A Qualitative Comparison of the Reactivities of 3,4,4,5-Tetrachloro-4H-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-4H-1,2,6-thiadiazine into 3,5-dichloro-4H-1,2,6-thiadiazin-4-one (up to 85%) and 2-(3,5-dichloro-4H-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-5H-1,2,3-dithiazol-5-one and 2-(4-chloro-5H-1,2,3-dithiazol-5-ylidene)malononitrile. Furthermore, cyclocondensation of 3,4,4,5-tetrachloro-4H-1,2,6-thiadiazine with 2-aminophenol and 1,2-benzenediamines gave fused 4H-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-4H-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;
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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-Thiaazizin-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-thiaazizin-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 6π 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-thiaazizin-4-imines (4) from 3,4,4,5-tetrachloro-4H-1,2,6-thiaazizin (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.

![Chemical structures and reactions](image)

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

2. Results and Discussion

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

Two methods exist in the literature for the preparation of the tetrachlorothiadiazine 1: the reaction of dichloromalononitrile (6) and SCl$_2$ [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 SCl$_2$ (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.

![Chemical structures and reactions](image)

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

3,5-Dichloro-4$H$-1,2,6-thiadiazin-4-one (3) can be prepared from the reaction of glacial formic acid with 3,4,4,5-tetrachloro-4$H$-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.
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to give 2-chloromalonamide (8) (Scheme 4) [26]. As such, we reinvestigated the transformation of tetrachlorothiadiazine 1 into the thiadiazinone 3 (Section 2.2.).

\[
\begin{align*}
1 & \xrightarrow{\text{HC02H}} 75\% \\
3 & \xrightarrow{\text{moist air}} 94\%
\end{align*}
\]

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

Comparing the syntheses of tetrachlorothiadiazine 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 tetrachlorothiadiazine 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 tetrachlorothiadiazine 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 tetrachlorothiadiazine 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 tetrachlorothiadiazine 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 tetrachlorothiadiazine 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 tetrachlorothiadiazine 1 and Appel’s salt 2 to thiadiazinone 3 and dithiazolone 9, respectively.

| Entry | Conditions a | Product Yields and Reaction Times |
|-------|--------------|-----------------------------------|
| 1     | HCO₂H (98%) neat | 3 (75%), 24 h 9 (89%), 2 h |
| 2     | HCO₂H (85%) b neat | 3 (0%), c 18 h 9 (72%), 1 h |
| 3     | AcOH neat | 3 (74%), 48 h 9 (60%), 2 h |
| 4     | NaNO₃ (1 equiv), DCM | 3 (nr), d 18 h 9 (72%), 18 h |
| 5     | NaNO₃ (1 equiv), MeCN | 3 (71%), 1.5 h 9 (77%), 18 h |
| 6     | AgNO₃ (1 equiv), MeCN | 3 (85%), 0.5 h 9 (72%), 1 min |
| 7     | Ag₂SO₄ (0.5 equiv), MeCN | 3 (77%), 4 h 9 (73%), 24 h |
| 8     | H₂O (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 tetrachlorothiadiazine 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 tetrachlorothiadiazine 1, and Appel’s salt 2, 2-(3,5-dichloro-4H-1,2,6-thiadiazin-4-ylidene)malononitrile (10) and 2-(4-chloro-5H-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 ylidenemalononitrile 10 from tetracyanoethylene (TCNE) and SCl₂.

2-(4-Chloro-5H-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-5H-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 tetrachlorothiadiazine 1 and Appel’s salt 2, the transformation of 1 into the ylidenemalononitrile 10 was explored: while the reaction of Appel’s salt 2 with TCNEO (1 equiv) in PhMe heated at reflux gave the ylide 11 in a 55% yield [32], under these reaction conditions, the tetrachlorothiadiazine 1 gave only a complex mixture of products containing a trace of the desired ylidenemalononitrile 10 by TLC. Similarly, while the reaction of dimethylsulfonium dicyanomethylide 14 with Appel’s salt 2 [36] affords the ylide 11 in medium to good yields (29%–72%) along with other side products, the analogous reaction of tetrachlorothiadiazine 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 SCl₂ [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 ylidenemalononitrile 11 (40%) [32], when the tetrachlorothiadiazine 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 ylidenemalononitrile 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 ylidenemalononitrile 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 the ylidenemalononitrile 10.

| Entry | 1 (mmol) | CH₂(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         | 64a             |

a Chromatography-free workup.
Attempts to develop a base-free protocol were less effective, as heating a PhMe solution of the tetrachlorothiadiazine 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-chlorobenzothiadiazole-2-carbonitrile (16) and 1H-benzothiadiazole-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.](image)

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-10H-[1,2,6]thiadiazino[3,4-b]quinoxaline (18) and 4-chlorobenzothiadiazole-2-carbonitrile (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.](image)

The dichloromethylene of the tetrachlorothiadiazine 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 tetrachlorothiadiazine 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 tetrachlorothiadiazine 1 that can presumably suffer from both halophilic and thiophilic attack, leading to its degradation.

Scheme 10. Reactions of the tetrachlorothiadiazine 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 thiadiazine 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 thiadiazine C-3 position to give 4-chloro-10-phenyl-10H-[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-10H-[1,2,6]thiadiazino[3,4-b]quinoxaline (19)

Interestingly, during the synthesis and isolation of 4-chloro-10H-[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-4H-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-4H-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; δC (125 MHz; CDCl3) 138.5 (s), 72.1 (s); νmax/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-4H-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; δC (125 MHz; CDCl3) 138.5 (s), 72.1 (s); νmax/cm⁻¹ 1582m, 1566m, 1144s, 1030s, 953m, 812m, 770s; identical to that described above.

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

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

This was performed according to the literature procedure [15]. 3,4,4,5-Tetrachloro-4H-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-4H-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); Rf 0.56 (n-hexane/DCM, 50:50); δC (125 MHz; CDCl₃) 157.5 (s), 149.8
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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 × 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-4H-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-5H-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-5H-1,2,3-dithiazol-5-one (9) (137 mg, 89%) as pale yellow plates, mp 35–36 °C (from pentane, lit. [17] 39 °C); Rf 0.48 (n-hexane/DCM, 60:40); δC (75 MHz; CDCl3) 183.3 (s), 147.0 (s); νmax/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-5H-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-5H-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-5H-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-4H-1,2,6-thiadiazine (1) to 2-(3,5-Dichloro-4H-1,2,6-thia
diazin-4-ylidene)malononitrile (10)

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

To a solution of 3,4,4,5-tetrachloro-4H-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-4H-1,2,6-thia
diazin-4-ylidene)malononitrile (10) (80 mg, 82%) as yellow plates, mp 133–134 °C (from c-hexane, lit. [31] 134–135 °C); Rf 0.65 (n-hexane/DCM, 20:80); δc (125 MHz; CDCl3) 138.8 (s), 136.5 (s), 112.0 (s), 81.2 (s); νmax/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⁺-CCl3N, 21), 134 (M⁺-CCl2N, 21), identical to an authentic sample [31].

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

To a solution of 3,4,4,5-tetrachloro-4H-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-4H-1,2,6-thia
diazin-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-4H-1,2,6-thiadiazine (1) with Dimethylsulfonium Dicyanomethylide (14)

To a solution of 3,4,4,5-tetrachloro-4H-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); Rf 0.41 (n-hexane/DCM, 60:40); νmax/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; δc (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 (C₅Cl₂N⁺, 28), 111 (C₆ClN⁺, 13), identical to an authentic sample [31]. Further elution (n-hexane/DCM, 20:80) gave 2-(3,5-dichloro-4H-1,2,6-thia
diazin-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); Rf 0.43 (n-hexane/DCM, 50:50); νmax/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, 876m, 868m, 800s, 763s, 748s; δH (500 MHz; DMSO-d6) 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); δC (125 MHz; DMSO-d6) 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⁺-CCN, 9), 144 (M⁺-CCNS, 11), 118 (5), 93 (CCNS⁺, 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.); Rf 0.17 (n-hexane/DCM, 50:50); νmax/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; δH (500 MHz; DMSO-d6) 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); δC (125 MHz; DMSO-d6) 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⁺-CCNS, 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-10H-[1,2,6]thiadiazino[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); Rf 0.81 (DCM); (found: C, 57.26; H, 2.54; N, 17.62. C₁₅H₁₀ClN₁₄S requires C, 57.60; H, 2.90; N, 17.91%); λmax (DCM)/nm 267 (log e 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); νmax/cm⁻¹ 3048w, 1593m, 1504m, 1497m, 1485m, 1450m, 1360s, 1317m, 1173w, 1157m, 941m, 932m, 876m, 764s, 750s, 731s, 714s; δH (500 MHz; DMSO-d6) 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); δC (125 MHz; DMSO-d6) 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-10H-[1,2,6]thiadiazino[3,4-b]quinoxaline (19)

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

To a stirred solution of 4-chloro-10H-[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); Rᵓ 0.59 (n-hexane/t-BuOMe, 40:60); νmax/cm⁻¹ 3412m, 3327m, 3132br, 2232m (C≡N), 1661s, 1611m, 1562m, 1557m, 1547m, 1532m, 1489m, 1437m, 1371m, 1360m, 1323w, 1254w, 1223m, 1171w, 1144m, 1123w, 1092w, 1013w, 963w, 918m, 760s, 754s, 741m; δH (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 = 8.3, 6.8, 1.4, Ar H), 5.42 (2H, br s, NH₂); δC (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), 1123w, 1092w, 1013w, 963w, 918m, 760s, 754s, 741m; 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-10H-[1,2,6]thiadiazino[3,4-b]quinoxaline (19) with HCl

To a stirred solution of 4-chloro-10H-[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); Rᵓ 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-4H-1,2,6-thiadiazine (1): its conversion to the useful scaffolds 3,5-dichloro-4H-1,2,6-thiadiazin-4-one (3) and 2-(3,5-dichloro-4H-1,2,6-thiadazin-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-4H-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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**Sample Availability:** Samples of the compounds are available from the authors.

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