

Article

A Qualitative Comparison of the Reactivities of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine and 4,5-Dichloro-1,2,3-dithiazolium Chloride

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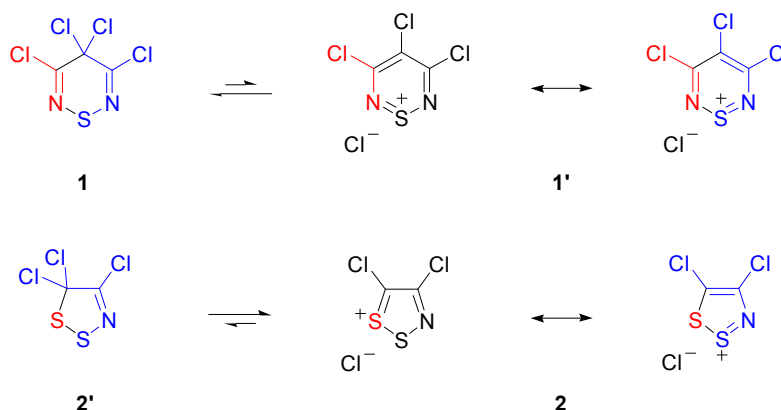
Abstract: The high yielding transformations of 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine into 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-one (up to 85%) and 2-(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)malononitrile (up to 83%) have been investigated and compared to the analogous transformations of the closely-related 4,5-dichloro-1,2,3-dithiazolium chloride (Appel's salt) into 4-chloro-5*H*-1,2,3-dithiazol-5-one and 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)malononitrile. Furthermore, cyclocondensation of 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine with 2-aminophenol and 1,2-benzenediamines gave fused 4*H*-1,2,6-thiadiazines in 68%–85% yields.

Keywords: heterocycle; 1,2,6-thiadiazines; Appel's salt; 1,2,3-dithiazoles

1. Introduction

3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**), which possesses a reactive geminal dichloromethylene, is related to highly-electrophilic 4,5-dichloro-1,2,3-dithiazolium chloride (**2**) (Appel's salt), in that substitution of the S-1 sulfur by a Cl–C=N unit affords 3,4,5-trichloro-1,2,6-thiadiazinium chloride (**1'**), the ionic form of **1** (Scheme 1). The late C. W. Rees recognized that the structural and electronic similarities implied that the C-4 position of tetrachlorothiadiazine **1** and the C-5 position of Appel's salt **2** could have similar chemical reactivities. Both of these compounds are useful and attractive heterocycles;

however, considerably more work has been reported for Appel's salt **2**, presumably owing to its more facile synthesis.



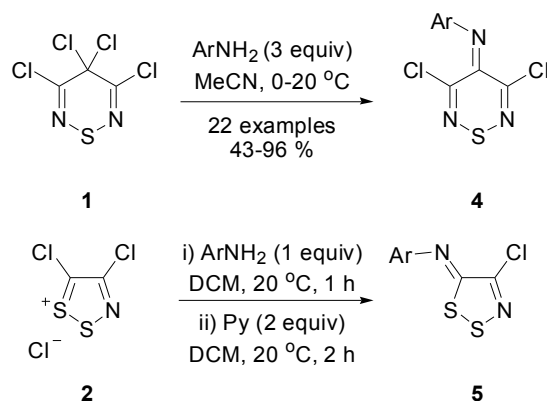
Scheme 1. Comparison of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**) with 4,5-dichloro-1,2,3-dithiazolium chloride (**2**).

Non-oxidized 4H-1,2,6-thiadiazines are rare, and accounts of their chemistry and applications are few. Mono-5-substituted-4H-1,2,6-thiadiazines have been investigated as plant antifungals [1–5], and to the best of our knowledge, these studies were not expanded. Furthermore, fused analogues were studied as examples of “extreme quinoids” that have an ambiguous aromatic character [6], while others displayed unusual liquid crystalline properties or behaved as near-infrared dyes [7,8]. Moreover, selected 4H-1,2,6-thiadiazines have been proposed as radical anion precursors for molecule-based magnetic and conducting functional materials [9]. 4H-1,2,6-Thiadiazin-4-one containing small molecules have been investigated as efficient electron donors in solution-processed bulk heterojunction solar cells [10], while in an effort to understand their optical properties, key 4H-1,2,6-thiadiazines have been characterized by resonance Raman (RR), absorption (UV-VIS) and photoluminescence (PL) spectroscopies [11]. For these potential applications to become reality, the chemistry of 4H-1,2,6-thiadiazines needs to be further developed. To date, the most commonly used non-S-oxidized 4H-1,2,6-thiadiazine scaffold is 3,5-dichloro-4H-1,2,6-thiadiazin-4-one (**3**), which is a precursor to many thiadiazine derivatives, via palladium-catalyzed C-C coupling reactions, such as Stille and Suzuki-Miyaura couplings, to give various 3,5-di(het)aryl substituted systems [12–14] and reactions with amines to give mono-, or 3,5-diamino-substituted systems [15], or polycyclic systems [16].

Appel's salt **2**, discovered in 1985, is readily prepared from chloroacetonitrile and disulfur dichloride [17] and has since found numerous uses as a scaffold for the synthesis of 1,2,3-dithiazole derivatives [18–21]. Dithiazolium **2** exists as a salt and not in the covalent form **2'**, and it is a planar and 6 π aromatic system, although worthy of note is the 5,5-difluoro analogue, which is a non-ionic covalent bound molecule that can be distilled and isolated as an oil [17]. The chemistry of the dithiazolium **2** is governed by the electrophilicity of the C-5 carbon, and it readily reacts with nucleophiles to give neutral 5H-1,2,3-dithiazoles.

Bearing in mind the similarities of the two reagents thiadiazine **1** and Appel's salt **2**, we began an investigation to compare their reactions with simple nucleophiles. Recently, the synthesis of *N*-aryl-3,5-dichloro-4H-1,2,6-thiadiazin-4-imines (**4**) from 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**) [22], by a simple reaction with aniline was investigated. This condensation is very similar to the reaction of anilines with Appel's salt **2** that gives (*Z*)-*N*-aryl-4-chloro-5H-1,2,3-dithiazol-5-imines **5** (Scheme 2) [23].

We now report the reactivity of thiadiazine **1** with three different types of nucleophiles: water, malononitrile and aromatic bisnucleophiles.

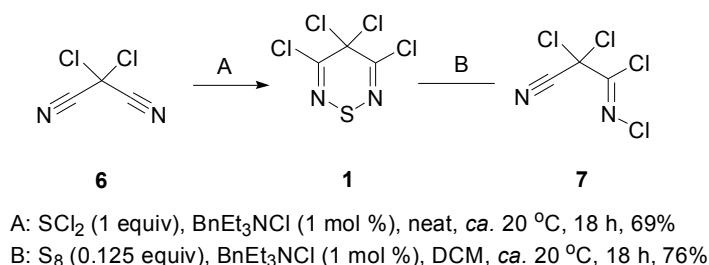


Scheme 2. Synthesis of synthesis of *N*-aryl-3,5-dichloro-4H-1,2,6-thiadiazin-4-imines (**4**) and (*Z*)-*N*-aryl-4-chloro-5H-1,2,3-dithiazol-5-imines (**5**).

2. Results and Discussion

2.1. Preparation of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**)

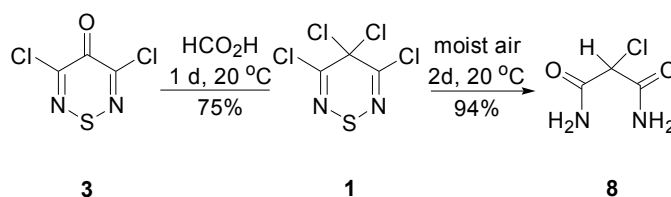
Two methods exist in the literature for the preparation of the tetrachlorothiadiazine **1**: the reaction of dichloromalononitrile (**6**) and SCl₂ [15] and the reaction of *N*-2,2-trichloro-2-cyanoacetimidoyl chloride (**7**) [24] with elemental sulfur. In our hands, both reactions worked well; however, the second method was preferred, as it gave better yields and avoided the use of the toxic and hard to access SCl₂ (Scheme 3). Compound **7**, even though it looks very reactive, was easy to prepare and isolate and can be stored for up to six months at 0 °C. Moreover, the two reports on the isolation of tetrachlorothiadiazine **1** gave conflicting distillation data for the product (100 °C, 8 mbar [25] vs. 90 °C, 4 mbar [26]). In our hands, the thiadiazine **1** distilled nicely at (90 °C, 30 mbar) as a pale yellow oil that crystallized on cooling to −20 °C [mp (DSC) onset: 10.3 °C, peak max: 12.8 °C] and can be stored for several months at −40 °C.



Scheme 3. Synthesis of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**).

3,5-Dichloro-4H-1,2,6-thiadiazin-4-one (**3**) can be prepared from the reaction of glacial formic acid with 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**) [15]. In our hands, this transformation was sensitive to the quality of the formic acid used as both a solvent and reagent. Interestingly, no other chemistry has been reported for tetrachlorothiadiazine **1** apart from this reaction and its degradation in moist air

to give 2-chloromalonamide (**8**) (Scheme 4) [26]. As such, we reinvestigated the transformation of tetrachlorothiadiazone **1** into the thiadiazinone **3** (Section 2.2.).



Scheme 4. Known reactions of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**).

Comparing the syntheses of tetrachlorothiadiazone **1** with dithiazolium **2**, it was clear that both required similarly hazardous reagents for their preparations. The synthesis of dithiazolium **2**, however, was clearly easier, as it required only commercially-available chloroacetonitrile and disulfur dichloride and can be isolated as a salt by simple filtration. On the other hand, the synthesis of the thiadiazine **1** required the use of chlorine gas to prepare the less readily-available dichloromalononitrile and SCl₂ reagents, and the product **1** was isolated by vacuum distillation.

2.2. Preparation of the Thiadiazinone **3** and Dithiazolone **9**

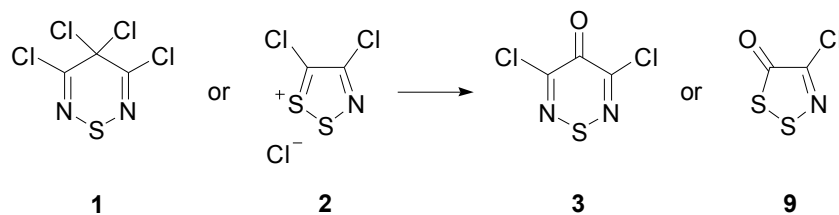
Both the covalent thiadiazine **1** and the ionic 1,2,3-dithiazolium **2** are hydrolytically unstable, reacting with water or even in moist air. However, while the degradation of dithiazolium **2** in moist air gives a brown mass from which the dithiazolone **9** can be isolated by sublimation [17], the analogous degradation of tetrachlorothiadiazone **1** leads to ring cleavage to afford 2-chloromalonamide (**8**) (Scheme 4) [26].

Several improved methods are known for the transformation of Appel's salt **2** to dithiazolone **9** [17,27], but only details of the formic acid-induced reaction have been reported for the hydrolysis of the tetrachlorothiadiazone **1** [1,2,15]. As such, we investigated other routes to synthesize the two ketones **3** and **9**.

The hydrolytic conditions investigated included treatment with formic acid, acetic acid, sodium and silver nitrates and DMSO (Table 1). The highest yielding (85%) and cleanest reaction conditions for the hydrolysis of the tetrachlorothiadiazone **1** into the thiadiazinone **3** involved the use of AgNO₃ in MeCN (Table 1, Entry 6), while for the hydrolysis of Appel's salt **2** to dithiazolone **9**, the cleanest conditions were using neat glacial formic acid (Table 1, Entry 1; 89%). While most procedures worked equally well for both transformations, significant differences in behavior were also observed.

The reaction of tetrachlorothiadiazone **1** with glacial formic acid (98% purity) gave the thiadiazinone **3** in a reasonable 75% yield, but the use of technical-grade formic acid (85% purity), containing *ca.* 15% water, led to degradation of the starting material, affording only a trace of 2-chloromalonamide (<1%). In contrast, Appel's salt **2** was less sensitive to the presence of water in the formic acid and with the respective reactions gave dithiazolone **9** in 89% and 71% yields (Table 1, Entries 1 and 2).

Moreover, the classical reaction of Appel's salt **2** with NaNO₃ (1 equiv) in dichloromethane (DCM), at *ca.* 20 °C, to give dithiazolone **9** in a 72% yield [17] failed to give any product with the tetrachlorothiadiazone **1**; however, when DCM was replaced by MeCN, the desired thiadiazinone **3** was obtained in a 71%–72% yield (Table 1, Entries 4 and 5). Presumably, the more polar MeCN encouraged the equilibrium between the covalent and ionic forms of thiadiazine **1** to shift favorably towards the latter.

Table 1. Hydrolysis of tetrachlorothiadiazone **1** and Appel's salt **2** to thiadiazinone **3** and dithiazolone **9**, respectively.

Entry	Conditions ^a	Product Yields and Reaction Times
1	HCO ₂ H (98%) neat	3 (75%), 24 h 9 (89%), 2 h
2	HCO ₂ H (85%) ^b neat	3 (0%), ^c 18 h 9 (72%), 1 h
3	AcOH neat	3 (74%), 48 h 9 (60%), 2 h
4	NaNO ₃ (1 equiv), DCM	3 (nr), ^d 18 h 9 (72%), 18 h
5	NaNO ₃ (1 equiv), MeCN	3 (71%), 1.5 h 9 (77%), 18 h
6	AgNO ₃ (1 equiv), MeCN	3 (85%), 0.5 h 9 (72%), 1 min
7	Ag ₂ SO ₄ (0.5 equiv), MeCN	3 (77%), 4 h 9 (73%), 24 h
8	H ₂ O (1 equiv), DMSO (1 mol %), MeCN	3 (0%), ^c 20 h 9 (86%), 1 h
9	DMSO (1 equiv), MeCN	3 (31%), 20 h 9 (83%), 1.5 h
10	DMSO neat	3 (45%), 1 h 9 (50%), 15 min

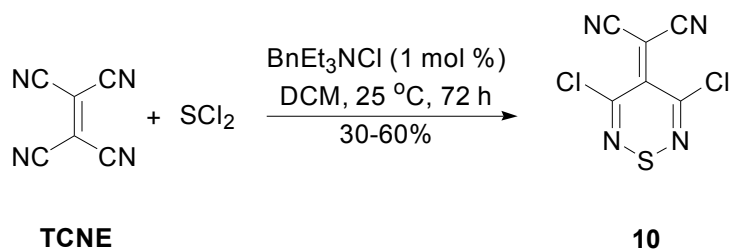
^a All reactions were performed at 20 °C. ^b Technical grade formic acid, contains 15% H₂O. ^c Degradation to chloromalonamide **8**. ^d nr = no reaction.

Finally, Appel's salt **2** can react with H₂O (1 equiv) in the presence of catalytic DMSO (Table 1, Entry 8) [27]; however, under these conditions, thiadiazine **1** gave only a trace of the desired ketone **3** (Table 1, Entry 8).

This study showed that the tetrachlorothiadiazone **1** and Appel's salt **2** have similar reactivity to many of the investigated reagents, indicating that both compounds, despite having a different form (covalent vs. ionic) are similarly electrophilic. However, thiadiazine **1**, which is non-aromatic, is more sensitive to the presence of water in the reaction conditions.

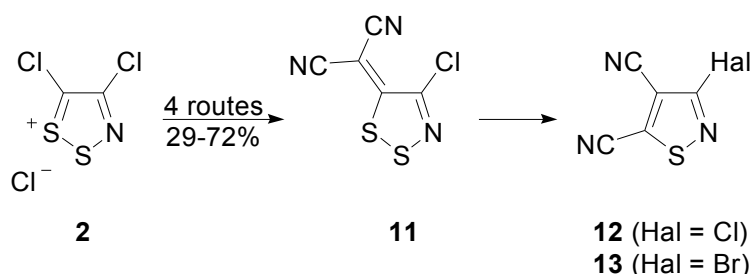
2.3. Preparation of Ylidenemalononitriles **10** and **11**

The ylidenemalononitriles derived from tetrachlorothiadiazone **1**, and Appel's salt **2**, 2-(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)malononitrile (**10**) and 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)malononitrile (**11**), respectively, are both known and are useful heterocycles. The ylidenemalononitrile **10** has been used for the synthesis of other thiadiazine derivatives, such as furo- [28] and pyrrolo-fused thiadiazines [16,28,29] (Scheme 5), while (1,2,6-thiadiazinylidene)malononitriles are desired as possible electron acceptors for organic photovoltaic (OPV) devices [11,30]. Interestingly, the ylidenemalononitrile **10** could not be prepared from the Knoevenagel condensation of the thiadiazinone **3** with malononitrile, but was accessible from the reaction of expensive tetracyanoethene (TCNE) with SCl₂. The reaction produced several minor side products and required chromatography to isolate the desired ylidene **10** in variable yields (30%–60%) [31]. These complications prevented scaling up the reaction and limited the supply of this useful ylidenemalononitrile.



Scheme 5. Preparation of the ylidene malononitrile **10** from tetracyanoethene (TCNE) and SCl_2 .

2-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)malononitrile (**11**) is a useful starting material for difficult to access 3-chloroisothiazole-4,5-dicarbonitrile (**12**) [32,33] and 3-bromoisothiazole-4,5-dicarbonitrile (**13**) (Scheme 6) [33,34]. Its preparation starting from Appel's salt **2** has been thoroughly investigated, and several syntheses have been reported, using malononitrile [32], tetracyanoethylene oxide (TCNEO) [32,35], halo-substituted malononitriles [34] and dimethylsulfonium dicyano-methylide [36].

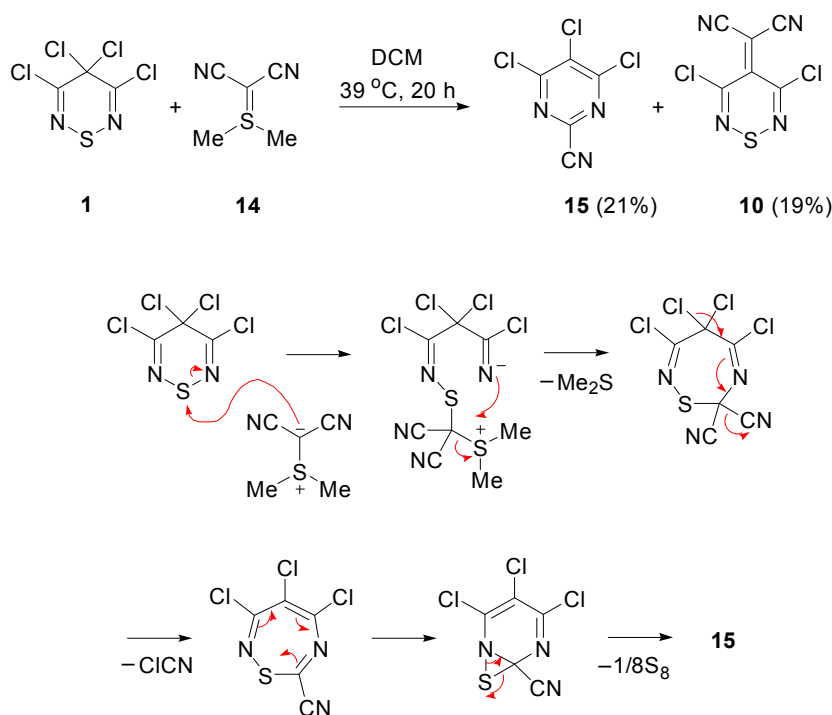


Scheme 6. Synthesis of 2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)malononitrile (**11**) from Appel's salt **2**. Structures of isothiazoles **12** and **13** derived from **11**.

In light of the similarities between the reactivity of tetrachlorothiadiazone **1** and Appel's salt **2**, the transformation of **1** into the ylidene malononitrile **10** was explored: while the reaction of Appel's salt **2** with TCNEO (1 equiv) in PhMe heated at reflux gave the ylidene **11** in a 55% yield [32], under these reaction conditions, the tetrachlorothiadiazone **1** gave only a complex mixture of products containing a trace of the desired ylidene malononitrile **10** by TLC. Similarly, while the reaction of dimethylsulfonium dicyanomethylide **14** with Appel's salt **2** [36] affords the ylidene **11** in medium to good yields (29%–72%) along with other side products, the analogous reaction of tetrachlorothiadiazone **1** with dicyanomethylide **14** was less effective, giving only a low 19% yield of ylidene **10** as the only product. Interestingly, performing the reaction at *ca.* 39 °C gave surprisingly a mixture of 4,5,6-trichloropyrimidine-2-carbonitrile (**15**) and the ylidene **10** in 21% and 19% yields, respectively (Scheme 7). The formation of the pyrimidine **15** from this reaction was intriguing, as this heterocycle was first observed in the abovementioned reaction of TCNE with SCl_2 [31]. A tentative mechanism for the formation of pyrimidine **15** is proposed below (Scheme 7).

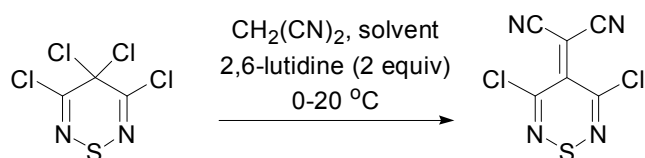
Despite the fact that the simple pyridine-mediated condensation of malononitrile with Appel's salt **2** gives only a low yield of ylidene malononitrile **11** (40%) [32], when the tetrachlorothiadiazone **1** was treated with malononitrile (1.1 equiv) and 2,6-lutidine (2 equiv) in dry DCM, at *ca.* 20 °C, the starting material was consumed quickly (TLC, 10 min) to give the ylidene malononitrile **10** in a 78% yield (Table 2, Entry 1). Attempts to improve the yield of this reaction involved screening the base [1,8-diazabicyclo [5.4.0]undec-7-ene (DBU), *i*-Pr₂NEt (Hünig's base), K₂CO₃, *t*-BuOK or K₃PO₄] and solvents (MeCN,

THF, PhMe), but these led to either degradation or to lower yields. Nevertheless, in DCM at *ca.* 20 °C using lutidine (2 equiv) as the base, increasing the equivalents of malononitrile from 1.1–1.5 equiv afforded the ylidene malononitrile **10** in a slightly better yield (82%), while a further increase to 2 equiv of malononitrile gave a similar 83% yield (Table 2, Entries 2 and 3). The reaction could be scaled up to 4 mmol, and while this led to a drop in yield (73%) (Table 2, Entry 5), it also enabled a chromatography free work-up that involved passing the reaction mixture through a short plug of SiO₂, washing the organic phase with 2M HCl and H₂O and precipitating the product from THF/pentane to give the ylidene **10** in a preparatively useful 64% yield (Table 2, Entry 6).



Scheme 7. Reaction of tetrachlorothiadiazine **1** with dimethylsulfonium dicyanomethylide **14** and the proposed mechanism for the formation of the pyrimidine **15**.

Table 2. Transformation of the tetrachlorothiadiazine **1** into to the ylidene malononitrile **10**.



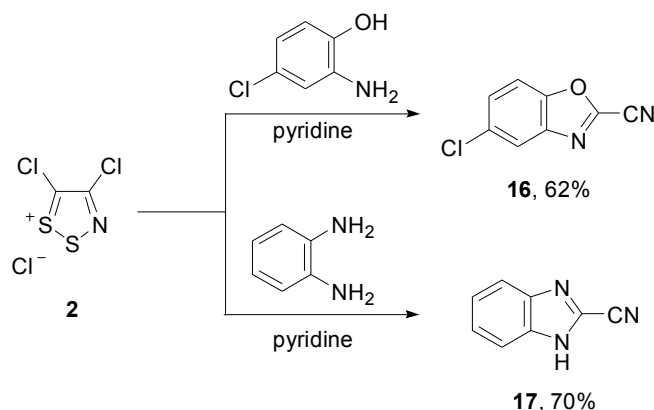
10						
Entry	1 (mmol)	CH ₂ (CN) ₂ (equiv)	DCM (mL)	Time (min)	Yield of 10 (%)	
1	0.42	1.1	1	10	78	
2	0.42	1.5	1	10	82	
3	0.42	2	1	10	83	
4	1	1.5	1	10	71	
5	2	1.5	4	30	73	
6	4	1.5	4	30	64 ^a	

^a Chromatography-free workup.

Attempts to develop a base-free protocol were less effective, as heating a PhMe solution of the tetrachlorothiadiazone **1** with malononitrile (2 equiv) at reflux (110 °C) led to complete consumption of the starting material only after 48 h and isolation of the desired ylidene **10** in a low 27% yield.

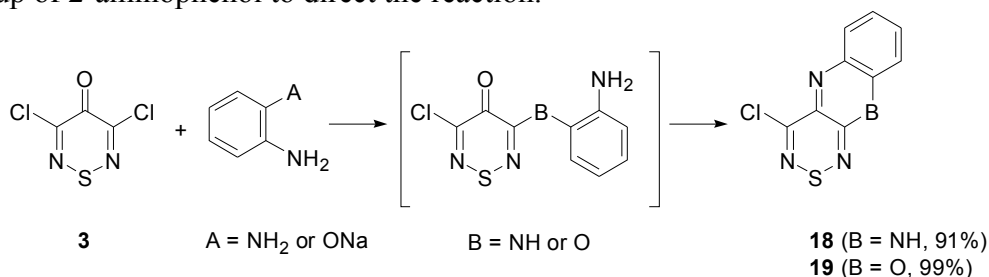
2.4. Cyclisation Reactions of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**)

The condensation of Appel's salt **2** with 2-amino-4-chlorophenol or benzene-1,2-diamine affords 5-chlorobenzo[*d*]oxazole-2-carbonitrile (**16**) and 1*H*-benzo[*d*]imidazole-2-carbonitrile (**17**), respectively (Scheme 8) [37].



Scheme 8. Reactions of Appel's salt **2** with 2-amino-4-chlorophenol or benzene-1,2-diamine.

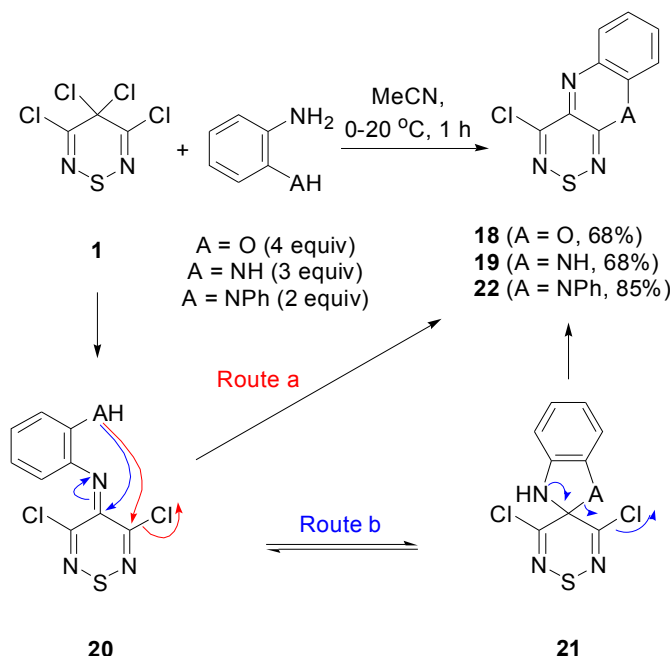
Moreover, the condensation reactions of the thiadiazinone **3** with benzene-1,2-diamine or sodium 2-aminophenoxide to give fused systems are known (Scheme 9) [16]. Even though the thiadiazinone **3** was inert to reactions with primary amines at the C-4 position, after an initial nucleophilic addition in the C-3 position, intramolecular cyclizations readily occur with bisnucleophiles to afford tricyclic systems in excellent yields, e.g., 4-chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**18**) and 4-chloro-benzo[5,6][1,4]oxazino[2,3-*c*][1,2,6]thiadiazine (**19**) (Scheme 9). Worthy of note was that while an excellent yield was reported for oxazine **19**, this required an initial base activation (deprotonation) of the hydroxy group of 2-aminophenol to direct the reaction.



Scheme 9. Reactions of thiadiazinone **3** with benzene-1,2-diamine and sodium 2-aminophenoxide.

The dichloromethylene of the tetrachlorothiadiazone **1** was expected to be more electrophilic and therefore more reactive than the C-3, C-4 and C-5 positions of the thiadiazinone **3**. As such, bisnucleophiles were anticipated to initially attack the geminal dichloromethylene. This reactivity mimics that of Appel's salt **2** (Scheme 8) with bisnucleophiles where the first nucleophilic displacement occurs at the more electrophilic C-5 position.

Treatment of the tetrachlorothiadiazone **1** with 2-aminophenol or benzene-1,2-diamine in MeCN at 20 °C for 1 h afforded the fused heterocycles **18** (68%) and **19** (68%), respectively (Scheme 10). Tentatively, the moderate yields (68%) can be attributed to the high reactivity of the tetrachlorothiadiazone **1** that can presumably suffer from both halophilic and thiophilic attack, leading to its degradation.



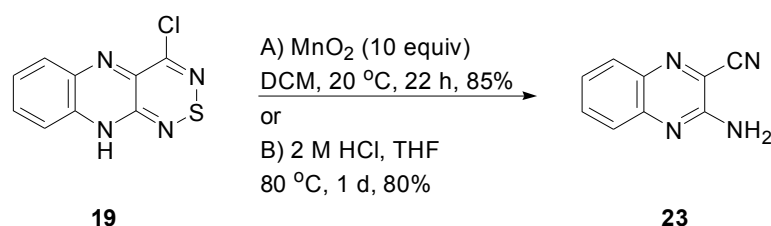
Scheme 10. Reactions of the tetrachlorothiadiazone **1** with 2-aminophenol, benzene-1,2-diamine and *N*-phenylbenzene-1,2-diamine.

A proposed mechanism for this transformation involves the initial formation of imine **20**, which we know from previous studies readily forms by reaction of thiadiazone **1** with arylamines [22]. Subsequently, two routes are proposed, either a 6-exo cyclisation to give the final products (Route a) or a 5-endo cyclisation occurs to form the spirocyclic compounds **21** that then ring-opens, assisted by electron release from both the nitrogen's lone pair and possibly the ring sulfur, subsequently cyclizing at the C-3 position (route b). Interestingly, when using *N*-phenylbenzene-1,2-diamine, an unsymmetrical diamine, the less reactive secondary amine ends up cyclizing on the thiadiazone C-3 position to give 4-chloro-10-phenyl-10*H*-[1,2,6][3,4-*b*]quinoxaline (**22**) in an 85% yield. While this route to tricyclic systems **18**, **19** and **22** was non-quantitative, it offered two distinct advantages: firstly, it avoided the need to access the thiadiazinone **3**, thereby reducing the number of steps to the final products, and secondly, it offered an alternative regioselectivity that avoided the need to base activate bisnucleophiles, such as the 2-aminophenol.

2.5. Reactivity of 4-Chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**)

Interestingly, during the synthesis and isolation of 4-chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**), we observed its decomposition to 3-aminoquinoxaline-2-carbonitrile (**23**). Traces of this product were initially observed during chromatography of quinoxaline **19**, so we decided to investigate the reactivity of this compound. Quinoxaline **19** was stable under basic conditions, as it was recovered unchanged after 48 h stirring in neat Et₃N, while it was unstable in acid, as heating a solution in glacial

AcOH at reflux for 15 min led to complete consumption of the starting material and isolation of 3-aminoquinoxaline-2-carbonitrile (**23**) as the only product in a 38% yield. Alternatively, heating a solution of **19** in aqueous HCl/THF at 80 °C gave the quinoxaline **23** in an 80% yield (Scheme 11).



Scheme 11. Conversion of 4-chloro-10H-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**) to 3-aminoquinoxaline-2-carbonitrile (**23**).

Furthermore, quinoxaline **19** was also unstable in oxidizing and reducing conditions. Namely, stirring a DCM solution of **19** with MnO₂ (10 equiv) at *ca.* 20 °C led to complete consumption of the starting material after 22 h and isolation of aminoquinazoline **23** in an 85% yield (Scheme 11). The dissolving metal reduction with Zn (4 equiv) in AcOH led to degradation of **19** and isolation of 3-aminoquinoxaline-2-carbonitrile (**23**) in only a low 6% yield.

Aminoquinoxaline **23** was previously prepared in a low yield by the reaction of 4-chloro-5-cyano-1,2,3-dithiazolium chloride with benzene-1,2-diamine [38]. Similar degradation reactions were also investigated for thiadiazines **18** and **22**; however, these gave complex mixtures of products (by TLC) and were not pursued further.

3. Experimental Section

3.1. General Methods and Materials

All chemicals were commercially available, except those whose synthesis is described. Anhydrous Na₂SO₄ 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 F₂₅₄) [39]. 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, Merck KGaA, Darmstadt, Germany). Melting points were determined using a PolyTherm-A, Wagner & Munz, Kofler—Hotstage Microscope apparatus (Wagner & Munz, Munich, Germany) or were determined using a TA Instruments differential scanning calorimeter (DSC) Q1000 with samples hermetically sealed in aluminum pans under an argon atmosphere; using heating rates of 5 °C/min (DSC melting points listed by onset and peak values). Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a Perkin-Elmer Lambda-25 UV-VIS spectrophotometer (Perkin-Elmer, Waltham, MA, USA), and inflections are identified by the abbreviation “inf”. IR spectra were recorded on a Shimadzu FTIR-NIR Prestige-21 spectrometer (Shimadzu, Kyoto, Japan) with the Pike Miracle Ge ATR accessory (Pike Miracle, Madison, WI, USA), and strong, medium and weak peaks are represented by s, m and w, respectively. ¹H- and ¹³C-NMR spectra were recorded on a Bruker Avance 300 (at 300 and 75 MHz, respectively, Bruker, Billerica, MA, USA) or a 500 machine (at 500 and 125 MHz,

respectively). Deuterated solvents were used for the homonuclear lock, and the signals are referenced to the deuterated solvent peaks. Attached-proton-test (APT) NMR studies identified quaternary and tertiary carbons, which are indicated by (s) and (d) notations, respectively. MALDI-TOF mass spectra were recorded on a Bruker Autoflex III Smartbeam instrument. Low resolution (EI) mass spectra were recorded on a Shimadzu Q2010 GC-MS with a direct inlet probe. Dichloromalononitrile (**6**) [24], *N*-2,2-trichloro-2-cyanoacetimidoyl chloride (**7**) [24] and dimethylsulfonium dicyanomethylide (**14**) [40] were prepared according to the reported procedures.

3.2. Preparation of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**)

3.2.1. Reaction of Dichloromalononitrile with SCl₂

Performed according to the literature procedure [26]. To a stirred solution of dichloromalononitrile (**6**) (100 g, 0.740 mol) was added BnEt₃NCl (1.69 g, 7.40 mmol), and the mixture was cooled in an ice bath (0 °C). Freshly distilled SCl₂ (76.2 g, 0.740 mol) was then added dropwise, the cooling bath removed and the mixture stirred overnight, protected with a CaCl₂ drying tube. After 18 h, the solvent was evaporated under vacuum and the product distilled under reduced pressure (90 °C, 30 mbar) to give 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**1**) (121.5 g, 69%) as a pale yellow oil that crystallized on cooling to −20 °C mp (DSC) onset: 10.3 °C, peak max: 12.8 °C; δ_C (125 MHz; CDCl₃) 138.5 (s), 72.1 (s); ν_{max}/cm^{−1} 1582m, 1566m, 1144s, 1030s, 953m, 812m, 770s; identical to an authentic sample.

3.2.2. Reaction of *N*-2,2-Trichloro-2-cyanoacetimidoyl Chloride (**4**) with S₈

This was performed according to the literature procedure [26]. A stirred solution of *N*-2,2-trichloro-2-cyanoacetimidoyl chloride (**7**) (41.2 g, 0.200 mol) in dry DCM (40 mL) was cooled in an ice bath (0 °C), and BnEt₃NCl (456 mg, 2.00 mmol) was added, followed by S₈ (6.40 g, 25.0 mmol) added in one portion. The cooling bath was then removed and the mixture stirred overnight, protected with a CaCl₂ drying tube. After 18 h, the product was distilled under reduced pressure (90 °C, 30 mbar) to give 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**1**) (36.2 g, 76%) as a pale yellow oil that crystallized on cooling to −20 °C mp (DSC) onset: 10.3 °C, peak max: 12.8 °C; identical to that described above.

3.3. Transformations of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**) to 3,5-Dichloro-4*H*-1,2,6-thiadiazin-4-one (**3**)

3.3.1. Reaction of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**) with Formic Acid

This was performed according to the literature procedure [15]. 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**) (59.5 g, 0.250 mol) was added dropwise to a cold (10 °C) stirred solution of 98% HCO₂H (175 mL). The cooling bath was then removed and the solution stirred overnight, protected with a CaCl₂ drying tube. After complete consumption of the starting material (TLC, 24 h), the mixture was poured into ice water and the precipitate collected, washed with water and dried under air to yield 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-one (**3**) (34.3 g, 75%) as yellowish needles, mp 81–82 °C (from *c*-hexane, lit. [15] 82–83 °C); R_f 0.56 (*n*-hexane/DCM, 50:50); δ_C (125 MHz; CDCl₃) 157.5 (s), 149.8

(s); $\nu_{\max}/\text{cm}^{-1}$ 1657s (C=O), 1501m, 1277w, 1265w, 1248m, 1227m, 1065s, 854m, 847w, 745s, identical to an authentic sample [15].

3.3.2. Reaction of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**) with Acetic Acid

3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**) (238 mg, 1.00 mmol) was added dropwise to a stirred solution of glacial AcOH (1 mL), and the solution was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until complete consumption of the starting material (TLC, 48 h). The mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 50:50) gave 3,5-dichloro-4H-1,2,6-thiadiazin-4-one (**3**) (135 mg, 74%) as yellowish needles, mp 81–82 °C (from *c*-hexane, lit. [15] 82–83 °C), identical to that described above.

3.3.3. Reaction of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**) with NaNO₃ in MeCN

To a solution of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**) (100 mg, 0.42 mmol) in dry MeCN (1 mL) was added NaNO₃ (39 mg, 0.46 mmol), and the mixture was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until consumption of the starting material (TLC, 1.5 h). The reaction mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 50:50) gave 3,5-dichloro-4H-1,2,6-thiadiazin-4-one (**3**) (55 mg, 71%) as yellowish needles, mp 81–82 °C (from *c*-hexane, lit. [15] 82–83 °C), identical to that described above.

3.3.4. Reaction of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**) with AgNO₃ in MeCN

To a solution of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**) (100 mg, 0.42 mmol) in dry MeCN (1 mL) was added AgNO₃ (71 mg, 0.42 mmol), and the mixture was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until consumption of the starting material (TLC, 30 min). A colorless precipitate formed that was filtered to give AgCl (52 mg, 87%). The filtrate was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 50:50) gave 3,5-dichloro-4H-1,2,6-thiadiazin-4-one (**3**) (65 mg, 85%) as yellowish needles, mp 81–82 °C (from *c*-hexane, lit. [15] 82–83 °C), identical to that described above.

3.3.5. Reaction of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**) with DMSO in MeCN

To a solution of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**) (238 mg, 1.00 mmol) in dry MeCN (10 mL) was added DMSO (71 μL , 1.0 mmol), and the mixture was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until consumption of the starting material (TLC, 20 h). The reaction mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 50:50) gave 3,5-dichloro-4H-1,2,6-thiadiazin-4-one (**3**) (57 mg, 31%) as yellowish needles, mp 81–82 °C (from *c*-hexane, lit. [15] 82–83 °C), identical to the one reported above.

3.3.6. Reaction of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (**1**) with Neat DMSO

A solution of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine (**1**) (238 mg, 1.00 mmol) in DMSO (2 mL) was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until consumption of the starting material (TLC, 1 h). Water (20 mL) was then added and the mixture extracted with *t*-BuOMe (3 \times 20 mL), the organic phase combined, dried (Na₂SO₄) and evaporated to give crude **3**. The crude product was then adsorbed

onto silica, and chromatography (*n*-hexane/DCM, 50:50) gave 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-one (**3**) (82 mg, 45%) as yellowish needles, mp 81–82 °C (from *c*-hexane, lit. [15] 82–83 °C), identical to the one reported above.

3.4. Transformations of 4,5-Dichloro-1,2,3-dithiazolium Chloride (**2**) into 4-Chloro-5*H*-1,2,3-dithiazol-5-one (**9**)

3.4.1. Reaction of 4,5-Dichloro-1,2,3-dithiazolium Chloride (**2**) with Formic Acid

Appel's salt **2** (208 mg, 1.00 mmol) was added to a stirred solution of HCO₂H (98%, 1 mL), and the solution was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until complete consumption of the starting material (2 h). The mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 60:40) gave 4-chloro-5*H*-1,2,3-dithiazol-5-one (**9**) (137 mg, 89%) as pale yellow plates, mp 35–36 °C (from pentane, lit. [17] 39 °C); *R*_f 0.48 (*n*-hexane/DCM, 60:40); δ_c (75 MHz; CDCl₃) 183.3 (s), 147.0 (s); ν_{max}/cm⁻¹ 1651s (C=O), 1612m, 1501m, 1337w, 1142w, 1021m, 1080w, 847m, 837m, 806w, 785m, identical to an authentic sample [17].

3.4.2. Reaction of 4,5-Dichloro-1,2,3-dithiazolium Chloride (**2**) with Acetic Acid

Appel's salt **2** (208 mg, 1.00 mmol) was added to a stirred solution of glacial AcOH (1 mL), and the solution was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until complete consumption of the starting material (2 h). The mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 60:40) gave 4-chloro-5*H*-1,2,3-dithiazol-5-one (**9**) (92 mg, 60%) as pale yellow plates, mp 35–36 °C (from pentane, lit. [17] 39 °C), identical to that described above.

3.4.3. Reaction of 4,5-Dichloro-1,2,3-dithiazolium Chloride (**2**) with NaNO₃ in MeCN

To a suspension of Appel's salt (**2**) (104 mg, 0.50 mmol) in dry MeCN (1 mL) was added NaNO₃ (43 mg, 0.50 mmol), and the mixture was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until consumption of the starting material (18 h). The mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 60:40) gave 4-chloro-5*H*-1,2,3-dithiazol-5-one (**9**) (59 mg, 77%) as pale yellow plates, mp 35–36 °C (from pentane, lit. [17] 39 °C), identical to that described above.

3.4.4. Reaction of 4,5-Dichloro-1,2,3-dithiazolium Chloride (**2**) with AgNO₃ in MeCN

To a suspension of Appel's salt (**2**) (104 mg, 0.50 mmol) in dry MeCN (1 mL) was added AgNO₃ (85 mg, 0.50 mmol), and the mixture was stirred at *ca.* 20 °C, protected with a CaCl₂ drying tube, until consumption of the starting material (1 min). A colorless precipitate formed that was filtered to give AgCl (72 mg, 100%). The filtrate was then adsorbed onto silica and chromatography (*n*-hexane/DCM, 60:40) gave 4-chloro-5*H*-1,2,3-dithiazol-5-one (**9**) (55 mg, 72%) as pale yellow plates, mp 35–36 °C (from pentane, lit. [17] 39 °C), identical to that described above.

3.5. Transformations of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**) to 2-(3,5-Dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)malononitrile (**10**)

3.5.1. Reaction of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**) with Malononitrile

To a solution of 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**1**) (100 mg, 0.42 mmol) in dry DCM (1 mL) was added malononitrile (42 mg, 0.63 mmol), and the solution was cooled in an ice bath (0 °C). 2,6-Lutidine (98 µL, 0.84 mmol) was then added dropwise to the stirred solution. The cooling bath was then removed and the solution stirred at *ca.* 20 °C until complete consumption of the starting material (TLC, 10 min). The reaction mixture was then poured onto a silica column, and chromatography (*n*-hexane/DCM, 20:80) gave 2-(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)malononitrile (**10**) (80 mg, 82%) as yellow plates, mp 133–134 °C (from *c*-hexane, lit. [31] 134–135 °C); R_f 0.65 (*n*-hexane/DCM, 20:80); δ_c (125 MHz; CDCl₃) 138.8 (s), 136.5 (s), 112.0 (s), 81.2 (s); $\nu_{\max}/\text{cm}^{-1}$ 2216m (C≡N), 1522m, 1508m, 1487m, 1288s, 1273m, 1144m, 1082m, 812m, 754s; m/z (EI) 230 (M⁺, 100), 204 (M⁺-CN, 2%), 195 (M⁺-Cl, 55), 169 (M⁺-CCIN, 21), 134 (M⁺-CCl₂N, 21), identical to an authentic sample [31].

3.5.2. Reaction of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**) with Malononitrile, Chromatography-Free (Table 2, Entry 6)

To a solution of 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**1**) (952 mg, 4.00 mmol) in dry DCM (4 mL) was added malononitrile (396 mg, 6.00 mmol), and the solution was cooled in an ice bath (0 °C). 2,6-Lutidine (0.930 mL, 8.00 mmol) was then added dropwise to the stirred solution. The cooling bath then removed and the solution stirred at *ca.* 20 °C until complete consumption of the starting material (TLC, 30 min). The reaction mixture was then passed through a plug of silica (DCM) and washed with 2 M HCl (2 × 10 mL) and H₂O (10 mL), evaporated and precipitated from THF/pentane to give 2-(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)malononitrile (**10**) (591 mg, 64%) as yellow plates, mp 133–134 °C (from *c*-hexane, lit. [31] 134–135 °C), identical to that described above.

3.5.3. Reaction of 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**1**) with Dimethylsulfonium Dicyanomethylide (**14**)

To a solution of 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**1**) (100 mg, 0.42 mmol) in dry DCM (1 mL) was added dimethylsulfonium dicyanomethylide (**14**) (58 mg, 0.46 mmol), and the mixture was heated at *ca.* 39 °C, protected with a CaCl₂ drying tube, until consumption of the starting material (20 h). The reaction mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 60:40) gave 4,5,6-trichloropyrimidine-2-carbonitrile (**15**) (18 mg, 21%) as colorless needles, mp 62–63 °C (sublimation, lit. [31] 64–65 °C); R_f 0.41 (*n*-hexane/DCM, 60:40); $\nu_{\max}/\text{cm}^{-1}$ 2423w and 2363w (C≡N) and 1530w (C=C), 1497s, 1350s, 1337m, 1315m, 1300m, 1275m, 1256m, 1209m, 1065m, 1057m, 910m, 832m, 818m, 770m; δ_c (125 MHz; CDCl₃) 161.1 (s), 139.7 (s), 133.2 (s), 113.4 (s); m/z (EI) 207 (M⁺, 100), 172 (M⁺-Cl, 50%), 120 (C₃Cl₂N⁺, 28), 111 (C₄ClN₂⁺, 13), identical to an authentic sample [31]. Further elution (*n*-hexane/DCM, 20:80) gave 2-(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)malononitrile (**10**) (18 mg, 19%) as yellow plates, mp 133–134 °C (from *c*-hexane, lit. [31] 134–135 °C), identical to that described above.

3.6. Cyclisation Reactions of 3,4,4,5-Tetrachloro-4H-1,2,6-thiadiazine (1)

3.6.1. Synthesis of 4-Chlorobenzo[5,6][1,4]oxazino[2,3-c][1,2,6]thiadiazine (18) (General Procedure)

To a cold (0 °C) stirred solution of tetrachlorothiadiazine **1** (238 mg, 1.00 mmol) in dry MeCN (5 mL) was added in one portion 2-aminophenol (436 mg, 4.00 mmol). The cooling bath was then removed and the solution stirred at *ca.* 20 °C protected with a CaCl₂ drying tube until complete consumption of the starting material (TLC, 1 h). The mixture was then adsorbed onto silica, and chromatography (*n*-hexane/DCM, 50:50) gave the title compound **18** (179 mg, 76%) as orange prisms, mp 157–160 °C (from EtOH, lit. [16] 158–163 °C); *R_f* 0.43 (*n*-hexane/DCM, 50:50); $\nu_{\max}/\text{cm}^{-1}$ 3103w and 3048w (Ar CH), 1614m, 1587m, 1547m, 1518m, 1456s, 1365m, 1331s, 1308m, 1294w, 1283m, 1244m, 1206m, 1184m, 1107m, 1059m, 1026m, 978m, 968m, 945m, 901s, 876s, 868m, 800s, 763s, 748s; δ_{H} (500 MHz; DMSO-*d*₆) 7.24 (1H, dd, *J* = 7.7, 1.4, Ar *H*), 7.18 (1H, ddd, *J* = 7.8, 7.8, 1.5, Ar *H*), 7.05 (1H, ddd, *J* = 7.6, 7.6, 0.9, Ar *H*), 6.89 (1H, d, *J* = 8.1, Ar *H*); δ_{C} (125 MHz; DMSO-*d*₆) 151.0 (s), 148.1 (s), 145.8 (s), 138.3 (s), 133.9 (s), 130.6 (d), 128.5 (d), 125.7 (d), 115.2 (d); *m/z* (EI) 237 (M⁺, 100%), 202 (M⁺-Cl, 5), 176 (M⁺-CCIN, 9), 144 (M⁺-CCINS, 11), 118 (5), 93 (CCINS⁺, 11), 64 (6), identical to an authentic sample.

3.6.2. Synthesis of 4-Chloro-10H-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (19)

Similar treatment of tetrachlorothiadiazine **1** (238 mg, 1.00 mmol) with benzene-1,2-diamine (432 mg, 3.00 mmol) gave, after the solvent was evaporated *in vacuo* and the crude product precipitated from EtOH (2 mL), the title compound **19** (160 mg, 68%) as purple needles, mp 310 °C (from EtOH, lit. [16] 310 °C subl.); *R_f* 0.17 (*n*-hexane/DCM, 50:50); $\nu_{\max}/\text{cm}^{-1}$ 3237w, 3188w, 3140w, 3069w and 3051w (Ar CH), 1605s, 1570w, 1514m, 1470m, 1414m, 1379s, 1275m, 1221m, 1115m, 957m, 924s, 878m, 800s, 766s, 741s; δ_{H} (500 MHz; DMSO-*d*₆) 10.19 (1H, s, NH), 6.93 (1H, ddd, *J* = 7.8, 7.8, 1.1, Ar *H*), 6.87 (1H, d, *J* = 8.2, Ar *H*), 6.66 (1H, ddd, *J* = 7.9, 7.9, 0.8, Ar *H*), 6.38 (1H, d, *J* = 7.9, Ar *H*); δ_{C} (125 MHz; DMSO-*d*₆) 149.9 (s), 142.2 (s), 139.7 (s), 136.4 (s), 135.8 (s), 130.5 (d), 128.3 (d), 123.1 (d), 113.5 (d); *m/z* (EI) 236 (M⁺, 100%), 201 (M⁺-Cl, 32), 174 (M⁺-CHCIN, 8), 168 (7), 162 (4), 154 (6), 149 (6), 143 (M⁺-CCINS, 21), 131 (6), 118 (6), 102 (5), 90 (9), 76 (C₆H₄⁺, 4), 69 (11), identical to the an authentic sample.

3.6.3. Synthesis of 4-Chloro-10-phenyl-10H-[1,2,6][3,4-*b*]quinoxaline (22)

Similar treatment of tetrachlorothiadiazine **1** (238 mg, 1.00 mmol) with *N*'-phenylbenzene-1,2-diamine (368 mg, 2.00 mmol) gave after chromatography (DCM) the title compound **22** (212 mg, 68%) as brown needles, mp 256–258 °C (from PhMe); *R_f* 0.81 (DCM); (found: C, 57.26; H, 2.54; N, 17.62. C₁₅H₉ClN₄S requires C, 57.60; H, 2.90; N, 17.91%); λ_{\max} (DCM)/nm 267 (log ϵ 4.37), 285 inf (4.29), 296 inf (4.24), 326 (4.14), 367 (3.94), 387 (3.98), 409 (3.83), 527 (3.68), 552 (3.69), 596 inf (3.44); $\nu_{\max}/\text{cm}^{-1}$ 3048w, 1593m, 1504m, 1497m, 1485m, 1450m, 1360s, 1317m, 1173w, 1157m, 941m, 932m, 876m, 764s, 750s, 731s, 714s; δ_{H} (500 MHz; DMSO-*d*₆) 7.58 (2H, dd, *J* = 7.4, 7.4, Ar *H*), 7.47 (1H, dd, *J* = 7.3, 7.3, Ar *H*), 7.33 (2H, d, *J* = 7.4, Ar *H*), 7.06 (1H, d, *J* = 7.5, Ar *H*), 6.87 (1H, dd, *J* = 7.4, 7.4, Ar *H*), 6.79 (1H, dd, *J* = 7.4, 7.4, Ar *H*), 5.66 (1H, d, *J* = 7.9, Ar *H*); δ_{C} (125 MHz; DMSO-*d*₆) 149.6 (s), 143.3 (s), 139.3 (s), 138.4 (s), 135.7 (s), 135.2 (s), 130.6 (d), 130.3 (d), 129.0 (d), 128.8 (d), 128.7 (d), 123.7 (d), 113.5 (d); *m/z* (MALDI-TOF) 314 (M⁺+2, 47%), 312 (M⁺, 95), 277 (M⁺-Cl, 100), 245 (M⁺-ClS, 36).

3.7. Reactivity of 4-Chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**)

3.7.1. Reaction of 4-Chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**) with MnO₂

To a stirred solution of 4-chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**) (47 mg, 0.20 mmol) in DCM (2 mL) at *ca.* 20 °C was added MnO₂ (174 mg, 2.0 mmol), and the mixture was protected with a CaCl₂ drying tube until complete consumption of the starting material (TLC, 22 h). The solid that formed was removed by filtration and the filtrate adsorbed onto silica and chromatographed (*n*-hexane/*t*-BuOMe, 40:60) to give 3-aminoquinoxaline-2-carbonitrile (**23**) (29 mg, 85%) as yellow needles, mp 209–210 °C (from *c*-hexane, lit. [38] 210 °C); *R_f* 0.59 (*n*-hexane/*t*-BuOMe, 40:60); $\nu_{\max}/\text{cm}^{-1}$ 3412m, 3327m, 3132 br, 2232m (C≡N), 1661s, 1611m, 1562m, 1557m, 1489m, 1437m, 1371m, 1360m, 1323w, 1254w, 1223m, 1171w, 1144m, 1123w, 1092w, 1013w, 963w, 918m, 760s, 754s, 741m; δ_{H} (500 MHz; CDCl₃) 7.94 (1H, dd, *J* = 8.4, 1.0, Ar *H*), 7.74 (1H, ddd, *J* = 8.4, 6.8, 1.4, Ar *H*), 7.69 (1H, dd, *J* = 8.5, 1.1, Ar *H*), 7.53 (1H, ddd, *J* = 8.3, 6.8, 1.4, Ar *H*), 5.42 (2H, br s, NH₂); δ_{C} (125 MHz; CDCl₃) 151.8 (s), 142.5 (s), 137.5 (s), 133.8 (d), 129.7 (d), 126.8 (d), 126.4 (d), 119.2 (s), 114.9 (s); *m/z* (EI) 170 (M⁺, 100%), 143 (M⁺-CHN, 33), 118 (17), 91 (C₆H₅N⁺, 13), 84 (13), 76 (C₆H₄⁺, 6), 66 (13), identical to an authentic sample [38].

3.7.2. Reaction of 4-Chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**) with HCl

To a stirred solution of 4-chloro-10*H*-[1,2,6]thiadiazino[3,4-*b*]quinoxaline (**19**) (47 mg, 0.20 mmol) in THF (4 mL) was added a 2 M aqueous HCl (4.0 mL, 8.0 mmol), and the mixture was stirred at *ca.* 80 °C until complete consumption of the starting material (TLC, 24 h). The mixture was then cooled to *ca.* 20 °C, and DCM (10 mL) was added, followed by saturated Na₂CO₃ until the pH reached 10. The organic phase was separated and the mixture further extracted with DCM (2 × 10 mL), and the combined organic phase was then dried (Na₂SO₄) and evaporated. The crude product was then adsorbed onto silica and chromatographed (*n*-hexane/*t*-BuOMe, 40:60) to give 3-aminoquinoxaline-2-carbonitrile (**23**) (27 mg, 80%) as yellow needles, mp 209–210 °C (from *c*-hexane, lit. [38] 210 °C); *R_f* 0.59 (*n*-hexane/*t*-BuOMe, 40:60), identical to that described above.

4. Conclusions

Three modes of reactivity were investigated for the sparingly explored 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**1**): its conversion to the useful scaffolds 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-one (**3**) and 2-(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)malononitrile (**10**) in 85% and 83% yields, respectively, and its transformation to tricyclic thiadiazines in good yields. The geminal dichloromethylene to ketone transformation was directly compared between thiadiazine **1** and Appel's salt **2**, and similarities and differences between the reactivity of the two reagents were identified. The reaction of thiadiazine **1** with dicyanomethylide **14** led to the isolation of an unexpected side product, 4,5,6-trichloropyrimidine-2-carbonitrile (**15**), the investigation of which is now under further study. The development of the chemistry of 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**1**) shows that this unexplored reagent can be a useful scaffold in the synthesis of valuable heterocycles.

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Author Contributions

A.S.K and P.A.K. designed the research, drafted and approved the manuscript; A.S.K. performed the synthetic work and analyzed the data.

Conflicts of Interest

The authors declare no conflict of interest.

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