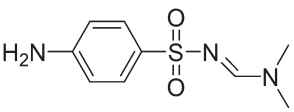
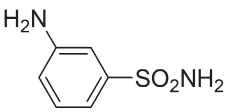
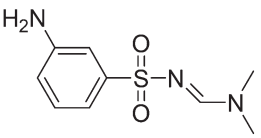
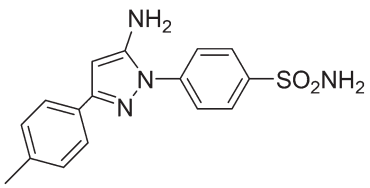
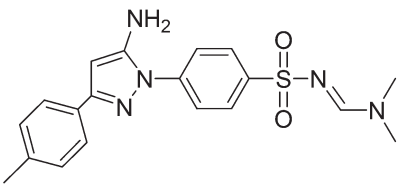
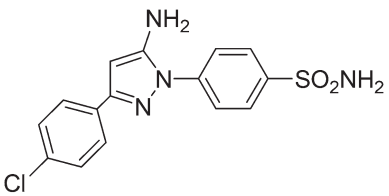
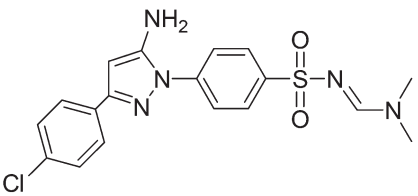
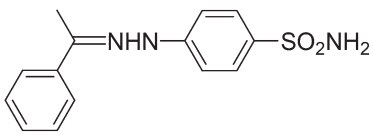
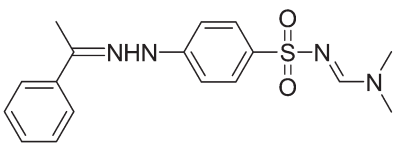
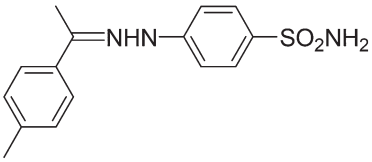
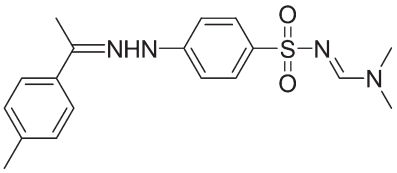
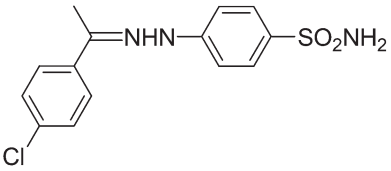
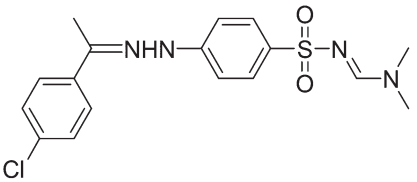
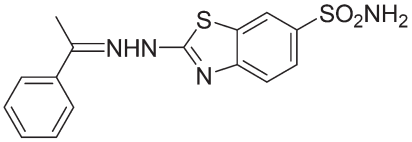
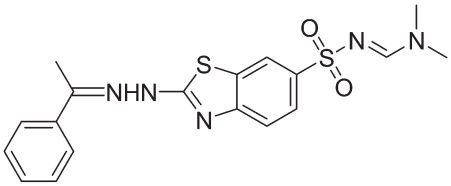
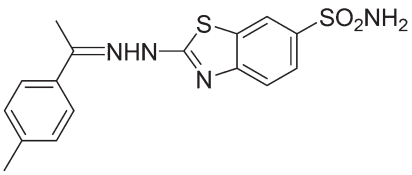
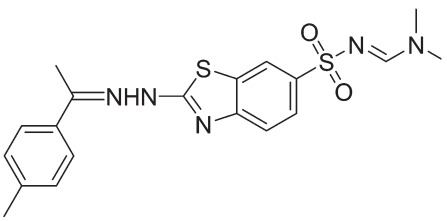
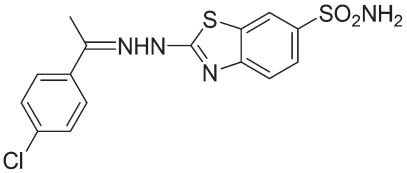
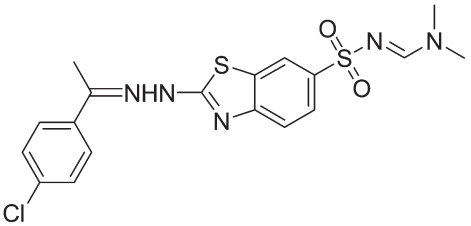
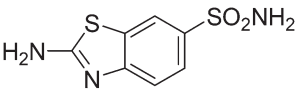
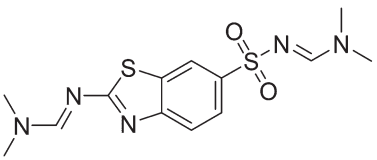
Entry	Substrate (S_{1-25})	Molar ratio of DMF-DMA required	Product (P_{1-25})[a]	% yield
9		1		97
10		1		98
11		4		95
12		4		95
13		1		96
14		1		92
15		1		98
16		1		98
17		1.1		94
18		1		96
19		1		98

Table 1 *(Contd.)*

Entry	Substrate ($\mathbf{S_{1-25}}$)	Molar ratio of DMF-DMA required	Product ($\mathbf{P_{1-25}}$)[a]	% yield
20		1		98
21		1		98
22		1		99
23		1.2		98
24		1.2		98
25		1 2		50 98

[a] Reactions were usually instantaneously complete, but in no case did the reaction take more than 15 minutes to reach completion.

5–7, 11–13, Table 1). However, 4 equivalents of DMF-DMA were required for substrates $\mathbf{S_{11}}$ and $\mathbf{S_{12}}$ bearing pyrazolyl moieties (entries 11 and 12, Table 1) for *N*-sulfonylformamidine protection and we are at a loss to explain this exceptional behaviour. No acceleration or retardation of the rate of reaction was observed upon changing the position of the substituent on the phenyl ring, and an instantaneous reaction was observed in all cases (entries 8–10, Table 1). Hereafter, we investigated if the developed protocol could be applied to aliphatic derivatives of sulfonamide by subjecting methanesulfonamide to similar conditions (entry 14, Table 1). An efficient and clean reaction was observed to afford the desired product in an excellent yield of 92%, indicating the generality of the procedure.

The selectivity of the developed protocol for sulfonamide groups over aromatic amino groups was also investigated. Interestingly, the reaction was found to be chemoselective for the sulfonamide group, as a single product was observed for 4-aminobenzenesulfonamide (entry 15, Table 1). This might be due to the higher acidity of the sulfonamide group compared to the amino group. A similar observation was reported in the case of 3-aminobenzenesulfonamide, where only the sulfonamide moiety was protected (entry 16, Table 1). Next, we attempted to see if an amino group attached to the aromatic

heterocyclic ring, such as pyrazole, can also be differentiated from the sulfonamide moiety attached to the phenyl ring. It was found that the reaction proceeds chemoselectively at the sulfonamide group (entries 17 and 18, Table 1), leaving the pyrazolylamino group unchanged. The hydrazones bearing a sulfonamide group (entries 19–24, Table 1) were the next to be treated with DMF-DMA under the developed conditions and the corresponding *N*-sulfonylformamidines were obtained in excellent yields while the NH from the hydrazones remained intact. However, the amino group of 2-amino-1,3-benzothiazole-6-sulfonamide was found to react under the described conditions to afford the fully protected product (entry 25, Table 1).[16] Considering the substitution at position-2 of benzothiazole, it is well known that the nature of benzothiazole as a whole is electron-withdrawing, keeping the lone-pair of electrons on the amino nitrogen busy within the ring, and thus making the amino functionality less basic.[17] It has recently been reported by us that an amino group not involved in any type of cyclization/aromatization through lone-pair of electrons is basic enough to become easily acylated by simply refluxing in acetic acid.[14g] On the other hand if the lone-pair of electrons on the amino group is being withdrawn, making it less basic, then it has to be refluxed/treated with acetic anhydride for acylation.[17] The newly developed DMF-DMA treatment protocol could be a better practical test for knowing the nature of an amino group in terms of relative basicity. This observation also allowed us to conclude that as the basicity of amino group (whether attached to aromatic or aliphatic moiety) decreases, the selectivity of DMF-DMA to distinguish between the amino and sulfonamido group vanishes and both get protected simultaneously when treated with DMF-DMA. Remarkably, the reaction could be readily scaled up to the multigram scale and the desired *N*-sulfonylformamidines could be obtained in good yield, thus rendering this methodology highly practical.

Conclusions

We have developed a metal and solvent free green and efficient protocol for the synthesis of *N*-sulfonylformamidines using neat *N*,*N*-dimethylformamide dimethylacetal (DMF-DMA). Reactions were performed at room temperature and were found to be independent of an attached electron-withdrawing or electron-donating group. In addition, *N*-sulfonylformamidine formation was accomplished chemoselectively in the presence of an amine group. Besides being solvent-free, the aqueous work-up further makes this synthesis greener, featuring high atom economy, easily available starting materials, a lack of microwave/conventional heating, operational simplicity, good tolerance to diverse functional groups and easy isolation.

Experimental section

General information

All reactions were carried out under atmospheric pressure. Melting points were determined in open glass capillaries in electrical melting point apparatus (Navyug Udyog, Ambala Cantt., India) and are uncorrected. The infrared (IR) spectra were recorded on a ABB MB 3000 DTGS FT-IR Spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded either in pure DMSO-d_6 or in $CDCl_3$–DMSO-d_6 mixtures on a Bruker NMR spectrometer at 300 MHz and 75.5 MHz respectively using tetramethylsilane (TMS) as internal standard. Mass spectra (DART-MS) were recorded on a AB Sciex 3200 Q Trap LC MS/MS Mass spectrometer having a DART (Direct Analysis in Real Time) source in +Q1 mode. Chemical shifts are expressed in δ, ppm. The purity of the compounds was checked by ^{1}H NMR and thin layer chromatography (TLC) on silica gel plates using a mixture of petroleum ether (60–80 °C) and ethyl acetate as eluent. Iodine or a UV lamp was used as a visualizing agent. Abbreviations 's' for singlet, 'd' for doublet, 'm' for multiplet, 'ex' for exchangeable proton are used for NMR assignments and 'vs' for very strong, 's' for strong, 'm' for medium, 'w' for weak for IR assignments. 'Mp' stands for melting point. DMF-DMA was procured from Spectrochem Private Limited, Mumbai, India.

General procedure for the synthesis of *N*-sulfonylformamidines

To neat DMF-DMA (6 mmol) was added benzenesulfonamide (6 mmol, $\mathbf{S_{1-25}}$) in a vial. The reaction mixture was magnetically stirred and the progress monitored through TLC (after taking a sample from stirred mixture and dissolving it in methanol for easy spotting on TLC plate). After completion of the reaction (less than 15 min in all cases), water was added to the reaction mixture where a precipitate of the product $\mathbf{P_{1-25}}$ was formed and then collected by filtration, followed by washing with diethyl ether and drying.

Note: Products $\mathbf{P_{11}}$, $\mathbf{P_{12}}$, $\mathbf{P_{17}}$ and $\mathbf{P_{18}}$ were extracted from water by ethyl acetate due to their partial solubility in water.

***N*-[(Dimethylamino)methylidene]benzenesulfonamide $\mathbf{P_1}$.** Mp 130–132 °C (lit.,[8a] 128–130 °C); ν_{max}/cm^{-1} 1620 vs (CN), 1335 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.90 (3H, s, NCH_3), 3.14 (3H, s, NCH_3), 7.49–7.60 (3H, m, Ar), 7.75–7.78 (2H, m, Ar), 8.21 (1H, s, CH=N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.5 (NCH_3), 41.3 (NCH_3), 126.3, 129.4, 132.1, 143.5, 160.2; DART MS *m*/*z* 213.19 $(M + H)^+$, $C_9H_{12}N_2O_2SH^+$ calcd 213.06.

***N*-[(Dimethylamino)methylidene]-4-methylbenzenesulfonamide $\mathbf{P_2}$.** Mp 137–139 °C (lit.,[13a] 133–134 °C); ν_{max}/cm^{-1} 1620 vs (CN), 1342 s and 1134 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.35 (3H, s, CH_3), 2.89 (3H, s, NCH_3), 3.13 (3H, s, NCH_3), 7.32 (2H, d, J = 8.4 Hz, Ar), 7.64 (2H, d, J = 8.4 Hz, Ar), 8.19 (1H, s, CH=N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 21.1 (CH_3), 35.4 (NCH_3), 41.4 (NCH_3), 126.2, 129.9, 139.7, 143.1, 159.7; DART MS *m*/*z* 227.21 $(M + H)^+$, $C_{10}H_{14}N_2O_2SH^+$ calcd 227.07.

4-Chloro-*N*-[(dimethylamino)methylidene]benzenesulfonamide $\mathbf{P_3}$. Mp 128–130 °C (lit.,[7] not given); ν_{max}/cm^{-1} 1620 vs (CN), 1342 s and 1142 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.91 (3H, s, NCH_3), 3.15 (3H, s, NCH_3), 7.60 (2H, d, J = 8.4 Hz, Ar), 7.78 (2H, d, J = 8.4 Hz, Ar), 8.22 (1H, s, CH=N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.5 (NCH_3), 41.5 (NCH_3), 128.1,

129.5, 137.6, 141.3, 159.9; DART MS *m*/*z* 247.19 $(M + H)^+$, $C_9H_{11}ClN_2O_2SH^+$ calcd 247.02.

***N*-[(Dimethylamino)methylidene]-4-iodobenzenesulfonamide P$_4$.** Mp 173–174 °C (lit.,[6b] 172–174 °C).

***N*-[(Dimethylamino)methylidene]-4-azidobenzenesulfonamide P$_5$.** Mp 154–156 °C (lit.,[6a] 155–156 °C).

Methyl 4-({[*N*-(dimethylamino)methylidene]amino}sulfonyl)benzoate P$_6$. Mp 163–165 °C (lit.,[7] not given); ν_{max}/cm^{-1} 1728 s (CO), 1628 vs (CN), 1335 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.92 (3H, s, NCH_3), 3.16 (3H, s, NCH_3), 3.88 (3H, s, OCH_3), 7.91 (2H, d, J = 7.8 Hz, Ar), 8.08 (2H, d, J = 7.8 Hz, Ar), 8.24 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.6 (NCH_3), 41.4 (NCH_3), 52.9 (OCH_3), 126.7, 130.2, 132.7, 147.5, 160.4, 165.7; DART MS *m*/*z* 271.17 $(M + H)^+$, $C_{11}H_{14}N_2O_4SH^+$ calcd 271.06.

***N*-[4-({[(Dimethylamino)methylidene]amino}sulfonyl)phenyl]-acetamide P$_7$.** Mp 196–198 °C (lit.,[7] not given); ν_{max}/cm^{-1} 3340 m (NH), 1697 s (CO), 1620 vs (CN), 1319 s and 1134 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.07 (3H, s, $NHCOCH_3$), 2.89 (3H, s, NCH_3), 3.12 (3H, s, NCH_3), 7.69 (4H, s, Ar), 8.17 (1H, s, CH═N), 10.25 (s, NHCO); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 24.4 ($NHCOCH_3$), 35.4 (NCH_3), 41.3 (NCH_3), 119.1, 127.4, 128.1, 137.4, 142.5, 159.9, 169.5 ($NHCOCH_3$).

***N*-[(Dimethylamino)methylidene]-3-iodobenzenesulfonamide P$_8$.** Mp 141–142 °C (lit.,[6b] 140–143 °C).

***N*-[(Dimethylamino)methylidene]-3-azidobenzenesulfonamide P$_9$.** Mp 135–137 °C (lit.,[6b] 136–138 °C).

***N*-[(Dimethylamino)methylidene]-3-nitrobenzenesulfonamide P$_{10}$.** Mp 140–142 °C; ν_{max}/cm^{-1} 1628 vs (CN), 1350 s and 1157 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.93 (3H, s, NCH_3), 3.17 (3H, s, NCH_3), 7.84 (1H, t, J = 7.8 Hz, Ar), 8.21 (1H, d, J = 7.8 Hz, Ar), 8.29 (1H, s, Ar), 8.41 (1H, d, J = 7.8 Hz, Ar), 8.47 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.6 (NCH_3), 41.6 (NCH_3), 120.8, 126.9, 131.5, 132.5, 144.6, 148.0, 160.3; DART MS *m*/*z* 258.21 $(M + H)^+$, $C_9H_{11}N_3O_4SH^+$ calcd 258.04.

***N*-[(Dimethylamino)methylidene]-4-(3,5-dimethyl-1*H*-pyrazol-1-yl)benzenesulfonamide P$_{11}$.** Mp 136–137 °C; ν_{max}/cm^{-1} 1628 vs (CN), 1342 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.18 (3H, s, CH_3), 2.35 (3H, s, CH_3), 2.93 (3H, s, NCH_3), 3.16 (3H, s, NCH_3), 6.12 (1H, s, pyrazole C_4-H), 7.67 (2H, d, J = 8.4 Hz, Ar), 7.85 (2H, d, J = 8.4 Hz, Ar), 8.24 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 12.8 (CH_3), 13.6 (CH_3), 35.5 (NCH_3), 41.4 (NCH_3), 108.7, 124.0, 127.5, 140.2, 141.2, 142.4, 149.4, 160.2; DART MS *m*/*z* 307.33 $(M + H)^+$, $C_{14}H_{18}N_4O_2SH^+$ calcd 307.11.

***N*-[(Dimethylamino)methylidene]-2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3-benzothiazole-6-sulfonamide P$_{12}$.** Mp 254–256 °C; ν_{max}/cm^{-1} 1636 vs (CN), 1535 s (CN), 1342 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.24 (3H, s, CH_3), 2.72 (3H, s, CH_3), 2.92 (3H, s, NCH_3), 3.15 (3H, s, NCH_3), 6.30 (1H, s, pyrazole C_4-H), 7.83 (1H, d, J = 8.7 Hz, Ar), 7.95 (1H, d, J = 8.7 Hz, Ar), 8.24 (1H, s, Ar), 8.53 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 13.6 (CH_3), 13.9 (CH_3), 35.5 (NCH_3), 41.5 (NCH_3), 111.6, 121.1, 122.5, 124.8, 132.9, 139.4, 142.9, 153.1, 153.5, 160.1, 164.3; DART MS *m*/*z* 364.21 $(M + H)^+$, $C_{15}H_{17}N_5O_2S_2H^+$ calcd 364.08.

***N*-[(Dimethylamino)methylidene]-2-iodo-1,3-benzothiazole-6-sulfonamide P$_{13}$.** Mp 188–190 °C; ν_{max}/cm^{-1} 1636 vs (CN), 1535 s (CN), 1342 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.92 (3H, s, NCH_3), 3.15 (3H, s, NCH_3), 7.88 (1H, d, J = 8.7 Hz, Ar), 8.03 (1H, d, J = 8.7 Hz, Ar), 8.23 (1H, s, CH═N), 8.58 (s, 1H, Ar); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.6 (NCH_3), 41.4 (NCH_3), 121.5, 123.2, 125.1, 136.4, 140.8, 152.5, 157.1, 160.2; DART MS *m*/*z* 395.98 $(M + H)^+$, $C_{10}H_{10}IN_3O_2S_2H^+$ calcd 395.92.

***N*-[(Dimethylamino)methylidene]methanesulfonamide P$_{14}$.** Mp 81–82 °C (lit.,[8a] 80–81 °C).

4-Amino-*N*-[(dimethylamino)methylidene]benzenesulfonamide P$_{15}$. Mp 167–169 °C (lit.,[18] 168.5–170 °C); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.86 (3H, s, NCH_3), 3.09 (3H, s, NCH_3), 5.80 (2H, s, ex, NH_2), 6.56 (2H, d, J = 8.4 Hz, Ar), 7.38 (2H, d, J = 8.4 Hz, Ar), 8.09 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.3 (NCH_3), 41.1 (NCH_3), 113.0, 128.1, 129.1, 152.3, 159.4.

3-Amino-*N*-[(dimethylamino)methylidene]benzenesulfonamide P$_{16}$. Mp 158–160 °C; ν_{max}/cm^{-1} 3464 w and 3364 w (NH), 1620 vs (CN), 1335 s and 1134 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.89 (3H, s, NCH_3), 3.13 (3H, s, NCH_3), 5.48 (2H, s, ex, NH_2), 6.68 (1H, d, J = 7.8 Hz, Ar), 6.83 (2H, J = 7.8 Hz, Ar), 6.95 (1H, s, Ar), 7.12 (1H, t, J = 7.8 Hz, Ar), 8.12 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.4 (NCH_3), 41.4 (NCH_3), 111.2, 113.9, 118.0, 130.1, 143.2, 148.9, 159.7; DART MS *m*/*z* 228.24 $(M + H)^+$, $C_9H_{13}N_3O_2SH^+$ calcd 228.07.

4-[5-Amino-3-(4-methylphenyl)-1*H*-pyrazol-1-yl]-*N*-[(dimethylamino)methylidene]benzenesulfonamide P$_{17}$. Mp 160–162 °C; ν_{max}/cm^{-1} 3364 w (NH), 1620 vs (CN), 1335 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.32 (3H, s, CH_3), 2.92 (3H, s, NCH_3), 3.16 (3H, s, NCH_3), 5.61 (2H, s, ex, NH_2), 5.91 (1H, s, pyrazole C_4-H), 7.21 (2H, d, J = 7.8 Hz, Ar), 7.65 (2H, d, J = 6.9 Hz, Ar), 7.86 (4H, s, Ar), 8.25 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 21.3 (CH_3), 35.5 (NCH_3), 41.3 (NCH_3), 88.3, 122.6, 125.5, 127.5, 129.5, 130.9, 137.5, 140.3, 142.3, 149.2, 151. 4, 160.2; DART MS *m*/*z* 384.39 $(M + H)^+$, $C_{19}H_{21}N_5O_2SH^+$ calcd 384.14.

4-[5-Amino-3-(4-chlorophenyl)-1*H*-pyrazol-1-yl]-*N*-[(dimethylamino)methylidene]benzenesulfonamide P$_{18}$. Mp 178–180 °C; ν_{max}/cm^{-1} 1628 vs (CN), 1335 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.92 (3H, s, NCH_3), 3.15 (3H, s, NCH_3), 5.68 (2H, s, ex, NH_2), 5.97 (1H, s, pyrazole C_4-H), 7.45 (2H, d, J = 8.1 Hz, Ar), 7.78 (2H, d, J = 8.1 Hz, Ar), 7.83–7.90 (4H, m, Ar), 8.24 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 35.5 (NCH_3), 41.4 (NCH_3), 88.5, 122.7, 127.1, 127.5, 128.7, 132.3, 132.9, 140.4, 142.1, 149.0, 150.4, 159.9; DART MS *m*/*z* 404.29 $(M + H)^+$, $C_{18}H_{18}ClN_5O_2SH^+$ calcd 404.08.

***N*-[(Dimethylamino)methylidene]-4-[2-(phenylethylidene)-hydrazino]benzenesulfonamide P$_{19}$.** Mp 251–252 °C; ν_{max}/cm^{-1} 3302 w (NH), 1628 vs (CN), 1589 s (CN), 1342 s and 1135 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.28 (3H, s, CH_3), 2.89 (3H, s, NCH_3), 3.12 (3H, s, NCH_3), 7.28–7.42 (5H, m, Ar), 7.60 (2H, d, J = 8.7 Hz, Ar), 7.80 (2H, d, J = 6.9 Hz, Ar), 8.15 (1H, s, CH═N), 9.72 (1H, br s, ex, NH); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 13.5 (CH_3), 35.3 (NCH_3), 41.2 (NCH_3), 112.5, 125.9,

127.9, 128.5, 128.7, 132.7, 139.2, 143.7, 149.0, 159.6; DART MS *m/z* 345.26 $(M + H)^+$, $C_{17}H_{20}N_4O_2SH^+$ calcd 345.13.

***N*-[(Dimethylamino)methylidene]-4-{2-[1-(4-methylphenyl)-ethylidene]hydrazino}benzenesulfonamide P$_{20}$.** Mp 180–182 °C; ν_{max}/cm^{-1} 3340 w (NH), 1620 vs (CN), 1589 s (CN), 1342 s and 1126 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.25 (3H, s, CH_3), 2.31 (3H, s, CH_3), 2.88 (3H, s, NCH_3), 3.11 (3H, s, NCH_3), 7.20 (2H, d, *J* = 8.1 Hz, Ar), 7.27 (2H, d, *J* = 8.4 Hz, Ar), 7.58 (2H, d, *J* = 8.4 Hz, Ar), 7.69 (2H, d, *J* = 8.1 Hz, Ar), 8.13 (1H, s, CH═N), 9.64 (1H, br s, ex, NH); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 13.5 (CH_3), 21.1 (CH_3), 35.3 (NCH_3), 41.2 (NCH_3), 112.5, 125.8, 127.9, 129.3, 132.5, 136.5, 137.9, 144.0, 149.1, 159.6; DART MS *m/z* 359.23 $(M + H)^+$, $C_{18}H_{22}N_4O_2SH^+$ calcd 359.14.

4-{2-[1-(4-Chlorophenyl)ethylidene]hydrazino}-*N*-[(dimethyl-amino)methylidene]-benzenesulfonamide P$_{21}$. Mp 170–172 °C; ν_{max}/cm^{-1} 3333 w (NH), 1620 vs (CN), 1589 s (CN), 1342 s and 1134 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.27 (3H, s, CH_3), 2.89 (3H, s, NCH_3), 3.12 (3H, s, NCH_3), 7.30 (2H, d, *J* = 8.7 Hz, Ar), 7.45 (2H, d, *J* = 8.7 Hz, Ar), 7.60 (2H, d, *J* = 8.7 Hz, Ar), 7.82 (2H, d, *J* = 8.7 Hz, Ar), 8.16 (1H, s, CH═N), 9.79 (1H, br s, ex, NH); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 13.4 (CH_3), 35.3 (NCH_3), 41.2 (NCH_3), 112.6, 127.6, 128.0, 128.7, 133.02, 133.07, 138.1, 142.5, 148.8, 159.6; DART MS *m/z* 379.16 $(M + H)^+$, $C_{17}H_{19}ClN_4O_2SH^+$ calcd 379.09.

***N*-[(Dimethylamino)methylidene]-2-[2-(1-phenylethylidene)-hydrazino]-1,3-benzothiazole-6-sulfonamide P$_{22}$.** Mp 229–231 °C; ν_{max}/cm^{-1} 3232 w (NH), 1628 vs (CN), 1551 s (CN), 1335 s and 1142 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.38 (3H, s, CH_3), 2.91 (3H, s, NCH_3), 3.14 (3H, s, NCH_3), 7.43–7.45 (4H, m, Ar), 7.67 (1H, d, *J* = 8.4 Hz, Ar), 7.82–7.84 (2H, m, Ar), 8.18–8.20 (2H, m, CH═N, Ar), 11.94 (1H, br s, ex, NH); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 14.8 (CH_3), 35.5 (NCH_3), 41.3 (NCH_3), 120.5, 124.8, 126.4, 128.9, 129.6, 136.3, 138.2, 160.1; DART MS *m/z* 402.02 $(M + H)^+$, $C_{18}H_{19}N_5O_2S_2H^+$ calcd 402.09.

***N*-[(Dimethylamino)methylidene]-2-{2-[1-(4-methylphenyl)-ethylidene]hydrazino}-1,3-benzothiazole-6-sulfonamide P$_{23}$.** Mp 216–218 °C; ν_{max}/cm^{-1} 1628 vs (CN), 1543 s (CN), 1342 s and 1142 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.35 (3H, s, CH_3), 2.50 (3H, s, CH_3), 2.90 (3H, s, NCH_3), 3.14 (3H, s, NCH_3), 7.25 (2H, d, *J* = 7.8 Hz, Ar), 7.43 (1H, br m, Ar), 7.66 (1H, d, *J* = 8.7 Hz, Ar), 7.72 (2H, d, *J* = 7.8 Hz, Ar), 8.17–8.20 (2H, m, CH═N, Ar), 11.88 (1H, br s, ex, NH); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 14.8 (CH_3), 21.2 (CH_3), 35.5 (NCH_3), 41.3 (NCH_3), 120.5, 124.7, 126.3, 129.4, 135.4, 136.2, 139.2, 160.0; DART MS *m/z* 416.32 $(M + H)^+$, $C_{19}H_{21}N_5O_2S_2H^+$ calcd 416.11.

2-{2-[1-(4-Chlorophenyl)ethylidene]hydrazino}-*N*-[(dimethyl-amino)methylidene]-1,3-benzothiazole-6-sulfonamide P$_{24}$. Mp 230–232 °C; ν_{max}/cm^{-1} 3240 w (NH), 1628 vs (CN), 1551 s (CN), 1342 s and 1142 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.36 (3H, s, CH_3), 2.90 (3H, s, NCH_3), 3.14 (3H, s, NCH_3), 7.43 (1H, br m, Ar), 7.51 (2H, d, *J* = 8.1 Hz, Ar), 7.66 (1H, d, *J* = 8.4 Hz, Ar), 7.83 (2H, d, *J* = 8.1 Hz, Ar), 8.16–8.20 (2H, m, CH═N, Ar); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 14.7 (CH_3), 35.4, 41.3, 120.6, 124.8, 128.1, 128.9, 134.3, 136.3, 137.0, 160.0; DART MS *m/z* 436.16 $(M + H)^+$, $C_{18}H_{18}ClN_5O_2S_2H^+$ calcd 436.05.

***N*-[(Dimethylamino)methylidene]-2{[dimethylamino)methylidene]amino}-1,3-benzothiazole-6-sulfonamide P$_{25}$.** Mp 212–214 °C; ν_{max}/cm^{-1} 1620 vs (CN), 1342 s and 1149 s (SO_2); δ_H (300 MHz; DMSO-d_6; Me_4Si) 2.90 (3H, s, NCH_3), 3.05 (3H, s, NCH_3), 3.14 (3H, s, NCH_3), 3.20 (3H, s, NCH_3), 7.62 (1H, d, *J* = 8.7 Hz, Ar), 7.68 (1H, d, *J* = 8.7 Hz, Ar), 8.20–8.22 (2H, m, CH═N, Ar), 8.54 (1H, s, CH═N); δ_C (75.5 MHz; DMSO-d_6; Me_4Si) 17.1 (CH_3), 114.8, 119.7, 128.1, 129.0, 129.1, 129.5, 130.2, 131.2, 131.6, 139.1, 147.8, 150.5, 153.5, 166.6, 171.2; DART MS *m/z* 340.17 $(M + H)^+$, $C_{13}H_{17}N_5O_2S_2H^+$ calcd 340.08.

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