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The Reaction of DABCO with 4-Chloro-5*H*-1,2,3-dithiazoles: Synthesis and Chemistry of 4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles

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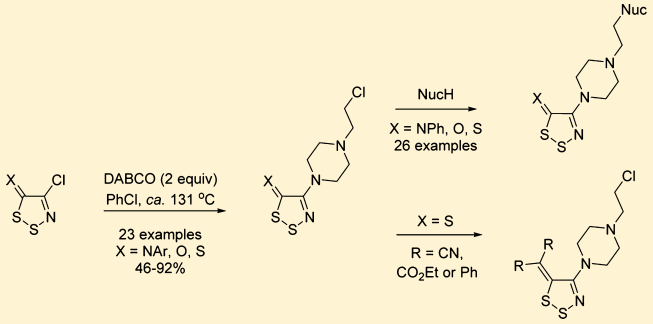
Supporting Information

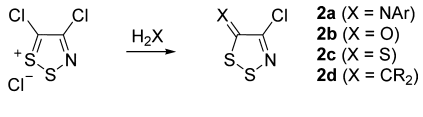
ABSTRACT: *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-anilines react with DABCO in hot PhCl to give *N*-{4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}-anilines in high yields (70−92%). The reaction also works with 4-chloro-5*H*-1,2,3-dithiazol-5-one and -thione, giving the corresponding products in 85% and 76% yields, respectively. While the reaction of several (4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)methanes with DABCO failed to give {4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}-methanes, these can be prepared in moderate yields via classical cycloaddition−retrocycloaddition strategies from 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole-5-thione. The 2-chloroethyl moiety on selected dithiazoles was also modified without cleavage of the 1,2,3-dithiazole by reaction with various nucleophiles, giving access to 4-[*N*-(2-substituted)piperazin-1-yl]-5*H*-1,2,3-dithiazoles in moderate to high yields.



1. INTRODUCTION

4,5-Dichloro-1,2,3-dithiazolium chloride (Appel salt) (**1**),[1] first prepared in 1985, provides access to many neutral 4-chloro-5*H*-1,2,3-dithiazoles **2**[2] (Scheme 1), several of which display

Scheme 1. Structure of Appel Salt 1 and Its Conversion to Neutral 5-Chloro-5*H*-1,2,3-dithiazoles 2a−d



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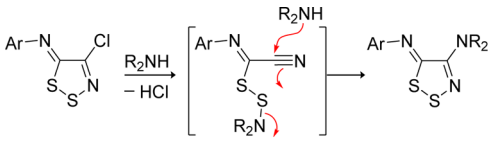
interesting biological activities such as antitumor,[3] antibacterial,[4] antifungal,[5] and herbicidal.[6] Recently, selected 1,2,3-dithiazoles inactivated the glutamine/amino acid transporter ASCT2,[7] while others elicited pigment loss on developing *Xenopus* embryos.[8]

Furthermore, 4-chloro-1,2,3-dithiazoles **2** are useful intermediates in organic synthesis.[2] Recent developments on the chemistry of 1,2,3-dithiazoles include their ring transformation to pyrazolo[3,4-*d*]thiazoles,[9] pyridothiazoles,[10] pyrido[2,3-*d*]-pyrimidines,[11] and the rare 1,2,4-dithiazine system (pyrazolo-[3,4-*e*][1,2,4]dithiazines and benzo[*e*][1,2,4]dithiazines).[12]

Despite the numerous reports on the ring transformations of 1,2,3-dithiazoles into other heterocycles and/or functionalities, and their interesting biological activities, there are only four reports on the functionalization of the dithiazole C4 position that maintain the integrity of the dithiazole ring.[13] The most general of which is the reaction of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines **2a** with dialkylamines, which gives *N*-(4-dialkylamino-5*H*-1,2,3-dithiazol-5-ylidene)anilines **4**.[13a] This reaction, however, suffers from variable yields, the formation of unknown side products, and lacks generality. The transformation proceeds via an addition of the nucleophile, ring-opening, and ring closure (ANRORC)[14] style mechanism where dialkylamine attacks the S2 ring sulfur, cleaving the 1,2,3-dithiazole to form an intermediate disulfide **3** that adds a second dialkylamine to the nitrile to give an amidine which then cyclizes onto the disulfide to release the initial dialkylamine (Scheme 2).

Rarer examples of C4 substitution reactions include the intramolecular cyclization of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-hydroxyaniline (**5a**) to benzo[*b*][1,2,3]dithiazolo-[5,4-*e*][1,4]oxazine (**6a**),[13b] which recently was extended to

Scheme 2. Reaction and Mechanism for the Transformation of *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines 2a to *N*-(4-Dialkylamino-5*H*-1,2,3-dithiazol-5-ylidene)anilines 4



2a **3** **4** (7-76%)

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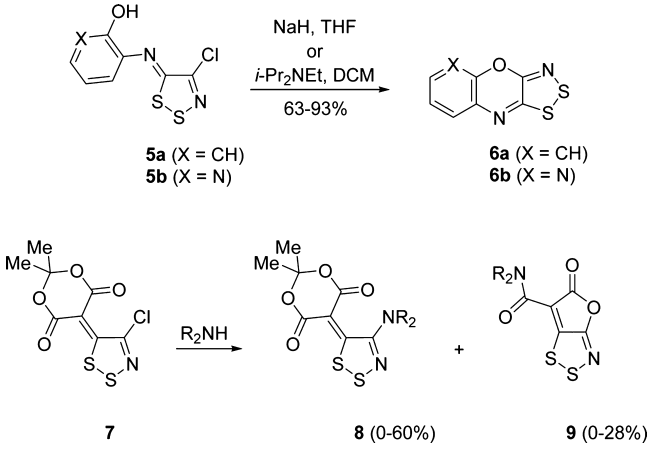
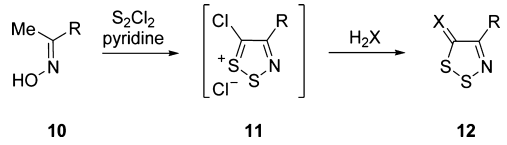
include a pyrido-fused analogue **6b**,[13c] and the reaction of 5-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**7**) with secondary dialkylamines to give 5-(4-dialkylamino-5*H*-1,2,3-dithiazol-5-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-diones **8** and 6-dialkylaminocarbamoyl-5-oxo-5*H*-furo[2,3-*d*][1,2,3]dithiazoles **9**[13d] (Scheme 3).

Scheme 3. Rare Examples for the Functionalization of the C4 Position of 1,2,3-Dithiazoles



Interestingly, 4-aryl- or 4-alkyl-substituted 1,2,3-dithiazoles **12** can also be prepared independently from the appropriate acetoximes **10**,[3,15] although the yields are often moderate to low owing to the difficulties in isolating and purifying the intermediate dithiazolium chlorides **11** (Scheme 4).

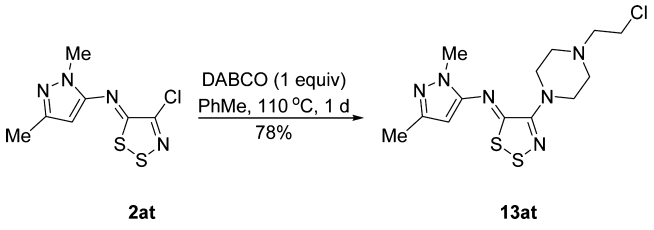
Scheme 4. Synthesis of 4-Substituted 1,2,3-Dithiazoles 12 from Acetoximes 10



During our recent work on *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amines,[12] we discovered that *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (**2at**) reacted with DABCO in hot toluene (110 °C) to give *N*-{[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}-1,3-dimethyl-1*H*-pyrazol-5-amine (**13at**) in 78% yield (Scheme 5).

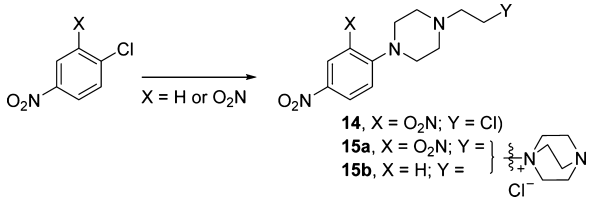
During this transformation, the dithiazole C4 position was substituted with an *N*-(2-chloroethyl)piperazinyl group, which presumably originated from ring-opening of quaternized DABCO by chloride.

Scheme 5. Reaction of *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (2at) with DABCO



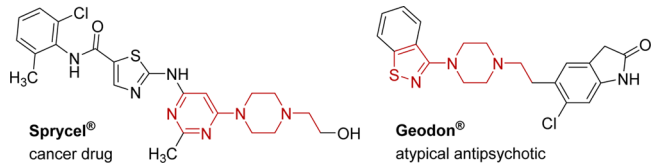
Ring-opening of quaternized DABCO in the presence of an external nucleophile was first invoked in 1963 when its acid-catalyzed polymerization was reported.[16] That same year, the reaction of DABCO with *p*-chloronitrobenzenes gave *N*-(2-chloroethyl)-*N*′-(4-nitrophenyl)piperazines **14** and/or *N*-{2-[*N*-(4-nitrophenyl)piperazin-1-yl]ethyl}-1,4-diazabicyclo-[2.2.2]octan-1-ium chlorides **15**[17] (Scheme 6).

Scheme 6. Reaction of *p*-Chloronitrobenzenes with DABCO



Despite these early observations and some sporadic reports,[18] only recently has the quaternization and subsequent ring-opening of DABCO been used as a strategy for the synthesis of compound libraries bearing a 2-substituted ethylpiperazine group.[19] Other bicyclic (e.g., quinuclidine)[20] and nonbicyclic[21] tertiary amines behave similarly under appropriate conditions.

Since the piperazine group frequently appears in biologically active compounds[22] and, in particular, the *N*-heteroaryl-*N*′-ethylpiperazine fragment is part of several approved drugs such as Sprycel (dasatinib) and Geodon (ziprasidone), we chose to develop this reaction further.



Herein, we report an investigation on the reaction of 4-chloro-5*H*-1,2,3-dithiazoles **2** with DABCO, which examines the scope and limitations of the reaction. Furthermore, facile functionalization of the obtained *N*-(2-chloroethyl)piperazinyl dithiazole products is demonstrated.

2. RESULTS AND DISCUSSION

2.1. Reaction of DABCO with 1,2,3-Dithiazoles. Initial investigations showed that the reaction of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (**2at**) with DABCO to give the *N*-{[*N*-(2-chloroethyl)-piperazin-1-yl]-5*H*-1,2,3-dithiazole **13at** was applicable to other 1,2,3-dithiazoles. As such, for the optimization of the reaction, with respect to the solvent, reagent concentrations, and reaction time, *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-aniline (**2aa**) was chosen. From the optimization the following were observed: (1) The choice of solvent was critical: in polar solvents, the dithiazole **2aa** reacted with DABCO even at *ca.* 20 °C to give multiple colorless products with no formation of the desired product; the fastest and cleanest reactions occurred in PhCl at *ca.* 131 °C. (2) The concentration of the reaction affected the yield: under concentrated reaction conditions (0.2 mmol of **2aa** in 2 mL), decomposition and higher yields of side products were observed. (3) Under more dilute reaction conditions (0.2 mmol of **2aa** in 8 mL), it was necessary to

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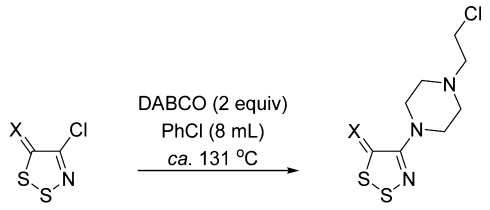
increase the quantity of DABCO to achieve a good reaction rate and limit side reactions. As such, the best conditions obtained from the optimization study were to treat the dithiazolimine **2aa** with DABCO (2 equiv) in PhCl (8 mL) for 4 h at *ca.* 131 °C, which gave *N*-{4-[*N*-(2-chloroethyl)-piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (**13aa**) in 79% yield (Table 1, entry 1). Nevertheless, even under these partially optimized conditions, it was not possible to completely avoid the formation of side products, which were tentatively assigned as *N*-{4-[*N*-(2-thiocyanatoethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (**16ah**), *N*-(2-chloroethyl)-*N*-phenylpiperazine-1-carbimidoyl cyanide (**17a**), and *N*-(2-{*N*-[5-(phenylimino)-5*H*-1,2,3-dithiazol-4-yl]piperazin-1-yl}ethyl)-1,4-diazabicyclo[2.2.2]octan-1-ium chloride (**18**) (Scheme 7). For a detailed discussion on the reaction optimization and spectroscopic characterization of the products, please see the Supporting Information (SI), section S2.1.

Table 1. Reaction of 4-Chloro-5*H*-1,2,3-dithiazoles 2 with DABCO



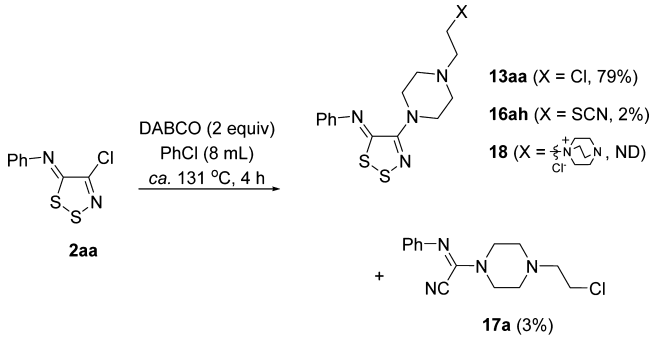
2 **13**

entry	dithiazole (X)	time (h)	yield (%)
1	**2aa** (PhN)	4	**13aa** (79)
2	**2ab** (2-MeC$_6$H$_4$N)	4.5	**13ab** (83)
3	**2ac** (2-MeOC$_6$H$_4$N)	2.5	**13ac** (91)
4	**2ad** (2-ClC$_6$H$_4$N)	1.25	**13ad** (90)
5	**2ae** (2-BrC$_6$H$_4$N)	1.25	**13ae** (92)
6	**2af** (2-O$_2$NC$_6$H$_4$N)	0.42	**13af** (88)
7	**2ag** (3-MeC$_6$H$_4$N)	5.5	**13ag** (82)
8	**2ah** (3-MeOC$_6$H$_4$N)	5.5	**13ah** (78)
9	**2ai** (3-BrC$_6$H$_4$N)	4.4	**13ai** (83)
10	**2aj** (4-MeC$_6$H$_4$N)	7.3	**13aj** (76)
11	**2ak** (4-MeOC$_6$H$_4$N)	7	**13ak** (70)
12	**2al** (4-BrC$_6$H$_4$N)	5	**13al** (80)
13	**2am** (4-O$_2$NC$_6$H$_4$N)	3	**13am** (74)
14	**2an** (4-NCC$_6$H$_4$N)	3.42	**13an** (82)
15	**2ao** (naphth-1-ylN)	3	**13ao** (76)
16	**2ap** (naphth-2-ylN)	5	**13ap** (77)
17	**2aq** (pyrid-2-ylN)	12	**13aq** (46)[a]
18	**2ar** (pyrid-3-ylN)	4	**13ar** (85)
19	**2as** (pyrazin-2-ylN)	12	**13as** (74)[b]
20	**2at** (pyrazol-5-ylN)	8.7	**13at** (79)
21	**2au** (thiazol-2-ylN)	12	**13au** (71)[c]
22	**2b** (O)	0.33	**13b** (85)
23	**2c** (S)	3	**13c** (76)
24	**2da** [C(CN)$_2$]	3	**13da** (–)[d]
25	**2db** [C(CO$_2$Et)$_2$]	5	**13db** (–)[d]

[a]40% recovered starting material. [b]15% recovered starting material. [c]8% recovered starting material. [d]Predominantly baseline material observed.

The partially optimized reaction conditions were then applied to a diverse library of 4-chloro-5*H*-1,2,3-dithiazoles **2** to investigate the scope and limitations of the reaction (Table 1). *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines bearing *ortho*-substituents (**2ab**–**af**) reacted faster than those containing only *meta*- or *para*-substituents, (**2ag**–**ai**) and (**2aj**–**an**), respectively (Table 1, entries 2–6 vs entries 7–14). Furthermore, within an *ortho*-, *meta*-, or *para*-substituted series, the reaction was faster in the presence of electron-withdrawing substituents. For example, within the *ortho*-substituted series, the reaction rate followed the trend Me < MeO < Br ≈ Cl < O_2N. *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)hetarylamines also worked well (Table 1, entries 18 and 20). The reactions of dithiazolimines **2aq**, **2as**, and **2au**, however, were slow, especially, in the case of the pyrid-2-yl analogue **2aq**, which, even after 12 h, gave the product in 46% yield, together with 40% recovered starting material. Longer reaction times or increasing the equivalents of DABCO did not improve product yield: in the first case, increasing the consumption of starting material failed to improve the product yield, and in the second case, a lower yield of the desired product was obtained.

Scheme 7. Reaction of Dithiazolimine 2aa with DABCO[a]



[a]ND = not determined. Recovered **2aa** (5%) also isolated.

4-Chloro-5*H*-1,2,3-dithiazol-5-one (**2b**) and -thione (**2c**) both reacted with DABCO to give the desired products **13b** and **13c** in 85% and 76% yields, respectively, and to the best of our knowledge, this is the first report for their modification at the C4 position: the structure of the thione **13c** was supported by single-crystal X-ray crystallography (see the SI, section S4.). Disappointingly, with the 4-chloro-5*H*-1,2,3-dithiazol-5-ylidenes **2d**, the desired products were not observed and predominantly intractable baseline material was obtained.

The relative reactivities of the dithiazoles toward DABCO suggested that the substituent at C5 affected the electrophilicity of the dithiazole ring. In the case of the *N*-aryl dithiazolimines **2a**, both steric and electronic factors were discernible. Owing to steric hindrance, *ortho*-substituted *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines **2ab**–**2af** were expected to have a greater torsion angle between the dithiazole and the *N*-aryl ring compared with their *meta*- and *para*-substituted analogues, **2ag**–**2ai** and **2aj**–**2an**, respectively. As the torsion angle increases, the conjugation between the *N*-aryl and the dithiazole decreases,[23] leading to an increase in the electrophilicity of the latter. The behavior of the *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)hetarylamines **2aq** and **2as** was more intriguing. Introducing the pyridyl (or pyrazinyl) ring was expected to increase the electrophilicity of the dithiazole owing to the electron-withdrawing character of the pyridyl ring. Nevertheless, the reaction times of the pyrid-3-yl- and the phenyl-substituted dithiazolimines, **2ar** and **2aa**, respectively, were similar, suggesting that the inductive electron-withdrawing power of the pyridyl nitrogen was not significant. Furthermore,

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in the case of the pyrid-2-yl-, pyrazin-2-yl-, and thiazol-2-yl-substituted dithiazolimines, **2aq**, **2as**, and **2au**, respectively, a long reaction time was observed. A similar behavior was observed in our previous study on the ring transformation of [(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]azines into azine fused thiazole-2-carbonitriles where, in the case of the pyrazin-2-yl analogue, the dithiazole, also, was more resistant to nucleophilic attack by the external nucleophile.[10] Tentatively, the reduced reactivity in these systems can be attributed to the presence of a nonbonding N···S1−S2 interaction (Figure 1).

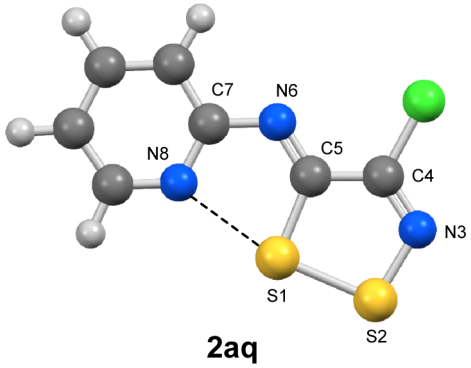
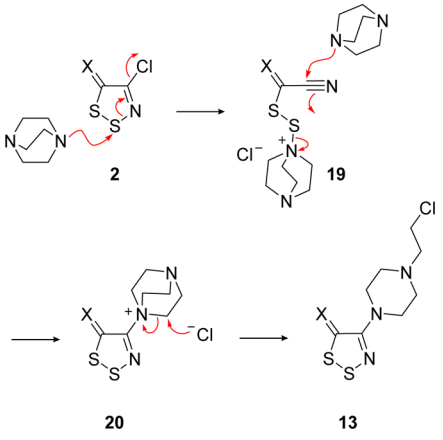


Figure 1. N···S interaction demonstrated for the *N*-{[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}pyrid-2-yl-amine **2aq** (optimized structure at the DFT RB3LYP/6-31g+(d,p) level of theory).

Nonbonding X···E−Y interactions (where X = N, O, or S and E = S, Se, or Te) have been extensively studied,[24] and the predominant factor responsible for their presence is electron donation from the lone pair of heteroatom X (n_X) to the antibonding orbital of the E−Y bond (σ^*_{E-Y}). This molecular orbital interaction, in our case, X = N and E−Y = S−S (i.e., $n_N \rightarrow \sigma^*_{S-S}$), leads to a lengthening of the S−S bond and increased electron density (reduced electrophilicity) at the S2 atom. For a more detailed discussion including computational studies, please see the SI, section S3.

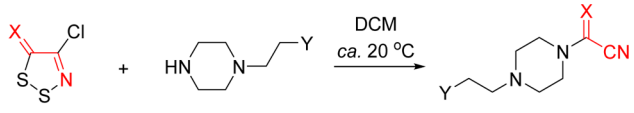
2.2. Mechanistic Rationale. A plausible mechanism for the formation of the 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles **13** involves the ANRORC-style[14] ring-opening of the 1,2,3-dithiazole by the nucleophilic DABCO to give a disulfide **19** (Scheme 8), analogous to the reaction of secondary dialkylamines with 1,2,3-dithiazoles.[13] Unlike the reactions of primary or secondary amines, the steric bulk of DABCO presumably prevents a second attack on the sulfur S2 by another DABCO, which limits the formation of side products that arise from cleavage of the disulfide chain.[25] As such, a second molecule of DABCO can competitively add to the more accessible nitrile to afford an amidine that then intramolecularly adds to the S2 sulfur, which now hosts a quaternized DABCO as a nucleofuge. The reaction sequence leads to the construction of a new 1,2,3-dithiazole **20** that now contains a quaternized DABCO at C4. Subsequent ring-opening of the quaternized DABCO by chloride gives the final product **13** (Scheme 8).

Scheme 8. Plausible Mechanism for the Formation of 4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles 13



The possibility that free *N*-(2-chloroethyl)piperazine (**21a**), which can form in the reaction mixture, reacted with the 4-chloro-5*H*-1,2,3-dithiazoles **2** to give the observed products was also considered. Treating the dithiazolimine **2aa** (0.2 mmol) with pure *N*-(2-chloroethyl)piperazine (**21a**) (2 equiv) in PhCl (8 mL) heated at reflux, however, gave a complex reaction mixture which, at 2 h, contained unreacted starting material **2aa** (37%), *N*-{4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (**13aa**) (6%), carbimidoyl cyanide **17a** (9%), and multiple unidentified colorless side products. Tentatively, this suggested that the reaction of the 1,2,3-dithiazoles **2** with free *N*-(2-chloroethyl)piperazine (**21a**) was not a major pathway leading to the formation of the *N*-{4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles **13**. Furthermore, when the dithiazoles **2a−c** were treated with pure *N*-(2-chloroethyl)piperazine (**21a**) or *N*-(2-cyanoethyl)piperazine (**21b**) under Kim's conditions,[25a] the carbimidoyl cyanides **17** were obtained in moderate to excellent yields, while no traces of the ANRORC products **13** were observed (Table 2).

Table 2. Reaction of 1,2,3-Dithiazoles 2 with *N*-[(2-Substituted)ethyl]piperazines 21 in DCM



2aa (X = PhN)
2b (X = O)
2c (X = S)

21a (Y = Cl)
21b (Y = CN)

17

entry	dithiazole	piperazine (equiv)	time (h)	X	Y	yields (%)
1	**2aa**	**21a** (5)	2.0	PhN	Cl	**17a** (67)[a]
2	**2aa**	**21b** (3)	4.5	PhN	CN	**17b** (98)
3	**2b**	**21a** (3)	0.33	O	Cl	**17c** (64)[a]
4	**2b**	**21b** (3)	0.33	O	CN	**17d** (75)
5	**2c**	**21a** (3)	0.17	S	Cl	**17e** (98)
6	**2c**	**21b** (3)	0.17	S	CN	**17f** (98)

[a]Complex reaction mixtures.

The possibility of a direct displacement of the C4 chlorine by DABCO cannot be eliminated but seems less probable since, to date, direct intermolecular nucleophilic attack at the 1,2,3-dithiazole C4 position has not been documented. Furthermore, Mulliken population analysis (see the SI, Table S3) shows significantly more positive character on S2 (0.301) than on C4 (0.078).

N-{4-[*N*-(2-Thiocyanatoethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (**16ah**) was obtained from nucleophilic displacement of the chloride by thiocyanate. Presumably,

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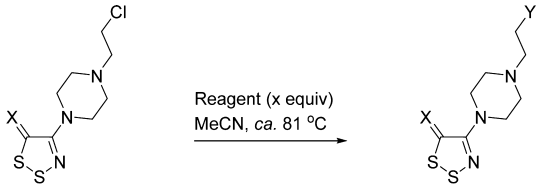
Table 3. Reaction of 4-[*N*-(2-Cyanoethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles 13aa, 13b, and 13c (0.1 mmol) with Various Nucleophiles in MeCN (2 mL) at *ca.* 81 °C



13aa (X = NPh)
13b (X = O)
13c (X = S)

16a (X = NPh)
16b (X = O)
16c (X = S)

			from **13aa**		from **13b**		from **13c**	
entry	reagent (equiv)	Y	time (h)	yield (%)	time (h)	yield (%)	time (h)	yield (%)
1	NaN_3 (1.1)	N_3	2.5	**16aa** (94)	5	**16ba** (97)	3	**16ca** (–)[a,g]
2	Bn(Me)NH (1.1)[b]	N(Me)Bn	7	**16ab** (63)	6	**16bb** (40)	8	**16cb** (53)
3	$PhNH_2$ (10)[c]	N(H)Ph	24	**16ac** (72)[e]	24	**16bc** (83)[e]	24	**16cc** (64)[e]
4	Ph(Me)NH (10)[d]	N(Me)Ph	24	**16ad** (54)[e]	24	**16bd** (78)[e]	38	**16 cd** (84)[e]
5	PhthNK (2)	NPhth	2.3	**16ae** (97)	1.5	**16be** (90)	3	**16ce** (91)
6	NaOAc (2)	OAc	10	**16af** (95)	8.5	**16bf** (93)	12	**16cf** (94)
7	NaOBz (1.1)	OBz	11	**16ag** (98)	5.5	**16bg** (97)	13	**16cg** (95)
8	KSCN (1.1)	SCN	1.6	**16ah** (91)	2.5	**16bh** (94)	4	**16ch** (90)
9	MBT[f] (1.1)[b]	S(benzothiazol-2-yl)	1.4	**16ai** (90)	2.5	**16bi** (81)	6	**16ci** (75)
10	KCN (1.1)	SCN	3	**16ah** (18)[a]	1.3	**16bh** (41)[g]	4	**16ch** (49)[g]

[a]Complex reaction mixture. [b]Used in combination with K_2CO_3 (1.1 equiv). [c]Reaction performed on a 0.4 mmol scale. [d]Reaction performed on a 0.8 mmol scale. [e]Yield for the HCl salt, isolated by filtration. [f]MBT = 2-mercaptobenzothiazole. [g]A significant amount of intractable polar material (baseline on TLC) was observed.

minor decomposition of the dithiazoles released cyanide, a typical thiophile (anthio anion), which, in the presence of sulfur, can generate thiocyanate.[26]

Carbimidoyl cyanides, analogous to **17**, were observed previously by Kim et al.,[25a,27] in the reaction of 1,2,3-dithiazoles **2a–c** with dialkylamines, and a mechanistic rationale was provided. A similar mechanism could take place in this case; however, the attacking nucleophile can be either DABCO or free *N*-(2-chloroethyl)piperazine (**21a**), which, as mentioned above, could be present in minor quantities in the reaction mixture.

N-(2-{*N*-[5-(Phenylimino)-5*H*-1,2,3-dithiazol-4-yl]-piperazin-1-yl}ethyl)-1,4-diazabicyclo[2.2.2]octan-1-ium chloride (**18**) presumably formed via nucleophilic attack of DABCO on the 2-chloroethyl moiety of the *N*-{4-[*N*-(2-chloroethyl)-piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (**13aa**). To support this, the dithiazolimine **13aa** was treated with DABCO (1 equiv) in PhCl (2 mL) at *ca.* 131 °C for 12 h, and not surprisingly, *N*-(2-{*N*-[5-(phenylimino)-5*H*-1,2,3-dithiazol-4-yl]piperazin-1-yl}-ethyl)-1,4-diazabicyclo[2.2.2]octan-1-ium chloride (**18**) was isolated in 64% yield, together with 36% recovered starting material.

2.3. Chemistry of 4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles. *2.3.1. Manipulations on the 2-Chloroethyl Moiety.* The 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles **13** contain a 2-chloroethyl group that can be modified by reaction with various nucleophiles. Nevertheless, in the presence of the 1,2,3-dithiazole, which hosts weak S–S and S–N bonds that are susceptible to thiophilic attack,[10,13a,25b,28] it was important to identify both nucleophiles and conditions that would not cleave the ring system.

A selection of N-, O-, and S-nucleophiles reacted cleanly with the *N*-(2-chloroethyl)piperazinyl dithiazoles **13aa**, **13b**, and **13c** in hot MeCN (*ca.* 81 °C) to give, predominantly, the desired *N*-[(2-(substituted)ethyl]piperazinyl products in good to excellent yields (Table 3). An exception was sodium azide (Table 3, entry 1), which reacted with the thione **13c** to give, after 3 h, a complex mixture, including unreacted starting material, which was not pursued further. Also, in the reactions with *N*-methylbenzylamine (Table 3, entry 2), significant quantities (10–20% by TLC) of starting material remained after 4–7 h. Increasing the equivalents of both *N*-methylbenzylamine and K_2CO_3 (up to 2 equiv) led to the completion of the reaction; however, no improvement on the product yields was observed. The reactions with aniline and *N*-methylaniline took significantly longer than the other nucleophiles (Table 3, entries 3 and 4); as such, these arylamines were used in excess (10 equiv). In these two cases, the desired products were precipitated out of the reaction as the hydrochloride salts. Furthermore, potassium cyanide was tested as C-nucleophile, but instead of the desired products **16aj–cj** (Y = CN), the thiocyanato adducts **16ah–ch** were obtained in low to moderate yields (Table 3, entry 10). Cyanide, which is thiophilic,[27] presumably preferentially attacked the dithiazoles S2 atom to cleave the ring and eventually expel thiocyanate that then reacted with intact dithiazoles at the 2-chloroethyl moiety to give the observed products.

2.3.2. Manipulations at the Dithiazole C5 Position. Having introduced the *N*-(2-chloroethyl)piperazinyl group at the dithiazole C4 position, we then considered whether in its presence we could also modify the C5 position. Since the reaction of (4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)methanes **2d** with DABCO failed to give the desired 4-[*N*-(2-chloroethyl)-piperazinyl]substituted dithiazoles **13d** (section 2.1.), we attempted to access these dithiazolylidenes from the dithiazolethione **13c**. Gratifyingly, treatment of thione **13c** with tetracyanoethylene oxide (TCNEO) or diazomalonate under the conditions specified in Scheme 9 gave the {4-[*N*-(2-

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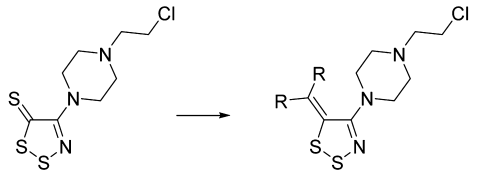
Scheme 9. Manipulation of the Dithiazole C5 Position of 4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole-5-thione (13c)



13c **13da** (R = CN)[i] **13db** (R = CO_2Et)[ii] **13dc** (R = Ph)[iii]

Reagents and Conditions: (i) TCNEO (2 equiv), PhMe, *ca.* 20 °C, 2 h, 33%; (ii) N_2=C(CO_2Et)$_2$ (3 equiv), CuBr (3 equiv), PhCl, *ca.* 131 °C, 3 h, 37%; (iii) N_2=CPh_2 (4 equiv), DCM, 20 °C, 20 h, 50%.

chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}-methanes **13da** and **13db** in 33% and 36% yields, respectively. Furthermore, treatment of thione **13c** with diphenydiazomethane gave the ylidene **13dc** in 50% yield. Worthy of note was that pure and recrystallized ylidene **13dc** was stable at *ca.* 20 °C for at least 1 month, in contrast to the analogous (4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)diphenylmethane (**2dc**) (R = Ph), which, when left standing overnight, decomposes to sulfur and 3-phenylbenzo[*b*]thiophene-2-carbonitrile.[29] Presumably, the piperazine at C5, which (a) releases electron density into the dithiazole, making it less electrophilic, and (b) is a poorer nucleofuge than chloride, makes the fragmentation of the dithiazole less facile.

3. CONCLUSIONS

A general and high yielding method for the C4 functionalization of 4-chloro-1,2,3-dithiazoles with a 2-(chloroethyl)-piperazinyl group has been developed. The reaction worked well with *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines **2a**, the 4-chloro-5*H*-1,2,3-dithiazol-5-one (**2b**), and -thione (**2c**), but with (4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)methanes **2d**, intractable baseline material was obtained. Nevertheless, several {4-[2-(chloroethyl)piperazinyl]-5*H*-1,2,3-dithiazol-5-ylidene}-methanes **13d** were prepared in modest yields via the C5 postfunctionalization of the 4-(2-chloroethyl)piperizinyl dithiazolethione **13c**. The *N*-(2-chloroethyl)piperazinyl group can also be further modified by reaction with various nucleophiles without degrading the dithiazole system. As such, the above synthetic protocols provide a general route for modifying the C4 position of 1,2,3-dithiazoles, giving access to products that can be further functionalized at either the 2-chloroethyl side chain or the C5 position. The compounds synthesized are currently under biological evaluation.

4. EXPERIMENTAL SECTION

4.1. General Methods and Materials. All chemicals were commercially available except those whose synthesis is described. All volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass backed thin-layer chromatography (TLC) plates (Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography was used throughout for all non-TLC scale chromatographic separations using silica gel 60 (<0.063 mm).[30] Melting points were determined using a hot stage microscope apparatus or a DSC with samples hermetically sealed in aluminum pans under an argon atmosphere, using heating rates of 5 °C/min. Solvents used for recrystallization are indicated after the melting point. UV/vis spectra were obtained using a UV/vis spectrophotometer, and inflections are identified by the abbreviation "inf". IR spectra were recorded on an FTIR spectrometer with a Ge ATR accessory, and strong, medium, and weak peaks are represented by s, m, and w, respectively. ^{1}H and ^{13}C NMR spectra were recorded at either 300 or 500 MHz and 75 or 125 MHz, respectively. Deuterated solvents were used for homonuclear lock, and the signals are referenced to the deuterated solvent peaks. APT NMR studies identified quaternary, tertiary, secondary, and primary carbons, which are indicated by (s), (d), (t), and (q) notations, respectively. MALDI-TOF MS were conducted on a time-of-flight (TOF) mass spectrometer. *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2aa**),[31] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-methylaniline (**2ab**),[32] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-methoxyaniline (**2ac**),[4c] 2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2ad**),[1a] 2-bromo-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2ae**),[31] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-nitroaniline (**2af**),[31] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-3-methoxyaniline (**2ah**),[31] 3-bromo-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2ai**),[32] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-methylaniline (**2aj**),[32] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-methoxyaniline (**2ak**),[1a] 4-bromo-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2al**),[13a] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-nitroaniline (**2am**),[1a] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-cyanoaniline (**2an**),[33] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)naphth-1-ylamine (**2ao**),[4c] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)naphth-2-ylamine (**2ap**),[32] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrid-2-ylamine (**2aq**),[31] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrid-3-ylamine (**2ar**),[34] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrazin-2-ylamine (**2as**),[34] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (**2at**),[9] *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-thiazol-2-ylamine (**2au**),[5c] 4-chloro-5*H*-1,2,3-dithiazol-5-one (**2b**),[35] 4-chloro-5*H*-1,2,3-dithiazole-5-thione (**2c**),[1a] 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)malononitrile (**2da**),[36] 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)malonate (**2db**),[29] *N*-(2-chloroethyl)piperazine dihydrochloride (**21a**·2HCl),[37] *N*-(2-cyanoethyl)piperazine (**21b**),[38] TCNEO,[39] diazomalonate,[40] and diphenyldiazomethane[41] were prepared according to literature procedures.

Crystallographic data for compound **13c** have been deposited with the Cambridge Crystallographic Data Centre with deposit no. CCDC 1426477. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; Fax: + 441223336033; E-mail: deposit@ccdc.cam.ac.uk.

4.2. Synthesis of Nonliterature *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines 2a. *4.2.1. N-(4-Chloro-5H-1,2,3-dithiazol-5-ylidene)-3-methylaniline (**2ag**) (Typical Procedure).* To a stirred suspension of 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.24 mmol) in DCM (4 mL) was added *m*-toluidine (52 μL, 0.24 mmol) in one portion. The mixture was stirred at *ca.* 20 °C for 2 h, and then Hünig's base (164 μL, 0.48 mmol) was added. The mixture was stirred for an additional 1 h. The mixture was then adsorbed onto silica and chromatographed (*n*-hexane/DCM, 90:10) to give the *title compound* **2ag** as yellow fibers (100.8 mg, 87%), mp 36−37 °C (*n*-pentane at *ca.* −40 °C); R_f 0.50 (*n*-hexane/DCM, 70:30); (found: C, 44.55; H, 2.91; N, 11.43. $C_9H_7ClN_2S_2$ requires: C, 44.53; H, 2.91; N, 11.54%); λ_{max} (DCM)/nm 308 inf (log ε 3.32), 377 (3.76), 386 inf (3.75), 408 inf (3.62); ν_{max}/cm^{-1} 3017w (aryl C-H), 2916w (alkyl C-H), 1589m, 1570s, 1531m, 1508w, 1481m, 1375w, 1329w, 1254m, 1169m, 1140m, 1086w, 1047w, 997m, 970w, 934m, 912m, 874s, 856s, 785m, 748s; δ_H (300 MHz; acetone-d_6) 7.39 (1H, dd, *J* 8.1, 8.1), 7.09 (1H, d, *J* 7.8), 7.05−7.03 (2H, m), 2.38 (3H, s); δ_C (125 MHz; acetone-d_6) 159.4 (s), 152.5 (s), 148.6 (s), 140.8 (s), 130.7 (d), 128.0 (d), 121.0 (d), 116.9 (d), 21.5 (q); MALDI-TOF MS (*m*/*z*): 245 (MH^+ + 2, 44%), 243 (MH^+, 100), 227 (9), 207 (90), 198 (7), 150 (3).

4.3. Synthesis of 4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles 13. *4.3.1. N-{4-[N-(2-Chloroethyl)piperazin-1-yl]-*

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*5H-1,2,3-dithiazol-5-ylidene}aniline (**13aa**) (Typical Procedure).* To a stirred solution of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2aa**) (45.7 mg, 0.20 mmol) in PhCl (8 mL) at *ca.* 20 °C was added in one portion DABCO (44.8 mg, 0.40 mmol). The mixture was then heated at *ca.* 131 °C for 4 h and then left to cool to *ca.* 20 °C. The mixture was poured onto a packed column of silica and eluted with *n*-hexane. Subsequent elution (*n*-hexane/Et_2O, 90:10) gave unreacted *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2aa**) (2.4 mg, 5%). Further elution (*n*-hexane/Et_2O, 80:20) gave the *title compound* **13aa** as yellow plates (53.6 mg, 79%), mp 73−74 °C (from *n*-hexane/*t*-BuOMe at *ca.* −20 °C); R_f 0.21 (*n*-hexane/Et_2O, 70:30); (found: C, 49.30; H, 5.11; N, 16.55. $C_{14}H_{17}ClN_4S_2$ requires: C, 49.33; H, 5.03; N, 16.44%); λ_{max} (DCM)/nm 237 inf (log ε 4.11), 281 inf (3.60), 379 (3.83); ν_{max}/cm^{-1} 3013w (aryl C-H), 2961w, 2845m and 2826m (alkyl C-H), 1593m, 1578s, 1518m, 1481m, 1464m, 1447m, 1385m, 1306m, 1294m, 1269m, 1250s, 1219m, 1202m, 1169m, 1138m, 1126m, 1080m, 1051m, 1034w, 993s, 953m, 907m, 858m, 829m, 793m, 764m, 727m; δ_H (500 MHz; $CDCl_3$) 7.43 (2H, dd, *J* 8.0, 8.0), 7.20 (1H, dd, *J* 7.5, 7.5), 7.12 (2H, dd, *J* 8.5, 1.0), 3.79 (4H, dd, *J* 5.0, 5.0), 3.62 (2H, t, *J* 7.0), 2.79 (2H, t, *J* 7.0), 2.67 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 160.6 (s), 158.3 (s), 152.5 (s), 129.7 (d), 125.6 (d), 119.4 (d), 59.8 (t), 52.8 (t), 48.3 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 343 (MH^+ + 2, 28%), 341 (MH^+, 100), 305 (63), 291 (27), 147 (9). Further elution (*n*-hexane/Et_2O, 60:40) gave *N*-{4-[*N*-(2-thiocyanatoethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (**16ah**) as yellow plates (1.3 mg, 2%); mp 86−87 °C (from *n*-hexane/*t*-BuOMe at *ca.* −20 °C); R_f 0.38 (*n*-hexane/*t*-BuOMe, 40:60); (found: C, 49.60; H, 4.73; N, 19.19. $C_{15}H_{17}N_5S_3$ requires: C, 49.56; H, 4.71; N, 19.27%); λ_{max} (DCM)/nm 244 inf (log ε 4.03), 279 (log ε 3.60), 381 (3.76); ν_{max}/cm^{-1} 3001w (aryl C-H), 2936w and 2820w (alkyl C-H), 2145m (C≡N), 1595m, 1578s, 1526m, 1481m, 1449m, 1431m, 1383m, 1377m, 1350m, 1310m, 1285m, 1269m, 1252s, 1215m, 1163m, 1140m, 1121m, 1082m, 1001m, 995m, 955m, 907m, 887m, 858m, 820m, 791m, 760s; δ_H (500 MHz; $CDCl_3$) 7.43 (2H, dd, *J* 7.8, 7.8), 7.21 (1H, dd, *J* 7.5, 7.5), 7.12 (2H, d, *J* 7.5), 3.78 (4H, dd, *J* 4.8, 4.8), 3.22 (2H, t, *J* 6.5), 2.80 (2H, t, *J* 6.5), 2.64 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 160.5 (s), 158.2 (s), 152.5 (s), 129.7 (d), 125.7 (d), 119.4 (d), 113.0 (s), 56.3 (t), 52.4 (t), 48.2 (t), 32.4 (t); MALDI-TOF MS (*m*/*z*): 364 (MH^+, 100%), 337 (6), 321 (50), 305 (4), 236 (56), 170 (4), 129 (7). Further elution (*n*-hexane/Et_2O, 40:60) gave *N*-(2-chloroethyl)-*N*-phenylpiperazine-1-carbimidoyl cyanide (**17a**) as colorless plates (1.8 mg, 3%), mp 45−46.5 °C (from *n*-hexane/Et_2O at *ca.* −40 °C), R_f 0.39 (DCM/*t*-BuOMe, 98:2); (found: C, 60.61; H, 6.12; N, 20.36. $C_{14}H_{17}ClN_4$ requires: C, 60.76; H, 6.19; N, 20.24%); λ_{max} (DCM)/nm 272 (log ε 3.96), 311 (3.79); ν_{max}/cm^{-1} 3055w (aryl C-H), 2947w and 2818w (alkyl C-H), 2228w (C≡N), 1612s, 1587s, 1449m, 1435m, 1368m, 1312m, 1290m, 1252m, 1204m, 1167m, 1132m, 1103w, 1072w, 1049w, 1030w, 1001m, 970m, 947w, 903w, 820m, 777m, 718m; δ_H (500 MHz; $CDCl_3$) 7.34 (2H, dd, *J* 7.8, 7.8), 7.14 (1H, dd, *J* 7.5, 7.5), 6.93 (2H, dd, *J* 8.2, 0.8), 3.73 (4H, br s), 3.63 (2H, t, *J* 6.5), 2.83 (2H, t, *J* 6.0), 2.65 (4H, br s); δ_C (125 MHz; $CDCl_3$) 148.1 (s), 133.9 (s), 129.1 (d), 124.6 (d), 121.4 (d), 108.2 (s), 59.4 (t), 52.3 (t), 40.6 (t), 29.7 (t); MALDI-TOF MS (*m*/*z*): 279 (MH^+ + 2, 42%), 277 (MH^+, 100), 250 (24), 241 (79), 227 (10), 224 (6), 188 (4), 147 (5), 129 (3), 118 (13).

*4.3.2. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-2-methylaniline (**13ab**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-methylaniline (**2ab**) (48.6 mg, 0.2 mmol) gave the *title compound* **13ab** as yellow plates (58.8 mg, 83%), chromatography eluent: *n*-hexane/Et_2O, 70:30; mp 97−99 °C (from *n*-hexane at *ca.* −40 °C); R_f 0.53 (*n*-hexane/Et_2O, 60:40); (found: C, 50.62; H, 5.51; N, 15.87. $C_{15}H_{19}ClN_4S_2$ requires: C, 50.76; H, 5.40; N, 15.79%); λ_{max} (DCM)/nm 279 inf (log ε 3.58), 371 (3.81); ν_{max}/cm^{-1} 3015w (aryl C-H), 2955w and 2824m (alkyl C-H), 1601m, 1593m, 1572m, 1530m, 1479m, 1456m, 1441m, 1387m, 1375m, 1352w, 1337w, 1310m, 1296m, 1271m, 1252m, 1221m, 1169m, 1130m, 1115m, 1078m, 1065m, 1055w, 1034m, 997s, 864m, 858m, 835m, 814m, 795m, 760m, 721s; δ_H (500 MHz; acetone-d_6) 7.32 (1H, d, *J* 7.5), 7.28 (1H, dd, *J* 7.8, 7.8), 7.12 (1H, ddd, *J* 7.5, 7.5, 1.0), 7.03 (1H, dd, *J* 8.0, 1.0), 3.79 (4H, dd, *J* 4.8, 4.8), 3.69 (2H, t, *J* 7.0), 2.76 (2H, t, *J* 6.8), 2.67 (4H, dd, *J* 5.0, 5.0), 2.18 (3H, s); δ_C (125 MHz; $CDCl_3$) 160.6 (s), 157.6 (s), 151.7 (s), 131.0 (d), 128.8 (s), 127.2 (d), 125.5 (d), 116.7 (d), 59.8 (t), 52.8 (t), 48.1 (t), 40.8 (t), 17.8 (q); MALDI-TOF MS (*m*/*z*): 357 (MH^+ + 2, 29%), 355 (MH^+, 64), 321 (4), 250 (100).

*4.3.3. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-2-methoxyaniline (**13ac**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-methoxyaniline (**2ac**) (51.7 mg, 0.2 mmol) gave the *title compound* **13ac** as yellow needles (68.2 mg, 91%), chromatography eluent: *n*-hexane/Et_2O, 60:40; mp 101−102 °C (from *n*-hexane); R_f 0.30 (*n*-hexane/Et_2O, 60:40); (found: C, 48.74; H, 4.99; N, 15.09. $C_{15}H_{19}ClN_4OS_2$ requires: C, 48.57; H, 5.16; N, 15.11%); λ_{max} (DCM)/nm 283 (log ε 3.68), 367 (3.80); ν_{max}/cm^{-1} 3007w (aryl C-H), 2940w and 2835m (alkyl C-H), 1601m, 1584m, 1530m, 1489m, 1464m, 1454m, 1437m, 1387m, 1379m, 1329w, 1310m, 1292m, 1277m, 1269m, 1256s, 1246m, 1227w, 1219m, 1209m, 1186m, 1161m, 1148w, 1123m, 1115m, 1078m, 1065w, 1047m, 1026m, 995s, 947w, 928w, 860m, 831m, 824m, 812m, 802m, 793m, 758s, 746m, 737m, 729m; δ_H (500 MHz; $CDCl_3$) 7.17 (1H, ddd, *J* 7.8, 7.8, 1.8), 7.06 (1H, dd, *J* 7.8, 1.8), 7.02−6.98 (2H, m), 3.84 (3H, s), 3.81 (4H, dd, *J* 4.8, 4.8), 3.62 (2H, t, *J* 7.0), 2.78 (2H, t, *J* 7.0), 2.67 (4H, dd, *J* 5.0, 5.0); δ_C (75 MHz; $CDCl_3$) 161.4 (s), 158.1 (s), 149.7 (s), 141.6 (s), 126.4 (d), 121.3 (d), 119.0 (d), 112.2 (d), 59.9 (t), 55.8 (q), 52.8 (t), 48.3 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 373 (MH^+ + 2, 25%), 371 (MH^+, 50), 338 (3), 306 (2), 266 (100).

*4.3.4. 2-Chloro-N-{[N-(2-chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**13ad**).* Similar treatment of 2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2ad**) (52.6 mg, 0.2 mmol) gave the *title compound* **13ad** as yellow needles (67.9 mg, 90%), chromatography eluent: *n*-hexane/Et_2O, 70:30; mp 95.5−96 °C (from *n*-hexane at *ca.* −20 °C); R_f 0.52 (*n*-hexane/Et_2O, 60:40); (found: C, 44.93; H, 4.42; N, 14.88. $C_{14}H_{16}Cl_2N_4S_2$ requires: C, 44.80; H, 4.30; N, 14.93%); λ_{max} (DCM)/nm 281 inf (log ε 3.73), 374 (3.87); ν_{max}/cm^{-1} 3065w and 3015w (aryl C-H), 2957m and 2826m (alkyl C-H), 1603s, 1580m, 1530m, 1464m, 1439m, 1389m, 1375m, 1352w, 1337w, 1310m, 1294m, 1271m, 1263m, 1252m, 1221m, 1204w, 1171m, 1130m, 1107m, 1078m, 1057m, 1034m, 999s, 951w, 935w, 866m, 856m, 833m, 808m, 793m, 754m, 748m, 725s, 700m; δ_H (500 MHz; $CDCl_3$) 7.48 (1H, dd, *J* 8.0, 1.5), 7.32 (1H, ddd, *J* 7.6, 7.6, 1.3), 7.16−7.11 (2H, m), 3.84 (4H, dd, *J* 4.8, 4.8), 3.62 (2H, t, *J* 7.0), 2.78 (2H, t, *J* 7.0), 2.68 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 162.6 (s), 157.9 (s), 149.6 (s), 130.5 (d), 128.1 (d), 126.2 (d), 125.7 (s), 118.8 (d), 59.8 (t), 52.8 (t), 48.4 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 377 (MH^+ + 2, 66%), 375 (MH^+, 79), 339 (4), 272 (37), 270 (100).

*4.3.5. 2-Bromo-N-{[N-(2-chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**13ae**).* Similar treatment of 2-bromo-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2ae**) (61.5 mg, 0.2 mmol) gave the *title compound* **13ae** as yellow plates (76.8 mg, 92%), chromatography eluent: *n*-hexane/Et_2O, 70:30; mp 63−65 °C (from *n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.26 (*n*-hexane/Et_2O, 70:30); (found: C, 40.21; H, 3.87; N, 13.33. $C_{14}H_{16}BrClN_4S_2$ requires: C, 40.06; H, 3.84; N, 13.35%); λ_{max} (DCM)/nm 352 inf (log ε 4.05), 269 inf (4.01), 377 (3.78); ν_{max}/cm^{-1} 3051w and 3005w (aryl C-H), 2941w and 2814m (alkyl C-H), 1589s, 1574s, 1522m, 1462m, 1449m, 1435m, 1385m, 1352w, 1337w, 1310m, 1290m, 1250m, 1217m, 1130m, 1080m, 1063w, 1043m, 1028m, 997s, 955w, 864m, 831m, 822w, 799m, 754s, 719m; δ_H (500 MHz; $CDCl_3$) 7.66 (1H, dd, *J* 8.0, 1.5), 7.36 (1H, ddd, *J* 7.6, 7.6, 1.3), 7.14 (1H, dd, *J* 8.0, 1.5), 7.05 (1H, ddd, *J* 7.8, 7.8, 1.3), 3.85 (4H, dd, *J* 4.8, 4.8), 3.61 (2H, t, *J* 7.0), 2.78 (2H, t, *J* 7.0), 2.67 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 162.5 (s), 157.8 (s), 151.1 (s), 133.5 (d), 128.9 (d), 126.5 (d), 118.6 (d), 115.7 (s), 59.8 (t), 52.8 (t), 48.4 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 423 (MH^+ + 4, 18%), 421 (MH^+ + 2, 80), 419 (MH^+, 71), 417 (M^+, 18), 387 (6), 316 (100), 314 (75).

*4.3.6. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-2-nitroaniline (**13af**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-nitroaniline (**2af**) (54.7 mg, 0.2 mmol) gave the *title compound* **13af** as a yellow microcrystalline powder (68.4 mg, 88%), chromatography eluent: *n*-hexane/Et_2O, 60:40; mp 120.5−

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122 °C (from *n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.33 (*n*-hexane/Et_2O, 60:40); (found: C, 43.66; H, 4.06; N, 18.40. $C_{14}H_{16}ClN_5O_2S_2$ requires: C, 43.58; H, 4.18; N, 18.15%); λ_{max} (DCM)/nm 255 inf (log ε 3.98), 364 (3.84); ν_{max}/cm^{-1} 3028w (aryl C-H), 2936w and 2820w (alkyl C-H), 1614m, 1599m, 1568m, 1518s (NO_2), 1464m, 1454m, 1445m, 1387m, 1335s (NO_2), 1304m, 1267m, 1256m, 1219m, 1163m, 1128m, 1103w, 1080m, 1061w, 1038w, 997m, 955m, 874m, 851m, 841m, 806w, 793m, 779m, 752m, 735m; δ_H (300 MHz; $CDCl_3$) 8.08 (1H, dd, *J* 8.3, 1.4), 7.66 (1H, ddd, *J* 7.8, 7.8, 1.3), 7.30 (1H, ddd, *J* 8.6, 7.4, 1.2), 7.17 (1H, dd, *J* 8.1, 1.2), 3.79 (4H, dd, *J* 5.0, 5.0), 3.61 (2H, t, *J* 6.9), 2.77 (2H, t, *J* 6.9), 2.65 (4H, dd, *J* 5.0, 5.0); δ_C (75 MHz; $CDCl_3$) 163.5 (s), 157.6 (s), 147.0 (s), 140.1 (s), 135.2 (d), 125.6 (d), 125.3 (d), 120.3 (d), 59.8 (t), 52.7 (t), 48.5 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 388 (MH^+ + 2, 30%), 386 (MH^+, 68), 349 (20), 281 (100), 105 (14).

*4.3.7. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-3-methylaniline (**13ag**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-3-methylaniline (**2ag**) (48.6 mg, 0.2 mmol) gave the *title compound* **13ag** as yellow plates (58.1 mg, 82%), chromatography eluent: *n*-hexane/Et_2O, 80:20; mp 110−112 °C (from *n*-hexane at *ca.* −40 °C); R_f 0.50 (*n*-hexane/Et_2O, 60:40); (found: C, 50.85; H, 5.53; N, 15.78. $C_{15}H_{19}ClN_4S_2$ requires: C, 50.76; H, 5.40; N, 15.79%); λ_{max} (DCM)/nm 278 inf (log ε 3.73), 372 (3.78); ν_{max}/cm^{-1} 3015w (aryl C-H), 2943w and 2847w (alkyl C-H), 1564s, 1516m, 1479m, 1460m, 1456m, 1450m, 1385m, 1371m, 1354w, 1335w, 1304m, 1294m, 1269m, 1254m, 1244m, 1219m, 1206m, 1169m, 1136m, 1126m, 1103w, 1092w, 1078m, 1061w, 1049w, 1034w, 999m, 991m, 953m, 930w, 901m, 876m, 851m, 833m, 826m, 797m, 781m, 745m, 733m, 704s; δ_H (500 MHz; $CDCl_3$) 7.32 (1H, dd, *J* 8.3, 8.3), 7.02 (1H, d, *J* 7.5), 6.94−6.93 (2H, m), 3.78 (4H, dd, *J* 4.8, 4.8), 3.62 (2H, t, *J* 7.0), 2.79 (2H, t, *J* 6.8), 2.66 (4H, dd, *J* 5.0, 5.0), 2.38 (3H, s); δ_C (75 MHz; $CDCl_3$) 160.3 (s), 158.2 (s), 152.5 (s), 139.6 (s), 129.5 (d), 126.4 (d), 120.1 (d), 116.0 (d), 59.8 (t), 52.7 (t), 48.2 (t), 40.8 (t), 21.5 (q); MALDI-TOF MS (*m*/*z*): 357 (MH^+ + 2, 34%), 355 (MH^+, 76), 321 (3), 250 (100).

*4.3.8. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-3-methoxyaniline (**13ah**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-3-methoxyaniline (**2ah**) (51.7 mg, 0.2 mmol) gave the *title compound* **13ah** as a yellow oil (57.9 mg, 78%), chromatography eluent: *n*-hexane/Et_2O, 70:30; R_f 0.30 (*n*-hexane/Et_2O, 60:40); (found: C, 48.62; H, 5.16; N, 15.23. $C_{15}H_{19}ClN_4OS_2$ requires: C, 48.57; H, 5.16; N, 15.11%); λ_{max} (DCM)/nm 273 (log ε 4.31), 385 (3.82); ν_{max}/cm^{-1} 3000w (aryl C-H), 2940w and 2832m (alkyl C-H), 1578s, 1522m, 1479m, 1464m, 1447m, 1433m, 1377m, 1310m, 1283m, 1248m, 1192m, 1163m, 1146s, 1080m, 1043m, 999m, 991m, 955m, 943m, 853m, 822m, 777m, 743m; δ_H (500 MHz; $CDCl_3$) 7.33 (1H, dd, *J* 8.0, 8.0), 6.75 (1H, ddd, *J* 8.3, 2.5, 0.7), 6.72 (1H, ddd, *J* 7.8, 2.0, 0.7), 6.66 (1H, dd, *J* 2.3, 2.3), 3.82 (3H, s), 3.78 (4H, dd, *J* 4.8, 4.8), 3.62 (2H, t, *J* 6.8), 2.79 (2H, t, *J* 7.0), 2.67 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 160.83 (s), 160.80 (s), 158.3 (s), 153.9 (s), 130.6 (d), 111.6 (d), 111.3 (d), 105.0 (d), 59.8 (t), 55.4 (q), 52.8 (t), 48.3 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 373 (MH^+ + 2, 39%), 371 (MH^+, 77), 337 (3), 266 (100).

*4.3.9. 3-Bromo-N-{[N-(2-chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**13ai**).* Similar treatment of 3-bromo-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2ai**) (61.5 mg, 0.2 mmol) gave the *title compound* **13ai** as a yellow microcrystalline powder (69.7 mg, 83%), chromatography eluent: *n*-hexane/Et_2O, 80:20; mp 52−53.5 °C (from *n*-hexane at *ca.* −40 °C); R_f 0.57 (*n*-hexane/Et_2O, 60:40); (found: C, 40.15; H, 3.76; N, 13.49. $C_{14}H_{16}BrClN_4S_2$ requires: C, 40.06; H, 3.84; N, 13.35%); λ_{max} (DCM)/nm 286 (log ε 3.56), 378 (3.81); ν_{max}/cm^{-1} 3022w (aryl C-H), 2953w and 2849m (alkyl C-H), 1605s, 1584m, 1562m, 1526m, 1464m, 1437m, 1414m, 1389m, 1375m, 1352w, 1337m, 1312m, 1294m, 1279m, 1258m, 1240m, 1207m, 1165m, 1150m, 1134m, 1105w, 1082m, 1061m, 999s, 991m, 945m, 889m, 878m, 866m, 822m, 804m, 773m, 760m, 733w; δ_H (500 MHz; acetone-d_6) 7.44 (1H, dd, *J* 8.0, 8.0), 7.40 (1H, ddd, *J* 8.0, 1.5, 1.5), 7.31 (1H, dd, *J* 2.0, 2.0), 7.14 (1H, ddd, *J* 7.7, 2.0, 1.3), 3.74 (4H, dd, *J* 5.0, 5.0), 3.68 (2H, t, *J* 7.0), 2.75 (2H, t, *J* 6.8), 2.66 (4H, dd, *J* 5.0, 5.0); δ_C (75 MHz; $CDCl_3$) 161.9 (s), 158.1 (s), 153.8 (s), 131.1 (d), 128.4 (d), 123.2 (s), 122.7 (d), 117.9 (d), 59.8 (t), 52.7 (t), 48.3 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 423 (MH^+ + 4, 17%), 421 (MH^+ + 2, 64), 419 (MH^+, 47), 417 (M^+, 11), 387 (12), 356 (2), 316 (100), 314 (78).

*4.3.10. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-4-methylaniline (**13aj**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-methylaniline (**2aj**) (48.6 mg, 0.2 mmol) gave the *title compound* **13aj** as yellow plates (53.9 mg, 76%), chromatography eluent: *n*-hexane/Et_2O, 80:20; mp 64.5−66 °C (from *n*-hexane at *ca.* −40 °C); R_f 0.42 (*n*-hexane/Et_2O, 60:40); (found: C, 50.52; H, 5.36; N, 15.82. $C_{15}H_{19}ClN_4S_2$ requires: C, 50.76; H, 5.40; N, 15.79%); λ_{max} (DCM)/nm 286 (log ε 3.62), 386 (3.81); ν_{max}/cm^{-1} 3022w (aryl C-H), 2965w and 2830w (alkyl C-H), 1609m, 1578s, 1566s, 1522m, 1501m, 1460m, 1456m, 1443m, 1387m, 1371m, 1354w, 1335w, 1308m, 1292m, 1271m, 1250s, 1215m, 1171m, 1136m, 1126m, 1111m, 1078m, 1061m, 1051w, 1032w, 997s, 966w, 951w, 864m, 839m, 818m, 797m, 756m, 725m, 718m; δ_H (300 MHz; acetone-d_6) 7.28 (2H, d, *J* 7.8), 7.05 (2H, d, *J* 8.1), 3.73 (4H, dd, *J* 5.0, 5.0), 3.67 (2H, t, *J* 6.9), 2.74 (2H, t, *J* 6.9), 2.64 (4H, dd, *J* 5.0, 5.0), 2.34 (3H, s); δ_C (75 MHz; acetone-d_6) 160.7 (s), 159.3 (s), 151.1 (s), 136.2 (s), 131.1 (d), 120.3 (d), 60.6 (t), 53.6 (t), 49.2 (t), 42.0 (t), 21.1 (q); MALDI-TOF MS (*m*/*z*): 357 (MH^+ + 2, 41%), 355 (MH^+, 100), 321 (3), 290 (2), 250 (74).

*4.3.11. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-4-methoxyaniline (**13ak**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-methoxyaniline (**2ak**) (51.7 mg, 0.2 mmol) gave the *title compound* **13ak** as yellow plates (51.9 mg, 70%), chromatography eluent: *n*-hexane/Et_2O, 70:30; mp 41−45 °C (from *n*-pentane/DCM at *ca.* −20 °C); R_f 0.33 (*n*-hexane/Et_2O, 60:40); (found: C, 48.69; H, 5.28; N, 14.99. $C_{15}H_{19}ClN_4OS_2$ requires: C, 48.57; H, 5.16; N, 15.11%); λ_{max} (DCM)/nm 293 (log ε 3.74), 389 (3.86), 403 inf (3.82); ν_{max}/cm^{-1} 3019w (aryl C-H), 2961w and 2847w (alkyl C-H), 1603m, 1564m, 1518m, 1501s, 1460m, 1452m, 1443m, 1387m, 1354w, 1337w, 1304m, 1294m, 1246s, 1219m, 1163m, 1136m, 1126m, 1109m, 1078m, 1061w, 1034m, 995m, 953m, 864m, 841m, 827m, 814m, 797m, 750m, 729m; δ_H (500 MHz; $CDCl_3$) 7.16 (2H, d, *J* 9.0), 6.96 (2H, d, *J* 9.0), 3.83 (3H, s), 3.77 (4H, dd, *J* 4.5, 4.5), 3.62 (2H, t, *J* 7.0), 2.78 (2H, t, *J* 7.0), 2.67 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 158.7 (s), 158.4 (s), 157.5 (s), 144.9 (s), 121.3 (d), 114.6 (d), 59.8 (t), 55.5 (q), 52.8 (t), 48.3 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 373 (MH^+ + 2, 29%), 371 (MH^+, 100), 339 (11), 306 (8), 266 (89).

*4.3.12. 4-Bromo-N-{[N-(2-chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**13al**).* Similar treatment of 4-bromo-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**2al**) (61.5 mg, 0.2 mmol) gave the *title compound* **13al** as yellow plates (67.2 mg, 80%), chromatography eluent: *n*-hexane/Et_2O, 80:20; mp 55−56 °C (*n*-hexane/Et_2O); R_f 0.47 (*n*-hexane/*t*-BuOMe, 60:40); (found: C, 40.14; H, 3.93; N, 13.34. $C_{14}H_{16}BrClN_4S_2$ requires: C, 40.06; H, 3.84; N, 13.35%); λ_{max} (DCM)/nm 247 inf (log ε 4.32), 278 inf (4.08), 387 (3.94); ν_{max}/cm^{-1} 2940w and 2814m (alkyl C-H), 1587s, 1574s, 1518m, 1477s, 1449m, 1395m, 1377m, 1352m, 1310m, 1290m, 1250s, 1211m, 1167m, 1130m, 1099m, 1069m, 1005s, 995s, 955m, 860m, 835m, 824m, 797m, 733m, 712m; δ_H (500 MHz; $CDCl_3$) 7.53 (2H, d, *J* 9.0), 7.00 (2H, d, *J* 8.5), 3.76 (4H, dd, *J* 5.0, 5.0), 3.61 (2H, t, *J* 7.0), 2.78 (2H, t, *J* 7.0), 2.65 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 161.1 (s), 158.2 (s), 151.3 (s), 132.8 (d), 121.3 (d), 118.5 (s), 59.8 (t), 52.7 (t), 48.3 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 423 (MH^+ + 4, 24%), 421 (MH^+ + 2, 72), 419 (MH^+, 51), 387 (6), 316 (100), 314 (65), 145 (3), 105 (4).

*4.3.13. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-4-nitroaniline (**13am**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-nitroaniline (**2am**) (0.2 mmol, 54.7 mg) gave the *title compound* **13am** as yellow plates/prisms (57.1 mg, 74%), chromatography eluent: *n*-hexane/Et_2O, 50:50; mp 95−96 °C (from *n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.43 (*n*-hexane/*t*-BuOMe, 40:60); (found: C, 43.67; H, 4.07; N, 18.20. $C_{14}H_{16}ClN_5O_2S_2$ requires: C, 43.58; H, 4.18; N, 18.15%); λ_{max} (DCM)/nm 284 (log ε 3.97), 323 (3.90), 411 (3.67); ν_{max}/cm^{-1} 3069w and 3030w (aryl C-H), 2946w and 2832w (alkyl C-H), 1593m, 1582m, 1514s, 1483m, 1454m,

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1389m, 1375m, 1339s, 1310m, 1294m, 1273w, 1256m, 1219m, 1209m, 1169m, 1128m, 1111m, 1078w, 1067w, 999m, 951w, 870m, 860m, 841w, 827m, 802m, 789m, 754m, 737m; δ_H (500 MHz; $CDCl_3$) 8.31 (2H, d, *J* 9.0), 7.20 (2H, d, *J* 9.0), 3.79 (4H, br s), 3.63 (2H, t, *J* 7.0), 2.81 (2H, t, *J* 6.8), 2.69 (4H, br s); δ_C (125 MHz; $CDCl_3$) 162.8 (s), 157.87 (s), 157.84 (s), 144.8 (s), 125.9 (d), 120.0 (d), 59.7 (t), 52.7 (t), 48.3 (t), 40.7 (t); MALDI-TOF MS (*m*/*z*): 388 (MH^+ + 2, 55%), 386 (MH^+, 99), 384 (38), 352 (6), 281 (100), 217 (5), 145 (11), 105 (16).

*4.3.14. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-4-cyanoaniline (**13an**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-cyanoaniline (**2an**) (50.7 mg, 0.2 mmol) gave the *title compound* **13an** as yellow plates (60.0 mg, 82%), chromatography eluent: *n*-hexane/Et_2O, 50:50; mp 100−102 °C (from *n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.25 (*n*-hexane/Et_2O, 60:40); (found: C, 49.33; H, 4.37; N, 19.20. $C_{15}H_{16}ClN_5S_2$ requires: C, 49.24; H, 4.41; N, 19.14%); λ_{max} (DCM)/nm 250 (log ε 4.36), 391 (3.88); ν_{max}/cm^{-1} 2938w and 2816w (alkyl C-H), 2224m (C≡N), 1603m, 1572s, 1508m, 1495m, 1462m, 1447m, 1410w, 1383m, 1373m, 1335w, 1310m, 1288m, 1275m, 1260m, 1252m, 1219m, 1202m, 1169m, 1144m, 1132m, 1111m, 1078w, 1053w, 993m, 955w, 864m, 847s, 833m, 824m, 808m, 797m, 735m; δ_H (300 MHz; $CDCl_3$) 7.72 (2H, d, *J* 8.4), 7.17 (2H, d, *J* 8.4), 3.77 (4H, dd, *J* 5.0, 5.0), 3.61 (2H, t, *J* 6.9), 2.79 (2H, t, *J* 6.9), 2.66 (4H, dd, *J* 5.0, 5.0); δ_C (75 MHz; $CDCl_3$) 162.5 (s), 158.0 (s), 156.1 (s), 134.1 (d), 120.2 (d), 118.8 (s), 108.6 (s), 59.8 (t), 52.7 (t), 48.4 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 368 (MH^+ + 2, 72%), 366 (MH^+, 100), 364 (25), 334 (7), 332 (11), 301 (3), 270 (3), 261 (97), 197 (3), 145 (3), 106 (12).

*4.3.15. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}naphth-1-ylamine (**13ao**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)naphth-1-ylamine (**2ao**) (55.8 mg, 0.2 mmol) gave the *title compound* **13ao** as yellow/orange plates (59.4 mg, 76%), chromatography eluent: *n*-hexane/Et_2O, 80:20; mp 121−122 °C (from *n*-hexane at *ca.* −40 °C); R_f 0.53 (*n*-hexane/Et_2O, 60:40); (found: C, 55.18; H, 4.94; N, 14.24. $C_{18}H_{19}ClN_4S_2$ requires: C, 55.30; H, 4.90; N, 14.33%); λ_{max} (DCM)/nm 286 (log ε 3.98), 391 (3.78); ν_{max}/cm^{-1} 3013w (aryl C-H), 2941w and 2806w (alkyl C-H), 1591m, 1578m, 1518m, 1503m, 1466m, 1439m, 1393m, 1385m, 1371m, 1367w, 1337w, 1308m, 1290m, 1261m, 1250m, 1213m, 1204m, 1173w, 1128m, 1105m, 1076m, 1016m, 993s, 970m, 953w, 881m, 853m, 833m, 818m, 802m, 789m, 772s, 729m; δ_H (500 MHz; $CDCl_3$) 8.02 (1H, d, *J* 8.5), 7.88 (1H, d, *J* 7.5), 7.72 (1H, d, *J* 8.0), 7.56−7.48 (3H, m), 7.28 (1H, d, *J* 7.0), 3.90 (4H, dd, *J* 5.0, 5.0), 3.64 (2H, t, *J* 7.0), 2.82 (2H, t, *J* 6.8), 2.72 (4H, dd, *J* 5.0, 5.0); δ_C (75 MHz; $CDCl_3$) 160.8 (s), 158.3 (s), 149.1 (s), 134.4 (s), 128.0 (d), 126.7 (d), 126.5 (s), 126.00 (d), 125.96 (d), 125.8 (d), 123.2 (d), 112.4 (d), 59.8 (t), 53.0 (t), 48.3 (t), 40.9 (t); MALDI-TOF MS (*m*/*z*): 393 (MH^+ + 2, 33%), 391 (MH^+, 77), 286 (100).

*4.3.16. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}naphth-2-ylamine (**13ap**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)naphth-2-ylamine (**2ap**) (55.8 mg, 0.2 mmol) gave the *title compound* **13ap** as yellow needles (60.2 mg, 77%), chromatography eluent: *n*-hexane/Et_2O, 80:20; mp 75−76 °C (from *n*-hexane at *ca.* −40 °C); R_f 0.43 (*n*-hexane/Et_2O, 60:40); (found: C, 55.47; H, 4.84; N, 14.47. $C_{18}H_{19}ClN_4S_2$ requires: C, 55.30; H, 4.90; N, 14.33%); λ_{max} (DCM)/nm 274 inf (log ε 4.11), 338 (3.70), 388 (3.80); ν_{max}/cm^{-1} 3017w (aryl C-H), 2961w and 2847w (alkyl C-H), 1562s, 1518m, 1503m, 1462m, 1450m, 1441w, 1433w, 1389m, 1371m, 1354w, 1335w, 1306m, 1296m, 1269m, 1250m, 1221m, 1206m, 1169m, 1157w, 1126m, 1101w, 1076m, 1059w, 1032w, 997m, 959m, 949m, 905m, 889m, 856m, 833m, 826m, 816m, 743s, 727m; δ_H (500 MHz; $CDCl_3$) 7.91 (1H, d, *J* 8.5), 7.84 (1H, d, *J* 8.0), 7.81 (1H, d, *J* 7.5), 7.56 (1H, d, *J* 2.0), 7.49 (1H, ddd, *J* 7.3, 7.3, 1.0), 7.46 (1H, ddd, *J* 7.5, 7.5, 1.5), 7.29 (1H, dd, *J* 8.5, 2.0), 3.83 (4H, dd, *J* 4.8, 4.8), 3.63 (2H, t, *J* 7.0), 2.81 (2H, t, *J* 7.0), 2.70 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 160.8 (s), 158.5 (s), 150.2 (s), 134.1 (s), 131.6 (s), 129.8 (d), 127.84 (d), 127.82 (d), 126.6 (d), 125.5 (d), 120.5 (d), 115.4 (d), 59.9 (t), 52.8 (t), 48.4 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 393 (MH^+ + 2, 23%), 391 (MH^+, 56), 356 (3), 286 (100).

*4.3.17. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}pyrid-2-ylamine (**13aq**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrid-2-ylamine (**2aq**) (45.9 mg, 0.2 mmol) gave the *title compound* **13aq** as yellow needles (31.5 mg, 46%), chromatography eluent: *n*-hexane/Et_2O, 50:50; mp 101−102 °C (from *n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.30 (*n*-hexane/Et_2O, 60:40); (found: C, 45.71; H, 4.68; N, 20.31. $C_{13}H_{16}ClN_5S_2$ requires: C, 45.67; H, 4.72; N, 20.49%); λ_{max} (DCM)/nm 244 (log ε 4.12), 299 (3.84), 408 (4.03), 423 (4.07); ν_{max}/cm^{-1} 2955w and 2837w (alkyl C-H), 1589m, 1564m, 1514m, 1485m, 1447m, 1433s, 1375m, 1356m, 1339w, 1308m, 1292m, 1261m, 1246m, 1144m, 1128m, 1101m, 1090w, 1070m, 1036w, 1015w, 999m, 961w, 851m, 891m, 876w, 835m, 816m, 799m, 785s, 739s, 719m; δ_H (300 MHz; $CDCl_3$) 8.61 (1H, ddd, *J* 8.5, 3.0, 1.0), 7.82 (1H, ddd, *J* 7.7, 7.7, 1.8), 7.49 (1H, d, *J* 8.1), 7.21 (1H, ddd, *J* 7.1, 5.0, 1.1), 3.86 (4H, br s), 3.68 (2H, t, *J* 6.9), 2.86 (2H, t, *J* 6.9), 2.79 (4H, dd, *J* 4.5, 4.5); δ_C (75 MHz; $CDCl_3$) 162.0 (s), 157.5 (s), 154.9 (s), 144.2 (d), 137.8 (d), 122.3 (d), 120.8 (d), 59.8 (t), 52.8 (t), 48.7 (t), 40.6 (t); MALDI-TOF MS (*m*/*z*): 344 (MH^+ + 2, 62%), 342 (MH^+, 100), 306 (6), 250 (12), 248 (30), 237 (72).

*4.3.18. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}pyrid-3-ylamine (**13ar**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrid-3-ylamine (**2ar**) (45.9 mg, 0.2 mmol) gave the *title compound* **13ar** as yellow needles (58.1 mg, 85%), chromatography eluent: *n*-hexane/Et_2O, 50:50; mp 83−84 °C (from *n*-hexane/DCM at *ca.* −40 °C); R_f 0.39 (DCM/Et_2O, 70:30); (found: C, 45.79; H, 4.63; N, 20.55. $C_{13}H_{16}ClN_5S_2$ requires: C, 45.67; H, 4.72; N, 20.49%); λ_{max} (DCM)/nm 279 (log ε 3.85), 384 (3.74); ν_{max}/cm^{-1} 3075w and 3013w (pyridyl C-H), 2926w and 2832m (alkyl C-H), 1584m, 1564s, 1558s, 1506s, 1474m, 1458m, 1447m, 1410m, 1375m, 1360m, 1339w, 1325w, 1308m, 1290m, 1275m, 1252s, 1223m, 1209m, 1190m, 1148m, 1130m, 1113m, 1094m, 1084m, 1074m, 1045m, 1011m, 999m, 974m, 955m, 934m, 868m, 833m, 810s, 793m, 739m, 708m; δ_H (500 MHz; $CDCl_3$) 8.46−8.44 (2H, m), 7.46 (1H, ddd, *J* 8.5, 2.5, 1.5), 7.36 (1H, dd, *J* 8.0, 5.0), 3.78 (4H, dd, *J* 4.8, 4.8), 3.62 (2H, t, *J* 6.8), 2.79 (2H, t, *J* 6.8), 2.67 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 162.8 (s), 158.1 (s), 148.4 (s), 146.7 (d), 142.0 (d), 126.4 (d), 124.1 (d), 59.8 (t), 52.7 (t), 48.4 (t), 40.8 (t); MALDI-TOF MS (*m*/*z*): 343 (M^+ + 2, 33%), 341 (M^+, 100), 304 (87).

*4.3.19. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}pyrazin-2-ylamine (**13as**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrazin-2-ylamine (**2as**) (46.1 mg, 0.2 mmol) gave the *title compound* **13as** as yellow needles (50.7 mg, 74%), chromatography eluent: DCM/Et_2O, 80:20; mp 140−141 °C (from *c*-hexane); R_f 0.35 (DCM/Et_2O, 60:40); (found: C, 42.19; H, 4.37; N, 24.34. $C_{12}H_{15}ClN_6S_2$ requires: C, 42.04; H, 4.41; N, 24.51%); λ_{max} (DCM)/nm 247 (log ε 4.17), 270 inf (3.93), 321 (3.87), 418 inf (4.08), 432 (4.14); ν_{max}/cm^{-1} 3057w and 3009w (pyrazinyl C-H), 2938w and 2837m (alkyl C-H), 1533m, 1514m, 1479s, 1456s, 1441m, 1408s, 1375m, 1358m, 1339m, 1314m, 1292m, 1275m, 1252s, 1196m, 1179m, 1157m, 1146m, 1128m, 1090m, 1070w, 1059w, 1013m, 999s, 955m, 928w, 895m, 845m, 837m, 816m, 797m, 754m, 733m, 716m, 706m; δ_H (300 MHz; $CDCl_3$) 3.84 (1H, d, *J* 1.5), 8.54 (1H, dd, *J* 2.7, 1.5), 8.41 (1H, d, *J* 2.7), 3.85 (4H, dd, *J* 5.0, 5.0), 3.65 (2H, t, *J* 7.1), 2.83 (2H, t, *J* 6.9), 2.76 (4H, dd, *J* 5.0, 5.0); δ_C (75 MHz; $CDCl_3$) 162.3 (s), 159.8 (s), 151.6 (s), 145.5 (d), 139.9 (d), 138.9 (d), 59.9 (t), 52.8 (t), 49.0 (t), 40.9 (t); MALDI-TOF MS (*m*/*z*): 345 (MH^+ + 2, 55%), 343 (MH^+, 100), 250 (6), 248 (16), 238 (79).

*4.3.20. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}-1,3-dimethyl-1H-pyrazol-5-amine (**13at**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (**2at**) (49.3 mg, 0.2 mmol) gave the *title compound* **13at** as yellow needles (56.7 mg, 79%), chromatography eluent: *n*-hexane/Et_2O, 50:50; mp 112−113 °C (from *c*-hexane); R_f 0.45 (DCM/Et_2O, 70:30); (found: C, 43.32; H, 5.27; N, 23.31. $C_{13}H_{19}ClN_6S_2$ requires: C, 43.51; H, 5.34; N, 23.42%); λ_{max} (DCM)/nm 244 (log ε 3.96), 249 inf (3.95), 281 (3.86), 345 inf (3.69), 360 inf (3.75), 377 inf (3.87), 395 (3.98), 414 (3.97); ν_{max}/cm^{-1} 2940w and 2820w (alkyl C-H), 1574m, 1514m, 1445m, 1400m, 1369m, 1306m, 1288m, 1248m, 1213w, 1173m, 1144m, 1128m, 1107w, 1082m, 1009m, 999m, 957w,

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876m, 831m, 806m, 754m, 727s; δ_H (500 MHz; $CDCl_3$) 6.27 (1H, s), 3.82 (3H, s), 3.77 (4H, dd, *J* 4.8, 4.8), 3.63 (2H, t, *J* 7.0), 2.80 (2H, t, *J* 7.0), 2.70 (4H, dd, *J* 4.8, 4.8), 2.33 (3H, s); δ_C (125 MHz; $CDCl_3$) 159.6 (s), 155.7 (s), 147.4 (s), 146.7 (s), 94.8 (d), 59.8 (t), 52.8 (t), 48.7 (t), 40.8 (t), 34.9 (q), 14.2 (q); MALDI-TOF MS (*m*/*z*): 361 (MH^+ + 2, 39%), 359 (MH^+, 100), 327 (15), 325 (22), 254 (70), 190 (11), 154 (7), 105 (11).

*4.3.21. N-{[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}thiazol-2-amine (**13au**).* Similar treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)thiazol-2-ylamine (**2au**) (47.1 mg, 0.2 mmol) gave the *title compound* **13au** as yellow/orange plates (44.5 mg, 64%), chromatography eluent: *n*-hexane/Et_2O, 80:20; mp 142−143 °C (from *c*-hexane); R_f 0.43 (*n*-hexane/Et_2O, 60:40); (found: C, 38.06; H, 4.12; N, 20.05. $C_{11}H_{14}ClN_5S_3$ requires: C, 37.98; H, 4.06; N, 20.13%); λ_{max} (DCM)/nm 261 (log ε 4.02), 275 inf (3.91), 335 (3.65), 402 inf (3.94), 419 (4.10), 438 (4.08); ν_{max}/cm^{-1} 3078w and 3065w (thiazolyl C-H), 2947w and 2826w (alkyl C-H), 1522m, 1481s, 1462m, 1447m, 1410m, 1381m, 1373m, 1335m, 1321m, 1308m, 1292m, 1271m, 1250m, 1215m, 1155s, 1136m, 1125m, 1105w, 1084m, 1074m, 1053w, 1032w, 997s, 866m, 847m, 829m, 802m, 773s, 760m, 735m, 704m; δ_H (500 MHz; $CDCl_3$) 7.75 (1H, d, *J* 4.0), 7.25 (1H, d, *J* 3.5), 3.79 (4H, dd, *J* 4.5, 4.5), 3.64 (2H, t, *J* 7.0), 2.81 (2H, t, *J* 7.0), 2.72 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 170.1 (s), 161.2 (s), 159.3 (s), 138.7 (d), 118.6 (d), 59.9 (t), 52.8 (t), 49.0 (t), 40.9 (t); MALDI-TOF MS (*m*/*z*): 350 (MH^+ + 2, 30%), 348 (MH^+, 58), 312 (5), 248 (8), 243 (100).

*4.3.22. 4-[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-one (**13b**).* Similar treatment of 4-chloro-5*H*-1,2,3-dithiazol-5-one (**2b**) (30.7 mg, 0.2 mmol) gave the *title compound* **13b** as yellow plates (45.3 mg, 85%), chromatography eluent: *n*-hexane/Et_2O, 70:30; mp (DSC) onset: 83.9 °C, peak max: 84.9 °C, decomp. onset: 191.6 °C, peak max: 193.4 °C (from *n*-hexane/*t*-BuOMe at *ca.* −20 °C); R_f 0.36 (*n*-hexane/*t*-BuOMe, 70:30); (found: C, 36.04; H, 4.59; N, 15.72. $C_8H_{12}ClN_3OS_2$ requires: C, 36.15; H, 4.55; N, 15.81%); λ_{max} (DCM)/nm 272 (log ε 2.96), 376 (3.82); ν_{max}/cm^{-1} 2940w and 2816m (alkyl C-H), 1667m, 1649m, 1632s, 1530m, 1452m, 1443m, 1387m, 1337m, 1327m, 1308m, 1294m, 1248s, 1231m, 1217m, 1146m, 1140m, 1128m, 1072m, 989s, 949m, 853m, 822m, 791m, 766m, 746m; δ_H (500 MHz; $CDCl_3$) 3.66 (4H, dd, *J* 4.8, 4.8), 3.60 (2H, t, *J* 6.8), 2.77 (2H, t, *J* 6.8), 2.62 (4H, dd, *J* 4.3, 4.3); δ_C (125 MHz; $CDCl_3$) 186.1 (s), 155.1 (s), 59.7 (t), 52.6 (t), 47.2 (t), 40.7 (t); MALDI-TOF MS (*m*/*z*): 268 (MH^+ + 2, 45%), 266 (MH^+, 100), 249 (29), 235 (39), 155 (53), 138 (5), 129 (5), 113 (7).

*4.3.23. 4-[N-(2-Chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazole-5-thione (**13c**).* Similar treatment of 4-chloro-5*H*-1,2,3-dithiazole-5-thione (**2c**) (33.9 mg, 0.2 mmol) gave the *title compound* **13c** as red plates (43.0 mg, 76%), chromatography eluent: *n*-hexane/Et_2O, 70:30; mp 68−69 °C (from *n*-hexane/*t*-BuOMe at *ca.* −20 °C); R_f 0.33 (*n*-hexane/*t*-BuOMe, 70:30); (found: C, 34.23; H, 4.27; N, 14.82. $C_8H_{12}ClN_3S_3$ requires: C, 34.09; H, 4.29; N, 14.91%); λ_{max} (DCM)/nm 254 inf (log ε 3.80), 327 (3.45), 457 (3.96), 536 inf (2.68); ν_{max}/cm^{-1} 2949w and 2820m (alkyl C-H), 1474m, 1447m, 1371m, 1354m, 1333m, 1300m, 1283m, 1260m, 1246s, 1209m, 1200m, 1123s, 1051s, 1003m, 982s, 853m, 829m, 818s, 799m, 745m; δ_H (500 MHz; $CDCl_3$) 3.69 (4H, br s), 3.62 (2H, t, *J* 6.8), 2.80 (2H, t, *J* 7.0), 2.68 (4H, dd, *J* 4.3, 4.3); δ_C (125 MHz; $CDCl_3$) 202.0 (s), 165.8 (s), 59.7 (t), 52.6 (t), 48.7 (t), 40.6 (t); MALDI-TOF MS (*m*/*z*): 283 (M^+ + 2, 34%), 281 (M^+, 100), 279 (41), 247 (20), 216 (14), 176 (32), 105 (12).

4.4. Synthesis of *N*-(2-Chloroethyl)piperazine (21a). To a stirred suspension of *N*-(2-chloroethyl)piperazine dihydrochloride (**21a**·2HCl) (500 mg, 2.26 mmol) in DCM (10 mL) was added DBU (675 μL, 4.51 mmol). The mixture was stirred at *ca.* 20 °C until all the solids dissolved. Then, the solvent was evaporated under reduced pressure at *ca.* 20 °C, the remaining residue was triturated with Et_2O (10 mL), and the solution was separated from the resultant gummy precipitation. The solvent was evaporated under reduced pressure to give *N*-(2-chloroethyl)piperazine (**21a**) as a colorless oil (218.5 mg, 65%), ν_{max}/cm^{-1} 3273m (N-H), 2941m and 2814m (alkyl C-H), 1645m, 1454m, 1371m, 1341m, 1321m, 1310m, 1269m, 1184m, 1142s, 1123s, 1061m, 1011m, 914m, 802s, 733s; δ_H (500 MHz; $CDCl_3$) N*H* resonance missing (deuterium exchanged), 3.58 (2H, t, *J* 7.2), 2.89 (4H, dd, *J* 4.8, 4.8), 2.70 (2H, t, *J* 7.0), 2.47 (4H, br s); δ_C (125 MHz; $CDCl_3$) 60.4 (t), 54.5 (t), 46.0 (t), 40.8 (t). Worthy of note was that the compound was stable at *ca.* 20 °C and suitable for subsequent chemistry for several hours but decomposed when left standing overnight.

4.5. Reaction of 4-Chloro-1,2,3-dithiazoles 2 with *N*-[2-(Substituted)ethyl]piperazines 21. *General Procedure*: A mixture of the appropriate 4-chloro-1,2,3-dithiazole **2aa**, **2b**, or **2c** (0.2 mmol) and *N*-(2-chloroethyl)piperazine (**21a**) or *N*-(2-cyanoethyl)piperazine (**21b**) (0.6 mmol) in DCM (4 mL) was stirred at *ca.* 20 °C for the time specified in Table 2. Then, the mixture was poured onto a packed column of silica and chromatographed to give the corresponding amidines **17a**−**f**.

*4.5.1. N-(2-Chloroethyl)-N-phenylpiperazine-1-carbimidoyl Cyanide (**17a**).* In this case, 148.6 mg (1 mmol) of *N*-(2-chloroethyl)-piperazine (**21a**) was used. Chromatography eluent: *n*-hexane/Et_2O, 70:30. Obtained as colorless plates (37.1 mg, 67%), mp 45−46.5 °C (from *n*-hexane/Et_2O at *ca.* −40 °C), identical to that described above.

*4.5.2. N-(2-Cyanoethyl)-N-phenylpiperazine-1-carbimidoyl Cyanide (**17b**).* Chromatography eluent: *n*-hexane/Et_2O, 20:80. Obtained as colorless prisms (52.4 mg, 98%), mp 41−43 °C (from *n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.31 (DCM/Et_2O, 90:10); (found: C, 67.53; H, 6.55; N, 26.03. $C_{15}H_{17}N_5$ requires: C, 67.39; H, 6.41; N, 26.20%); λ_{max} (MeCN)/nm 270 (log ε 4.07), 301 inf (3.89); ν_{max}/cm^{-1} 3057w (aryl C-H), 2949w and 2824w (alkyl C-H), 2249w and 2228w (C≡N), 1612s, 1589s, 1485w, 1449m, 1425m, 1368m, 1331w, 1290m, 1252m, 1215m, 1179m, 1169m, 1142m, 1107w, 1072w, 1001m, 970m, 943m, 905m, 816m, 779m, 718m; δ_H (500 MHz; $CDCl_3$) 7.34 (2H, dd, *J* 7.8, 7.8), 7.14 (1H, dd, *J* 7.3, 7.3), 6.93 (2H, dd, *J* 8.5, 1.0), 3.72 (4H, dd, *J* 5.0, 5.0), 2.76 (2H, t, *J* 6.8), 2.62 (4H, dd, *J* 5.0, 5.0), 2.55 (2H, t, *J* 7.0); δ_C (125 MHz; $CDCl_3$) 148.1 (s), 133.9 (s), 129.1 (d), 124.6 (d), 121.4 (d), 118.4 (s), 108.2 (s), 53.1 (t), 52.0 (t), 45.6 (t), 16.1 (t); MALDI-TOF MS (*m*/*z*): 268 (MH^+, 100%), 241 (68), 227 (65), 198 (5), 172 (48), 129 (9), 124 (33), 97 (5), 77 (2), 55 (2).

*4.5.3. N-(2-Chloroethyl)piperazine-1-carbonyl Cyanide (**17c**).* Chromatography eluent: *n*-hexane/Et_2O: 30:70. Obtained as colorless needles (25.9 mg, 64%), mp 39.5−41 °C (from *n*-hexane/Et_2O at *ca.* −20 °C); R_f 0.42 (DCM/Et_2O, 90:10); (found: C, 47.47; H, 6.13; N, 20.67. $C_8H_{12}ClN_3O$ requires: C, 47.65; H, 6.00; N, 20.84%); λ_{max} (MeCN)/nm 231 (log ε 3.89); ν_{max}/cm^{-1} 2932w, 2820w and 2778w (alkyl C-H), 2230w (C≡N), 1672s (C═O), 1578w, 1522w, 1441m, 1379w, 1366m, 1354m, 1314m, 1285m, 1267m, 1250m, 1227m, 1180w, 1144m, 1130m, 1038m, 997m, 945m, 885w, 858w, 808w, 758m, 719m; δ_H (500 MHz; $CDCl_3$) 3.78 (2H, dd, *J* 5.0, 5.0), 3.67 (2H, dd, *J* 5.0, 5.0), 3.58 (2H, t, *J* 6.8), 2.79 (2H, t, *J* 6.5), 2.64 (2H, dd, *J* 5.0, 5.0), 2.56 (2H, dd, *J* 5.3, 5.3); δ_C (125 MHz; $CDCl_3$) 143.1 (s), 110.1 (s), 59.1 (t), 52.9 (t), 51.8 (t), 46.9 (t), 42.2 (t), 40.7 (t); MALDI-TOF MS (*m*/*z*): 204 (MH^+ + 2, 29%), 202 (MH^+, 85), 166 (100), 113 (13).

*4.5.4. N-(2-Cyanoethyl)piperazine-1-carbonyl Cyanide (**17d**).* Chromatography eluent: *n*-hexane/Et_2O, 10:90. Obtained as colorless needles (28.9 mg, 75%), mp 61.5−63.5 °C (from *n*-pentane/Et_2O at *ca.* −20 °C); R_f 0.30 (DCM/Et_2O, 90:10); (found: C, 56.15; H, 6.37; N, 29.02. $C_9H_{12}N_4O$ requires: C, 56.24; H, 6.29; N, 29.15%); λ_{max} (MeCN)/nm 231 (log ε 3.80); ν_{max}/cm^{-1} 2955w, 2814w and 2772w (alkyl C-H), 2255w and 2226w (C≡N), 1667s (C═O), 1460m, 1452m, 1435m, 1423m, 1375m, 1360m, 1350m, 1329m, 1298m, 1285m, 1254m, 1229m, 1142m, 1109m, 1045m, 1016m, 993m, 962w, 934m, 891m, 760m; δ_H (500 MHz; $CDCl_3$) 3.79 (2H, dd, *J* 5.3, 5.3), 3.67 (2H, dd, *J* 5.3, 5.3), 2.74 (2H, t, *J* 6.8), 2.63 (2H, dd, *J* 5.0, 5.0), 2.55 (2H, dd, *J* 5.3, 5.3), 2.53 (2H, t, *J* 6.8); δ_C (125 MHz; $CDCl_3$) 143.1 (s), 118.2 (s), 110.1 (s), 52.8 (t), 52.5 (t), 51.5 (t), 46.8 (t), 42.1 (t), 16.2 (t); MALDI-TOF MS (*m*/*z*): 193 (MH^+, 40%), 192 (M^+, 100), 152 (6), 100 (60), 91 (42).

*4.5.5. N-(2-Chloroethyl)piperazine-1-carbothioyl Cyanide (**17e**).* Chromatography eluent: *n*-hexane/Et_2O, 50:50. Obtained as yellow plates (42.7 mg, 98%), mp 108−109 °C (from *c*-hexane); R_f 0.63 (DCM/Et_2O, 90:10); (found: C, 44.25; H, 5.45; N, 19.41. $C_8H_{12}ClN_3S$ requires: C, 44.13; H, 5.56; N, 19.30%); λ_{max} (DCM)/

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nm 320 (log ε 4.16); ν_{max}/cm^{-1} 2934w, 2801w and 2778w (alkyl C-H), 2224w (C≡N), 1508s (C═O), 1462m, 1437m, 1375m, 1350m, 1312m, 1283m, 1265m, 1238m, 1166m, 1140m, 1128m, 1101m, 1076m, 1045m, 1030m, 1007m, 943m, 910w, 872w, 758m; δ_H (300 MHz; $CDCl_3$) 4.17 (2H, dd, *J* 5.3, 5.3), 4.09 (2H, dd, *J* 5.1, 5.1), 3.60 (2H, t, *J* 6.5), 2.82 (2H, t, *J* 6.6), 2.72 (2H, dd, *J* 5.3, 5.3), 2.67 (2H, dd, *J* 5.3, 5.3); δ_C (75 MHz; $CDCl_3$) 163.9 (s), 111.6 (s), 58.7 (t), 53.4 (t), 52.7 (t), 51.5 (t), 46.8 (t), 40.7 (t); MALDI-TOF MS (*m*/*z*): 220 (MH^+ + 2, 31%), 218 (MH^+, 74), 216 (100), 184 (25), 175 (7), 139 (7), 113 (12), 106 (27).

*4.5.6. N-(2-Cyanoethyl)piperazine-1-carbothioyl Cyanide (**17f**).* Chromatography eluent: *n*-hexane/Et_2O, 20:80. Obtained as yellow plates (41.0 mg, 98%), mp 125−126 °C (from *c*-hexane/1,2-DCE); R_f 0.45 (DCM/Et_2O, 90:10); (found: C, 51.95; H, 5.87; N, 26.79. $C_9H_{12}N_4S$ requires: C, 51.90; H, 5.81; N, 26.90%); λ_{max} (DCM)/nm 320 (log ε 4.11); ν_{max}/cm^{-1} 2965w and 2830m (alkyl C-H), 2249w and 2224w (C≡N), 1510s, 1466m, 1449m, 1437m, 1381m, 1350m, 1333m, 1300m, 1283m, 1269m, 1242m, 1211w, 1196m, 1140m, 1101m, 1076w, 1032m, 1015m, 993m, 941m, 910w, 874w, 824w, 758m; δ_H (300 MHz; $CDCl_3$) 4.17 (2H, dd, *J* 5.3, 5.3), 4.09 (2H, dd, *J* 5.1, 5.1), 2.76 (2H, t, *J* 6.8), 2.71 (2H, dd, *J* 5.1, 5.1), 2.65 (2H, dd, *J* 5.1, 5.1), 2.55 (2H, t, *J* 6.6); δ_C (75 MHz; $CDCl_3$) 163.9 (s), 118.1 (s), 111.5 (s), 53.3 (t), 52.4 (t), 52.3 (t), 51.1 (t), 46.7 (t), 16.2 (t); MALDI-TOF MS (*m*/*z*): 209 (MH^+, 100%), 192 (5), 182 (16), 175 (50), 168 (77), 141 (3), 113 (19), 97 (63).

4.6. Reaction of *N*-{4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (13aa) with DABCO. To a stirred solution of *N*-{4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}aniline (**13aa**) (68.2 mg, 0.2 mmol) in PhCl (2 mL) at *ca.* 20 °C was added in one portion DABCO (22.4 mg, 0.2 mmol), and the mixture was then heated at *ca.* 131 °C for 12 h. Then, the mixture was allowed to cool to *ca.* 20 °C and filtered, and the collected solid was washed with *n*-hexane to give *N-(2-{N-[5-(phenylimino)-5H-1,2,3-dithiazol-4-yl]piperazin-1-yl}ethyl)-1,4-diazabicyclo[2.2.2]octan-1-ium chloride* (**18**) as yellow glassy plates (58.2 mg, 64%), decomp. (DSC) onset: 198.5 °C, peak max: 201.7 °C (precipitated from DCM with *n*-pentane/Et_2O, followed by sonication in MeCN); (found: C, 52.96; H, 6.40; N, 18.46. $C_{20}H_{29}ClN_6S_2$ requires: C, 53.02; H, 6.45; N, 18.55%); λ_{max} (DCM)/nm 241 inf (log ε 4.01), 274 inf (3.84), 380 (3.75); ν_{max}/cm^{-1} 3005w (aryl C-H), 2965w, 2886w and 2832m (alkyl C-H), 1597s, 1584s, 1533m, 1483m, 1445m, 1393m, 1339w, 1312m, 1277w, 1267w, 1244s, 1213w, 1200w, 1182w, 1150m, 1101m, 1078m, 1061m, 1003m, 995m, 949m, 905m, 899m, 858m, 849m,843m, 822m, 795m, 762m; δ_H (300 MHz; $CDCl_3$) 7.40 (2H, dd, *J* 7.8, 7.8), 7.17 (1H, dd, *J* 7.5, 7.5), 7.08 (2H, dd, *J* 8.7, 1.2), 3.90 (2H, dd, *J* 5.1, 5.1), 3.83 (6H, dd, *J* 7.2, 7.2), 3.71 (4H, br s), 3.19 (6H, dd, *J* 7.2, 7.2), 2.89 (2H, dd, *J* 4.8, 4.8), 2.68 (4H, dd, *J* 4.5, 4.5); δ_C (75 MHz; $CDCl_3$) 160.4 (s), 158.1 (s), 152.4 (s), 129.7 (d), 125.6 (d), 119.3 (d), 59.7 (t), 52.8 (t), 52.6 (t), 52.0 (t), 48.1 (t), 45.4 (t); MALDI-TOF MS (*m*/*z*): 417 (M^+, 22%), 327 (30), 305 (100), 250 (7), 138 (10), 113 (3), 70 (3). The filtrate was adsorbed onto silica and chromatographed (*n*-hexane/Et_2O, 80:20) to give unreacted *N*-{4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazol-5-ylidene}-aniline (**X**) (24.4 mg, 36%).

4.7. Reactions of 4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazoles 13 with Nucleophiles. *4.7.1. Reaction with Sodium Azide (General Procedure).* To a stirred solution of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.10 mmol) in MeCN (2 mL) at *ca.* 20 °C was added in one portion NaN_3 (7.2 mg, 0.11 mmol). The mixture was then heated at *ca.* 81 °C for the time specified in Table 3 (entry 1) and then left to cool to *ca.* 20 °C. The mixture was adsorbed onto silica, and chromatography (*n*-hexane/Et_2O, 90:10) gave, in some cases, traces of unreacted starting material. Further elution gave the corresponding 4-[*N*-(2-azidoethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **16aa**−**ca**.

*4.7.1.1. N-{4-[N-(2-Azidoethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**16aa**).* Chromatography eluent: *n*-hexane/Et_2O, 70:30. Obtained as yellow needles (32.8 mg, 94%); mp 42.5−44.5 °C (*n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.48 (*n*-hexane/Et_2O, 60:40); (found: C, 48.48; H, 5.02; N, 28.13. $C_{14}H_{17}N_7S_2$ requires: C, 48.40; H, 4.93; N, 28.22%); λ_{max} (DCM)/nm 283 (log ε 3.61), 382 (3.83); ν_{max}/cm^{-1} 2938m and 2814m (alkyl C-H), 2099s (N≡N), 1582s, 1574s, 1522m, 1483m, 1449m, 1379m, 1350m, 1304m, 1285m, 1250s, 1144m, 1072m, 1051m, 1001m, 993s, 955m, 907m, 858m, 831m, 818m, 793m, 762s; δ_H (300 MHz; $CDCl_3$) 7.43 (2H, dd, *J* 8.0, 8.0), 7.20 (1H, dd, *J* 7.5, 7.5), 7.12 (2H, d, *J* 8.1), 3.79 (4H, dd, *J* 5.0, 5.0), 3.38 (2H, t, *J* 6.0), 2.67−2.63 (6H, m); δ_C (75 MHz; $CDCl_3$) 160.6 (s), 158.3 (s), 152.5 (s), 129.7 (d), 125.6 (d), 119.3 (d), 57.2 (t), 52.8 (t), 48.3 (t), 48.1 (t); MALDI-TOF MS (*m*/*z*): 348 (MH^+, 100%), 314 (19), 291 (23), 283 (6), 275 (5), 236 (82), 172 (8), 111 (5), 67 (11).

*4.7.1.2. 4-[N-(2-Azidoethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-one (**16ba**).* Chromatography eluent: *n*-hexane/Et_2O, 70:30. Obtained as a yellow oil (26.4 mg, 97%), R_f 0.68 (DCM/*t*-BuOMe, 90:10); (found: C, 35.19; H, 4.26; N, 30.71. $C_8H_{12}N_6OS_2$ requires: C, 35.28; H, 4.44; N, 30.86%); λ_{max} (DCM)/nm 276 (log ε 3.35), 376 (3.79); ν_{max}/cm^{-1} 2941w and 2816m (alkyl C-H), 2099m (N≡N), 1659s, 1651s, 1530m, 1449m, 1383m, 1348m, 1304m, 1285m, 1246m, 1144m, 1067m, 988m, 953m, 816m, 800m, 768m; δ_H (500 MHz; $CDCl_3$) 3.65 (4H, dd, *J* 4.8, 4.8), 3.36 (2H, t, *J* 5.8), 2.63 (2H, t, *J* 6.0), 2.60 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 186.1 (s), 155.1 (s), 57.1 (t), 52.6 (t), 48.0 (t), 47.2 (t); MALDI-TOF MS (*m*/*z*): 272 (M^+, 100%), 270 (59), 228 (13), 215 (21), 213 (18), 199 (8).

4.7.2. Reaction with N-Benzylmethylamine (General Procedure). To a stirred solution of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.10 mmol) in MeCN (2 mL) at *ca.* 20 °C was added in one portion *N*-benzylmethylamine (14.2 μL, 0.11 mmol) and then powdered K_2CO_3 (15.2 mg, 0.11 mmol). The mixture was then heated at *ca.* 81 °C for the time specified in Table 3 (entry 2) and then left to cool to *ca.* 20 °C. The mixture was filtered and washed with DCM, and the filtrate was adsorbed onto silica and chromatographed (*n*-hexane/Et_2O, 70:30) to give unreacted starting material. Further elution gave the corresponding 4-(*N*-{2-[benzyl-(methyl)amino]ethyl}piperazin-1-yl)-5*H*-1,2,3-dithiazole **16ab**−**cb**.

*4.7.2.1. N-[4-(N-{2-[Benzyl(methyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazol-5-ylidene]aniline (**16ab**).* Chromatography eluent: Et_2O. Obtained as yellow plates (22.5 mg, 63%); mp 89.5−91 °C (MeCN at *ca.* −40 °C); R_f 0.38 (Et_2O); (found: C, 62.18; H, 6.33; N, 16.59. $C_{22}H_{27}N_5S_2$ requires: C, 62.09; H, 6.39; N, 16.46%); λ_{max} (DCM)/nm 290 (log ε 3.56), 383 (3.79); ν_{max}/cm^{-1} 2922m, 2851m and 2806m (alkyl C-H), 1595m, 1585m, 1522m, 1483m, 1460m, 1447m, 1379m, 1323w, 1308w, 1292m, 1271m, 1252m, 1213w, 1177m, 1130m, 1121m, 1080m, 1018m, 993m, 957m, 914w, 858m, 831m, 787m, 766m, 746m; δ_H (500 MHz; acetone-d_6) 7.47 (2H, dd, *J* 8.0, 8.0), 7.36−7.34 (2H, m), 7.30 (2H, dd, *J* 7.5, 7.5), 7.22 (2H, dd, *J* 7.5, 7.5), 7.13 (2H, dd, *J* 8.5, 1.0), 3.72 (4H, dd, *J* 4.8, 4.8), 3.52 (2H, s), 2.58 (4H, dd, *J* 5.3, 5.3), 2.55 (4H, s), 2.20 (3H, s); δ_C (500 MHz; acetone-d_6) 161.8 (s), 159.3 (s), 154.0 (s), 140.8 (s), 130.8 (d), 129.7 (d), 129.0 (d), 127.7 (d), 126.4 (d), 120.2 (d), 63.3 (t), 57.3 (t), 55.7 (t), 54.1 (t), 49.4 (t), 43.0 (q); MALDI-TOF MS (*m*/*z*): 426 (MH^+, 100%), 424 (62), 392 (6), 333 (29), 305 (77), 275 (3), 148 (82), 134 (5).

*4.7.2.2. 4-(N-{2-[Benzyl(methyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazol-5-one (**16bb**).* Chromatography eluent: Et_2O/acetone (95:5). Obtained as an unstable yellow oil (14.0 mg, 40%), which was fully characterized as the dihydrochloride salt. 4-(*N*-{2-[Benzyl-(methyl)amino]ethyl}piperazin-1-yl)-5*H*-1,2,3-dithiazol-5-one (**16bb**) was dissolved in DCM and purged with HCl (g) for 5 s. The precipitated salt was filtered and washed with DCM to give *4-(N-{2-[benzyl(methyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazol-5-one dihydrochloride* (**16bb**·2HCl) as a microcrystalline pale yellow powder, decomp. (DSC) onset: 222.6 °C, peak max: 223.4 °C; (found: C, 45.28; H, 5.79; N, 13.09. $C_{16}H_{24}Cl_2N_4OS_2$ requires: C, 45.39; H, 5.71; N, 13.23%); λ_{max} (H_2O)/nm 262 (3.21), 369 (3.79); ν_{max}/cm^{-1} 2359brm (N^+-H), 1649s, 1520m, 1495m, 1479w, 1460m, 1449m, 1398m, 1389m, 1362w, 1315m, 1279m, 1261m, 1211w, 1196m, 1177w, 1144w, 1119m, 1061m, 1043m, 966m, 947m, 924m, 837m, 822m, 797m, 752s, 706s; δ_H (500 MHz; D_2O) 7.61−7.55 (5H, m), 4.49 (2H, s), 3.87 (4H, br s), 3.75−3.63 (4H, m), 3.47 (4H, br s), 2.92 (3H, s); δ_C [125 MHz; D_2O (0.5 mL) + DMSO-d_6 (0.1 mL)] 189.1

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(s), 156.7 (s), 132.6 (d), 132.2 (d), 131.1 (d), 129.9 (s), 62.3 (t), 53.4 (t), 51.7 (t), 50.3 (t), 45.9 (t), 41.1 (q); MALDI-TOF MS (*m*/*z*): 351 (MH^+, 100%), 258 (5), 230 (77), 148 (69), 90 (5).

*4.7.2.3. 4-(N-{2-[Benzyl(methyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazol-5-thione (**16cb**).* Chromatography eluent: Et_2O/acetone (95:5). Obtained as an unstable red oil (19.5 mg, 53%), which was fully characterized as the dihydrochloride salt. 4-(*N*-{2-[Benzyl(methyl)amino]ethyl}piperazin-1-yl)-5*H*-1,2,3-dithiazole-5-thione (**16cb**) was dissolved in DCM and purged with HCl (g) for 5 s. The precipitated salt was filtered and washed with DCM to give *4-(N-{2-[benzyl(methyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazol-5-thione dihydrochloride* (**16cb**·2HCl) as microcrystalline red powder, decomp. (DSC) onset: 209.4 °C, peak max: 214.0 °C; (found: C, 43.80; H, 5.41; N, 12.67. $C_{16}H_{24}Cl_2N_4S_3$ requires: C, 43.73; H, 5.50; N, 12.75%); λ_{max} (H_2O)/nm 235 (log ε 3.91), 315 (3.25), 441 (3.88); ν_{max}/cm^{-1} 2984w and 2916w (alkyl C-H), 2419m (N^+-H), 1609w, 1493m, 1477m, 1452m, 1396m, 1337m, 1279m, 1261s, 1213w, 1182w, 1167m, 1152m, 1123s, 1076m, 1049m, 1043m, 1030m, 991m, 964s, 922m, 856w, 849m, 839m, 824m, 804m, 785m, 741m, 708m; δ_H (500 MHz; D_2O) 7.61−7.57 (5H, m), 4.49 (2H, s), 3.90 (4H, br s), 3.74−3.69 (4H, m), 3.52 (4H, br s), 2.93 (3H, s); δ_C [125 MHz; D_2O + DMSO-d_6 (1 drop)] 203.7 (s), 167.1 (s), 132.6 (d), 132.2 (d), 131.1 (d), 129.8 (s), 62.4 (t), 53.6 (t), 51.8 (t), 50.2 (t), 47.5 (t), 41.3 (q); MALDI-TOF MS (*m*/*z*): 367 (MH^+, 85%), 365 (100), 335 (6), 274 (3), 246 (92), 148 (75), 134 (4).

4.7.3. Reaction with Aniline (General Procedure). To a stirred suspension of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.40 mmol) in dry and deaerated MeCN (2 mL) at *ca.* 20 °C under an argon atmosphere was added dropwise aniline (365 μL, 4.0 mmol). The mixture was then heated at *ca.* 81 °C under argon for the time specified in Table 3 (entry 3) and then left to cool to *ca.* 20 °C. The mixture was then cooled to *ca.* −20 °C for 12 h, and the resultant precipitate was collected by filtration and washed with cold MeCN to give the corresponding 4-{*N*-[2-(phenylamino)ethyl]-piperazin-1-yl}-5*H*-1,2,3-dithiazole hydrochloride **16ac**−**cc**.

*4.7.3.1. N-(4-{N-[2-(Phenylamino)ethyl]piperazin-1-yl}-5H-1,2,3-dithiazol-5-ylidene)aniline Hydrochloride (**16ac**).* Obtained as yellow needles (124.3 mg, 72%); mp (DSC) onset: 195.6 °C, peak max: 198.6 °C, decomp. onset: 200.5 °C, peak max: 201.4 °C (from EtOH); (found: C, 55.23; H, 5.65; N, 16.04. $C_{20}H_{24}ClN_5S_2$ requires: C, 55.35; H, 5.57; N, 16.14%); λ_{max} (MeOH)/nm 244 (log ε 4.35), 285 (3.76), 379 (3.79); ν_{max}/cm^{-1} 3250m (N-H), 3113w and 3024w (aryl C-H), 2585m and 2475m (N^+-H), 1603m, 1562s, 1526m, 1501m, 1483m, 1466m, 1441m, 1381m, 1310m, 1277m, 1258m, 1229m, 1182m, 1128m, 1086m, 1053m, 1026m, 1007m, 970s, 941m, 864m, 822m, 785m, 756s; δ_H (500 MHz; DMSO-d_6 at *ca.* 80 °C) two N*H* resonances missing (deuterium exchanged), 7.48 (2H, dd, *J* 7.8, 7.8), 7.24 (1H, dd, *J* 7.3, 7.3), 7.15−7.10 (4H, m), 6.68 (2H, d, *J* 7.5), 6.62 (1H, dd, *J* 7.3, 7.3), 4.08 (4H, br s), 3.53 (2H, t, *J* 6.3), 3.42 (4H, br s), 3.30 (2H, t, *J* 6.3); δ_C (125 MHz; DMSO-d_6) 160.6 (s), 157.1 (s), 152.2 (s), 147.7 (s), 129.8 (d), 128.9 (d), 125.5 (d), 119.1 (d), 116.4 (d), 112.3 (d), 54.3 (t), 50.4 (t), 44.6 (t), 37.1 (t); MALDI-TOF MS (*m*/*z*): 398 (MH^+, 100%), 363 (12), 305 (87), 279 (42), 236 (5).

*4.7.3.2. 4-{N-[2-(Phenylamino)ethyl]piperazin-1-yl}-5H-1,2,3-dithiazol-5-one Hydrochloride (**16bc**).* Obtained as yellow needles (118.6 mg, 83%), mp 179−181 °C (from EtOH); (found: C, 47.00; H, 5.27; N, 15.72. $C_{14}H_{19}ClN_4OS_2$ requires: C, 46.85; H, 5.34; N, 15.61%); λ_{max} (MeOH)/nm 245 (log ε 4.23), 293 (3.46), 373 (3.87); ν_{max}/cm^{-1} 3258m (N-H), 3026w (aryl C-H), 2848w (alkyl C-H), 2569m (N^+-H), 1663s (C═O), 1605s, 1530m, 1499m, 1474m, 1443m, 1435m, 1387m, 1360m, 1310m, 1271m, 1248s, 1225m, 1182m, 1130m, 1086m, 1051m, 1032m, 970s, 945m, 891m, 814m, 758s; δ_H (500 MHz; DMSO-d_6 at *ca.* 80 °C) two N*H* resonances missing (deuterium exchanged), 7.11 (2H, dd, *J* 8.5, 7.5), 6.68 (2H, dd, *J* 8.5, 1.0), 6.61 (1H, ddd, *J* 7.3, 7.3, 1.0), 3.92 (4H, br s), 3.52 (2H, t, *J* 6.3), 3.37 (4H, br s), 3.26 (2H, t, *J* 6.3); δ_C (125 MHz; DMSO-d_6) 186.3 (s), 154.7 (s), 147.7 (s), 128.9 (d), 116.4 (d), 112.3 (d), 54.3 (t), 50.2 (t), 43.7 (t), 37.1 (t); MALDI-TOF MS (*m*/*z*): 323 (MH^+, 100%), 262 (2), 230 (71), 206 (2), 119 (9).

*4.7.3.3. 4-{N-[2-(Phenylamino)ethyl]piperazin-1-yl}-5H-1,2,3-dithiazole-5-thione Hydrochloride (**16cc**).* Obtained as red plates (96.0 mg, 64%), decomp. (DSC) onset: 190.1 °C, peak max: 194.5 °C (from $CHCl_3$/EtOH); (found: C, 44.80; H, 5.09; N, 14.81. $C_{14}H_{19}ClN_4S_3$ requires: C, 44.85; H, 5.11; N, 14.94%); λ_{max} (MeOH)/nm 243 (log ε 4.28), 273 inf (3.75), 320 inf (3.35), 450 (3.92); ν_{max}/cm^{-1} 3246m (N-H), 2571m (N^+-H), 1603m (C═S), 1526m, 1497m, 1481m, 1433m, 1385m, 1350m, 1308m, 1250s, 1225m, 1179m, 1146m, 1121m, 1080m, 1047m, 993m, 968s, 885m, 841m, 824m, 806m, 748s; δ_H (500 MHz; DMSO-d_6 at *ca.* 80 °C) two N*H* resonances missing (deuterium exchanged), 7.11 (2H, dd, *J* 8.5, 7.0), 6.68 (2H, d, *J* 7.5), 6.61 (1H, dd, *J* 7.3, 7.3), 3.96 (4H, br s), 3.52 (2H, t, *J* 6.3), 3.40 (4H, br s), 3.29 (2H, t, *J* 6.5); δ_C (125 MHz; DMSO-d_6) 202.1 (s), 165.0 (s), 147.7 (s), 128.9 (d), 116.4 (d), 112.3 (d), 54.2 (t), 50.4 (t), 45.2 (t), 37.1 (t); MALDI-TOF MS (*m*/*z*): 339 (MH^+, 100%), 246 (59), 120 (3).

4.7.4. Reaction with N-Methylaniline (General Procedure). To a stirred suspension of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.80 mmol) in dry and deaerated MeCN (2 mL) at *ca.* 20 °C under an argon atmosphere was added dropwise *N*-methylaniline (867 μL, 8.0 mmol). The mixture was then heated at *ca.* 81 °C under argon for the time specified in Table 3 (entry 4) and then left to cool to *ca.* 20 °C. The mixture was then cooled to *ca.* −20 °C for 12 h, and the resultant precipitate was collected by filtration and washed with cold MeCN to give the corresponding 4-{*N*-[2-(phenylamino)ethyl]piperazin-1-yl}-5*H*-1,2,3-dithiazole hydrochloride **16ad**−**cd**.

*4.7.4.1. N-[4-(N-{2-[Methyl(phenyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazol-5-ylidene]aniline Hydrochloride (**16ad**).* In this case, the mixture was cooled to *ca.* −40 °C for 24 h. Obtained as yellow prisms (194. 2 mg, 54%); mp (DSC) onset: 186.2 °C, peak max: 191.8 °C, decomp. onset: 194.2 °C, peak max: 196.6 °C (from EtOH); (found: C, 56.28; H, 5.96; N, 15.58. $C_{21}H_{26}ClN_5S_2$ requires: C, 56.30; H, 5.85; N, 15.63%); λ_{max} (MeOH)/nm 253 (log ε 4.45), 277 inf (4.05), 379 (3.83); ν_{max}/cm^{-1} 3053w and 3028w (aryl C-H), 2951w and 2932w (alkyl C-H), 2365m (N^+-H), 1595s, 1585s, 1531m, 1510m, 1479m, 1454m, 1443m, 1398m, 1381m, 1369m, 1283m, 1250m, 1219m, 1159m, 1123m, 1086m, 1072m, 1036m, 1020m, 989m, 970s, 928m, 858m, 849m, 839m, 793m, 781m, 772m, 752s, 748s, 706s; δ_H (500 MHz; DMSO-d_6 at *ca.* 80 °C) one N*H* resonance missing (deuterium exchanged), 7.48 (2H, dd, *J* 8.0, 7.5), 7.25−7.18 (3H, m), 7.14 (2H, dd, *J* 8.5, 1.0), 6.86 (2H, d, *J* 8.0), 6.70 (1H, dd, *J* 7.3, 7.3), 4.06 (4H, br s), 3.82 (2H, t, *J* 7.5), 3.41 (4H, br s), 3.26 (2H, t, *J* 7.3), 2.95 (3H, s); δ_C (75 MHz; DMSO-d_6) 160.6 (s), 157.1 (s), 152.2 (s), 148.3 (s), 129.8 (d), 129.0 (d), 125.5 (d), 119.1 (d), 116.5 (d), 112.3 (d), 51.0 (t), 50.4 (t), 45.9 (t), 44.7 (t), 37.8 (q); MALDI-TOF MS (*m*/*z*): 412 (MH^+, 100%), 377 (2), 305 (65), 134 (37).

*4.7.4.2. 4-(N-{2-[Methyl(phenyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazol-5-one Hydrochloride (**16bd**).* Obtained as yellow plates (232.5 mg, 78%), mp (DSC) onset: 178.8 °C, peak max: 182.8 °C, decomp. onset 186.2 °C, peak max: 191.9 °C (from EtOH); (found: C, 48.20; H, 5.52; N, 15.00. $C_{15}H_{21}ClN_4OS_2$ requires: C, 48.31; H, 5.68; N, 15.02%); λ_{max} (MeOH)/nm 254 (log ε 4.25), 301 (3.48), 372 (3.82); ν_{max}/cm^{-1} 3024w (aryl C-H), 2911w (alkyl C-H); 2409m (N^+-H), 1638s (C═O), 1507m, 1526m, 1508s, 1462m, 1445m, 1383m, 1360m, 1281m, 1271m, 1236m, 1211m, 1194m, 1184m, 1161w, 1111m, 1094m, 1076m, 1049w, 1038m, 991m, 959s, 862m, 845m, 822m, 789m, 745s; δ_H (500 MHz; DMSO-d_6 at *ca.* 80 °C) one N*H* resonance missing (deuterium exchanged), 7.20 (2H, dd, *J* 8.5, 7.5), 6.85 (2H, d, *J* 8.0), 6.70 (1H, dd, *J* 7.3, 7.3), 3.91 (4H, br s), 3.81 (2H, t, *J* 7.5), 3.36 (4H, br s), 3.22 (2H, t, *J* 7.5), 2.93 (3H, s); δ_C (125 MHz; DMSO-d_6) 186.3 (s), 154.7 (s), 148.2 (s), 129.0 (d), 116.6 (d), 112.3 (d), 51.0 (t), 50.1 (t), 45.8 (t), 43.8 (t), 37.8 (q); MALDI-TOF MS (*m*/*z*): 337 (MH^+, 100%), 274 (4), 246 (5), 230 (59), 134 (18), 132 (15).

*4.7.4.3. 4-(N-{2-[Methyl(phenyl)amino]ethyl}piperazin-1-yl)-5H-1,2,3-dithiazole-5-thione Hydrochloride (**16cd**).* Obtained as red plates (237.2 mg, 84%), decomp. (DSC) onset: 186.7 °C, peak max: 191.3 °C (from $CHCl_3$/EtOH); (found: C, 46.35; H, 5.53; N, 14.38. $C_{15}H_{21}ClN_4S_3$ requires: C, 46.32; H, 5.44; N, 14.40%); λ_{max} (MeOH)/

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nm 241 inf (log ε 4.30), 253 (4.40), 284 inf (3.82), 320 inf (3.52), 450 (4.02); ν_{max}/cm^{-1} 3051w (aryl C-H), 2936w (alkyl C-H), 2401m (N^+-H), 1597m (C═S), 1508m, 1485m, 1435m, 1422m, 1383m, 1377m, 1366m, 1275m, 1252m, 1229m, 1215m, 1198m, 1159m, 1121m, 1105m, 1076m, 1028m, 1015m, 988m, 970m, 918w, 866w, 829m, 820m, 800m, 743s; δ_H (500 MHz; DMSO-d_6 at *ca.* 80 °C) one N*H* resonance missing (deuterium exchanged), 7.20 (2H, dd, *J* 8.8, 7.3), 6.85 (2H, d, *J* 8.0), 6.70 (1H, dd, *J* 7.3, 7.3), 3.95 (4H, br s), 3.81 (2H, t, *J* 7.5), 3.40 (4H, br s), 3.25 (2H, t, *J* 7.3), 3.11 (2H, br s), 2.93 (3H, s); δ_C (125 MHz; DMSO-d_6) 202.1 (s), 165.0 (s), 148.2 (s), 129.0 (d), 116.5 (d), 112.3 (d), 51.0 (t), 50.4 (t), 45.9 (t), 45.2 (t), 37.8 (q); MALDI-TOF MS (*m*/*z*): 353 (MH^+, 60%), 351 (100), 319 (4), 246 (67), 244 (34), 220 (3), 134 (61), 132 (27).

4.7.5. Reaction with Potassium Phthalimide (General Procedure). To a stirred solution of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.10 mmol) in MeCN (2 mL) at *ca.* 20 °C was added in one portion potassium phthalimide (37 mg, 0.20 mmol). The mixture was then heated at *ca.* 81 °C for the time specified in Table 3 (entry 5) and then left to cool to *ca.* 20 °C. The mixture was adsorbed onto silica, and chromatography (*n*-hexane/Et_2O, 90:10) gave, in some cases, traces of unreacted starting material. Further elution gave the corresponding 4-[*N*-(2-phthalimidoethyl)-piperazin-1-yl]-5*H*-1,2,3-dithiazole **16ae**−**ce**.

*4.7.5.1. N-{4-[N-(2-Phthalimidoethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**16ae**).* Chromatography eluent: *n*-hexane/Et_2O, 50:50. Obtained as yellow needles (43.9 mg, 97%); mp 115−116 °C (from *n*-hexane/*t*-BuOMe at *ca.* −40 °C); R_f 0.29 (*n*-hexane/Et_2O, 60:40); (found: C, 58.57; H, 4.61; N, 15.59. $C_{22}H_{21}N_5O_2S_2$ requires: C, 58.52; H, 4.69; N, 15.51%); λ_{max} (DCM)/nm 243 (log ε 4.38), 281 (4.01), 382 (3.77); ν_{max}/cm^{-1} 2941w and 2828w (alkyl C-H), 1767m, 1705s (C═O), 1591m, 1578m, 1522m, 1481m, 1452m, 1437m, 1395m, 1387m, 1360m, 1325m, 1281m, 1271m, 1244m, 1209m, 1144m, 1115m, 1105m, 1078m, 1013m, 993m, 918m, 860m, 814m, 797m, 766m, 760m, 714s, 706m; δ_H (300 MHz; $CDCl_3$) 7.88−7.82 (2H, m), 7.75−7.68 (2H, m), 7.42 (2H, dd, *J* 7.8, 7.8), 7.19 (1H, dd, *J* 7.5, 7.5), 7.11 (2H, d, *J* 8.1), 3.85 (2H, t, *J* 6.5), 3.70 (4H, dd, *J* 4.8, 4.8), 2.71−2.65 (6H, m); δ_C (75 MHz; $CDCl_3$); 168.3 (s), 160.6 (s), 158.4 (s), 152.5 (s), 133.9 (d), 132.2 (s), 129.7 (d), 125.6 (d), 123.2 (d), 119.4 (d), 55.7 (t), 52.6 (t), 48.5 (t), 35.2 (t); MALDI-TOF MS (*m*/*z*): 452 (MH^+, 100%), 418 (2), 236 (58), 217 (4).

*4.7.5.2. 4-[N-(2-Phthalimidoethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-one (**16be**).* Chromatography eluent: *n*-hexane/Et_2O, 40:60. Obtained as pale yellow cotton fibers (33.7 mg, 90%), mp 136−138 °C (from *c*-hexane); R_f 0.36 (*n*-hexane/*t*-BuOMe, 50:50); (found: C, 51.13; H, 4.36; N, 14.73. $C_{16}H_{16}N_4O_3S_2$ requires: C, 51.05; H, 4.28; N, 14.88%); λ_{max} (DCM)/nm 242 (log ε 4.17), 276 (4.17), 377 (3.70); ν_{max}/cm^{-1} 2941w and 2845w (alkyl C-H), 1767m, 1705s (C═O), 1667s (C═O), 1530m, 1464m, 1452m, 1441m, 1396m, 1387m, 1341m, 1335m, 1300m, 1269m, 1246m, 1207m, 1202m, 1144m, 1128m, 1099m, 1074m, 1026m, 1009m, 991m, 874m, 820m, 808m, 791m; δ_H (500 MHz; $CDCl_3$) 7.81−7.79 (2H, m), 7.72−7.67 (2H, m), 3.81 (2H, t, *J* 6.3), 3.53 (4H, dd, *J* 4.5, 4.5), 2.64 (2H, t, *J* 6.5), 2.59 (4H, dd, *J* 4.8, 4.8); δ_C (125 MHz; $CDCl_3$) 186.0 (s), 168.2 (s), 155.1 (s), 133.8 (d), 132.0 (s), 123.1 (d), 55.5 (t), 52.4 (t), 47.3 (t), 35.0 (t); MALDI-TOF MS (*m*/*z*): 377 (MH^+, 100%), 375 (64), 345 (30), 316 (72), 285 (75), 214 (9), 174 (35), 124 (4).

*4.7.5.3. 4-[N-(2-Phthalimidoethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-thione (**16ce**).* Chromatography eluent: *n*-hexane/Et_2O, 40:60. Obtained as red plates (35.6 mg, 91%), mp 165.5−167.5 °C (from *c*-hexane/1,2-DCE); R_f 0.55 (DCM/Et_2O, 80:20); (found: C, 49.11; H, 4.04; N, 14.18. $C_{16}H_{16}N_4O_2S_3$ requires: C, 48.96; H, 4.11; N, 14.27%); λ_{max} (DCM)/nm 242 (log ε 4.41), 267 (4.12), 331 inf (2.49), 458 (4.00); ν_{max}/cm^{-1} 2830w and 2810w (alkyl C-H), 1761m, 1701s (C═O), 1479m, 1474m, 1441m, 1402m, 1379m, 1358m, 1325m, 1277m, 1271m, 1242s, 1200m, 1190m, 1173m, 1146m, 1123s, 1103m, 1055m, 1040m, 1015m, 984m, 920m, 891m, 858m, 826m, 812m, 764m, 721s; δ_H (500 MHz; $CDCl_3$) 7.86−7.83 (2H, m), 7.73−7.70 (2H, m), 3.87 (2H, br s), 3.64 (4H, br s), 2.72 (6H, br s); δ_C (125 MHz; $CDCl_3$) 202.0 (s), 168.3 (s), 165.9 (s), 133.9 (d), 132.2 (s), 123.2 (d), 55.6 (t), 52.5 (t), 48.7 (t), 35.0 (t); MALDI-TOF MS (*m*/*z*): 393 (MH^+, 100%), 358 (42), 328 (13), 288 (7), 217 (47), 203 (9), 177 (37), 174 (48).

4.7.6. Reaction with Sodium Acetate (General Procedure). To a stirred solution of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.10 mmol) in MeCN (2 mL) at *ca.* 20 °C was added in one portion NaOAc (16.4 mg, 0.20 mmol). The mixture was then heated at *ca.* 81 °C for the time specified in Table 3 (entry 6) and then left to cool to *ca.* 20 °C. The mixture was adsorbed onto silica, and chromatography (*n*-hexane/Et_2O, 90:10) gave traces of unreacted starting material. Further elution gave the corresponding 4-[*N*-(2-acetoxyethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **16af**−**16cf**.

*4.7.6.1. N-{4-[N-(2-Acetoxyethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**16af**).* Chromatography eluent: *n*-hexane/Et_2O, 20:80. Obtained as a yellow oil (34.6 mg, 95%); R_f 0.35 (*t*-BuOMe); (found: C, 53.01; H, 5.43; N, 15.21. $C_{16}H_{20}N_4O_2S_2$ requires: C, 52.73; H, 5.53; N, 15.37%); λ_{max} (DCM)/nm 243 inf (log ε 3.98), 280 (3.59), 382 (3.71); ν_{max}/cm^{-1} 2940w and 2826w (alkyl C-H), 1738s (C═O), 1595m, 1582m, 1574m, 1522m, 1485m, 1449m, 1379m, 1306m, 1233s, 1150m, 1078m, 1043m, 993m, 905w, 858m, 826m, 795m, 762m; δ_H (500 MHz; $CDCl_3$) 7.43 (2H, dd, *J* 7.8, 7.8), 7.20 (1H, dd, *J* 7.3, 7.3), 7.13 (2H, d, *J* 8.0), 4.25 (2H, t, *J* 5.8), 3.80 (4H, br s), 2.72−2.69 (6H, m), 2.08 (3H, s); δ_C (125 MHz; $CDCl_3$) 170.9 (s), 160.6 (s), 158.3 (s), 152.5 (s), 129.7 (d), 125.6 (d), 119.3 (d), 61.6 (t), 56.7 (t), 53.0 (t), 48.2 (t), 21.0 (q); MALDI-TOF MS (*m*/*z*): 365 (MH^+, 100%), 331 (4), 236 (76), 86 (21).

*4.7.6.2. 4-[N-(2-Acetoxyethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-one (**16bf**).* Chromatography eluent: *n*-hexane/Et_2O, 20:80. Obtained as yellow prisms (26.8 mg, 93%); mp 32.5−34 °C (*n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.20 (*n*-hexane/*t*-BuOMe, 50:50); (found: C, 41.50; H, 5.28; N, 14.36. $C_{10}H_{15}N_3O_3S_2$ requires: C, 41.51; H, 5.23; N, 14.52%); λ_{max} (DCM)/nm 276 (log ε 3.81), 376 (3.71); ν_{max}/cm^{-1} 2941w and 2822w (alkyl C-H), 1736m, 1659s, 1651m, 1530m, 1449m, 1383m, 1306m, 1236s, 1150m, 1043m, 988m, 816m; δ_H (500 MHz; $CDCl_3$) 4.20 (2H, t, *J* 5.8), 3.64 (4H, dd, *J* 4.8, 4.8), 2.66 (2H, t, *J* 5.8), 2.60 (4H, dd, *J* 4.8, 4.8), 2.06 (3H, s); δ_C (125 MHz; $CDCl_3$) 186.1 (s), 170.9 (s), 155.1 (s), 61.5 (t), 56.6 (t), 52.8 (t), 47.2 (t), 21.0 (q); MALDI-TOF MS (*m*/*z*): 290 (MH^+, 100), 288 (56), 230 (38), 229 (41), 87 (23).

*4.7.6.3. 4-[N-(2-Acetoxyethyl)piperazin-1-yl]-5H-1,2,3-dithiazole-5-thione (**16cf**).* Chromatography eluent: *n*-hexane/Et_2O, 20:80. Obtained as a red oil (29.0 mg, 94%); R_f 0.21 (DCM/*t*-BuOMe, 90:10); (found: C, 39.42; H, 4.82; N, 13.63. $C_{10}H_{15}N_3O_2S_3$ requires: C, 39.33; H, 4.95; N, 13.76%); λ_{max} (DCM)/nm 259 inf (log ε 3.92), 327 (3.49), 457 (3.99), 538 inf (2.75); ν_{max}/cm^{-1} 2940w and 2822w (alkyl C-H), 1736m, 1732m, 1485m, 1445m, 1375m, 1306m, 1236s, 1125s, 1051m, 1007w, 980m, 812m; δ_H (500 MHz; $CDCl_3$) 4.21 (2H, t, *J* 5.8), 3.67 (4H, dd, *J* 4.3, 4.3), 2.68 (2H, t, *J* 6.0), 2.65 (4H, dd, *J* 4.8, 4.8), 2.06 (3H, s); δ_C (125 MHz; $CDCl_3$) 202.0 (s), 170.9 (s), 165.9 (s), 61.6 (t), 56.6 (t), 52.9 (t), 48.8 (t), 21.0 (q); MALDI-TOF MS (*m*/*z*): 306 (MH^+, 100%), 304 (32), 246 (17), 86 (10).

4.7.7. Reaction with Sodium Benzoate (General Procedure). To a stirred solution of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.10 mmol) in MeCN (2 mL) at *ca.* 20 °C was added in one portion NaOBz (15.9 mg, 0.11 mmol). The mixture was then heated at *ca.* 81 °C for the time specified in Table 3 (entry 7) and then left to cool to *ca.* 20 °C. The mixture was adsorbed onto silica, and chromatography (*n*-hexane/Et_2O, 90:10) gave traces of unreacted starting material. Further elution gave the corresponding 4-[*N*-(2-benzoyloxyethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **16ag**−**cg**.

*4.7.7.1. N-{4-[N-(2-Benzoyloxyethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**16ag**).* Chromatography eluent: *n*-hexane/Et_2O, 80:20. Obtained as a yellow microcrystalline powder (41.6 mg, 98%); mp 55−56.5 °C (from *n*-hexane/*t*-BuOMe at *ca.* −40 °C); R_f 0.43 (*n*-hexane/*t*-BuOMe, 40:60); (found: C, 59.35; H, 5.01; N, 13.33. $C_{21}H_{22}N_4O_2S_2$ requires: C, 59.13; H, 5.20; N, 13.14%); λ_{max} (DCM)/nm 272 inf (log ε 3.74), 281 (3.71), 294 inf (3.61), 382 (3.80); ν_{max}/cm^{-1} 3063w and 3009w (aryl C-H), 2806w and 2754w (alkyl C-H), 1713s (C═O), 1574s, 1524m, 1487m, 1450m, 1400m, 1362m, 1314m, 1275s, 1246m, 1234m, 1173m, 1148m, 1107m, 1069m, 1030m, 1016m, 991m, 949m, 934m, 856m, 826m, 804m, 791m, 766m,

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708s; δ_H (500 MHz; $CDCl_3$) 8.04 (2H, d, *J* 7.0), 7.57 (1H, dd, *J* 7.5, 7.5), 7.47−7.42 (4H, m), 7.20 (1H, dd, *J* 7.5, 7.5), 7.12 (2H, d, *J* 7.5), 4.53 (2H, br s), 3.83 (4H, br s), 2.90 (2H, br s), 2.79 (4H, br s); δ_C (125 MHz; $CDCl_3$) 166.4 (s), 160.6 (s), 158.2 (s), 152.5 (s), 133.0 (d), 130.1 (s), 129.7 (d), 129.6 (d), 128.4 (d), 125.6 (d), 119.4 (d), 62.3 (t), 56.7 (t), 53.0 (t), 48.2 (t); MALDI-TOF MS (*m*/*z*): 427 (MH^+, 100%), 393 (6), 305 (19), 276 (2), 236 (83), 192 (4), 149 (49), 104 (4).

*4.7.7.2. 4-[N-(2-Benzoyloxyethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-one (**16bg**).* Chromatography eluent: *n*-hexane/Et_2O, 80:20. Obtained as yellow needles (34.2 mg, 97%), mp 59−61.5 °C (from *n*-hexane/Et_2O at *ca.* −20 °C); R_f 0.43 (DCM/Et_2O, 90:10); (found: C, 51.12; H, 4.84; N, 11.84. $C_{15}H_{17}N_3O_3S_2$ requires: C, 51.26; H, 4.88; N, 11.96%); λ_{max} (DCM)/nm 274 (log ε 3.93), 281 inf (3.90), 377 (3.73); ν_{max}/cm^{-1} 3067w and 3030w (aryl C-H), 2833w and 2851w (alkyl C-H), 1722s (C═O), 1659s, 1601m, 1526m, 1450m, 1445m, 1414m, 1383m, 1331m, 1312m, 1279s, 1267s, 1250m, 1225m, 1194m, 1177m, 1152m, 1119m, 1070m, 1026m, 989m, 955m, 816m; δ_H (500 MHz; $CDCl_3$) 8.03 (2H, d, *J* 7.0), 7.56 (1H, dd, *J* 7.5, 7.5), 7.44 (2H, dd, *J* 7.8, 7.8), 4.47 (2H, t, *J* 5.8), 3.65 (4H, dd, *J* 4.8, 4.8), 2.82 (2H, t, *J* 5.8), 2.68 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 186.1 (s), 166.4 (s), 155.1 (s), 133.0 (d), 130.0 (s), 129.5 (d), 128.4 (d), 62.4 (t), 56.6 (t), 52.9 (t), 47.3 (t); MALDI-TOF MS (*m*/*z*): 352 (MH^+, 100%), 350 (61), 291 (47), 260 (14), 230 (37), 149 (19), 104 (7).

*4.7.7.3. 4-[N-(2-Benzoyloxyethyl)piperazin-1-yl]-5H-1,2,3-dithiazole-5-thione (**16cg**).* Chromatography eluent: *n*-hexane/Et_2O, 80:20. Obtained as a red oil (34.8 mg, 95%), R_f 0.54 (DCM/*t*-BuOMe, 90:10); (found: C, 49.15; H, 4.73; N, 11.32. $C_{15}H_{17}N_3O_2S_3$ requires: C, 49.02; H, 4.66; N, 11.43%); λ_{max} (DCM)/nm 256 inf (log ε 3.95), 268 inf (3.92), 280 inf (3.82), 289 inf (3.70), 327 (3.45), 457 (3.97); ν_{max}/cm^{-1} 2932w and 2826w (alkyl C-H), 1717m (C═S), 1601w, 1485m, 1445m, 1379m, 1314m, 1271s, 1246m, 1175m, 1125m, 1070m, 1051m, 1026m, 980m, 810m; δ_H (500 MHz; $CDCl_3$) 8.04 (2H, d, *J* 7.0), 7.57 (1H, dd, *J* 7.5, 7.5), 7.45 (2H, dd, *J* 7.8, 7.8), 4.50 (2H, br s), 3.70 (4H, br s), 2.87 (2H, br s), 2.76 (4H, br s); δ_C (125 MHz; $CDCl_3$) 202.0 (s), 166.4 (s), 165.8 (s), 133.1 (d), 130.1 (s), 129.6 (d), 128.4 (d), 62.3 (t), 56.6 (t), 52.9 (t), 48.8 (t); MALDI-TOF MS (*m*/*z*): 368 (MH^+, 100%), 335 (12), 305 (4), 246 (61), 149 (30), 105 (8).

4.7.8. Reaction with Potassium Thiocyanate (General Procedure). To a stirred solution of the appropriate 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.10 mmol) in MeCN (2 mL) at *ca.* 20 °C was added in one portion KSCN (10.7 mg, 0.11 mmol). The mixture was then heated at *ca.* 81 °C for the time specified in Table 3 (entry 8) and then left to cool to *ca.* 20 °C. The mixture was adsorbed onto silica, and chromatography (*n*-hexane/Et_2O, 90:10) gave, in some cases, traces of unreacted starting material. Further elution gave the corresponding 4-[*N*-(2-thiocyanatoethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole **16ah**−**ch**.

*4.7.8.1. N-{4-[N-(2-Thiocyanatoethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}aniline (**16ah**).* Chromatography eluent: *n*-hexane/Et_2O, 60:40. Obtained as yellow needles (33.1 mg, 91%); mp 86−87 °C (from *n*-hexane/*t*-BuOMe at *ca.* −20 °C); R_f 0.38 (*n*-hexane/*t*-BuOMe, 40:60); identical to that described above.

*4.7.8.2. 4-[N-(2-Thiocyanatoethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-one (**16bh**).* Chromatography eluent: *n*-hexane/Et_2O, 50:50. Obtained as pale yellow prisms (27.3 mg, 94%), mp 92−93 °C (from *c*-hexane); R_f 0.32 (*n*-hexane/*t*-BuOMe, 50:50); (found: C, 37.33; H, 4.04; N, 19.32. $C_9H_{12}N_4OS_3$ requires: C, 37.48; H, 4.19; N, 19.43%); λ_{max} (DCM)/nm 276 (log ε 3.61), 377 (3.80); ν_{max}/cm^{-1} 3015w (aryl C-H), 2954w and 2824m (alkyl C-H), 2156m (C≡N), 1643s (C═O), 1618m, 1522m, 1450m, 1387m, 1368m, 1335m, 1308m, 1277m, 1252s, 1225s, 1163m, 1144m, 1125m, 1103m, 1072m, 1059m, 1007m, 989s, 962m, 949m, 851m, 824m, 803m, 760m; δ_H (500 MHz; $CDCl_3$) 3.64 (4H, dd, *J* 5.0, 5.0), 3.20 (2H, t, *J* 6.5), 2.78 (2H, t, *J* 6.5), 2.59 (4H, dd, *J* 4.8, 4.8); δ_C (125 MHz; $CDCl_3$) 186.0 (s), 155.0 (s), 112.9 (s), 56.1 (t), 52.2 (t), 47.0 (t), 32.1 (t); MALDI-TOF MS (*m*/*z*): 289 (MH^+, 100%), 287 (78), 262 (49), 228 (49), 216 (5).

*4.7.8.3. 4-[N-(2-Thiocyanatoethyl)piperazin-1-yl]-5H-1,2,3-dithiazole-5-thione (**16ch**).* Chromatography eluent: *n*-hexane/Et_2O, 50:50. Obtained as red plates (27.5 mg, 90%), mp 104.5−105.5 °C (from *n*-hexane/*t*-BuOMe at *ca.* −20 °C); R_f 0.55 (DCM/Et_2O, 90:10); (found: C, 35.71; H, 3.79; N, 18.36. $C_9H_{12}N_4S_4$ requires: C, 35.50; H, 3.97; N, 18.40%); λ_{max} (DCM)/nm 252 inf (log ε 3.87), 330 (3.40), 456 (3.93), 540 inf (2.48); ν_{max}/cm^{-1} 2943w and 2824m (alkyl C-H), 2151m (C≡N), 1479m, 1441m, 1381m, 1369m, 1356m, 1312m, 1288m, 1265m, 1250s, 1211m, 1202m, 1136m, 1121s, 1101m, 1065m, 1053m, 1042m, 1001m, 982s, 853m, 827m, 795m, 762m; δ_H (500 MHz; $CDCl_3$) 3.67 (4H, br s), 3.21 (2H, t, *J* 6.5), 2.80 (2H, t, *J* 6.5), 2.65 (4H, dd, *J* 5.0, 5.0); δ_C (125 MHz; $CDCl_3$) 202.0 (s), 165.8 (s), 112.9 (s), 56.2 (t), 52.2 (t), 48.7 (t), 32.3 (t); MALDI-TOF MS (*m*/*z*): 305 (MH^+, 61%), 303 (100), 278 (58), 271 (10), 246 (21), 177 (3), 129 (6).

4.7.9. Reaction with 2-Mercaptobenzothiazole (General Procedure). To a stirred solution of the appropriate 4-[*N*-(2-chloroethyl)-piperazin-1-yl]-5*H*-1,2,3-dithiazole **13** (0.10 mmol) in MeCN (2 mL) at *ca.* 20 °C was added in one portion 2-mercaptobenzothiazole (18.4 μL, 0.11 mmol) and then powdered K_2CO_3 (0.11 mmol, 15.2 mg). The mixture was then heated at *ca.* 81 °C for the time specified in Table 3 (entry 9) and then left to cool to *ca.* 20 °C. The mixture was filtered and washed with DCM, and the filtrate was adsorbed onto silica and chromatographed to give the corresponding 4-{*N*-[2-(benzo[*d*]thiazol-2-ylthio)ethyl]piperazin-1-yl}-5*H*-1,2,3-dithiazole **16ai**−**ci**.

*4.7.9.1. N-(4-{N-[2-(Benzo[d]thiazol-2-ylthio)ethyl]piperazin-1-yl}-5H-1,2,3-dithiazol-5-ylidene)aniline (**16ai**).* Chromatography eluent: *n*-hexane/Et_2O, 40:60. Obtained as yellow plates (42.8 mg, 90%); mp 118−119 °C (from *n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.35 (*n*-hexane/Et_2O, 50:50); (found: C, 53.55; H, 4.56; N, 14.79. $C_{21}H_{21}N_5S_4$ requires: C, 53.48; H, 4.49; N, 14.85%); λ_{max} (DCM)/nm 243 (log ε 4.31), 282 (4.23), 290 (4.19), 301 (4.11), 381 (3.77); ν_{max}/cm^{-1} 3067w and 3024w (aryl C-H), 2841m and 2826m (alkyl C-H), 1591m, 1572s, 1516m, 1485m, 1462m, 1454m, 1447m, 1427m, 1377m, 1371m, 1360m, 1312m, 1292m, 1269m, 1254m, 1242m, 1211m, 1206m, 1132m, 1080m, 1016m, 993s, 953m, 858m, 845m, 829m, 793m, 754s, 723m; δ_H (300 MHz; $CDCl_3$) 7.86 (1H, d, *J* 8.1), 7.76 (1H, d, *J* 7.8), 7.46−7.38 (3H, m), 7.29 (1H, dd, *J* 7.5, 7.5), 7.20 (1H, dd, *J* 7.4, 7.4), 7.13 (2H, d, *J* 8.1), 3.79 (4H, dd, *J* 4.8, 4.8), 3.56 (2H, t, *J* 7.1), 2.87 (2H, t, *J* 7.1), 2.71 (4H, dd, *J* 5.0, 5.0); δ_C (75 MHz; $CDCl_3$) 166.9 (s), 160.7 (s), 158.3 (s), 153.2 (s), 152.5 (s), 135.3 (s), 129.7 (d), 126.0 (d), 125.6 (d), 124.2 (d), 121.5 (d), 121.0 (d), 119.4 (d), 57.1 (t), 52.6 (t), 48.3 (t), 30.8 (t); MALDI-TOF MS (*m*/*z*): 471 (M^+, 52%), 437 (7), 304 (100), 235 (8), 193 (30).

*4.7.9.2. 4-{N-[2-(Benzo[d]thiazol-2-ylthio)ethyl]piperazin-1-yl}-5H-1,2,3-dithiazol-5-one (**16bi**).* Chromatography eluent: *n*-hexane/Et_2O, 30:70. Obtained as a yellow needles (32.4 mg, 81%), mp 69−70 °C (*n*-hexane/Et_2O at *ca.* −40 °C); R_f 0.67 (DCM/Et_2O, 90:10); (found: C, 45.51; H, 4.13; N, 14.12. $C_{15}H_{16}N_4OS_4$ requires: C, 45.43; H, 4.07; N, 14.13%); λ_{max} (DCM)/nm 245 inf (log ε 4.12), 281 (4.26), 289 inf (4.21), 302 (4.10), 377 (3.84); ν_{max}/cm^{-1} 3057w (aryl C-H), 2934m and 2812m (alkyl C-H), 1659s (C═O), 1530m, 1454m, 1427s, 1385m, 1308m, 1273m, 1248m, 1128m, 1074m, 989s, 816m, 756s, 725m; δ_H (500 MHz; $CDCl_3$) 7.85 (1H, d, *J* 8.0), 7.74 (1H, d, *J* 8.0), 7.41 (1H, dd, *J* 7.8, 7.8), 7.29 (1H, dd, *J* 7.5, 7.5), 3.66 (4H, dd, *J* 4.5, 4.5), 3.54 (2H, t, *J* 7.3), 2.85 (2H, t, *J* 6.0), 2.66 (4H, br s); δ_C (125 MHz; $CDCl_3$) 186.1 (s), 166.7 (s), 155.1 (s), 153.1 (s), 135.2 (s), 126.0 (d), 124.2 (d), 121.4 (d), 121.0 (d), 57.0 (t), 52.4 (t), 47.2 (t), 30.6 (t); MALDI-TOF MS (*m*/*z*) 397 (MH^+, 100%), 305 (7), 230 (62), 194 (5), 138 (3).

*4.7.9.3. 4-{N-[2-(Benzo[d]thiazol-2-ylthio)ethyl]piperazin-1-yl}-5H-1,2,3-dithiazole-5-thione (**16ci**).* Chromatography eluent: *n*-hexane/Et_2O, 30:70. Obtained as an unstable red oil (33.7 mg, 75%), which was characterized as the hydrochloride salt. 4-{*N*-[2-(Benzo[*d*]thiazol-2-ylthio)ethyl]piperazin-1-yl}-5*H*-1,2,3-dithiazole-5-thione (**16ci**) was dissolved in MeCN/DCM (2:1, 5 mL) and purged with HCl (g) for 5−10 s. To the mixture was added *n*-pentane, and the resulting precipitate was collected by filtration and washed with *n*-pentane to give *4-{N-[2-(benzo[d]thiazol-2-ylthio)ethyl]piperazin-1-yl}-5H-1,2,3-dithiazole-5-thione hydrochloride* (**16ci**·HCl) as a red microcrystalline powder, decomp. (DSC) onset: 182.2 °C, peak max: 186.6

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°C; (found: C, 39.97; H, 3.70; N, 12.37. $C_{15}H_{17}ClN_4S_5$ requires: C, 40.12; H, 3.82; N, 12.48%); λ_{max} (MeOH)/nm 225 (log ε 4.39), 234 inf (4.29), 243 inf (4.20), 278 (4.23), 288 inf (4.17), 301 (4.06), 330 inf (3.34), 450 (3.87); ν_{max}/cm^{-1} 3063w (aryl C-H), 2884w and 2938w (alkyl C-H), 2556m (N^+-H), 1481m, 1456m, 1427m, 1402m, 1391m, 1342m, 1333m, 1265m, 1190m, 1132m, 1123m, 1086m, 1061m, 1032m, 1001m, 974m, 957m, 932m 868m, 826m, 810m, 750s, 721m, 706m; δ_H (500 MHz; DMSO-d_6) 11.44 (1H, br s), 8.04 (1H, d, *J* 7.5), 7.90 (1H, d, *J* 8.0), 7.50 (1H, dd, *J* 7.5, 7.5), 7.40 (1H, dd, *J* 7.5, 7.5), 4.40 (2H, d, *J* 13.0), 3.83 (2H, t, *J* 7.5), 3.70 (2H, d, *J* 11.0), 3.59 (2H, t, *J* 7.8), 3.40 (2H, dd, *J* 12.5, 12.5), 3.33−3.22 (2H, m); δ_C (125 MHz; $CDCl_3$) 202.1 (s), 165.0 (s), 164.8 (s), 152.4 (s), 134.7 (s), 126.4 (d), 124.7 (d), 121.8 (d), 121.3 (d), 54.3 (t), 50.4 (t), 45.2 (t), 26.1 (t); MALDI-TOF MS (*m*/*z*): 413 (MH^+, 100%), 379 (6), 246 (77).

4.8. Chemistry of 4-[*N*-(2-Chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole-5-thione (13c). *4.8.1. Reaction with TCNEO.* To a stirred solution of 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole-5-thione (**13c**) (28.2 mg, 0.1 mmol) in toluene (0.5 mL) at *ca.* 20 °C was added TCNEO (28.8 mg, 0.2 mmol) in one portion, and the mixture was left to stir at this temperature for 2 h. Then, the reaction mixture was diluted with *n*-hexane/DCM and poured onto a packed column of silica, and chromatography (DCM/Et_2O 30:70) gave the desired product together with unidentified side products. A second chromatography (Et_2O) gave pure *2-{4-[N-(2-chloroethyl)-piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}malononitrile* (**13da**) as orange needles (10.5 mg, 33%), decomp. (DSC) onset: 160.1 °C, peak max: 161.1 °C (from Et_2O at *ca.* −20 °C); R_f 0.76 (Et_2O); (found: C, 42.13; H, 3.75; N, 22.19. $C_{11}H_{12}ClN_5S_2$ requires: C, 42.10; H, 3.85; N, 22.32%); λ_{max} (DCM)/nm 243 (log ε 3.78), 270 inf (3.57), 380 inf (3.65), 445 (4.10); ν_{max}/cm^{-1} 2941w, 2843w and 2818w (alkyl C-H), 2208m (C≡N), 1487m, 1468s, 1464s, 1454m, 1371m, 1356m, 1339m, 1312m, 1294w, 1275m, 1260m, 1211m, 1159m, 1148m, 1125m, 1084m, 1001m, 939m, 895m, 851m, 837m, 826m, 814s, 737w, 710m; δ_H (500 MHz; $CDCl_3$) 3.60 (2H, t, *J* 6.8), 3.25 (4H, br s), 2.80 (2H, t, *J* 7.0), 2.77 (4H, dd, *J* 4.5, 4.5); δ_C (125 MHz; $CDCl_3$) 167.9 (s), 162.1 (s), 116.3 (s), 112.6 (s), 65.4 (s), 59.4 (t), 51.9 (t), 51.3 (t), 40.9 (t); MALDI-TOF MS (*m*/*z*): 316 (MH^+ + 2, 25%), 314 (MH^+, 67), 278 (100), 264 (8), 242 (2), 226 (3), 147 (7).

4.8.2. Reaction with Diazomalonate. To a stirred solution of diazomalonate (56.0 mg, 0.3 mmol) in PhCl (2 mL) at *ca.* 20 °C was added 4-[*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole-5-thione (**13c**) (28.2 mg, 0.1 mmol) and CuBr (43.2 mg, 0.3 mmol), and the mixture was heated under vigorous reflux (external temperature *ca.* 170 °C) for 3 h. Then, the mixture was left to cool to *ca.* 20 °C and then poured onto a packed column of silica. Chromatography (*n*-hexane/Et_2O, 90:10) gave unreacted diazomalonate and thione **13c**. Further elution (*n*-hexane/Et_2O, 60:40) gave an unidentified yellow side product (2.7 mg). A last elution (*n*-hexane/Et_2O, 60:40) gave *diethyl 2-{4-[N-(2-chloroethyl)piperazin-1-yl]-5H-1,2,3-dithiazol-5-ylidene}malonate* (**13db**) as yellow plates (14.0 mg, 37%), mp 74−75 °C (from *n*-hexane/Et_2O at *ca.* −20 °C); R_f 0.33 (*n*-hexane/Et_2O, 60:40); (found: C, 44.03; H, 5.31; N, 10.36. $C_{15}H_{22}ClN_3O_4S_2$ requires: C, 44.17; H, 5.44; N, 10.30%); λ_{max} (DCM)/nm 269 inf (log ε 3.24), 421 (3.96); ν_{max}/cm^{-1} 2984w, 2961w, 2938w, 2839w and 2803w (alkyl C-H), 1697m, 1651m, 1518m, 1479m, 1456m, 1366m, 1321m, 1281m, 1254m, 1238s, 1171m, 1138w, 1121m, 1099m, 1065w, 1034m, 1015m, 1007m, 991m, 935m, 862m, 839m, 810m, 785m, 772m, 748m, 727m; δ_H (500 MHz; $CDCl_3$) 4.32 (2H, q, *J* 7.0), 4.30 (2H, q, *J* 7.2), 3.59 (2H, t, *J* 7.0), 3.11 (2H, br s), 2.96 (2H, br s), 2.83 (2H, br s), 2.76 (2H, t, *J* 7.0), 2.32 (2H, br s), 1.32 (3H, t, *J* 7.3), 1.31 (3H, t, *J* 7.0); δ_C (125 MHz; $CDCl_3$) 167.0 (s), 165.6 (s), 164.7 (s), 154.9 (s), 112.5 (s), 62.1 (t), 61.7 (t), 59.8 (t), 52.2 (t), 51.7 (t), 40.8 (t), 14.2 (q), 14.0 (q); MALDI-TOF MS (*m*/*z*): 409 (M^+ + 2, 48%), 407 (M^+, 72), 369 (44), 361 (100), 331 (12), 145 (22).

4.8.3. Reaction with Diphenyldiazomethane. To a stirred solution of diphenyldiazomethane (77.7 mg, 0.4 mmol) in DCM (1 mL) was added 4-*N*-(2-chloroethyl)piperazin-1-yl]-5*H*-1,2,3-dithiazole-5-thione (**13c**) (28.2 mg, 0.1 mmol), and the mixture was left stirring at *ca.* 20 °C for 20 h. Then, the mixture was diluted with *n*-hexane and poured onto a packed column of silica, and chromatography (DCM) gave the desired product as a mixture with multiple colorless side products. A second chromatography (*n*-hexane/Et_2O, 60:40) gave pure *4-[N-(2-chloroethyl)piperazin-1-yl]-5-(diphenylmethylene)-5H-1,2,3-dithiazole* (**13dc**) as orange needles (20.7 mg, 50%), mp 122−124 °C (from *n*-hexane/Et_2O at *ca.* −20 °C); R_f 0.48 (*n*-hexane/Et_2O, 60:40); (found: C, 60.76; H, 5.26; N, 10.22. $C_{21}H_{22}ClN_3S_2$ requires: C, 60.63; H, 5.33; N, 10.10%); λ_{max} (DCM)/nm 264 (log ε 4.19), 286 inf (4.26), 432 (3.76); ν_{max}/cm^{-1} 3063w and 3026w (aryl C-H), 2951w, 2882w, 2841m and 2822m (alkyl C-H), 1520m, 1503m, 1491m, 1464m, 1445m, 1381m, 1368m, 1360m, 1306m, 1288m, 1267m, 1254m, 1209m, 1159m, 1138m, 1126m, 1103w, 1086m, 1074m, 1034w, 999m, 974w, 951w, 926w, 905w, 853m, 824m, 802m, 785m, 770s, 754m, 733m, 708s; δ_H (500 MHz; CD_3CN at *ca.* 65 °C) 7.42−7.39 (3H, m), 7.37−7.31 (3H, m), 7.24−7.21 (2H, m), 7.11−7.09 (2H, m), 3.47 (2H, t, *J* 6.5), 2.98 (4H, dd, *J* 4.5, 4.5), 2.47 (2H, t, *J* 6.8), 1.89 (4H, br s); δ_C (125 MHz; $CDCl_3$) 162.1 (s), 144.8 (s), 141.6 (s), 140.4 (s), 133.2 (s), 131.6 (d), 129.3 (d), 129.0 (d), 128.17 (d), 128.15 (d), 127.3 (d), 59.6 (t), 51.2 (t), 48.8 (t), 40.5 (t); MALDI-TOF MS (*m*/*z*): 417 (M^+ + 2, 14%), 415 (M^+, 25), 380 (8), 348 (14), 320 (29), 177 (2), 147 (100), 118 (37).

4.9. X-ray Crystallographic Studies. Data were collected on an Oxford Diffraction Supernova diffractometer, equipped with a CCD area detector utilizing Cu−Kα radiation (λ = 1.5418 Å). A suitable crystal was attached to glass fibers using paratone-N oil and transferred to a goniostat, where it was cooled for data collection. Unit cell dimensions were determined and refined by using 2064 ($3.29 \leq \theta \leq 72.43$) reflections. Empirical absorption corrections (multiscan based on symmetry-related measurements) were applied using CrysAlis RED software.[42] The structures were solved by direct method and refined on F^2 using full-matrix least-squares using SHELXL97.[43] Software packages used: CrysAlis CCD[42] for data collection, CrysAlis RED[42] for cell refinement and data reduction, WINGX for geometric calculations,[44] and DIAMOND[45] for molecular graphics. The non-H atoms were treated anisotropically. The hydrogen atoms were placed in calculated, ideal positions and refined as riding on their respective carbon atoms.

4.9.1. Crystal Refinement Data for Compound 13c. $C_8H_{12}ClN_3S_3$, *M* = 281.84, monoclinic, space group $P2_1/n$, *a* = 11.0496(4) Å, *b* = 7.8673(2) Å, *c* = 13.8104(5) Å, α = 90°, β = 103.673(4)°, γ = 90°, *V* = 1166.52(7) Å^3, *Z* = 4, *T* = 100(2) K, ρ_{calcd} = 1.605 g cm^{-3}, $2\theta_{max}$ = 67. Refinement of 136 parameters on 2075 independent reflections out of 5856 measured reflections (R_{int} = 0.0323) led to R_1 = 0.0348 [$I > 2\sigma(I)$], wR_2 = 0.4198 (all data), and *S* = 1.092, with the largest difference peak and hole of 0.385 and −0.510 e^{-3}, respectively.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02497.

Extended discussion on the optimization of the reaction of compound **2aa** with DABCO; structure elucidation discussions for compounds **13aa**, **16ah**, **17a**, and **18**; detailed discussion on the N···S interaction including computational studies; ellipsoid representation of the crystal structure for compound **13c**; and copies of 1D ^{1}H and ^{13}C NMR spectra of all compounds (PDF)

Atomic Cartesian coordinates and computed energies of dithiazoles **2aa**, **2aq**, **2as**, and **2au** (PDF)

Crystallographic data for compound **13c** (CIF)

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Notes

The authors declare no competing financial interest.

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