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Facile, efficient and eco-friendly synthesis of 5-sulfenyl tetrazole derivatives of indoles and pyrroles

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ABSTRACT

A concise, two-step eco-friendly approach towards the synthesis of 5-sulfenyl tetrazole derivatives of indoles and pyrroles, is reported. The synthesis comprises the oxone-mediated thiocyanation of the starting heterocycles towards intermediate 3-thiocyanato indoles and 2-thiocyanato pyrroles, and their subsequent treatment with sodium azide in 2-propanol/water under zinc bromide promotion.

The tetrazoles are five-membered ring 6π-heterocycles, containing four contiguous nitrogen atoms.[1a] They are not found in Nature;[1b] however, tetrazole derivatives possess interesting applications in agriculture, pharmacy, photography and as components of explosives. In medicinal chemistry, they are employed as metabolically-stable carboxylic acid isosteres.[2]

5-Substituted tetrazoles are usually prepared by a [3+2] cycloaddition reaction between organic nitriles and hydrazoic acid,[3] commonly generated in situ from azides, including NaN_3,[4] $TMSN_3$,[5a,b] tin[5c,d] and organoaluminium azides,[5e,f] and DPPA,[5g] and protic or Lewis acids such as I_2,[6a] $NaHSO_4/SiO_2$,[6a] TMSCl,[6b] $Et_3N{\cdot}HCl$,[6c] NH_4Cl,[7a] $NH_4Cl/LiCl$,[7b] Cu_2O,[7c] $AlCl_3$[7d] and $FeCl_3$.[4a] An intramolecular version has also been reported, employing an organic azide moiety.[8]

More recently, the use zinc promoters, especially $ZnBr_2$ in water-based solvents, has greatly simplified the synthesis.[9] Variations including mesoporous ZnS nanospheres,[10a] Zn/Al hydrotalcite,[10b] Bu_2SnO[10c] and $ZnCl_2$ under solventless conditions have also been reported.[10d] Ionic liquids[10e] and a catalyst-free method in glycerol[10f] have been proposed as alternative media.

Thiocyanates are versatile chemical intermediates, which embody a strategically useful entry to various derivatives carrying C–S bonds.[11] Thiocyanation of heteroaromatics has been carried out by reaction with inorganic thiocyanate salts under assistance by different acid catalysts or oxidants. Acids include montmorillonite K-10,[12a] acid alumina,[12b] TsOH[12c] and Amberlyst-15,[12d] while oxidants encompass HIO_3,[13a] I_2O_5,[13b] I_2/MeOH,[13c] CAN,[13d] $Mn(OAc)_3$,[13e] $FeCl_3$,[13f] DDQ,[13g] H_2O_2[13h] and Oxone®,[13i] among others.

5-Sulfenyl tetrazoles are a small and special group of tetrazoles that can be found as a distinguished motif in active pharmaceutical ingredients, such as cefamandol and latamoxef, and other potentially bioactive molecules (Fig. 1).[14]

5-Sulfenyl tetrazoles have been occasionally synthesized from thiocyanates and inorganic azides during studies on 5-substituted tetrazoles.[7a,b,9a]

In addition, 1-substituted 5-thiotetrazoles have been used as capping agents for stabilization of gold nanoparticles,[15a] while 5-ethyl- and 5-benzyl-thio-1*H*-tetrazole are used as 1*H*-tetrazole replacements in oligonucleotide synthesis.[15b,c] The sulfur atom of the thioether group conveys better solubility and turns the tetrazole ring more acidic than the corresponding 5-alkyl tetrazoles, improving their ability to act as activators.[16]

NH_4Cl[15,17] and $ZnBr_2$[4b] have been employed as promoters for the synthesis of 5-thio- and 5-seleno tetrazoles; $Et_3N{\cdot}HCl$[18a] and magnetic Fe_3O_4 nanoparticles have also been used recently.[18b] Additionally, 5-alkyl(aryl)thiotetrazoles, were advantageously prepared in a toluene-water biphasic system under phase-transfer catalysis which eased work-up operations,[17b] and further, Et_2AlN_3 was also used as a source of the azide ion.[5e,f]

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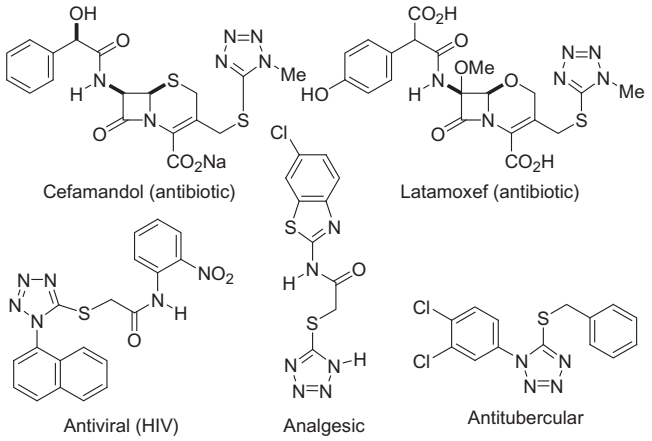
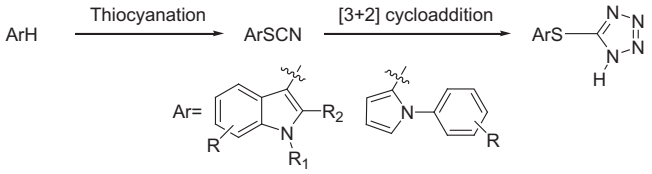


Figure 1. Examples of bioactive 5-sulfenyl tetrazoles.



Scheme 1. Proposed reaction sequence towards 5-sulfenyl tetrazoles.

Taking into account our interest in the development of new approaches to the synthesis of polysubstituted nitrogen heterocycles with potential as bioactive compounds, herein we wish to report the synthesis of 5-sulfenyl tetrazole derivatives of indoles and pyrroles in a two-step sequence involving the thiocyanation of the substituted heterocycles and the subsequent reaction of the resulting thiocyanates with NaN_3 under $ZnBr_2$ promotion, as shown in Scheme 1.

The different starting indoles (**1**) were synthesized according to the literature.[19] The intermediate thiocyanates **3** and **4** were prepared by reaction of the indoles and *N*-phenyl pyrroles (**2**)[20] with NH_4SCN, employing oxone as oxidizing agent. Following an adaptation of the work of Wu[13i] and based on our previous results,[20] the amount of NH_4SCN was limited to 1 mmol/mmol of heterocycle in order to avoid formation of polythiocyanated compounds.

In all cases (Table 1), the thiocyanation was efficient and furnished the expected compounds in short times and with high regioselectivity. Only 3-substituted indoles and 2-substituted pyrroles were obtained.[21] In their infrared spectra, all compounds exhibited the typical CN stretching band of the SCN moiety at 2100–2200 cm^{-1} and a resonance at 110–113 ppm in the ^{13}C NMR spectra. The mechanism of the thiocyanation has been studied.[13i]

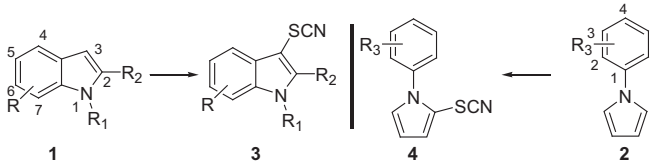
With the thiocyanato derivatives in hand, the next step was the [3+2] cycloaddition towards the tetrazoles. This was attempted under different conditions and later optimized, by systematically changing the solvent, amount of NaN_3 and promoter. The effects of time and reaction temperature were also studied, with the results summarized in Table 2.

Employing the protocols of the groups of Das[6a] (entry 1) and Hallberg,[22] low product yields and incomplete consumption of the starting material were observed (entry 2). On the other hand, use of glycerol as the reaction medium without promoter (entry 3)[10f] and water as the sole solvent[9a] gave no product (entry 4). However, the approach reported by the group of Suresh babu[4b] met with better luck, furnishing 89% of the expected heterocycle (entry 5). Apparently, in this case the addition of 2-propanol was a key for the success of transformation.

Based on this result, it was decided to investigate the substitution of $ZnBr_2$ with $ZnCl_2$, observing that this caused an increase of the reaction time to 7 h, while reducing the yields to 53% (entry 6). A decrease in the amount of solvent (from 30 to 10 mL) allowed decreasing the reaction time while maintaining the yields (entry 7). Lowering the amount of NaN_3 to 1.2 equiv and further decreasing the amount of the solvent mixture to 6 mL/mmole of thiocyanate (entry 8) resulted in 94% yield of the tetrazole, after 2 h. However, reducing the amount of promoter and running the reaction at 70 °C or room temperature (entries 9–11) proved nonsatisfactory.

These tests demonstrated the need of stoichiometric amounts of the promoter and high temperatures for satisfactory results

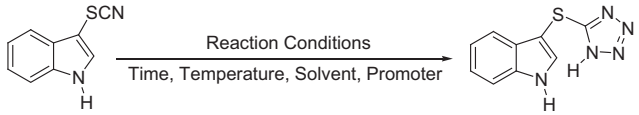
Table 1
Synthesis of thiocyanates **3** and **4** by reaction of indoles **1** and pyrroles **2** with NH_4SCN and Oxone® in MeOH



Entry No	R	R_1	R_2	R_3	Prod. No	Time (h)	Yield[a] (%)
1	H	H	H	—	**3a**	1	93
2	5-Br	H	H	—	**3b**	3	90
3	5-(*p*-Tolyl)	H	H	—	**3c**	4	80
4	H	H	Me	—	**3d**	2	91
5	H	Me	H	—	**3e**	2	96
6	H	n-C_8H_{17}	H	—	**3f**	5	95
7	H	Ph	H	—	**3g**	3.5	90
8	Br	Me	H	—	**3h**	3	95
9	—	—	—	H	**4a**	2	89
10	—	—	—	4-OMe	**4b**	0.5	92
11	—	—	—	4-Cl	**4c**	1.5	92
12	—	—	—	3-Cl	**4d**	1.5	90
13	—	—	—	2-Cl	**4e**	1.5	90

[a] Isolated yields after column chromatography.

Table 2
Optimization of the synthesis of the 5-sulfenyl tetrazoles



Entry No	Solvent (mL)	NaN_3 (equiv)	Promoter (equiv)	Temp (°C)	Time (h)	Yield[a] (%)
1	DMF (1.5)	1.5	I_2 (0.06)	120	4	76
2	DMF (1.0)	1.1	NH_4Cl (1.2)	160	0.25	64[b]
3	Glycerol (20)	1.2	—	110	6	—
4	H_2O (10)	1.1	$ZnBr_2$ (1.0)	Reflux	5	—
5	H_2O/2-PrOH (1:1, 30)	2.5	$ZnBr_2$ (1.0)	Reflux	5	89
6	H_2O/2-PrOH (1:1, 10)	2.5	$ZnCl_2$ (1.0)	Reflux	7	53
7	H_2O/2-PrOH (1:1, 10)	2.5	$ZnBr_2$ (1.0)	Reflux	4	87
8	H_2O/2-PrOH (1:1, 6)	1.2	$ZnBr_2$ (1.0)	Reflux	2	94
9	H_2O/2-PrOH (1:1, 6)	1.2	$ZnBr_2$ (0.5)	Reflux	3	78
10	H_2O/2-PrOH (1:1, 6)	1.2	$ZnBr_2$ (1.0)	r.t.	3	39
11	H_2O/2-PrOH (1:1, 6)	1.2	$ZnBr_2$ (1.0)	70	3	64

[a] Isolated yields after column chromatography.
[b] Performed under microwave irradiation.

and defined the optimum conditions as those employed in entry 8.[23]

In order to assess the scope and limitations of the transformation, the 3-thiocyanato-1*H*-indoles prepared as shown in Table 1 were submitted to the optimized conditions, with the results displayed in Table 3. All tetrazole products are novel. Their structures were fully characterized by ^1H and ^{13}C NMR analysis, FT-IR spectroscopy and elemental analysis or HRMS.[24] The tetrazole carbon atoms displayed a characteristic signal in a very narrow region (δ 154–156 ppm) of the ^{13}C NMR spectrum.

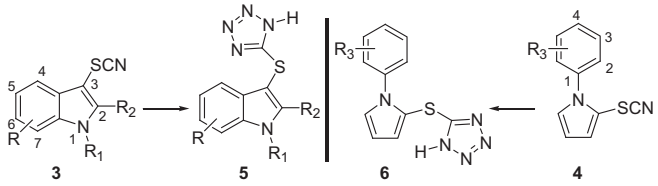
It was observed that the less substituted heterocycle (entry 1) reacted more rapidly than its congeners. On the other hand, substituents exert a large influence. For the *N*-substituted compounds, **3e** reacted faster than **3f** but furnished comparatively lower yields of product (entries 5 and 6). However, introduction of a 5-Br substituent improved the yields at the expense of an increase in the reaction time (entries 5 and 8), compared with the non-methylated analogue **3c** (entry 2).

For the series of tetrazoles derived from 1-aryl-2-thiocyanato-1*H*-pyrroles (**4a**–**e**), the reaction times were generally shorter and the yields remained good to excellent. No significant steric (entry 13) nor electronic (entries 9–11) effects were observed.

The reaction mechanism for the synthesis of tetrazoles has been discussed elsewhere. Pioneering research by Himo et al.,[25a] based on computational and experimental studies, demonstrated the role of Zn in the synthesis of tetrazoles. Using MeCN, MeN_3 and $ZnBr_2$, they were able to prove that there is a significant decrease in the activation energy of the reaction when the nitrogen of the nitrile group is coordinated to the Lewis acid. Whereas binding of Zn^{II} to the azide ion gave calculated activation energy of 34 and 36 kcal mol^{-1} for tetrahedral and octahedral coordinating zinc ions, respectively, when Zn^{II} was connected to the nitrogen atom of the nitrile, the activation energy dropped to 25–30 kcal mol^{-1}. Activation of the nitrile substrate is also the basis of the mode of action of a new organocatalyst for the synthesis of tetrazoles.[6b]

In conclusion, a two step synthesis of new 5-thio-tetrazoles derived from 3-thiocyanato-1*H*-indoles and 2-thiocyanato-1-phenyl pyrroles, is reported. The NH_4SCN/oxone reagent combination was employed for the thiocyanation stage, affording good to excellent yields of the thiocyanate intermediates. The [3+2]

Table 3
Synthesis of 5-sulfenyl tetrazoles **5** and **6** by reaction of 3-indolyl (**3**) and 2-pyrrolyl (**4**) thiocyanates



Entry No	R	R_1	R_2	R_3	St. mat./prod. no	Time (h)	Yield[a] (%)
1	H	H	H	—	**3a/5a**	2	94
2	5-Br	H	H	—	**3b/5b**	3.5	92
3	5-(*p*-Tolyl)	H	H	—	**3c/5c**	4	87
4	H	H	Me	—	**3d/5d**	4	87
5	H	Me	H	—	**3e/5e**	3	83
6	H	n-C_8H_{17}	H	—	**3f/5f**	4.5	95
7	H	Ph	H	—	**3g/5g**	4	90
8	5-Br	Me	H	—	**3h/5h**	4.5	97
9	—	—	—	H	**4a/6a**	2	89
10	—	—	—	4-OMe	**4b/6b**	3	95
11	—	—	—	4-Cl	**4c/6c**	3	81
12	—	—	—	3-Cl	**4d/6d**	2	96
13	—	—	—	2-Cl	**4e/6e**	2	92

[a] Isolated yields after column chromatography.

cycloaddition step towards tetrazoles was optimized with regard to reaction temperature, concentration of the reactants, solvent composition and amounts of NaN_3 and $ZnBr_2$ promoter, to efficiently deliver the products in short times. The use of a hydroalcoholic medium turns the procedure eco-friendly and amenable to use in synthetic organic chemistry.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.01.101.

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21. Typical procedure for the synthesis of the thiocyanates: A magnetically stirred mixture of the indole (1.0 mmol) and NH_4SCN (114 mg, 1.5 mmol) in MeOH (10 mL), was treated with Oxone (921 mg, 1.5 mmol), and the reaction was stirred at room temperature until complete consumption of the starting material (TLC). Water (30 mL) was added and the products were extracted with EtOAc (3 × 10 mL). The organic phase was dried ($MgSO_4$), concentrated under reduced pressure and the residue was purified by chromatography (hexane/EtOAc, 90:10).
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23. Typical procedure for the synthesis of the 5-sulfenyl tetrazoles: A stirred mixture of the thiocyanate (1 mmol, 1.0 equiv) NaN_3 (1.2 equiv) and $ZnBr_2$ (1.0 equiv) in 2-PrOH/H_2O (1:1, 6 mL) was refluxed until complete consumption of the starting material (2–4.5 h). After cooling to room temperature, the reaction was acidified with 1 M HCl (10 mL) and diluted with EtOAc (15 mL). The aqueous phase was extracted with EtOAc (2 × 20 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc to EtOAc/MeOH 90:10).
24. Characterization of selected compounds: ^{1}H and ^{13}C NMR were run at 400 and 100 MHz, respectively, with the samples dissolved in DMSO-d_6. 3-((1*H*-Tetrazol-5-yl)thio)-1*H*-indole (**5a**). Beige solid, mp: 210.4–211.6 °C. IR (KBr, *ν*): 3269, 2336, 1653, 1508, 1310, 1042, 746 and 604 cm^{-1}. ^{1}H NMR *δ*: 11.83 (s, 1H), 7.91 (d, 1H, *J* = 2.3 Hz), 7.55 (d, 1H, *J* = 8.0 Hz), 7.49 (d, 1H, *J* = 7.8 Hz), 7.23–7.20 (m, 1H) and 7.14–7.10 (m, 1H). ^{13}C NMR *δ*: 155.3, 136.6, 133.1, 128.3, 122.3, 120.4, 117.9, 112.9 and 94.0. EI-MS (*m*/*z*, rel int., %): 218 [(M+1)$^+$, 2], 217 (M$^+$, 5), 160 (29), 148 (100), 89 (19) and 77 (19). Anal. Calcd: C, 49.76; H, 3.25. Found: C, 50.09; H, 3.55. 3-((1*H*-Tetrazol-5-yl)thio)-5-bromo-1*H*-indole (**5b**). Beige solid, mp: 209.5–211.3 °C. IR (KBr, *ν*): 3274, 2364, 1566, 1309, 1217, 1109, 1033, 795 and 746 cm^{-1}. ^{1}H NMR *δ*: 12.00 (s, 1H), 7.93 (d, 1H, *J* = 2.5 Hz), 7.64 (s, 1H), 7.49 (d, 1H, *J* = 8.6 Hz) and 7.31 (dd, 1H, *J* = 8.6 Hz, 0.9 Hz). ^{13}C NMR *δ*: 155.1, 135.4, 134.6, 130.4, 125.0, 120.3, 114.5, 113.3 and 94.2. EI-MS (*m*/*z*, rel int.,%): 296 [(M+2)$^+$, 34], 295 [(M+1)$^+$, 4], 294 (M$^+$, 31), 239 (64), 227 (97), 225 (100), 173 (40), 148 (37), 120 (52), 114 (16) and 45 (34). HRMS obsd *m*/*z*: 317.9429; $C_9H_6BrN_5SNa$ [M+Na]$^+$ requires *m*/*z* 317.9425. 3-((1*H*-Tetrazol-5-yl)thio)-5-(*p*-tolyl)-1*H*-indole (**5c**). Brown solid, mp 213.3–215.5 °C. IR (KBr, *ν*): 3263, 2331, 1502, 1473, 1308, 1108, 1036 and 799 cm^{-1}. ^{1}H NMR *δ*: 11.81 (s, 1H), 7.90 (s, 1H), 7.65 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.52–7.50 (m, 3H), 7.23 (d, 2H, *J* = 7.4 Hz), 2.33 (s, 3H). ^{13}C NMR *δ*: 154.9, 137.9, 135.6, 135.3, 133.2, 132.7, 128.9, 128.5, 126.1, 121.2, 115.1, 112.4, 94.3 and 20.1. EI-MS (*m*/*z*, rel int.,%): 308 [(M+1)$^+$, 2], 307 (M$^+$, 11), 277 (18), 238 (44), 173 (100), 11 (21), 77 (9) and 45 (21). Anal. Calcd: C, 62.58; H, 4.26. Found: C, 62.68; H, 4.68. 3-((1*H*-Tetrazol-5-yl)thio)-2-methyl-1*H*-indole (**5d**). Beige solid, mp: 184.5–185.7 °C. IR (KBr, *ν*): 3339, 3052, 2332, 1546, 1518, 1314, 1035 and 742 cm^{-1}. ^{1}H NMR *δ*: 11.68 (s, 1H), 7.43–7.39 (m, 2H), 7.16–7.12 (m, 1H), 7.09–7.06 (m, 1H) and 2.52 (s, 3H). ^{13}C NMR *δ*: 155.2, 143.1, 135.5, 129.2, 121.4, 120.0, 117.1, 111.3, 91.3 and 11.6. EI-MS (*m*/*z*, rel int.,%): 233 [(M+2)$^+$, 2], 233 [(M+1)$^+$, 5], 231 (M$^+$, 34), 174 (33), 162 (100), 130 (32), 118 (67) and 77 (27). HRMS obsd *m*/*z*: 254.0471; $C_{10}H_9N_5SNa$ [M+Na]$^+$ requires *m*/*z* 254.0476. 3-((1*H*-Tetrazol-5-yl)thio)-1-methyl-1*H*-indole (**5e**). Beige solid, mp: 179.9–181.4 °C. IR (KBr, *ν*): 3394, 3110, 2331, 1517, 1243, 1028 and 744 cm^{-1}. ^{1}H NMR *δ*: 7.87 (s, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.29–7.26 (m, 1H), 7.18–7.14 (m, 1H) and 3.85 (s, 3H). ^{13}C NMR *δ*: 155.2, 137.1, 136.6, 128.6, 122.2, 120.4, 118.0, 110.5, 92.9 and 32.7. EI-MS (*m*/*z*, rel int.,%): 231 (M$^+$, 4), 174 (27), 162 (100), 118 (15) and 77 (16). Anal. Calcd: C, 51.93; H, 3.92. Found: C, 51.99; H, 3.99. 3-((1*H*-Tetrazol-5-yl)thio)-1-octyl-1*H*-indole (**5f**). Yellow solid, mp: 95.4–96.9 °C. IR (KBr, *ν*): 3444, 2953, 2923, 2852, 2713, 1613, 1508, 1492, 1457, 1299, 1165, 1020 and 738 cm^{-1}. ^{1}H NMR *δ*: 7.91 (s, 1H), 7.59

(d, 1H, J = 8.1 Hz), 7.47 (d, 1H, J = 7.7 Hz), 7.27–7.23 (m, 1H), 7.16–7.12 (m, 1H), 4.22 (t, 2H, J = 6.8 Hz), 1.85–1.75 (m, 2H), 1.28–1.22 (m, 10H) and 0.85–0.83 (m, 3H). ^{13}C NMR δ: 155.1, 136.4, 135.5, 128.6, 122.1, 120.3, 118.1, 110.6, 93.0, 45.8, 30.9, 29.3, 28.3, 25.9, 21.7 and 13.6. EI-MS (m/z, rel int.,%): 331 [(M+2)$^+$, 2], 330 [(M+1)$^+$, 7], 329 (M$^+$, 33), 272 (57), 260 (59), 162 (100), 130 (28), 77 (8), 57 (26) and 41 (50). Anal. Calcd: C, 61.97; H, 7.04. Found: C, 61.74; H, 7.23. 3-((1*H*-Tetrazol-5-yl)thio)-1-phenyl-1*H*-indole (**5g**). Yellow solid, mp: 153.1–154.3 °C. IR (KBr, ν): 3033, 2331, 1598, 1499, 1457, 1231, 1017, 746 and 695 cm^{-1}. ^{1}H NMR $\delta\delta$: 8.22 (d, J = 0.9 Hz, 1H), 7.66–7.56 (m, 6H), 7.49–7.45 (m, 1H), 7.33–7.29 (m, 1H) and 7.26–7.22 (m, 1H). ^{13}C NMR δ: 154.9, 137.9, 136.0, 135.5, 129.8, 129.1, 127.3, 124.2, 123.5, 121.6, 118.6, 111.1 and 96.9. EI-MS (m/z, rel int.,%): 294 [(M+1)$^+$, 5], 293 (M$^+$, 29), 236 (36), 224 (100), 121 (21) and 77 (40). HRMS obsd m/z: 316.0614; $C_{15}H_{11}N_5SNa$ [M+Na]$^+$ requires m/z 316.0633. 3-((1*H*-Tetrazol-5-yl)thio)-5-bromo-1-methyl-1*H*-indole (**5h**). Beige solid, mp: 205.5–207.0 °C. IR (KBr, ν): 3394, 1509, 1465, 1242, 795 and 614 cm^{-1}. ^{1}H NMR δ: 7.87 (s, 1H), 7.62 (d, J = 1.7 Hz, 1H), 7.52 (d, J = 8.7 Hz, 1H), 7.36 (dd, J = 8.7 Hz, 1.8 Hz, 1H) and 3.82 (s, 3H). ^{13}C NMR δ: 155.2, 137.6, 135.8, 130.6, 124.7, 120.5, 113.2, 112.8, 94.3 and 33.0. EI-MS (m/z, rel int.,%): 310 [(M+2)$^+$, 35], 309 [(M+1)$^+$, 5], 308 (M$^+$, 35), 253 (48), 241 (97), 239 (100), 162 (24), 117 (32) and 77 (7). HRMS obsd m/z: 331.9575; $C_{10}H_8BrN_5SNa$ [M+Na]$^+$ requires m/z 331.9581. 5-((1-Phenyl-1*H*-pyrrol-2-yl)thio)-1*H*-tetrazole (**6a**). Yellow solid, mp: 160.1–161.4 °C. IR (KBr, ν): 3048, 2366, 1595, 1498, 1322, 1038, 766 and 740 cm^{-1}. ^{1}H NMR δ: 7.45–7.34 (m, 6H), 6.82 (dd, J = 3.6 Hz, 1.6 Hz, 1H) and 6.40–6.38 (m, 1H). ^{13}C NMR δ: 155.0, 138.3, 128.7, 128.1, 127.7, 126.0, 121.6, 111.4 and 109.9. EI-MS (m/z, rel int.,%): 244 [(M+1)$^+$, 2], 243 (M$^+$, 6), 242 (37), 185 (34), 174 (45), 173 (100), 172 (48), 130 (16), 115 (19), 77 (65), 70 (26) and 51 (39). HRMS obsd m/z: 266.0465; $C_{11}H_9N_5SNa$ [M+Na]$^+$ requires m/z 266.0476. 5-((1-(4-Methoxyphenyl)-1*H*-pyrrol-2-yl)thio)-1*H*-tetrazole (**6b**). White solid, mp: 210.0–211.4 °C. IR (KBr, ν): 3012, 2360, 1517, 1250, 1039, 837 and 740 cm^{-1}. ^{1}H NMR δ: 7.27–7.24 (m, 3H), 6.96 (d, J = 8.9 Hz, 2H), 6.78 (dd, J = 3.6 Hz, 1.7 Hz, 1H), 6.39–6.35 (m, 1H) and 3.76 (s, 3H). ^{13}C NMR δ: 158.6, 155.1, 131.3, 128.4, 127.5, 121.2, 113.9, 111.5, 109.6 and 55.2. EI-MS (m/z, rel int.,%): 275 [(M+2)$^+$, 2], 274 [(M+1)$^+$, 6], 273 (M$^+$, 37), 216 (20), 204 (100), 173 (37), 92 (15) and 77 (20). Anal. Calcd: C, 52.73; H, 4.06. Found: C, 52.86; H, 4.31. 5-((1-(4-Chlorophenyl)-1*H*-pyrrol-2-yl)thio)-1*H*-tetrazole (**6c**). Orange solid, mp: 171.2–173.1 °C. IR (KBr, ν): 3129, 3010, 2362, 1494, 1311, 1094, 837 and 739 cm^{-1}. ^{1}H NMR δ: 7.50 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 8.8, 2H), 7.35 (dd, 1H, J = 3.0 Hz, 1.8 Hz), 6.82 (dd, J = 3.7, 1.8, 1H) and 6.40 (dd, 1H, J = 3.7 Hz, 3.0 Hz). ^{13}C NMR δ: 155.0, 137.2, 132.4, 128.8 128.3, 127.9, 122.0, 111.6 and 110.2. EI-MS (m/z, rel int.,%): 279 [(M+2)$^+$, 6], 278 [(M+1)$^+$, 2], 277 (M$^+$, 18), 219 (19), 173 (100), 111 (13) and 75 (19). HRMS obsd m/z: 300.0074; $C_{11}H_8ClN_5SNa$ [M+Na]$^+$ requires m/z 300.0087.

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