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The conversion of [(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]azines into azine fused thiazole-2-carbonitriles†‡

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The thermolysis of several *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-*n*-amines (where *n* = 2, 3 and 4) gives a mixture of thiazolopyridine-2-carbonitriles in low to moderate yields. Introduction, by design, of a chlorine substituent at the C2 or C4 position of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine and other selected azines enables a $BnEt_3NI$ mediated ANRORC style ring transformation that provides fourteen heteroazine fused thiazole-2-carbonitriles in moderate to near quantitative yields. The synthesis described herein therefore provides a facile high yielding two-step route to heteroazine fused thiazole-2-carbonitriles starting from 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt) and *ortho*- or *para*-chloro substituted *meta*-aminoazines.

1. Introduction

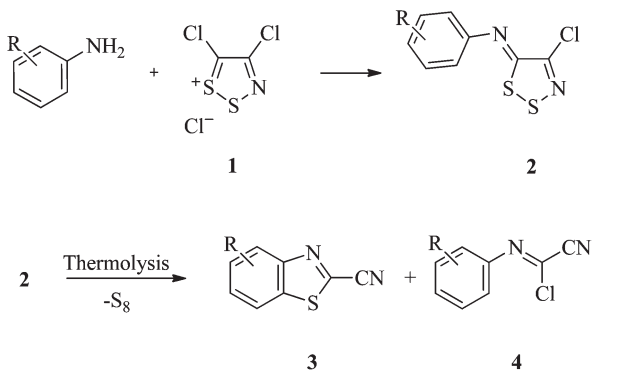
4,5-Dichloro-1,2,3-dithiazolium chloride (Appel salt) **1**[1] was prepared over 25 years ago and its chemistry has been exploited extensively to prepare many neutral 5*H*-1,2,3-dithiazoles. Several excellent reviews have appeared,[2] and some 1,2,3-dithiazoles show interesting biological activity as fungicides,[3] antibacterials,[4] or as inhibitors of the glutamine/amino acid transporter (ASCT2).[5] 1,2,3-Dithiazolyls are also of interest in the materials sciences as potential conductors and/or organic magnets.[6]

Additionally, neutral 4-chloro-1,2,3-dithiazoles are useful for the preparation of difficult to access cyano substituted heteroarenes. In particular, 1,2,3-dithiazolylidenes have been converted into thiazoles,[7] isothiazoles,[8] 1,2,4-thiadiazoles,[9] 1,3,4-thiadiazoles,[7b,10] and the rare 3*H*-pyrrole system,[11] as well as benzo fused heterocycles such as indoles,[12] benzothiazoles,[13] benzimidazoles,[14] benzoxazines,[15] and quinazolines.[12,16] Acyclic functionalities such as isothiocyanates and thiocyanoformamides can also be prepared from neutral 1,2,3-dithiazolylidenamines (dithiazolimines).[16c,17]

Despite their synthetic utility the library of dithiazolimines prepared from Appel salt **1** is comprised mainly of analogues where the dithiazolimine moiety is bound to a benzene ring. Some examples also exist where the dithiazole moiety is bound to 5-membered heteroles,[17b,18] and recently we extended this library by preparing several dithiazolimines bound to 6-membered heteroazines.[19]

The thermolysis of [(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-amino]arenes **2** to give arene fused thiazole-2-carbonitriles has been, in most part, limited to the preparation of benzothiazole-2-carbonitriles **3** (Scheme 1). The reactions are accompanied by the formation of elemental sulfur (S_8) and when the aniline substituent is electron poor the arylcarbonocyanidimidic chlorides **4**[20] are also formed. A mechanistic rationale for the formation of both products has been proposed by Rees.[13a,20]

Benzothiazole is a privileged bicyclic ring system and many benzothiazole-2-carboxamides, which can be readily derived from benzothiazole-2-carbonitriles, possess useful physical



Scheme 1

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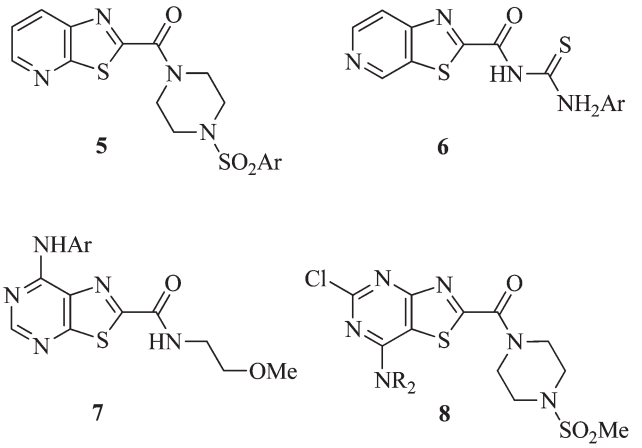
†Dedicated to the memory of Dr Van-Duc Le.

‡Electronic supplementary information (ESI) available: The study on the thermolysis of (dithiazolylidene)pyridinamines and related experimental procedures. ^1H and ^{13}C NMR spectra for all new compounds. See DOI: 10.1039/c2ob26993g

and biological properties.[21] Interesting biological activity is also shown by isosteric heteroazine fused thiazole-2-carboxamides, including anticoagulant (*e.g.*, the thiazolo[5,4-*b*]pyridines **5**)[22] or antiviral behavior (*e.g.*, the thiazolo[5,4-*c*]-pyridines **6**),[23] and inhibition of kinases (*e.g.*, the thiazolo[5,4-*d*]-pyrimidines **7**[24] and thiazolo[4,5-*d*]pyrimidines **8**[25]).



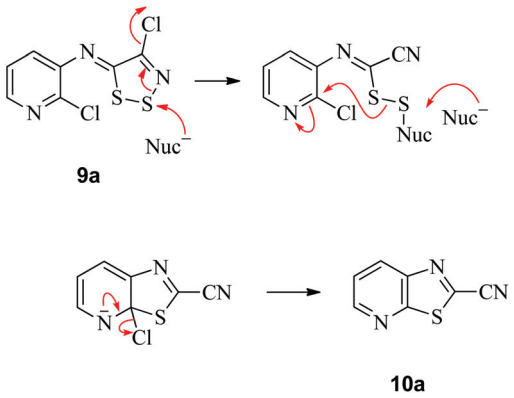
Unlike benzothiazoles,[21,26] routes to heteroazine fused thiazoles (heteroarenothiazoles) are less well developed.[26,27] By analogy with the formation of benzothiazole-2-carbonitriles **3** (Scheme 1) the thermolysis of our recently prepared [(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]azines[19] could provide a facile route to azine fused thiazole-2-carbonitriles.

Herein, having investigated and ascertained the limitations of the thermolysis reactions of *N*-heteroazine dithiazolimines (see ESI‡), we describe an efficient catalytic thiophile assisted addition of the nucleophile, ring opening, and ring closure (ANRORC) strategy, to obtain a series of azine fused thiazole-2-carbonitriles in high to near quantitative yields.

2. Results and discussion

Attempts to prepare thiazolopyridines *via* the thermolysis of various (dithiazol-5-ylidene)pyridinamines gave only low to moderate yields of the desired products together with several minor side products (for an account see ESI‡). In light of the comparative π electron deficiency of pyridine we then considered the thiophile assisted ANRORC[28] style ring transformation of dithiazoles which we and others have previously demonstrated with success.[3c,13–15,16a,b,d,29] Tentatively, we postulated that the generation of a nucleophilic S1 atom could be trapped at the pyridyl's more electrophilic sites. Furthermore, by introducing a suitable nucleofuge at these positions such as a halogen, the cyclisation step could occur *via* a facile intramolecular nucleophilic aromatic substitution thus avoiding the need for oxidative rearomatisation (Scheme 2).

Gratifyingly, the thiophile assisted ANRORC-style ring transformation of 2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-pyridin-3-amine (**9a**) with $BnEt_3NHal$ (Hal = Cl, Br, I) gave as the only product the thiazolo[5,4-*b*]pyridine **10a** in moderate to



Scheme 2

Table 1 Reaction of 2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9a**) (0.19 mmol) with R_4NHal in dry PhCl (2 ml) at *ca.* 132 °C under an argon atmosphere

			Yields (%)	
Entry	R_4NHal (equiv.)	Time (h)	S_8	**10a**
1	$BnEt_3NCl$ (1)	9	94	89
2	Et_4NBr (1)	11	84	99
3	$BnEt_3NI$ (1)	0.33	84	66
4	$BnEt_3NI$ (0.50)	1.25	99	92
5	$BnEt_3NI$ (0.25)	2	100	92
6	$BnEt_3NI$ (0.05)	24	83	98

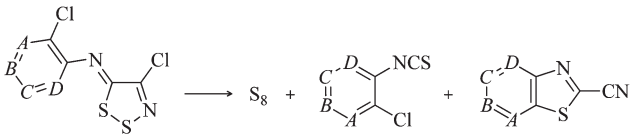
quantitative yields. The reaction was optimized with respect to solvent, equivalents of reagents and atmosphere (Table 1).

Under atmospheric air or in non-dried and degassed solvents the reaction mixture was complex providing the desired product in moderate to low yields. When the reaction took place in anhydrous conditions and in dry and degassed chlorobenzene then the product was obtained in high yields. The reactions with chloride or bromide (Table 1, entries 1 and 2, respectively) took significantly longer to consume the starting dithiazole than with iodide (entry 3). Furthermore, $BnEt_3NI$ could be used in catalytic amounts (5 mol%), although this led to longer reaction times (20 h *vs.* 2 h with 100 mol% of $BnEt_3NI$) (compare entries 3 to 6, Table 1). While only the results in chlorobenzene are shown in Table 1 we note that dry degassed benzene, toluene and xylene can also be used without significant changes in the product yield.

In light of this success, we prepared a range of 2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)heteroarylamines using the standard method for the condensation of Appel salt **1** with aminoheteroazines[19] and treated these dithiazolylidenamines with our optimized conditions. In nearly all cases, the desired heteroarenothiazole-2-carbonitrile was obtained in excellent yield (Table 2).

A selection of 2-chloro-*N*-(dithiazolylidene)pyridin-3-amines bearing substituents at the pyridyl C4 and C5 positions reacted with $BnEt_3NI$ to give near quantitative yields of the corresponding thiazolopyridines (entries 3–7). Similarly, the

Table 2 Reaction of (dithiazolylidene)heteroarylamines **9a–n** (0.19 mmol) with $BnEt_3NI$ (5 mol%) in dry PhCl (2 ml) at *ca.* 132 °C under an argon atmosphere



9a-n **11a & 11b** **10a-n**

Entry	Dithiazole **9**	*A*	*B*	*C*	*D*	Time (h)	Yields (%) **11**	Yields (%) **10**
1	**9a**	N	CH	CH	CH	24	—	**10a** (98)
2	**9b**	CH	CH	N	CH	20	—	**10b** (99)
3	**9c**	N	CH	CH	CMe	31	—	**10c** (98)
4	**9d**	N	CH	CMe	CH	51	—	**10d** (98)
5	**9e**	N	CH	CCl	CH	41	—	**10e** (97)
6	**9f**	N	CH	CBr	CH	36	—	**10f** (92)
7	**9g**	N	CH	Cl	CH	51	—	**10g** (93)
8	**9h**	N	COMe	CH	CH	43	**11a** (12)	**10h** (36)
9	**9i**	N	CCl	CH	CH	48	**11b** (13)	**10i** (43)
10	**9j**	N	CH	N	CH	31	—	**10j** (97)
11	**9k**	N	CH	N	CCl	26	—	**10k** (80)
12	**9l**	N	CMe	N	CCl	27	—	**10l** (89)
13	**9m**	N	CCl	N	CH	35	—	**10m** (93)
14	**9n**	N	CH	CH	N	132	—	**10n** (42)[a]

[a] Yield based on 10% recovered starting dithiazolimine **9n**.

reaction with 4-chloro-*N*-(dithiazolylidene)pyridin-3-amine **9b** gave the thiazolo[4,5-*c*]pyridine **10b** in 99% yield (entry 2). The exceptions, however, were the pyridine analogs bearing a substituent at the pyridyl C6 position (Table 2, entries 8 and 9), where the desired thiazolopyridines **10h** and **10i** were obtained in low to moderate yields, 36 and 43%, respectively, together with isothiocyanates **11a** and **11b** isolated as minor side products, 12 and 13%, respectively. Furthermore, diazines such as the pyrimidine analogues **9j–m** gave thiazolopyrimidines in good to excellent yields (Table 2, entries 10–13), however, the reaction of the pyrazine analogue **9n** (entry 14) could not be brought to completion even after 5 days; repeating the reaction with 1 equivalent of $BnEt_3NI$ also led to incomplete consumption of starting dithiazole after 12 hours and a complex reaction mixture.

To the best of our knowledge, with the exception of compound **10a**, the above heteroarenothiazole-2-carbonitriles are all new and their synthesis described herein presents a facile, high yielding two step preparation starting from readily available 4,5-dichloro-1,2,3-dithiazolium chloride and an appropriately halo substituted aminoheteroazine. The compounds all bear a potentially useful C2 nitrile, which can readily be further modified, adding additional value to the method.

3. Conclusions

The thermolysis of readily prepared *N*-(4-chloro-5*H*-1,2,3-dithiazolylidene)pyridineamines affords molecular sulfur and thiazolopyridines in low to moderate yields. However, by switching to an ANRORC style ring transformation, 2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9a**) treated with a catalytic amount of $BnEt_3NI$ (5 mol%) as the thiophile gave thiazolo[5,4-*b*]pyridine-2-carbonitrile (**10a**) in near quantitative yield. In this way, fourteen heteroarenothiazole-2-carbonitriles were prepared in two steps and in high overall yield *via* readily available Appel salt **1**.

4. Experimental

4.1. General methods and materials

DCM was freshly distilled from CaH_2 under argon. Reactions were protected from atmospheric moisture by $CaCl_2$ drying tubes. Anhydrous Na_2SO_4 was used for drying organic extracts, and 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 (Merck 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 Merck Silica Gel 60 (less than 0.063 mm).[30] Melting points were determined using a PolyTherm-A, Wagner & Munz, Koefler-Hotstage Microscope apparatus or a TA Instruments DSC Q1000 with samples hermetically sealed in aluminum pans under an argon atmosphere, using heating rates of 5 °C min^{-1}. Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a Perkin-Elmer Lambda-25 UV/vis spectrophotometer and inflections are identified by the

abbreviation "inf". IR spectra were recorded on a Shimadzu FTIR-NIR Prestige-21 spectrometer with a Pike *Miracle* 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 on a Bruker Avance 500 machine (at 500 and 125 MHz, respectively). Deuterated solvents were used for homonuclear lock and the signals are referenced to the deuterated solvent peaks. Low resolution (EI) mass spectra were recorded on a Shimadzu Q2010 GCMS with a direct inlet probe or on an Agilent 6890/5973N GCMS. MALDI-TOF MS were conducted on a Bruker BIFLEX III time-of-flight (TOF) mass spectrometer. High resolution (EI) mass spectra were recorded on an Autospec 'Q' machine. 4,5-Dichloro-1,2,3-dithiazolium chloride (**1**),[1] and dithiazoles (*Z*)-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9a**)[19] and (*Z*)-4-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9b**)[19] were prepared according to literature procedures.

4.2. Synthesis of [(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-amino]azines

4.2.1. (*Z*)-2-Chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-methylpyridin-3-amine (9c) (typical procedure). To a stirred suspension of 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) in DCM (4 ml) at *ca.* 20 °C and protected with a $CaCl_2$ drying tube was added 2-chloro-4-methylpyridin-3-amine (68.4 mg, 0.48 mmol). The reaction mixture was left to stir at *ca.* 20 °C for 1 h and then to this was added 2,6-lutidine (112 μl, 0.96 mmol) and the mixture was stirred at *ca.* 20 °C for an additional 2 h. The reaction mixture was then adsorbed onto silica and chromatographed to afford the *title compound* **9c** (80.1 mg, 60%) as yellow needles, mp (DSC) onset: 156.2 °C, peak max: 158.6 °C (from cyclohexane); R_f 0.58 (DCM); (found: C, 34.39; H, 1.80; N, 15.02. $C_8H_5Cl_2N_3S_2$ requires: C, 34.54; H, 1.81; N, 15.11%); λ_{max} (DCM) 234 (log ε 3.05), 278 (2.70), 352 (2.90); ν_{max}/cm^{-1} 3057w (Ar CH), 2974w and 2918w (CH_3), 1599s, 1574m, 1555m, 1514m, 1454w, 1437w, 1364s, 1281w, 1261w, 1240w, 1211s, 1182m, 1150m, 1088w, 1030w, 1007w, 883s, 858s, 814s, 779s; δ_H (500 MHz; $CDCl_3$) 8.13 (1H, d, *J* 5.0), 7.16 (1H, dd, *J* 5.0, 0.5), 2.21 (3H, s); δ_C (125 MHz; $CDCl_3$) 163.3 (s), 146.6 (s), 145.6 (d), 144.5 (s), 140.1 (s), 139.2 (s), 125.1 (d), 17.5 (q); MALDI-TOF MS (*m*/*z*): 282 (MH^+ + 4, 10%), 280 (MH^+ + 2, 70), 278 (MH^+, 100).

4.2.2. (*Z*)-2-Chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-5-methylpyridin-3-amine (9d). Similar treatment of 2-chloro-5-methylpyridin-3-amine (68.4 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 μl, 0.96 mmol) gave the *title compound* **9d** (109.5 mg, 82%) as yellow needles, mp 130–131 °C (from cyclohexane); R_f 0.42 (hexane–DCM, 3 : 7); (found: C, 34.71; H, 1.81; N, 14.98. $C_8H_5Cl_2N_3S_2$ requires: C, 34.54; H, 1.81; N, 15.11%); λ_{max} (DCM) 232 (log ε 3.50), 287 (3.10), 363 (3.25); ν_{max}/cm^{-1} 3042w (Ar CH), 2922w (CH_3), 1576s, 1545m, 1503m, 1493m, 1414m, 1393m, 1379m, 1290w, 1250w, 1221w, 1204s, 1142m, 1082s, 1038w, 976w, 907w, 864s, 854m, 800m, 750s; δ_H (500 MHz; acetone-d_6) 8.10 (1H, dd, *J* 2.0, 0.5), 7.48 (1H, dd, *J* 2.0, 1.0), 2.36 (3H, s); δ_C (125 MHz; $CDCl_3$) 162.6 (s), 147.4 (s), 146.8 (d), 144.5 (s), 139.4 (s), 133.8 (s), 127.8 (d), 17.8 (q); MALDI-TOF MS (*m*/*z*): 282 (MH^+ + 4, 7%), 280 (MH^+ + 2, 75), 278 (MH^+, 100).

4.2.3. (*Z*)-2,5-Dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (9e). Similar treatment of 2,5-dichloropyridin-3-amine (78.2 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 μl, 0.96 mmol) gave the *title compound* **9e** (117.5 mg, 82%) as orange needles, mp 152.5–153 °C (from cyclohexane); R_f 0.70 (hexane–DCM, 3 : 7); (found: C, 28.05; H, 0.68; N, 14.00. $C_7H_2Cl_3N_3S_2$ requires: C, 28.16; H, 0.68; N, 14.07%); λ_{max} (DCM) 233 (log ε 3.11), 293 (2.72), 364 (2.88); ν_{max}/cm^{-1} 3080w, 3053w and 3040w (Ar CH), 1574s, 1545m, 1535m, 1493s, 1402s, 1383m, 1263w, 1234w, 1217w, 1200m, 1161w, 1146m, 1126s, 1090m, 1080m, 930s, 897w, 866m, 856m, 795m; δ_H (500 MHz; $CDCl_3$) 8.23 (1H, d, *J* 2.5), 7.46 (1H, d, *J* 2.5); δ_C (125 MHz; $CDCl_3$) 163.6 (s), 147.4 (s), 145.3 (s), 144.8 (d), 140.5 (s), 131.3 (s), 127.1 (d); MALDI-TOF MS (*m*/*z*): 302 (MH^+ + 4, 24%), 300 (MH^+ + 2, 100), 298 (MH^+, 71).

4.2.4. (*Z*)-5-Bromo-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (9f). Similar treatment of 5-bromo-2-chloropyridin-3-amine (99.6 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 μl, 0.96 mmol) gave the *title compound* **9f** (133.4 mg, 81%) as orange needles, mp (DSC) onset: 172.6 °C, peak max: 173.9 °C (from cyclohexane–DCE); R_f 0.70 (hexane–DCM, 3 : 7); (found: C, 24.36; H, 0.67; N, 12.18. $C_7H_2BrCl_2N_3S_2$ requires: C, 24.51; H, 0.59; N, 12.25%); λ_{max} (DCM) 231 (log ε 3.31), 294 (2.91), 361 (3.03); ν_{max}/cm^{-1} 3075w (Ar CH), 1570s, 1541m, 1530m, 1518m, 1491s, 1400s, 1375m, 1263w, 1233w, 1215w, 1198m, 1159w, 1142m, 1119m, 1082s, 905s, 868s, 854s, 791m; δ_H (500 MHz; DMSO-d_6) 8.43 (1H, d, *J* 2.0), 8.08 (1H, d, *J* 2.5); δ_C (125 MHz; DMSO-d_6) 165.1 (s), 146.3 (d), 145.9 (s), 145.8 (s), 140.2 (s), 130.4 (d), 119.4 (s); MALDI-TOF MS (*m*/*z*): 346 (MH^+ + 4, 44%). 344 (MH^+ + 2, 100), 342 (MH^+, 54).

4.2.5. (*Z*)-2-Chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-5-iodopyridin-3-amine (9g). Similar treatment of 2-chloro-5-iodopyridin-3-amine (122.1 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 μl, 0.96 mmol) gave the *title compound* **9g** (151.7 mg, 81%) as yellow needles, mp 177.1–179.1 °C (from cyclohexane–DCE); R_f 0.70 (hexane–DCM, 3 : 7); (found: C, 21.63; H, 0.54; N, 10.84. $C_7H_2Cl_2IN_3S_2$ requires: C, 21.55; H, 0.52; N, 10.77%); λ_{max} (DCM) 232 (log ε 3.34), 299 (2.82), 365 (2.98); ν_{max}/cm^{-1} 3069w (Ar CH), 1564s, 1535w, 1520m, 1508m, 1487s, 1400s, 1375m, 1265w, 1229w, 1198m, 1142m, 1117m, 1076s, 889s, 868s, 851m, 789m; δ_H (500 MHz; DMSO-d_6) 8.51 (1H, d, *J* 2.0), 8.14 (1H, d, *J* 2.0); δ_C (125 MHz; DMSO-d_6) 164.9 (s), 151.3 (d), 146.0 (s), 145.8 (s), 140.9 (s), 135.5 (d), 93.2 (s); MALDI-TOF MS (*m*/*z*): 394 (MH^+ + 4, 6%), 392 (MH^+ + 2, 65), 390 (MH^+, 100).

4.2.6. (*Z*)-2-Chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-6-methoxypyridin-3-amine (9h). Similar treatment of 2-chloro-6-methoxypyridin-3-amine (76.1 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 μl, 0.96 mmol) gave the *title compound*

9h (127.1 mg, 90%) as orange plates, mp 139.6–140.8 °C (from cyclohexane); R_f 0.75 (hexane–DCM, 3 : 7); (found: C, 32.70; H, 1.62; N, 14.16. $C_8H_5Cl_2N_3OS_2$ requires: C, 32.66; H, 1.71; N, 14.28%); λ_{max} (DCM) 244 (log ε 3.09), 295 (2.90), 381 (2.82), 420 inf (2.62); ν_{max}/cm^{-1} 2997w and 2959w (CH_3), 1582s, 1547w, 1470s, 1441w, 1416m, 1364s, 1308s, 1258m, 1171w, 1155w, 1132m, 1070m, 1018s, 903m, 858s, 826s, 770s; δ_H (500 MHz; $CDCl_3$) 7.46 (1H, d, *J* 8.5), 6.77 (1H, d, *J* 8.5), 3.97 (3H, s); δ_C (125 MHz; $CDCl_3$) 161.2 (s), 161.1 (s), 147.7 (s), 139.8 (s), 137.8 (s), 130.4 (d), 110.3 (d), 54.4 (q); MALDI-TOF MS (*m*/*z*): 298 (MH^+ + 4, 8%), 296 (MH^+ + 2, 53), 294 (MH^+, 100).

4.2.7. (*Z*)-2,6-Dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-pyridin-3-amine (9i). Similar treatment of 2,6-dichloropyridin-3-amine (78.2 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 µl, 0.96 mmol) gave the *title compound* **9i** (121.8 mg, 85%) as yellow plates, mp 109.8–110.8 °C (from cyclohexane); R_f 0.70 (hexane–DCM, 2 : 8); (found: C, 28.22; H, 0.68; N, 13.95. $C_7H_2Cl_3N_3S_2$ requires: C, 28.16; H, 0.68; N, 14.07%); λ_{max} (DCM) 242 (log ε 3.25), 288 (3.02), 368 (2.96); ν_{max}/cm^{-1} 3042w (Ar CH), 1574s, 1557m, 1547m, 1504m, 1491m, 1412s, 1350m, 1248m, 1234s, 1150m, 1136s, 1076m, 1007w, 935w, 866s, 814s, 797s; δ_H (500 MHz; $CDCl_3$) 7.44 (1H, d, *J* 8.0), 7.36 (1H, d, *J* 8.0); δ_C (125 MHz; $CDCl_3$) 163.2 (s), 147.4 (s), 146.3 (s), 143.9 (s), 141.6 (s), 129.9 (d), 124.1 (d); MALDI-TOF MS (*m*/*z*): 302 (MH^+ + 4, 34%), 300 (MH^+ + 2, 91), 298 (MH^+, 100).

4.2.8. (*Z*)-4-Chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-pyrimidin-5-amine (9j). Similar treatment of 4-chloropyrimidin-5-amine (62.2 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 µl, 0.96 mmol) gave the *title compound* **9j** (99.3 mg, 78%) as orange plates, mp (DSC) onset: 124.8 °C, peak max: 126.8 °C (from cyclohexane); R_f 0.47 (DCM); (found: C, 27.13; H, 0.83; N, 21.09. $C_6H_2Cl_2N_4S_2$ requires: C, 27.18; H, 0.76; N, 21.13%); λ_{max} (DCM) 232 (log ε 3.11), 276 (2.73), 365 (2.88); ν_{max}/cm^{-1} 1593s, 1578m, 1551m, 1524m, 1416m, 1391s, 1290m, 1211m, 1179w, 1161m, 1123m, 1103m, 916m, 895w, 860s, 791m; δ_H (500 MHz; $CDCl_3$) 8.86 (1H, s), 8.52 (1H, s); δ_C (125 MHz; $CDCl_3$) 164.2 (s), 155.4 (d), 152.0 (s), 147.6 (d), 147.4 (s), 143.5 (s); MALDI-TOF MS (*m*/*z*): 269 (MH^+ + 4, 9%), 267 (MH^+ + 2, 74), 265 (MH^+, 100).

4.2.9. (*Z*)-4,6-Dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrimidin-5-amine (9k). Similar treatment of 4,6-dichloropyrimidin-5-amine (78.7 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 µl, 0.96 mmol) gave the *title compound* **9k** (132.3 mg, 50%) as colorless prisms, mp (DSC) onset: 195.7 °C, peak max: 197.3 °C (from cyclohexane); R_f 0.53 (hexane–DCM, 3 : 7); (found: C, 23.97; H, 0.35; N, 18.65. $C_6HCl_3N_4S_2$ requires: C, 24.05; H, 0.34; N, 18.70%); λ_{max} (DCM) 236 (log ε 3.13), 278 (2.92), 357 (3.03); ν_{max}/cm^{-1} 3076w (Ar CH), 1591s, 1580m, 1560w, 1528m, 1506s, 1404m, 1375w, 1356s, 1323w, 1294w, 1236w, 1227w, 1179m, 1165m, 1144w, 968w, 878m, 858w, 816s, 793s, 770m; δ_H (500 MHz; $CDCl_3$) 8.63 (1H, s); δ_C (125 MHz; $CDCl_3$) 165.3 (s), 153.7 (d), 151.2 (s), 146.8 (s), 140.8 (s); MALDI-TOF MS (*m*/*z*): 303 (MH^+ + 4, 35%), 301 (MH^+ + 2, 100), 299 (MH^+, 93).

4.2.10. (*Z*)-4,6-Dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-methyl-pyrimidin-5-amine (9l). Similar treatment of 4,6-dichloro-2-methylpyrimidin-5-amine (85.4 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 µl, 0.96 mmol) gave the *title compound* **9l** (106.9 mg, 71%) as yellow prisms, mp (DSC) onset: 178.1 °C, peak max: 179.7 °C (from cyclohexane); R_f 0.50 (hexane–DCM, 2 : 8); (found: C, 26.73; H, 0.94; N, 17.84. $C_7H_3Cl_3N_4S_2$ requires: C, 26.81; H, 0.96; N, 17.86%); λ_{max} (DCM) 235 (log ε 3.19), 281 (2.92), 358 (3.00); ν_{max}/cm^{-1} 1605m, 1589s, 1543m, 1487m, 1410m, 1362w, 1304m, 1290m, 1177w, 1163m, 1140w, 1034w, 1007w, 918w, 908w, 887w, 872s, 816s, 773s, 764m; δ_H (500 MHz; $CDCl_3$) 2.72 (3H, s); δ_C (125 MHz; $CDCl_3$) 165.3 (s), 164.6 (s), 150.8 (s), 146.8 (s), 138.0 (s), 25.1 (q); MALDI-TOF MS (*m*/*z*): 317 (MH^+ + 4, 18%), 315 (MH^+ + 2, 100), 313 (MH^+, 82).

4.2.11. (*Z*)-2,4-Dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrimidin-5-amine (9m). Similar treatment of 5-amino-2,4-dichloropyrimidine (78.7 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 µl, 0.96 mmol) gave the *title compound* **9m** (98.0 mg, 77%) as red prisms, mp 117.2–118.2 °C (from cyclohexane); R_f 0.60 (hexane–DCM, 3 : 7); (found: C, 24.16; H, 0.36; N, 18.77. $C_6HCl_3N_4S_2$ requires: C, 24.05; H, 0.34; N, 18.70%); λ_{max} (DCM) 235 (log ε 3.14), 289 (2.74), 367 (2.95); ν_{max}/cm^{-1} 1572m, 1553s, 1514w, 1495m, 1481m, 1408w, 1385s, 1315m, 1271m, 1258m, 1204m, 1188m, 1155w, 1096w, 872s, 806s, 756s; δ_H (500 MHz; $CDCl_3$) 8.43 (1H, s); δ_C (125 MHz; $CDCl_3$) 164.6 (s), 156.1 (s), 153.6 (s), 149.6 (d), 147.4 (s), 142.1 (s); MALDI-TOF MS (*m*/*z*): 303 (MH^+ + 4, 9%), 301 (MH^+ + 2, 74), 299 (MH^+, 100).

4.2.12. (*Z*)-3-Chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-pyrazin-2-amine (9n). Similar treatment of 3-chloropyrazin-2-amine (62.2 mg, 0.48 mmol) with 4,5-dichloro-1,2,3-dithiazolium chloride (**1**) (100 mg, 0.48 mmol) and 2,6-lutidine (112 µl, 0.96 mmol) gave the *title compound* **9n** (114.5 mg, 90%) as orange needles, mp (DSC) onset: 247.6 °C, peak max: 249.6 °C (from cyclohexane–DCE); R_f 0.50 (hexane–DCM, 1 : 1); (found: C, 27.14; H, 0.79; N, 21.12. $C_6H_2Cl_2N_4S_2$ requires: C, 27.18; H, 0.76; N, 21.13%); λ_{max} (DCM) 230 (log ε 3.62), 247 (3.66), 255 inf (3.62), 314 (3.47), 328 inf (3.38), 384 inf (3.55), 398 (3.84), 417 (3.97), 439 (3.80); ν_{max}/cm^{-1} 1516m, 1501m, 1464s, 1423m, 1387s, 1354w, 1323w, 1277w, 1215w, 1192m, 1163w, 1094m, 1078w, 1069m, 1001w, 951w, 908m, 874s, 837m, 800m, 777w; δ_H (500 MHz; DMSO-d_6) 8.74 (1H, d, *J* 3.0), 8.43 (1H, d, *J* 2.5); δ_C (125 MHz; DMSO-d_6) 162.3 (s), 148.9 (s), 148.6 (s), 145.4 (s), 139.9 (d), 138.3 (d); MALDI-TOF MS (*m*/*z*): 269 (MH^+ + 4, 6%), 267 (MH^+ + 2, 65), 265 (MH^+, 100).

4.3. Treatment of [*N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-amino]azines with $BnEt_3NI$

4.3.1. Thiazolo[5,4-*b*]pyridine-2-carbonitrile (10a) (typical procedure). To a mixture of (*Z*)-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9a**) (50.2 mg, 0.19 mmol)

and $BnEt_3NI$ (3.0 mg, 9.5 μmol) under an argon atmosphere was added dry and degassed PhCl (2 ml). The reaction mixture was immersed into a preheated Wood's metal bath at *ca.* 150 °C and left to stir at reflux until all the starting material was consumed (controlled by TLC). Later, the reaction mixture was removed from Wood's metal bath and allowed to cool to *ca.* 20 °C, dissolved with DCM (10 ml) and adsorbed onto silica. Chromatography (hexane) gave S_8 (5.0 mg, 83%), further elution (DCM) gave the *title compound* **10a** (30.0 mg, 98%) as colorless cotton fibers, mp (DSC) onset: 133.6 °C, peak max: 134.3 °C (lit.,[31] 135 °C) (from cyclohexane); R_f 0.50 (hexane–DCM, 2 : 8); (found: C, 52.07; H, 2.00; N, 25.92. $C_7H_3N_3S$ requires: C, 52.16; H, 1.88; N, 26.07%); λ_{max} (DCM) 243 inf (log ε 2.72), 247 (2.74), 274 (2.92), 303 (2.82); ν_{max}/cm^{-1} 3107w and 3065w (Ar CH), 2236w (C≡N), 1574w, 1551m, 1466m, 1441s, 1377m, 1279m, 1248m, 1223w, 1204w, 1167m, 1155m, 1119w, 1090w, 1042w, 880w, 810s; δ_H (500 MHz; $CDCl_3$) 8.82 (1H, dd, *J* 4.5, 1.5), 8.49 (1H, dd, *J* 8.5, 1.5), 7.63 (1H, dd, *J* 8.5, 4.5); δ_C (125 MHz; $CDCl_3$) 157.5 (s), 150.9 (d), 145.2 (s), 137.7 (s), 132.6 (d), 122.9 (d), 112.5 (s); *m*/*z* (EI) 161 (M^+, 100%), 109 (26), 103 (12), 82 (24), 70 (18), 64 (6), 51 (6).

4.3.2. Thiazolo[4,5-*c*]pyridine-2-carbonitrile (10b). Similar treatment of (*Z*)-4-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9b**) (50.2 mg, 0.19 mmol) gave S_8, and the *title compound* **10b** (30.3 mg, 99%) as colorless needles, mp (DSC) onset: 187.2 °C, peak max: 187.8 °C (from cyclohexane); R_f 0.61 (DCM–*t*-BuOMe, 9 : 1); (found: C, 52.19; H, 1.77; N, 25.95. $C_7H_3N_3S$ requires: C, 52.16; H, 1.88; N, 26.07%); λ_{max} (DCM) 241 (log ε 3.51), 279 (3.35), 298 inf (3.01); ν_{max}/cm^{-1} 3094w and 3065w (Ar CH), 2232w (C≡N), 1576m, 1526w, 1458m, 1437s, 1416m, 1387w, 1275m, 1231m, 1196s, 1157s, 1123w, 1084m, 1036m, 922m, 881m, 822s; δ_H (500 MHz; $CDCl_3$) 9.56 (1H, s), 8.75 (1H, d, *J* 5.5), 7.97 (1H, dd, *J* 5.5, 0.5); δ_C (125 MHz; $CDCl_3$) 148.5 (s), 147.8 (d), 146.5 (d), 142.8 (s), 137.9 (s), 116.4 (d), 112.2 (s); *m*/*z* (EI) 161 (M^+, 100%), 134 (7), 109 (25), 82 (61), 69 (16), 64 (8), 52 (5).

4.3.3. 7-Methylthiazolo[5,4-*b*]pyridine-2-carbonitrile (10c). Similar treatment of (*Z*)-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4-methylpyridin-3-amine (**9c**) (52.9 mg, 0.19 mmol) gave S_8, and the *title compound* **10c** (32.6 mg, 98%) as colorless needles, mp (DSC) onset: 176.9 °C, peak max: 177.5 °C (from cyclohexane); R_f 0.50 (hexane–DCM, 2 : 8); (found: C, 54.76; H, 2.79; N, 23.92. $C_8H_5N_3S$ requires: C, 54.84; H, 2.88; N, 23.98%); λ_{max} (DCM)/nm 229 (log ε 2.80), 241 (2.82), 245 (2.82), 280 (3.17), 296 inf (3.03), 311 inf (2.83); ν_{max}/cm^{-1} 3071w (Ar CH), 2922w and 2866w (CH_3), 2234m (C≡N), 1566s, 1466m, 1441s, 1373m, 1344m, 1273m, 1242m, 1219w, 1207w, 1165m, 1142s, 1103w, 1034w, 1003w, 901w, 891w, 872m, 841s; δ_H (500 MHz; $CDCl_3$) 8.64 (1H, d, *J* 4.5), 7.40 (1H, dd, *J* 4.8, 0.8), 2.81 (3H, d, *J* 0.5); δ_C (125 MHz; $CDCl_3$) 157.5 (s), 150.7 (d), 145.5 (s), 144.9 (s), 136.1 (s), 123.5 (d), 112.7 (s), 17.8 (q); MALDI-TOF MS (*m*/*z*): 176 (MH^+, 100%).

4.3.4. 6-Methylthiazolo[5,4-*b*]pyridine-2-carbonitrile (10d). Similar treatment of (*Z*)-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-5-methylpyridin-3-amine (**9d**) (52.9 mg, 0.19 mmol) gave S_8, and the *title compound* **10d** (32.6 mg, 98%) as colorless needles, mp (DSC) onset: 180.6 °C, peak max: 181.5 °C (from cyclohexane); R_f 0.50 (hexane–DCM, 2 : 8); (found: C, 54.76; H, 2.93; N, 23.87. $C_8H_5N_3S$ requires: C, 54.84; H, 2.88; N, 23.98%); λ_{max} (DCM)/nm 228 (log ε 3.26), 246 inf (3.29), 250 (3.33), 272 (3.44), 314 (3.33); ν_{max}/cm^{-1} 3057w (Ar CH), 2928w and 2859w (CH_3), 2236m (C≡N), 1539m, 1466m, 1439s, 1383w, 1360m, 1307w, 1265s, 1240w, 1188w, 1171m, 1155s, 1134m, 1086w, 1047w, 1013w, 978m, 889s, 762w; δ_H (500 MHz; $CDCl_3$) 8.66 (1H, d, *J* 2.0), 8.27 (1H, dd, *J* 1.8, 0.8), 2.57 (3H, s); δ_C (125 MHz; $CDCl_3$) 154.7 (s); 152.4 (d), 145.4 (s), 137.5 (s), 133.4 (s), 132.2 (d), 112.7 (s), 18.5 (q); MALDI-TOF MS (*m*/*z*): 176 (MH^+, 100%).

4.3.5. 6-Chlorothiazolo[5,4-*b*]pyridine-2-carbonitrile (10e). Similar treatment of (*Z*)-2,5-dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9e**) (56.4 mg, 0.19 mmol) gave S_8, and the *title compound* **10e** (36.1 mg, 97%) as colorless needles, mp (DSC) onset: 142.3 °C, peak max: 143.1 °C (from cyclohexane); R_f 0.70 (hexane–DCM, 2 : 8); (found: C, 42.83; H, 1.02; N, 21.39. $C_7H_2ClN_3S$ requires: C, 42.98; H, 1.03; N, 21.48%); λ_{max} (DCM)/nm 230 (log ε 3.16), 247 inf (2.93), 252 (2.97), 270 (3.00), 275 inf (2.97), 318 (2.90), 325 inf (2.84); ν_{max}/cm^{-1} 3073w (Ar CH), 2239w (C≡N), 1528m, 1445s, 1360m, 1281m, 1252s, 1229m, 1211w, 1157s, 1146s, 1094s, 1078w, 941s, 893s; δ_H (500 MHz; $CDCl_3$) 8.78 (1H, d, *J* 2.5), 8.47 (1H, d, *J* 2.5); δ_C (125 MHz; $CDCl_3$) 155.0 (s), 150.1 (d), 145.6 (s), 139.5 (s), 131.8 (s), 131.7 (d), 112.2 (s); MALDI-TOF MS (*m*/*z*): 198 (MH^+ + 2, 30%), 196 (MH^+, 100).

4.3.6. 6-Bromothiazolo[5,4-*b*]pyridine-2-carbonitrile (10f). Similar treatment of (*Z*)-5-bromo-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3-amine (**9f**) (65.2 mg, 0.19 mmol) gave S_8, and the *title compound* **10f** (42.0 mg, 92%) as colorless needles, mp (DSC) onset: 151.3 °C, peak max: 152.0 °C (from cyclohexane); R_f 0.70 (hexane–DCM, 2 : 8); (found: C, 34.97; H, 0.84; N, 17.45. $C_7H_2BrN_3S$ requires: C, 35.02; H, 0.84; N, 17.50%); λ_{max} (DCM)/nm 230 (log ε 3.40), 248 inf (3.10), 253 (3.12), 271 (3.10), 276 inf (3.07), 319 (2.98), 325 inf (2.94); ν_{max}/cm^{-1} 3046m (Ar CH), 2236w (C≡N), 1526m, 1443s, 1431m, 1360m, 1283w, 1254s, 1227w, 1155s, 1138m, 1096m, 1069w, 918s, 910s; δ_H (500 MHz; $CDCl_3$) 8.86 (1H, d, *J* 2.0), 8.64 (1H, d, *J* 2.5); δ_C (125 MHz; $CDCl_3$) 155.5 (s), 152.0 (d), 146.1 (s), 139.2 (s), 134.7 (d), 119.8 (s), 112.1 (s); MALDI-TOF MS (*m*/*z*): 242 (MH^+ + 2, 100%), 240 (MH^+, 81).

4.3.7. 6-Iodothiazolo[5,4-*b*]pyridine-2-carbonitrile (10g). Similar treatment of (*Z*)-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-5-iodo-pyridin-3-amine (**9g**) (74.1 mg, 0.19 mmol) gave S_8, and the *title compound* **10g** (50.7 mg, 93%) as colorless needles, mp 153.3–154.3 °C (from cyclohexane); R_f 0.70 (hexane–DCM, 2 : 8); (found: C, 29.38; H, 0.76; N, 14.58. $C_7H_2IN_3S$ requires: C, 29.29; H, 0.70; N, 14.64%); λ_{max} (DCM)/nm 235 (log ε 3.46), 255 (3.29), 267 inf (3.16), 278 inf (3.07), 327 (2.91); ν_{max}/cm^{-1} 3061w and 3042m (Ar CH), 2236w (C≡N), 1522m, 1449s, 1433m, 1356m, 1287m, 1250s, 1223w, 1182w, 1150s, 1128m, 1098m, 1090m, 1070w, 905s; δ_H (500 MHz; $CDCl_3$) 8.98 (1H, d, *J* 2.0), 8.83 (1H, d, *J* 2.0); δ_C (125 MHz; $CDCl_3$) 156.5 (d), 156.1 (s), 146.6 (s), 140.6 (d), 138.6 (s), 112.1 (s), 91.2 (s); MALDI-TOF MS (*m*/*z*): 288 (MH^+, 100%).

4.3.8. 2-Chloro-3-isothiocyanato-6-methoxypyridine (11a) and 5-methoxythiazolo-[5,4-*b*]pyridine-2-carbonitrile (10h). Similar treatment of (*Z*)-2-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-6-methoxypyridin-3-amine (**9h**) (55.9 mg, 0.19 mmol) gave after chromatography (hexane) S_8, followed by (hexane–DCM, 1 : 1) *2-chloro-3-isothiocyanato-6-methoxypyridine* (**11a**) (4.6 mg, 12%) as colorless plates, mp 86.1–86.6 °C (from pentane); R_f 0.71 (hexane–DCM, 1 : 1); (found: C, 42.03; H, 2.64; N, 14. 00. $C_7H_2IN_3S$ requires: C, 41.90; H, 2.51; N, 13.96%); λ_{max} (DCM)/nm 233 (log ε 3.17), 269 inf (2.98), 280 (3.15), 292 (3.14); ν_{max}/cm^{-1} 2959w, 2924m and 2853w (CH_3), 2204w, 2135m and 2075m (N═C═S), 1593m, 1549m, 1477s, 1441w, 1416m, 1371m, 1358s, 1315s, 1271m, 1261m, 1180m, 1130w, 1074s, 1016s, 962w, 935m, 881m, 826s, 804w; δ_H (500 MHz; $CDCl_3$) 7.42 (1H, d, *J* 8.5), 6.66 (1H, d, *J* 8.5), 3.94 (3H, s); δ_C (125 MHz; $CDCl_3$) 161.2 (s), 145.6 (s), 140.0 (s), 136.7 (d), 120.2 (s), 110.2 (d), 54.6 (q); *m*/*z* (EI) 202 (M^+ + 2, 36%), 200 (M^+, 100), 173 (16), 171 (43), 165 (9), 159 (6), 157 (13), 150 (6), 143 (4), 137 (3), 135 (16), 96 (42), 76 (4), 70 (11), 64 (15), 52 (3). Further elution (hexane–DCM, 2 : 8) gave *5-methoxythiazolo[5,4-b]pyridine-2-carbonitrile* (**10h**) (13.1 mg, 36%) as colorless plates, mp (DSC) onset: 128.2 °C, peak max: 128.6 °C (from cyclohexane); R_f 0.63 (hexane–DCM, 2 : 8); (found: C, 50.29; H, 2.67; N, 21.91. $C_8H_5N_3OS$ requires: C, 50.25; H, 2.64; N, 21.98%); λ_{max} (DCM)/nm 250 (log ε 3.97), 257 (3.46), 290 inf (3.40), 314 (3.80), 322 (3.80); ν_{max}/cm^{-1} 3067w (Ar CH), 2970w and 2945w (CH_3) 2236m (C≡N), 1585s, 1545m, 1479s, 1439s, 1425w, 1410w, 1366s, 1329m, 1296s, 1277s, 1186w, 1153s, 1120m, 1080m, 1009s, 974w, 903w, 847m, 837s, 760w; δ_H (500 MHz; $CDCl_3$) 8.26 (1H, d, *J* 9.0), 7.02 (1H, d, *J* 9.0), 4.05 (3H, s); δ_C (125 MHz; $CDCl_3$) 164.6 (s), 155.7 (s), 141.2 (s), 134.4 (d), 132.7 (s), 113.1 (d) 113.0 (s), 54.7 (q); MALDI-TOF MS (*m*/*z*): 192 (MH^+, 100%).

4.3.9. 2,6-Dichloro-3-isothiocyanatopyridine (11b) and 5-chlorothiazolo[5,4-*b*]-pyridine-2-carbonitrile (10i). Similar treatment of (*Z*)-2,6-dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-pyridin-3-amine (**9i**) (56.7 mg, 0.19 mmol) gave after chromatography (hexane) S_8, followed by (hexane–DCM, 1 : 1) *2,6-dichloro-3-isothiocyanatopyridine* (**11b**) as colorless plates (4.2 mg, 13%), mp (DSC) onset: 64.3 °C, peak max: 66.0 °C (from pentane); R_f 0.44 (hexane–DCM, 7 : 3); (found: C, 35.28; H, 1.07; N, 13.58. $C_6H_2Cl_2N_2S$ requires: C, 35.14; H, 0.98; N, 13.66%); λ_{max} (DCM)/nm 232 (log ε 2.95), 282 (2.78), 297 (2.85); ν_{max}/cm^{-1} 3084w and 3049w (Ar CH), 2224w, 2054s (N═C═S), 1537m, 1423s, 1348s, 1323m, 1238m, 1188m, 1152s, 1132s, 1088m, 968w, 939s, 876s, 810m; δ_H (500 MHz; acetone-d_6) 7.95 (1H, d, *J* 8.0), 7.59 (1H, d, *J* 8.5); δ_C (125 MHz; $CDCl_3$) 147.7 (s), 147.1 (s), 142.7 (s), 135.9 (d), 127.1 (s), 123.7 (d); *m*/*z* (EI) 208 (M^+ + 4, 14%), 206 (M^+ + 2, 37), 204 (M^+, 100), 171 (11), 169 (30), 110 (10), 98 (3), 85 (3), 76 (6), 64 (5). Further elution (hexane–DCM, 2 : 8) gave *5-chlorothiazolo[5,4-b]pyridine-2-carbonitrile* (**10i**) as colorless needles (13.3 mg, 43%), mp (DSC) onset: 153.7 °C, peak max: 154.6 °C (from cyclohexane); R_f 0.70 (hexane–DCM, 2 : 8); (found: C, 42.87; H, 1.07; N, 21.39. $C_7H_2ClN_3S$ requires: C, 42.98; H, 1.03; N, 21.48%); λ_{max} (DCM)/nm 247 inf (log ε 2.77), 253 (2.87), 281 (3.05), 305 (3.21), 314 (3.16); ν_{max}/cm^{-1} 3090w and 3051w (Ar CH), 2232w (C≡N), 1572s, 1539m, 1452s, 1422m, 1375w, 1354s, 1337m, 1288m, 1271m, 1244w, 1177m, 1152s, 1125m, 1082m, 881m, 843s, 783w, 766m; δ_H (500 MHz; $CDCl_3$) 8.42 (1H, d, *J* 9.0), 7.62 (1H, d, *J* 8.5); δ_C (125 MHz; $CDCl_3$) 156.7 (s), 152.4 (s), 144.3 (s), 137.8 (s), 134.5 (d), 124.2 (d), 112.2 (s); MALDI-TOF MS (*m*/*z*): 198 (MH^+ + 2, 27%), 196 (MH^+, 100).

4.3.10. Thiazolo[5,4-*d*]pyrimidine-2-carbonitrile (10j). Similar treatment of (*Z*)-4-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrimidin-5-amine (**9j**) (50.4 mg, 0.19 mmol) gave S_8, and the *title compound* **10j** (29.9 mg, 97%) as colorless plates, mp (DSC) onset: 160.8 °C, peak max: 161.9 °C (from cyclohexane); R_f 0.50 (DCM); (found: C, 44.26; H, 1.28; N, 34.50. $C_6H_2N_4S$ requires: C, 44.44; H, 1.24; N, 34.55%); λ_{max} (DCM)/nm 236 (log ε 2.99), 239 (3.00), 271 (3.16), 277 (3.16), 285 (3.09); ν_{max}/cm^{-1} 3036w (Ar CH), 2237w (C≡N), 1562m, 1514m, 1445m, 1431m, 1371s, 1306m, 1242w, 1211m, 1157s, 1099m, 1084m, 928m, 880w, 858w, 831w, 762m; δ_H (500 MHz; $CDCl_3$) 9.59 (1H, s), 9.33 (1H, s); δ_C (125 MHz; $CDCl_3$) 164.7 (s), 156.7 (d), 153.8 (d), 143.3 (s), 138.7 (s), 111.9 (s); MALDI-TOF MS (*m*/*z*): 163 (MH^+, 100%).

4.3.11. 7-Chlorothiazolo[5,4-*d*]pyrimidine-2-carbonitrile (10k). Similar treatment of (*Z*)-4,6-dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrimidin-5-amine (**9k**) (56.9 mg, 0.19 mmol) gave S_8, and the *title compound* **10k** (29.9 mg, 80%) as colorless plates, mp (DSC) onset: 117.4 °C, peak max: 118.1 °C (from cyclohexane); R_f 0.47 (hexane–DCM, 2 : 8); (found: C, 36.75; H, 0.56; N, 28.53. C_6HClN_4S requires: C, 36.65; H, 0.51; N, 28.50%); λ_{max} (DCM)/nm 239 inf (log ε 3.08), 242 (3.08), 278 (3.19), 285 inf (3.15); ν_{max}/cm^{-1} 2234w (C≡N), 1545s, 1499s, 1443m, 1429m, 1422s, 1364w, 1341s, 1254w, 1229m, 1206w, 1165m, 1142w, 1119s, 997w, 970w, 951w, 899w, 870m, 839s, 775m; δ_H (500 MHz; $CDCl_3$) 9.09 (1H, s); δ_C (125 MHz; $CDCl_3$) 165.1 (s), 157.2 (s), 156.0 (d), 141.4 (s), 138.7 (s), 111.6 (s); *m*/*z* (EI) 198 (M^+ + 2, 39%), 196 (M^+, 100), 161 (80), 134 (16), 117 (2), 111 (4), 82 (27), 76 (4), 70 (14).

4.3.12. 7-Chloro-5-methylthiazolo[5,4-*d*]pyrimidine-2-carbonitrile (10l). Similar treatment of (*Z*)-4,6-dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-methylpyrimidin-5-amine (**9l**) (59.6 mg, 0.19 mmol) gave S_8, and the *title compound* **10l** (35.6 mg, 89%) as colorless needles, mp (DSC) onset: 94.9 °C, peak max: 96.3 °C (from pentane); R_f 0.50 (hexane–DCM, 2 : 8); (found: C, 39.96; H, 1.48; N, 26.49. $C_7H_3ClN_4S$ requires: C, 39.91; H, 1.44; N, 26.60%); λ_{max} (DCM)/nm 244 (log ε 3.14), 286 (3.25); ν_{max}/cm^{-1} 2237w (C≡N), 1557s, 1493m, 1450m, 1420m, 1406m, 1356w, 1321w, 1296w, 1227m, 1215m, 1179m, 1126s, 1103w, 1065w, 1030w, 910m, 853m, 837m, 791w, 772w; δ_H (500 MHz; $CDCl_3$) 2.89 (3H, s); δ_C (125 MHz; $CDCl_3$) 167.7 (s), 165.5 (s), 156.4 (s), 139.3 (s), 137.2 (s), 111.7 (s), 26.0 (q); *m*/*z* (EI) 212 (M^+ + 2, 25%), 210 (M^+, 61), 175 (100), 134 (32), 117 (3), 111 (3), 82 (26), 70 (12).

4.3.13. 5-Chlorothiazolo[5,4-*d*]pyrimidine-2-carbonitrile (10m). Similar treatment of (*Z*)-2,4-dichloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrimidin-5-amine (**9m**) (56.9 mg, 0.19 mmol) gave S_8, and the *title compound* **10m** (34.7 mg, 93%) as colorless needles, mp (DSC) onset: 158.7 °C, peak

max: 159.6 °C (from cyclohexane); R_f 0.60 (hexane–DCM, 2 : 8); (found: C, 36.57; H, 0.54; N, 28.41. C_6HClN_4S requires: C, 36.55; H, 0.51; N, 28.50%); λ_{max} (DCM)/nm 229 (log ε 3.17), 242 (3.21), 272 inf (3.10), 280 (3.32), 284 (3.35), 294 (3.33); ν_{max}/cm^{-1} 2243w (C≡N), 1556s, 1512s, 1447m, 1358s, 1248w, 1227m, 1200s, 1182s, 1177s, 1138m, 1126w, 1094m, 939m, 883m, 799w, 772; δ_H (500 MHz; $CDCl_3$) 9.44 (1H, s); δ_C (125 MHz; $CDCl_3$) 166.5 (s), 159.5 (s), 155.5 (d), 142.3 (s), 138.9 (s), 111.6 (s); MALDI-TOF MS (*m*/*z*): 198 (M^+ + 2, 27%), 196 (M^+, 100).

4.3.14. Thiazolo[4,5-*b*]pyrazine-2-carbonitrile (10n). Similar treatment of (*Z*)-3-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrazin-2-amine (**9n**) (50.4 mg, 0.19 mmol) gave after chromatography (hexane) S_8, then (DCM) recovered (*Z*)-3-chloro-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyrazin-2-amine (**9n**) (5.0 mg, 10%) as orange needles, mp (DSC) onset: 247.6 °C, peak max: 249.6 °C (from cyclohexane–DCE); identical to that described above. Further elution (DCM–*t*-BuOMe, 9 : 1) gave the *title compound* **10n** (11.7 mg, 38%) as colorless needles, mp (DSC) onset: 119.8 °C, peak max: 120.4 °C (from cyclohexane); R_f 0.73 (DCM–*t*-BuOMe, 9 : 1); (found: C, 44.35; H, 1.25; N, 34.47. $C_6H_2N_4S$ requires: C, 44.44; H, 1.24; N, 34.55%); λ_{max} (DCM)/nm 258 inf (log ε 2.90), 268 (2.99), 278 (2.99), 306 (3.30), 312 (3.31); ν_{max}/cm^{-1} 3073w and 3040w (Ar CH), 2234 (C≡N), 1524m, 1464m, 1443m, 1352m, 1333m, 1310m, 1248w, 1229m, 1207s, 1150s, 1123w, 1094m, 1036m, 903m, 874m, 845m, 785w, 764w; δ_H (500 MHz; $CDCl_3$) 8.96 (1H, d, *J* 2.0), 8.80 (1H, d, *J* 2.5); δ_C (125 MHz; $CDCl_3$) 155.8 (s), 151.5 (s), 145.1 (d), 144.6 (d), 141.7 (s), 112.0 (s); MALDI-TOF MS (*m*/*z*): 163 (MH^+, 100%).

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References

1 (*a*) R. Appel, H. Janssen, M. Siray and F. Knoch, *Chem. Ber.*, 1985, **118**, 1632–1643; (*b*) P. A. Koutentis, *Molecules*, 2005, **10**, 346–359.
2 (*a*) O. A. Rakitin, (ed. in chief A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor), in *Comprehensive Heterocyclic Chemistry III*, ed. V. V. Zhdankin, Elsevier, Oxford, 2008, ch. 6.01, vol. 6, pp. 1–36; (*b*) L. S. Konstantinova and O. A. Rakitin, *Russ. Chem. Rev.*, 2008, **77**, 521–546; (*c*) K. Kim, *Sulfur Rep.*, 1998, **21**, 147–207; (*d*) K. Kim, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1997, **120**, 229–244.
3 (*a*) J. E. Moore, *US Pat.*, 4,059,590, 1977; (*b*) R. Appel, H. Janssen, I. Haller and M. Plempel, *DE Pat.*, 2,848,221, 1980; (*c*) T. Besson, C. W. Rees, G. Cottenceau and A. M. Pons, *Bioorg. Med. Chem. Lett.*, 1996, **6**, 2343–2348.
4 (*a*) G. Cottenceau, T. Besson, V. Gautier, C. W. Rees and A. M. Pons, *Bioorg. Med. Chem. Lett.*, 1996, **6**, 529–532; (*b*) V. Thiery, C. W. Rees, T. Besson, G. Cottenceau and A. M. Pons, *Eur. J. Med. Chem.*, 1998, **33**, 149–153; (*c*) R. W. Joseph, D. L. Antes and P. Osei-Gyimah, *US Pat.*, 5,688,744, 1997.
5 F. Oppedisano, M. Catto, P. A. Koutentis, O. Nicolotti, L. Pochini, M. Koyioni, A. Introcaso, S. S. Michaelidou, A. Carotti and C. Indiveri, *Toxicol. Appl. Pharmacol.*, 2012, **265**, 93–102.
6 (*a*) T. M. Barclay, L. Beer, A. W. Cordes, R. T. Oakley, K. E. Preuss, N. J. Taylor and R. W. Reed, *Chem. Commun.*, 1999, 531–532; (*b*) L. Beer, A. W. Cordes, R. C. Haddon, M. E. Itkis, R. T. Oakley, R. W. Reed and C. M. Robertson, *Chem. Commun.*, 2002, 1872–1873.
7 (*a*) V. N. Yarovenko, A. A. Es'kov, P. A. Kondrashev, A. V. Ignatenko, I. V. Zavarzin, L. G. Vorontsova, I. P. Sedishev, M. M. Krayushkin and Z. A. Starikova, *Heterocycles*, 2005, **65**, 1601–1608; (*b*) I. C. Christoforou, A. S. Kalogirou and P. A. Koutentis, *Tetrahedron*, 2009, **65**, 9967–9972.
8 (*a*) K. Emayan, R. F. English, P. A. Koutentis and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3345–3349; (*b*) D. Clarke, K. Emayan and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1998, 77–82; (*c*) P. A. Koutentis and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1998, 2505–2509; (*d*) I. C. Christoforou, P. A. Koutentis and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1236–1241; (*e*) Y.-G. Chang, K. Kim and Y. J. Park, *J. Heterocycl. Chem.*, 2002, **39**, 29–36.
9 (*a*) T. Iwakawa and A. Murabayashi, *Heterocycles*, 1999, **51**, 811–819; (*b*) L. S. Konstantinova, O. A. Rakitin, C. W. Rees, T. Torroba, A. J. P. White and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2243–2248.
10 (*a*) V.-D. Le, C. W. Rees and S. Sivadasan, *Tetrahedron Lett.*, 2000, **41**, 9407–9411; (*b*) C. W. Rees, S. Sivadasan, A. J. P. White and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1535–1542.
11 P. A. Koutentis, C. W. Rees, A. J. P. White and D. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1998, 2765–2769.
12 S. S. Michaelidou and P. A. Koutentis, *Tetrahedron*, 2009, **65**, 8428–8433.
13 (*a*) C. W. Rees, *J. Heterocycl. Chem.*, 1992, **29**, 639–651; (*b*) T. Besson, M. J. Dozias, J. Guillard and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1998, 3925–3926.
14 O. A. Rakitin, C. W. Rees and O. G. Vlasova, *Tetrahedron Lett.*, 1996, **37**, 4589–4592.

15 T. Besson, G. Guillaumet, C. Lamazzi and C. W. Rees, *Synlett*, 1997, 704–706.
16 (*a*) T. Besson and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1996, 2857–2860; (*b*) T. Besson, M.-J. Dozias, J. Guillard, P. Jacquault, M.-D. Legoy and C. W. Rees, *Tetrahedron*, 1998, **54**, 6475–6484; (*c*) Y.-G. Chang and K. Kim, *Heterocycles*, 1999, **51**, 2653–2666; (*d*) T. Besson, J. Guillard and C. W. Rees, *Tetrahedron Lett.*, 2000, **41**, 1027–1030; (*e*) W. R. Bowman, M. O. Cloonan, A. J. Fletcher and T. Stein, *Org. Biomol. Chem.*, 2005, **3**, 1460–1467.
17 (*a*) R. F. English, O. A. Rakitin, C. W. Rees and O. G. Vlasova, *J. Chem. Soc., Perkin Trans. 1*, 1997, 201–205; (*b*) H. S. Lee, Y. G. Chang and K. Kim, *J. Heterocycl. Chem.*, 1998, **35**, 659–668; (*c*) S. S. Michaelidou and P. A. Koutentis, *Synthesis*, 2009, 4167–4174.
18 (*a*) P. G. Baraldi, M. G. Pavani, M. C. Nuñez, P. Brigidi, B. Vitali, R. Gambari and R. Romagnoli, *Bioorg. Med. Chem.*, 2002, **10**, 449–456; (*b*) A. M. Cuadro and J. Alvarez-Builla, *Tetrahedron*, 1994, **50**, 10037–10046.
19 P. A. Koutentis, M. Koyioni and S. S. Michaelidou, *Molecules*, 2011, **16**, 8992–9002.
20 T. Besson and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1995, 1659–1662.
21 (*a*) V. Facchinetti, R. da R. Reis, C. R. B. Gomes and T. R. A. Vasconcelos, *Mini-Rev. Org. Chem.*, 2012, **9**, 44–53; (*b*) P. S. Yadav and S. G. P. Devprakash, *Int. J. Pharm. Sci. Drug Res.*, 2011, **3**, 1–7; (*c*) B. Chen and W. Heal, (ed. in chief A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor), in *Comprehensive Heterocyclic Chemistry III*, ed. J. A. Joule, Elsevier, Oxford, 2008, ch. 4.06, vol. 4, pp. 692–695.
22 (*a*) S. Komoriya, S. Kobayashi, K. Osanai, T. Yoshino, T. Nagata, N. Haginoya, Y. Nakamoto, A. Mochizuki, T. Nagahara, M. Suzuki, T. Shimada, K. Watanabe, Y. Isobe and T. Furugoori, *Bioorg. Med. Chem.*, 2006, **14**, 1309–1330; (*b*) N. Haginoya, S. Kobayashi, S. Komoriya, T. Yoshino, T. Nagata, Y. Hirokawa and T. Nagahara, *Bioorg. Med. Chem.*, 2004, **12**, 5579–5586.
23 A. Phadke, D. Chen, M. Deshpande, A. Thurkauf, X. Wang, Y. Shen, C. Liu, J. Quinn, J. Ohkanda and S. Li, *US Pat.*, 2006/25416, 2006.
24 Y. Sugihara and Y. Kawakita, *Eur. Pat.*, 1,731,523, 2006.
25 G. M. Castanedo, J. L. Gunzner, K. Malesky, A. G. Olivero, S. Wang, I. Chuckowree, S. Oxenford, N. C. Wan, A. Folkes, B.-Y. Zhu, D. P. Sutherlin and S. Mathieu, *WO Pat.*, 2009/42607, 2009.
26 (*a*) A. Gupta and S. Rawat, *J. Curr. Pharm. Res.*, 2010, **3**, 13–23; (*b*) H. Ulrich, in *Benzothiazoles (Update 2010) in Science of Synthesis Knowledge Updates 2010/1, Product Class 18*, ed. E. Schaumann, Georg Thieme, Stuttgart, 2010, ch. 11.18, pp. 393–404; (*c*) H. Ulrich, in *Benzothiazoles and Related Compounds in Science of Synthesis, Product Class 18*, ed. E. Schaumann, Georg Thieme, Stuttgart, 2002, ch. 11.18, vol. 11, pp. 835–912.
27 (*a*) B. R. Buckley, (ed. in chief A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor), in *Comprehensive Heterocyclic Chemistry III*, ed. R. C. F. Jones, Elsevier, Oxford, 2008, ch. 10.08, vol. 10, pp. 431–491; (*b*) M. H. Elnagdi, N. Al-Awadi and I. A. Abdelhamid, (ed. in Chief A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor), in *Comprehensive Heterocyclic Chemistry III*, ed. R. C. F. Jones, Elsevier, Oxford, 2008, ch. 10.12, vol. 10, pp. 599–660; (*c*) F. Aldabbagh, (ed. in chief A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor), in *Comprehensive Heterocyclic Chemistry III*, ed. R. C. F. Jones, Elsevier, Oxford, 2008, ch. 10.13, vol. 10, pp. 661–702.
28 (*a*) H. C. Van der Plas, *Adv. Heterocycl. Chem.*, 1999, **74**, 9–86; (*b*) H. C. Van der Plas, *Adv. Heterocycl. Chem.*, 1999, **74**, 87–151.
29 I. C. Christoforou, P. A. Koutentis and S. S. Michaelidou, *ARKIVOC*, 2006, **7**, 207–223.
30 L. M. Harwood, *Aldrichimica Acta*, 1985, **18**, 25–25.
31 J. Bourdais, D. Abenhaim, B. Sabourald and A. Lorre, *J. Heterocycl. Chem.*, 1976, **13**, 491–496.