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The synthesis of pyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitriles from (4*H*-1,2,6-thiadiazin-4-ylidene)malononitriles

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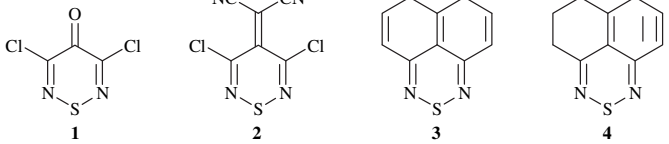
ABSTRACT

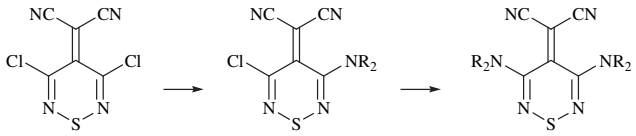
[3,5-Bis(dialkylamino)-4*H*-1,2,6-thiadiazin-4-ylidene]propanedinitriles **6a–c**, react with sodium methoxide or ethoxide to give the corresponding 6-alkoxy-4-dialkylamino substituted pyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitriles **7a–f** in variable yields. These new compounds are fully characterised and two rational mechanisms are proposed for their formation.

1. Introduction

Various oxidised 1,2,6-thiadiazines such as the sulfoxides and, more importantly, the sulfones have received considerable attention in various areas of applied chemistry including the pharmaceutical,[1] agrochemical[2] and materials[3] sectors. Surprisingly little, however, has appeared in the literature on non-oxidised 4*H*-1,2,6-thiadiazines. Monocyclic 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-one **1**[4] and its 4-dicyanomethylene derivative **2**[5,6] have been prepared and both are useful precursors to several polycyclic 1,2,6-thiadiazine systems.[7] Furthermore, many mono-chloro derivatives of thiadiazinone **1** have high fungicidal activity,[8] while fused 4*H*-1,2,6-thiadiazines such as acenaphtho[5,6-*cd*][1,2,6]thiadiazine **3**,[9,10] and naphtho[1,8-*cd*:4,5-*c*′*d*′]bis[1,2,6]thiadiazine **4**,[11] have been studied as examples of 'extreme quinoids', that have ambiguous aromatic character. More recently Torroba et al. prepared cyclopenta[1,2,6]thiadiazines starting from cyclic enaminonitriles,[12,13] some of which displayed unusual liquid crystalline properties or behaved as near infra-red dyes. The synthesis and chemistry of 1,2,6-thiadiazines has been reviewed.[14]



As part of our ongoing studies on both 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-one **1** and 3,5-dichloro-4-dicyanomethylene-4*H*-1,2,6-thiadiazine **2** we investigated the nucleophilic displacement of halide by dialkylamines, which in general proceeded smoothly and in high yield. Treatment of 3,5-dichloro-4-dicyanomethylene-4*H*-1,2,6-thiadiazine **2** with secondary alkylamines gave first the deep red monoamino mono-chloro derivatives **5** and then the blue 3,5-bisamino compounds **6**, both in good yields.[15]



Surprisingly, when these displacements were carried out in ethanol, additional minor fluorescent products could be observed (by TLC). Control studies showed that these new products, which were identified as pyrrolo[2,3-*c*][1,2,6]thiadiazines, could be formed in moderate to good yield by reacting the 3,5-bis(dialkylamino)-4-dicyanomethylene-4*H*-1,2,6-thiadiazines **6** with sodium alkoxide.

2. Results and discussion

In preliminary studies, when (3,5-dimorpholino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6a** was treated with morpholine in EtOH, two minor fluorescent products were observed, one yellow and one orange in colour. Both compounds were unstable, however they could be isolated and fully characterised. The less polar product that was yellow in solution [λ_{max}(DCM) 457 nm (log ε 3.82)], was isolated as orange needles [mp 163–165 °C (cyclohexane)] and gave a correct elemental analysis for the formula $C_{12}H_{13}N_5O_2S$, that supported a molecular parent ion of *m*/*z* 291 Da (100%) from EI mass

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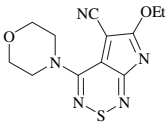
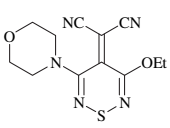
spectrometry. This suggested the loss of one morpholino group and the gain of an ethoxide group. A single stretching band in the IR spectrum at ν(C≡N) 2212 cm^{-1} supported the presence of a cyano functionality, while ^{1}H and ^{13}C NMR spectroscopy indicated the presence of an OEt group and the loss of the symmetry of the starting thiadiazine. Tentatively, the above data suggested one of two possible structures: The bicyclic 6-ethoxy-4-morpholinopyrrolo[2,3-*c*][1,2,6]-thiadiazine-5-carbonitrile **7a** or the monocyclic (3-ethoxy-5-morpholino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **8**. The two possibilities could be differentiated based on the compounds colour. Monodialkylamino substituted (thiadiazin-4-ylidene)propanedinitriles **5** are deep red in colour and do not fluoresce, while fused bicyclic systems such as the furo-fused thiadiazine **9**[15] and the pyrrolo-fused thiadiazine **10**,[6] are significantly less coloured and display a notable but weak fluorescence. On the basis that the isolated compound was yellow in colour and showed a weak fluorescence we tentatively concluded to it being the fused pyrrolothiadiazine **7a**.



7a



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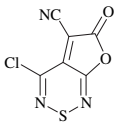

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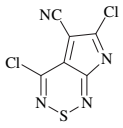
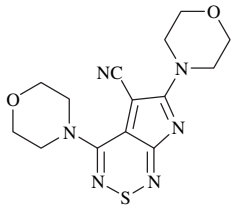


10

The more polar product that was orange in solution [λ_{max}(DCM) 490 nm (log ε 3.60)], and was isolated as red needles that were unstable [mp 228–230 °C (cyclohexane)]. This compound gave a correct elemental analysis for the formula $C_{14}H_{16}N_6O_2S$ and LREI mass spectrometry gave a molecular parent ion of *m*/*z* 332 Da (100%) indicating this was an isomer of the initial (3,5-dimorpholino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6a**. A single stretching band in the IR spectrum at ν(C≡N) 2204 cm^{-1} indicated the presence of a cyano group that was supported by a ^{13}C NMR resonance at 117.7 ppm. ^{1}H and ^{13}C NMR spectroscopy indicated loss of the symmetry of the starting thiadiazine and the presence of two independent morpholino groups. In light of the above data and the fluorescent nature of the new product we tentatively assigned the compound to be 4,6-dimorpholinopyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitrile **11**. Worthy of note was that, despite the 10π aromatic nature of this ring system, the dimorpholinopyrrolothiadiazine **11** was sufficiently unstable that it decomposed on storage. Presumably, a combination of the presence of two electron releasing morpholino groups that increased the electron density in the molecules heteroaromatic core, and the more rigid structure owed to the ring fusion, made the compound oxidatively less stable.

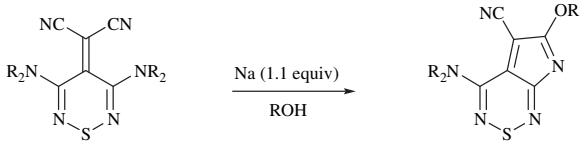


11

To date there are only two reported examples of this bicyclic ring system: The first, 4,6-dichloropyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitrile **10** was prepared in low yield (20%) via an unexpected isomerisation of dicyanomethylene thiadiazine **2** when treated with monosulfur dichloride and benzyltriethylammonium chloride in DCM,[6] and the second, 4-anilino-5-cyano-7-phenyl-6-phenyliminopyrrolo[2,3-*c*][1,2,6]thiadiazine, was prepared in very low yield (5%) on reacting dicyanomethylene thiadiazine **2** with aniline.[15] Nevertheless, this bicyclic system has appeared as part of larger polyheteroarenes.[7]

On the basis of the rarity of this pyrrolo[2,3-*c*][1,2,6]thiadiazine system we investigated further the formation of both pyrrolo[2,3-*c*][1,2,6]thiadiazines **7** and **11** from the starting 3,5-bis(dialkylamino)-1,2,6-thiadiazines **6**. We were able to show that treatment of 3,5-bis(dialkylamino)thiadiazines **6a–c** with sodium alkoxides in alcohol gave moderate to good yields of 6-alkoxy-4-(dialkylamino)pyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitriles **7a–f** (Table 1).

Table 1
Treatment of [3,5-bis(dialkylamino)-4*H*-1,2,6-thiadiazin-4-ylidene]propanedinitriles **6** (0.1 mmol) with alkoxide (1.1 equiv)

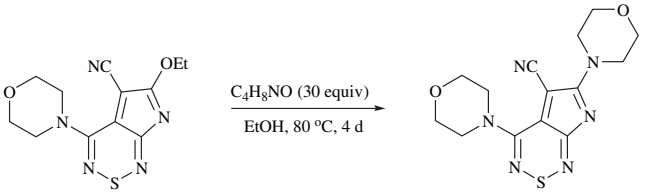


6a-c **7a-f**

6 (R_2N)	ROH	Temp (°C)	Time (h)	Yield (%)
6a (Morpholino)	EtOH	80	4	**7a** (90)[a]
6a (Morpholino)	MeOH	65	24	**7b** (92)
6b (Piperidino)	EtOH	80	24	**7c** (33)
6b (Piperidino)	MeOH	65	72	**7d** (26)
6c (Pyrrolidino)	EtOH	80	2	**7e** (37)
6c (Pyrrolidino)	MeOH	65	24	**7f** (25)

[a] 4,6-Dimorpholinopyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitrile **11** was also isolated (4%).

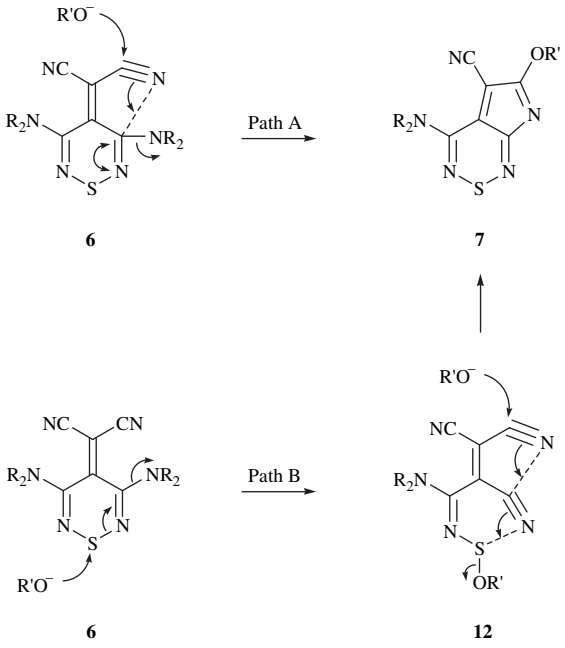
The best yields were obtained with the 3,5-bismorpholinothiadiazine **6a**, which on treatment with methoxide or ethoxide gave the corresponding 6-ethoxy and 6-methoxy pyrrolo[2,3-*c*]-[1,2,6]thiadiazines **7a** (90%) and **7b** (92%), respectively. The bispiperidino and bispyrrolidinothiadiazines were less reactive under similar reaction conditions and gave only moderate yields of the corresponding alkoxy derivatives. Additional minor fluorescent byproducts were also isolated in some reactions but their full characterization was not practical owing to their instability. Nevertheless, the reaction of (3,5-dimorpholino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6a** with ethoxide at ca. 80 °C, did afford 4,6-dimorpholinopyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitrile **11** as a minor byproduct (4%). The formation of this product from the reaction indicated that morpholine freed from the starting thiadiazine could compete with alkoxide as nucleophile, reacting either with the unreacted bisamine **6a** or displacing ethoxide from product **7a**. To investigate the formation of product **11** we reacted the 6-ethoxypyrrolothiadiazine **7a** with morpholine (30 equiv) and obtained the 4,6-dimorpholinopyrrolothiadiazine **11** in 48% yield.



7a **11** (48%)

2.1. Mechanistic rationale for the conversion of (thiadiazin-4-ylidine)propanedinitrile into pyrrolo-[2,3-*c*][1,2,6]thiadiazine

The cyclisation could proceed via two possible pathways (Scheme 1). The first (Path A) invoked alkoxide addition to the



Scheme 1.

nitrile to generate a reactive amidine that subsequently cyclised directly on to the thiadiazine C-3 carbon, eliminating the C-3 substituent. Despite this 'simplicity', the mechanism has drawbacks owing to the poor nucleofuge behaviour of dialkylamines. A second more elaborate ANRORC[16,17] style mechanism (Path B) involved nucleophilic attack by alkoxide on the thiadiazine ring sulfur leading to ring opening and concominant elimination of the C-3 thiadiazine substituent to give the tricyanovinyl intermediate **12**. The generation of the new triple bonded nitrile could act as a thermodynamic driving force for such a ring opening.[18] This tricyanovinyl species could then trap a second nucleophile resulting in a cascade cyclisation to afford the observed pyrrolo[2,3-*c*][1,2,6]thiadiazine **7**. Similar cyclisations of phthalonitriles afford 3-alkoxy-1*H*-isoindoles.[19–25]

It was expected that the latter mechanism would be less efficient and lead to more complex reaction mixtures, which could explain the variable yields, however no byproducts have been isolated to support either mechanism. The comparatively high yields in the reaction of the 3,5-bis(dimorpholino)thiadiazine **6a** may reflect the better nucleofugacity of morpholine compared to either piperidine or pyrrolidine.

An attempt to extend this cyclisation by treating [3,5-bis(phenylsulfide)-4*H*-1,2,6-thiadiazin-4-ylidene]propanedinitrile with ethoxide led to a complex reaction. TLC analysis of the reaction mixture indicated the presence of free thiophenol, however no fluorescent products were visible on irradiation with 365 nm light, possibly implying the pyrrolo[2,3-*c*][1,2,6]thiadiazine ring system was not present. Despite this limitation, the chemistry provided a route to the rare pyrrolo[2,3-*c*][1,2,6]thiadiazines. Additional study is required to understand better the reaction mechanism and its synthetic potential.

3. Experimental

3.1. General

Solvents EtOH and MeOH were freshly distilled from CaH_2 under argon. Reactions were protected by $CaCl_2$ drying tubes. Anhydrous sodium sulfate was used for drying organic extracts and all volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass backed thin layer chromatography (TLC) plates (Merck Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography was used throughout for all non-TLC scale chromatographic separations using Merck Silica Gel 60 (less than 0.063 mm). Melting points were determined using a Wagner & Munz Polytherm A hot stage microscope apparatus. Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a Perkin Elmer Lambda 25 UV/vis spectrometer and inflections are identified by the abbreviation 'inf'. IR spectra were recorded on a Shimadzu IR Prestige-21 spectrometer fitted with a Pike miracle ATR attachment and strong, medium and weak peaks are represented by s, m and w, respectively. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 machine (at 300 and 75 MHz, respectively). Deuterated solvents were used for homonuclear lock and the signals are referenced to the deuterated solvent peaks. Mass spectra were recorded on a GC-2010 Shimadzu mass spectrometer. VG Autospec 'Q' mass spectrometer. Petroleum ether refers to light petroleum, bp 40–60 °C. (3,5-Dimorpholino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6a**,[15] (3,5-dipiperidino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6b**,[15] (3,5-dipyrrolidino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6c**[15] and 3,5-bis(phenylthio)-4-dicyanomethylene-4*H*-1,2,6-thiadiazine,[15] were prepared according to literature procedures.

*3.1.1. 6-Ethoxy-4-morpholinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile **7a**. Typical Procedure*: To a stirred solution of sodium metal (2.3 mg, 0.11 mmol) in dry EtOH (2 mL) at 20 °C, was added (3,5-dimorpholino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6a** (33 mg, 0.1 mmol). The mixture was heated to ca. 80 °C for 4 h and then allowed to cool to ca. 20 °C. Adsorption of the reaction mixture onto silica and chromatography (petroleum ether/DCM, 1:1) gave the *title compound* **7a** (23.7 mg, 90%) as orange needles, mp 163–165 °C (cyclohexane) (Found: C, 49.34; H, 4.40; N, 23.95. $C_{12}H_{13}N_5O_2S$ requires C, 49.47; H, 4.50; N, 24.04%); λ_{max}(DCM)/nm 457 (log ε 3.82); ν_{max}(ATR)/cm^{-1} 2212m (C≡N), 1570m, 1531m, 1460w, 1442w, 1417m, 1381w, 1315s, 1267m, 1103s, 1018s, 984w, 902m, 879m, 852s, 788s, 725m; δ_H(300 MHz; $CDCl_3$) 4.71 (2H, q, *J* 6.9, OCH_2CH$_3$), 3.94 (4H, t, *J* 4.0, OCH_2), 3.60 (4H, t, *J* 4.15, NCH_2), 1.52 (3H, t, *J* 6.9, CH_3); δ_C(75 MHz; $CDCl_3$) 174.4, 159.0, 154.8, 119.3, 114.1, 83.9 (*C*C≡N), 67.5 (OCH_2), 66.2 (OCH_2), 49.5 (NCH_2), 14.4 (CH_3); *m*/*z* (EI) 291 (M^+, 100%), 205 ($M^+-C_4H_8NO$, 15), 204 (32), 179 (7), 177 (39), 150 (13), 86 ($C_4H_8NO^+$, 81), 57 (16), 56 (24), (Found: M^+, 291.0793. $C_{12}H_{13}N_5O_2S$ requires M, 291.0790). Further elution (DCM) gave *4,6-dimorpholinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile* **11** (1.3 mg, 4%) as red needles, mp 228–230 °C (cyclohexane) (Found: C, 50.50; H, 4.76; N, 25.19. $C_{14}H_{16}N_6O_2S$ requires C, 50.59; H, 4.85; N, 25.28%); λ_{max}(DCM)/nm 490 (log ε 3.60), 326 (3.64); ν_{max}(ATR)/cm^{-1} 2204m (C≡N), 1571s, 1543m, 1431m, 1114s, 910m, 862m, 787m; δ_H(300 MHz; DMSO-d_6) 3.04 (4H, t, *J* 4.62, OCH_2), 2.88 (4H, t, *J* 4.3, OCH_2), 2.83 (4H, t, *J* 4.66, NCH_2), 1.57 (4H, t, *J* 1.6, NCH_2); δ_C(75 MHz; C_5D_5N) 165.7, 161.3, 154.2, 117.7 (C≡N), 83.0, 66.6 (OCH_2), 66.1 (OCH_2), 50.1 (NCH_2), 47.5 (NCH_2); *m*/*z* (EI) 332 (M^+, 100%), 246 ($M^+-C_4H_8NO$, 5), 217 (27), 189 (25), 162 (10), 129 (36), 86 ($C_4H_8NO^+$, 83), 77 (13), 56 (64).

*3.1.2. 6-Methoxy-4-morpholinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile **7b**.* Similar treatment of (3,5-dimorpholino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6a** with a stirred solution of sodium metal in dry MeOH for 24 h at ca. 65 °C, gave after chromatography (petroleum ether/DCM, 1:1) the *title compound* **7b** (22.9 mg, 92%) as orange needles, mp 152–153 °C (cyclohexane) (Found: C, 47.72; H, 3.95; N, 25.29. $C_{11}H_{11}N_5O_2S$ requires C, 47.64; H, 4.00; N, 25.26%); λ_{max}(DCM)/nm 457 (log ε 3.87), 294 (3.88), 230

(3.87); ν_{max}(ATR)/cm^{-1} 2212m (C≡N), 1564m, 1529m, 1463m, 1429w, 1419w, 1383m, 1317s, 1296w, 1261m, 1205w, 1107s, 999m, 950m, 893m, 864s, 800s, 759m, 727m; δ_H(300 MHz; $CDCl_3$) 4.30 (3H, s, OC*H*$_3$), 3.95 (4H, t, *J* 4.7, OC*H*$_2$), 3.62 (4H, t, *J* 4.7, NC*H*$_2$); δ_C(75 MHz; $CDCl_3$) 174.9, 158.8, 154.9, 119.3, 114.1, 83.6 (*C*CN), 66.2 (OCH$_2$), 58.0 (OCH$_3$), 49.5 (NCH$_2$); *m*/*z* (EI) 277 (M$^+$, 100%), 246 (M$^+$−CH$_3$O, 6), 220 (6), 191 (29), 86 ($C_4H_8NO^+$, 78), 84 (10), 56 (26), (Found: M$^+$, 277.0633. $C_{11}H_{11}N_5O_2S$ requires M, 277.0631).

3.1.3. 6-Ethoxy-4-piperidinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile ***7c***. Similar treatment of (3,5-dipiperidino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6b** with a stirred solution of sodium metal in dry EtOH for 24 h at ca. 80 °C gave after chromatography (petroleum ether/DCM, 1:1) the *title compound* **7c** (8.6 mg, 33%) as orange needles, mp 103–105 °C (pentane) (Found: C, 54.07; H, 5.09; N, 24.22. $C_{13}H_{15}N_5OS$ requires C, 53.96; H, 5.23; N, 24.20%); λ_{max}(DCM)/nm 466 (log ε 3.82), 295 (3.88), 229 (3.88); ν_{max}(ATR)/cm^{-1} 2927w, 2853w, 2210m (C≡N), 1568s, 1530m, 1466w, 1431w, 1417w, 1381w, 1309s, 1285w, 1255w, 1220w, 1184w, 1088w, 1030m, 1005w, 984w, 905w, 783s, 725m; δ_H(300 MHz; $CDCl_3$) 4.69 (2H, q, *J* 7.1, OC*H*$_2$CH$_3$), 3.57 (4H, t, *J* 5.3, NC*H*$_2$), 1.72–1.81 (6H, m, C*H*$_2$), 1.51 (3H, t, *J* 7.1, C*H*$_3$); δ_C(75 MHz; $CDCl_3$) 173.9, 158.6, 155.0, 119.0, 114.1, 83.5 (*C*CN), 67.1 (OCH$_2$O), 50.2 (NCH$_2$), 25.3 (NCH$_2$CH$_2$), 24.2 (CH$_2$), 14.5 (CH$_3$); *m*/*z* (EI) 289 (M$^+$, 51%), 260 (10), 245 (3), 84 ($C_5H_{10}N^+$, 100), 56 (19).

3.1.4. 6-Methoxy-4-piperidinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile ***7d***. Similar treatment of (3,5-dipiperidino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6b** with a stirred solution of sodium metal in dry MeOH for 72 h at ca. 65 °C, gave after chromatography (petroleum ether/DCM, 1:2) the *title compound* **7d** (6.4 mg, 26%) as orange needles, mp 104–105 °C (pentane) (Found: C, 52.39; H, 4.69; N, 25.36. $C_{12}H_{13}N_5OS$ requires C, 52.35; H, 4.76; N, 25.44%); λ_{max}(DCM)/nm 466 (log ε 3.75), 294 (3.78), 229 (3.80); ν_{max}(ATR)/cm^{-1} 2937w, 2852w, 2214m (C≡N), 1564m, 1528m, 1458w, 1440m, 1398s, 1356w, 1334w, 1311m, 1277w, 1255m, 1197w, 1105w, 999m, 926w, 945m, 920m, 895w, 864m, 785m, 727m; δ_H(300 MHz; $CDCl_3$) 4.30 (3H, s, OC*H*$_3$), 3.58 (4H, app. s, NCH$_2$C*H*$_2$), 1.76 (6H, app. d, C*H*$_2$); δ_C(75 MHz; $CDCl_3$) 174.4, 158.2, 155.1, 118.9, 114.0, 83.0 (*C*CN), 57.7 (OCH$_3$), 50.1 (NCH$_2$), 25.2 (CH$_2$), 24.2 (CH$_2$); *m*/*z* (EI) 275 (M$^+$, 54%), 218 (4), 191 (M$^+$−C$_5$H$_{10}$N, 9), 84 ($C_5H_{10}N^+$, 100), 56 (18), (Found: M$^+$, 275.0839. $C_{12}H_{13}N_5OS$ requires M, 275.0841).

3.1.5. 6-Ethoxy-4-pyrrolidinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile ***7e***. Similar treatment of (3,5-dipyrrolidino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6c** with a stirred solution of sodium metal in dry EtOH for 4 h at ca. 80 °C, gave after chromatography (petroleum ether/DCM, 1:1) the *title compound* **7e** (9.2 mg, 37%) as orange needles, mp 147–149 °C (cyclohexane) (Found: C, 52.43; H, 4.71; N, 25.37. $C_{12}H_{13}N_5OS$ requires C, 52.35; H, 4.76; N, 25.44%); λ_{max}(DCM)/nm 486 (log ε 4.06), 291 (4.03), 259 (3.92), 227 (3.90); ν_{max}(ATR)/cm^{-1} 2965w, 2670w, 2214m (C≡N), 1562s, 1520s, 1443s, 1387m, 1342m, 1309m, 1296s, 1105w, 1028m, 924w, 870m, 808s, 773m, 723s; δ_H(300 MHz; $CDCl_3$) 4.66 (2H, q, *J* 7.1, OC*H*$_2$CH$_3$), 3.90 (4H, app. s, NC*H*$_2$), 2.07 (4H, t, *J* 6.3, NCH$_2$C*H*$_2$), 1.51 (3H, t, *J* 7.1, C*H*$_3$); δ_C(75 MHz; $CDCl_3$) 173.5, 156.2, 151.6, 115.9, 115.1, 83.9 (*C*CN), 66.7 (OCH$_2$), 50.4 (NCH$_2$), 25.53 (CH$_2$), 14.5 (CH$_3$); *m*/*z* (EI) 275 (M$^+$, 52%), 260 (13), 247 (16), 219 (16), 70 ($C_4H_8N^+$, 100), (Found: M$^+$, 275.0839. $C_{12}H_{13}N_5OS$ requires M, 275.0841).

3.1.6. 6-Methoxy-4-pyrrolidinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile ***7f***. Similar treatment of (3,5-dipyrrolidino-4*H*-1,2,6-thiadiazin-4-ylidene)propanedinitrile **6c** with a stirred solution of sodium metal in dry MeOH for 24 h at ca. 65 °C, gave after chromatography (petroleum ether/DCM, 1:1) the *title compound* **7f** (8.7 mg, 37%) as orange needles, mp 190–191 °C (cyclohexane) (Found: C, 50.53; H, 4.12; N, 26.73. $C_{11}H_{11}N_5OS$ requires C, 50.56; H, 4.24; N, 26.80%); λ_{max}(DCM)/nm 486 (log ε 3.91), 289 (3.94); ν_{max}(ATR)/cm^{-1} 2958w, 2854w, 2216m (C≡N), 1566s, 1523s, 1460m, 1390s, 1296m, 964m, 912w, 808m, 759m; δ_H(300 MHz; $CDCl_3$) 4.30 (3H, s, OC*H*$_3$), 3.91 (4H, t, *J* 6.7, NC*H*$_2$), 2.05–2.10 (4H, m, 2×C*H*$_2$); δ_C(75 MHz; $CDCl_3$) 174.0, 155.9, 151.7, 115.9, 115.1, 80.9 (*C*CN), 57.5 (OCH$_3$), 50.5 (NCH$_2$), 25.5 (NCH$_2$CH$_2$); *m*/*z* (EI) 261 (M$^+$, 54%), 245 (18), 232 (14), 191 (M$^+$−C$_4$H$_8$N, 16), 177 (15), 91 (15), 70 ($C_4H_8N^+$, 100), (Found: M$^+$, 261.0685. $C_{11}H_{11}N_5OS$ requires M, 261.0684).

3.1.7. Reaction of 6-ethoxy-4-morpholinopyrrolo[2,3-c][1,2,6]thiadiazine-5-carbonitrile ***7a*** *with morpholine.* To a stirred solution of 6-ethoxy-4-morpholinopyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitrile **7a** (29.1 mg, 0.10 mmol) in dry EtOH (2 mL) at ca. 20 °C was added morpholine (260 μL, 3 mmol). The mixture was heated to ca. 80 °C for 4 d and then allowed to cool to ca. 20 °C. Adsorption of the reaction mixture onto silica and chromatography (DCM) gave 4,6-dimorpholinopyrrolo[2,3-*c*][1,2,6]thiadiazine-5-carbonitrile **11** (15.9 mg, 48%) as red crystals, mp 228–230 °C (cyclohexane), identical to that described above.

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