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The rapid preparation of 2-aminosulfonamide-1,3,4-oxadiazoles using polymer-supported reagents and microwave heating

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Abstract—Herein, we report on the preparation of a library of 5-substituted-2-amino-1,3,4-oxadiazoles and the corresponding thiadiazole analogues. Presented is a one-pot preparation of the 2-aminosulfonylated analogues through a three component coupling of an acylhydrazine, an isocyanate and sulfonyl chloride promoted by a polymer-supported phosphazine base under microwave dielectric heating. Also described is the optimization process and details pertaining to the elucidation of the reaction products.

1. Introduction

As part of an ongoing investigation into small molecule binders as potential modulators of therapeutic targets we required an expedient synthetic route to the versatile compound class **1** (5-substituted-2-amino-1,3,4-oxadiazoles; Figure 1) which had been identified as an excellent structural template for rapid chemical elaboration. Indeed, 1,3,4-oxadiazoles and the related 1,3,4-thiadiazolium derivatives have attracted considerable interest in medicinal chemistry as surrogates of carboxylic acids, esters and carboxamides;[1] moreover, these compounds have also demonstrated a broad spectrum of biological activity in both agrochemical and pharmaceutical fields showing antibacterial,[2] antimicrobial,[3] insecticidal,[4] herbicidal/fungicidal,[5] anti-inflammatory,[6] hypoglycaemic,[7] and hypotension[8] characteristics. In particular the 2-amino-1,3,4-oxadiazoles **1** have recently been reported to exhibit promising anti-tumour activity.[9]

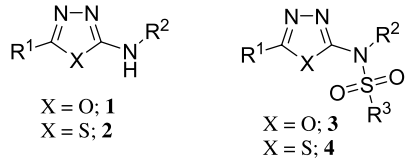

Figure 1. 5-Substituted-2-amino-1,3,4-oxadiazoles **1**, 5-substituted-2-amino-1,3,4-thiodiazoles **2**, 2*N*,5-disubstituted 2-amino-1,3,4-oxadiazoles **3** and 2*N*,5-disubstituted-2-amino-1,3,4-thiodiazoles **4**.

The classical synthesis of oxadiazoles usually involves rather harsh reaction conditions employing for example, $SOCl_2$, $POCl_3$, strong mineral acids or various mercury salts,[10] although a few more recent publications have reported milder cyclisation methods albeit for specifically substituted molecules.[11] In an attempt to avoid the use of these potentially problematic reagents and nongeneral conditions a number of groups have developed alternative procedures more amenable to automated high throughput synthesis. In 2001 Brain et al. reported on the synthesis of simple 1,3,4-oxadiazoles via cyclodehydration of 1,2-diacylhydrazines using a polymer-supported Burgess reagent or the polymer-bound phosphazine base PS-BEMP[12] in the presence of toluenesulfonyl chloride as a dehydrating agent.[13] Brown[14] and Kilburn[15] have also shown that 2-amino-1,3,4-oxadiazoles of type **1** can be prepared in excellent yields on solid phase from the corresponding immobilised 1,4-disubstituted semicarbazides using either 1,3-diisopropylcarbodiimide (DIPC), 1,3-dicyclohexylcarbodiimide (DCC) or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl) as the cyclisation mediator. However, these latter on-bead preparations are somewhat restrictive because of the necessity for extended reaction times (as well as attachment and cleavage steps) and the inherent difficulties of monitoring the reactions progress especially for the preparation of diverse compound libraries. In addition they are often difficult to directly scale up in order to prepare significant quantities of material for further processing

Keywords: Polymer-supported reagents; Oxaziazole; Thiadiazole; Combinatorial chemistry; Microwave.
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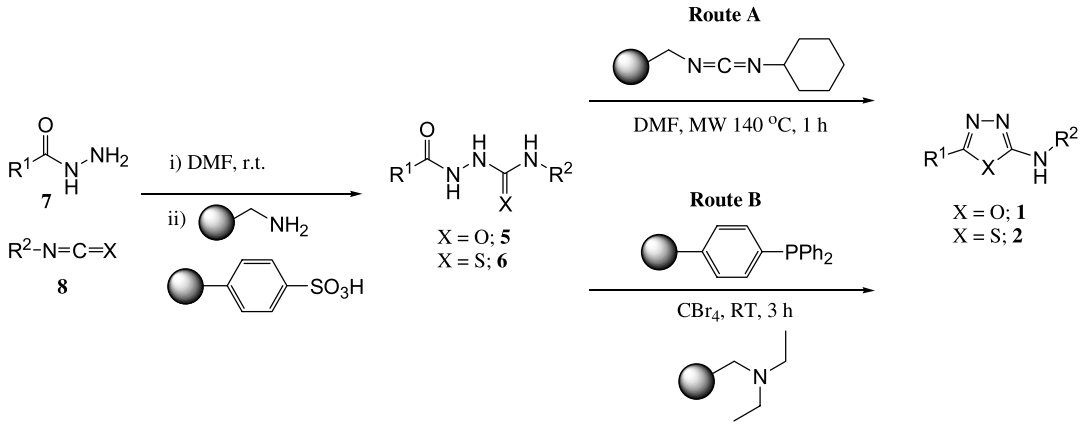


Scheme 1. Preparation of 1,4-disubstituted-(thio)semicarbazides **5/6** and their transformation to 5-substituted-2-amino-1,3,4-oxadiazoles **1** using (a) polymer-supported DCC reagent and (b) carbon tetrabromide and supported triphenylphosphine.

without intensive optimization. Due to our extensive experience and successes in the fields of solid-supported reagents[16] and microwave-assisted[17] organic chemistry we decided to investigate the symbiotic combination of these two enabling technologies to the rapid generation of combinatorial libraries based on the general structures **1**–**4** (Fig. 1).[18]

2. Results and discussion

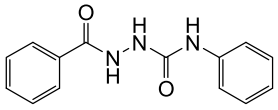
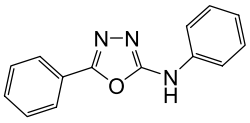
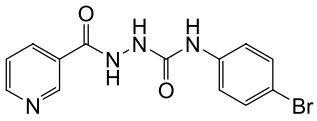
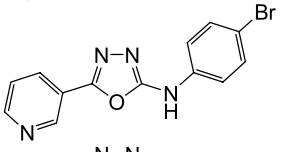
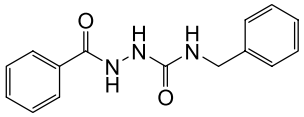
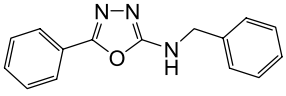
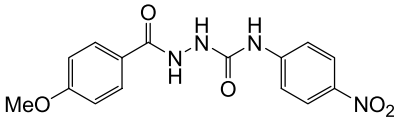
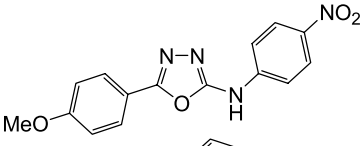
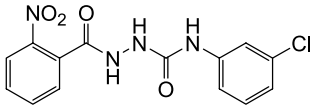
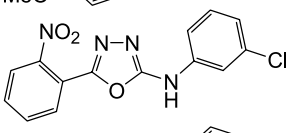
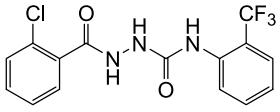
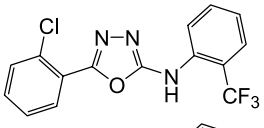
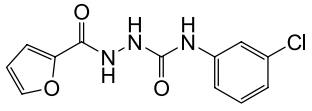
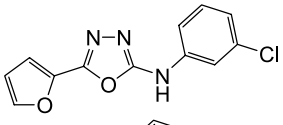
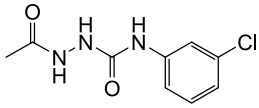
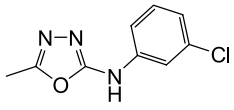
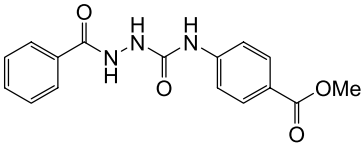
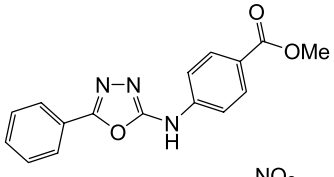
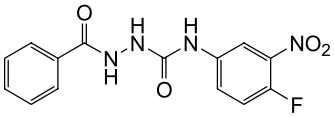
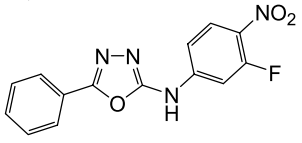
As a result of the literature precedent for successful on bead synthesis we initially investigated the analogous solution phase cyclisation of a range of semicarbazides **5** promoted by an immobilised DCC reagent[19] (Scheme 1; Route A). The prerequisite 1,4-disubstituted (thio)semicarbazides **5/6** were prepared directly via a condensation reaction of the appropriately substituted acylhydrazine **7** and the iso(thio)-cyanate **8**. The reaction conditions were not optimized to maximize the attainable yield but biased to facilitate rapid access to the clean products. Therefore, following a scavenging sequence utilizing a mixture of macroporous sulfonic acid and aminomethyl polystyrene to sequester any unreacted hydrazine **7** and/or iso(thio)cyanate **8** the semicarbazides **5** or **6** were isolated in moderate to high yields but in all cases in excellent purity (Fig. 2).[20] The semicarbazides **5/6** thus prepared were analyzed by LC-MS with a small subset being further characterised by ^{1}H NMR (all compounds exceeded a required 95% minimum purity). The cyclodehydration of a selection of the semicarbazide compounds **5** with a resin bound DCC equivalent (6 equiv) in DMF at 140 °C (1 h) under microwave irradiation[21] was encouraging, leading cleanly to the desired heterocyclic product (Scheme 1; Route A; Table 1). Repeating the reaction in the absence of the supported DCC resulted in no cyclisation and permitted quantitative recovery of the starting material.

Although the described protocol was extremely effective for the cyclisation we were unable to devise a generic procedure that permitted a significant reduction in the number of equivalents of the supported DCC reagent. This proved somewhat problematic (especially for scaling) because the use of six equivalents required large volumes of solvent due to the resins swelling characteristics in DMF and also the need for effective post reaction washing in order to facilitate the isolation of the product. Experiments involving different solvents systems or substitution of the core resin matrix[22] as well as altering other reaction parameters (time, temperature, concentration) failed to give any significant benefits in terms of higher yields or potential scalability. It should be noted that during the preparation of these compound libraries Evans and co-workers reported[23] on the same preparative route to compounds of type **1** using a polymer-supported (PS) DCC cyclisation procedure at 80 °C (reaction times of 60 h). Their protocol also required the use of five equivalents of the immobilised reagent.

We therefore pursued an alternative approach to inducing cyclisation using a mixture of a PS-triphenylphosphine equivalent and carbon tetrabromide.[24] In order to regulate the pH of the system an immobilised triethylamine variant was also added (Scheme 1; Route B). This proved to be a particularly effective combination giving excellent conversions to the corresponding oxadiazoles although the initial purity (~78–92%) of the product was somewhat lower than for the material obtained in the previous PS-DCC mediated method. However, we discovered that simple filtration of the reaction mixture through a functionalised silica packed cartridge (aminopropyl-NH_2) significantly improved the purity (>95% as determined by LC-MS; Table 2).[25]

Having determined two routes to the 2-amino heterocycles **1**, we turned our attention to methods for the direct preparation of the correspondingly sulfonylated material as our intended targets for biological evaluation. Our premise was, that in accordance with the work by Brain et al.[14] we could facilitate the desired cyclisation of **5** using a combination of PS-BEMP and an excess of an appropriately functionalised sulfonyl chloride, which would then lead directly to the protected sulfonamide **3** in a one-pot combinatorial fashion. Indeed, this proved a successful strategy enabling the preparation of a small exploratory compound set based on the 1,4-disubstituted semicarbazides **5** and a selection of 25 commercially available sulfonyl chlorides (Table 3). The optimised conditions were eventually found to be treatment of semicarbazide **5** with PS-BEMP (3.5 equiv) and sulfonyl chloride (2.3 equiv) in acetonitrile at 150 °C. The choice of solvent proved critical (see later discussion) as did the number of equivalents of

Table 1. 2-Amino-1,3,4-oxadiazoles **1** prepared using an PS- DCC reagent (Scheme 1; Route A)

Entry	Substrate	Product	Isolated yield
1			73
2			81
3			70
4			88
5			69
6			64
7			77
8			76
9			80
10			83

All compounds showed a purity >95% as determined by LC-MS.

the two reagents which were configured to suppress the formation of the unprotected amine **1**, which at lower concentrations was always present as a major by-product. However, this observation was of obvious interest with respect to the preparation of compound **1** and hence it was decided to further investigate the feasibility of devising two parallel synthetic routes, which would lead respectively to the sulfonamide **3** and the unprotected heterocycle **1** by simple modification of the reaction parameters.

2.1. 2-Amino-1,3,4-oxadiazoles the effect of the base

Initial observations concerning the reactions of the semicarbazides **5** with PS-BEMP and toluene-4-sulfonyl chloride **11** (TsCl) indicated that it was critical to use an excess of the immobilised phosphazine base. Lower quantities (<2 equiv) always resulted in efficient cyclodehydration but the product mixture comprised of varying amounts of the sulfonamide protected material **3** and free heterocyclic amine **1**. Altering the ratio of sulfonyl chloride beyond two equivalents had little effect on the product composition if sub-quantities of PS-BEMP were used. In order to fully evaluate the effect of the base concentration and its identity a more comprehensive screening programme was conducted (for selected results see Table 4).

From the tabulated information it is evident that there is a specific correlation between the relative basicity of the

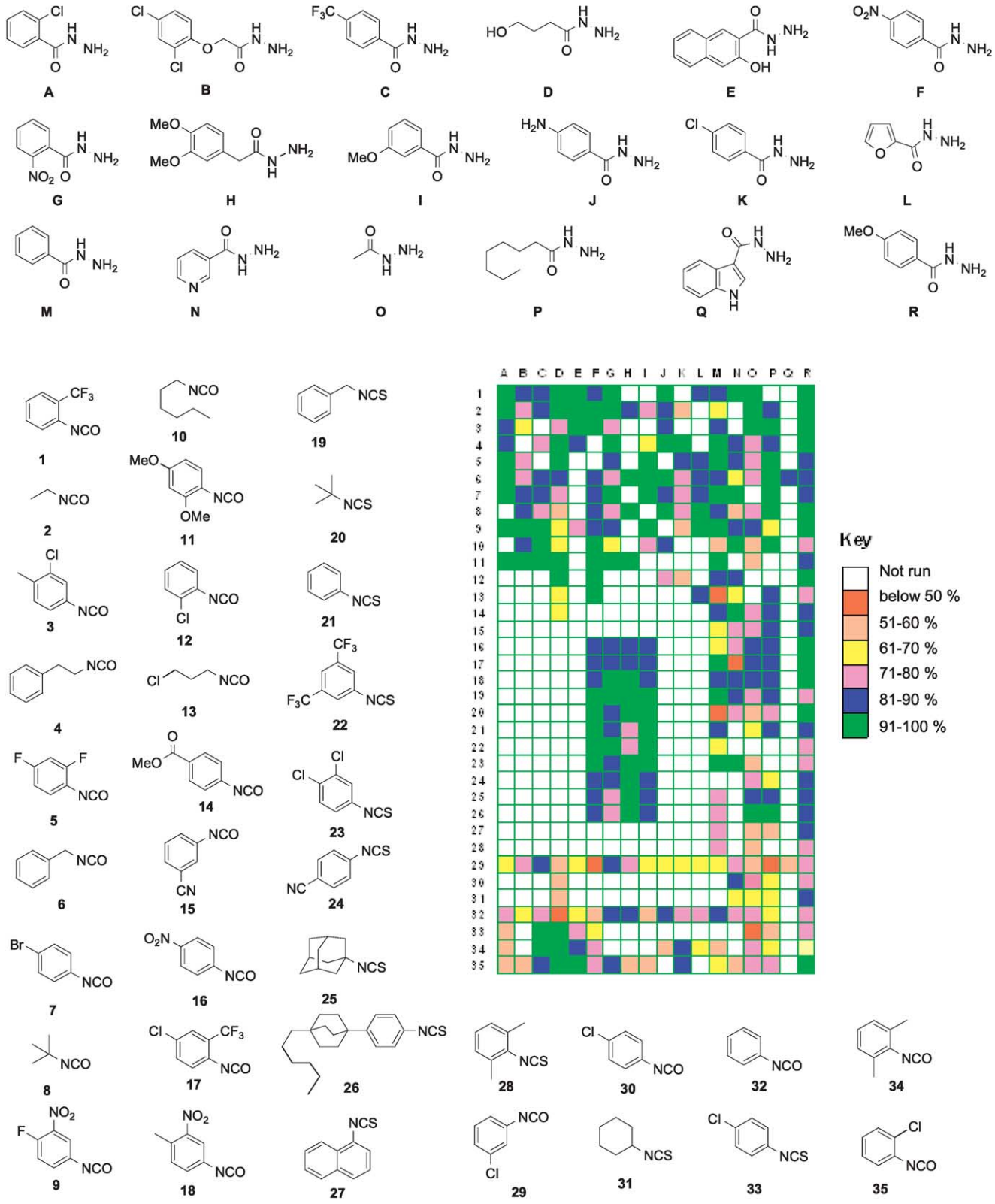


Figure 2.

polymer and the proportions of starting material **34**, cyclised adduct **35** and protected product **36** present in the final reaction mixture. The more basic polymers PS-BEMP and the polymer-bound guanidine base 1,3,4,6,7,8-hexahydro-1-methyl-2*H*-pyrimido[1,2-*a*]pyrimidine (PS-TBD) gave good conversions to the cyclised products **35** and **36**. Whereas, the more weakly basic species such as PS-diisopropylethylamine (PS-DIEA), the tetraalkylammonium carbonate (PS-$NaCO_3$), PS-morpholine (PS-NMM) and Amberlyst A21, although all showing some ability to promote the initial condensation reaction, failed to catalyse the following sulfonation step (only 13% for PS-NMM;

Table 2. Preparation of 2-amino-1,3,4-oxadiazoles using PS-triphenylphosphine and carbon tetrabromide (Scheme 1; Route B)

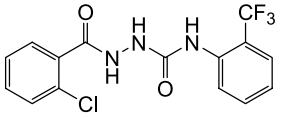
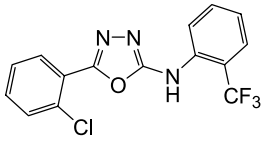
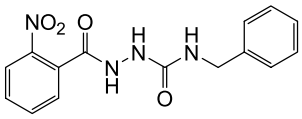
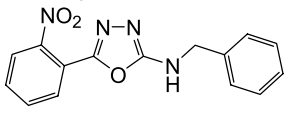
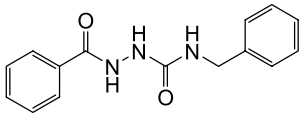
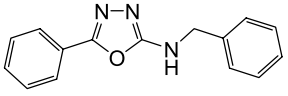
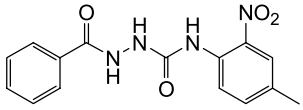
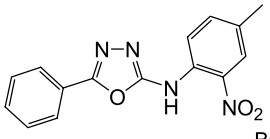
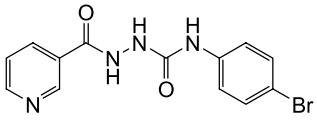
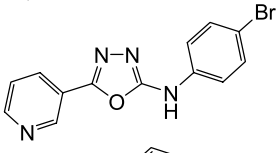
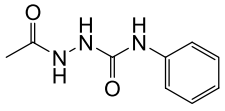
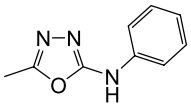
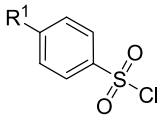
Entry	Substrate	Product	Yield
1			68
2			71
3			77
4			59
5			83
6			81

Table 4, entry 21). Interestingly, both polymer-bound dimethylaminopyridine (PS-DMAP) and to some extent polyvinyl pyridine (PVP) were effective additives for catalysing the initial cyclisation step presumably by formation of a more activated sulfonylating agent,[26] although being weak bases they do not assist the subsequent protection step. This seemed to present an ideal solution to our requirements providing with a simple substitution of the polymeric resins the selective formation of either of the two desired products **35** or **36**. Unfortunately, on a more extensive evaluation the cyclisation reaction catalysed by PS-DMAP proved to be very substrate dependent and variable amounts of starting material **5** were always detected at the end of reaction (3–12%). However, due to the difference in solubility and basicity between the starting material **5** and product **1**, a relatively simple catch and release purification was possible using a sulfonic acid silica bonded sorbent (SCX-II) giving products of >98% purity on release. Therefore, in a typical procedure, the urea, prepared in situ from an acylhydrazide **7** and isocyanate **8** in THF, was cyclodehydrated in a microwave oven (120 °C, 30 min) in the presence of PS-DMAP (3 equiv) and TsCl (2 equiv). Using this procedure a small collection of 120 compounds was formed in moderate to good yields (Table 5 for a representative sample).

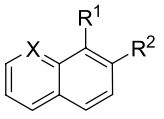
2.2. Sulfonamide protected 2-amino-1,3,4-oxadiazoles the effect of the solvent

A number of potential solvents systems were screened for the one-pot cyclisation/protection sequence leading to compounds of type **3**. The solvents dichloromethane,

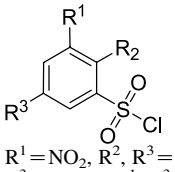
Table 3. The various sulfonic acid chlorides used in the construction of heterocyclic sulfonamides **3**



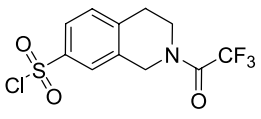
R^1=H, **9**; Ph, **10**; Me, **11**; MeO, **12**; F, **13**; Cl, **14**; Br, **15**; I, **16**; NO_2, **17**; $MeSO_2$, **18**; butoxy, **19**; CF_3, **20**; PhO, **21**.



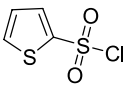
R^1=H, R^2=SO_2Cl, X=CH, **22**; R^1=SO_2Cl, R^2=H, X=CH, **23**; R^1=SO_2Cl, R^2=H, X=N, **24**.



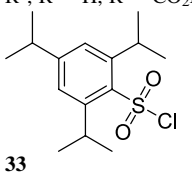
R^1=NO_2, R^2, R^3=H, **25**; R^1=CF_3, R^2=H, R^3=Br, **26**; R^1, R^3=H, R^2=CF_3, **27**; R^1, R^3=H, R^2=CN, **28**; R^1, R^3=H, R^2=NO_2, **29**; R^1, R^3=H, R^2=CO_2Me, **30**.



31

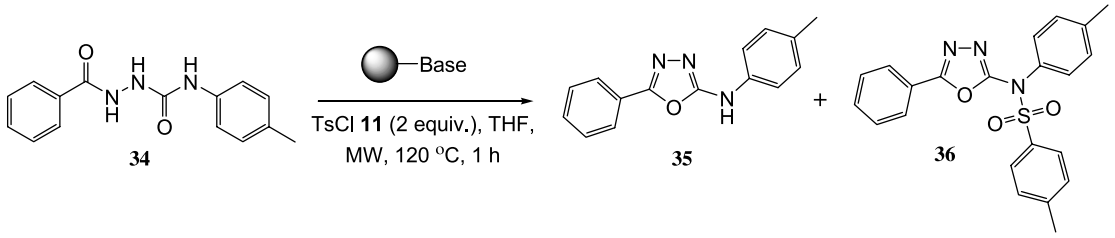


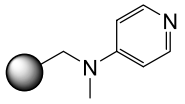
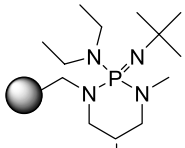
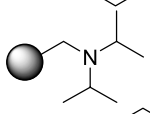
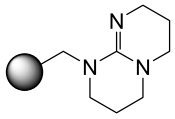
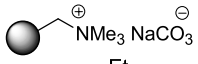
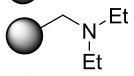
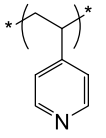
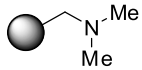
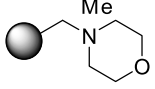
32



33

Table 4. Optimisation of the immobilised base used for the cyclodehydration of urea compound **34**



Entry	Base	Polymer structure	Equiv	**34**[a]	**35**[a]	**36**[a]
1	No base[b]		—	88	12	—
2	PS-DMAP		5		95	—
3			3	12	88	—
4			1	52	48	—
5[c]			2	38	62	—
6			2	28	72	—
7			2.5	24	76	—
8	PS-BEMP		5	—	—	99
9			3.5	—	—	99
10			2	—	16	84
11			1	—	48	52
12	PS-DIEA		5	55	45	—
13	PS-TBD		5	—	60	40
14			3	2	86	20
15			1	22	56	22
16	PS-$NaCO_3$		5	80	20	—
17	PS-TEA		5	64	36	—
18	PVP[c]		5	61	39	—
19			5	45	55	—
20	Amberlyst A21		5	82	18	—
21	PS-NMM		5	42	45	13

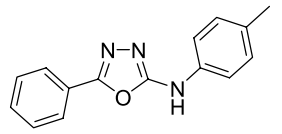
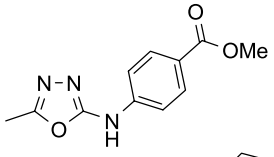
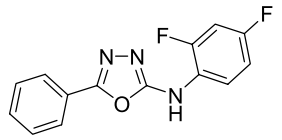
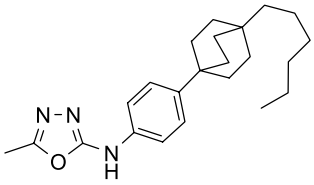
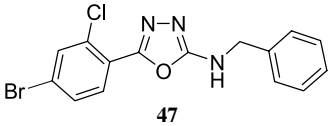
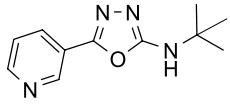
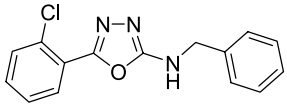
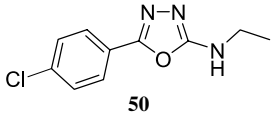
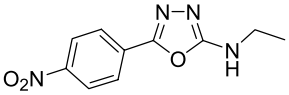
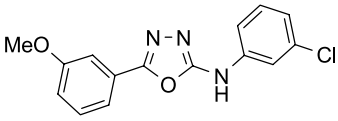
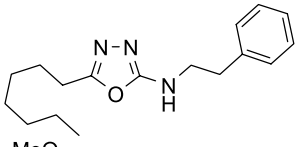
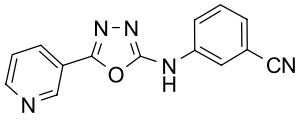
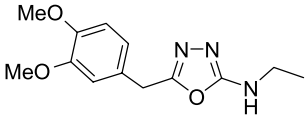
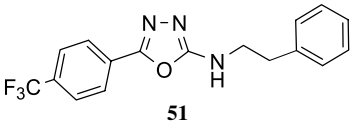
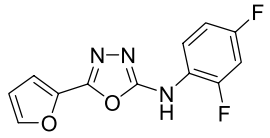
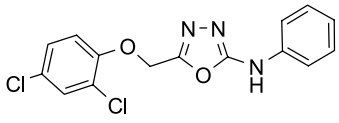
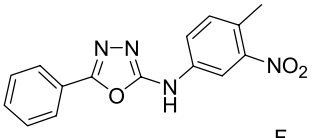
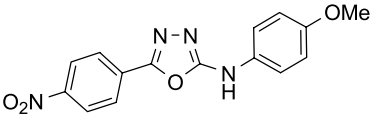
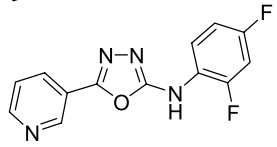
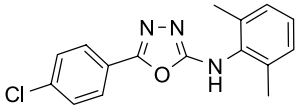
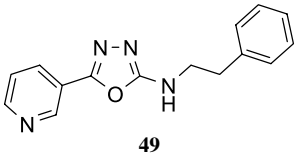
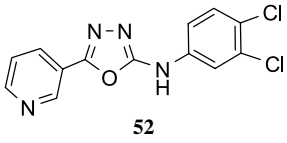
[a] Determined by LC-MS, 254 nm detection.
[b] Heated for 1 h at 120 °C in tetrahydrofuran.
[c] Heated for 30 min at 120 °C.

chloroform, 1,2-dichlorobenzene and toluene all gave complex mixtures under the standard conditions (PS-BEMP (3.5 equiv), TsCl (2.2 equiv) at 120 °C for 20 min) (Scheme 2). The use of dimethylformaldehyde (DMF) also proved problematic giving a single alternative product which was later identified as the sulfonyl protected enol derivative. When the reaction was carried out in THF or similarly 1,4-dioxane all the starting material was consumed but the solution upon isolation contained two compounds with identical molecular weights in a 4:1 ratio.

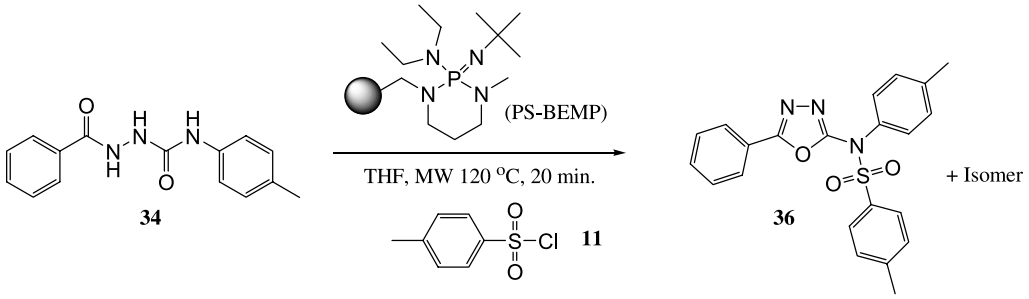
There are a number of potential structural isomers which could be formed through the cyclodehydration and resulting protection sequence of the semicarbazide compounds **5**. The most likely rationalization for the formation of two species under our reaction conditions would be as a consequence of the bidentate nucleophilic behavior of the intermediate heterocycle **1** through tautomerism with the imino-oxadiazoline form **37** (Scheme 3). These two species could then react independently with the electrophile at either the ring or exocyclic nitrogens leading to two distinct regioisomers **3** and **38**.[27] Presumably, the driving force for the formation of compound **38** would be the avoidance of steric congestion around the *N*-5 site that would be apparent in the bis-substituted amine isomer **3**.

In addition we must also consider the possible heterocyclic structures that could result from nucleophilic attack of the (5-*N*) nitrogen to form the alternative cyclisation product namely the 1,3,4-triazole **39** and its subsequently sulfonylated derivatives **41** and **42** (Scheme 3). In order to gain some insight into the reaction and determine the potential for any

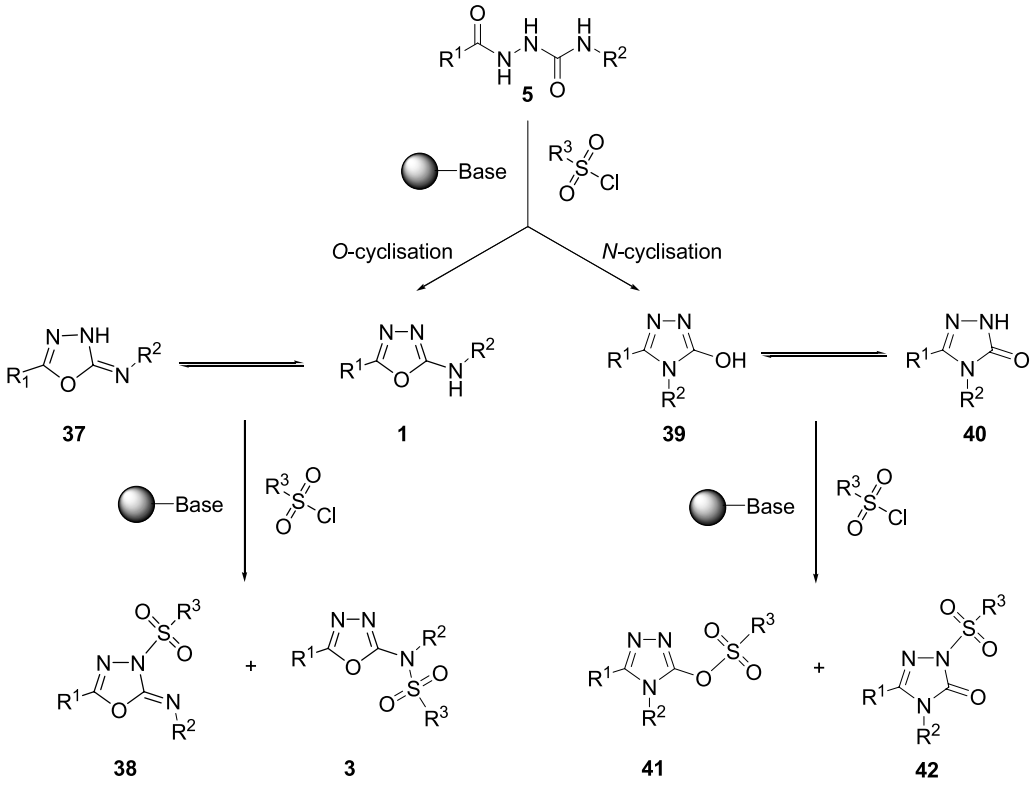
Table 5. 2-Amino-1,3,4-oxadiazoles synthesis

Entry	Product	Yield	Entry	Product	Yield
1		60	12		53
2		55	13		59
3	 **47**	82	14		68
4		56	15	 **50**	75
5	 **48**	78	16		77
6		72	17		82
7		77	18	 **51**	77
8		64	19		64
9		52	20		80
10		88	21		68
11	 **49**	90	22	 **52**	76

experimental control of the regioselectivity we embarked on a more detailed study of the reaction components of the model system depicted in Scheme 2. Preliminary investigations of the IR spectra and attempted correlation to the literature reported compounds proved inconclusive. Therefore, a selection of acyl semicarbazide derivatives **5** were analyzed and a characteristic C=O stretching band in the range of 1710–1665 cm^{-1} was identified which in the corresponding major cyclisation products was replaced with equally strong absorptions between 1655 and 1600 cm^{-1} corresponding to the finger print region for a C=N stretch consistent with a cyclic strained structure. The



Scheme 2. Model system for reaction optimization.



Scheme 3. Tautomerism in the 2-amino-1,3,4-oxadiazoles **1**;[28] formation of compounds **3** and **38**. The alternative cyclisation product 1,3,4-triazole **39** and the possible sulfonyl protected forms **41** and **42**.

imino-oxadiazoline species **37** would be expected to show a higher absorbance at 1695–1640 cm^{-1} in accordance with the exocyclic C═NR stretch as seen in IR spectra of mixtures containing the minor product.[29] Alternatively, compound **42** would be expected to display a characteristic absorption frequency corresponding to the carbonyl (C═O; 1725–1695 cm^{-1}) signal which was not observed.[30] From these pieces of data we could provisionally propose the structures **3** (major product) and **38** (minor product) to the isomer mixtures. In addition more indirect evidence to support the presence of structure **38** was found when upon attempted separation the minor regioisomer decomposed to yield the derivative of form **1**. However, in order to fully validate the identity of the two product components we decided to prepare by know literature methods[31] compounds **35** and **43** which were subsequently sulfonylated (TsCl **11**),[32] resulting in the clean formation of two additional compounds **36** and **44**, respectively for which single crystal X-ray data was obtained (Fig. 3). We were therefore able to immediately match the major products from the reactions of **34** and **11** with PS-BEMP, namely **36** (Scheme 2) and in the case of PS-DMAP product **35** (Table 4) which also matches the decomposition product of the minor isomer from the model system. In addition the possible structure regioisomer **44** could be conclusively eliminated from consideration as a possible candidate for the minor isomeric partner of **35**. Interestingly, all attempts to prepare the alternative regioisomer of **44** based on the structure **40** failed allowing only isolation of compound **44**. Presumably, the sulfonamide **44** is favored because of the lability of the *O*-sulfonyl and the potential for steric hindrance with the adjacent *N*-tolyl group which prevents the *O*-protected assembly.

A number of other substrates showed the same behavior giving two regioisomers (Table 6). In all cases attempted isolation of the minor product resulted in its decomposition and only the nonsulfonylated material **1** could be recovered. Indeed, even on standing at ambient temperature the minor

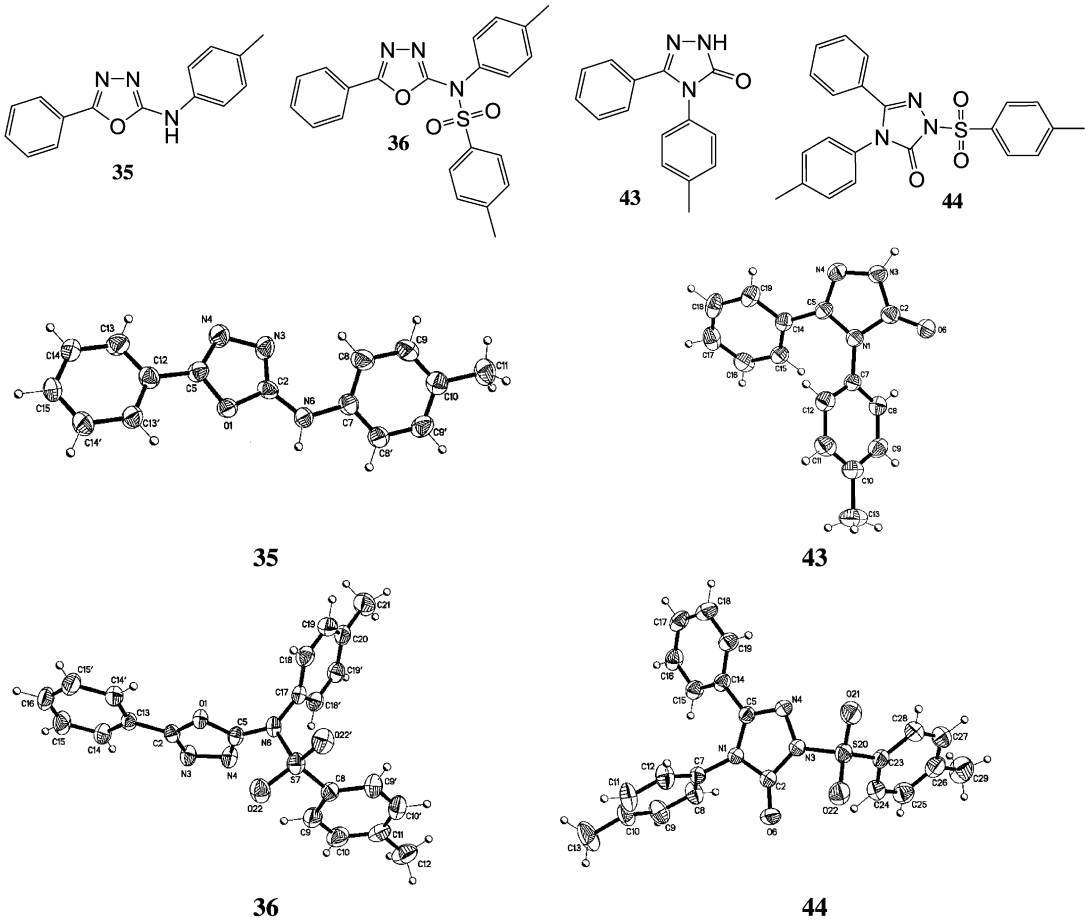


Figure 3. X-ray crystal structures for compounds **35**, **36**, **43** and **44**.

product spontaneously eliminated the corresponding sulfonic acid to give the 2-amino-ozadiazole **1**. This process could be accelerated with the addition of an alcoholic solvent such as methanol/water or by the addition of a nucleophilic amine leading to the formation of the sulfonamide adduct.

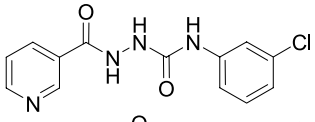
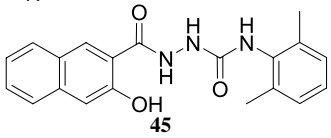
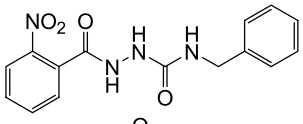
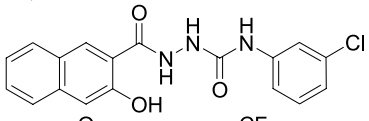
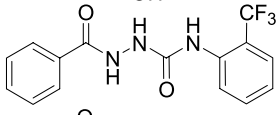
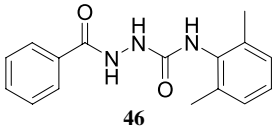
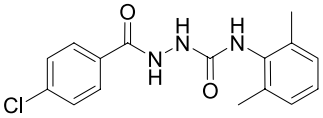
The synthetic inconvenience of producing a mixed regioisomer product was avoided in the majority of cases by simply changing the solvent to acetonitrile. This proved highly beneficial yielding the protected oxazolidine **3** as the exclusive product after only 15 min although this required the temperature to be elevated to 150 °C. At lower temperatures extended reaction times were required and the final products purity was lower. Again, work-up and purification was facile requiring only filtration through a short plug of silica and solvent evaporation. Although the use of acetonitrile as the solvent did result in the formation of a single product, in the majority of cases certain compounds were still obtained as mixtures, the exact ratio was found to be highly dependant on the steric nature of the coupling partners. However, in all cases the use of acetonitrile always gave a preferentially biased mixture in favour of the oxadiazole **3** (Table 6).

Accordingly a library of *N*-substituted-2-amino-1,3,4-oxazolidines **3** were prepared from the previously described urea library **5** (Table 7; see Fig. 2 for details of the semicarbazides **5** and Table 3 for a list of the sulfonyl chlorides employed). In total, a compound collection comprising of over 850 distinct and isolated compounds was generated. All compound purities were determined by LC-MS and a small random selection of the compounds were chosen for full characterisation.

2.3. Cyclodehydration of thiosemicarbazides 6

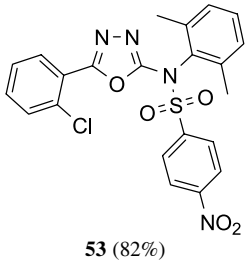
In addition to the formation of the oxadiazole species **3** we were also interested in preparing the corresponding 2-amino-1,3,4-thiadiazole analogues **4**. When the same standardized reaction conditions were applied to the cyclisation of the thiosemicarbazides **6**, a substrate dependant transformation to either the thiadiazoles **4** or oxadiazoles **3** occurred (Table 8). The selectivity of the reaction was found to be highly dependant on the electronic characteristics of the R^1 and R^2 substituents. Rationalization of the differing reactivity of the thiourea compounds **6** could be ascribed to the relative nucleophilicity of the thiocarbonyl and carbonyl functionality as influenced by the interaction of electron-withdrawing or electron-donating groups. In entries 4–10 (Table 8), the pyridine ring (likewise the 4-nitro group in entries 27–29; Table 8) reduces the electron density of the acylhydrazine moiety. This would result in an increase in acidity of the *N*-2 proton permitting rapid enol tautomerism. Facile *O*-sulfonylation of the enolate would yield a reactive intermediate possessing an electrophilic centre and associated leaving group. Spontaneous intramolecular cyclisation through attack of

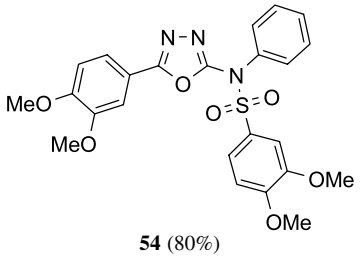
Table 6. Effect of solvent on product composition

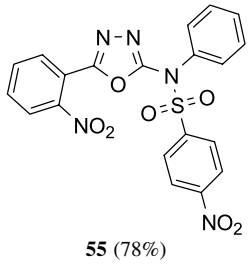
Substrate	RSO_2Cl	Solvent	Ratio 3:38
	**14**	THF MeCN	6:5 3:1
 **45**	**14**	THF MeCN	1:1 5:2
	**15**	THF MeCN	3:2 5:1
	**27**	THF MeCN	1:1 4:1
	**32**	THF MeCN	6:1 20:1
 **46**	**12**	THF MeCN	3:1 9:1
	**12**	THF MeCN	3:2 5:1

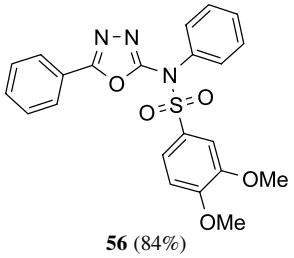
the thiocarbonyl would then lead to exclusive formation of the thiadiazole product **4**. To a lesser extent the same effect can also be seen in entries 1–3 where the phenyl group would likewise assist the deprotonation step (PS-BEMP is well known to be able to remove N–H amidic protons). Conversely, electron donating or simple alkyl groups at R^1 would increase the nucleophilicity of the sulfur in the thiourea making this the more likely centre for sulfonylation and therefore creation of the required leaving group (in addition to arguments of activation following the above argument for the *N*-2 proton acidity). Again, the analogous intramolecular cyclisation by the carbonyl oxygen would result in formation of the alternative product the oxadiazole **3**. As can be see from entries 17–19 (Table 8) the two processes are quite finely balanced although there is probably some inherent bias towards the formation of the

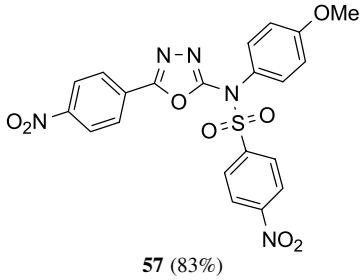
Table 7. Examples of N-substituted-2-sulfonamide-1,3,4-oxadiazoles prepared from semicarbazide library **5**


53 (82%)


54 (80%)


55 (78%)


56 (84%)


57 (83%)

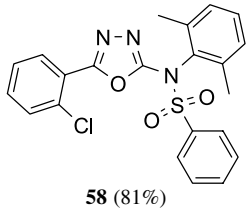
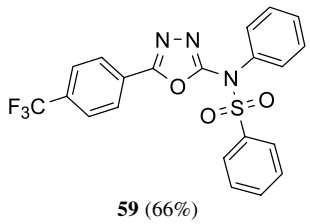
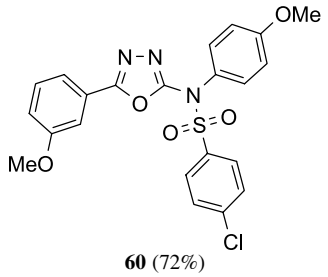

58 (81%)

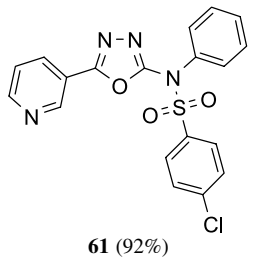
Table 7 (*continued*)



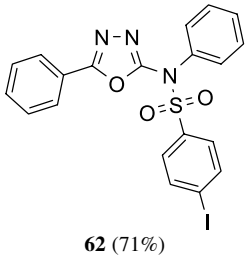
59 (66%)



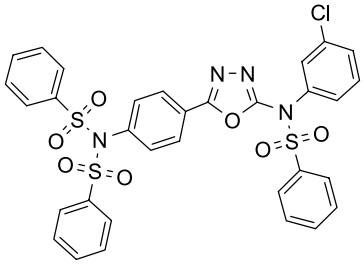
60 (72%)



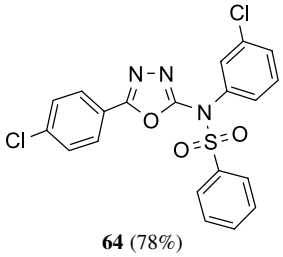
61 (92%)



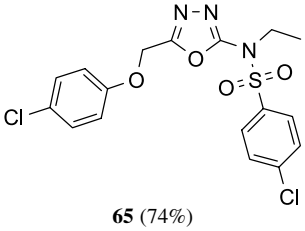
62 (71%)



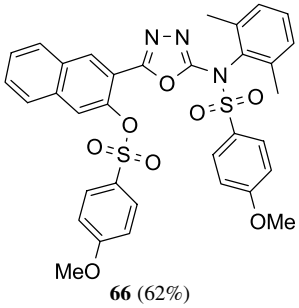
63 (49%)



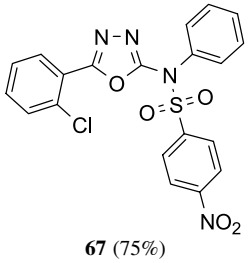
64 (78%)



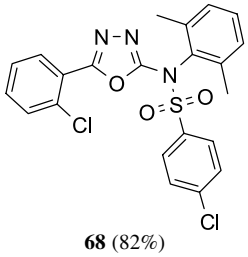
65 (74%)



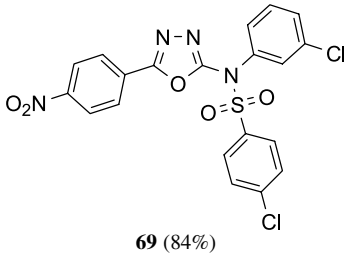
66 (62%)



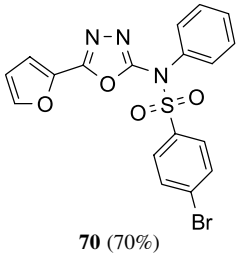
67 (75%)



68 (82%)



69 (84%)



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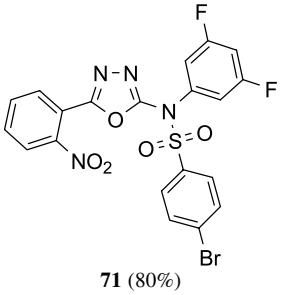

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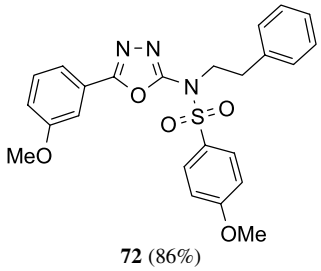
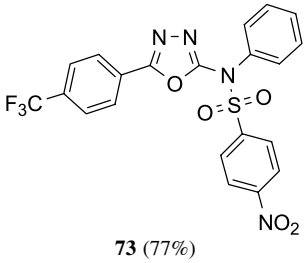


72 (86%)



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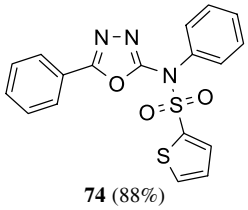
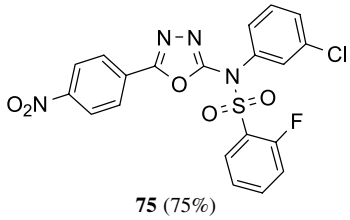


74 (88%)



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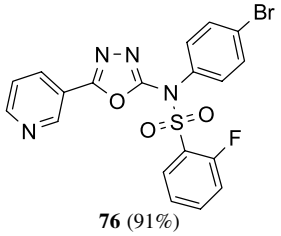

76 (91%)

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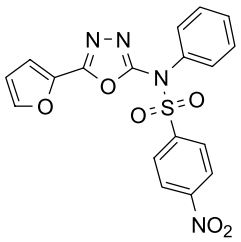
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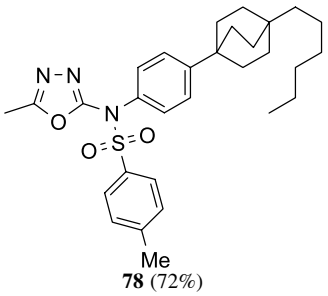
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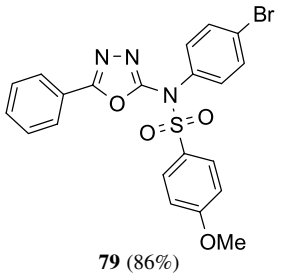
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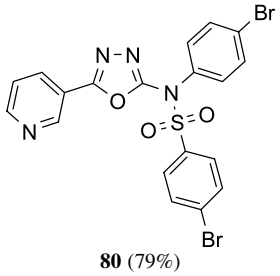
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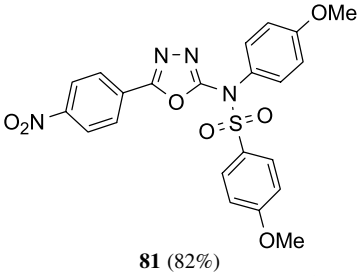
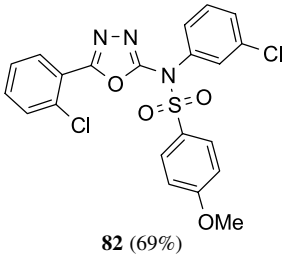
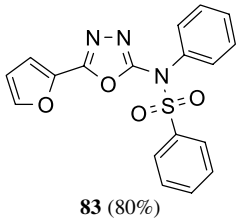
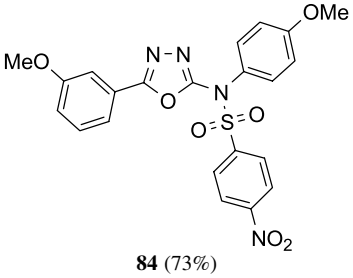
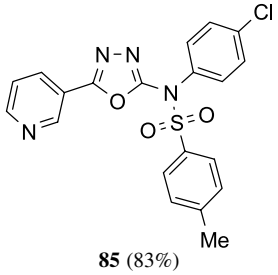
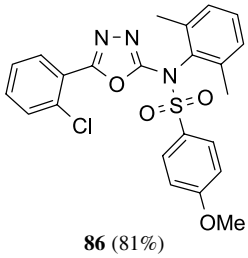

81 (82%)

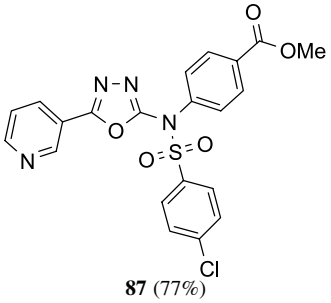

82 (69%)


83 (80%)


84 (73%)


85 (83%)


86 (81%)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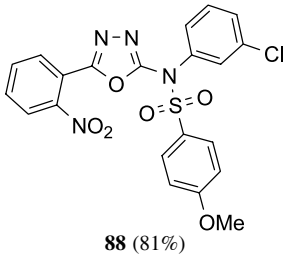
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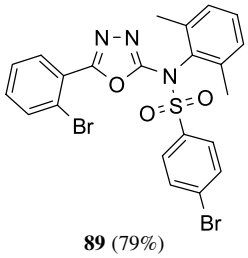
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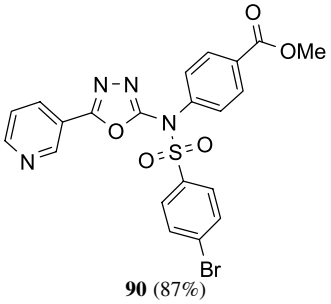
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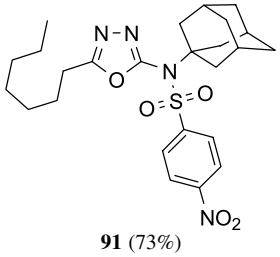
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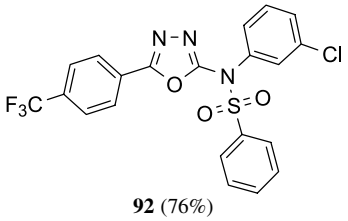
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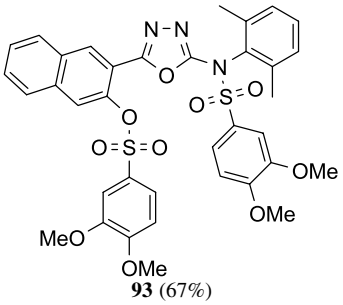
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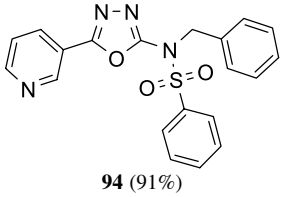
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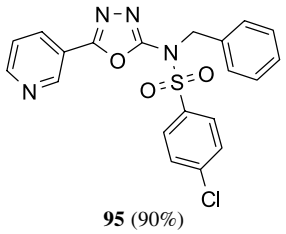
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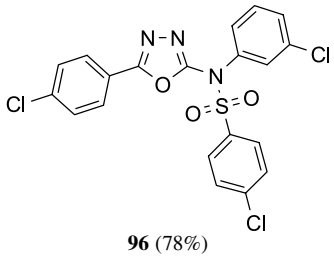
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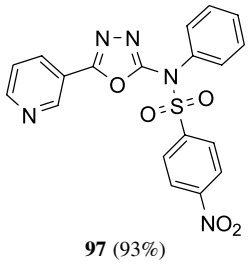
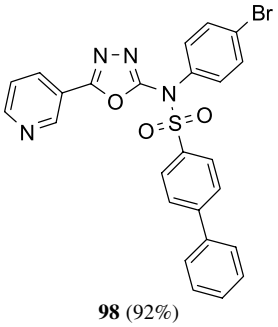
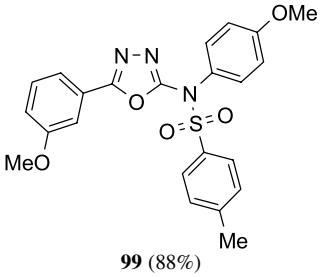
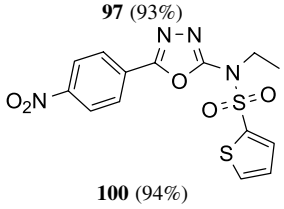

97 (93%)


98 (92%)


99 (88%)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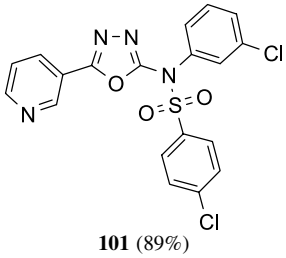
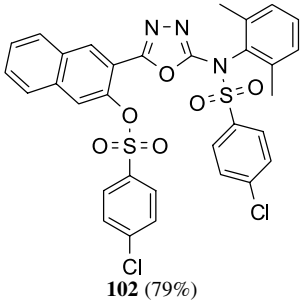
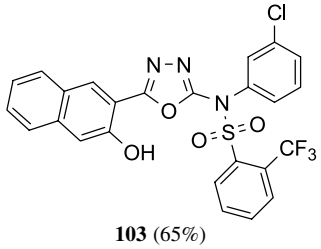

101 (89%)


102 (79%)


103 (65%)

thiadiazole product **4** because of the higher oxophilicity of the sulfonyl chloride reagents.

2.4. Single pot strategy

We next turned our attention to enhancing this synthetic methodology by validating a new three step one-pot synthetic procedure. According to this protocol the 1,2-diacylhydrazine **3** was generated in situ starting from acylhydrazide and isocyanate in acetonitrile at ambient temperature; after stirring the reaction mixture for 5 min PS-BEMP and the corresponding sulfonyl chloride was added and the mixture heated under microwave irradiation at 150 °C for 15 min (Table 9). In general the final compounds were obtained in high purity and yield, with the exception of compounds derived from sulfonyl chlorides substituted in the ortho position (Table 9; entries 15–18). This was consistent with the observations from the previous preparation (see Table 8).

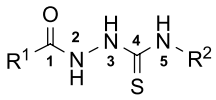
3. Conclusion

In conclusion we have successfully developed and validated two convenient routes to 5-substituted-2-amino-1,3,4-oxadiazoles **2** and their 2-aminosulfonylated derivatives **4** using polymer-supported reagents to expedite their preparation and purification. In total over 15 hundred discrete compounds have been prepared which are being screening and evaluated against a range of medicinal and agrochemical targets.

4. Experimental

Poly-DMAP was pre-washed with DCM, MeOH, Et_2O then dried at 60 °C for 20 h. Tetrahydrofuran (THF) was distilled over sodium benzophenone and dichloromethane over calcium hydride. All others solvents and reagents were used as supplied unless otherwise specified. Analytical TLC was peformed using precoated glass-backed plates (Merck Kieselgel 60 F254) and visualized by ultra-violet radiation, acidic ammonium molybdate (IV) or potassium permanganate. ^{1}H spectra were recorded on a Bruker Advance DPX-400 or DPX-500 spectrometer with residual chloroform as the internal reference (δ_H=7.26 ppm). ^{13}C NMR spectra were recorded in $CDCl_3$ on the same spectrometers with the central peak of chloroform as the internal reference (δ_C=77.0 ppm). DEPT 135 and two-dimensional (COSY, HMQC and HMBC) NMR spectroscopy were used, where appropriate, to aid in the assignment of signal in the ^{1}H and ^{13}C NMR spectra. Infra-red spectra were recorded on a Perkin–Elmer Spectrum One FT-IR spectrometer neat, letters in the parentheses refer to relative absorbancy of the peak w-weak less than 40% of the main peak, m-medium ca. 41–74% of the main peak, s-strong greater than 74% of the most intense peak. LC-MS analysis was performed on a Hewlett–Packard HPLC 1100 chromatograph (Mercury hexyl-phenyl column) attached to a HP LC/MSD Platform LC APCI mass spectrometer. Elution was carried out using the gradient given in Table A.

Table 8. Cyclodehydration reaction on thiourea derivatives **6**



6

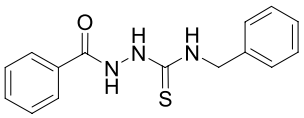
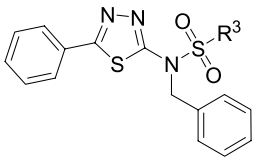
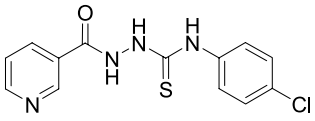
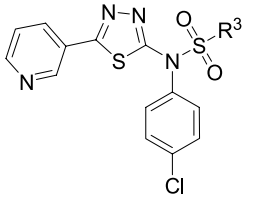
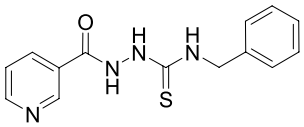
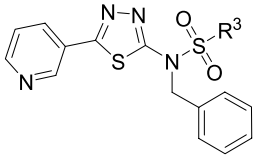
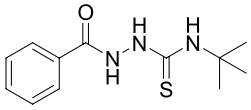
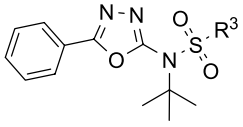
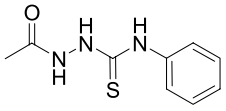
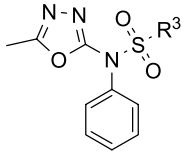
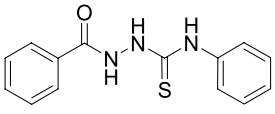
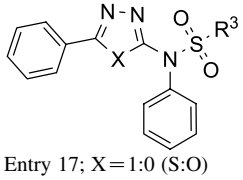
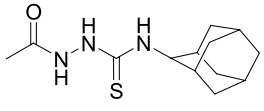
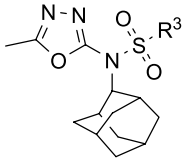
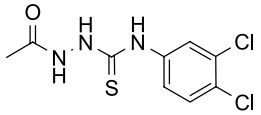
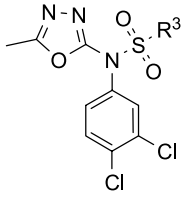
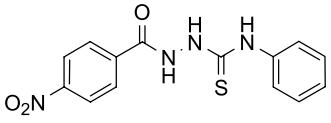
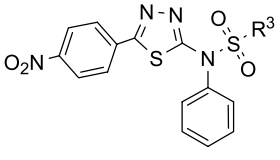
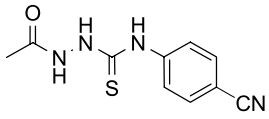
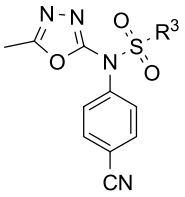
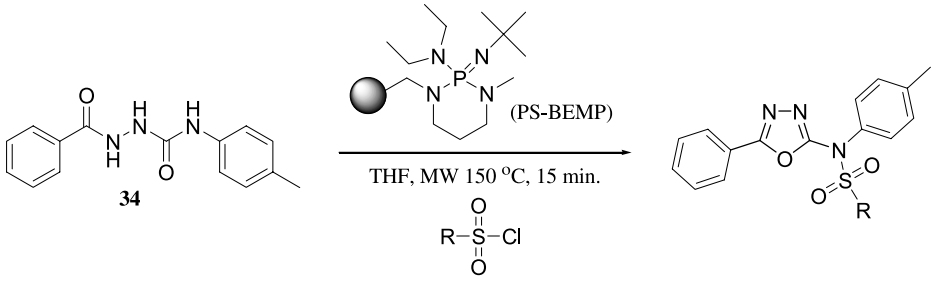
Entry	Substrate	R^3SO_2Cl	Product[a]	Yield[b]	Purity[c]
1		**12**		83	90
2		**13**		80	90
3		**22**		84	90
4		**14**		70	90
5		**11**		79	95
6		**13**		77	95
7		**14**		76	92
8		**11**		98	98
9		**10**		89	98
10		**16**		70	95
11		**32**		89	90
12		**13**		80	90
13		**13**		81	90
14		**17**		80	90
15		**14**		80	90
16		**11**		89	90
17		**32**		98	98
18		**12**		83	95
19		**13**		88	98
			Entry 17; X = 1:0 (S:O) Entry 18; X = 2:1 (S:O) Entry 19; X = 9:5 (S:O)		
20		**13**		70	90
21		**14**		81	90
22		**11**		78	95
23		**13**		85	90
24		**17**		88	90
25		**14**		88	90
26		**10**		90	90
27		**12**		79	95
28		**13**		81	95
29		**14**		90	95

Table 8 (*continued*)

Entry	Substrate	R^3SO_2Cl	Product[a]	Yield[b]	Purity[c]
30		**11**		65	90
31		**13**		75	95
32		**17**		81	95

[a] General reaction conditions used were: substrate (0.5 mmol), BEMP (4.3 equiv, 2.2 mmol/g from Fluka) and sulfonylchloride (2.3 equiv) were irradiated in a microwave apparatus at 150 °C for 20 min.
[b] Yields of isolated products.
[c] Determined by LC-MS, 254 nm detection.

Table 9. Data for the synthesis of 2-sulfonamide-1,3,4-oxadiazoles **3** in a single pot reaction sequence, RSO_2Cl compounds are listed in Table 3



Entry	RSO_2Cl	Yield (%)[a]	Purity (%)[b]
1	**10**	78	>99
2	**13**	61	>99
3	**14**	75	>99
4	**28**	80	>99
5	**15**	80	98
6	**16**	65	98
7	**11**	77	>99
8	**12**	73	98
9	**17**	43	95
10	**20**	71	95
11	**19**	58	95
12	**21**	72	>99
13	**18**	68	95
14	**10**	70	>99
15	**28**	49	89
16	**30**	44	> 70
17	**27**	60	>75
18	**26**	42	> 70
19	**31**	70	>99
20	**32**	60	>99
21	**22**	66	85
22	**23**	75	90

[a] Yields of isolated products.
[b] Determined by LC-MS, 254 nm detection.

Table A. Elution gradient for LC-MS

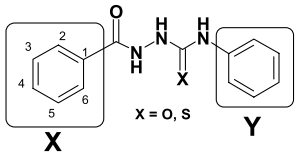
Time/min	A %[a]	B %[b]	Flow rate (mL/min)
0.00	95	5	0
3.00	5	95	0.6
5.00	5	95	0.6
5.50	95	5	0.6
8.00	95	5	0.6

[a] Water + 0.1% trifluoroacetic acid.
[b] Acetonitrile + 0.1% trifluoroacetic acid.

4.1. Preparation of 1,4-disubstituted (thio)semicarbazide 2

Isothiocyanate or isocyanate (5.5 mmol) was added to a solution of substituted hydrazines (5 mmol) in DMF (10 mL) and stirred for 4 h at ambient temperature. The reaction mixture was added to a suspension of polymer-supported sulfonic acid (MP-TsOH) (1.4 mmol, 1.5 mmol g^{-1}) and polymer supported-amine ($PS\text{-}NH_2$)

(1.4 mmol, 1.3 mmol N/g) in DMF (10 mL) and stirred for a further 12 h at ambient temperature. The resulting suspension was filtered to remove polymer-supported reagents and the solvent was removed in vacuo.



4.1.1. 1-(4-Chlorobenzoyl)-4-(2,6-dimethylphenyl)semicarbazide. LC-MS R_f 3.222 M+H 318.1; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 10.38 (1H, br s, NH), 8.10 (1H, br s, NH), 8.04 (1H, br s, NH), 7.94 (2H, d, J=8.8 Hz, H_X-2/6), 7.53 (2H, d, J=8.8 Hz, H_X-3/5), 7.04 (3H, m, H_Y-3/4/5), 2.19 (6H, s, 2×Me).

4.1.2. 1-Benzoyl-4-(*p*-tolyl)semicarbazide 34. LC-MS R_f 3.543 M+H 270.1; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 10.27 (1H, br s, NH), 8.77 (1H, br s, NH), 8.18 (1H, br s, NH), 7.94 (2H, d, J=7.6 Hz, H_X-2/6), 7.60 (1H, t, J=7.4 Hz, H_X-4), 7.52 (2H, br t, H_X-3/5), 7.38 (2H, d, J=8.1 Hz, H_Y-3/5), 7.04 (2H, d, J=8.1 Hz, H_Y-2/6), 2.23 (3H, s, Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 166.79 (C), 156.06 (C), 137.48 (C), 132.09 (CH), 133.00 (C), 131.06 (C), 129.39 (CH), 128.72 (CH), 127.92 (CH), 119.02 (CH), 20.69 (CH_3). IR ν (neat)=3263.6 (w), 3059.1 (w), 1651 (m), 1644.4 (s), 1594.0 (m), 1537.7 (s), 1515.3 (m), 1493.0 (m), 1343.9 (m), 1329.9 (m), 1307.9 (m), 1290.3 (m), 1231.7 (s), 1193.3 (m), 916.8 (m), 826.3 (m), 807.8 (m), 784.8 (m), 774.7 (w), 755.6 (w), 687.6 (s) cm^{-1}. HRMS Calcd for $C_{15}H_{16}N_3O_2$ 270.1243; found 270.1239.

4.1.3. 1-Benzoyl-4-(2,6-dimethylphenyl)semicarbazide 46. LC-MS R_f 2.853 M+H 286.1; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 10.28 (1H, br s, NH), 8.07 (1H, br s, NH), 8.02 (1H, br s, NH), 7.94 (2H, d, J=7.3 Hz, H_X-2/6), 7.94 (1H, t, J=7.3 Hz, H_X-4), 7.47 (2H, t, J=7.3 Hz, H_X-3/5), 7.03 (3H, m, H_Y-3/4/5), 2.20 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 166.89 (C), 157.03 (C), 136.42 (C), 135.77 (C), 133.15 (C), 131.99 (CH), 128.62 (CH), 128.01 (CH), 127.91 (CH), 126.35 (CH), 18.53 (CH_3).

4.1.4. 1-(1*H*-indol-3-carbonyl)-4-benzyl semicarbazide. LC-MS R_f 3.008 M+H 309.1; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 10.86 (1H, br s, NH), 9.88 (1H, br s, NH), 8.63 (1H, br s, NH), 8.05 (1H, br s, NH), 7.62 (1H, d, J=8.2 Hz), 7.41 (2H, d, J=8.2 Hz), 7.35 (1H, d, J=8.2 Hz), 7.25 (4H, m), 7.09 (1H, t, J=7.7 Hz), 6.98 (1H, t, J=7.4 Hz), 6.94 (1H, t, J=7.4 Hz), 3.62 (2H, s, CH_2).

4.1.5. 1-Hexyl-4-(4-methoxyphenyl) semicarbazide. LC-MS R_f 3.699 M+H 308.2; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 9.53 (1H, br s, NH), 8.46 (1H, br s, NH), 7.87 (1H, br s, NH), 7.32 (2H, d, J=8.3 Hz, X), 6.82 (2H, d, J=8.3 Hz, X), 3.68 (3H, s, OMe), 2.11 (2H, t, J=7.4 Hz, H_X-1), 1.52 (2H, m, H_X-2), 1.13 (8H, m), 0.84 (3H, t, J=7.2 Hz, H_X-7); ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 172.58 (C), 156.00 (C), 154.83 (C), 133.06 (C), 120.55 (CH), 114.19 (CH), 55.50 (CH_3), 33.57 (CH_2), 31.54 (CH_2), 28.95 (CH_2), 28.83 (CH_2), 25.27 (CH_2), 22.42 (CH_2), 14.29 (CH_3).

4.1.6. 1-Pentyl-4-(4-methoxyphenyl)semicarbazide. LC-MS R_f 2.622 M+H 299.1; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 9.84 (1H, br s, NH), 7.95 (1H, br s, NH), 7.90 (1H, br s, NH), 7.64 (2H, d, J=8.8 Hz, H_X-2/6), 7.06 (3H, m, H_Y-3/4/5), 6.57 (2H, d, J=8.8 Hz, H_X-3/5), 5.64 (2H, s, NH_2), 2.20 (6H, s, 2×Me).

4.1.7. 1-Nicotinoyl-4-(3-chloropropane)semicarbazide. LC-MS R_f 1.025 M+H 257.0; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 10.32 (1H, br s, NH), 9.05 (1H, br s, NH), 8.72 (1H, br s, NH), 8.22 (1H, dt, J=7.7, 1.6 Hz, X), 7.95 (1H, s, X), 7.53 (1H, dd, J=X Hz, X), 6.72 (1H, br s, X), 3.62 (2H, t, J=6.6 Hz, H_Y-3), 3.15 (2H, dt, J=6.6, 6.0 Hz, H_Y-1), 1.85 (3H, tt, J=6.6, 6.0 Hz, H_Y-2).

4.1.8. 1-(4-Nitrobenzoyl)-4-(4-methoxyphenyl)semicarbazide. LC-MS R_f 2.990 M+H 331.1; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 10.58 (1H, br s, NH), 8.72 (1H, br s, NH), 8.31 (2H, d, J=8.8 Hz, H_X-3/5), 8.21 (1H, br s, NH), 8.12 (2H, d, J=8.8 Hz, H_X-2/6), 7.35 (2H, d, J=8.8 Hz, H_Y-2/6), 6.83 (2H, d, J=8.8 Hz, H_Y-3/5), 3.70 (3H, s, OMe).

4.1.9. 1-(Propan-3-ol)-4-(4-methoxyphenyl)semicarbazide. LC-MS R_f 1.630 M+H 250.1; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 9.53 (1H, br s, NH), 8.48 (1H, br s, NH), 7.84 (1H, br s, NH), 7.32 (2H, d, J=8.7 Hz, X), 6.82 (2H, d, J=8.7 Hz, H_Y-3/5), 3.69 (3H, s, OMe), 3.41 (2H, m, H_X-3), 2.17 (2H, t, J=7.5 Hz, H_X-1), 1.69 (2H, m, H_X-2).

4.1.10. 1-(3-Hydroxynaphthoyl-2-)-4-(2,6-dimethylphenyl)semicarbazide 45. LC-MS (Method B) R_f 4.00 M+H 348.3; ^{1}H NMR (d_6-DMSO; 600 MHz) δ ppm 11.52 (1H, br s, OH), 10.58 (1H, br s, NH), 8.53 (1H, br s, NH), 8.38 (1H, br s, NH), 8.11 (1H, s), 7.87 (1H, d, J=8.4 Hz), 7.73 (1H, d, J=8.4 Hz), 7.50 (1H, m), 7.35 (1H, m), 7.26 (1H, s), 7.04 (3H, m), 2.20 (6H, s, 2×Me).

4.1.11. 1-Nicotinoyl-4-*tert*-butyl semicarbazide. LC-MS (Method B) R_f 2.60 M−H 236.4; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 10.26 (1H, br s, NH), 9.03 (1H, d, J=2.2 Hz, H_X-2), 8.73 (1H, dd, J=4.7, 1.8 Hz, H_X-4), 8.21 (1H, dt, J=8.05, 1.8 Hz, H_X-6), 7.72 (1H, br s, NH), 7.52 (1H, dd, J=8.05, 4.7 Hz, H_X-5), 6.18 (1H, br s, NH), 1.24 (9H, s, 3×Me).

4.1.12. 1-Nicotinoyl-4-hexyl semicarbazide. LC-MS R_f 2.443 M+H 265.2; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 10.30 (1H, br s, NH), 9.05 (1H, d, J=1.8 Hz, H_X-2), 8.72 (1H, dd, J=4.8, 1.8 Hz, H_X-4), 8.22 (1H, dt, J=8.05, 1.8 Hz, H_X-6), 7.88 (1H, br s, NH), 7.53 (1H, ddd, J=8.05, 4.8, 0.7 Hz, H_X-5), 6.56 (1H, t, J=5.12 Hz, NH), 3.02 (2H, m, H_Y-1), 1.39 (2H, m, H_Y-2), 1.25 (6H, m), 1.24 (3H, t, J=7.3 Hz, Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 165.30 (C), 158.54 (C), 152.49 (CH), 148.94 (CH), 135.68 (CH), 128.84 (C), 123.82 (CH), 39.60 (CH_2), 31.42 (CH_2), 30.18 (CH_2), 26.34 (CH_2), 22.44 (CH_2), 14.29 (CH_3).

4.1.13. 1-Methyl-4-(adamantane)thiosemicarbazide. LC-MS R_f 3.004 M+H 268.1; ^{1}H NMR (d_6-DMSO;

600 MHz) δ ppm 9.64 (1H, br s, NH), 8.92 (1H, br s, NH), 7.06 (1H, br s, NH), 2.18 (6H, m), 1.98 (3H, m), 1.85 (3H, s, H_Z-Me), 1.60 (6H, m); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 186.76 (C), 170.50 (C), 41.32 (CH_2), 36.35 (CH_2), 29.43 (CH), 29.41 (CH), 21.07 (CH_3).

4.1.14. 1-(3-Methoxyphenyl)-4-(3-nitro-4-fluorophenyl)-semicarbazide. LC-MS R_f 2.727 M+H 315.1; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 10.29 (1H, br s, NH), 9.34 (1H, br s, NH), 8.50 (1H, br s, NH), 8.40 (1H, dd, J=6.8, 2.7 Hz), 7.84 (1H, m), 7.51–7.47 (3H, m), 7.45 (1H, t, J=7.9 Hz), 7.14 (1H, m), 3.81 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 166.59 (C), 159.55 (C), 148.69 (C), 137.13 (C), 137.10 (C), 136.65 (C), 134.25 (C), 129.91 (CH), 120.22 (CH), 118.98 (CH), 118.77 (CH), 118.09 (CH), 115.17 (CH), 113.09 (CH), 55.70 (CH_3).

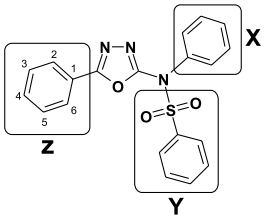
4.1.15. 1-(3,4-Dimethoxyphenylmethylene)-4-ethyl semicarbazide. LC-MS R_f 1.966 M+H 282.1; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 9.64 (1H, br s, NH), 7.70 (1H, br s, NH), 6.90 (1H, br s, NH), 6.85 (1H, d, J=8.2 Hz), 6.78 (1H, d, J=8.2 Hz), 6.26 (1H, m), 3.72 (3H, s, OMe), 3.69 (3H, s, OMe), 3.34 (2H, s, CH_2Ph), 3.05 (2H, m, H_Y-1), 0.93 (3H, t, J=7.05 Hz, H_Y-2); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 170.55 (C), 158.30 (C), 148.78 (C), 147.83 (C), 128.54 (C) 121.69 (CH), 113.25 (CH), 112.02 (CH), 55.87 (CH_3), 55.73 (CH_3), 40.12 (CH_2), 34.35 (CH_2), 15.86 (CH_3).

4.2. General procedure for 1

A mixture of acylhydrazide **3** (0.5 mmol) and isocyanate **4** (1 equiv) in CH_3CN (5 mL) in a microwave tube was stirred for 5 min. PS-BEMP (4.3 equiv, 2.2 mmol/g from Fluka) and sulfonylchloride (2.3 equiv) were added and the reaction was irradiated in a microwave apparatus at 150 °C for 20 min. After cooling to room temperature in the microwave cavity the reaction mixture was purified on silica cartridge using DCM (15 mL) as eluent. The organic solvent were evaporated and the residue precipitated with Et_2O or iPr$_2$O.

4.3. General procedure for 2

A mixture of acylhydrazide **3** (0.5 mmol) and isocyanate **4** (1 equiv) in THF (5 mL) in a microwave tube was stirred for 5 min. PS-DMAP (3 equiv, 2.2 mmol/g from Fluka) and TsCl (1.8 equiv) were added and the reaction was irradiated in a microwave apparatus at 120 °C for 30 min. After cooling to room temperature in the microwave cavity the reaction mixture was purified on SCXII cartridge.



4.3.1. (5-Phenyl-[1,3,4]oxadiazol-2-yl)-4-methylbenzeneamine 35. LC-MS R_f 3.028 M+H 252.1; ^{1}H NMR ($CDCl_3$; 600 MHz) δ ppm 9.64 (1H, br s, NH), 8.81 (2H, m, H_Z-2/6), 7.37 (5H, m, H_Z-3/4/5 and H_X-3/4), 6.92 (2H, d, J=8.3 Hz, H_X-2/6), 2.11 (3H, s, H_X-Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 135.94 (C), 133.56 (C), 131.59 (C), 130.51 (CH), 129.44 (CH), 128.79 (CH), 125.68 (CH), 124.28 (C), 117.59 (CH), 95.23 (C), 20.57 (CH_3). IR ν (neat)=3292 (w), 3045.1 (w), 1610.8 (s), 1580.3 (s), 1556.9 (m), 1543.3 (m), 1516.5 (m), 1488.4 (m), 1446.8 (w), 1417.4 (w), 1321.4 (w), 1298.8 (w), 1287.0 (w), 1244.0 (w), 1231.1 (w), 1127.6 (w), 1067.4 (w), 1049.7 (m), 1024.4 (m), 958.9 (w), 866.8 (w), 817.3 (s), 797.6 (m), 767.2 (s), 718.8 (s), 680.6 (s) cm^{-1}. HRMS Calcd for $C_{15}H_{14}N_3O$ 252.1137; found 252.1139. Anal. ($C_{15}H_{13}N_3O$) Calcd C 71.70, H 5.21, N 16.72, O 6.37; found C 71.79, H 5.20, N 16.77, O 6.24. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre under the deposition number 252367.

4.3.2. 4-Methyl-*N*-(5-phenyl-[1,3,4]oxadiazol-2-yl)-*N*-4-methylbenzenesulfonamide 36. LC-MS R_f 3.559 M+H 406.1; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 7.88 (2H, m, H_Z-2/6), 7.77 (2H, d, J=8.4 Hz, H_Y-2/6), 7.64–7.55 (3H, m), 7.51 (2H, m), 7.26 (2H, d, J=8.6 Hz), 7.21 (2H, d, J=8.6 Hz), 2.43 (3H, s, Me), 2.31 (3H, s, Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 163.38 (C), 158.66 (C), 146.02 (C), 140.06 (C), 134.08 (CH), 133.10 (C), 131.88 (C), 130.98 (CH), 130.48 (CH), 129.87 (CH), 128.82 (CH), 128.77 (CH), 126.68 (CH), 123.21 (C), 21.55 (CH_3), 21.05 (CH_3). IR ν (neat)=1596.1 (w), 1564.1 (s), 1542.4 (m), 1506.9 (m), 1490.1 (m), 1449.4 (m), 1361.2 (s), 1294.7 (w), 1266.9 (m), 1208.0 (m), 1190.0 (m), 1167.2 (s), 1021.8 (m), 965.9 (m), 957.7 (m), 936.3 (s), 815.1 (s), 777.0 (m), 711.0 (s), 685.9 (s), 666.5 (s) cm^{-1}. HRMS Calcd for $C_{22}H_{20}N_3O_3S$ 406.1225; found 406.1220. Anal. ($C_{22}H_{19}N_3O_3S$) Calcd C 65.17, H 4.72, N 10.36, O 11.84, S 7.91; found C 65.29, H 4.88, N 10.21. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre under the deposition number 252366.

4.3.3. 5-Phenyl-4-*p*-tolyl-2,4-dihydro-[1,2,4]triazol-3-one 43. MS R_f 3.721 M+H 252.10; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 7.41–7.24 (5H, m, Ph), 7.19 (2H, d, J=8.05 Hz, H_Y-3/5), 7.08 (2H, d, J=8.05 Hz, H_Y-2/6), 2.33 (3H, s, Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 155.01 (C), 145.77 (C), 138.38 (C), 131.53 (C), 130.13 (CH), 130.09 (CH), 128.86 (C), 127.92 (CH), 127.85 (CH), 127.53 (C), 21.04 (CH_3). IR ν (neat)=3151.7 (w), 3040.0 (w), 1692.5 (s), 1579.2 (w), 1550.9 (w), 1514.8 (m), 1494.3 (w), 1448.4 (m), 1417.3 (m), 1328.4 (m), 1180.1 (w), 1141.8 (w), 1108.5 (w), 1039.9 (w), 967.4 (w), 939.0 (w), 803.7 (m), 776.2 (s), 745.6 (s), 696.6 (s), 676.8 (w) cm^{-1}. HRMS Calcd for $C_{15}H_{14}N_3O$ 252.1137; found 252.1144. Anal. ($C_{15}H_{13}N_3O$) Calcd C 71.70, H 5.21, N 16.72, O 6.37; found C 71.67, H 5.23, N 16.78, O 6.31. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre under the deposition number 252368.

4.3.4. 5-Phenyl-2-(toluene-4-sulfonyl)-4-*p*-tolyl-2,4-dihydro-[1,2,4]triazol-3-one 44. MS R_f 2.987 M+H 406.1; ^{1}H NMR (d_6-DMSO; 400 MHz) δ ppm 7.94 (2H, d, J=8.05 Hz), 7.52 (2H, d, J=8.05 Hz), 7.44 (1H, m), 7.39–7.30 (4H, m), 7.30–7.15 (4H, m), 2.41 (3H, s, Me), 2.28 (3H, s, Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 150.68 (C),

148.36 (C), 146.56 (C), 139.45 (C), 134.20 (C), 131.40 (CH), 130.73 (CH), 130.27 (CH), 130.19 (C), 128.95 (CH), 128.69 (CH), 128.19 (CH), 128.08 (CH), 125.69 (C), 21.58 (CH_3), 21.05 (CH_3). IR ν (neat)=1739.1 (s), 1593.1 (w), 1548.0 (w), 1515.4 (m), 1496.7 (m), 1450.5 (m), 1386.1 (s), 1318.4 (m), 1207.6 (s), 1191.9 (s), 1175.5 (s), 1149.8 (m), 1091.4 (m), 1073.7 (w), 963.1 (m), 846.7 (w), 823.0 (m), 785.2 (m), 739.0 (s), 692.7 (s), 661.6 (s) cm^{-1}. HRMS Calcd for $C_{22}H_{20}N_3O_3S$ 406.1225; found 406.1229. ($C_{22}H_{19}N_3O_3S$) Calcd C 65.17, H 4.72, N 10.36, O 11.84, S 7.91; found C 65.20, H 4.78, N 10.42. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre under the deposition number 252365.

4.3.5. Benzyl-[5-(4-bromo-2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]amine 47. ^{1}H NMR ($CDCl_3$; 400 MHz) δ ppm 8.04 (1H, d, J=2.6 Hz, H_Z-6), 7.50 (1H, dd, J=8.4, 2.6 Hz, H_Z-Ar), 7.45–7.30 (6H, m, H_Z-Ar/H_X-Ph), 5.12 (1H, t, J=5.6 Hz, NH), 4.63 (2H, d, J=5.6 Hz, H_X-1).

4.3.6. Ethyl-[5-(4-nitrophenyl)-[1,3,4]oxadiazol-2-yl]-amine 48. LC-MS R_f 2.926 M+H 235.1; ^{1}H NMR ($CDCl_3$; 400 MHz) δ ppm 8.32 (2H, d, J=9.15 Hz, H_Z-3/5), 8.08 (2H, d, J=9.15 Hz, H_Z-2/6), 4.80 (1H, br t, NH), 3.53 (2H, dq, J=7.1, 5.8 Hz, H_X-1), 1.34 (3H, t, J=7.1 Hz, H_X-2).

4.3.7. Phenethyl-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-amine 49. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 9.05 (1H, d, J=1.6 Hz, H_Z-2), 8.82 (1H, d, J=4.7, 1.6 Hz, H_Z-4), 8.26 (1H, ddd, J=7.9, 2.2, 1.9 Hz, H_Z-6), 7.66 (1H, ddd, J=7.9, 4.7, 1.6 Hz, H_Z-5), 7.24 (5H, m, H_X-Ph), 4.12 (2H, t, J=7.25 Hz, H_X-1), 3.05 (2H, t, J=7.25 Hz, H_X-2); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.05 (C), 158.77 (C), 153.04 (CH), 147.34 (CH), 142.66 (CH), 137.82 (C), 135.77 (C), 134.34 (CH), 130.75 (CH), 129.37 (CH), 128.88 (CH), 35.10 (CH_2), 31.15 (CH_2). IR ν (neat)=1675.8 (m), 1632.3 (w), 1585.2 (m), 1568.1 (m), 1545.3 (m), 1370.2 (m), 1199.9 (s), 1165.0 (s), 1128.9 (s), 1023.9 (m), 1006.7 (m), 822.9 (m), 799.2 (m), 757.6 (s), 720.0 (s), 701.1 (s), 683.3 (s) cm^{-1}. HRMS Calcd for $C_{15}H_{15}N_4O$ 267.1246; found 267.1249.

4.3.8. [5-(4-Chlorophenyl)-[1,3,4]oxadiazol-2-yl]-ethyl-amine 50. LC-MS R_f 3.188 M+H 224.0 and 226.0; ^{1}H NMR ($CDCl_3$; 400 MHz) δ ppm 7.85 (2H, d, J=8.8 Hz, H_Z-3/5), 7.43 (2H, d, J=8.8 Hz, H_Z-2/6), 4.96 (1H, br s, NH), 3.49 (2H, dq, J=7.3, 5.8 Hz, H_X-1), 1.34 (3H, t, J=7.3 Hz, H_X-2).

4.3.9. Phenethyl-[5-(4-trifluoromethylphenyl)-[1,3,4]-oxadiazol-2-yl]amine 51. LC-MS R_f 3.697 M+H 334.1; ^{1}H NMR ($CDCl_3$; 400 MHz) δ ppm 8.02 (2H, d, J=8.05 Hz, H_Z-3/5), 7.73 (2H, d, J=8.05 Hz, H_Z-2/6), 7.34 (2H, m, H_X-Ph), 7.25 (3H, m, H_X-Ph), 4.96 (1H, t, J=6.4 Hz, NH), 3.76 (2H, dt, J=7.3, 6.4 Hz, H_X-1), 3.02 (2H, t, J=7.3 Hz, H_X-2).

4.3.10. (3,4-Dichlorophenyl)-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)amine 52. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 11.20 (1H, br s, NH), 9.08 (1H, dd, J=2.2, 0.6 Hz, H_Z-2), 8.76 (1H, dd, J=4.7, 1.6 Hz, H_Z-4), 8.27 (1H, dt, J=8.2, 1.9 Hz, H_Z-6), 7.95 (1H, d, J=2.5 Hz, H_X-2), 7.63 (1H, d, J=8.8 Hz, H_X-5), 7.62 (1H, ddd, J=8.2, 4.7, 0.95 Hz, H_Z-5), 7.55 (1H, dd, J=8.8, 2.5 Hz, H_X-6); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 160.15 (C), 156.78 (C), 152.19 (C), 146.85 (CH), 139.09 (C), 133.70 (CH), 131.88 (C), 131.49 (CH), 124.18 (CH), 123.98 (C), 120.69 (C), 118.82 (CH), 117.93 (CH). IR ν (neat)=1634.4 (s), 1610.8 (m), 1588.5 (s), 1571.4 (m), 1556.9 (m), 1549.5 (m), 1477.1 (s), 1401.9 (m), 1302.2 (w), 1250.2 (w), 1135.1 (w), 1058.2 (m), 1027.9 (m), 957.4 (m), 867.8 (m), 813.7 (m), 797.5 (s), 700.5 (s), 681.9 (m), 674.3 (m) cm^{-1}. HRMS Calcd for $C_{13}H_9N_4OCl_2$ 307.0153; found 307.0145.

4.3.11. *N*-[5-(2-Chlorophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-(2,6-dimethylphenyl)-4-nitro-benzenesulfonamide 53. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 8.56 (2H, d, J=9.1 Hz, H_Y-3/5), 8.42 (2H, d, J=9.1 Hz, H_Y-2/6), 7.84 (1H, d, J=7.6, 1.6 Hz, H_Z-Ar), 7.63 (2H, m, 2×H_Z-Ar), 7.55 (1H, m, H_Z-Ar), 7.36 (1H, t, J=7.6 Hz, H_X-4), 7.26 (2H, d, J=7.6 Hz, H_X-3/5), 2.10 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 160.74 (C), 158.20 (C), 151.55 (C), 143.07 (C), 134.10 (C), 134.20 (C), 133.92 (CH), 132.14 (C), 131.77 (CH), 131.49 (CH), 131.19 (CH), 130.79 (CH), 129.85 (CH), 128.40 (CH), 125.42 (CH), 122.40 (C), 18.53 (CH_3). IR ν (neat)=1630.2 (m), 1606.9 (w), 1556.8 (m), 1530.1 (s), 1515.6 (s), 1488.1 (w), 1449.1 (w), 1404.8 (w), 1384.0 (s), 1347.4 (s), 1318.2 (w), 1304.9 (w), 1278.9 (m), 1196.1 (w), 1176.8 (s), 1165.2 (s), 1110.9 (m), 1084.1 (m), 1010.2 (m), 928.8 (m), 905.8 (m), 888.3 (s), 861.6 (s), 853.9 (s), 769.2 (m), 758.9 (m), 738.6 (s), 695.1 (s), 679.9 (s) cm^{-1}. HRMS Calcd for $C_{22}H_{17}N_4O_5SCl$ 485.0686; found 485.0702.

4.3.12. 3,4-Dimethoxy-*N*-[5-(3,4-dimethoxyphenyl)-[1,3,4]oxadiazol-2-yl]-*N*-phenyl-benzenesulfonamide 54. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 7.52–7.45 (3H, m), 7.38 (1H, dd, J=2.5, 1.6 Hz), 7.31 (1H, d, J=2.5 Hz), 7.23 (1H, d, J=8.8 Hz), 7.20 (1H, ddd, J=8.2, 2.5, 0.95 Hz), 7.02 (2H, d, J=9.1 Hz), 3.90 (3H, s, OMe), 3.85 (3H, s, OMe), 3.80 (3H, s, OMe), 3.79 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 163.21 (C), 160.53 (C), 160.13 (C), 159.08 (C), 154.30 (C), 149.18 (C), 131.29 (CH), 130.81 (CH), 129.11 (C), 128.02 (C), 124.53 (C), 123.34 (CH), 119.04 (CH), 118.59 (CH), 115.30 (CH), 111.88 (CH), 111.61 (CH), 111.02 (CH), 56.53 (CH_3), 56.26 (CH_3), 55.99 (CH_3), 55.92 (CH_3). IR ν (neat)=1604.9 (w), 1586.8 (w), 1560.3 (m), 1542.6 (m), 1508.4 (s), 1491.9 (s), 1462.4 (m), 1445.5 (w), 1436.9 (w), 1411.7 (w), 1364,2 (s), 1346.5 (w), 1320.8 (w), 1267.4 (s), 1250.8 (m), 1232.6 (s), 1202.4 (m), 1183.8 (m), 1163.6 (s), 1137.8 (m), 1096.3 (m), 1071.3 (w), 1030.2 (s), 1017.8 (s), 990.6 (w), 951.4 (m), 925.9 (m), 873.5 (w), 852.3 (s), 833.0 (w), 797.4 (m), 767.4 (w), 723.0 (m), 700.2 (m), 674.7 (s) cm^{-1}. HRMS Calcd for $C_{24}H_{24}N_3O_7S$ 498.1335; found 498.1345.

4.3.13. 4-Nitro-*N*-[5-(2-nitrophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-phenyl-benzenesulfonamide 55. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 8.51 (2H, d, J=9.1 Hz, H_Y-3/5), 8.19 (1H, m, H_Z-5), 8.16 (2H, d, J=9.1 Hz, H_Y-2/6), 7.99–7.90 (3H, m, H_Z-3/4/6), 7.54 (3H, m, 3×H_X-Ar), 7.38 (2H, m, 2×H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 160.13 (C), 158.92 (C), 151.47 (C), 148.07 (C), 141.95 (C), 135.86 (C), 134.40 (CH), 134.21 (CH), 132.00 (CH), 130.90 (CH), 130.66 (CH), 130.58 (CH), 129.31 (CH),

125.44 (CH), 125.40 (CH), 116.98 (C). IR ν (neat)=1608.2 (w), 1573.0 (w), 1557.4 (m), 1529.3 (s), 1486.8 (w), 1405.2 (w), 1382.7 (m), 1365.4 (w), 1342.1 (s), 1315.7 (w), 1273.8 (m), 1200.9 (m), 1177.1 (s), 1085.8 (w), 1021.8 (w), 963.3 (w), 942.6 (m), 913.0 (w), 854.7 (s), 789.4 (m), 738.5 (s), 711.1 (m), 697.4 (s), 680.4 (s), 654.8 (s) cm^{-1}. HRMS Calcd for $C_{20}H_{14}N_5O_7S$ 468.0614; found 468.0700.

4.3.14. 3,4-Dimethoxy-*N*-phenyl-*N*-(5-phenyl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 56. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.90 (2H, m), 7.62 (3H, m), 7.50 (4H, m), 7.38 (2H, m), 7.29 (1H, d, J=2.5 Hz), 7.23 (1H, d, J=8.8 Hz), 3.90 (3H, s, OMe), 3.88 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 163.51 (C), 158.81 (C), 154.36 (C), 149.17 (C), 136.83 (C), 132.73 (CH), 130.24 (CH), 129.94 (CH), 129.92 (C), 129.12 (CH), 127.92 (C), 126.78 (CH), 123.37 (CH), 123.35 (CH), 111.94 (CH), 111.01 (CH), 56.55 (CH_3), 56.25 (CH_3). IR ν (neat)=1592.4 (w), 1568.1 (w), 1536.9 (s), 1508.4 (s), 1490.8 (m), 1470.3 (w), 1452.5 (w), 1439.3 (w), 1414.3 (s), 1366.5 (m), 1281.9 (m), 1264.0 (s), 1242.6 (m), 1182.8 (w), 1167.1 (s), 1143.5 (m), 1092.1 (s), 1019.3 (s), 964.3 (w), 946.0 (w), 916.6 (w), 887.6 (w), 846.5 (w), 819.5 (w), 767.9 (w), 717.7 (m), 699.2 (m), 691.9 (s), 685.5 (s), 675.6 (s), 654.5 (w) cm^{-1}. HRMS Calcd for $C_{22}H_{20}N_3O_5S$ 438.1124; found 438.1113.

4.3.15. *N*-(4-Methoxy-phenyl)-4-nitro-*N*-[5-(4-nitrophenyl)-[1,3,4]oxadiazol-2-yl]-benzenesulfonamide 57. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.52 (2H, d, J=8.5 Hz, H_Y-3/5), 8.39 (2H, d, J=8.8 Hz, H_Z-3/5), 8.21 (2H, d, J=8.5 Hz, H_Y-2/6), 8.10 (2H, d, J=8.8 Hz, H_Z-2/6), 7.33 (2H, d, J=8.7 Hz, H_X-2/6), 7.04 (2H, d, J=8.7 Hz, H_X-3/5), 3.79 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.79 (C), 160.80 (C), 159.03 (C), 151.34 (C), 149.64 (C), 143.52 (C), 141.95 (C), 130.95 (CH), 130.66 (CH), 128.10 (CH), 128.04 (C), 125.30 (CH), 125.02 (CH), 115.49 (CH), 55.97 (CH_3). IR ν (neat)=1606.4 (w), 1555.9 (w), 1542.2 (w), 1531.6 (s), 1519.1 (s), 1506.1 (s), 1448.5 (w), 1379.8 (m), 1341.5 (s), 1314.8 (m), 1305.0 (m), 1255.9 (s), 1195.3 (w), 1170.5 (s), 1110.8 (m), 1101.1 (w), 1057.5 (m), 1034.8 (m), 1009.5 (m), 914.8 (w), 897.9 (w), 854.0 (s), 831.8 (w), 739.3 (s), 716.4 (w), 703.8 (m), 680.5 (m) cm^{-1}. HRMS Calcd for $C_{21}H_{17}N_5O_8S$ 498.0720; found 498.0773.

4.3.16. *N*-[5-(2-Chlorophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-(2,6-dimethylphenyl)benzenesulfonamide 58. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.16 (2H, dd, J=8.5, 1.3 Hz, H_Y-2/6), 7.88 (2H, m), 7.77 (2H, m), 7.64 (2H, m), 7.54 (1H, m), 7.32 (1H, m), 7.23 (2H, X, m), 2.09 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 160.49 (C), 158.60 (C), 139.00 (C), 138.13 (C), 135.63 (CH), 134.58 (C), 133.86 (CH), 132.10 (C), 131.73 (CH), 131.48 (CH), 130.51 (CH), 130.22 (CH), 129.72 (CH), 129.25 (CH), 128.40 (CH), 122.55 (C), 18.41 (CH_3). IR ν (neat)=1581.0 (m), 1566.9 (s), 1532.4 (w), 1448.8 (m), 1363.6 (s), 1289.9 (m), 1278.7 (w), 1195.4 (w), 1179.7 (s), 1088.5 (m), 1027.0 (w), 966.9 (w), 943.5 (m), 900,4 (w), 777.7 (m), 728.2 (s), 718.8 (m), 684.0 (s) cm^{-1}. HRMS Calcd for $C_{22}H_{19}N_3O_3SCl$ 440.0836; found 440.0840.

4.3.17. *N*-Phenyl-*N*-[5-(4-trifluoromethylphenyl)-[1,3,4]-oxadiazol-2-yl]benzenesulfonamide 59. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.13–7.71 (9H, m), 7.58–7.34 (6H, m); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.35 (C), 159.04 (C), 136.97 (C), 136.41 (C), 135.45 (CH), 130.46 (CH), 130.31 (CH), 130.19 (CH), 129.96 (CH), 128.88 (CH), 127.65 (CH), 127.12 (C), 126.90 and 126.87 (CF_3). IR ν (neat)=1538.6 (s), 1492.7 (w), 1447.7 (w), 1397.7 (w), 1325.9 (s), 1284.1 (w), 1182.3 (m), 1163.7 (m), 1123.1 (m), 1092.8 (m), 1066.7 (m), 1011.7 (w), 964.1 (w), 944.7 (w), 915.3 (w), 853.6 (m), 757.5 (w), 724.6 (s), 715.8 (m), 695.0 (s), 683.0 (s) cm^{-1}. HRMS Calcd for $C_{21}H_{15}N_3O_3SF_3S$ 446.0786; found 446.0923.

4.3.18. 4-Chloro-*N*-[5-(4-methoxyphenyl)-[1,3,4]oxadiazol-2-yl]-*N*-3-methoxyphenyl-benzenesulfonamide 60. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.91 (2H, d, J=8.6 Hz, H_Y-2/6), 7.80 (2H, d, J=8.6 Hz, H_Y-3/5), 7.51 (1H, t, J=8.0 Hz, H_Z-Ar), 4.47 (1H, dt, J=8.0, 1.3 Hz, H_Z-Ar), 7.38 (1H, dd, J=2.5, 1.6 Hz, H_Z-2), 7.30 (2H, d, J=9.1 Hz, H_X-3/5), 7.21 (1H, ddd, J=8.0, 2.5, 1.3 Hz, H_Z-Ar), 7.05 (2H, d, J=9.1 Hz, H_X-2/6), 3.83 (3H, s, OMe), 3.80 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 163.39 (C), 160.68 (C), 160.10 (C), 158.68 (C), 140.39 (C), 135.75 (C), 131.29 (CH), 130.80 (CH), 130.32 (CH), 128.59 (C), 124.43 (C), 119.12 (CH), 118.68 (CH), 115.47 (CH), 111.62 (CH), 56.00 (CH_3), 55.90 (CH_3). IR ν (neat)=1563.9 (m), 1542.9 (m), 1506.6 (m), 1493.8 (m), 1381.8 (s), 1368.9 (m), 1277.7 (w), 1250.5 (m), 1234.1 (m), 1182.9 (w), 1171.1 (s), 1089.4 (m), 1028.4 (m), 956.9 (w), 935.0 (w), 847.7 (w), 792.8 (w), 756.3 (s), 721.5 (m), 705.3 (m), 686.4 (w) cm^{-1}. HRMS Calcd for $C_{22}H_{19}N_3O_5SCl$ 472.0734; found 472.0558.

4.3.19. 4-Chloro-*N*-phenyl-*N*-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 61. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 9.08 (1H, d, J=1.6 Hz, H_Z-2), 8.81 (1H, dd, J=5.0, 1.6 Hz, H_Z-4), 8.24 (1H, dt, J=7.9, 1.6 Hz, H_Z-6), 7.92 (2H, d, J=8.8 Hz, H_Y-2/6), 7.80 (2H, d, J=8.8 Hz, H_Y-3/5), 7.63 (1H, ddd, J=7.9, 5.0, 0.95 Hz, H_Z-5), 7.52 (3H, m, H_X-Ar), 7.40 (2H, m, H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.88 (C), 158.78 (C), 153.17 (CH), 147.50 (CH), 140.53 (C), 136.27 (C), 135.66 (C), 134.55 (CH), 130.87 (CH), 130.58 (CH), 130.41 (CH), 130.39 (CH), 129.24 (CH), 124.82 (CH), 120.03 (C). IR ν (neat)=1608.1 (w), 1579.3 (w), 1561.2 (w), 1532.6 (s), 1487.7 (w), 1476.5 (w), 1401.0 (s), 1382.2 (m), 1370.3 (m), 1294.7 (m), 1198.8 (m), 1177.5 (s), 1098.6 (s), 1082.6 (m), 1056.6 (m), 1019.7 (w), 1012.5 (w), 960.8 (m), 916.7 (w), 889.8 (w), 822.0 (w), 753.6 (s), 721.0 (m), 705.4 (m), 693.0 (s), 668.1 (m) cm^{-1}. HRMS Calcd for $C_{19}H_{13}N_4O_3SCl$ 413.0475; found 413.0507.

4.3.20. 4-Iodo-*N*-phenyl-*N*-(5-phenyl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 62. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.12 (2H, d, J=8.85 Hz, H_Y-2/6), 7.90 (2H, d, J=6.9 Hz, H_Z-2/6), 7.64 (2H, d, J=8.85 Hz, H_Y-3/5), 7.58 (3H, m, H_Z-3/4/5), 7.51 (3H, m, 3×H_X-Ar), 7.39 (2H, m, 2×H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 163.61 (C), 158.42 (C), 139.13 (CH), 136.54 (C), 136.37 (C), 132.76 (CH), 130.49 (CH), 130.41 (CH), 130.30 (CH), 129.95 (CH), 129.15 (CH), 126.83 (CH), 123.25 (C). IR ν (neat)=1593.6 (w), 1566.9 (s), 1536.9 (s), 1488.6 (s), 1455.2 (w), 1411.4 (m), 1385.2 (m), 1371.1 (m), 1279.1 (m), 1188.0 (m), 1170.1 (s), 1093.1 (m), 1052.1 (m), 1025.6 (m), 1004.1 (s), 961.9 (m), 942.9 (m), 915.5 (m), 888.3 (m),

816.1 (s), 734.4 (s), 715.3 (s), 684.9 (m) cm^{-1}. HRMS Calcd for $C_{20}H_{15}N_3O_3SI$ 503.9879; found 503.9961.

4.3.21. *N*-[5-(*N*,*N*-Dibenzenesulfonamide-4-aminophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-(3-chlorophenyl)benzenesulfonamide 63. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.98–7.93 (4H, m), 7.89–7.82 (7H, m), 7.77–7.69 (6H, m), 7.62 (1H, ddd, $J=8.2$, 2.3, 1.0 Hz), 7.54 (1H, t, $J=8.2$ Hz), 7.50 (1H, t, $J=1.9$ Hz), 7.37 (1H, t, $J=8.2$, 1.9, 0.95 Hz), 7.27 (2H, d, $J=7.5$); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.60 (C), 158.57 (C), 138.66 (C), 137.54 (C), 136.83 (C), 136.63 (C), 135.68 (CH), 135.43 (CH), 134.13 (C), 132.99 (CH), 131.82 (CH), 130.57 (CH), 130.33 (CH), 130.20 (CH), 129.18 (CH), 128.94 (CH), 128.53 (CH), 128.07 (CH), 128.00 (CH), 125.20 (C). IR ν (neat)= 1608.9 (w), 1581.9 (w), 1566.1 (m), 1544.6 (m), 1477.6 (m), 1447.9 (m), 1380.1 (s), 1361.7 (s), 1301.7 (w), 1281.0 (w), 1261.1 (m), 1208.1 (w), 1161.0 (s), 1089.7 (s), 956.2 (m), 958.0 (m), 912.5 (s), 820.5 (m), 795.9 (m), 762.9 (m), 753.1 (m), 718.9 (s), 693.8 (m), 681.2 (s) cm^{-1}. HRMS Calcd for $C_{32}H_{23}N_4O_7S_3Cl$ 707.0496; found 707.0684.

4.3.22. *N*-(3-Chlorophenyl)-*N*-[5-(4-chlorophenyl)-[1,3,4]oxadiazol-2-yl]benzenesulfonamide 64. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.93 (2H, d, $J=8.2$ Hz, H_Y-2/6), 7.90 (2H, d, $J=8.5$ Hz, H_Z-2/6), 7.86 (1×H, m, H_Y-4), 7.73 (2H, m, H_Y-3/5), 7.66 (2H, d, $J=8.5$ Hz, H_Z-3/5), 7.61 (1H, ddd, $J=8.2$, 1.9, 1.0 Hz, H_X-Ar), 7.53 (1H, t, $J=8.2$ Hz, H_X-5), 7.49 (1H, t, $J=1.9$ Hz, H_X-2), 7.36 (1H, ddd, $J=8.2$, 1.9, 1.0 Hz, H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.85 (C), 158.31 (C), 137.52 (C), 137.47 (C), 136.65 (C), 135.64 (CH), 134.13 (C), 131.81 (CH), 130.57 (CH), 130.29 (CH), 130.13 (CH), 129.19 (CH), 128.92 (CH), 128.64 (CH), 127.99 (CH), 122.23 (C). IR ν (neat)=1623.5 (w), 1589.4 (s), 1565.6 (s), 1542.1 (s), 1482.2 (s), 1448.0 (m), 1373.4 (m), 1171.0 (s), 1090.2 (s), 1047.8 (w), 1012.8 (s), 964.0 (w), 834.7 (m), 780.8 (m), 753.5 (m), 722.7 (s), 682.3 (s) cm^{-1}. HRMS Calcd for $C_{20}H_{14}N_3O_3SCl_2$ 446.0133; found 446.0210.

4.3.23. 4-Chloro-*N*-[5-(2,4-dichlorophenoxymethyl)-[1,3,4]oxadiazol-2-yl]-*N*-ethyl-benzenesulfonamide 65. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.99 (2H, d, $J=8.8$ Hz, H_Y-2/6), 7.73 (2H, d, $J=8.8$ Hz, H_Y-3/5), 7.64 (1H, d, $J=2.5$ Hz, H_Z-5), 7.42 (1H, dd, $J=8.8$, 2.5 Hz, H_Y-7), 7.35 (1H, d, $J=8.8$ Hz, H_Y-8), 5.51 (2H, s, CH-$_2$O), 3.89 (2H, q, $J=6.9$ Hz, H_X-1), 1.22 (3H, t, $J=6.9$ Hz, H_X-2); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 160.87 (C), 158.97 (C), 152.21 (C), 140.11 (C), 136.72 (C), 130.32 (CH), 130.08 (CH), 130.05 (CH), 128.65 (C), 126.61 (CH), 123.49 (C), 116.80 (CH), 61.35 (CH_2), 46.48 (CH_2), 14.56 (CH_3). IR ν (neat)=1606.7 (w), 1554.1 (s), 1537.3 (m), 1478.9 (s), 1421.1 (m), 1381.7 (w), 1367.1 (m), 1286.9 (m), 1267.0 (m), 1244.0 (m), 1228.7 (m), 1176.4 (s), 1166.9 (s), 1093.8 (m), 1085.0 (m), 1058.1 (m), 1024.8 (m), 882.7 (m), 824.9 (m), 805.0 (s), 766.9 (s), 757.2 (s), 724.2 (m) cm^{-1}. HRMS Calcd for $C_{17}H_{16}N_3O_4SCl_2$ 428.0239; found 428.0241.

4.3.24. 4-Methoxybenzenesulfonic acid 3-{5-[(2,6-dimethylphenyl)-(4-methoxybenzenesulfonyl)-amino]-[1,3,4]oxadiazol-2-yl}naphthalen-2-yl ester 66. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.38 (1H, s), 8.12 (1H, d, $J=7.6$ Hz), 8.10 (2H, d, $J=8.9$ Hz), 8.04 (1H, d, $J=7.9$ Hz), 7.91 (1H, s), 7.72–7.64 (2H, m), 7.44 (2H, d, $J=8.9$ Hz), 7.34 (1H, dd, $J=8.2$, 6.9 Hz), 7.27 (2H, d, $J=9.14$ Hz), 7.25 (2H, m), 6.92 (2H, d, $J=9.1$ Hz), 3.90 (3H, s, OMe), 3.80 (3H, s, OMe), 2.17 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 164.68 (C), 164.66 (C), 159.66 (C), 158.68 (C), 142.81 (C), 139.16 (C), 134.64 (C), 134.47 (C), 132.09 (CH), 131.83 (CH), 131.13 (C), 130.89 (CH), 130.44 (CH), 129.78 (CH), 129.75 (CH), 129.53 (C), 129.20 (CH), 128.37 (CH), 124.96 (C), 122.61 (CH), 116.44 (C), 115.33 (CH), 115.23 (CH), 56.48 (CH_3), 56.36 (CH_3), 18.52 (CH_3). IR ν (neat)=15.93.3 (m), 1578.4 (m), 1556.8 (m), 1496.6 (m), 1442.7 (w), 1366.1 (s), 1314.4 (w), 1264.1 (s), 1194.5 (m), 1166.6 (s), 1132.9 (m), 1091.3 (s), 1027.3 (m), 959.0 (w), 938.5 (m), 912.6 (m), 824.3 (s), 803.9 (s), 775.9 (s), 763.7 (s), 715.8 (m), 685.6 (s) cm^{-1}. HRMS Calcd for $C_{34}H_{30}N_3O_8S_2$ 672.1474; found 672.1455.

4.3.25. *N*-[5-(2-Chlorophenyl)-[1,3,4]oxadiazol-2-yl]-4-nitro-*N*-phenyl-benzenesulfonamide 67. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.53 (2H, d, $J=9.1$ Hz, H_Y-3/5), 8.20 (2H, d, $J=9.1$ Hz, H_Y-2/6), 7.88 (1H, dd, $J=7.9$, 1.6 Hz, H_X-Ar), 7.68 (2H, m), 7.55 (4H, m), 7.42 (2H, m); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.55 (C), 158.55 (C), 151.46 (C), 142.08 (C), 135.96 (C), 134.00 (CH), 132.19 (C), 131.71 (CH), 131.60 (CH), 130.70 (CH), 130.55 (CH), 129.42 (CH), 128.41 (CH), 125.43 (CH), 122.34 (C). IR ν (neat)=1607.6 (w), 1566.4 (m), 1536.8 (s), 1486.8 (w), 1460.2 (w), 1404.9 (w), 1381.7 (s), 1365.1 (w), 1348.7 (s), 1317.7 (w), 1273.7 (m), 1243.6 (w), 1201.8 (m), 1175.1 (s), 1101.8 (m), 1085.6 (m), 1020.6 (m), 962.7 (m), 943.1 (m), 912.6 (m), 861.9 (m), 854.9 (m), 765.9 (m), 748.4 (w), 739.2 (s), 696.9 (m), 680.6 (s), 657.9 (s) cm^{-1}. HR-MS Calcd for $C_{20}H_{14}N_4O_5ClS$: 457.0373; found 457.0372.

4.3.26. 4-Chloro-*N*-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-(2,6-dimethylphenyl)benzenesulfonamide 68. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.19 (2H, d, $J=8.85$ Hz, H_Y-2/6), 7.85 (3H, m, H_Y-3/5/H_Z-Ar), 7.65 (2H, m, 2×H_Z-Ar), 7.53 (1H, m, H_Z-Ar), 7.35 (1H, t, $J=7.6$ Hz, H_X-4), 7.26 (2H, d, $J=7.6$ Hz, H_X-3/5), 2.12 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 160.53 (C), 158.42 (C), 140.74 (C), 138.96 (C), 136.87 (C), 134.37 (C), 133.87 (CH), 132.11 (C), 131.74 (CH), 131.47 (CH), 131.29 (CH), 130.62 (CH), 130.40 (CH), 129.77 (CH), 128.39 (CH), 122.49 (C), 18.46 (CH_3). IR ν (neat)=1578.9 (w), 1563.6 (s), 1539.0 (w), 1462.9, 1368.1 (s), 1290.7 (w), 1279.3 (m), 1167.1 (s), 1090.3 (m), 1079.5 (m), 1024.1 (w), 932.4 (m), 839.8 (m), 828.9 (m), 783.1 (w), 753.2 (s), 728.0 (m), 705.3 (m), 692.9 (m) cm^{-1}. HR-MS Calcd for $C_{22}H_{18}N_3O_3SCl_2$: 474.0446; found 474.0467.

4.3.27. 4-Chloro-*N*-(3-chlorophenyl)-*N*-[5-(4-nitrophenyl)-[1,3,4]oxadiazol-2-yl]-benzenesulfonamide 69. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.40 (2H, d, $J=9.1$ Hz, H_Z-3/5), 8.12 (2H, d, $J=9.1$ Hz, H_Z-2/6), 7.97 (2H, d, $J=8.9$ Hz, H_Y-2/6), 7.83 (2H, d, $J=8.9$ Hz, H_Y-3/5), 7.64 (1H, ddd, $J=8.1$, 2.1, 1.0 Hz, H_X-Ar), 7.58 (1H, br t, $J=2.1$ Hz, H_X-2), 7.56 (1H, d, $J=8.0$ Hz, H_X-Ar), 7.41 (1H, ddd, $J=8.0$, 2.1, 1.0 Hz, H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.88 (C), 158.80 (C), 149.70 (C), 140.81 (C), 137.23 (C), 135.38 (C), 134.23 (C), 131.89 (CH), 131.00 (CH), 130.84 (CH), 130.47 (CH), 129.51 (C), 128.90 (CH), 128.28 (CH), 125.12 (CH). IR ν

(neat)=1610.3 (w), 1573.8 (s), 1538.6 (s), 1515.4 (s), 1484.7 (m), 1473.7 (m), 1429.2 (m), 1398.1 (m), 1356.7 (m), 1340.2 (s), 1300.8 (m), 1282.2 (s), 1210.4 (w), 1180.3 (m), 1168.6 (s), 1087.3 (s), 1054.2 (m), 1024.6 (w), 1001.7 (w), 967.9 (s), 943.2 (m), 922.2 (w), 853.0 (s), 831.6 (m), 817.7 (w), 782.5 (w), 762.6 (s), 740.8 (s), 715.9 (s), 683.0 (s), 656.9 (s) cm^{-1}. HRMS Calcd for $C_{20}H_{13}N_4O_5SCl$ 490.9984; found 490.9965.

4.3.28. 4-Bromo-*N*-(5-furan-2-yl-[1,3,4]oxadiazol-2-yl)-*N*-phenyl-benzenesulfonamide 70. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.05 (1H, dd, $J=1.8$, 0.8 Hz, H_Z-3), 7.94 (2H, d, $J=8.8$ Hz, H_Y-2/6), 7.80 (2H, d, $J=8.8$ Hz, H_Y-3/5), 7.50 (3H, m, H_X-2/4/6), 7.39 (2H, m, H_X-3/5), 7.32 (1H, dd, $J=3.6$, 0.8 Hz, H_Z-5), 6.78 (1H, dd, $J=3.6$, 1.8 Hz, H_Z-4); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 157.70 (C), 156.55 (C), 147.76 (CH), 138.28 (C), 136.22 (C), 136.00 (C), 133.32 (CH), 130.82 (CH), 130.57 (CH), 130.44 (CH), 129.71 (C), 129.14 (CH), 115.54 (CH), 113.15 (CH). IR ν (neat)=1592.6 (w), 1573.7 (s), 1545.9 (m), 1491.5 (w), 1455.7 (w), 1360.0 (w), 1350.0 (w), 1285.6 (m), 1264.5 (m), 1218.9 (m), 1163.6 (s), 1042.1 (m), 1021.4 (m), 1011.7 (m), 837.5 (m), 744.2 (s), 697.4 (m), 688.6 (m) cm^{-1}. HR-MS Calcd for $C_{18}H_{12}N_3O_4SBr$: 445.98106; found 445.9787.

4.3.29. 4-Bromo-*N*-[5-(2,4-difluorophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-(2-nitrophenyl)benzenesulfonamide 71. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.18 (1H, m), 7.98–7.87 (7H, m), 7.62 (2H, m), 7.30 (1H, m); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 158.77 (C), 157.99 (C), 147.53 (C), 135.58 (C), 133.85 (CH), 133.62 (CH), 133.22 (CH), 133.14 (CH), 132.96 (CH), 131.37 (CH), 130.34 (CH), 130.00 (CH), 129.66 (C), 124.85 (CH), 116.33 (C), 113.08, 112.87 (CF), 105.76, 105.75, 105.57 (CF). IR ν (neat)=1589.7 (m), 1572.3 (m), 1557.5 (s), 1530.2 (s), 1502.0 (s), 1471.5 (w), 1384.7 (m), 1343.9 (m), 1277.5 (w), 1246.4 (w), 1187.6 (s), 1178.3 (s), 1142.5 (m), 1090.1 (m), 1010.1 (w), 984.3 (w), 961.1 (w), 928.0 (m), 852.5 (m), 787.9 (w), 744.2 (s), 709.7 (m) cm^{-1}. HRMS Calcd for $C_{20}H_{12}N_4O_5SBRf._2$ 536.9680; found 536.9692.

4.3.30. 4-Methoxy-*N*-[5-(3-methoxyphenyl)-[1,3,4]oxadiazol-2-yl]-*N*-phenethyl-benzenesulfonamide 72. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.91 (2H, d, $J=8.8$ Hz, H_Y-2/6), 7.53 (1H, t, $J=7.8$ Hz, H_Z-Ar), 7.48 (1H, d, $J=7.8$ Hz, H_Z-Ar), 7.33 (1H, m, H_Z-2), 7.28 (7H, m, Ph/H_Y-3/5), 7.25 (1H, m, H_Z-Ar), 7.20 (1H, m, H_Z-Ar), 4.11 (2H, t, $J=7.25$ Hz, H_X-1), 3.88 (3H, s, OMe), 3.89 (3H, s, OMe), 3.00 (2H, t, $J=7.25$ Hz, H_X-2); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 163.75 (C), 162.10 (C), 159.59 (C), 158.12 (C), 137.40 (C), 130.77 (CH), 130.28 (CH), 128.78 (CH), 128.57 (C), 128.35 (CH), 126.50 (CH), 124.09 (C), 118.43 (CH), 117.95 (CH), 114.81 (CH), 110.87 (CH), 55.87 (CH_3), 55.40 (CH_3), 51.16 (CH_2), 34.41 (CH_2). IR ν (neat)=1592.7 (m), 1575.2 (s), 1544.8 (s), 1491.9 (m), 1367.2 (m), 1349.1 (m), 1316.9 (w), 1285.2 (m), 1263.5 (s), 1218.4 (m), 1174.1 (w), 1155.9 (s), 1040.9 (s), 1020.9 (s), 1010.1 (m), 867.3 (m), 836.7 (s), 805.5 (m), 785.0 (s), 756.0 (m), 745.3 (m), 708.5 (m), 687.3 (s), 680.3 (s) cm^{-1}. HRMS Calcd for $C_{24}H_{24}N_3O_5S$ 466.1437; found 466.1439.

4.3.31. 4-Nitro-*N*-phenyl-*N*-[5-(4-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]benzenesulfonamide 73. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.53 (2H, d, $J=9.1$ Hz, H_Y-3/5), 8.21 (2H, d, $J=9.1$ Hz, H_Y-2/6), 8.09 (2H, d, $J=8.2$ Hz, H_Z-3/5), 7.97 (2H, d, $J=8.2$ Hz, H_Z-2/6), 7.53 (3H, m, H_X-2/4/6), 7.43 (2H, m, H_X-3/5); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.46 (C), 158.64 (C), 151.48 (C), 142.03 (C), 125.94 (C), 130.86 (CH), 130.73 (CH), 130.54 (CH), 129.44 (CH), 127.76 (CH), 127.04 (C), 126.93 (C), 126.90 (CH), 125.44 (CH). IR ν (neat)=1597.8 (w), 1568.5 (w), 1541.3 (s), 1530.1 (s), 1504.8 (w), 1489.3 (w), 1423.9 (w), 1406.4 (m), 1347.2 (m), 1322.5 (s), 1284.3 (m), 1167.6 (s), 1124.6 (s), 1094.6 (m), 1067.1 (s), 1051.3 (m), 1026.7 (m), 1013.2 (m), 962.4 (w), 943.4 (w), 916.5 (w), 888.3 (w), 852.0 (s), 821.1 (w), 746.5 (m), 738.6 (s), 717.1 (m), 693.7 (s), 681.5 (s), 666.2 (m) cm^{-1}. HRMS Calcd for $C_{21}H_{14}N_4O_5SF_3$ 491.0637; found 491.0654.

4.3.32. Thiophene-2-sulfonic acid phenyl-(5-phenyl-[1,3,4]oxadiazol-2-yl)amide 74. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.24 (1H, dd, $J=5.0$, 1.3 Hz, H_Y-3), 7.90 (2H, d, $J=6.9$ Hz, H_Z-2/6), 7.86 (1H, dd, $J=3.8$, 1.3 Hz, H_Y-5), 7.61 (3H, m, H_Z-3/4/5), 7.50 (3H, m, H_X-2/4/6), 7.40 (2H, m, H_X-3/5), 7.35 (1H, dd, $J=5.0$, 3.8 Hz, H_Y-4); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.83 (C), 158.55 (C), 153.15 (CH), 147.49 (CH), 135.57 (C), 134.52 (CH), 133.39 (CH), 132.45 (CH), 131.41 (CH), 124.80 (CH), 123.93 (C), 120.01 (C), 117.71 (CH), 117.52 (CH). IR ν (neat)=1593.6 (w), 1568.0 (w), 1536.5 (s), 1485.6 (m), 1452.5 (w), 1412.4 (m), 1396.4 (m), 1374.7 (m), 1341.4 (w), 1296.4 (w), 1280.4 (m), 1227.8 (w), 1170.9 (s), 1094.8 (s), 1070.6 (m), 1053.0 (m), 1027.7 (m), 1015.4 (s), 961.2 (m), 942.7 (m), 913.8 (m), 887.6 (m), 856.8 (m), 775.7 (m), 751.6 (w), 728.0 (s), 717.4 (s), 693.0 (s), 676.0 (s) cm^{-1}. HRMS Calcd for $C_{18}H_{14}N_3O_3S_2$ 384.0477; found 384.0489.

4.3.33. *N*-(3-Chlorophenyl)-2-fluoro-*N*-[5-(4-nitrophenyl)-[1,3,4]oxadiazol-2-yl]benzenesulfonamide 75. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.41 (2H, d, $J=9.1$ Hz, H_Z-2/6), 8.12 (2H, d, $J=9.1$ Hz, H_Z-3/5), 8.03 (2H, m, 2×H_Y-Ar), 7.64 (1H, ddd, J=8.2, 2.2, 0.95 Hz, H_X-Ar), 7.61 (4H, m, 2×H_Y-Ar, 2×H_X-Ar), 7.39 (1H, ddd, $J=7.9$, 2.2, 0.95 Hz, H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 167.25 (C), 165.22 (C), 161.90 (C), 158.86 (C), 149.70 (C), 137.30 (C), 134.21 (C), 132.53 (CH), 132.45 (CH), 131.86 (CH), 130.78 (CH), 129.48 (CH), 128.90 (C), 128.26 (CH), 128.17 (CH), 125.11 (CH), 117.73 (CH), 117.55 (CH). IR ν (neat)=1574.3 (s), 1541.0 (s), 1523.8 (s), 1487.0 (w), 1473.7 (w), 1429.7 (w), 1399.0 (w), 1361.7 (m), 1340.4 (s), 1300.2 (w), 1286.7 (w), 1236.9 (m), 1177.0 (s), 1157.8 (s), 1094.5 (s), 1052.9 (m), 968.3 (m), 943.9 (w), 918.3 (w), 893.9 (w), 853.8 (s), 842.0 (s), 833.2 (m), 781.8 (w), 754.4 (w), 716.0 (s), 707.0 (m), 693.7 (m), 683.4 (s), 672.2 (s) cm^{-1}. HRMS Calcd for $C_{20}H_{13}N_4O_5SFCl$ 475.0279; found 475.0259.

4.3.34. *N*-(4-Bromophenyl)-2-fluoro-*N*-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 76. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 9.06 (1H, dd, $J=2.2$, 0.6 Hz, H_Z-2), 8.80 (1H, dd, $J=4.7$, 1.6 Hz, H_Z-4), 8.25 (1H, ddd, $J=8.0$, 2.2, 1.6 Hz, H_Z-6), 8.00 (2H, m), 7.69 (2H, d, $J=8.8$ Hz, H_X-3 and H_X-5), 7.61 (1H, ddd, $J=8.0$, 4.7, 0.95 Hz, Hz-5), 7.57 (2H, app. t, $J=8.8$ Hz, H_Y-4 and H_Y-5), 7.29 (2H, d, $J=8.8$ Hz, H_X-2 and H_X-6); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 167.18 (C), 165.15 (C),

161.82 (C), 158.55 (C), 153.15 (CH), 147.49 (CH), 135.57 (C), 134.52 (CH), 133.39 (CH), 132.45 (CH), 132.36 (CH), 131.41 (CH), 124.80 (CH), 123.93 (C), 120.01 (C), 117.71 (CH), 117.52 (CH). IR ν (neat)=1585.6 (m), 1568.9 (w), 1537.7 (s), 1489.8 (s), 1404.1 (m), 1381.0 (w), 1365.5 (m), 1340.0 (w), 1292.9 (m), 1240.5 (m), 1211.4 (w), 1175.1 (s), 1149.1 (s), 1096.4 (s), 1066.4 (m), 1012.8 (m), 961.9 (m), 924.4 (w), 838.8 (m), 817.9 (m), 703.1 (s), 664.9 (s) cm^{-1}. HRMS Calcd for $C_{19}H_{13}N_4O_3SBRf$ 474.9876; found 474.9901.

4.3.35. *N*-(5-Furan-2-yl-[1,3,4]oxadiazol-2-yl)-4-nitro-*N*-phenyl-benzenesulfonamide 77. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.51 (2H, d, J=8.9 Hz, H_Y-2/6), 8.14 (2H, d, J=8.9 Hz, H_Y-3/5), 8.03 (1H, dd, J=1.89, 0.6 Hz, H_Z-3), 7.52 (3H, m, H_X-3/4/5), 7.40 (2H, m, H_X-2/6), 7.33 (1H, dd, J=3.5, 0.6 Hz, H_Z-5), 6.78 (1H, dd, J=3.5, 1.9 Hz, H_Z-4); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 157.46 (C), 156.63 (C), 151.46 (C), 147.83 (CH), 141.92 (C), 138.21 (C), 135.94 (C), 130.81 (CH), 130.70 (CH), 130.55 (CH), 129.25 (CH), 125.41 (CH), 115.68 (C), 113.18 (C). IR ν (neat)=1630.4 (w), 1607.0 (w), 1556.9 (m), 1531.3 (s), 1516.0 (m), 1488.3 (w), 1449.3 (w), 1404.5 (w), 1383.8 (s), 1366.7 (w), 1347.8 (s), 1317.7 (w), 1304.8 (w), 1279.1 (m), 1196.1 (w), 1178.0 (s), 1165.8 (s), 1111.2 (m), 1084.8 (m), 1010.6 (m), 985.5 (w), 970.6 (m), 929.5 (m), 906.0 (m), 889.0 (m), 862.2 (m), 854.1 (m), 768.6 (m), 759.0 (m), 739.9 (s), 695.8 (s), 680.8 (s) cm^{-1}. HRMS Calcd for $C_{18}H_{13}N_4O_6S$ 413.0556; found 413.0566.

4.3.36. *N*-(4-hexyl-bicyclo[2.2.2]oct-1-yl)-4-methyl-*N*-(5-methyl-[1,3,4]oxadiazol-2-yl)-benzenesulfonamide 78. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.73 (2H, d, J=8.5 Hz, H_Y-2/6), 7.49 (2H, d, J=8.5 Hz, H_Y-3/5), 7.40 (2H, d, J=8.8 Hz, H_X-3/5), 7.15 (2H, d, J=8.8 Hz, H_Y-2/6), 2.39 (3H, s, H_Z-Me), 2.38 (3H, s, Me), 1.74 (6H, m), 1.44 (6H, m), 1.24 (10H, m), 0.86 (3H, t, J=7.3 Hz, H_Y-Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 164.11 (C), 158.55 (C), 152.10 (C), 145.89 (C), 134.40 (C), 133.96 (C), 130.50 (C), 130.49 (CH), 128.76 (CH), 128.63 (C), 128.41 (CH), 127.37 (CH), 41.68 (CH_2), 32.45 (CH_2), 31.79 (CH_2), 31.41 (CH_2), 30.19 (CH_2), 23.62 (CH_2), 22.55 (CH_2), 21.63 (CH_3), 14.42 (CH_3), 11.34 (CH_3). IR ν (neat)=2918.8 (s), 2853.2 (s), 1614.5 (w), 1596.8 (w), 1540.9 (s), 1510.9 (m), 1437.2 (w), 1411.1 (s), 1385.6 (m), 1303.7 (w), 1243.9 (m), 1185.4 (m), 1175.1 (s), 1094.7 (s), 1050.6 (w), 1019.2 (m), 962.2 (m), 916.4 (m), 810.0 (s) cm^{-1}. HRMS Calcd for $C_{30}H_{40}N_3O_3S$ 522.2790; found 522.2793.

4.3.37. *N*-(4-Bromophenyl)-4-methoxy-*N*-(5-phenyl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 79. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.91 (2H, d, J=6.9 Hz, H_Z-2/6), 7.85 (2H, d, J=9.1 Hz, H_Y-2/6), 7.70 (2H, d, J=8.8 Hz, H_X-2/6), 7.60 (3H, dm, J=6.9 Hz, H_Z-3/4/5), 7.33 (2H, d, J=8.8 Hz, H_X-3/5), 7.22 (2H, d, J=9.1 Hz, H_Y-3/5), 3.91 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 164.64 (C), 163.50 (C), 158.45 (C), 136.00 (C), 133.29 (CH), 132.72 (CH), 131.40 (CH), 131.21 (CH), 129.95 (CH), 127.86 (C), 126.81 (CH), 123.57 (C), 123.31 (C), 115.42 (CH), 56.46 (CH_3). IR ν (neat)=1593.2 (m), 1569.5 (m), 1542.1 (m), 1496.5 (m), 1485.6 (m), 1449.9 (w), 1399.8 (w), 1367.3 (m), 1296.4 (s), 1185.1 (m), 1159.4 (s), 1088.8 (s), 1068.6 (m), 1022.7 (m), 1011.8 (s), 960.5 (w), 920.8 (m), 833.1 (m), 802.8 (m), 775.8 (w), 706.0 (s), 680.0 (s), 689.7 (s), 665.7 (s) cm^{-1}. HRMS Calcd for $C_{21}H_{17}N_3O_4SBr$ 486.0123; found 486.0148.

4.3.38. 4-Bromo-*N*-(4-bromophenyl)-*N*-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-benzenesulfonamide 80. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 9.06 (1H, dd, J=2.2, 0.7 Hz, H_Z-2), 8.82 (1H, dd, J=5.0, 1.6 Hz, H_Z-4), 8.25 (1H, dt, J=7.9, 2.1 Hz, H_Z-6), 7.97 (2H, d, J=8.5 Hz, H_Y-2/6), 7.86 (2H, d, J=8.5 Hz, H_Y-3/5), 7.73 (2H, d, J=8.8 Hz, H_X-3/5), 7.62 (1H, ddd, J=7.9, 5.0, 0.7 Hz, H_Z-5), 7.38 (2H, d, J=8.8 Hz, H_X-2/6); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.82 (C), 158.48 (C), 153.17 (CH), 147.50 (CH), 35.82 (C), 135.50 (C), 134.56 (CH), 133.43 (CH), 133.42 (CH), 131.43 (CH), 130.91 (CH), 129.91 (C), 124.83 (C), 123.99 (C), 120.01 (CH). IR ν (neat)=1609.1 (w), 1586.2 (m), 1571.2 (m), 1539.3 (s), 1493.3 (m), 1481.2 (m), 1403.5 (s), 1389.6 (m), 1382.2 (m), 1369.4 (m), 1294.7 (m), 1208.9 (w), 1170.3 (s), 1097.9 (m), 1085.7 (m), 1011.5 (s), 963.2 (m), 926.4 (m), 898.0 (m), 822.9 (s), 811.6 (m), 743.5 (s), 721.3 (m), 701.1 (s) cm^{-1}. HRMS Calcd for $C_{19}H_{13}N_4O_3SBr_2$ 534.9075; found 534.9110.

4.3.39. 4-Methoxy-*N*-(4-methoxyphenyl)-*N*-[5-(4-nitrophenyl)-[1,3,4]oxadiazol-2-yl]benzenesulfonamide 81. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.39 (2H, d, J=9.1 Hz, H_Z-2/6), 8.10 (2H, d, J=9.1 Hz, H_Z-3/5), 7.86 (2H, d, J=8.8 Hz, H_Y-2/6), 7.26 (2H, d, J=8.3 Hz, H_X-3/5), 7.23 (2H, d, J=8.8 Hz, H_Y-3/5), 7.01 (2H, d, J=8.3 Hz, H_X-2/6), 3.85 (3H, s, OMe), 3.79 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 164.54 (C), 161.61 (C), 160.58 (C), 159.72 (C), 149.65 (C), 142.66 (CH), 131.41 (CH), 130.92 (CH), 128.96 (C), 128.86 (C), 128.15 (C), 128.06 (CH), 125.13 (CH), 115.34 (CH), 56.44 (CH_3), 56.00 (CH_3). IR ν (neat)=1594.6 (w), 1571.7 (m), 1535.2 (s), 1514.8 (s), 1496.0 (m), 1399.4 (w), 1366.4 (w), 1340.7 (s), 1301.9 (w), 1286.4 (w), 1256.4 (s), 1185.6 (w), 1164.7 (s), 1092.7 (m), 1058.8 (m), 1028.6 (m), 962.2 (m), 913.7 (w), 889.9 (w), 856.1 (m), 830.4 (m), 802.3 (m), 757.7 (w), 718.6 (m), 696.0 (w) cm^{-1}. HRMS Calcd for $C_{22}H_{19}N_4O_7S$ 483.0974; found 483.0991.

4.3.40. *N*-(3-Chlorophenyl)-*N*-[5-(4-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-4-methoxybenzenesulfonamide 82. LC-MS R_f 4.261 M+H 476.0; ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.92 (2H, dX, J=8.5 Hz, H_Z-2/6), 7.86 (2H, d, J=8.8 Hz, H_Y-2/6), 7.68 (2H, d, J=8.5 Hz, H_Z-3/5), 7.63 (1H, ddd, J=8.2, 1.9, 0.95 Hz, H_X-Ar), 7.54 (1H, t, J=8.2 Hz, H_X-Ar), 7.50 (1H, t, J=2.2 Hz, H_X-2), 7.32 (1H, ddd, J=8.2, 1.9, 0.95 Hz, H_X-Ar), 7.24 (2H, d, J=8.8 Hz, H_Y-3/5), 3.91 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 164.72 (C), 162.72 (C), 158.50 (C), 137.76 (C), 137.42 (C), 134.09 (C), 131.77 (CH), 131.46 (CH), 130.42 (CH), 130.14 (CH), 129.15 (CH), 128.63 (CH), 127.90 (CH), 127.79 (C), 122.26 (C), 115.43 (CH), 56.49 (CH_3). IR ν (neat)=1587.3 (m), 1579.0 (m), 1561.0 (m), 1540.5 (s), 1496.4 (m), 1483.1 (s), 1472.7 (m), 1439.7 (m), 1424.2 (w), 1396.1 (m), 1370.4 (m), 1303.8 (w), 1287.3 (w), 1262.5 (s), 1211.6 (m), 1184.7 (m), 1175.5 (m), 1162.3 (s), 1091.4 (s), 1055.2 (m), 1023.1 (m), 1011.5 (m), 969.2 (m), 943.5 (w), 921.9 (w), 899.0 (w), 871.6 (w), 834.6 (m), 827.5 (s), 805.9 (s), 782.3 (m), 746.7 (m), 733.7 (m), 726.0

(s), 713.7 (m), 682.9 (s), 670.7 (s) cm^{-1}. HRMS Calcd for $C_{21}H_{16}N_3O_4SCl_2$ 476.0239; found 476.0250.

4.3.41. *N*-(5-Furan-2-yl-[1,3,4]oxadiazol-2-yl)-*N*-phenyl-benzenesulfonamide 83. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.04 (1H, dd, $J=1.9$, 0.6 Hz, H_Z-3), 7.90 (2H, dd, $J=8.2$, 0.95 Hz, H_Y-2/6), 7.82 (1H, m, H_Y-4), 7.71 (2H, m, $2\times H_Y$-Ar), 7.49 (3H, m, $2\times H_Z$-Ar, H_X-5), 6.80 (1H, dd, $J=3.7$, 1.9 Hz, H_Z-4); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 157.86 (C), 156.59 (C), 147.76 (CH), 138.32 (C), 136.84 (C), 136.42 (C), 135.42 (CH), 130.41 (CH), 130.34 (CH), 130.18 (CH), 129.04 (CH), 128.85 (CH), 115.51 (CH), 113.15 (CH). IR ν (neat)=1551.8 (s), 1519.7 (s), 1491.0 (m), 1450.7 (m), 1425.1 (w), 1416.9 (w), 1402.9 (w), 1385.4 (m), 1289.7 (w), 1162.1 (s), 1094.8 (m), 1087.8 (m), 1027.2 (w), 1006.2 (m), 964.5 (w), 934.4 (m), 914.9 (w), 756.4 (s), 722.5 (s), 694.3 (s), 684.4 (s), 664.9 (m) cm^{-1}. HRMS Calcd for $C_{18}H_{14}N_3O_4S$ 368.0705; found 368.0760.

4.3.42. *N*-[5-(3,4-Dimethoxyphenyl)-[1,3,4]oxadiazol-2-yl]-4-nitro-*N*-phenyl-benzenesulfonamide 84. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.50 (2H, d, $J=8.75$ Hz, H_Y-3/5), 8.15 (2H, d, $J=8.75$ Hz, H_Y-2/6), 7.51 (1H, t, $J=7.9$ Hz, H_Z-5), 7.46 (1H, dt, $J=7.9$, 1.3 Hz, H_Z-6), 7.36 (1H, dt, $J=1.6$, 1.3 Hz, H_Z-2), 7.32 (2H, d, $J=8.8$ Hz, H_X-3/5), 7.20 (1H, ddd, $J=7.9$, 1.6, 1.3 Hz, H_Z-4), 7.03 (2H, d, $J=8.8$ Hz, H_X-2/6), 3.93 (3H, s, OMe), 3.90 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 163.51 (C), 160.82 (C), 160.10 (C), 158.42 (C), 151.38 (C), 142.10 (C), 131.32 (CH), 130.88 (CH), 130.66 (CH), 128.28 (C), 125.37 (CH), 124.35 (C), 119.19 (CH), 118.74 (CH), 115.58 (CH), 111.68 (CH), 56.04 (CH_3), 55.92 (CH_3). IR ν (neat)=1603.3 (w), 1559.6 (w), 1543.4 (m), 1524.8 (s), 1493.4 (s), 1464.6 (m), 1440.0 (m), 1417.5 (w), 1404.4 (w), 1384.6 (s), 1371.0 (m), 1347.7 (m), 1293.0 (m), 1278.0 (m), 1250.1 (s), 1229.5 (s), 1201.5 (w), 1172.2 (s), 1109.3 (m), 1088.3 (m), 1053.2 (w), 1026.1 (s), 999.5 (w), 971.8 (w), 930.4 (m), 874.3 (w), 852.1 (s), 833.8 (s), 803.9 (m), 792.1 (m), 736.8 (s), 719.8 (m), 702.3 (m), 684.0 (s) cm^{-1}. HRMS Calcd for $C_{22}H_{19}N_4O_7S$ 483.0974; found 483.1003.

4.3.43. *N*-(4-Chlorophenyl)-4-methyl-*N*-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 85. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 9.09 (1H, dd, $J=2.1$, 0.6 Hz, H_Z-2), 8.73 (1H, dd, $J=5.0$, 1.6 Hz, H_Z-4), 8.31 (1H, ddd, $J=8.3$, 2.1, 1.6 Hz, H_Z-6), 7.96 (2H, d, $J=8.2$ Hz, H_Y-2/6), 7.59 (2H, d, $J=8.9$ Hz, $2\times H_X$-Ar), 7.57 (1H, ddd, $J=8.3$, 5.0, 1.6 Hz, H_Z-5), 7.52 (2H, d, $J=8.2$ Hz, H_Y-3/5), 7.32 (2H, d, $J=8.9$ Hz, $2\times H_X$-Ar), 2.41 (3H, s, Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 163.17 (C), 163.07 (C), 152.35 (CH), 148.22 (CH), 146.49 (C), 136.83 (C), 135.17 (CH), 133.91 (C), 131.95 (CH), 130.82 (CH), 130.37 (CH), 130.34 (C), 128.99 (C), 128.61 (CH), 124.78 (CH), 21.67 (CH_3). IR ν (neat)=1639.4 (w), 1593.8 (m), 1566.8 (m), 1542.5 (w), 1528.3 (w), 1488.5 (s), 1424.7 (s), 1412.8 (s), 1368.1 (s), 1293.9 (m), 1274.7 (m), 1187.2 (m), 1174.1 (s), 1162.9 (m), 1088.4 (s), 1026.3 (m), 1015.9 (s), 964.0 (m), 931.6 (m), 813.5 (s), 772.1 (m), 703.1 (s), 663.4 (s) cm^{-1}. HRMS Calcd for $C_{20}H_{15}N_4O_3SCl$ 427.0632; found 427.0620.

4.3.44. 4-Methoxy-*N*-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-(2,6-dimethylphenyl)benzenesulfonamide 86. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.10 (2H, d, $J=9.1$ Hz, H_Y-2/6), 7.83 (1H, dd, $J=7.9$, 1.6 Hz, H_Z-Ar), 7.63 (2H, m, $2\times H_Z$-Ar), 7.52 (1H, m, H_Z-Ar), 7.42 (1H, m), 7.30 (1H, t, $J=7.6$ Hz, H_X-4), 7.26 (2H, d, $J=9.1$ Hz, H_Y-3/5), 7.24 (2H, d, $J=7.6$ Hz, H_X-3/5), 3.90 (3H, s, OMe), 2.11 (6H, s, $2\times$Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 164.71 (C), 160.21 (C), 158.73 (C), 138.93 (C), 134.78 (CH), 133.79 (C), 132.08 (C), 131.80 (CH), 131.68 (CH), 131.47 (CH), 130.38 (CH), 129.65 (CH), 129.35 (C), 128.40 (CH), 122.59 (C), 115.31 (CH), 56.48 (CH_3), 18.47 (CH_3). IR ν (neat)=1291.8 (m), 1582.5 (m), 1564.7 (m), 1545.5 (m), 1496.9 (m), 1460.2 (w), 1442.6 (w), 1380.7 (w), 1368.1 (s), 1291.8 (m), 1264.0 (s), 1188.8 (m), 1161.6 (s), 1085.5 (m), 1023.4 (m), 974.3 (w), 927.3 (m), 888.7 (m), 834.8 (s), 804.7 (m), 776.0 (w), 729.4 (s), 669.5 (s) cm^{-1}. HRMS Calcd for $C_{23}H_{21}N_3O_4SCl$ 470.0941; found 470.0926.

4.3.45. 3-[(4-Chlorobenzenesulfonyl)-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-amino]benzoic acid methyl ester 87. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 9.08 (1H, dd, $J=2.2$, 0.6 Hz, H_Z-2), 8.80 (1H, dd, $J=4.7$, 1.6 Hz, H_Z-4), 8.26 (1H, ddd, $J=8.2$, 2.2, 1.6 Hz, H_Z-6), 8.10 (1H, m, H_X-Ar), 7.92 (3H, m, H_Y-2/6, H_X-Ar), 7.80 (2H, d, $J=8.8$ Hz, H_Y-3/5), 7.69 (2H, m, H_X-Ar), 7.60 (1H, ddd, $J=8.2$, 4.7, 0.95 Hz, H_Z-5), 3.89 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 165.47 (C), 161.92 (C), 158.55 (C), 153.16 (CH), 147.51 (CH), 140.76 (C), 136.57 (C), 135.35 (C), 134.56 (CH), 134.07 (CH), 131.76 (C), 131.12 (CH), 131.10 (CH), 130.94 (CH), 130.47 (CH), 129.91 (CH), 124.81 (CH), 120.04 (C), 53.03 (CH_3). IR ν (neat)=1715.8 (s), 1606.8 (w), 1582.2 (m), 1536.7 (m), 1540.4 (s), 1485.1 (m), 1473.2 (w), 1432.1 (m), 1406.2 (s), 1367.9 (m), 1294.3 (s), 1274.6 (s), 1207.5 (w), 1175.8 (s), 1159.5 (m), 1112.0 (w), 1099.0 (s), 1082.5 (s), 1063.9 (m), 1018.1 (m), 1009.5 (m), 1003.9 (m), 993.1 (s), 984.0 (s), 960.4 (m), 893.4 (m), 831.7 (m), 809.3 (m), 759.7 (s), 753.0 (s), 719.9 (m), 709.0 (m), 700.7 (s), 686.1 (s), 655.0 (s) cm^{-1}. HRMS Calcd for $C_{21}H_{16}N_4O_5SCl$ 471.0530; found 471.0518.

4.3.46. *N*-(3-Chloro-4-methylphenyl)-4-methoxy-*N*-[5-(2-nitrophenyl)-[1,3,4]oxadiazol-2-yl]benzenesulfonamide 88. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.19 (1H, m, H_Z-5), 7.97 (3H, m, H_Z-3/4/6), 7.82 (2H, d, $J=9.1$ Hz, H_Y-2/6), 7.48 (1H, d, $J=8.5$ Hz, H_X-5), 7.40 (1H, d, $J=2.5$ Hz, H_X-2), 7.21 (2H, d, $J=9.1$ Hz, H_Y-3/5), 7.17 (1H, dd, $J=8.5$, 2.5 Hz, H_X-6), 3.90 (3H, s, OMe), 2.37 (3H, s, Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 164.71 (C), 159.79 (C), 159.25 (C), 148.10 (C), 138.33 (C), 135.16 (C), 134.33 (CH), 134.15 (C), 134.08 (CH), 132.54 (CH), 131.89 (CH), 131.41 (CH), 129.50 (CH), 127.88 (CH), 127.74 (C), 125.34 (CH), 117.10 (C), 115.41 (CH), 56.47 (CH_3), 19.80 (CH_3). IR ν (neat)=1592.5 (m), 1570.5 (m), 1531.4 (s), 1489.0 (m), 1442.0 (w), 1367.2 (m), 1348.1 (m), 1309.6 (w), 1262.8 (s), 1186.6 (m), 1162.6 (s), 1090.3 (m), 1052.5 (m), 1024.6 (m), 965.9 (w), 945.0 (w), 914.6 (w), 852.4 (w), 834.9 (w), 802.8 (w), 786.7 (w), 755.1 (w), 715.0 (w), 700.6 (m), 669.9 (s) cm^{-1}. HRMS Calcd for $C_{21}H_{16}N_4O_6SCl$ 487.0479; found 487.0498.

4.3.47. 4-Bromo-*N*-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-*N*-(2,6-dimethylphenyl)benzenesulfonamide 89. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 8.09 (2H, d, $J=8.8$ Hz,

H_Y-2/6), 8.00 (2H, d, J=8.8 Hz, H_Y-3/5), 7.84 (1H, dd, J=7.9, 1.6 Hz, H_Z-Ar), 7.63 (2H, m, H_Z-Ar), 7.54 (1H, m, H_Z-Ar), 7.31 (1H, t, J=7.9 Hz, H_X-4), 7.22 (2H, d, J=7.6 Hz, H_X-3/5), 2.10 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 160.52 (C), 158.41 (C), 138.96 (C), 137.29 (C), 134.36 (C), 133.88 (CH), 133.36 (CH), 132.11 (C), 131.75 (CH), 131.48 (CH), 131.27 (CH), 130.62 (CH), 129.92 (C), 129.77 (CH), 128.40 (CH), 122.49 (C), 18.48 (CH_3). IR ν (neat)=1563.2 (s), 1539.8 (m), 1462.9 (w), 1444.5 (w), 1368.5 (s), 1290.6 (m), 1279.6 (m), 1188.8 (w), 1166.0 (s), 1083.6 (w), 1066.9 (w), 932.7 (m), 826.9 (m), 782.4 (m), 763.1 (s), 740.8 (s), 727.5 (s) cm^{-1}. HRMS Calcd for $C_{22}H_{18}N_3O_3SBr_2$ 561.9436; found 561.9388.

4.3.48. 3-[(4-Bromobenzenesulfonyl)-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-amino]benzoic acid methyl ester 90. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 9.04 (1H, dd, J=2.2, 0.95 Hz, H_Z-2), 8.81 (1H, dd, J=4.7, 1.6 Hz, H_Z-4), 8.26 (1H, ddd, J=7.9, 2.2, 1.6 Hz, H_Z-6), 8.10 (1H, m, H_Z-Ar), 7.98 (2H, d, J=8.8 Hz, H_X-3/5), 7.96 (1H, m), 7.84 (2H, d, J=8.8 Hz, H_X-2/6), 7.68 (2H, m, 2×H_Y-Ar), 7.63 (1H, ddd, J=7.9, 4.7, 0.95 Hz, H_Z-5), 3.88 (3H, s, OMe); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 165.47 (C), 161.91 (C), 158.54 (C), 153.17 (CH), 147.51 (CH), 136.57 (C), 135.79 (C), 134.57 (CH), 134.07 (CH), 133.43 (CH), 131.75 (C), 131.13 (CH), 131.11 (CH), 130.90 (CH), 129.96 (CH), 129.92 (C), 124.82 (CH), 120.04 (C), 53.04 (CH_3). IR ν (neat)=1716.4 (s), 1606.7 (w), 1583.4 (w), 1572.6 (m), 1563.1 (m), 1540.4 (s), 1484.0 (m), 1467.6 (m), 1432.8 (m), 1406.0 (m), 1388.6 (m), 1368.0 (m), 1294.9 (s), 1274.1 (s), 1207.7 (m), 1169.3 (s), 1159.6 (s), 1099.5 (m), 1083.1 (m), 1064.8 (m), 1016.9 (w), 1004.2 (m), 993.4 (m), 960.5 (m), 891.9 (m), 829.2 (m), 755.1 (m), 745.8 (s), 720.0 (s), 699.9 (s), 686.5 (s), 654.0 (m) cm^{-1}. HRMS Calcd for $C_{21}H_{16}N_4O_5SBr$ 515.00225; found 515.0037.

4.3.49. *N*-Adamantan-1-yl-*N*-(5-hexyl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 91. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 8.26 (2H, d, J=9.1 Hz, H_X-3/5), 7.81 (2H, d, J=9.1 Hz, H_X-2/6), 2.60 (2H, t, J=7.25 Hz, H_Z-1-CH_2), 2.04 (3H, m), 1.91 (5H, m), 1.60 (8H, m), 1.26 (8H, m), 0.83 (3H, t, J=6.9 Hz, H_Z-Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 161.97 (C), 147.24 (C), 144.06 (C), 142.61 (C), 127.28 (CH), 125.03 (CH), 41.40 (CH_2), 36.35 (CH_2), 31.56 (CH_2), 29.33 (CH), 28.74 (CH_2), 28.67 (CH_2), 26.42 (CH_2), 24.86 (CH_2), 22.49 (CH_2), 14.38 (CH_3). IR ν (neat)=2903.7 (s), 2850.1 (s), 1625.9 (s), 1573.3 (s), 1515.5 (w), 1468.9 (w), 1454.3 (w), 1389.7 (w), 1361.6 (m), 1334.3 (m), 1307.2 (m), 1249.0 (w), 1225.3 (w), 1180.2 (m), 1136.3 (w), 976.0 (w), 932.1 (m), 852.7 (m), 817.0 (w), 727.8 (m) cm^{-1}. HRMS Calcd for $C_{25}H_{35}N_4O_5S$ 503.2328; found 503.2298.

4.3.50. *N*-(3-Chlorophenyl)-*N*-[5-(4-trifluoromethylphenyl)-[1,3,4]oxadiazol-2-yl]benzenesulfonamide 92. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 8.11 (2H, d, J=8.2 Hz), 7.96 (3H, m), 7.88 (1H, m), 7.74 (2H, m), 7.61 (1H, ddd, J=8.0, 2.1, 1.1 Hz, H_X-Ar), 7.54 (1H, t, J=8.0 Hz, H_X-Ar), 7.51 (1H, t, J=2.1 Hz, H_X-Ar), 7.39 (1H, ddd, J=8.0, 2.1, 1.1 Hz, H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.39 (C), 158.69 (C), 137.47 (C), 136.66 (C), 135.66 (CH), 134.15 (C), 131.79 (CH), 130.61 (CH), 130.28 (CH), 129.29 (CH), 128.96 (CH), 128.09 (CH), 127.67 (CH), 126.92 and 126.89 and 126.86 and 126.83 (CF_3). IR ν (neat)=1571.3 (w), 1537.7 (s), 1505.9 (w), 1472.4 (w), 1449.9 (w), 1424.9 (w), 1367.2 (w), 1327.9 (s), 1285.5 (w), 1181.6 (m), 1161.1 (s), 1123.8 (m), 1095.6 (s), 1068.9 (s), 1015.3 (m), 968.5 (m), 946.4 (m), 925.6 (w), 847.4 (s), 788.9 (m), 745.0 (m), 719.3 (s), 679.8 (s) cm^{-1}. HR-MS Calcd for $C_{20}H_{14}N_3O_3ClF_3S$: 480.0347; found 480.0401.

4.3.51. 3,4-Dimethoxybenzenesulfonic acid 3-{5-[(3,4-dimethoxy-benzenesulfonyl)-(2,6-dimethylphenyl)-amino]-[1,3,4]oxadiazol-2-yl}naphthalen-2-yl ester 93. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 8.44 (1H, s), 8.12 (1H, dd, J=7.9 Hz), 8.03 (1H, d, J=7.9 Hz), 7.90 (1H, s), 6.68 (3H, m), 7.33 (1H, m), 7.29 (1H, d, J=8.8 Hz), 7.23 (2H, m), 7.17 (1H, dd, J=8.5, 2.5 Hz), 7.08 (1H, d, J=2.2 Hz), 6.98 (1H, d, J=8.8 Hz), 3.91 (3H, s, OMe), 3.81 (6H, s, 2×OMe), 3.60 (3H, s, OMe), 2.13 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 159.68 (C), 158.83 (C), 154.60 (C), 154.58 (C), 149.25 (C), 149.23 (C), 142.86 (C), 139.12 (C), 134.81 (C), 134.42 (C), 131.93 (CH), 131.13 (C), 130.40 (CH), 129.79 (CH), 129.67 (CH), 129.27 (C), 129.12 (CH), 128.39 (CH), 128.35 (CH), 124.87 (C), 123.79 (CH), 123.17 (CH), 122.42 (CH), 116.65 (C), 112.03 (CH), 111.69 (CH), 111.57 (CH), 110.81 (CH), 56.60 (CH_3), 56.46 (CH_3), 56.32 (CH_3), 56.09 (CH_3), 18.47 (CH_3). IR ν (neat)=1630.3 (w), 1582.9 (m), 1544.4 (m), 1508.2 (s), 1464.3 (m), 1441.8 (m), 1407.5 (m), 1369.6 (s), 1264.3 (s), 1238.2 (s), 1188.5 (m), 1174.0 (m), 1163.4 (m), 1140.5 (s), 1092.2 (s), 1054.3 (w), 1013.5 (s), 928.3 (w), 911.8 (m), 893.8 (m), 854.8 (w), 817.4 (m), 765.9 (s), 741.2 (m) cm^{-1}. HRMS Calcd for $C_{36}H_{34}N_3O_{10}S_2$ 732.1686; found 732.1684.

4.3.52. *N*-Benzyl-*N*-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 94. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 9.10 (1H, dd, J=2.5, 0.95 Hz, H_Z-2), 8.72 (1H, dd, J=5.0, 1.6 Hz, H_Z-4), 8.30 (1H, ddd, J=8.2, 2.2, 1.6 Hz, H_Z-6), 8.00 (2H, dd, J=7.25, 0.95 Hz, H_Y-2/6), 8.81 (1H, m, H_Y-4), 7.69 (2H, m, H_Y-3/5), 7.56 (1H, ddd, J=8.2, 5.0, 0.95 Hz, H_Z-5), 7.40 (2H, m, 2×H_X-Ar), 7.33 (2H, m, 2×H_X-Ar), 7.29 (1H, m, H_X-Ar), 5.23 (2H, s, NCH_2); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.95 (C), 161.85 (C), 152.29 (CH), 148.19 (CH), 137.10 (C), 135.82 (C), 135.41 (CH), 135.16 (CH), 130.57 (CH), 128.97 (CH), 128.31 (CH), 128.28 (CH), 127.72 (CH), 126.13 (C), 124.74 (CH), 53.10 (CH_2). IR ν (neat)=1584.6 (w), 1570.1 (w), 1494.8 (w), 1444.0 (s), 1413.5 (s), 1366.8 (s), 1336.2 (m), 1275.3 (m), 1252.8 (m), 1185.5 (m), 1166.3 (s), 1105.1 (m), 1088.8 (m), 1077.7 (m), 1025.6 (m), 1012.4 (s), 983.0 (m), 971.9 (m), 832.6 (s), 820.7 (m), 806.0 (m), 760.1 (s), 722.0 (s) cm^{-1}. HR-MS Calcd for $C_{20}H_{17}N_4O_3S$: 393.1021; found 393.1014.

4.3.53. *N*-Benzyl-4-chloro-*N*-(5-pyridin-3-yl-[1,3,4]-oxadiazol-2-yl)benzenesulfonamide 95. ^{1}H NMR (d_6-DMSO; 500 MHz) δ ppm 9.06 (1H, dd, J=2.2, 0.95 Hz, H_Z-2), 8.69 (1H, dd, J=4.7, 1.6 Hz, H_Z-4), 8.22 (1H, ddd, J=7.9, 2.2, 1.6 Hz, H_Z-6), 7.90 (2H, d, J=8.8 Hz, H_Y-2/6), 7.61 (2H, d, J=8.8 Hz, H_Y-3/5), 7.50 (1H, ddd, J=7.9, 4.7, 0.95 Hz, H_Z-5), 7.40 (2H, m, 2×H_X-Ar), 7.29 (3H, m, 3×H_X-Ar), 5.20 (2H, s, H_X-1); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.86 (C), 161.58 (C),

152.00 (CH), 148.10 (CH), 140.61 (C), 135.90 (C), 135.37 (C), 134.80 (CH), 130.35 (CH), 129.40 (CH), 128.74 (CH), 128.38 (CH), 128.18 (CH), 126.16 (C), 124.39 (CH), 53.27 (CH_2). IR ν (neat)=1584.6 (m), 1565.9 (m), 1496.4 (m), 1479.4 (m), 1446.9 (s), 1419.3 (s), 1401.2 (m), 1357.9 (s), 1274.5 (m), 1250.3 (m), 1165.6 (s), 1108.6 (m), 1083.7 (m), 1019.9 (m), 1013.2 (m), 980.9 (m), 848.4 (m), 837.3 (m), 823.1 (m), 756.6 (s), 748.2 (s), 696.3 (s), 656.7 (s) cm^{-1}. HR-MS Calcd for $C_{20}H_{15}N_4O_3SCl$: 427.0553; found 427.0632.

4.3.54. 4-Chloro-*N*-(3-chloro-phenyl)-*N*-[5-(4-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]benzenesulfonamide 96. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 7.83 (2H, d, J=8.5 Hz, H_Y-2/6), 7.90 (2H, d, J=8.8 Hz, H_Z-2/6), 7.83 (2H, d, J=8.5 Hz, H_Y-3/5), 7.68 (2H, d, J=8.8 Hz, H_Z-3/5), 7.63 (1H, ddd, J=8.2, 2.4, 1.0 Hz, H_X-Ar), 7.56 (2H, m, 2×H_X-Ar), 7.39 (1H, ddd, J=7.9, 2.4, 1.0 Hz, H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.76 (C), 158.17 (C), 140.73 (C), 137.46 (C), 137.33 (C), 135.41 (C), 134.21 (C), 131.90 (CH), 130.74 (CH), 130.46 (CH), 130.15 (CH), 130.09 (CH), 129.35 (CH), 128.67 (CH), 128.09 (CH), 122.21 (C). IR ν (neat)=1605.4 (w), 1584.2 (s), 1562.8 (s), 1541.8 (s), 1474.3 (s), 1376.3 (m), 1302.3 (w), 1281.7 (w), 1172.2 (s), 1091.9 (s), 1055.1 (m), 1028.7 (w), 1012.3 (s), 964.1 (m), 946.8 (m), 833.6 (m), 784.2 (m), 757.2 (s), 729.3 (m), 704.5 (m), 682.4 (s) cm^{-1}. HR-MS Calcd for $C_{20}H_{13}N_3O_3SCl_3$: 479.9743; found 479.9767.

4.3.55. 4-Nitro-*N*-phenyl-*N*-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 97. ^1H NMR (d_6-DMSO; 500 MHz) δ ppm 9.08 (1H, dd, J=2.1, 0.95 Hz, H_Z-2), 8.81 (1H, dd, J=4.7, 1.6 Hz, H_Z-4), 8.54 (2H, d, J=8.8 Hz, H_Y-3/5), 8.26 (1H, dd, J=7.9, 2.1 Hz, H_Z-6), 8.20 (2H, d, J=8.8 Hz, H_Y-2/6), 7.64 (1H, ddd, J=7.9, 4.7, 0.95 Hz, H_Z-5), 7.52 (3H, m, 2×H_X-Ar), 7.41 (2H, m, 2×H_X-Ar); ^{13}C NMR (d_6-DMSO; 125 MHz) δ ppm 162.01 (C), 158.54 (C), 153.22 (CH), 151.47 (C), 147.54 (CH), 142.01 (C), 135.98 (C), 134.62 (CH), 130.81 (C), 130.72 (CH), 130.53 (CH), 129.34 (CH), 125.44 (CH), 124.84 (CH), 119.97 (C). IR ν (neat)=1606.9 (w), 1579.3 (w), 1567.4 (w), 1538.9 (m), 1524.7 (s), 1488.5 (m), 1406.4 (s), 1370.1 (w), 1345.9 (s), 1312.3 (m), 1290.2 (m), 1173.3 (s), 1121.6 (w), 1096.2 (m), 1052.4 (s), 1027.7 (s), 1008.4 (s), 959.9 (m), 914.8 (w), 888.8 (w), 854.3 (s), 815.0 (m), 754.5 (m), 738.9 (s), 723.1 (m), 698.9 (s), 683.9 (s), 666.6 (m) cm^{-1}. HR-MS Calcd for $C_{19}H_{14}N_5O_5S$: 424.0716; found 424.0734.

4.3.56. Biphenyl-4-sulfonic acid (4-bromophenyl)-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)amide 98. ^1H NMR ($CDCl_3$; 400 MHz) δ ppm 9.19 (1H, dd, J=2.2, 0.7 Hz, H_Z-2), 8.77 (1H, dd, J=4.7, 1.5 Hz, H_Z-4), 8.29 (1H, ddd, J=8.05, 2.2, 1.5 Hz, H_Z-6), 7.96 (2H, d, J=8.4 Hz, H_Y-2/6), 7.76 (2H, d, J=8.4 Hz, H_Y-3/5), 7.64 (2H, m), 7.57 (2H, d, J=8.7 Hz, H_X-2/6), 7.53–7.40 (4H, m), 7.29 (2H, d, J=8.7 Hz, H_X-3/5).

4.3.57. 4-Methoxy-N-[5-(3-methoxyphenyl)-[1,3,4]oxadiazol-2-yl]-*N*-4-methylbenzenesulfonamide 99. ^1H NMR ($CDCl_3$; 400 MHz) δ ppm 7.88 (2H, d, J=8.8 Hz, H_Y-2/6), 7.55 (1H, dt, J=8.05, 1.4 Hz, H_Z-Ar), 7.52 (1H, m, H_Z-Ar), 7.41 (1H, t, J=8.05 Hz, H_Z-Ar), 7.24 (2H, d, J=8.4 Hz, H_X-2/6), 7.21 (2H, d, J=8.4 Hz, H_X-3/5), 7.08 (1H, ddd, J=8.4, 2.6, 1.1 Hz, H_Z-Ar), 7.02 (2H, d, J=8.8 Hz, H_Y-3/5), 3.91 (3H, s, OMe), 3.86 (3H, s, OMe), 2.40 (3H, s, Me).

4.3.58. Thiophene-2-sulfonic acid ethyl-[5-(4-nitro-phenyl)-[1,3,4]oxadiazol-2-yl]amide 100. LC-MS R_f 3.755 M+H 381.0; ^1H NMR ($CDCl_3$; 400 MHz) δ ppm 8.40 (2H, d, J=8.8 Hz, H_Z-3/5), 8.21 (2H, d, J=8.8 Hz, H_Z-2/6), 7.85 (1H, dd, J=4.0, 1.5 Hz, H_Y-4), 7.73 (1H, d, J=5.1, 1.5 Hz, H_Y-5), 7.18 (1H, dd, J=5.1, 4.0 Hz, H_Y-4), 4.08 (2H, q, J=7.1 Hz, H_X-1), 1.42 (3H, t, J=7.1 Hz, H_X-2).

4.3.59. 4-Chloro-*N*-(3-chlorophenyl)-*N*-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)benzenesulfonamide 101. LC-MS R_f 4.509 M+H 446.9; ^1H NMR ($CDCl_3$; 400 MHz) δ ppm 9.18 (1H, br s, H_Z-2), 8.77 (1H, d, J=4.0 Hz, H_Z-4), 8.26 (1H, dt, J=8.05, 1.8 Hz, H_Z-6), 7.85 (2H, d, J=8.78 Hz, H_Y-2/6), 7.54 (2H, d, J=7.78 Hz, H_Y-3/5), 7.48–7.31 (4H, m), 7.23 (1H, m); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 162.67 (C), 159.02 (C), 153.22 (CH), 148.17 (CH), 141.85 (C), 138.34 (C), 136.10 (C), 135.73 (C), 134.38 (CH), 131.04 (CH), 130.78 (CH), 130.71 (CH), 130.00 (CH), 129.45 (CH), 127.26 (C), 124.19 (CH), 120.26 (C). IR ν (neat)=1571.8 (m), 1541.9 (s0, 1529.8 (s), 1488.8 (m), 1473.9 (m), 1416.7 (m), 1395.9 (w), 1372.9 (m), 1286.9 (m), 1173.9 (s), 1161.9 (m), 1081.0 (s), 1047.7 (w), 971.7 (m), 945.5 (w), 928.8 (w), 853.2 (w), 831.0 (m), 760.2 (s), 739.6 (m), 712.5 (m), 684.9 (s), 656.2 (m) cm^{-1}.

4.3.60. 4-Chloro-benzenesulfonic acid 3-{5-[(4-chloro-benzenesulfonyl)-(2,6-dimethylphenyl)amino]-[1,3,4]-oxadiazol-2-yl}-naphthalen-2-yl ester 102. LC-MS R_f 5.261 M+H 680.0; ^1H NMR ($CDCl_3$; 400 MHz) δ ppm 8.20 (1H, s), 8.09 (2H, d, J=8.8 Hz), 7.77 (3H, m), 7.57–7.39 (6H, m), 7.22 (2H, d, J=8.4 Hz), 7.19 (1H, m), 7.10 (2H, d, J=7.7 Hz), 2.11 (6H, s, 2×Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 160.45 (C), 159.12 (C), 143.24 (C), 141.51 (C), 141.81 (C), 139.69 (C), 137.68 (C), 134.86 (C), 134.48 (C), 133.31 (C), 132.12 (CH), 131.48 (C), 131.24 (CH), 130.58 (CH), 130.34 (CH), 129.94 (CH), 129.90 (CH), 129.61 (CH), 129.01 (CH), 128.30 (CH), 128.21 (CH), 122.51 (CH), 116.58 (C), 19.02 (CH_3). IR ν (neat)=1543.8 (s), 1473.8 (m), 1358.9 (s), 1281.9 (m), 1191.0 (s), 1176.2 (s), 1085.9 (s), 1015.2 (m), 933.9 (m), 897.6 (m), 817.0 (s), 779.6 (s), 758.3 (s), 703.7 (m), 669.6 (m) cm^{-1}.

4.3.61. *N*-(3-Chloro-4-methylphenyl)-*N*-[5-(3-hydroxy-naphthalen-2-yl)-[1,3,4]oxadiazol-2-yl]-2-trifluoro-methylbenzenesulfonamide 103. LC-MS R_f 4.965 M+H 560.0; ^1H NMR ($CDCl_3$; 400 MHz) δ ppm 8.54 (1H, m), 8.37 (1H, m), 8.14 (1H, m), 8.02–7.86 (3H, m), 7.84–7.67 (3H, m), 7.62–7.55 (3H, m), 7.49 (1H, m), 7.20 (1H, m), 2.32 (3H, s, Me); ^{13}C NMR (d_6-DMSO; 100 MHz) δ ppm 162.18 (C), 158.85 (C), 142.86 (C), 138.82 (C), 135.32 (C), 140.05 (C), 134.95 (CH), 134.78 (C), 134.66 (CH), 134.06 (CH), 133.30 (CH), 133.05 (C), 132.96 (CH), 132.48 (CH), 131.97 (CH), 131.55 (C), 130.02 (CH), 129.69 (CH), 129.13 (CH), 128.20 (CH), 128.17 (C), 127.75 (CH), 122.13 (CH), 116.76 (C), 20.27 (CH_3). IR ν (neat)=1628.6 (m), 1607.4 (m), 1544.8 (m), 1513.5 (w), 1496.3 (m), 1466.4 (w), 1439.5 (w), 11406.5 (w), 1353.9 (s), 1311.1 (s), 1274.0 (m), 1188.8

(m), 1177.8 (s), 1146.5 (s), 1115.9 (s), 1095.1 (w), 1047.6 (m), 1034.1 (m), 1025.4 (m), 907.8 (m), 892.4 (m), 827.5 (s), 805.6 (s), 796.6 (s), 743.5 (s), 720.9 (s), 690.0 cm^{-1}.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2005.03.062

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19. PS-carbodiimide (1.1–1.13 mmol g^{-1}) available from Argonaut Technologies was used without further purification.
20. For the pyridyl derivative (*N*; Fig. 2) a benzaldehyde functionalised resin (PS-benzaldehyde; polystyrene backbone 1–2% cross-linked with divinylbenzene available from Argonaut Technologies) was substituted for the sulfonic acid. Additionally, for the chloroalkyl containing isocyanate reactions the aminomethylpolystyrene was excluded from the scavenging process.
21. A mono-mode single cavity microwave instrument with pressure and temperature sensing, and an integrated liquid handling robot (Emrys Synthesizer) was used for the library preparation and an Emrys optimizer EXP for investigative and early stage development work. Both machines are available from Personal Chemistry a subdivision of Biotage.
22. *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide on polystyrene (EDC polymer bound) available from Aldrich cat. no. 09657 and *N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide on JandaJel both proved to be less effective for this cyclisation.
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