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Ring transformations of 2-hydroxy-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes

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Dedicated to the memory of Professor Alan R. Katritzky who sadly passed away on the 10th Feb. 2014

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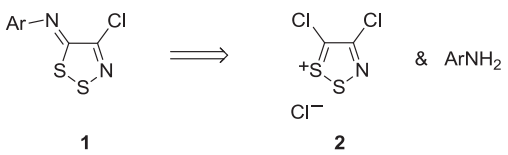
The cyclisation reactions of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene-amino)phenol (**5a**), 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**) and 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) are investigated. Thermolysis in hot PhCl (132 °C) or under solvent free conditions at ca. 200 °C gave benzo[*d*]oxazole-2-carbonitrile (**4a**), oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) and oxazolo[4,5-*b*]pyridine-2-carbonitrile (**4c**) in high yields, while treatment with either NaH in dry THF at 66 °C or with *i*-Pr_2NEt in DCM at 20 °C gave benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**), [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**) and oxazolo[4,5-*b*]pyridine (**4c**), respectively. The transformation of benzoxazine **6a** and the pyridoxazine **6b** into the corresponding oxazoles **4a** and **4b** was also investigated, and tentative mechanistic pathways for these transformations are proposed.

1. Introduction

(4-Chloro-1,2,3-dithiazol-5*H*-ylideneamino)(het)arenes **1**, can be readily prepared in good to excellent yields[1–3] from the reaction of a primary (het)arylamine with 4,5-dichloro-1,2,3-dithiazolium chloride **2** (Appel salt)[1] followed by treatment with a tertiary amine base (2 equiv) (Scheme 1). They can also be formed from the reaction of *N*-aryl-*S*,*S*-dimethylsulfimides,[4] *N*-aryl-1,1,1-trimethyl-*N*-(trimethylsilyl) silanamines,[1] or tetrazoles[5] with Appel salt **2**.



1 2

Scheme 1. Synthesis of (dithiazolylideneamino)arenes **1** from Appel salt **2**.

Early reports on the biological activity of [(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]arenes showed that some 1,2,3-dithiazoles have antifungal[6] and herbicidal[7] activities, while more recently, interesting antitumour,[8] antibacterial[9] activities and inactivation of the glutamine/amino acid transporter ASCT2[10] have been demonstrated. Furthermore, benzo and heteroazine fused 1,2,3-dithiazoles are of interest to the material sciences.[11]

In addition, (4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes are useful precursors to other heterocycles through *A*ddition of the *N*ucleophile, *R*ing *O*pening, and *R*ing *C*losure (ANRORC)[12] style ring transformations.[13] For example, thiazoles,[14] 1,3,4-thiadiazoles[14] and heteroazine fused thiazoles[15] have been prepared via ANRORC type transformations,[16] while the thermolysis of (1,2,3-dithiazolylideneamino)arenes can afford (het)areno fused thiazoles,[15–17] 1,2,4,-dithiazines,[18] imidazoles[19] oxazoles[17c,20] and oxazines.[21] Moreover, 1,2,3-dithiazolylideneamines have also been used to prepare acyclic functionalities such as isothiocyanates[22] and thiocyanoformamides.[2,23]

Several examples of (4-chloro-5*H*-1,2,3-dithiazol-5-ylidene amino)arene ring transformations involve a nucleophilic *ortho* substituent on the arene. Where the *ortho* substituent is a primary, secondary[19,24] or even a tertiary amine,[25] thermolysis affords the analogous imidazole-2-carbonitriles **3**, and when the *ortho* substituent is a hydroxyl group the analogous benzo[*d*]oxazole-2-carbonitrile (**4a**) forms (Scheme 2).[17a,20] Surprisingly, in the latter case, treatment of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino) phenol (**5a**) with NaH in dry THF gave benzo[*b*][1,2,3]dithiazolo [5,4-*e*][1,4]oxazine (**6a**) (Scheme 2).[17a]

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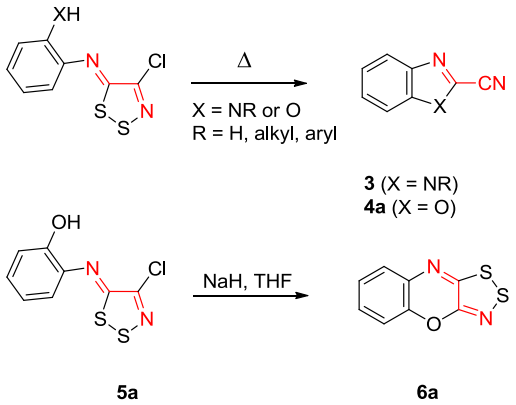


Scheme 2. Ring transformations of (dithiazolylideneamino)arenes bearing a nucleophilic *ortho* substituent on the arene.

The latter cyclisation is analogous to the base (NaH or *i*-Pr_2NEt in THF or K_2CO_3 in MeCN) catalysed cyclisation of 2-(4-chloro-3*H*-1,2-dithiol-3-ylideneamino)phenols **7**, prepared from 3,4,5-trichloro-1,2-dithiolium chloride (**8**) (Boberg salt)[26] and 2-aminophenols, to give 1,2-dithiolo[4,3-*b*][1,4]benzoxazines **9**, in moderate yields (39–45%) (Scheme 3).[27]

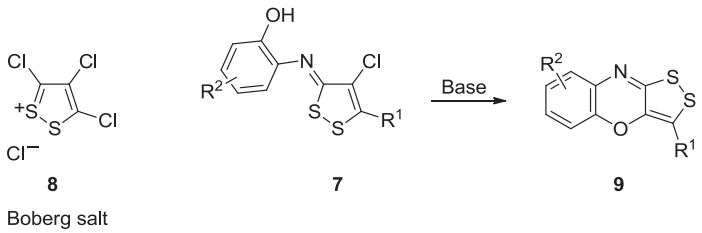
via an ANRORC style mechanism where the amine attacks the ring sulfur to generate a disulfide intermediate that then recyclises. Kim et al. has reported several examples of ANRORC style indirect displacement of the Cl by amines.[28,29]

In light of our access to 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene amino)phenol (**5a**), 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneam ino)pyridin-2-ol (**5b**) and 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) and our on-going interest in the chemistry of Appel salt **2** we probed this chemistry further. Our aims were to identify additional examples and to improve the reaction conditions leading to the fused oxazines, to determine the influence of additional ring nitrogens, and to propose mechanistic pathways for the products formed.

2. Results and discussion

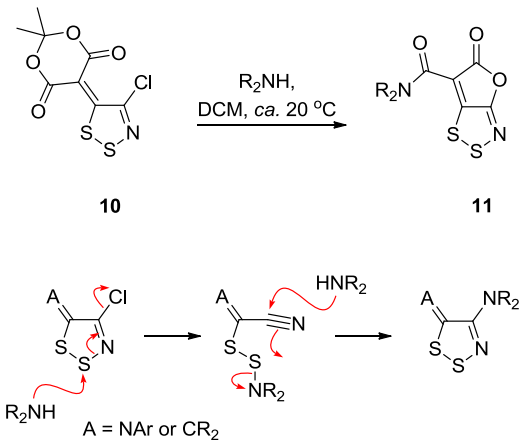
2.1. Synthesis of fused oxazoles and oxazines

2.1.1. Synthesis of dithiazolimine starting materials. 2-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**), 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**) and 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) were prepared from Appel salt **2** and the corresponding *ortho* hydroxy amino arenes **12** (Scheme 5).



Scheme 3. Cyclisation of 2-(4-chloro-3*H*-1,2-dithiol-3-ylideneamino)phenols **7**.

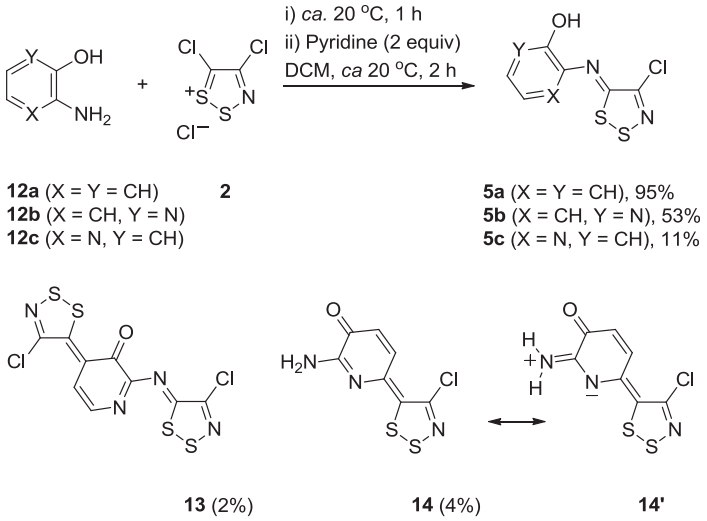
Direct displacement of the dithiazoles C4 chlorine atom has proved to be difficult,[17a] and the intramolecular cyclisation of the (dithiazolylideneamino)phenol **5a** to afford the benzoxazine **6a** is a very rare example of a cyclisation onto the dithiazole C4 position that maintains the integrity of the dithiazole ring. The only other known example is the reaction of 5-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**10**) with secondary alkylamines to yield 6-carbamoyl-5-oxo-5*H*-furo[2,3-*d*][1,2,3]dithiazoles (**11**) (Scheme 4).[28] However, this cyclisation proceeds



Scheme 4. Example of intramolecular cyclisation onto the dithiazole C4 position that maintains the integrity of the dithiazole ring, and the proposed mechanism for the ANRORC mediated indirect displacement of the C4 chlorine by amine.

Interestingly, the pyridin-3-ol **5c** was obtained only in 11% yield, and was accompanied by several deeply coloured side products. Two of these were isolable and tentatively assigned as (*Z*)-4-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-2-[(*Z*)-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]pyridin-3(4*H*)-one (**13**) (2%) and (*Z*)-2-amino-6-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)pyridin-3(6*H*)-one (**14**) (4%), respectively, and were a reminder that electron rich arenes can react directly via the ring carbon in an enolic[30] or enaminic[17e,18] manner.

Compound **13** was obtained as blue dust, mp 288–289 °C (from DCE). Elemental analysis and LR (EI) mass spectrometry supported the molecular formula $C_9H_2Cl_2N_4OS_4$; a clear two chlorine isotope pattern was observed for the parent ion [*m*/*z* 384 (M^++4, 2%), 382 (M^++2, 4), 380 (M^+, 8)]. UV/vis spectroscopy showed a λ_{max} of 614 nm (log ε 3.52) that suggested the compound had extended conjugation. ^{1}H NMR spectroscopy showed two doublets at 9.23 and 8.08 ppm with *J* values of 6.0 and 5.5 Hz, respectively. The small *J* values observed in the ^{1}H NMR data supported a 5,6-unsubstituted pyridine since $^1J_{H4H5}$ couplings are typically larger than $^1J_{H5H6}$ couplings (7–9 vs 4–6 Hz).[31] ^{13}C NMR spectroscopy, revealed the presence of nine carbon resonances of which seven were quaternaries and two secondaries. Based on these data a bis-dithiazole structure was proposed for compound **13**, however, a number of geometric isomers are possible. Of these, the *Z,Z* isomer has two favourable non-bonding interactions: the first interaction between the S1 sulfur atom of the dithiazolylidene and the oxygen atom of the carbonyl group, and the second between the S1 sulfur atom of the other dithiazolimine and the pyridone nitrogen atom. The non-bonding interaction between the S1 sulfur



Scheme 5. Reaction of Appel salt **2** with *ortho* hydroxy amino arenes **12**.

of the dithiazole ring and the oxygen atom of the carbonyl group is supported by the absence of a carbonyl stretch in the FTIR data.[32] Tentatively, based on these data the more stable isomer was proposed to be the structure shown (Scheme 5).

Compound **14** was obtained as lusterous bronze coloured prisms, mp >300 °C (from DCE). Elemental analysis and LR (EI) mass spectrometry supported the molecular formula $C_7H_4ClN_3OS_2$; a clear one chlorine isotope pattern was observed for the parent ion [*m*/*z* (EI) 247 (M^++2, 28%), 245 (M^+, 64)]. UV/vis spectroscopy showed a λ_{max} at 612 nm (log ε 3.35) suggesting the compound had extended conjugation. ^{1}H NMR spectroscopy identified one D_2O exchangeable broad doublet integrating for two Hs at 7.27 ppm, indicating the presence of a primary amine with hindered rotation on the NMR timescale, presumably owing to a significant contribution of the resonance form **14′**. The amine group was additionally supported by IR bands at ν(N–H) 3300 and 3486 cm^{-1}. ^{1}H NMR spectroscopy also identified two doublets, which belonged to aromatic hydrogens [8.50 (*J* 9.5 Hz) and 6.34 (*J* 9.0 Hz) ppm], both integrating for 1H. The large *J* couplings suggested a 2,3,6-trisubstituted pyridine.[31] Tentatively, based on these data, structure **14** was proposed, however, identifying a specific geometrical isomer proved elusive.

2.1.2. Thermolysis and base mediated ring transformations. The relative thermal stability of the 2-hydroxy(dithiazolylideneamino) arenes **5a**–**c** was indicated during their isolation and purification: both the (dithiazolylideneamino)phenol and pyridin-3-ol **5a** and **5c**, respectively, can be recrystallised as yellow cotton fibres from warm *c*-hexane, however, the (dithiazolylideneamino)pyridin-2-ol **5b** was unstable and partly cyclised into oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) affording also traces of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**). Purification of the (dithiazolylideneamino)pyridin-2-ol **5b** was, therefore, carried out via precipitation in *n*-pentane from THF.

The instability of dithiazole **5b** in hot *c*-hexane prompted an examination of the thermal behaviour of all three dithiazoles by differential scanning calorimetry (DSC) and also in a range of aromatic solvents: PhH (bp 80 °C), PhMe (bp 110 °C) and PhCl (bp 132 °C). DSC of all three dithiazoles **5a**–**c** indicated that on melting all three dithiazoles **5a**–**c** were thermally unstable (Table 1).

In hot PhCl all three dithiazoles **5a**–**c** were converted into their respective fused 2-cyano oxazoles: benzo[*d*]oxazole-2-carbonitrile (**4a**), oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) and oxazolo[4,5-*b*]pyridine-2-carbonitrile (**4c**) and elemental sulfur. The relative order of reactivity was **5b**>**5a**>**5c** (Table 2, entries 1–3). Solutions of dithiazoles **5a** and **5c** in hot PhH were stable even after 24 h, however, in hot PhMe, only the dithiazole **5c** was completely stable. In contrast, the dithiazole **5b** after 24 h in hot PhMe showed consumption of the starting material and only traces of both oxazole **4b** and oxazine **6b** (by TLC), while the dithiazole **5a** in hot PhMe was converted slowly (48 h) into the oxazole **4a** (80%) and elemental sulfur.

Table 1
Differential scanning calorimetery (DSC) data for the 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes **5a**–**c**[a]

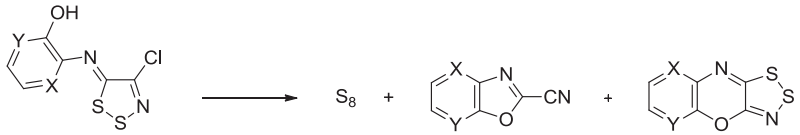
Entry	5	Mp (°C)		Decomp. (°C)		Decomp. (°C)	
		Onset	Peak	Onset	Peak	Onset	Peak
1	**5a**	107.9	109.0	110.1[b]	112.0[b]	—	—
2	**5b**	100.1	106.4	107.2[b]	109.3[b]	142.5[b]	145.0[b]
3	**5c**	138.4	138.9	139.7[c]	139.8[c]	148.7[b]	154.2[b]

[a] Samples were run (1–2 mg) in hermetic aluminium pans under argon atmosphere with a 5 °C/min heating rate.
[b] Exotherm.
[c] Endotherm.

Under solvent free conditions the thermolysis of all three 2-hydroxy-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes **5a**–**c** under an argon atmosphere at ca. 200 °C for 1–5 min, gave the corresponding fused oxazoles **4a**–**c** in 60–85% yield, together with some S_8 (60–90%) (Table 2, entries 4–6). Thermolysis of the (dithiazolylideneamino)pyridin-2-ol **5b** also gave a small quantity of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**) (1%) (Table 2, entry 5). The reaction of the dithiazoles **5a**–**c** with NaH (1.1–2 equiv) in dry THF for 2 h heated at ca. 66 °C was less predictable (Table 2, entries 7–9): dithiazoles **5a** and **5b** gave the expected oxazine products **6a** and **6b** in 65 and 42% yields, respectively, while the dithiazole **5c** gave only the oxazolo[4,5-*b*]pyridine **4c** in a relatively high yield (88%, Table 2, entry 9). The very different behaviour of the dithiazole **5c** towards NaH was also seen when the base was replaced by tertiary amine bases: treating the dithiazoles **5a** and **5b** with *i*-Pr_2NEt (1.1 equiv) in DCM at ca. 20 °C for 0.5 and 7 days, respectively (Table 2, entries 10 and 11) afforded the tricyclic oxazines **6a** and **6b** in 93 and 63% yields, respectively, while the analogous treatment of the dithiazole **5c** gave the oxazolo[4,5-*b*]pyridine **4c** in 73% yield (Table 2, entry 12).

Interestingly, while the dithiazoles **5a**–**c** reacted relatively quickly with trialkylamines such as Et_3N, *i*-Pr_2NEt or DBU, they

Table 2
Thermolysis and base reactions of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes **5a**–**c** (0.20 mmol)



5a-c **4a-c** **6a-c**

Entry	X	Y	Conditions	Yields (%)		
				S_8	**4**	**6**
1	CH	CH	PhCl, 132 °C, 15 h, argon	98	**4a** (83)	—
2	CH	N	PhCl, 132 °C, 1 h, argon	100	**4b** (96)	—
3	N	CH	PhCl, 132 °C, 3 d, argon	95	**4c** (72)	—
4	CH	CH	200 °C, 1 min, argon	60	**4a** (85)	—
5	CH	N	200 °C, 2 min, argon	90	**4b** (66)	**6b** (1)
6	N	CH	200 °C, 5 min, argon	90	**4c** (84)	—
7	CH	CH	NaH (2 equiv), THF, 66 °C, 2 h	55	**4a** (Trace)	**6a** (65)
8	CH	N	NaH (1.1 equiv), THF, 66 °C, 2 h	Traces	**4b** (Trace)	**6b** (42)
9	N	CH	NaH (2 equiv), THF, 66 °C, 2 h	88	**4c** (88)	—
10	CH	CH	*i*-Pr_2NEt (1.1 equiv), DCM, 20 °C, 12 h	Traces	**4a** (1)	**6a** (93)
11	CH	N	*i*-Pr_2NEt (1.1 equiv), DCM, 20 °C, 7 d	Traces	**4b** (Trace)	**6b** (63)
12	N	CH	*i*-Pr_2NEt (1.1 equiv), DCM, 20 °C, 4 d	85	**4c** (73)	—

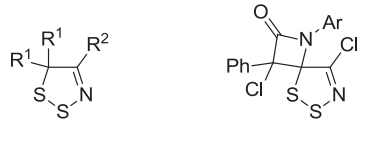
were much less reactive to the weaker aromatic bases pyridine and 2,6-lutidine. In these cases, the use of only 1.1 equiv of base led to recovered unreacted dithiazoles, although the reaction could be brought to completion by using a large excess of base (4 equiv).

These results demonstrated that during the thermolysis, not only oxazoles but also traces of the fused oxazines formed and that the presence and position of an additional pyridyl nitrogen affected the outcome of both the thermal ring contraction and the base mediated intramolecular cyclisations. More specifically, the thermolysis of the pyridin-3-ol **5c** took longer than the 'parent' phenol **5a** while that of the pyridin-2-ol **5b** was considerably faster. Furthermore, while base treatment of both the 'parent' phenol **5a** and the pyridin-2-ol **5b** gave the corresponding fused oxazines **6a** and **6b**, respectively, treatment of the pyridine-3-ol **5c** gave only the oxazole **4c**.

2.2. Mechanistic rationale

A rational mechanism for the formation of both the oxazoles **4** and the oxazines **6** must take into account that the dithiazole C5 position is more electrophilic than the C4 position. Rees[17a] postulated that on base catalysed deprotonation the *ortho* hydroxyl group cyclises onto the electrophilic C5 position to give a spirocyclic intermediate **15** that can fragment via path A to form the oxazine or via path B to form the oxazole (Scheme 6).

Similar 5,5-disubstituted 1,2,3-dithiazoles to the proposed spirocyclic intermediate **15** are known, such as the 5,5-difluoro-1,2,3-dithiazole **16a**,[1] the dithiazole ketals **16b**[33] and the spirocyclic lactams **17**.[32b]



16a (R^1 = F, R^2 = Cl)
16b (R^1 = OEt, R^2 = Ar)

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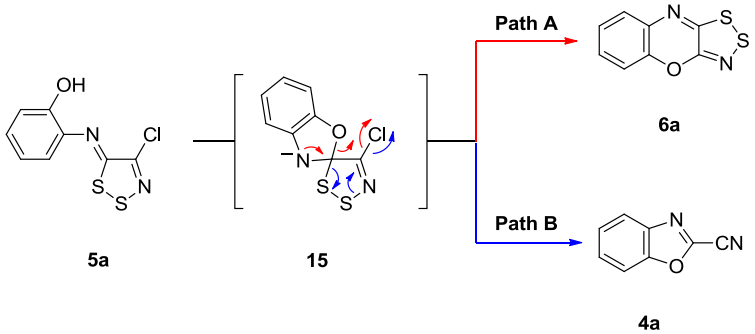
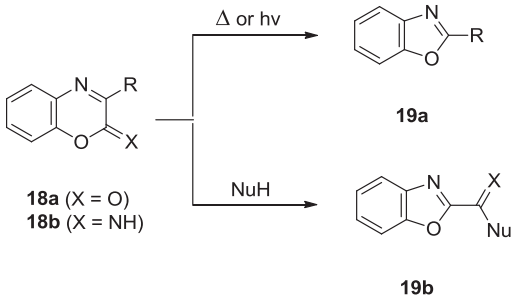
Rees also claimed that the oxazine **6a** was not a precursor to the benzoxazole **4a** since a pure sample was thermally stable at 200 °C.[17a] Nevertheless, ring contractions of 2*H*-benzo[*b*][1,4]oxazin-2-ones **18a** (X=O)[34] and 2*H*-benzo[*b*][1,4]oxazin-2-imines **18b** (X=NH)[35] into benzoxazoles **19a** and **19b** are known, and typically initiated by either thermolysis,[34i,j] photolysis[34a,g] or by nucleophiles such as hydroxide,[34b–d,35] alcohols,[34f] alkylamines[34e,f,k] and hydrazines[34h,k] (Scheme 7).



Scheme 6. Proposed mechanism for the formation of both the oxazoles and the oxazines from dithiazolimine **5a**.



Scheme 7. Ring contractions of benzoxazinones **18a** and benzoxazin-2-imines **18b** to benzoxazoles **19a** and **19b**.

The thermolysis of the dithiazoles **5** to give the oxazoles **4** leads to the formation of thiophilic by-products such as HCl and 'active' sulfur, which could affect the stability of any oxazine **6** that may form. As such, we reinvestigated the thermal stability of the oxazines **6a** and **6b**.

Heating benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**) or [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**) in either isoquinoline at 150 °C or in PhCl at ca. 132 °C for 24 h, led to no decomposition indicating that under these conditions both compounds were thermally stable. DSC studies, however, showed that the benzoxazine **6a** had an exothermic decomposition peak at 276.1 °C (onset peak at 274.6 °C), while the pyridoxazine **6b** had endothermic decomposition peaks at 224.0 °C (onset: 222.4 °C) and 265.2 °C (onset: 263.8 °C), significantly past their melting points. In light of this data, neat samples of the oxazines **6a** and **6b** were thermolysed at ca. 275 and 230 °C, respectively, to afford the benzoxazole **4a** and the oxazolopyridine **4b** in 27 and 65% yields, respectively. These reaction conditions were more aggressive than those required to directly convert the 2-hydroxy(dithiazolylideneamino)arenes **5a** and **5b** into the corresponding oxazoles. Nevertheless, since trace amounts of acid, base or other nucleophiles are often formed as by-products in these thermolyses, we reinvestigated the oxazine to oxazole ring contractions in the presence of basic (pyridine, Et_3N), thiophilic ($BnEt_3NCl$) and acidic (phenol, $TsOH\cdot H_2O$) additives to examine if the reaction temperatures could be lowered (Table 3).

Table 3
Ring contractions of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6a**) and [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**)

6a (X = CH)
6b (X = N)

4a (X = CH)
4b (X = N)

Entry	Solvent	Additive (equiv)	Temp (°C)	Time (h)	X	S_8 (%)	**4** (%)
1	Neat	—	275	7 min	CH	55	**4a** (27)
2	Neat	—	230	10 min	N	97	**4b** (65)
3	PhCl	Et_3N (1)	132	24	CH	85	**4a** (45)
4	PhCl	Et_3N (1)	132	24	N	80	**4b** (40)
5	PhCl	$BnEt_3NCl$ (1)	132	12	CH	71	**4a** (35)
6	PhCl	$BnEt_3NCl$ (1)	132	5	N	38	**4b** (42)
7	PhCl	$TsOH\cdot H_2O$ (1)	132	24	CH	nr[a]	nr[a]
8	PhCl	$TsOH\cdot H_2O$ (1)	132	2	N	83	**4b** (49)
9	PhMe	$TsOH\cdot H_2O$ (1)	110	3	N	41	**4b** (47)
10	PhCl	$TsOH\cdot H_2O$ (0.05)	132	20	N	86	**4b** (50)

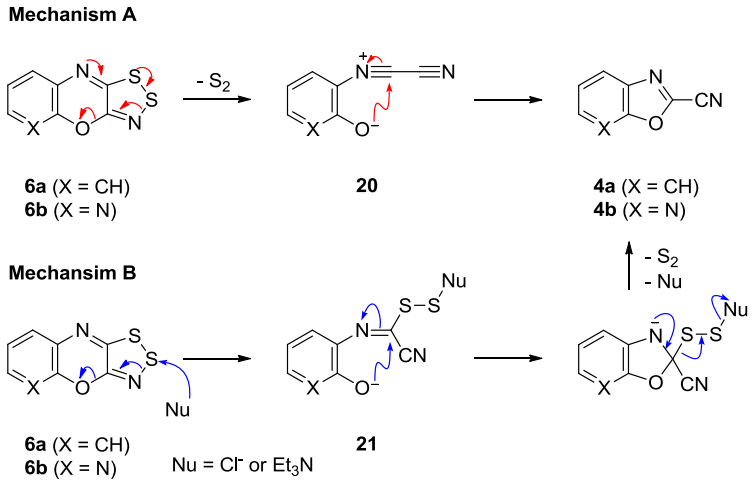
[a] nr=No reaction.

When solutions of the benzoxazine **6a** or the pyridoxazine **6b** in PhCl were heated at reflux (ca. 132 °C) in the presence of pyridine (1 equiv) both oxazines were stable but in the presence of Et_3N (1 equiv) they were converted into the benzoxazole **4a** (45%) and oxazolopyridine **4b** (40%), respectively, together with some elemental sulfur (Table 3, entries 3 and 4). Similar products and yields were also obtained when the trialkylamine was replaced by non-basic but thiophilic $BnEt_3NCl$ (1 equiv), and interestingly, in these cases (Table 3, entries 5 and 6), the reactions were notably faster (5–12 h vs 24 h) than those involving Et_3N. Moreover, in the presence of phenol or 3-hydroxypyridine (1 equiv), which are weak acids no reactions took place, however, when $TsOH\cdot H_2O$ (1 equiv) was added in either PhCl at ca. 132 °C or in PhMe at ca. 110 °C the pyridoxazine **6b** was converted to the oxazolopyridine **4b** (Table 3, entries 8 and 9) while the benzoxazine **6a** was stable (Table 3, entry 7). Interestingly, only catalytic amounts of $TsOH\cdot H_2O$ (5 mol %) were needed to trigger the ring contraction of the pyridoxazine **6b** (Table 3, entry 10).

We also considered the stability of the oxazines **6a** and **6b** under the conditions of the ring contraction of dithiazoles **5a** and **5b** in hot PhCl. As such, equimolar quantities of dithiazoles **5a** and **5b** were mixed with oxazines **6a** and **6b**, respectively, and heated in PhCl at 132 °C until complete consumption of the imine (TLC, 3 and 5 h, respectively). At this temperature, the pure oxazines **6a** and **6b** were shown previously to be stable, however, the reaction of dithiazole **5a** gave elemental sulfur, the benzoxazole **4a** (120% based on consumed **5a**) and recovered oxazine **6a** (42%), while the reaction of dithiazole **5b** gave elemental sulfur, the oxazole **4b** (62% based on consumed **5b**) and recovered oxazine **6b** (76%). The data indicated that the oxazines **6a** and **6b**, were thermally unstable under the reaction conditions, and in the case of the dithiazole **5a** a total benzoxazole yield of 120% supported that the oxazine **6a** had contributed to formation of the benzoxazole **4a**. As such, we can conclude that while pure samples of oxazines **6** are indeed thermally stable as reported by Rees, in the presence of either acid or chloride and possibly other halophiles, they are labile and can therefore also be sources of the oxazoles isolated during the direct thermolysis of the dithiazoles **5a**–**c**.

Formally the transformation of the oxazine **6** to the oxazole **4** required the loss of diatomic sulfur (S_2) and tentatively this can occur via a stepwise mechanism that involves ring opening-ring closing steps (mechanism A) (Scheme 8). The oxazine nitrogen lone pair could release electron density into the dithiazole ring leading to fragmentation via loss of S_2 and formation of a highly electrophilic nitrilium carbonitrile intermediate **20**. This could subsequently trap the phenoxide (where X=CH) or the pyridoxide (where X=N) to give the observed oxazoles **4a** and **4b**, respectively. The addition of acid could assist the ring transformation by protonating the pyridyl nitrogen and thus facilitating cleavage of the C–O bond. When Et_3N or $BnEt_3NCl$ was added an alternative mechanism (mechanism B) can be invoked that involves thiophilic attack on the dithiazole ring sulfur to give intermediate **21**, which subsequently eliminates sulfur and cyclises to the observed oxazoles. Similar thiophilic reactions between amines[29] or tetraalkylammonium halides[36] and neutral dithiazoles leading to ANRORC-style[37] ring transformations have been reported.

A tentative explanation for the failure to isolate the isomeric pyridoxazine **6c** in the reactions of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) can be that this compound, which has two amidine like nitrogen atoms, must be more basic and prone to protonation, and as such, if the oxazine had formed it may have rearranged rapidly in the presence of traces of H^+ to the



Scheme 8. Possible mechanisms: the transformation of oxazine to oxazole.

oxazolo[4,5-*b*]pyridine (**4c**). This and other aspects of this chemistry are now under further study.

3. Conclusions

Thermolysis of the dithiazolylidenes **5a**, **5b** and **5c** in hot PhCl (132 °C) or under solvent free conditions at ca. 200 °C afforded benzo[*d*]oxazole-2-carbonitrile (**4a**), oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) and oxazolo[4,5-*b*]pyridine-2-carbonitrile (**4c**) in high yields, respectively. Treatment of the dithiazolylidenes **5a**, **5b** and **5c** with either NaH in dry THF at 66 °C or with *i*-Pr_2NEt in DCM at 20 °C afforded benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**), [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine **6b** and oxazolo[4,5-*b*]pyridine (**4c**), respectively, with the latter milder conditions providing the higher yields. The benzoxazine **6a** and the pyridoxazine **6b** can be thermolysed either neat or in PhCl solutions in the presence of either Et_3N (1 equiv) or $BnEt_3NCl$ (1 equiv) to give the corresponding oxazoles in moderate yields. In the presence of $TsOH{\cdot}H_2O$ though, a solution of benzoxazine **6a** in PhCl heated to reflux was stable, while a solution of the pyridoxazine **6b** rapidly converted into the corresponding oxazole. Tentative mechanistic pathways for these transformations have been proposed.

4. Experimental

4.1. General procedures

All chemicals were commercially available except those whose synthesis is described. DMF was dried by azeotropically removing water with benzene and then distilling under vacuum over dried 4 Å molecular sieves and then kept under an argon atmosphere in a desiccator. 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}).[38] 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). Melting points were determined using a TA Instruments DSC Q1000 with samples hermetically sealed in aluminium pans under an argon atmosphere; using heating rates of 5 °C/min (DSC mp listed by onset and peak values). Solvents used for recrystallisation 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 Pike *Miracle* Ge ATR accessory and strong, medium and weak peaks are represented by s, m and w, respectively. ^1H 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. CH assignments are made based on DEPT 135 spectroscopy. Low-resolution (EI) mass spectra were recorded on a Shimadzu Q2010 GCMS with direct inlet probe. MALDI TOF mass spectra were recorded on a Bruker Autoflex III Smartbeam instrument, while ESI-APCI$^+$ mass spectra were recorded on a Model 6110 Quadrupole MSD, Agilent Technologies. 2-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**)[2] and 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**)[3] were prepared according to literature procedures.

4.2. Synthesis of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (5c)

To a stirred solution of 4,5-dichloro-1,2,3-dithiazolium chloride **2** (956 mg, 4.59 mmol) in DCM (10 mL) at ca. 20 °C and protected with a $CaCl_2$ drying tube was added 2-aminopyridin-3-ol (**12c**). After 1 h, to the reaction mixture was added, dropwise, pyridine (743 μL, 9.18 mmol) and left to stir at ca. 20 °C for an additional 2 h. The reaction mixture was adsorbed onto silica and chromatography (*n*-hexane) gave S_8 (traces). Further elution (*n*-hexane/DCM, 4:1) gave 4-chloro-5*H*-1,2,3-dithiazole-5-thione (10 mg, 6%) and further elution (*n*-hexane/DCM, 3:7) gave the title compound **5c** as orange cotton fibres (6.5 mg, 11%), mp 142–143 °C (from *c*-hexane/EtOH); R_f 0.84 (*n*-hexane/DCM, 3:7). Found C, 34.35; H, 1.56; N, 16.95. $C_7H_4ClN_3OS_2$ requires C, 34.22; H, 1.64; N, 17.10%; λ_{max} (DCM)/nm 247 (log ε 2.74), 265 inf (2.40), 304 (2.47), 387 inf (2.66), 407 (2.90), 428 (2.96), 454 (2.71); ν_{max}/cm^{-1} 3466w and 3366w (OH), 1599w, 1572m, 1516s, 1491s, 1462m, 1433s, 1403w, 1337m, 1287m, 1271m, 1231s, 1186s, 1153s, 1105m, 1053m, 964w, 908m, 878s, 826m, 795s, 779s, 764s; δ_H (500 MHz; DMSO-d_6) 10.33 (1H, s, O*H*), 8.15 (1H, dd, *J* 5.0, 1.0, Py *H*-4), 7.44 (1H, dd, *J* 8.0, 1.0, Py *H*-5), 7.33 (1H, dd, *J* 8.0, 5.0, Py *H*-6); δ_C (75 MHz; DMSO-d_6) 156.1 (s), 149.3 (s), 148.3 (s), 143.4 (s), 133.7 (d), 123.7 (d), 123.6 (d); *m*/*z* (EI) 247 (M^++2, 14%), 245 (M^+,

34), 210 (14), 178 (4), 146 (100), 120 (9), 102 (8), 94 (41), 70 (12), 64 (38), 53 (10). Found M^+, 244.9489. $C_7H_4ClN_3OS_2$ requires M, 244.9484. Further elution (DCM) gave *(E)-6-(4-chloro-5H-1,2,3-dithiazol-5-ylidene)-2-[(Z)-(4-chloro-5H-1,2,3-dithiazol-5-ylidene) amino]pyridin-3(6H)-one* (**13**) as a blue dust (2.7 mg, 3%), mp 288–289 °C (from DCE); R_f 0.41 (DCM). Found C, 28.51; H, 0.50; N, 15.02. $C_9H_2Cl_2N_4OS_4$ requires C, 28.35; H, 0.53; N, 14.69%; λ_{max} (DCM)/nm 260 (log ε 2.34), 268 (2.32), 331 (1.81), 418 (1.74), 615 (2.09); ν_{max}/cm^{-1} 2922w, 2847w, 1570w, 1503m, 1485m, 1447m, 1424m, 1367w, 1360w, 1325s, 1288m, 1240s, 1209m, 1105w, 1047m, 941w, 914w, 883m, 851w, 824m, 808w, 789m, 779m; δ_H (500 MHz; TFA-d_1) 9.23 (1H, *J* 6.0, Py *H*), 8.08 (1H, *J* 5.5, Py *H*); δ_C (125 MHz; TFA-d_1) 164.4 (s), 162.9 (s), 155.5 (s), 146.3 (s), 141.0 (s), 129.6 (d), 129.3 (s), 119.9 (d); *m*/*z* (EI) 384 (M^++4, 7%), 382 (M^++2, 22), 380 (M^+, 25), 347 (13), 345 (M^+–Cl, 25), 310 (4), 283 (39), 281 (100), 253 (5), 231 (14), 229 (33), 220 (4), 214 (4), 192 (3), 166 (10), 160 (7), 142 (8), 140 (14), 137 (7), 134 (11), 102 (14), 99 (11), 96 (16), 85 (11), 82 (17), 76 (18), 70 (21), 64 (80), 57 (14). Further elution (DCM/*t*-BuOMe, 9:1) gave *(E)-2-amino-6-(4-chloro-5H-1,2,3-dithiazol-5-ylidene)pyridin-3(6H)-one* (**14**) as lustrous bronze coloured prisms (2.4 mg, 4%), mp (DSC) onset: 156.6 °C peak max: 168.5 °C (decomp.) (from DCE); R_f 0.53 (DCM/*t*-BuOMe, 9:1). Found: C, 34.37; H, 1.72; N, 16.97. $C_7H_4ClN_3OS_2$ requires C, 34.22; H, 1.64; N, 17.10%; λ_{max} (DCM)/nm 281 (log ε 3.73), 298 inf (3.66), 422 inf (3.21), 549 (4.19); ν_{max}/cm^{-1} 3486w and 3300m (NH_2), 3215w, 1612w, 1554m, 1541s, 1511s, 1449m, 1428s, 1407s, 1365s, 1333w, 1318m, 1235s, 1206m, 1139m, 1079m, 960w, 875m, 831m, 812s, 753w; δ_H (500 MHz; DMSO-d_6) 8.51 (1H, *J* 9.5, Py *H*), 7.49 (1H, br s, NH_2), 7.06 (1H, br s, NH_2), 6.34 (1H, *J* 9.0, Py *H*); δ_C (125 MHz; DMSO-d_6) 173.9 (s), 154.2 (s), 147.4 (s), 141.4 (s), 135.6 (s), 127.9 (d), 121.0 (d); *m*/*z* (EI) 247 (M^++2, 28%), 245 (M^+, 64), 217 (4), 210 (14), 182 (13), 178 (28), 175 (35), 156 (8), 150 (5), 140 (14), 124 (9), 110 (16), 104 (35), 96 (31), 93 (31), 82 (80), 76 (84), 70 (60), 64 (100), 53 (37).

4.3. Thermolysis of 2-hydroxy-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes in PhCl at reflux

*4.3.1. Thermolysis of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) phenol (**5a**) (typical procedure: see Table 1).* A stirred solution of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**) (48.8 mg, 0.20 mmol) in PhCl (2 mL) was heated at ca. 132 °C, until no starting materials remained (TLC, 15 h). On cooling to ca. 20 °C the reaction mixture was adsorbed onto silica and chromatography (*n*-hexane) gave S_8 (12.5 mg, 98%). Further elution (*n*-hexane/DCM, 6:4) gave benzo[*d*]oxazole-2-carbonitrile (**4a**) (23.9 mg, 83%) as colourless needles, mp 99–100 °C (lit.[39] 102–104 °C) (from *c*-hexane); R_f 0.57 (*n*-hexane/DCM, 6:4); λ_{max} (DCM)/nm 273 inf (log ε 3.19); ν_{max}/cm^{-1} 2251m (C≡N), 1794w, 1611m, 1603m, 1530m, 1476m, 1445s, 1429w, 1371w, 1341s, 1287w, 1275w, 1258m, 1233w, 1219w, 1171s, 1163w, 1136w, 1105m, 993m, 953s, 895m, 953s, 895m, 854w, 837w, 818s, 760s; δ_H (300 MHz; $CDCl_3$) 7.90–7.86 (1H, m, Ph *H*), 7.67–7.49 (3H, m, Ph *H*); δ_C (75 MHz; $CDCl_3$) 150.3 (s), 139.4 (s), 137.2 (s), 129.1 (d), 126.5 (d), 121.9 (d), 111.5 (d), 109.1 (s); *m*/*z* (EI) 144 (M^+, 100%), 116 (8), 92 (120), 64 (35).

*4.3.2. Thermolysis of 3-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**).* Similar treatment of 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**) (49.2 mg, 0.20 mmol) gave S_8 (12.8 mg, 100%). Further elution (*n*-hexane/DCM, 4:6) gave *oxazolo[5,4-b]pyridine-2-carbonitrile* (**4b**) (27.8 mg, 96%) as colourless needles, mp 105–106 °C (from *c*-hexane); R_f 0.67 (*n*-hexane/DCM, 4:6). Found C, 57.86; H, 2.10; N, 28.88. $C_7H_3N_3O$ requires C, 57.94; H, 2.08; N, 28.96%; λ_{max} (DCM)/nm 247 inf (log ε 2.63), 327 (2.57), 418 (2.68); ν_{max}/cm^{-1} 2257w (C≡N), 1609m, 1599m, 1524m, 1476w, 1400s, 1362w, 1333s, 1279m, 1231s, 1167w, 1153m, 1117w, 1032w, 1005w, 993w, 953m, 901m, 845w, 829s, 816s, 806s, 773s; δ_H (300 MHz; $CDCl_3$) 8.63 (1H, dd, *J* 1.5, 4.8, Py *H*-4 or 6), 8.26 (1H, dd, *J* 1.65, 7.95, Py *H*-6 or 4), 7.56 (1H, dd, *J* 4.8, 8.1, Py *H*-5); δ_C (75 MHz; $CDCl_3$) 158.3 (s), 149.3 (d), 137.5 (s), 131.2 (s), 131.1 (d), 122.9 (d), 108.6 (s); *m*/*z* (EI) 145 (M^+, 100%), 117 (82), 65 (35), 64 (20), 54 (8), 51 (4).

*4.3.3. Thermolysis of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**).* Similar treatment of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) (49.2 mg, 0.20 mmol) gave S_8 (12.2 mg, 95%) and *oxazolo[4,5-b]pyridine-2-carbonitrile* (**4c**) (20.9 mg, 72%) as colourless needles, mp 49–50 °C (from *c*-hexane); R_f 0.20 (*n*-hexane/DCM, 4:6). Found C, 57.86; H, 2.10; N, 28.88. $C_7H_3N_3O$ requires C, 57.94; H, 2.08; N, 28.96%; λ_{max} (DCM)/nm 245 (log ε 2.63), 292 (3.09), 304 inf (2.89); ν_{max}/cm^{-1} 3043w, 2259w (C≡N), 1715w, 1700w, 1684w, 1653w, 1611m, 1537m, 1506w, 1403s, 1321m, 1293w, 1260m, 1251w, 1223m, 1212w, 1171m, 1111w, 1030m, 954m, 844m, 828m, 795s, 780s; δ_H (300 MHz; $CDCl_3$) 8.80 (1H, d, *J* 4.45, Py *H*-4 or 6), 8.04 (1h, dd, *J* 1.4, 8.4, Py *H*-6 or 4), 7.59 (1H, dd, *J* 4.7, 8.4, Py *H*-5); δ_C (75 MHz; $CDCl_3$) 152.4 (s), 149.6 (d), 143.2 (s), 139.6 (s), 123.8 (d), 120.0 (d), 108.5 (s); *m*/*z* (EI) 145 (M^+, 98%), 94 (6), 93 (100), 65 (49), 64 (23).

4.4. Solvent-free thermolysis of 2-hydroxy-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes

*4.4.1. Thermolysis of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) phenol (**5a**) (typical procedure: see Table 1).* Neat 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**) (48.8 mg, 0.20 mmol) was heated at ca. 200 °C for 1 min in argon atmosphere. On cooling to ca. 20 °C the reaction mixture was adsorbed onto silica and chromatography (*n*-hexane) gave S_8 (4.7 mg, 60%). Further elution (*n*-hexane/DCM, 6:4) gave benzo[*d*]oxazole-2-carbonitrile (**4a**) (24.7 mg, 85%) as colourless needles, mp 99–100 °C (lit.[39] 102–104 °C) (from *c*-hexane), identical to that described above.

*4.4.2. Thermolysis of 3-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**).* Similar treatment of 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**) (49.2 mg, 0.20 mmol) at ca. 200 °C for 2 min gave S_8 (11.5 mg, 90%). Further elution (*n*-hexane/DCM, 4:6) gave *oxazolo[5,4-b]pyridine-2-carbonitrile* (**4b**) (19.1 mg, 66%) as colourless needles, mp 105–106 °C (from *c*-hexane), identical to that described above. Further elution (DCM) gave *[1,2,3]dithiazolo[5,4-e]pyrido[3,2-b][1,4] oxazine* **6b** (0.4 mg, 1%) as orange fibres, mp 217–218 °C (from *c*-hexane/EtOH); R_f 0.32 (DCM). Found C, 40.26; H, 1.40; N, 20.09. $C_7H_3N_3OS_2$ requires C, 40.18; H, 1.45; N, 20.08%; λ_{max} (DCM)/nm 272 inf (log ε 2.45), 308 (2.35), 383 inf (3.02), 411 (3.17), 434 inf (3.04); ν_{max}/cm^{-1} 3044w, 3007w, 1582m, 1562s, 1501s, 1423s, 1287m, 1269w, 1234s, 1192m, 1123m, 1076m, 1045m, 982w, 932m, 856w, 806s, 756s, 727m; δ_H (300 MHz; DMSO-d_6) 7.92 (1H, d, *J* 4.1, Py *H*), 7.52 (1H, d, *J* 7.3, Py *H*), 7.14 (1H, dd, *J* 5.0, 7.0, Py *H*); δ_C (75 MHz; DMSO-d_6) 166.2 (s), 152.4 (s), 150.5 (s), 144.3 (d), 133.4 (d), 127.8 (s), 122.4 (d); *m*/*z* (EI) 209 (M^+, 100%), 135 (54), 108 (17), 103 (10), 76 (13), 70 (16), 64 (24). Found M^+, 208.9718. $C_7H_3N_3OS_2$ requires M, 208.9718.

*4.4.3. Thermolysis of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**).* Similar treatment of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) (49.2 mg, 0.20 mmol) at ca. 200 °C for 5 min gave S_8 (11.5 mg, 90%) and

oxazolo[4,5-b]pyridine-2-carbonitrile (**4c**) (24.4 mg, 84%) as colourless needles, mp 49–50 °C (from *c*-hexane), identical to that described above.

4.5. Reaction of 2-hydroxy-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes with NaH

*4.5.1. Reaction of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) phenol (**5a**) with NaH (typical procedure: see Table 1).* To a stirred solution of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**) (48.8 mg, 0.20 mmol) in dry THF (2 mL) at ca. 20 °C and protected with a $CaCl_2$ drying tube was added NaH (9.6 mg, 0.40 mmol) and the mixture was then heated at ca. 66 °C until no more starting material remained (TLC, 2 h). The reaction mixture was adsorbed onto silica and chromatography (*n*-hexane) gave S_8 (7.0 mg, 55%). Further elution (*n*-hexane/DCM, 6:4) gave benzo[*d*]oxazole-2-carbonitrile (**4a**) (traces) as colourless needles, mp 99–100 °C (from *c*-hexane), identical to that described above. Further elution (*n*-hexane/DCM, 3:7) gave benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**) (27.0 mg, 65%) as orange fibres, mp 183–184 °C (from *c*-hexane/EtOH). Found C, 46.24; H, 2.03; N, 13.38. $C_8H_4N_2OS_2$ requires C, 46.14; H, 1.94; N, 13.45%; R_f 0.67 (*n*-hexane/DCM, 3:7); λ_{max} (DCM)/nm 272 inf (log ε 2.45), 308 (2.35), 383 inf (3.02), 411 (3.17), 434 inf (3.04); ν_{max}/cm^{-1} 1584w, 1570w, 1560s, 1499w, 1491m, 1476m, 1458m, 1437w, 1371w, 1302m, 1285w, 1273w, 1236m, 1207m, 1190w, 1113m, 1049s, 974w, 939m, 926s, 856w, 841w; δ_H (300 MHz; DMSO-d_6) 7.12–7.10 (3H, m, Ph *H*), 7.01–6.99 (1H, m, Ph *H*); δ_C (75 MHz; DMSO-d_6) 165.1 (s), 150.5 (s), 143.9 (s), 131.9 (s), 127.6 (d), 125.5 (d), 125.3 (d), 115.15 (d); *m*/*z* (EI) 208 (M^+, 100%), 144 (17), 122 (12), 104 (91), 90 (22), 78 (10), 76 (13), 70 (21), 64 (78), 51 (29).

*4.5.2. Reaction of 3-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) pyridin-2-ol (**5b**) with NaH.* Similar treatment of 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**) (49.2 mg, 0.20 mmol) with NaH (5.3 mg, 0.22 mmol) gave oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) (traces) as colourless needles, mp 105–106 °C (from *c*-hexane), identical to that described above. Further elution (DCM) gave *[1,2,3]dithiazolo[5,4-e]pyrido[3,2-b][1,4]oxazine* **6b** (17.6 mg, 42%) as orange fibres, mp 217–218 °C (from *c*-hexane/EtOH), identical to that described above.

*4.5.3. Reaction of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) pyridin-3-ol (**5c**) with NaH.* Similar treatment of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) (49.2 mg, 0.20 mmol) with NaH (9.6 mg, 0.40 mmol) gave oxazolo[4,5-*b*]pyridine-2-carbonitrile (**4c**) (25.5 mg, 88%) as colourless needles, mp 49–50 °C (from *c*-hexane), identical to that described above.

4.6. Reaction of 2-hydroxy-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)arenes with base

*4.6.1. Reaction of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) phenol (**5a**) with base (typical procedure: see Table 1).* To a stirred solution of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**) (48.8 mg, 0.20 mmol) in DCM (2 mL) at ca. 20 °C and protected with a $CaCl_2$ drying tube, was added *i*-Pr_2NEt (37.7 μL, 0.22 mmol) and the mixture was left to stir until no more starting material remained (TLC, 12 h). The reaction mixture was adsorbed onto silica and chromatography (*n*-hexane) gave S_8 (traces). Further elution (*n*-hexane/DCM, 6:4) gave benzo[*d*]oxazole-2-carbonitrile (**4a**) (0.3 mg, 1%) as colourless needles, mp 99–100 °C (from *c*-hexane), identical that described above. Further elution (*n*-hexane/DCM, 3:7) gave benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**) (38.7 mg, 93%) as orange fibres, mp 183–184 °C (from *c*-hexane/EtOH), identical that described above.

*4.6.2. Reaction of 3-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) pyridin-2-ol (**5b**) with base.* Similar treatment of 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene-amino)pyridin-2-ol (**5b**) (49.2 mg, 0.20 mmol) with *i*-Pr_2NEt (37.7 μL, 0.22 mmol) gave oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) (traces) as colourless needles, mp 105–106 °C (from *c*-hexane), identical to that described above. Further elution (DCM) gave [1,2,3]dithiazolo[5,4-*e*]pyrido[3,2-*b*][1,4]oxazine (**6b**) (26.3 mg, 63%) as orange fibres, mp 217–218 °C (from *c*-hexane/EtOH), identical to that described above.

*4.6.3. Reaction of 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) pyridin-3-ol (**5c**) with base.* Similar treatment of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-3-ol (**5c**) (49.2 mg, 0.20 mmol) with *i*-Pr_2NEt (37.7 μL, 0.22 mmol) gave oxazolo[4,5-*b*]pyridine-2-carbonitrile (**4c**) (21.2 mg, 73%) as colourless needles, mp 49–50 °C (from *c*-hexane), identical to the that described above.

4.7. Thermolysis reaction of fused [1,2,3]dithiazolo[5,4-*e*][1,4]oxazines

*4.7.1. Thermolysis reaction of benzo[b][1,2,3]dithiazolo[5,4-e][1,4] oxazine (**6a**) (typical procedure: see Table 3).* Neat benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine **6a** (41.6 mg, 0.20 mmol) in argon atmosphere was heated at ca. 275 °C for 7 min. On cooling to ca. 20 °C the reaction mixture was adsorbed onto silica and chromatography (*n*-hexane) gave S_8 (7.0 mg, 55%). Further elution (*n*-hexane/DCM, 6:4) gave the benzo[*d*]oxazole-2-carbonitrile **4a** (7.8 mg, 27%) as colourless needles, mp 99–100 °C (from *c*-hexane) identical to an authentic sample.

*4.7.2. Thermolysis of [1,2,3]dithiazolo[5,4-e]pyrido[2,3-b][1,4]oxazine (**6b**).* Similar treatment of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**) (42.0 mg, 0.20 mmol) at ca. 230 °C for 10 min gave S_8 (12.4 mg, 97%) and oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) (19.0 mg, 65%) as colourless needles, mp 105–106 °C (from *c*-hexane) identical to that described previously.

4.8. Reaction of fused [1,2,3]dithiazolo[5,4-*e*][1,4]oxazines with base

*4.8.1. Reaction of benzo[b][1,2,3]dithiazolo[5,4-e][1,4]oxazine (**6a**) with base (typical procedure: see Table 3).* To a stirred solution of benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**) (41.6 mg, 0.20 mmol) in PhCl (2 mL) at ca. 20 °C and protected with a $CaCl_2$ drying tube, was added Et_3N (27.9 μL, 0.20 mmol). The mixture was then heated at ca. 132 °C, until no starting materials remained (TLC, 24 h). Chromatography (*n*-hexane) gave S_8 (10.9 mg, 85%) and further elution gave benzo[*d*]oxazole-2-carbonitrile (**4a**) (13.0 mg, 45%) as colourless needles, mp 99–100 °C (from *c*-hexane), identical to an authentic sample.

*4.8.2. Reaction of [1,2,3]dithiazolo[5,4-e]pyrido[2,3-b][1,4]oxazine (**6b**) with base.* Similar treatment of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**) (42.0 mg, 0.20 mmol) with Et_3N (27.9 μL, 0.20 mmol) gave S_8 (10.2 mg, 80%) and further elution gave oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) (11.6 mg, 40%) as colourless needles, mp 105–106 °C (from *c*-hexane) identical to that described above.

4.9. Reactions of oxazines 6a and 6b with $BnEt_3NCl$

*4.9.1. Reaction of benzo[b][1,2,3]dithiazolo[5,4-e][1,4]oxazine (**6a**) with $BnEt_3NCl$ (typical procedure: see Table 3).* To a stirred solution

of benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**) (41.6 mg, 0.20 mmol) in PhCl (2 mL) at ca. 20 °C and protected with a $CaCl_2$ drying tube was added $BnEt_3NCl$ (45.6 mg, 0.20 mmol). The mixture was then heated at ca. 132 °C, until no starting materials remained (TLC, 12 h). Chromatography (*n*-hexane) gave S_8 (9.1 mg, 71%) and further elution (*n*-hexane/DCM, 6:4) gave benzo[*d*]oxazole-2-carbonitrile (**4a**) (10.1 mg, 35%) as colourless needles, mp 99–100 °C (from *c*-hexane), identical to an authentic sample.

*4.9.2. Reaction of [1,2,3]dithiazolo[5,4-e]pyrido[2,3-b][1,4]oxazine (**6b**) with $BnEt_3NCl$.* Similar treatment of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**) (42.0 mg, 0.20 mmol) with $BnEt_3NCl$ (45.6 mg, 0.20 mmol) gave S_8 (4.9 mg, 38%) and oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) (12.2 mg, 42%) as colourless needles, mp 105–106 °C (from *c*-hexane), identical to that described above.

4.10. Reaction of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (6b) with $TsOH\cdot H_2O$

To a stirred solution of [1,2,3]dithiazolo[5,4-*e*]pyrido[2,3-*b*][1,4]oxazine (**6b**) (42.0 mg, 0.20 mmol) in PhCl (2 mL) at ca. 20 °C and protected with a $CaCl_2$ drying tube was added $TsOH\cdot H_2O$ (1.9 mg, 0.010 mmol). The mixture was then heated at ca. 132 °C, until no starting materials remained (TLC, 20 h). Chromatography (*n*-hexane) gave S_8 (11.0 mg, 86%) and further elution gave oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) (14.5 mg, 50%) as colourless needles, mp 105–106 °C (from *c*-hexane), identical to that described above.

4.11. Stability study of oxazines in the presence of 2-hydroxy (dithiazolylideneamino)arenes

*4.11.1. Reaction of benzo[b][1,2,3]dithiazolo[5,4-e][1,4]oxazine (**6a**) and 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**) (typical procedure).* A stirred solution of benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**) (41.6 mg, 0.20 mmol) and 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)phenol (**5a**) (50.0 mg, 0.20 mmol) in PhCl (2 mL), protected with a $CaCl_2$ drying tube was heated at ca. 132 °C until the dithiazole **5a** was consumed (TLC). Chromatography (*n*-hexane) gave S_8 (15.8 mg, 78%) and further elution (*n*-hexane/DCM, 6:4) gave benzo[*d*]oxazole-2-carbonitrile (**4a**) (34.6 mg, 120%) as colourless needles, mp 99–100 °C (from *c*-hexane), identical to an authentic sample. A final elution (*n*-hexane/DCM, 3:7) gave recovered benzo[*b*][1,2,3]dithiazolo[5,4-*e*][1,4]oxazine (**6a**) (17.3 mg, 42%) as orange fibres, mp 183–184 °C (from *c*-hexane/EtOH), identical to an authentic sample.

*4.11.2. Reaction of [1,2,3]dithiazolo[5,4-e]pyrido[3,2-b][1,4]oxazine (**6b**) and 3-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**).* Similar treatment of [1,2,3]dithiazolo[5,4-*e*]pyrido[3,2-*b*][1,4]oxazine (**6b**) (42.0 mg, 0.20 mmol) and 3-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)pyridin-2-ol (**5b**) (49.2 mg, 0.20 mmol) gave S_8 (11.3 mg, 66%) and oxazolo[5,4-*b*]pyridine-2-carbonitrile (**4b**) (18.1 mg, 62%) as colourless needles, mp 105–106 °C (from *c*-hexane) identical to that described previously and recovered [1,2,3]dithiazolo[5,4-*e*]pyrido[3,2-*b*][1,4]oxazine (**6b**) (31.9 mg, 76%) as orange fibres, mp 217–218 °C (from *c*-hexane/EtOH), identical to that described above.

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