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Synthesis of Fused 1,2,4-Dithiazines and 1,2,3,5-Trithiazepines

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Supporting Information

ABSTRACT: Reacting (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amines **5** with Et_2NH and then with concd H_2SO_4 gives 5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitriles **7** in good yields (74−85%) and 6*H*-pyrazolo-[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitriles **9** as minor products (0−6%). Furthermore, the 1,3-dimethylpyrazole analogue **5a** was transformed into the dithiazine **7a** in two discrete steps, allowing the isolation of a disulfide intermediate (*Z*)-2-[(diethylamino)disulfan-yl]-2-[(1*H*-pyrazol-5-yl)imino]-acetonitrile (**8a**). The one-pot, two-step reaction also worked with electron-rich hydroxy- and methoxy-substituted anilines. Thermolysis of the pyrazolo[3,4-*e*][1,2,4]dithiazines **7** gave the ring-contracted 1*H*-pyrazolo[3,4-*d*]thiazole-5-carbonitriles **6** (94−100%). With active sulfur, 1,3-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (**7a**) gave 1,3-dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile (**9a**), but on prolonged reaction times, it gave 5,7-dimethyl-5*H*-[1,2,3]-dithiazolo[4,5-*b*]pyrazolo[3,4-*e*][1,4]thiazine (**13**). Finally, in the absence of acid, heating a solution of (*Z*)-2-[(diethylamino)-disulfanyl]-2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)imino]acetonitrile (**8a**) gave 4,6,10,12-tetramethyl-6*H*-pyrazolo[3,4-*f*]pyrazolo-[3′,4′:4,5]pyrimido[6,1-*d*][1,2,3,5]trithiazepine-8,12*b*(10*H*)-dicarbonitrile (**19**) (67%).

1. INTRODUCTION

1,2-Dithiines,[1] which are six-membered heterocycles with two adjacent sulfur atoms, have attracted considerable attention because of their unusual red color,[2] questions about their structure and their potential antiaromaticity,[2a,3] their occurrence in plants,[4] and their interesting biological activities,[5] such as antibiotic,[6] antiviral,[7] nematicidal,[8] insecticidal,[9] and antifungal activities[10] and DNA-cleaving properties.[11]

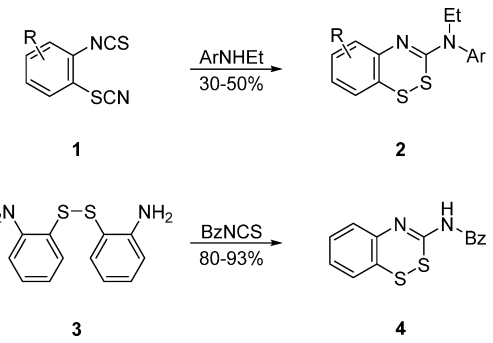
1,2-dithiine 1,2,3-dithiazine 1,2,4-dithiazine

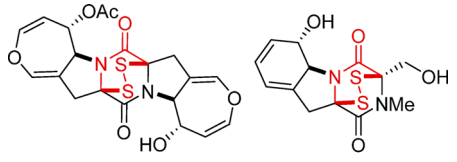
Aza analogues of 1,2-dithiines are less well-known. The two isomeric monoaza dithiines, the 1,2,3- and 1,2,4-dithiazines, are both rare systems with limited reports on their synthesis and chemistry. To the best of our knowledge, there are three reports describing the synthesis of monocyclic 8π 1,2,3-dithiazines,[12] whereas for 8π 1,2,4-dithiazines, there are only two reports on the synthesis of benzo-fused analogues (Scheme 1).[13]

The first, and more general, synthesis of 3-anilino-1,2,4-benzodithiazines **2** involved the condensation of *N*-ethylaniline or 4-bromo-*N*-ethylaniline with substituted *o*-thiocyanatophenylisothiocyanates **1**,[13a] whereas more recently, another benzo-fused analogue **4** was isolated from the reaction of 2,2′-diaminodiphenyl disulfide (**3**) with *N*-benzoyl thiocyanate.[13b]

Interestingly, di- and tetrahydro-1,2,4-dithiazines are more common.[14] Bridged analogues of 3,6-dihydro-1,2,4-dithiazin-5-ones are also present in natural products and possess interesting biological activities such as antibacterial (e.g., hyalodendrin),[15] antiviral (e.g., aranotin),[16] and antitumor (e.g., gliotoxin).[17]

Scheme 1. Known Syntheses of 1,2,4-Dithiazines





Aranotin[16] Gliotoxin[17]

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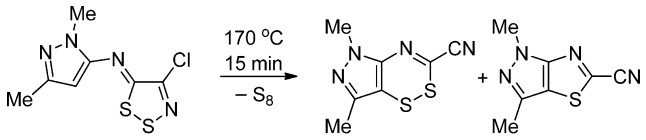
During our recent work on the thermolysis of readily available (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amines **5**,[18] which gives elemental sulfur and pyrazolo[3,4-*d*]thiazoles **6**, we also obtained an unidentified minor side product. Herein, we report the structural elucidation of this minor product, which is a rare example of a fused 1,2,4-dithiazine. Furthermore, we describe an optimized synthesis of this heterocycle and studies related to its chemistry.

2. RESULTS AND DISCUSSION

2.1. Synthesis of Pyrazolo- and Benzo-Fused 1,2,4-Dithiazines. Thermolysis of (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (**5a**) at ca. 170 °C for 15 min gave S_8, 1,3-dimethyl-1*H*-pyrazolo[3,4-*d*]-thiazole-5-carbonitrile (**6a**), and a minor previously unidentified red colored side product **7a**.[18] Spectroscopic data for this minor side product, which included single-crystal X-ray crystallography (see Supporting Information, section S1.1), identified the compound as 5,7-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (**7a**) (Scheme 2).

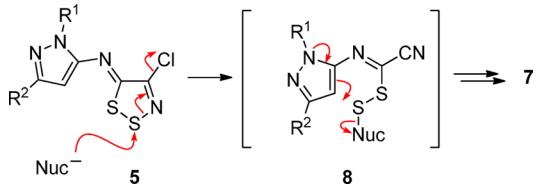
Scheme 2. Thermolysis of (*Z*)-*N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (5a)



5a **7a** (2%) **6a** (77%)

A plausible addition of the nucleophile, ring opening, and ring closure (ANRORC)[19] mechanism can be proposed for the formation of the pyrazolo[3,4-*e*][1,2,4]dithiazine **7a**: thiophilic attack on the S-2 sulfur atom of the dithiazolylidene **5** by chloride or an equivalent nucleophile released during the thermolysis can give the intermediate disulfide **8**. In the presence of the electron-rich enaminic C-4 position of the pyrazole ring, the disulfide **8** could undergo an intramolecular cyclization to give the observed product **7** (Scheme 3).

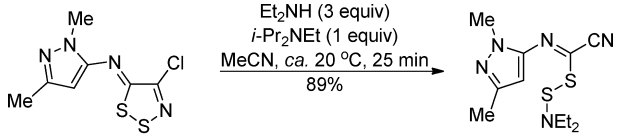
Scheme 3. Proposed Disulfide Intermediate 8 Involved in the Transformation of Dithiazole 5 into Dithiazine 7



Intermediates analogous to disulfide **8** are frequently proposed in reactions involving thiophile-mediated ring transformations of *N*-(5*H*-1,2,3-dithiazolylidene)amines.[20] Typical thiophiles that induce ring transformation of 5*H*-1,2,3-dithiazolylidenes include triphenylphosphine (Ph_3P),[20f,21] 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU),[20d] tetraalkylammonium halides (R_4NHal),[20a] and dialkylamines,[20g,i,22] whereas other less common reagents include Grignard reagents,[20e] phosphoranes,[20h] and sodium hydride.[23] Reaction of the dithiazolylidene **5a** with common thiophiles (R_4NHal, Ph_3P, DBU), however, gave either mixtures of thiazole **6a** and dithiazine **7a** in low to moderate yields or no formation of the desired product.

Nevertheless, Kim et al. have described the synthesis of stable disulfides from *N*-(dithiazolylidene)amines on treatment with either phosphoranes[20h] or dialkylamines.[22] As such, a two-step route to the dithiazine **7a** was developed via the synthesis and isolation of the postulated disulfide intermediate. In our hands, the dialkylamine-mediated ring opening of dithiazolylidene **5a** worked well with Et_2NH (3 equiv) in combination with Hünig's base (*i*-Pr_2NEt, 1 equiv) in MeCN at ca. 20 °C for 25 min to give disulfide **8a** in 89% yield (Scheme 4). Spectroscopic

Scheme 4. Preparation of (*Z*)-2-[(Diethylamino)disulfanyl]-2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)imino]acetonitrile (8)

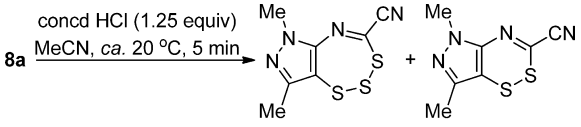


5a **8a**

data and single-crystal X-ray diffraction study supported the structure of the disulfide (see Supporting Information, section S1.2). Additional details on the optimization of this reaction are presented in the Supporting Information (section S2.1).

Attempts to convert disulfide **8a** into the desired dithiazine **7a** under nonacidic reaction conditions failed to give the expected dithiazine, presumably owing to the poor nucleofugality of the diethylamide, but they did lead to interesting new chemistry (see Section 2.4). As such, we treated disulfide **8a** with a range of acids. Fortunately, a solution of disulfide **8a** in MeCN treated with a slight excess of concd HCl (1.25 equiv) at ca. 20 °C for 5 min gave the red colored dithiazine **7a** in 82% yield together with a yellow colored minor side product, identified from the spectroscopic data and by X-ray crystallography (see Supporting Information, section S1.3) as 6,8-dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile (**9a**) (Scheme 5).

Scheme 5. Acid-Mediated Conversion of the Disulfide 8a into the 1,2,3,5-Trithiazepine 9a and the 1,2,4-Dithiazine 7a



9a (5%) **7a** (82%)

Interestingly, the choice of acid used for this transformation was important: the use of concd H_2SO_4 instead of concd HCl led to mainly unreacted starting disulfide and low yields (12%) of the desired dithiazine. Further details on the optimization can be found in the Supporting Information (section S2.2).

With a two-step procedure successfully developed, a one-pot, two-step process was elucidated: treatment of dithiazolylidene **5a** with Et_2NH (3 equiv) and *i*-Pr_2NEt (1 equiv) at ca. 20 °C for 25 min led to formation of the desired disulfide **8a** (by TLC). To the reaction mixture was then added concd HCl (4 equiv), and after 5 min, the reaction was worked-up to afford the desired dithiazine **7a** and trithiazepine **9a** as major and minor products in 61 and 5% yields, respectively. Interestingly,

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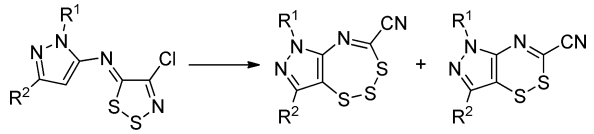
under these one-pot conditions, the concd HCl could be substituted for concd H_2SO_4 (5 equiv), which gave dithiazine **7a** in an improved yield of 74%. Further details on the optimization can be found in the Supporting Information (section S2.3). This one-pot, two-step reaction protocol was successfully applied to a range of 1,3-disubstituted (dithiazolylidene)pyrazolamines **5** (Table 1).

Table 1. One-Pot Transformation of (*Z*)-*N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amines 5 (0.2 mmol) into 5*H*-Pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitriles 7[a]



5 **9** **7**

entry	R^1	R^2	yields (%)	
1	Me	Me	**9a** (5)	**7a** (74)
2	Me	Ph	**9b** (5)	**7b** (75)
3	Bn	Me	**9c** (6)	**7c** (78)
4	Bn	Ph	**9d** (–)[b]	**7d** (85)[b]
5	Ph	Me	**9e** (0)	**7e** (85)
6[c]	Ph	Ph	**9f** (0)	**7f** (80)

[a]Reagents and conditions: (i) Et_2NH (3 equiv), *i*-Pr_2NEt (1 equiv), MeCN, ca. 20 °C, 25 min; (ii) concd H_2SO_4 (5 equiv), ca. 20 °C, 5 min [b]Compounds **7d** and **9d** (ratio **7d**/**9d**, 14:1 by ^1H NMR) were inseparable by chromatography; however, a microanalytically pure sample of dithiazine **7d** was obtained after recrystallization. [c]A trace of the pyrazolothiazole **6f** was observed (by TLC).

With these results in hand, we envisioned that the transformation of (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amines **5** to 5*H*-pyrazolo[3,4-*e*][1,2,4]-dithiazine-3-carbonitriles **7** could also be applied to other electron-rich arenes. As such, a series of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines **10** was subjected to the optimized one-pot conditions (Scheme 6).

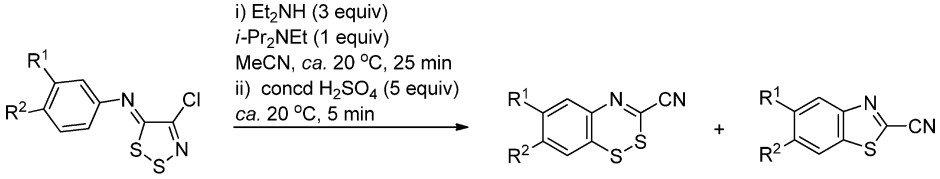
Treatment of the least activated *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**10a**) with Et_2NH and then concd H_2SO_4 led only to a complex reaction mixture, and no traces of either 1,2,4-benzodithiazine **11a** or benzothiazole **12a** were detected. Nevertheless, the introduction of electron-releasing groups such as methoxy and hydroxy groups (**10b–d**) did lead to formation of the 1,2,4-benzodithiazines. In particular, the most activated dithiazolylidene **10d** (R^1 = HO, R^2 = MeO) led to the formation of 1,2,4-benzodithiazine **11d** in a 70% yield together with a small quantity of the benzothiazole **12d** (13%). Interestingly, the isolated reaction products indicated the cyclization occurred regioselectively para to the more dominant electron-releasing substituent.

2.2. Transformation of 5,7-Dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile to 6,8-Dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile. The formation of the 5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitriles **7** was, in most cases, accompanied by a small quantity of 1,2,3,5-trithiazepines **9**, which were relatively unstable and on silica (2D-TLC) converted back into 1,2,4-dithiazines **7**. The formation and instability of trithiazepines **9** suggested that an equilibrium may exist between the dithiazine, the trithiazepine, and an active form of sulfur, similar to that observed between 1,2,3-trithioles and 1,2,3,4,5-pentathiepins.[24] Related transformations also included the conversion of bridged 3,6-dihydro-1,2,4-dithiazin-5-ones to bridged 4,7-dihydro-1,2,3,5-trithiazepin-6-ones and vice versa[25] and an interesting quantitative conversion of (1*R*,1′*R*)-diborn-2-eno[2,3-*c*;3′,2′-*e*][1,2]dithiine to (1*R*,1′*R*)-diborn-2-eno[2,3-*d*;3′,2′-*f*][1,2,3]-trithiepine, which was facilitated by the release of ring strain on going from a six- to a seven-membered ring.[26]

Initially, we investigated the transformation of 5,7-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (**7a**) into 6,8-dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile (**9a**) by heating to reflux a mixture of the dithiazine **7a** and sulfur (10 equiv) in various solvents (MeCN, DMF, acetone, DCM, $CHCl_3$, THF, PhCl, 1,4-dioxane, CS_2, *n*-heptane, and *c*-hexane). Degradation was observed (by TLC) in either DMF or acetone, whereas a small amount of trithiazepine **9a** was observed in MeCN, THF, and 1,4-dioxane. A significant formation of trithiazepine **9a** was noted only in PhCl; however, at the reflux temperature of PhCl (bp 131 °C), the formation of thiazole **6a** (15%) was also observed (Table 2, entry 1). Repeating the reaction in PhCl at a lower temperature (ca. 100 °C) led, after 16 h, to only a small quantity of trithiazepine **9a** (6%) (Table 2, entry 2). Gratifyingly, when either a catalytic (0.1 equiv) or stoichiometric (1.0 equiv) quantity of DABCO was added to the reaction mixture (Table 2, entries 3 and 4), after only 20 and 6 min, respectively, trithiazepine **9a** could be isolated in 43 and 47% yields, based on recovered unreacted dithiazine **7a**. This conversion could also be achieved more slowly (ca. 5 h) at lower reaction temperatures, ca. 40 °C, but the overall yields of trithiazepine **9a** and recovered dithiazine **7a** were poor (Table 2, entry 5).

Interestingly, under these conditions, a trace of a new orange colored side product was observed, which, from the

Scheme 6. Conversion of *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)anilines 10 into Benzo[*e*][1,2,4]dithiazine-3-carbonitriles 11



10a (R^1 = R^2 = H)
10b (R^1 = MeO, R^2 = H)
10c (R^1 = HO, R^2 = H)
10d (R^1 = HO, R^2 = MeO)

11a (0%)
11b (17%)
11c (55%)
11d (70%)

12a (0%)
12b (8%)
12c (12%)
12d (13%)

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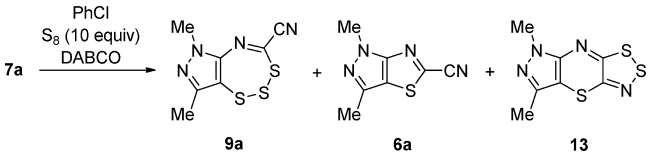
Table 2. Transformation of 5,7-Dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (7a) (0.1 mmol) to 6,8-Dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile (9a)



entry	temp (°C)	DABCO (equiv)	time (h)	yields (%)[a] 7a[b]	9a	6a	13
1	131	0	16	33	18	22	0
2	100	0	16	69	19	0	0
3	100	0.1	0.33	44	43	0	trace
4	100	1.0	0.10	45	47	0	trace
5	40	1.0	5	31	20	0	trace
6	100	1.0	16	trace	trace	17	23
7	60	1.0	27	12	7	15	27

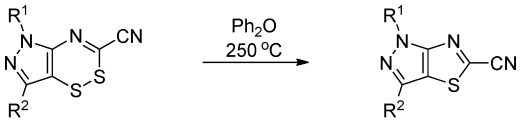
[a]Yields based on recovered dithiazine **7a**. [b]Recovered dithiazine **7a**.

spectroscopic and crystallographic data, was identified as 5,7-dimethyl-5*H*-[1,2,3]dithiazolo[4,5-*b*]pyrazolo[3,4-*e*][1,4]-thiazine (**13**) (see Supporting Information, section S1.4). When 1 equiv of DABCO and longer reaction times (16 h) were used the pyrazolo[3,4-*e*][1,4]thiazine **13** was isolated in 23%, accompanied by the formation of thiazole (17%) (Table 2, entry 6). Decreasing the reaction temperature to ca. 60 °C did not improve the yield of the thiazine **13**, nor did it avoid the formation of thiazole **6a** (Table 2, entry 7).

Presumably, ring opening of dithiazine **7a** or even trithiazepine **9a** mediated by the postulated thiophilic DABCO/S_8 adduct **14**[27] afforded a species such as compound **15**. Rotation of the imine bond can bring the nitrile group close to the pyrazole C-4 thiolate (species **16**), and a cascade cyclization and concomitant loss of sulfur via a chain extension mechanism[28] could lead to the formation of the tricyclic 1,4-thiazine **13** (Scheme 7).

2.3. Thermolysis of 5*H*-Pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitriles 7. 1,2,4-Dithiazines are structurally similar to 1,2-dithiines and therefore could readily extrude sulfur thermally[26,29] or photochemically[30] to give the more aromatic and thermally stable thiazoles. In our hands, a DCM solution of dithiazine **7a** exposed to intense sunlight or to irradiation at 365 nm from a hand-held UV/vis lamp appeared to be stable. Nevertheless, DSC studies indicated that the dithiazines **7** were thermally labile, and the subsequent thermolysis of the dithiazines **7** in diphenyl ether at ca. 250 °C gave the corresponding thiazoles **6** in near quantitative yields (Table 3).

Table 3. Thermolysis of 5*H*-Pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitriles 7 (0.1 mmol) To Give 1*H*-Pyrazolo[3,4-*d*]thiazole-5-carbonitriles 6



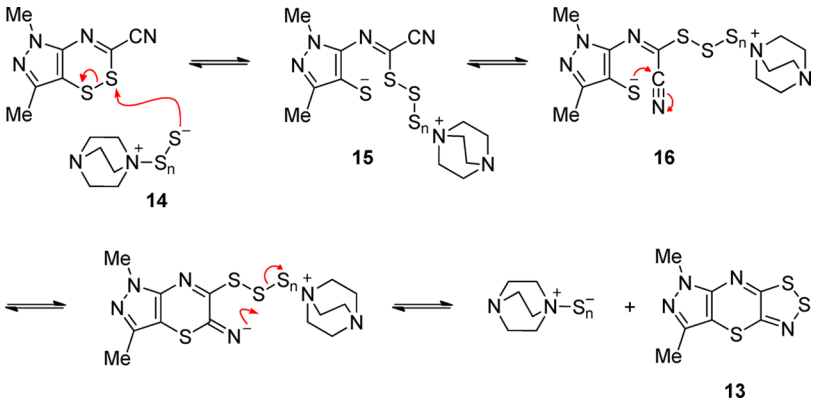
entry	R^1	R^2	decomp onset[a] (°C)	time (min)	yields **6** (%)
1	Me	Me	[b]	30	**6a** (100)
2	Me	Ph	175.9	30	**6b** (95)
3	Bn	Me	171.8	25	**6c** (95)
4	Bn	Ph	187.3	35	**6d** (94)
5	Ph	Me	157.2	20	**6e** (100)
6	Ph	Ph	149.2	25	**6f** (100)

[a]Decomp onset temperatures determined using DSC at a heating rate of 5 °C/min under an argon atmosphere. [b]No decomp onset was determined, as compound **7a** had a low bp (onset, 189.6 °C; peak max, 198.3 °C) and escaped from the sealed DSC pan.

The reaction mechanism for this ring contraction is probably similar to that for the ring contraction of the analogous 1,2-dithiins into thiophenes.[26,29c,31] A thermally mediated 6π electrocyclic ring opening of the dithiazine can lead to the formation of a [4-thioxo-1*H*-pyrazol-5(4*H*)-ylidene]-carbamothioyl cyanide **17**, which, aided by the electron-releasing pyrazole N-1 atom, can then recyclize to the thiazolo intermediate **18**. This can then lose sulfur via a sulfur chain extension mechanism[28] to afford the fully aromatic pyrazolo-[3,4-*d*]thiazole **6** (Scheme 8).

2.4. Unexpected Chemistry of Disulfide 8a. TLC analysis of a solution of the disulfide **8a** in MeCN that had been left to stand at ca. 20 °C over 3 days indicated the gradual disappearance of the disulfide and formation of some elemental sulfur, $Et_2NS_nNEt_2$ (n = 1–3) (by TLC), and a colorless product isolated in 40% yield, which was identified by single-crystal X-ray diffraction study as 4,6,10,12-tetramethyl-6*H*-

Scheme 7. Tentative Mechanistic Rationale for the Formation of 5,7-Dimethyl-5*H*-[1,2,3]dithiazolo[4,5-*b*]pyrazolo[3,4-*e*][1,4]thiazine (13)



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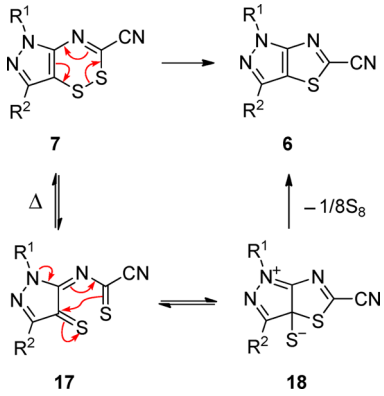
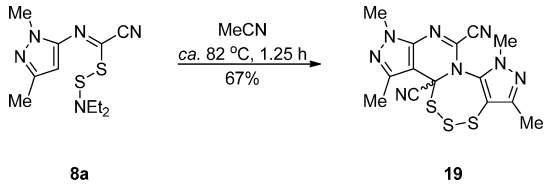
Scheme 8. Tentative Mechanism for the Ring Contraction of 1,2,4-Dithiazines 7 into Thiazoles 6



pyrazolo[3,4-*f*]pyrazolo[3′,4′:4,5]pyrimido[6,1-*d*][1,2,3,5]-trithiazepine-8,12*b*(10*H*)-dicarbonitrile (**19**) (see Supporting Information, section S1.5). When a solution of the disulfide **8a** (0.2 mmol) in MeCN (4 mL) was heated at ca. 82 °C for ca. 1 h, tetracycle **19** was obtained in a surprisingly good yield of 67% (Scheme 9). Interestingly, at ca. 82 °C, a trace of the

Scheme 9. Formation of 4,6,10,12-Tetramethyl-6*H*-pyrazolo[3,4-*f*]pyrazolo[3′,4′:4,5]pyrimido[6,1-*d*][1,2,3,5]trithiazepine-8,12*b*(10*H*)-dicarbonitrile (19) from Disulfide 8a



expected dithiazine **7a** was observed (by TLC) at the beginning of the reaction, but this was quickly consumed. Furthermore, a pure sample of the tetracycle **19** in PhCl heated to ca. 131 °C for 12 h was stable (by TLC).

Formally, this tetracyclic product **19** can form from the Diels–Alder cycloaddition of one dithiazine **7a** and one trithiazepine **9a** followed by loss of diatomic sulfur; however, preliminary studies suggest that this cycloaddition/retro-cycloaddition pathway was not valid: a 1:1 equimolar mixture of dithiazine **7a** and trithiazepine **9a** in MeCN heated to reflux gave no tetracycle **19**. As such, we tentatively propose a stepwise mechanism that invoked the enaminic character of one pyrazole and the highly electrophilic carbon of the exocyclic imine of a second pyrazole **8a** (Scheme 10).

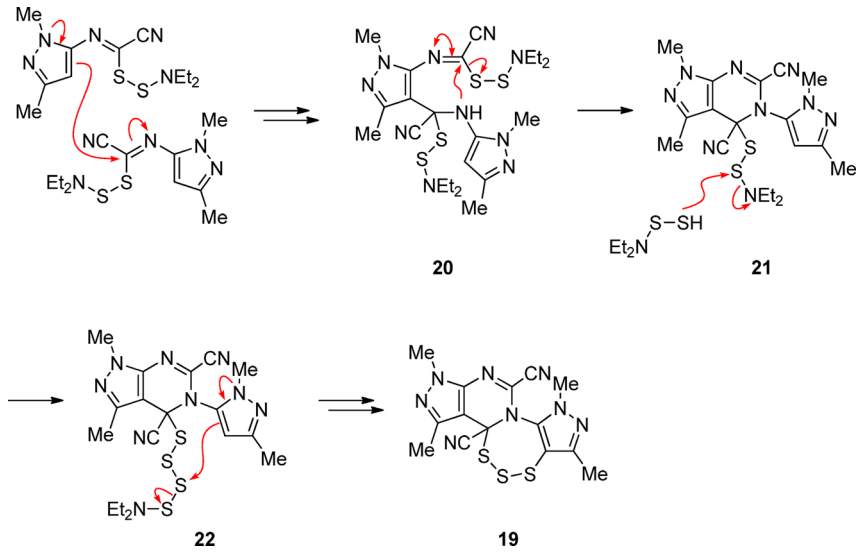
Electrophilic substitution at the pyrazole C-4 carbon by the imine of a second pyrazole **8a** can give a coupled species **20** that can undergo an intramolecular cyclization to provide the pyrazolo[3,4-*d*]pyrimidine intermediate **21** and a species akin to *N*,*N*-diethyldisulfanamine. The latter small molecule can act as an active form of sulfur to extend the disulfide chain of **21** to give a species similar to **22** that undergoes as final cyclization to the observed tetracyclic **19**.

To the best of our knowledge, monocyclic or fused 1,2,3,5-trithiazepines have not been reported. Bridged 4,7-dihydro-1,2,3,5-trithiazepin-6-ones, however, appear in several fungal metabolites and, like their analogous 3,6-dihydro-1,2,4-dithiazin-5-ones, possess interesting biological activities.[32] The scope of this transformation, details regarding its mechanism, and the biological properties of tetracycle **19** are now under investigation.

3. CONCLUSIONS

An efficient one-pot, two-step route to pyrazole fused 1,2,4-dithiazine-3-carbonitriles **7** has been developed starting from *N*-(4-chloro-1,2,3-dithiazolylidene)pyrazol-5-amines **5**, which can be readily prepared in one-step from 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt) and the appropriate 5-aminopyrazole.[18] The reaction requires the use of a dialkylamine to ring open the dithiazole to afford an isolable disulfide intermediate **8**, which on treatment with acid cyclizes to give mainly the desired dithiazines **7** (74–85%) accompanied by small quantities of 1,2,3,5-trithiazepines **9** (0–6%). In the presence of active sulfur, 1,3-dimethyl-5*H*-pyrazolo[3,4-*e*]-[1,2,4]dithiazine-3-carbonitrile (**7a**) can be converted into

Scheme 10. Tentative Mechanism for the Formation of 4,6,10,12-Tetramethyl-6*H*-pyrazolo[3,4-*f*]pyrazolo[3′,4′:4,5]pyrimido[6,1-*d*][1,2,3,5]trithiazepine-8,12*b*(10*H*)-dicarbonitrile (19) from Disulfide 8a



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trithiazepine **9a** in yields as high as 47%. Interestingly, extending the reaction times (>16 h) serendipitously afforded pyrazolo[3,4-*e*][1,4]thiazine **13**. Other unexpected chemistry occurred when disulfide **8a** was heated in neat acetonitrile, affording the unusual tetracyclic 6*H*-pyrazolo[3,4-*f*]pyrazolo-[3′,4′:4,5]pyrimido[6,1-*d*][1,2,3,5]trithiazepine **19**. The reactions described above demonstrate that 4-chloro-1,2,3-dithiazoles can now can be used to provide facile access to fused 1,2,4-dithiazines, a difficult-to-access and potentially interesting ring system.

4. EXPERIMENTAL SECTION

4.1. General Methods and Materials. All chemicals were commercially available except those whose synthesis is described. All volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass-backed thin-layer chromatography (TLC) plates (Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography was used throughout for all non-TLC scale chromatographic separations using silica gel 60 (less than 0.063 mm).[33] Melting points were determined using a Koefler–Hotstage microscope apparatus or a DSC with samples hermetically sealed in aluminum pans under an argon atmosphere, using heating rates of 5 °C/min. Solvents used for recrystallization are indicated after the melting point. UV/vis spectra were obtained using a UV/vis spectrophotometer, and inflections are identified by the abbreviation "inf". IR spectra were recorded on a FTIR spectrometer with a Ge ATR accessory, and strong, medium, and weak peaks are represented by s, m, and w, respectively. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively. Deuterated solvents were used for homonuclear lock, and the signals are referenced to the deuterated solvent peaks. APT NMR studies identified quaternary, tertiary, secondary, and primary carbons, which are indicated by (s), (d), (t), and (q) notations, respectively. MALDI-TOF MS was conducted on a time-of-flight (TOF) mass spectrometer or on a EI GC-MS. (*Z*)-*N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amines (**5a**–**f**),[18] (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline (**10a**),[34] (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-3-methoxyaniline (**10b**),[34] and (*Z*)-5-[(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]-2-methoxyphenol (**10d**)[35] were prepared according to literature procedures.

4.2. Stepwise Synthesis of 5,7-Dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (7a). *4.2.1. (Z)-2-[(Diethylamino)disulfanyl-2-(1,3-dimethyl-1H-pyrazol-5-yl)imino]-acetonitrile (8a).* To a stirred suspension of (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1,3-dimethyl-1*H*-pyrazol-5-amine (**5a**) (49.3 mg, 0.2 mmol) in MeCN (4 mL) at ca. 20 °C was added Hünig's base (34.5 μL, 0.2 mmol) followed by diethylamine (63.0 μL, 0.6 mmol). After 25 min stirring, the reaction mixture was diluted with *n*-hexane and poured onto a packed silica column. Elution with DCM/*t*-BuOMe (90:10) afforded a mixture from which the volatiles were removed under vacuum. The remaining residue was diluted with DCM, adsorbed onto silica, and chromatographed (DCM/*t*-BuOMe, 95:5) to give the title compound **8a** (50 mg, 89%) as beige needles: mp (DSC) onset, 64.4 °C; peak max, 65.0 °C; decomp. onset, 91.5 °C; peak max, 99.4 °C (from *n*-pentane at ca. −20 °C). R_f 0.43 (DCM). (Found: C, 46.53; H, 5.99; N, 24.66. $C_{11}H_{17}N_5S_2$ requires: C, 46.62; H, 6.05; N, 24.71%.) λ_{max}(DCM) 246 (log ε 3.96), 352 (4.16). ν_{max}/cm^{-1} 3138w (Ar CH), 2972m, 2934m and 2870w (CH_2 and CH_3), 2214m (C≡N), 1557m, 1512m, 1470m, 1445m, 1375m, 1368m, 1348m, 1302m, 1173m, 1163m, 1098w, 1065s, 1043s, 1011s, 920m, 914m, 847m, 795m. δ_H(500 MHz; $CDCl_3$) major 6.27 (1H, s), 3.86 (3H, s), 3.09 (4H, q, *J* = 7.3 Hz), 2.28 (3H, s), 1.21 (6H, t, *J* = 7.0 Hz); minor 6.63 (1H, s), 3.85 (3H, s), 3.03 (4H, q, *J* = 7.2 Hz), 2.28 (3H, s), 1.20 (6H, t, *J* = 7.3 Hz) (major/minor, 5:1). δ_C (125 MHz, $CDCl_3$) major 147.8 (s), 143.5 (s), 138.8 (s), 113.2 (s), 100.8 (d), 52.3 (t), 35.3 (q), 13.93 (q), 13.1 (q); minor 148.2 (s), 144.4 (s), 137.3 (s), 109.8 (s), 95.1 (d), 52.2 (t), 35.0 (q), 13.94 (q), 13.2 (q). MALDI-TOF MS (*m*/*z*): 285 (M^+ + 2, 57%), 284 (M^+ + 1, 99), 213 (100), 181 (69), 104 (47), 71 (52).

4.2.2. Treatment of (Z)-2-[(Diethylamino)disulfanyl-2-(1,3-dimethyl-1H-pyrazol-5-yl)imino]acetonitrile (8a) with Concentrated HCl. To a stirred solution of (*Z*)-2-[(diethylamino)disulfanyl-2-(1,3-dimethyl-1*H*-pyrazol-5-yl)imino]acetonitrile (**8a**) (28.3 mg, 0.1 mmol) in MeCN (2 mL) at ca. 20 °C was added in one portion concd HCl (11 μL, 0.125 mmol). After 5 min stirring, the mixture was adsorbed onto silica and chromatographed (*n*-hexane/*t*-BuOMe, 90:10) to give 6,8-dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile (**9a**) (1.3 mg, 5%) as yellow needles: mp (DSC) onset, 66.7 °C; peak max, 71.7 °C; decomp. onset, 166.8 °C; peak max, 185.7 °C (from *n*-pentane at ca. −20 °C). R_f 0.40 (*n*-hexane/*t*-BuOMe, 80:20). (Found: C, 34.57; H, 2.41; N, 23.24. $C_7H_6N_4S_3$ requires: C, 34.69; H, 2.50; N, 23.12%.) λ_{max}(DCM) 301 (log ε 3.58), 373 (3.65), 414 inf (3.26). ν_{max}/cm^{-1} 2949w and 2922w (CH_3), 2218w (C≡N), 1584m, 1481m, 1427m, 1422s, 1387m, 1342m, 1306m, 1198w, 1121w, 1080m, 1042s, 1018m, 995m, 901m, 754s. δ_H (500 MHz, $CDCl_3$) 3.96 (3H, s), 2.28 (3H, s). δ_C (125 MHz, $CDCl_3$) 146.1 (s), 140.7 (s), 127.8 (s), 121.0 (s), 114.6 (s), 36.7 (q), 12.5 (q). MALDI-TOF MS (*m*/*z*): 243 (M^+ + 1, 28%), 242 (M^+, 65), 241 (M^+ − 1, 100), 178 (32), 177 (75). Further elution (*n*-hexane/*t*-BuOMe, 90:10) gave 5,7-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (**7a**) as red needles (17.2 mg, 82%): mp (DSC) onset, 98.2 °C; peak max, 98.6 °C, bp onset, 189.6 °C; peak max, 198.3 °C (from *n*-hexane). R_f 0.32 (*n*-hexane/*t*-BuOMe, 80:20). (Found: C, 40.10; H, 2.69; N, 26.54. $C_7H_6N_4S_2$ requires: C, 39.98; H, 2.88; N, 26.65%.) λ_{max}(DCM) 288 (log ε 3.82), 357 inf (3.60), 377 (3.64), 521 (2.81). ν_{max}/cm^{-1} 2943w (CH_3), 2218m (C≡N), 1504s, 1495m, 1452m, 1377m, 1337w, 1292m, 1209w, 1177w, 1103m, 1065s, 1045m, 1038m, 988w, 912m, 764w, 746m. δ_H (500 MHz, $CDCl_3$) 3.78 (3H, s), 2.19 (3H, s). δ_C (125 MHz, $CDCl_3$) 146.3 (s), 143.2 (s), 126.2 (s), 113.0 (s), 94.5 (s), 35.4 (q), 12.1 (q). MALDI-TOF MS (*m*/*z*): 212 (M^+ + 2, 26%), 211 (M^+ + 1, 81), 210 (M^+, 100), 195 (56).

4.3. One-Pot Transformation of (*Z*)-*N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amines 5 to 5*H*-Pyrazolo-[3,4-*e*][1,2,4]dithiazine-3-carbonitriles 7. *General Procedure.* To a stirred suspension of the appropriate (*Z*)-*N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-1*H*-pyrazol-5-amine **5** (0.2 mmol) in MeCN (4 mL) at ca. 20 °C was added Hünig's base (34.5 μL, 0.2 mmol) followed by diethylamine (63.0 μL, 0.6 mmol). After 25 min stirring, to the mixture was added in one portion concd H_2SO_4 (55 μL, 1 mmol). The mixture was stirred for 5 min and then adsorbed onto silica and chromatographed to give the corresponding 6*H*-pyrazolo-[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitriles **9** and 5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitriles **7**.

4.3.1. 5,7-Dimethyl-5H-pyrazolo[3,4-e][1,2,4]dithiazine-3-carbonitrile (7a). Chromatography eluent: *n*-hexane/*t*-BuOMe, 90:10. Obtained as red needles (31 mg, 74%): mp (DSC) onset, 98.2 °C; peak max, 98.6 °C, bp onset, 189.6 °C; peak max, 198.3 °C (from *n*-hexane). R_f 0.32 (*n*-hexane/*t*-BuOMe, 80:20). Identical to that described above.

4.3.2. 5-Methyl-7-phenyl-5H-pyrazolo[3,4-e][1,2,4]dithiazine-3-carbonitrile (7b). Chromatography eluent: *n*-hexane/*t*-BuOMe, 98:2. Obtained as red needles (41 mg, 75%): mp (DSC) onset, 106.8 °C; peak max, 108.5 °C; decomp. onset, 175.9 °C; peak max, 211.4 °C (from *n*-hexane). R_f 0.38 (*n*-hexane/*t*-BuOMe, 90:10). (Found: C, 52.86; H, 2.89; N, 20.58. $C_{12}H_8N_4S_2$ requires: C, 52.92; H, 2.96; N, 20.57%.) λ_{max}(DCM) 255 (log ε 4.31), 325 inf (3.51), 409 (3.59), 508 (2.77). ν_{max}/cm^{-1} 2945w (CH_3), 2222w (C≡N), 1522m, 1481m, 1454m, 1431m, 1308m, 1204w, 1180w, 1169w, 1074m, 1045m, 1009m, 916w, 868w, 772s, 746m. δ_H (500 MHz, $CDCl_3$) 7.68 (2H, d, *J* = 8.0 Hz), 7.45 (2H, dd, *J* = 7.3, 7.3 Hz), 7.38 (1H, dd, *J* = 7.5, 7.5 Hz), 3.91 (3H, s). δ_C (125 MHz, $CDCl_3$) 146.9 (s), 145.6 (s), 130.8 (s), 128.9 (d), 128.8 (d), 126.7 (d), 126.3 (d), 113.0 (s), 93.8 (s), 35.9 (q). MALDI-TOF MS (*m*/*z*): 274 (M^+ + 2, 15%), 273 (M^+ + 1, 59), 272 (M^+, 100), 257 (69), 168 (7).

4.3.3. 5-Benzyl-7-methyl-5H-pyrazolo[3,4-e][1,2,4]dithiazine-3-carbonitrile (7c). Chromatography eluent: *n*-hexane/*t*-BuOMe, 95:5. Obtained as red oil (45 mg, 78%), (DSC) decomp. onset, 171.8 °C; peak max, 204.1 °C. R_f 0.31 (*n*-hexane/*t*-BuOMe, 90:10). (Found: C, 54.60; H, 3.39; N, 19.54. $C_{13}H_{10}N_4S_2$ requires: C, 54.52; H, 3.52; N,

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19.56%.) λ_{max}(DCM) 295 (log ε 3.68), 357 inf (3.59), 377 (3.63), 522 (2.77). ν_{max}/cm^{-1} 3065w and 3032w (Ar CH), 2928w and 2853w (CH_2 and CH_3), 2220w (C≡N), 1514m, 1497m, 1460m, 1454m, 1441m, 1375w, 1358w, 1314m, 1294m, 1279m, 1227w, 1204w, 1182w, 1144m, 1094m, 1061m, 1030m, 1003w, 918m, 907m, 820w, 758m, 735s. δ_H (500 MHz, $CDCl_3$) 7.35−7.29 (3H, m), 7.24 (2H, d, J = 7.3 Hz), 5.25 (2H, s), 2.20 (3H, s). δ_C (125 MHz, $CDCl_3$) 146.1 (s), 143.8 (s), 135.5 (s), 128.8 (d), 128.2 (d), 127.9 (d), 126.2 (s), 113.1 (s), 95.0 (s), 52.3 (t), 12.3 (q). MALDI-TOF MS (m/z): 288 (M^+ + 2, 63%), 287 (M^+ + 1, 93), 286 (M^+, 100), 253 (36), 245 (12), 195 (12), 182 (22), 104 (7), 91 (98).

*4.3.4. 5-Benzyl-7-phenyl-5H-pyrazolo[3,4-e][1,2,4]dithiazine-3-carbonitrile (**7d**).* Chromatography eluent: *n*-hexane/*t*-BuOMe, 95:5. Obtained as brown needles (59 mg, 85%): mp (DSC) onset, 130.3 °C; peak max, 134.3 °C; decomp. onset, 187.3 °C; peak max, 208.5 °C (from *c*-hexane). R_f 0.52 (*n*-hexane/*t*-BuOMe, 90:10). (Found: C, 61.92; H, 3.62; N, 15.94. $C_{18}H_{12}N_4S_2$ requires: C, 62.05; H, 3.47; N, 16.08%.) λ_{max}(DCM) 253 (log ε 4.32), 305 inf (3.62), 407 (3.62), 520 (2.77). ν_{max}/cm^{-1} 3063w and 3032w (Ar CH), 2976w and 2940w (CH_2), 2222w (C≡N), 1530m, 1495m, 1481m, 1464w, 1452m, 1427m, 1354m, 1331m, 1317m, 1294m, 1283m, 1180m, 1132m, 1067m, 1026w, 1009m, 916w, 907w, 872w, 772s, 731s. δ_H (500 MHz, $CDCl_3$) 7.71 (2H, d, J = 7.0 Hz), 7.44 (2H, dd, J = 7.5, 7.5 Hz), 7.39−7.30 (6H, m), 5.39 (2H, s). δ_C (125 MHz, $CDCl_3$) one C (d) resonance missing 146.6 (s), 146.0 (s), 135.3 (s), 130.8 (s), 128.87 (d), 128.85 (d), 128.3 (d), 127.9 (d), 126.8 (d), 126.2 (s), 113.1 (s), 94.2 (s), 52.8 (t). MALDI-TOF MS (m/z): 350 (M^+ + 2, 36%), 349 (M^+ + 1, 80), 348 (M^+, 100), 315 (11), 257 (14), 245 (30), 90 (80). The dithiazine **7d** coeluted on chromatography with the trithiazepine **9d**; nevertheless, a microanalytically pure sample of compound **7d** was obtained by recrystallization.

*4.3.5. 7-Methyl-5-phenyl-5H-pyrazolo[3,4-e][1,2,4]dithiazine-3-carbonitrile (**7e**).* Chromatography eluent: *n*-hexane/*t*-BuOMe, 95:5. Obtained as brown needles (46 mg, 85%): mp (DSC) onset, 90.2 °C; peak max, 91.4 °C; decomp. onset, 157.2 °C; peak max, 179.8 °C (from *n*-pentane at ca. −20 °C). R_f 0.44 (*n*-hexane/*t*-BuOMe, 90:10). (Found: C, 53.01; H, 2.87; N, 20.56. $C_{12}H_8N_4S_2$ requires: C, 52.92; H, 2.96; N, 20.57%.) λ_{max}(DCM) 239 (log ε 4.24), 307 (3.63), 359 inf (3.60), 401 (3.76), 520 (2.87). ν_{max}/cm^{-1} 3105w, 3082w and 3049w (Ar CH), 2924 (CH_3), 2216w (C≡N), 1591m, 1504s, 1464m, 1435m, 1418m, 1368w, 1352m, 1319w, 1163m, 1107m, 1074m, 1057m, 1024m, 1001w, 964w, 932w, 907m, 854m, 760s, 733s. δ_H (500 MHz, $CDCl_3$) 7.59 (2H, d, J = 8.0 Hz), 7.47 (2H, dd, J = 8.0, 8.0 Hz), 7.37 (1H, dd, J = 7.5, 7.5 Hz), 2.32 (3H, s). δ_C (125 MHz, $CDCl_3$) 146.0 (s), 144.6 (s), 137.6 (s), 129.2 (d), 128.0 (d), 125.4 (s), 122.7 (d), 113.1 (s), 98.1 (s), 12.4 (q). MALDI-TOF MS (m/z): 274 (M^+ + 2, 25%), 273 (M^+ + 1, 100), 272 (M^+, 44), 246 (5), 239 (19), 240 (22), 231 (13), 220 (35), 209 (22), 198 (3), 155 (5).

*4.3.6. 5,7-Diphenyl-5H-pyrazolo[3,4-e][1,2,4]dithiazine-3-carbonitrile (**7f**).* Chromatography eluent: *n*-hexane/*t*-BuOMe, 95:5. Obtained as orange/brown cotton fibers (54 mg, 80%): mp (DSC) onset, 144.7 °C; peak max, 147.0 °C; decomp. onset, 149.2 °C; peak max, 164.2 °C (from *n*-hexane at ca. −20 °C). R_f 0.56 (*n*-hexane/*t*-BuOMe, 90:10). (Found: C, 61.08; H, 2.94; N, 16.57. $C_{17}H_{10}N_4S_2$ requires: C, 61.06; H, 3.01; N, 16.75%.) λ_{max}(DCM) 239 (log ε 4.25), 267 (4.33), 332 inf (3.53), 422 (3.67), 509 inf (2.93). ν_{max}/cm^{-1} 3061w (Ar CH), 2218w (C≡N), 1595m, 1518m, 1499s, 1477m, 1460m, 1454m, 1427m, 1344m, 1319m, 1300m, 1236w, 1202m, 1152m, 1090m, 1072m, 1055m, 1026m, 1003m, 982m, 903m, 835m, 764s, 758s, 731m. δ_H (500 MHz, $CDCl_3$) 7.81 (2H, d, J = 7.0 Hz), 7.71 (2H, d, J = 8.0 Hz), 7.53−7.48 (4H, m), 7.45−7.41 (2H, m). δ_C (125 MHz, $CDCl_3$) 146.7 (s), 146.6 (s), 137.7 (s), 130.6 (s), 129.23 (d), 129.20 (d), 129.0 (d), 128.3 (d), 127.0 (d), 125.4 (s), 123.1 (d), 113.1 (s), 97.3 (s). MALDI-TOF MS (m/z): 336 (M^+ + 2, 22%), 335 (M^+ + 1, 63), 334 (M^+, 100), 301 (12), 282 (13), 271 (3), 231 (36), 198 (3), 155 (4).

*4.3.7. 6,8-Dimethyl-6H-pyrazolo[3,4-f][1,2,3,5]trithiazepine-4-carbonitrile (**9a**).* Chromatography eluent: *n*-hexane/*t*-BuOMe (90:10). Obtained as yellow needles (2.4 mg, 5%): mp (DSC) onset, 66.7 °C; peak max, 71.7 °C; decomp. onset, 166.8 °C; peak max, 185.7 °C (from *n*-pentane at ca. −20 °C). R_f 0.40 (*n*-hexane/*t*-BuOMe, 80:20). Identical to that described above.

*4.3.8. 6-Methyl-8-phenyl-6H-pyrazolo[3,4-f][1,2,3,5]-trithiazepine-4-carbonitrile (**9b**).* Chromatography eluent: *n*-hexane/*t*-BuOMe, 90:10. Obtained as pale yellow needles (3.0 mg, 5%): mp 104−106 °C (from *n*-pentane at ca. −20 °C). R_f 0.40 (*n*-hexane/*t*-BuOMe, 90:10). (Found: C, 47.30; H, 2.54; N, 18.32. $C_{12}H_8N_4S_3$ requires: C, 47.35; H, 2.65; N, 18.41%.) λ_{max}(DCM) 250 (log ε 4.32), 295 inf (3.79), 385 (3.95). ν_{max}/cm^{-1} 3059w (Ar CH), 2947w (CH_3), 2218w (C≡N), 1589m, 1558m, 1506m, 1456m, 1448m, 1433m, 1414m, 1387w, 1341w, 1317m, 1306m, 1200w, 1182w, 1157w, 1146w, 1076m, 1020m, 1003m, 914m, 853w, 770s, 758m. δ_H (500 MHz, $CDCl_3$) 7.68 (2H, d, J = 8.0 Hz), 7.47 (2H, dd, J = 7.5, 7.5 Hz), 7.42 (1H, dd, J = 7.5, 7.5 Hz), 4.08 (3H, s). δ_C (125 MHz, $CDCl_3$) 148.9 (s), 141.1 (s), 131.2 (s), 128.9 (d), 128.7 (d), 128.3 (s), 127.8 (d), 120.5 (s), 114.5 (s), 37.2 (q). MALDI-TOF MS (m/z): 306 (M^+ + 2, 48%), 305 (M^+ + 1, 100), 304 (M^+, 86), 242 (18), 241 (70), 240 (33). Although the compound was obtained microanalytically pure by recrystallization, it was not very stable in solution and afforded a trace of dithiazine **7b**, which was visible in the NMR.

*4.3.9. 6-Benzyl-8-methyl-6H-pyrazolo[3,4-f][1,2,3,5]trithiazepine-4-carbonitrile (**9c**).* Chromatography eluent: *n*-hexane/*t*-BuOMe, 90:10. Obtained as yellow needles (3.8 mg, 6%): mp (DSC) onset, 115.0 °C; peak max, 118.7 °C; decomp. onset, 171.6 °C; peak max, 193.3 °C (from *n*-pentane at ca. −20 °C). R_f 0.52 (*n*-hexane/*t*-BuOMe, 90:10). (Found: C, 48.98; H, 3.06; N, 17.43. $C_{13}H_{10}N_4S_3$ requires: C, 49.04; H, 3.17; N, 17.60%.) λ_{max}(DCM) 303 (log ε 3.76), 370 (3.88), 407 inf (3.57). ν_{max}/cm^{-1} 2212w (C≡N), 1582m, 1558w, 1539w, 1522w, 1506w, 1497m, 1477m, 1454m, 1422m, 1402m, 1360w, 1346w, 1323m, 1296m, 1279w, 1204w, 1152w, 1076m, 1055s, 1028m, 1003m, 947w, 905m, 818w, 795w, 768s, 735s. δ_H (500 MHz, $CDCl_3$) 7.36−7.28 (5H, m), 5.47 (2H, s), 2.29 (3H, s). δ_C (125 MHz, $CDCl_3$) 146.6 (s), 140.2 (s), 136.0 (s), 128.8 (d), 128.13 (d), 128.12 (d), 128.0 (s), 121.4 (s), 114.5 (s), 53.3 (t), 12.7 (q). MALDI-TOF MS (m/z): 320 (M^+ + 2, 78%), 319 (M^+ + 1, 80), 318 (M^+, 28), 310 (7), 286 (18), 278 (6), 256 (40), 255 (100), 91 (86).

4.4. Synthesis of (*Z*)-3-[(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]phenol (10c). To a stirred suspension of 4,5-dichloro-1,2,3-dithiazolium chloride (500 mg, 2.4 mmol) in DCM (10 mL) protected by $CaCl_2$ drying tube at ca. 20 °C was added 3-aminophenol (262 mg, 2.4 mmol) in one portion. After 2 h, to the reaction mixture was added Hünig's base (835 μL, 4.8 mmol). After an additional 1 h, the mixture was adsorbed on silica and chromatographed (DCM) to give unidentified minor red side products. Further elution (DCM/*t*-BuOMe, 95:5) gave (*Z*)-3-[(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)amino]phenol (**10c**) as yellow plates (245 mg, 42%): mp 102−104 °C (from *c*-hexane/1,2-DCE). R_f 0.45 (DCM/*t*-BuOMe, 96:4). (Found: C, 39.19; H, 1.93; N, 11.36. $C_8H_5ClN_2OS_2$ requires: C, 39.27; H, 2.06; N, 11.45%.) λ_{max}(DCM) 377 (log ε 3.74). ν_{max}/cm^{-1} 3242m (OH), 1585s, 1574s, 1518w, 1503w, 1476m, 1462m, 1314m, 1300m, 1281m, 1227m, 1173s, 1136m, 1078m, 997m, 959m, 897s, 866m, 808m, 787m, 754m. δ_H (500 MHz, DMSO-d_6) 9.73 (1H, br s), 7.27 (1H, dd, J = 8.0, 8.0 Hz), 6.65 (1H, dd, J = 8.0, 1.5 Hz), 6.62 (1H, dd, J = 8.0, 1.5 Hz), 6.59 (1H, dd, J = 2.0, 2.0 Hz). δ_C (125 MHz, DMSO-d_6) 159.0 (s), 158.6 (s), 152.1 (s), 146.7 (s), 130.7 (d), 113.2 (d), 109.7 (d), 105.8 (d). m/z (EI) 246 (M^+ + 2, 21%), 244 (M^+, 51), 209 (19), 183 (16), 151 (8), 145 (13), 119 (100), 93 (21), 91 (14), 64 (37).

4.5. One-Pot Transformation of *N*-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-anilines 10 to Benzo[*e*][1,2,4]dithiazine-3-carbonitriles 11. *General Procedure.* To a stirred suspension of the appropriate *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)aniline **10** (0.2 mmol) in MeCN (4 mL) at ca. 20 °C was added Hünig's base (34.5 μL, 0.2 mmol) followed by diethylamine (63.0 μL, 0.6 mmol). After 25 min stirring, to the mixture was added in one portion concd H_2SO_4 (55 μL, 1 mmol). The mixture was stirred for 5 min and then adsorbed on silica and chromatographed to give the corresponding benzo[*e*]-[1,2,4]dithiazine-3-carbonitriles **11** and benzo[*d*]thiazole-2-carbonitriles **12**.

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*4.5.1. 6-Methoxybenzo[e][1,2,4]dithiazine-3-carbonitrile (**11b**).* Chromatography eluent: *n*-hexane/*t*-BuOMe, 90:10. Obtained as red plates (7.6 mg, 17%): mp (DSC) onset, 129.1 °C; peak max, 129.5 °C; decomp. onset, 130.5 °C; peak max, 153.0 °C (from *c*-hexane). R_f 0.71 (*n*-hexane/DCM, 50:50). (Found: C, 48.51; H, 2.73; N, 12.50. $C_9H_6N_2OS_2$ requires: C, 48.63; H, 2.72; N, 12.60%.) λ_{max}(DCM) 258 (log ε 4.13), 279 inf (3.88), 350 (3.56), 481 (2.67). ν_{max}/cm^{-1} 2972w, 2848w, 2228w (C≡N), 1595m, 1557m, 1530m, 1468m, 1437m, 1398w, 1310m, 1277m, 1236s, 1196w, 1165m, 1128m, 1069m, 1057s, 1024m, 951m, 851m, 816s, 754m. δ_H (500 MHz, $CDCl_3$) 7.24−7.22 (1H, m), 6.94−6.92 (2H, m), 3.84 (3H, s). δ_C (125 MHz, $CDCl_3$) 161.0 (s), 145.5 (s), 133.6 (s), 129.7 (d), 117.7 (d), 112.9 (s), 112.5 (d), 109.9 (s), 55.8 (q). MALDI-TOF MS (*m*/*z*): 224 (M^+ + 2, 19%), 223 (M^+ + 1, 64), 222 (M^+, 96), 204 (100).

*4.5.2. 6-Hydroxybenzo[e][1,2,4]dithiazine-3-carbonitrile (**11c**).* Chromatography eluent: DCM. Obtained as red prisms (23 mg, 55%): mp (DSC) onset, 148.2 °C; peak max, 150.6 °C; decomp. onset, 152.9 °C; peak max, 156.7 °C (from $CHCl_3$). R_f 0.60 (DCM/*t*-BuOMe, 96:4). (Found: C, 46.25; H, 1.86; N, 13.33. $C_8H_4N_2OS_2$ requires: C, 46.14; H, 1.94; N, 13.45%.) λ_{max}(DCM) 256 (log ε 3.94), 277 inf (3.69), 346 (3.38), 482 (2.41). ν_{max}/cm^{-1} 3379m (OH), 2241m (C≡N), 1609w, 1560m, 1541m, 1506w, 1470m, 1431m, 1333m, 1290s, 1250m, 1227m, 1217m, 1152s, 1136w, 1126m, 1067m, 1051m, 963m, 878m, 822s, 766m. δ_H (500 MHz, $CDCl_3$) 7.21−7.20 (1H, m), 6.89−6.87 (2H, m), 5.57 (1H, br s). δ_C (125 MHz, $CDCl_3$) 157.2 (s), 145.4 (s), 133.9 (s), 130.0 (d), 118.4 (d), 114.6 (d), 112.8 (s), 110.2 (s). MALDI-TOF MS (*m*/*z*): 210 (M^+ + 2, 17%), 209 (M^+ + 1, 100), 208 (M^+, 22).

*4.5.3. 6-Hydroxy-7-methoxybenzo[e][1,2,4]dithiazine-3-carbonitrile (**11d**).* Chromatography eluent: DCM. Obtained as red needles (33 mg, 70%): mp (DSC) onset, 172.8 °C; peak max, 174.6 °C; decomp. onset, 175.4 °C; peak max, 177.8 °C (from *c*-hexane/DCM). R_f 0.40 (DCM). (Found: C, 45.34; H, 2.46; N, 11.58. $C_9H_6N_2O_2S_2$ requires: C, 45.37; H, 2.54; N, 11.76%.) λ_{max}(DCM) 271 (log ε 4.35), 359 (3.76), 485 (3.20). ν_{max}/cm^{-1} 3372m (OH), 3005w (Ar CH), 2990w, 2945w and 2837w (CH_3), 2239m (C≡N), 1609m, 1562m, 1522m, 1497s, 1462m, 1449m, 1433m, 1342m, 1283s, 1260s, 1225m, 1207m, 1179m, 1171m, 1157m, 1061m, 1051m, 1040m, 1009m, 874s, 812m, 766m. δ_H (500 MHz, $CDCl_3$) 6.98 (1H, s), 6.74 (1H, s), 5.72 (1H, s), 3.96 (3H, s). δ_C (125 MHz, $CDCl_3$) 148.5 (s), 147.0 (s), 139.9 (s), 128.5 (s), 114.5 (d), 113.1 (s), 110.3 (d), 109.7 (s), 56.5 (q). MALDI-TOF MS (*m*/*z*): 240 (M^+ + 2, 26%), 239 (M^+ + 1, 100), 238 (M^+, 63), 220 (30), 212 (10), 206 (22), 205 (12).

*4.5.4. 5-Methoxybenzo[d]thiazole-2-carbonitrile (**12b**).* Chromatography eluent: *n*-hexane/*t*-BuOMe, 90:10. Obtained as colorless needles (3.0 mg, 8%): mp 94−96 °C, lit.[36] 99−100 °C (from *c*-hexane). R_f 0.68 (DCM). λ_{max}(DCM) 287 (log ε 4.05), 295 inf (4.05), 349 (3.62). δ_H (500 MHz, $CDCl_3$) 7.82 (1H, d, *J* = 9.0 Hz), 7.63 (1H, d, *J* = 2.5 Hz), 7.28 (1H, dd, *J* = 9.0, 2.5 Hz), 3.92 (3H, s). δ_C (125 MHz, $CDCl_3$) 160.2 (s), 153.9 (s), 137.1 (s), 127.4 (s), 121.9 (d), 120.1 (d), 113.1 (s), 106.1 (d), 55.8 (q). MALDI-TOF MS (*m*/*z*): 192 (M^+ + 2, 91%), 191 (M^+ + 1, 100).

*4.5.5. 5-Hydroxybenzo[d]thiazole-2-carbonitrile (**12c**).* Chromatography eluent: DCM/*t*-BuOMe, 95:5. Obtained as colorless needles (4.2 mg, 12%): mp (DSC) onset, 192.1 °C; peak max, 193.2 °C, lit.[37] 193.5−194 °C (from *c*-hexane/$CHCl_3$). R_f 0.40 (DCM/*t*-BuOMe, 92:8). λ_{max}(DCM) 285 (log ε 4.06), 295 inf (3.99), 341 (3.61). δ_H (500 MHz, $CDCl_3$) 7.82 (1H, d, *J* = 9.0 Hz), 7.62 (1H, d, *J* = 2.5 Hz), 7.23 (1H, dd, *J* = 9.0, 2.5 Hz), 5.69 (1H, s). δ_C (125 MHz, DMSO-d_6) 158.0 (s), 153.3 (s), 137.1 (s), 125.8 (s), 123.4 (d) 119.7 (d), 113.5 (s), 108.2 (d). MALDI-TOF MS (*m*/*z*): 178 (M^+ + 2, 44%), 177 (M^+ + 1, 100), 164 (11), 159 (38), 151 (53).

*4.5.6. 5-Hydroxy-6-methoxybenzo[d]thiazole-2-carbonitrile (**12d**).* Chromatography eluent: DCM/*t*-BuOMe, 95:5. Obtained as colorless plates (5.4 mg, 13%): mp 173−175 °C (from *c*-hexane/$CHCl_3$). R_f 0.69 (DCM/*t*-BuOMe, 90:10). (Found: C, 52.50; H, 3.01; N, 13.58. $C_9H_6N_2O_2S$ requires: C, 52.42; H, 2.93; N, 13.58%.) λ_{max}(DCM) 266 (log ε 3.76), 312 (4.03), 335 (3.75). ν_{max}/cm^{-1} 3292w (OH), 2226m (C≡N), 1551m, 1485m, 1466w, 1452m, 1423m, 1354w, 1288s, 1234m, 1204m, 1182m, 1128m, 1047m, 1007m, 907w, 856m, 835m, 827m, 777m. δ_H (500 MHz, $CDCl_3$) 7.68 (1H, s), 7.31 (1H, s), 6.01 (1H, br s), 4.04 (3H, s). δ_C (125 MHz, $CDCl_3$) 149.3 (s), 147.5 (s), 147.3 (s), 133.8 (s), 128.0 (s), 113.3 (s), 108.6 (d), 100.9 (d), 56.5 (q). MALDI-TOF MS (*m*/*z*): 208 (M^+ + 2, 8%), 207 (M^+ + 1, 54), 193 (26), 192 (100), 191 (6), 181 (20), 175 (7).

4.6. Transformation of 5,7-Dimethyl-5*H*-pyrazolo[3,4-*e*]-[1,2,4]dithiazine-3-carbonitrile (7a) to 6,8-Dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile (9a). A mixture of 5,7-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (**7a**) (21 mg, 0.1 mmol), S_8 (256 mg, 1 mmol), and DABCO (11.2 mg, 0.1 mmol) in PhCl (2 mL) was heated in a preheated Wood's metal bath at ca. 100 °C. After 6 min, the reaction was cooled to ca. 0 °C, filtered, and washed with *n*-hexane to remove excess sulfur. The filtrate was poured onto packed silica and chromatographed (*n*-hexane/*t*-BuOMe, 90:10) to give 6,8-dimethyl-6*H*-pyrazolo[3,4-*f*]-[1,2,3,5]trithiazepine-4-carbonitrile (**9a**) (6.3 mg, 26%) as yellow needles: mp (DSC) onset, 66.7 °C; peak max, 71.7 °C; decomp. onset, 166.8 °C; peak max, 185.7 °C (from *n*-pentane at ca. −20 °C). R_f 0.40 (*n*-hexane/*t*-BuOMe, 80:20). Identical to that described above. Further elution (*n*-hexane/*t*-BuOMe, 90:10) gave unreacted 5,7-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (**7a**) as red needles (9.5 mg, 45%): mp (DSC) onset, 98.2 °C; peak max, 98.6 °C, bp onset, 189.6 °C; peak max, 198.3 °C (from *n*-hexane). R_f 0.32 (*n*-hexane/*t*-BuOMe, 80:20). Identical to that described above.

4.7. Transformation of 5,7-Dimethyl-5*H*-pyrazolo[3,4-*e*]-[1,2,4]dithiazine-3-carbonitrile (7a) to 5,7-Dimethyl-5*H*-[1,2,3]-dithiazolo[4,5-*b*]pyrazolo[3,4-*e*][1,4]thiazine (13). A mixture of 5,7-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile (**7a**) (21 mg, 0.1 mmol), S_8 (256 mg, 1.0 mmol), and DABCO (11.2 mg, 0.1 mmol) in PhCl (2 mL) was heated at ca. 100 °C. After 16 h, the reaction was cooled to ca. 0 °C, filtered, and washed with DCM to remove excess sulfur. The filtrate was adsorbed onto silica and chromatographed (*n*-hexane) to give sulfur. Further elution (DCM) gave traces of 6,8-dimethyl-6*H*-pyrazolo[3,4-*f*][1,2,3,5]trithiazepine-4-carbonitrile (**9a**) and 5,7-dimethyl-5*H*-pyrazolo[3,4-*e*][1,2,4]-dithiazine-3-carbonitrile (**7a**). Further elution (DCM) gave 1,3-dimethyl-1*H*-pyrazolo[3,4-*d*]thiazole-5-carbonitrile (**6a**) as colorless needles (3.0 mg, 17%): mp 99−100.5 °C, lit.[18] 99−100.5 °C (from *c*-hexane). R_f 0.20 (DCM). δ_H (500 MHz, $CDCl_3$) 4.07 (3H, s), 2.47 (3H, s). *m*/*z* (EI) 178 (M^+, 100%), 163 (15), 85 (94), 70 (86), 58 (8). Identical to an authentic sample. Further elution (DCM) gave 5,7-dimethyl-5*H*-[1,2,3]dithiazolo[4,5-*b*]pyrazolo[3,4-*e*][1,4]thiazine (**13**) (5.5 mg, 23%) as orange needles: mp (DSC) onset, 186.6 °C; peak max, 187.6 °C (from *c*-hexane). R_f 0.24 (*n*-hexane/*t*-BuOMe, 80:20). (Found: C, 34.58; H, 2.39; N, 22.98. $C_7H_6N_4S_3$ requires: C, 34.69; H, 2.50; N, 23.12%.) λ_{max}(DCM) 275 (log ε 4.19), 347 (3.20), 359 inf (3.17), 436 inf (3.62), 457 inf (3.77), 480 (3.84), 505 inf (3.70). ν_{max}/cm^{-1} 2947w and 2918w (CH_3), 1508m, 1504m, 1474m, 1454m, 1369m, 1358m, 1288m, 1101m, 1057m, 989w, 945m, 854m, 735s. δ_H (500 MHz, $CDCl_3$) 3.71 (3H, s), 2.08 (3H, s). δ_C (125 MHz, $CDCl_3$) 171.0 (s), 148.9 (s), 141.1 (s), 140.9 (s), 91.0 (s), 34.2 (q), 12.0 (q). MALDI-TOF MS (*m*/*z*): 244 (M^+ + 2, 15%), 243 (M^+ + 1, 40), 242 (M^+, 100).

4.8. Thermolysis of 5*H*-Pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitriles 7. *General Procedure.* A stirred solution of the appropriate 5*H*-pyrazolo[3,4-*e*][1,2,4]dithiazine-3-carbonitrile **7** (0.1 mmol) in Ph_2O (1 mL) was heated at ca. 250 °C. After consumption of the starting material (by TLC) the mixture was adsorbed onto silica and chromatographed.

*4.8.1. 1,3-Dimethyl-1H-pyrazolo[3,4-d]thiazole-5-carbonitrile (**6a**).* Chromatography eluent: DCM/*t*-BuOMe, 90:10. Obtained as colorless needles (17.8 mg, 100%): mp 99−100.5 °C, lit.[18] 99−100.5 °C (from *c*-hexane). R_f 0.20 (DCM). δ_H (500 MHz, $CDCl_3$) 4.07 (3H, s), 2.47 (3H, s). *m*/*z* (EI) 178 (M^+, 100%), 163 (15), 85 (94), 70 (86), 58 (8). Identical to that described above.

*4.8.2. 1-Methyl-3-phenyl-1H-pyrazolo[3,4-d]thiazole-5-carbonitrile (**6b**).* Chromatography eluent: DCM. Obtained as colorless needles (22.8 mg, 95%): mp (DSC) onset, 170.5 °C; peak max, 171.3 °C (from *c*-hexane). R_f 0.53 (DCM). δ_H (500 MHz, $CDCl_3$) 7.80 (2H,

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d, J = 7.0 Hz), 7.50 (2H, dd, J = 7.5, 7.5 Hz), 7.40 (1H, dd, J = 7.3, 7.3 Hz), 4.21 (3H, s). MALDI-TOF MS (m/z): 240 (M^+, 100). Identical to an authentic sample.[18]

4.8.3. 1-Benzyl-3-methyl-1H-pyrazolo[3,4-d]thiazole-5-carbonitrile (6c). Chromatography eluent: DCM. Obtained as colorless prisms (24.1 mg, 95%): mp 91−93 °C (from *n*-pentane at ca. −20 °C). R_f 0.56 (DCM). δ_H (500 MHz, DMSO-d_6) 7.34−7.25 (5H, m), 5.54 (2H, s), 2.42 (3H, s). MALDI-TOF MS (m/z): 255 (M^+ + 1, 100), 242 (15), 91 (55). Identical to an authentic sample.[18]

4.8.4. 1-Benzyl-3-phenyl-1H-pyrazolo[3,4-d]thiazole-5-carbonitrile (6d). Chromatography eluent: *n*-hexane/DCM, 50:50. Obtained as beige needles (29.7, 94%): mp 113.5−114.5 °C (from *c*-hexane). R_f 0.50 (*n*-hexane/DCM, 50:50). δ_H (500 MHz, $CDCl_3$) 7.82 (2H, d, J = 7.0 Hz), 7.49 (2H, dd, J = 7.8, 7.8 Hz), 7.44−7.38 (3H, m), 7.37−7.29 (3H, m), 5.66 (2H, s). MALDI-TOF MS (m/z): 317 (M^+ + 1, 100%), 91 (90). Identical to an authentic sample.[18]

4.8.5. 3-Methyl-1-phenyl-1H-pyrazolo[3,4-d]thiazole-5-carbonitrile (6e). Chromatography eluent: *n*-hexane/DCM, 50:50. Obtained as beige plates (24 mg, 100%): mp 127−128.5 °C (from *c*-hexane). R_f 0.50 (*n*-hexane/DCM, 50:50). δ_H (500 MHz, $CDCl_3$) 8.12 (2H, d, J = 8.0 Hz), 7.51 (2H, dd, J = 8.0, 8.0 Hz), 7.31 (1H, dd, J = 7.3, 7.3 Hz), 2.59 (3H, s). MALDI-TOF MS (m/z): 241 (M^+ + 1, 100%), 205 (18). Identical to an authentic sample.[18]

4.8.6. 1,3-Diphenyl-1H-pyrazolo[3,4-d]thiazole-5-carbonitrile (6f). Chromatography eluent: *n*-hexane/DCM, 60:40). Obtained as yellow needles (30 mg, 100%): mp (DSC) onset, 185.2 °C; peak max, 185.6 °C (from *c*-hexane). R_f 0.46 (*n*-hexane/DCM, 70:30). δ_H (500 MHz, $CDCl_3$) 8.26 (2H, dd, J = 8.5, 1.0 Hz), 7.93 (2H, dd, J = 8.0, 1.0 Hz), 7.58−7.53 (4H, m), 7.46 (1H, dd, J = 7.3, 7.3 Hz), 7.36 (1H, dd, J = 7.5, 7.5 Hz). MALDI-TOF MS (m/z): 303 (M^+ + 1, 92%), 302 (M^+, 100). Identical to an authentic sample.[18]

4.9. Transformation of (*E*)-2-[(Diethylamino)disulfanyl-2-(1,3-dimethyl-1*H*-pyrazol-5-yl)imino]acetonitrile (8a) to 4,6,10,12-Tetramethyl-6*H*-pyrazolo[3,4-*f*]pyrazolo[3′,4′:4,5]-pyrimido[6,1-*d*][1,2,3,5]trithiazepine-8,12*b*(10*H*)-dicarbonitrile (19). A stirred solution of (*Z*)-2-[(diethylamino)disulfanyl-2-(1,3-dimethyl-1*H*-pyrazol-5-yl)imino]acetonitrile (**8a**) (56.7 mg, 0.2 mmol) in MeCN (4 mL) was heated at ca. 82 °C for 1.25 h. The mixture was left to cool at ca. 20 °C, diluted with *n*-hexane, and poured onto a packed silica column. Chromatography (*n*-hexane) gave sulfur and $Et_2NS_xEt_2N$. Further elution (*n*-hexane/acetone, 90:10) gave 4,6,10,12-tetramethyl-6*H*-pyrazolo[3,4-*f*]pyrazolo[3′,4′:4,5]pyrimido-[6,1-*d*][1,2,3,5]trithiazepine-8,12b-(10*H*)-dicarbonitrile (**19**) (26.0 mg, 67%) as colorless prisms: mp (DSC) onset, 209.7 °C; peak max, 211.4 °C; decomp. onset, 213.5 °C; peak max, 215.2 °C (from *c*-hexane). R_f 0.60 (DCM/*t*-BuOMe, 96:4). (Found: C, 43.22; H, 3.14; N, 28.77. $C_{14}H_{12}N_8S_3$ requires: C, 43.28; H, 3.11; N, 28.84%.) λ_{max}(DCM) 236 (log ε 4.14), 336 (3.82). ν_{max}/cm^{-1} 2995w, 2949w and 2926w (CH_3), 2245w (C≡N), 1578s, 1555m, 1522m, 1493m, 1452m, 1437m, 1412m, 1377m, 1364m, 1287s, 1242m 1186m, 1113m, 1096m, 1063w, 1040m, 1009w, 989m, 955m, 912m, 847m, 799m, 752s. δ_H (500 MHz, $CDCl_3$) 3.89 (3H, s), 3.80 (3H, s), 2.37 (3H, s), 2.35 (3H, s). δ_C (125 MHz, $CDCl_3$) 149.5 (s), 143.6 (s), 140.5 (s), 138.5 (s), 128.6 (s), 119.4 (s), 111.1 (s), 110.3 (s), 94.5 (s), 63.8 (s), 36.2 (q), 34.6 (q), 12.6 (q), 12.0 (q). MALDI-TOF MS (m/z): 390 (M^+ + 2, 15%), 389 (M^+ + 1, 22), 388 (M^+, 86%), 377 (11), 368 (27), 323 (100), 153 (7).

4.10. X-ray Crystallographic Studies. Data were collected on an Oxford-Diffraction Supernova diffractometer, equipped with a CCD area detector utilizing Mo Kα radiation (λ = 0.71073 Å). A suitable crystal was attached to glass fibers using paratone-N oil and transferred to a goniostat, where it were cooled for data collection. Unit cell dimensions were determined and refined by using 1396 ($3.83 \le \theta \le 29.44°$) reflections for **7a**, 1925 ($3.61 \le \theta \le 28.38°$) reflections for **8a**, 1339 ($3.99 \le \theta \le 28.13°$) reflections for **9a**, 1061 ($3.73 \le \theta \le 27.93°$) reflections for **13**, and 2589 ($3.90 \le \theta \le 28.84°$) reflections for **19**. Empirical absorption corrections (multiscan based on symmetry-related measurements) were applied using CrysAlis RED software.[38] The structure was solved by direct methods using SIR92[39] and refined on F^2 using full-matrix least-squares with SHELXL97.[40] The following software packages were used: CrysAlis CCD[38] for data collection, CrysAlis RED[38] for cell refinement and data reduction, WINGX for geometric calculations,[41] and DIAMOND[42] for molecular graphics. The non-H atoms were treated anisotropically. All hydrogen atoms were placed in calculated, ideal positions and refined as riding on their respective carbon atoms.

4.10.1. Crystal Refinement Data for Compound 7a. $C_7H_6N_4S_2$, M = 210.30, monoclinic, space group $P2_1/c$, a = 3.9220(3) Å, b = 16.8520(14) Å, c = 13.4334(11) Å, α = 90(3)°, β = 94.338(8)°, γ = 90°, V = 885.32(12) Å^3, Z = 4, T = 100(2) K, ρ_{calcd} = 1.578 g cm^{-3}, $2\theta_{max}$ = 25. Refinement of 118 parameters on 1565 independent reflections out of 2092 measured reflections (R_{int} = 0.0440) led to R_1 = 0.0392 [$I > 2s(I)$], wR_2 = 0.1006 (all data), and S = 1.052, with the largest difference peak and hole of 0.403 and −0.371 e^{-3}, respectively.

4.10.2. Crystal Refinement Data for Compound 8a. $C_{11}H_{17}N_5S_2$, M = 283.44, triclinic, space group $P\bar{1}$, a = 7.9239(7) Å, b = 8.1833(6) Å, c = 11.9333(11) Å, α = 86.140(7)°, β = 78.319(8)°, γ = 65.964(8)°, V = 691.97(11) Å^3, Z = 2, T = 100(3) K, ρ_{calcd} = 1.360 g cm^{-3}, $2\theta_{max}$ = 25. Refinement of 163 parameters on 2445 independent reflections out of 4661 measured reflections (R_{int} = 0.0540) led to R_1 = 0.0503 [$I > 2s(I)$], wR_2 = 0.1466 (all data), and S = 1.076, with the largest difference peak and hole of 0.493 and −0.566 e^{-3}, respectively.

4.10.3. Crystal Refinement Data for Compound 9a. $C_7H_6N_4S_3$, M = 242.32, triclinic, space group $P\bar{1}$, a = 7.8861(6) Å, b = 8.2893(10) Å, c = 8.3398(9) Å, α = 113.381(11)°, β = 99.470(8)°, γ = 97.678(8)°, V = 481.53(10) Å^3, Z = 2, T = 100(2) K, ρ_{calcd} = 1.671 g cm^{-3}, $2\theta_{max}$ = 25. Refinement of 128 parameters on 1697 independent reflections out of 2833 measured reflections (R_{int} = 0.0343) led to R_1 = 0.0442 [$I > 2s(I)$], wR_2 = 0.1059 (all data), and S = 1.036, with the largest difference peak and hole of 0.418 and −0.395 e^{-3}, respectively.

4.10.4. Crystal Refinement Data for Compound 13. $C_7H_6N_4S_3$, M = 242.32, monoclinic, space group $P2_1$, a = 3.8380(4) Å, b = 7.3609(8) Å, c = 16.2830(17) Å, α = 90°, β = 92.324(10)°, γ = 90°, V = 459.64(8) Å^3, Z = 2, T = 100(2) K, ρ_{calcd} = 1.751 g cm^{-3}, $2\theta_{max}$ = 25. Refinement of 127 parameters on 1131 independent reflections out of 1598 measured reflections (R_{int} = 0.0304) led to R_1 = 0.0432 [$I > 2s(I)$], wR_2 = 0.1051 (all data), and S = 1.062, with the largest difference peak and hole of 0.433 and −0.353 e^{-3}, respectively.

4.10.5. Crystal Refinement Data for Compound 19. $C_{14}H_{12}N_8S_3$, M = 388.53, monoclinic, space group $P2_1/c$, a = 9.7319(4) Å, b = 18.6419(9) Å, c = 9.2096(5) Å, α = 90°, β = 94.930(4)°, γ = 90°, V = 1664.64(14) Å^3, Z = 4, T = 100(2) K, ρ_{calcd} = 1.550 g cm^{-3}, $2\theta_{max}$ = 25. Refinement of 226 parameters on 2928 independent reflections out of 3538 measured reflections (R_{int} = 0.0322) led to R_1 = 0.0438 [$I > 2s(I)$], wR_2 = 0.1222 (all data), and S = 1.062, with the largest difference peak and hole of 0.644 and −0.624 e^{-3}, respectively.

■ ASSOCIATED CONTENT

Supporting Information

Structure elucidation discussions, and ellipsoid representations of the crystal structures for compounds **7a**, **8a**, **9a**, **13**, and **19**. Extended discussion on optimizing the conversion of **5a** into **8a**, **8a** into **7a**, and **5a** into **7a**. Copies of 1D ^{1}H and ^{13}C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data for compounds **7a**, **8a**, **9a**, **13**, and **19** has been deposited with the Cambridge Crystallographic Data Centre with deposit nos. CCDC 1013809, 1013810, 1017374, 1017375, and 1013811, respectively. This data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +441223336033; e-mail: deposit@ccdc.cam.ac.uk).

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to the memory of Professor Charles W. Rees, who passed away on September 21st, 2006.

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