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Aust. J. Chem. **2010**, *63*, 785–791

N,*N*-Dialkyl-*N*′-Chlorosulfonyl Chloroformamidines in Heterocyclic Synthesis. Part IX.* Novel Triazolo-Fused Thiatriazoles and Pyrazolo-Fused Oxathiazines

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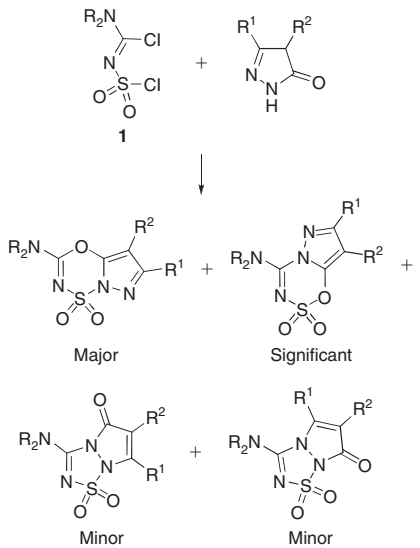
N,*N*-dialkyl-*N*′-chlorosulfonyl chloroformamidines **1** reacted with 4-substituted urazoles **2** to give [1,2,4]triazolo[1,2-*b*][1,2,3,5]thiatriazoles **3** in a selective 1,2-NN dinucleophilic mode of reaction. The reaction of **1** with N^1-substituted pyrazol-5-ones **4** afforded pyrazolo[4,3-*e*][1,4,3]oxathiazines **5** via selective 1,3-CCO dinucleophilic substitution. Compounds **3** and **5** were the sole products isolated from the respective reactions and both represent new ring systems.

Manuscript received: 24 November 2009.
Manuscript accepted: 15 January 2010.

Introduction

We recently reported[1] that the reaction between *N*,*N*-dialkyl *N*′-chlorosulfonyl chloroformamidines **1** and *N*-unsubstituted pyrazol-3-ones produced the previously unknown pyrazolo[3,2-*b*][1,2,3,5]oxathiadiazine and pyrazolo[2,3-*e*][1,4,3,5]oxathiadiazine ring systems, along with, in minor proportion(s), one or two trioxo isomers of the rare pyrazolo[1,2-*b*][1,2,3,5]thiatriazole ring system (Scheme 1). The four possible products from this reaction apparently arise from numerous tautomeric forms available to *N*-unsubstituted pyrazol-3-ones.[1]

We were interested in trying to constrain the regiochemical outcome of this or similar multisite reactions by restricting the number of tautomeric forms available to the starting dinucleophile. We envisaged that in this way, fewer products would be created, rather than mixtures of several isomers. The feasibility of this approach was explored and this paper details the outcomes.

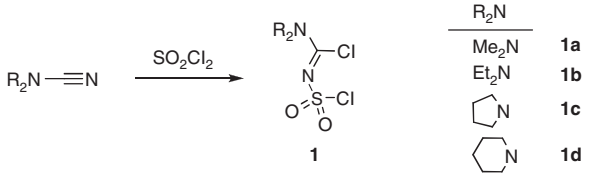


Scheme 1.

Results and Discussion

The dichlorides **1a**–**d** were readily prepared[1,2] from sulfuryl chloride and the corresponding dialkyl cyanamide (Scheme 2).

In place of *N*-unsubstituted pyrazol-3-ones, which on reaction with dichlorides **1** gave mainly 1,3-NCO disubstituted products and little 1,2-NN disubstituted products, we chose to use 4-substituted urazoles **2**. These compounds cannot exist as tautomers containing an NH–C–OH moiety and therefore cannot act as 1,3-NCO dinucleophiles. It is known that 4-phenylurazole reacts smoothly with acetic anhydride to afford the 1,2-diacetylated product in almost quantitative yield.[3] Therefore,



Scheme 2. General synthesis of dichlorides **1**.

*Part VIII, published in *Aust. J. Chem.* **2010**, *63*, 659.

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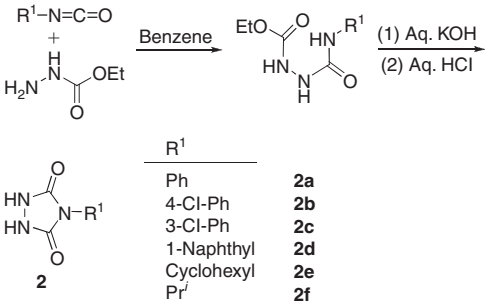
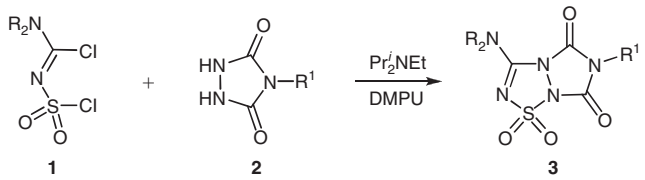


Scheme 3. General synthesis of urazoles **2**.



Scheme 4.

Table 1. Synthesis of the [1,2,4]triazolo[1,2-*b*][1,2,3,5]thiatriazoles 3

R_2N	R^1	Product	Yield [%]
Me_2N (**1a**)	Ph (**2a**)	**3a**	50
Et_2N (**1b**)	Ph (**2a**)	**3b**	31
N (**1c**)	Ph (**2a**)	**3c**	60
Me_2N (**1a**)	4-Cl-Ph (**2b**)	**3d**	54
N (**1c**)	3-Cl-Ph (**2c**)	**3e**	73
N (**1d**)	1-Naphthyl (**2d**)	**3f**	55
Me_2N (**1a**)	Cyclohexyl (**2e**)	**3g**	29
Me_2N (**1a**)	Pr^i (**2f**)	**3h**	16

we were confident that 4-substituted urazoles **2** would react with dichlorides **1** through the two nitrogen atoms, N1 and N2.

The 4-substituted urazoles **2a**–**f** were synthesized from ethyl hydrazinecarboxylate and the appropriate isocyanate (Scheme 3).[4]

The reaction of dichlorides **1** with 4-substituted urazoles **2** in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (dimethylpropylene urea, DMPU), in the presence of Hünig's base, readily gave [1,2,4]triazolo[1,2-*b*][1,2,3,5]thiatriazoles **3**, the first reported representatives of this ring system, as the sole isolated product (Scheme 4, Table 1).

The [1,2,4]triazolo[1,2-*b*][1,2,3,5]thiatriazoles **3** were isolated in high purity after simple precipitation from the DMPU-based reaction mixture (by the addition of ethyl acetate and water) and washing with dilute hydrochloric acid. The relatively low yields of diethylamino derivative **3b** and alkyl-substituted compounds **3g** and **3h** may be simply a result of their greater solubility in organic solvents. No attempts were made to isolate further amounts of these products from the mother liquor.

The products **3** were stable, colourless, crystalline solids; however, we were not able to recrystallize them from methanol or ethanol. After boiling in these solvents, significant decomposition was observed by NMR spectroscopy. Nevertheless, recrystallization to analytical purity was possible from isopropanol or from ethanol/chloroform or isopropanol/acetone mixtures.

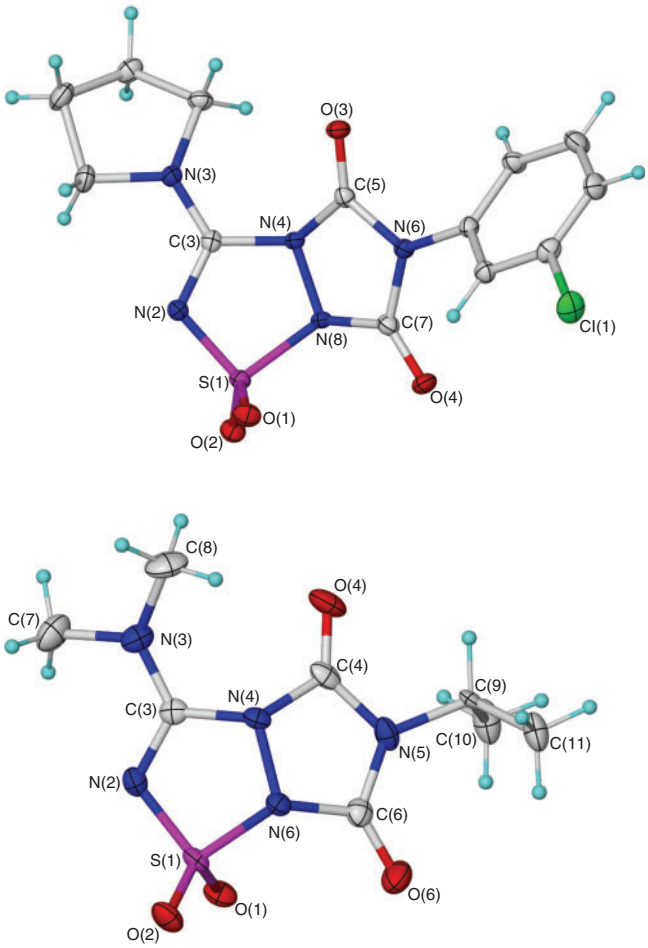


Fig. 1. *ORTEP* diagrams of **3e** and **3h**.

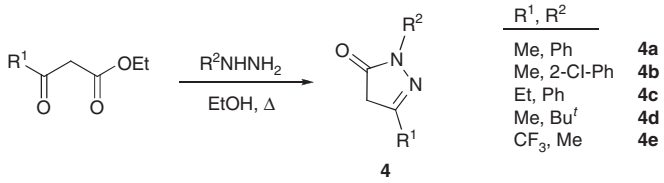
The structural assignments for **3a**–**h** were confirmed by X-ray crystallographic analyses of **3e** and **3h** as typical representatives (Fig. 1 and Table 3).

As predicted, ring formation to produce compounds **3** proceeded via the 1,2-NN dinucleophilic mode of addition.

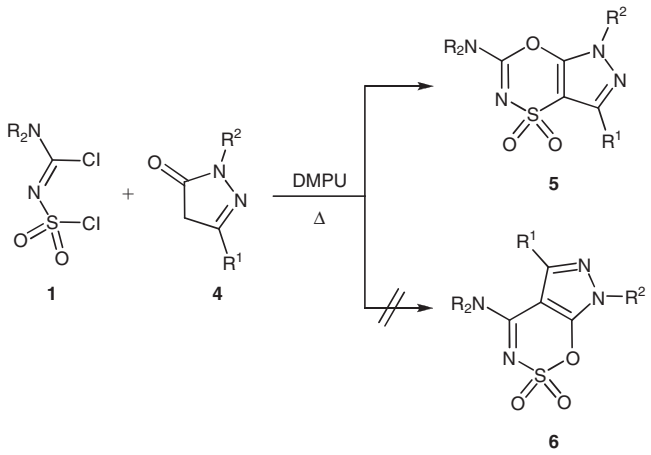
With a method in hand that selectively gave fused, bicyclic products arising from 1,2-NN dinucleophilic reaction, we turned our attention toward attempting to alter the course of the reaction between pyrazol-3-ones and dichlorides **1** so as to obtain fused cyclic products involving C-substitution. Employing N^1-substituted pyrazol-5-ones, which are substituted at the nitrogen atom directly adjacent to the carbonyl group, should block both of the 1,2-NN and 1,3-NCO modes of reaction and we expected that this should ensure 1,3-CCO dinucleophilic substitution, because such pyrazolones are well known to acylate at C4 (and sometimes at N2 or the exocyclic oxygen atom).[5–7]

N-Substituted pyrazolones **4a**–**e** were synthesized from the appropriate β-ketoesters and monosubstituted hydrazines (Scheme 5).[8]

Treatment of pyrazolones **4** with dichlorides **1** at 80°C in DMPU indeed effected 1,3-CCO dinucleophilic substitution to form 3-dialkylamino-1,1-dioxo-1λ^6-pyrazolo[4,3-*e*][1,4,3]oxathiazines **5** (Scheme 6, Table 2). These compounds



Scheme 5. General synthesis of pyrazolones **4**.



Scheme 6.

Table 2. Synthesis of the pyrazolo[4,3-*e*][1,4,3]oxathiazines 5

R_2N	R^1	R^2	Product	Yield [%]
Me_2N (**1a**)	Me	Ph (**4a**)	**5a**	61
N (**1c**)	Me	2-Cl-Ph (**4b**)	**5b**	72
N (**1d**)	Me	2-Cl-Ph (**4b**)	**5c**	56
N (**1c**)	Et	Ph (**4c**)	**5d**	37
Me_2N (**1a**)	Me	Bu^t (**4d**)	**5e**	20
Et_2N (**1b**)	Me	Bu^t (**4d**)	**5f**	26
Me_2N (**1a**)	CF_3	Me (**4e**)	**5g**	59
Et_2N (**1b**)	CF_3	Me (**4e**)	**5h**	34
N (**1d**)	CF_3	Me (**4e**)	**5i**	50

are the first reported representatives of the pyrazolo[4,3-*e*][1,4,3]oxathiazine ring system.

Usually, the pyrazolo[4,3-*e*][1,4,3]oxathiazines **5** were precipitated from the reaction mixture in high purity by our favoured[9] ethyl acetate/water workup procedure. No other products were isolated. In the case of compound **5a**, the whole reaction mixture was analyzed and extensive chromatography did not reveal the presence of any additional isomeric products.

The derivatives of the new heterocyclic system described above were all stable, colourless, crystalline solids unaffected by recrystallization from alcohols.

Spectroscopic studies alone were not sufficient to distinguish between the two possible isomeric structures **5** and **6**; therefore structural assignments for compounds listed in Table 2 were based on X-ray crystallographic analyses of representative compounds **5a**, **5c**, and **5f** (Fig. 2, Table 3).

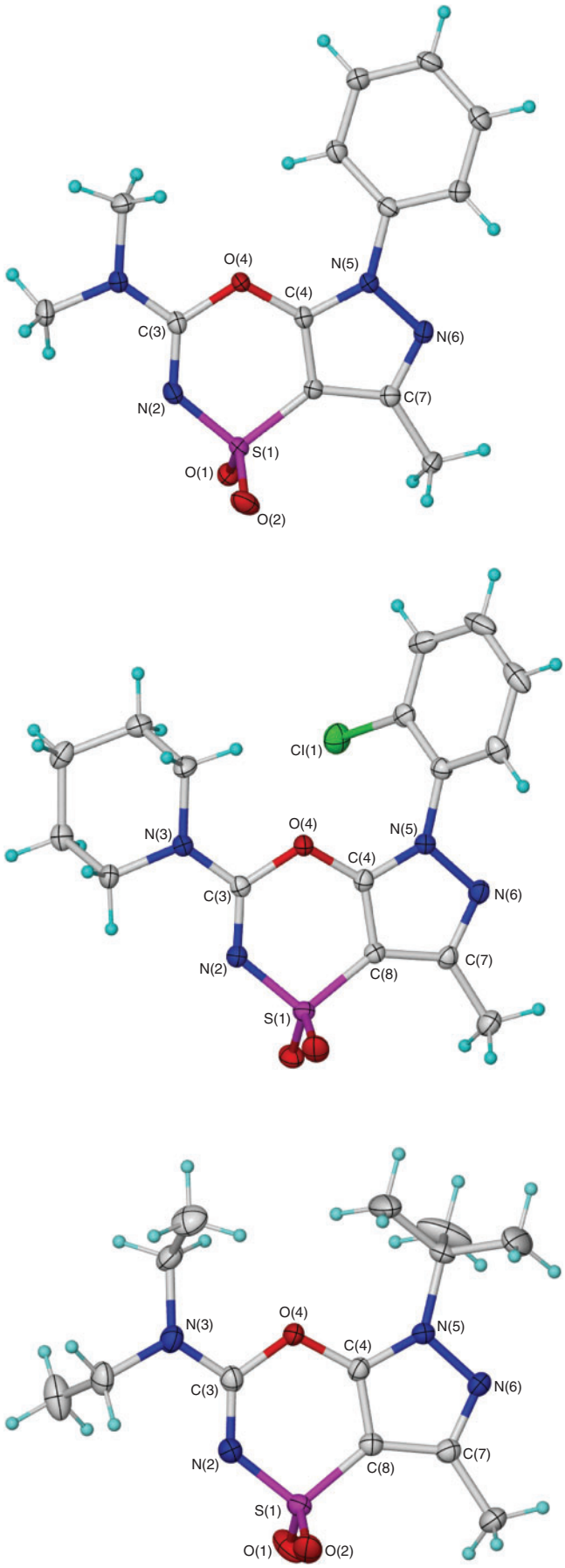


Fig. 2. *ORTEP* diagrams of **5a**, **5c**, and **5f**.

Table 3. Crystal data and structure refinement for 3e, 3h, 5a, 5c, 5f

	3e	3h	5a	5c	5f
CCDC no.	755596	755595	755593	755594	755592
Empirical formula	$C_{13}H_{12}ClN_5O_4S$	$C_8H_{13}N_5O_4S$	$C_{13}H_{14}N_4O_3S$	$C_{16}H_{17}ClN_4O_3S$	$C_{13}H_{22}N_4O_3S$
Formula weight	369.79	275.29	306.34	380.85	314.41
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/n$	$P2_1/c$	$P2_1/c$	$P2_1/c$
Unit cell dimensions					
a [Å]	10.7866(1)	8.6770(2)	9.2397(3)	10.2794(2)	19.3970(6)
b [Å]	12.7327(2)	13.4273(4)	16.1650(5)	19.924(4)	18.0859(7)
c [Å]	11.8309(2)	10.9685(3)	9.3633(4)	9.2248(1)	9.0451(3)
α [°]	90	90	90	90	90
β [°]	103.803 (1)	111.7350(10)	103.471(1)	114.510(1)	91.449(2)
γ [°]	90	90	90	90	90
Volume [Å^3]	1577.96(4)	1187.07(6)	1360.02(8)	1719.0(3)	3172.12(19)
Z	4	4	4	4	8
ρ (calc.) [mg m^{-3}]	1.557	1.540	1.496	1.472	1.317
μ [mm^{-1}]	0.404	0.290	0.255	0.368	0.220
Crystal size [mm]	0.33 × 0.25 × 0.25	0.25 × 0.25 × 0.13	0.30 × 0.30 × 0.25	0.30 × 0.20 × 0.08	0.25 × 0.25 × 0.20
θ range [°]	2.30 to 27.50	2.51 to 27.49	2.27 to 27.50	2.04 to 27.50	2.49 to 27.50
N_{total}	22431	7545	16515	17351	30704
N (R_{int})	3611 (0.061)	2668 (0.062)	3111 (0.061)	3874 (0.068)	7205 (0.054)
N_{obs} [$I > 2\sigma(I)$]	2857	2057	2284	2677	5570
R indices [$I > 2\sigma(I)$]					
R_1	0.0359	0.0618	0.0443	0.0469	0.0499
wR_2	0.0796	0.1666	0.1049	0.1081	0.1076
R indices (all data)					
R_1	0.0555	0.0811	0.0720	0.0805	0.0696
wR_2	0.0888	0.1842	0.1183	0.1263	0.1194
GoF (on F^2)	1.041	1.031	1.028	1.042	1.045

Ring formation to produce the fused oxathiazines **5** proceeds such that the carbon atom of **4** reacts with the sulfamoyl chloride moiety of **1** and the oxygen atom bonds with the amidine carbon atom. This mode of reaction parallels that observed with 4-hydroxy-2-pyrone derivatives and 1,3-dimethylbarbituric acid (other compounds with an enolizable methylene group), which were reported earlier.[10]

Conclusion

The dichloro compounds **1**, readily available and versatile 1,3-dielectrophiles, have been shown to react with 4-substituted urazoles **2** via selective 1,2-NN dinucleophilic substitution to give 3-dialkylamino-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-*b*][1,2,3,5]thiatriazoles **3**. Reaction of dichlorides **1** with *N*-substituted pyrazolones **4** afforded 3-dialkylamino-1,1-dioxo-1λ^6-pyrazolo[4,3-*e*][1,4,3]oxathiazines **5**, which arise from selective 1,3-CCO dinucleophilic substitution. Compounds **3** and **5** represent hitherto unreported heterocyclic ring systems.

Experimental

Methods and Materials

Analytical and spectroscopic methods were described previously.[1]

The urazoles **2a**,[4] **2b**,[11] **2c**,[11] **2d**,[12] **2e**,[13] **2f**[14] were all synthesized from ethyl hydrazinecarboxylate and the appropriate isocyanate using the procedure of Cookson et al.[4] The pyrazolones **4c**,[15] **4d**,[16] and **4e**[17] were all prepared from the appropriate β-ketoester and monosubstituted hydrazine by the method of Taylor and McKillop.[8] Other materials were obtained from commercial sources.

General Synthesis Procedure for 6-Substituted 3-Dialkylamino-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazoles *3a–i*

N,*N*-Diisopropylethylamine (5 mmol) was added to a stirred mixture of the 4-substituted urazole **2** (2 mmol), the dichloro compound **1** (3 mmol), and DMPU (2 mL). The resulting mixture was stirred at room temperature for at least 3 h. Ethyl acetate (5 mL) was added, followed by water (10 mL). The mixture was stirred vigorously for at least 10 min. The precipitate was collected and the solid was stirred in dilute hydrochloric acid (2 M, 5 mL) for a few minutes before being filtered and the collected solid washed sequentially with water, ethyl acetate and diethyl ether.

The following compounds were prepared by the above procedure:

3-Dimethylamino-6-phenyl-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole *3a*

Obtained as an off-white solid in 50% yield. Recrystallized from ethanol/chloroform (~4:1); colourless needles, mp 191.5–192.5°C. (Found: C 42.6, H 3.7, N 22.5%; M$^{+\bullet}$ 309.0517. $C_{11}H_{11}N_5O_4S$ requires C 42.7, H 3.6, N 22.6%; M$^{+\bullet}$ 309.0526). δ_H (400 MHz, $CDCl_3$) 7.55–7.42 (5H, m, ArH), 3.39 (3H, s, NCH_3), 3.25 (3H, s, NCH_3). δ_C (50 MHz, $CDCl_3$) 150.8, 148.8, 148.5, 129.9, 129.7, 129.6, 126.0, 41.8, 40.3. *m/z* (EI) 309 (42%, M$^{+\bullet}$), 190 (100).

3-Diethylamino-6-phenyl-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole ***3b***

Obtained in 31% yield after radial chromatography (50–100% dichloromethane in light petroleum, then 0–5% ethyl acetate in dichloromethane) and recrystallization from isopropanol; nacreous plates, mp 170–171°C. (Found: C 46.2, H 4.7, N 21.0%; $M^{+\bullet}$ 337.0831. $C_{13}H_{15}N_5O_4S$ requires C 46.3, H 4.5, N 20.8%; $M^{+\bullet}$ 337.0839). δ_H (400 MHz, $CDCl_3$) 7.55–7.42 (5H, m, ArH), 3.75 (2H, q, *J* 7.1, NCH_2) 3.61 (2H, q, *J* 7.2, NCH_2), 1.38 (3H, t, *J* 7.1, CH_3), 1.32 (3H, t, *J* 7.2, CH_3). δ_C (100 MHz, $CDCl_3$) 149.8, 148.8, 148.2, 129.9, 129.7, 129.6, 126.0, 46.7, 44.7, 13.3, 11.7. *m/z* (EI) 337 (31%, $M^{+\bullet}$), 218 (100).

3-Pyrrolidin-1-yl-6-phenyl-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole ***3c***

Obtained as a white solid in 60% yield. Recrystallized from ethanol/chloroform (~3:2); small, colourless needles, mp 218–220°C. (Found: C 46.4, H 3.9, N 20.8%; $M^{+\bullet}$ 335.0676. $C_{13}H_{13}N_5O_4S$ requires C 46.6, H 3.9, N 20.9%; $M^{+\bullet}$ 335.0683). δ_H (500 MHz, $CDCl_3$) 7.54–7.42 (5H, m, ArH), 3.98 (2H, t, *J* 7, NCH_2) 3.68 (2H, t, *J* 7, NCH_2), 2.12–2.00 (4H, m, CH_2CH_2). δ_C (125 MHz, $CDCl_3$) 148.6, 148.5, 148.0, 129.8, 129.7, 129.6, 126.0, 52.4, 50.7, 26.1, 24.5. *m/z* (EI) 335 (45%, $M^{+\bullet}$), 216 (100).

6-(4-Chlorophenyl)-3-dimethylamino-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole ***3d***

Obtained as a white solid in 54% yield. Recrystallized from isopropanol/acetone (~1:1); colourless crystals, mp 210–212°C. (Found: C 38.5, H 2.9, N 20.3%; $M^{+\bullet}$ 343.0127. $C_{11}H_{10}ClN_5O_4S$ requires C 38.4, H 2.9, N 20.4%; $M^{+\bullet}$ 343.0137). δ_H (400 MHz, $CDCl_3$) 7.50 (2H, m, ArH), 7.41 (2H, m, ArH), 3.39 (3H, s, NCH_3), 3.25 (3H, s, NCH_3). δ_C (125 MHz, $CDCl_3$) 150.7, 148.5, 148.1, 135.9, 129.9, 128.0, 127.1, 41.9, 40.3. *m/z* (EI) 343/345 (35/14%, $M^{+\bullet}$), 190 (100).

6-(3-Chlorophenyl)-3-pyrrolidin-1-yl-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole ***3e***

Obtained as a colourless powder in 73% yield. Recrystallized from isopropanol/acetone (~1:1) to give colourless prisms, mp 217.5–219.5°C. (Found: C 42.3, H 3.4, N 19.0, S 8.6%; $M^{+\bullet}$ 369.0294. $C_{13}H_{12}ClN_5O_4S$ requires C 42.2, H 3.3, N 18.9, S 8.7%; $M^{+\bullet}$ 369.0293). δ_H (400 MHz, $CDCl_3$) 7.51–7.49 (1H, m, ArH), 7.48–7.44 (2H, m, ArH), 7.41–7.36 (1H, m, ArH), 3.97 (2H, t, *J* 6.5, CH_2N), 3.69 (2H, t, *J* 6.5, CH_2N), 2.14–2.01 (4H, m, 2 × CH_2). δ_H (400 MHz, [D_6]DMSO) 7.67–7.49 (4H, m, ArH), 3.89 (2H, t, *J* 6.5, CH_2N), 3.54 (2H, t, *J* 6.5, CH_2N), 1.94 (4H, m, 2 × CH_2). δ_C (100 MHz, $CDCl_3$) 148.2, 148.1, 147.9, 135.3, 130.7, 130.6, 130.1, 126.1, 124.0, 52.4, 50.8, 26.1, 24.5. δ_C (100 MHz, [D_6]DMSO) 148.0, 147.9, 147.3, 133.2, 131.1, 130.8, 129.5, 126.7, 125.5, 52.5, 50.5, 25.4, 23.9. *m/z* (EI) 369/371 (41/16%, $M^{+\bullet}$), 216 (100), 153/155 (24/8), 96 (55). Colourless single crystals suitable for X-ray analysis were obtained by slow evaporation of an acetone solution.

6-Naphth-1-yl-3-piperidin-1-yl-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole ***3f***

Obtained as an off-white solid in 55% yield. Recrystallized from isopropanol/acetone (~2:1); colourless prisms, mp 215–216°C. (Found: C 54.4, H 4.6, N 17.6%; $M^{+\bullet}$ 399.0990. $C_{18}H_{17}N_5O_4S$ requires C 54.1, H 4.3, N 17.5%; $M^{+\bullet}$ 399.0996). δ_H (500 MHz, $CDCl_3$) 8.04 (1H, d, *J* 8.2, ArH), 7.96 (1H, d, *J* 7.3, ArH), 7.72 (1H, dd, *J* 8.2, 0.7, ArH), 7.64–7.56 (3H, m, ArH), 7.52 (1H, dd, *J* 7.3, 1.1, ArH), 3.77 (2H, m, NCH_2), 3.74 (2H, m, NCH_2), 1.79 (4H, m, 2 × CH_2), 1.73 (2H, m, CH_2). δ_C (125 MHz, $CDCl_3$) 149.35, 149.34, 148.8, 134.4, 131.6, 129.2, 128.8, 128.3, 127.2, 127.0, 125.4, 125.3, 121.3, 51.7, 49.6, 25.7, 24.8, 23.4. *m/z* (EI) 399 (48%, $M^{+\bullet}$), 230 (41), 169 (100).

6-Cyclohexyl-3-dimethylamino-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole ***3g***

Obtained as a white solid in 29% yield. Recrystallized from isopropanol/acetone (~2:1); colourless plates, mp 184–185°C. (Found: C 41.9, H 5.5, N 22.0%; $M^{+\bullet}$ 315.0988. $C_{11}H_{17}N_5O_4S$ requires C 41.9, H 5.4, N 22.2%; $M^{+\bullet}$ 315.0996). δ_H (500 MHz, $CDCl_3$) 3.89 (1H, tt, *J* 12.4, 3.9, CHN), 3.33 (3H, s, NCH_3), 3.20 (3H, s, NCH_3), 2.10–2.00 (2H, m), 1.90–1.76 (4H, m), 1.71–1.65 (1H, m), 1.37–1.14 (3H, m). δ_C (125 MHz, $CDCl_3$) 151.0, 149.8, 149.3, 54.5, 41.7, 40.1, 28.8, 25.5, 24.7. *m/z* (EI) 315 (11%, $M^{+\bullet}$), 233 (94), 190 (52), 83 (72), 71 (100).

3-Dimethylamino-6-prop-2-yl-1,1,5,7-tetraoxo-1λ^6-[1,2,4]triazolo[1,2-b][1,2,3,5]thiatriazole ***3h***

Obtained as a white solid in 16% yield. Recrystallized from isopropanol/acetone (~2:1); colourless prisms, mp 189.5–190.5°C. (Found: C 35.0, H 4.8, N 25.2%; $M^{+\bullet}$ 275.0679. $C_8H_{13}N_5O_4S$ requires C 34.9, H 4.8, N 25.4%; $M^{+\bullet}$ 275.0683). δ_H (500 MHz, $CDCl_3$) 4.31 (1H, septet, *J* 6.9, CH), 3.34 (3H, s, NCH_3), 3.21 (3H, s, NCH_3), 1.47 (6H, d, *J* 6.9, $C(CH_3)_2$). δ_C (125 MHz, $CDCl_3$) 151.0, 149.7, 149.3, 47.2, 41.7, 40.1, 19.2. *m/z* (EI) 275 (40%, $M^{+\bullet}$), 233 (54), 190 (98), 70 (100).

General Synthesis Procedure for 3-Dialkylamino-1,1-dioxo-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazines ***5***

A stirred mixture of the *N*-substituted pyrazolone **4** (2 mmol), the dichloro compound **1** (2.5 mmol), and DMPU (2 mL) was heated at 80°C for 10–11 h. The mixture was cooled and slowly diluted with water (10 mL) and then ethyl acetate (5 mL). The mixture was stirred vigorously for at least 15 min. The precipitate was collected by filtration and washed sequentially with 5% aqueous NaOH solution, water and diethyl ether.

The following compounds were prepared by the above procedure:

3-Dimethylamino-1,1-dioxo-7-methyl-5-phenyl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine ***5a***

The reaction mixture was diluted with water only. The resulting sticky orange precipitate was collected and dissolved in dichloromethane. The filtrate was extracted several times with dichloromethane. The combined extracts were added to the solution of the precipitate and the whole was washed with 5% aqueous sodium hydroxide solution and then water. The solvent was removed under reduced pressure. The aqueous phase slowly yielded additional precipitate after several hours. All product samples obtained were chromatographed over silica gel (dichloromethane/light petroleum, 1:1), affording the title compound in 61% yield. Recrystallized from acetonitrile/dichloromethane; colourless crystals, mp 240–242°C (dec.). (Found: C 51.2, H 4.6, N 18.4; $M^{+\bullet}$ 306.0779. $C_{13}H_{14}N_4O_3S$ requires C 51.0, H 4.6, N 18.3%; $M^{+\bullet}$ 306.0781). δ_H (300 MHz, $CDCl_3$) 7.60–7.56 (2H, m, ArH), 7.54–7.49 (2H, m, ArH), 7.44–7.39 (1H, m, ArH), 3.21 (3H, s, NCH_3), 3.14 (3H, s, NCH_3), 2.54 (3H, s, CH_3). δ_C (75 MHz, $CDCl_3$) 147.9, 145.0, 144.5, 136.3,

129.6, 128.3, 122.1, 100.9, 39.0, 36.6, 13.5. *m/z* (EI) 306 (24%, $M^{+\bullet}$), 236 (100), 174 (3), 105 (59), 77 (29), 67 (88).

5-(2-Chlorophenyl)-1,1-dioxo-7-methyl-3-pyrrolidin-1-yl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine ***5b***

Obtained in 72% yield after column chromatography (silica gel, dichloromethane). Recrystallized from ethanol; colourless crystals, mp 242–243°C (dec.). (Found: C 49.4, H 4.1, N 15.3%; $M^{+\bullet}$ 366.0537. $C_{15}H_{15}ClN_4O_3S$ requires C 49.1, H 4.1, N 15.3%; $M^{+\bullet}$ 366.0553). δ_H (300 MHz, $CDCl_3$) 7.56–7.54 (1H, m, Ar), 7.49–7.44 (3H, m, Ar), 3.59 (2H, br s, NCH_2), 3.39 (2H, br s, NCH_2), 2.53 (3H, s, CH_3), 1.96–1.94 (4H, m, CH_2CH_2). δ_C (50 MHz, $CDCl_3$) 146.3, 145.9, 145.2, 133.3, 131.2, 130.7, 130.5, 129.2, 128.0, 100.5, 48.6, 46.6, 25.3, 24.6, 13.6. *m/z* (EI) 366 (28%, $M^{+\bullet}$), 272 (12), 270 (28), 150 (13), 139 (18), 67 (100).

5-(2-Chlorophenyl)-1,1-dioxo-7-methyl-3-piperidin-1-yl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine ***5c***

Obtained in 56% yield after chromatography (silica gel, dichloromethane/light petroleum, 1:1). Recrystallized from ethanol; colourless crystals, mp 243–244°C (dec.). (Found: C 50.7, H 4.5, N 14.8%; $M^{+\bullet}$ 380.0698. $C_{16}H_{17}ClN_4O_3S$ requires C 50.5, H 4.5, N 14.7%; $M^{+\bullet}$ 380.0704). δ_H (300 MHz, $CDCl_3$) 7.59–7.58 (1H, m, Ar), 7.56–7.46 (3H, m, Ar), 3.70 (2H, br s, NCH_2), 3.40 (2H, br s, NCH_2), 2.55 (3H, s, CH_3), 1.65 (6H, br s, $CH_2CH_2CH_2$). δ_C (50 MHz, $CDCl_3$) 146.4, 146.3, 145.2, 133.5, 131.2, 130.6, 130.5, 129.3, 128.1, 100.6, 47.5, 45.5, 25.6, 24.9, 23.7, 13.6. *m/z* (EI) 380 (28%, $M^{+\bullet}$), 272 (15), 270 (40), 150 (17), 139 (21), 111 (26), 67 (100).

1,1-Dioxo-7-ethyl-5-phenyl-3-pyrrolidin-1-yl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine ***5d***

Obtained as a light grey solid in 37% yield after sequential boiling with isopropanol and trituration with dichloromethane. Recrystallized from ethanol; fine, colourless needles, mp 216.5–217.5°C. (Found: C 55.6, H 5.3, N 16.5%; $M^{+\bullet}$ 346.1090. $C_{16}H_{18}N_4O_3S$ requires C 55.5, H 5.2, N 16.2%; $M^{+\bullet}$ 346.1094). δ_H (500 MHz, $CDCl_3$) 7.63–7.59 (2H, m, Ar), 7.53–7.48 (2H, m, Ar), 7.42–7.37 (1H, m, Ar), 3.65 (2H, t, *J* 6.6, NCH_2), 3.58 (2H, t, *J* 6.6, NCH_2), 2.93 (2H, q, *J* 7.6, CH_2), 2.07–1.96 (4H, m, CH_2CH_2), 1.42 (3H, t, *J* 7.6, CH_3). δ_C (125 MHz, $CDCl_3$) 150.1, 146.0, 145.0, 136.5, 129.6, 128.1, 121.9, 100.5, 48.7, 46.8, 25.5, 24.7, 21.9, 12.4. *m/z* (EI) 346 (24%, $M^{+\bullet}$), 250 (87), 105 (38), 81 (100).

*5-*tert*-Butyl-3-dimethylamino-1,1-dioxo-7-methyl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine* ***5e***

Obtained in 20% yield after recrystallization from aqueous isopropanol; flat, colourless needles, mp 206–208°C. (Found: C 46.4, H 6.3, N 19.8%; $M^{+\bullet}$ 286.1089. $C_{11}H_{18}N_4O_3S$ requires C 46.1, H 6.3, N 19.6%; $M^{+\bullet}$ 286.1094). δ_H (500 MHz, $CDCl_3$) 3.20 (3H, s, NCH_3), 3.19 (3H, s, NCH_3), 2.43 (3H, s, CH_3), 1.61 (9H, s, $C(CH_3)_3$). δ_C (125 MHz, $CDCl_3$) 148.3, 145.0, 141.2, 99.8, 60.6, 39.1, 36.8, 29.1, 13.4. *m/z* (EI) 286 (45%, $M^{+\bullet}$), 216 (48), 71 (37), 67 (100).

*5-*tert*-Butyl-3-diethylamino-1,1-dioxo-7-methyl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine* ***5f***

Obtained as a colourless solid in 26% yield after chromatography (silica gel, 5% ethyl acetate in dichloromethane). Recrystallized from isopropanol; colourless plates, mp 187.5–189°C. (Found: C 49.8, H 6.9, N 17.7%; $M^{+\bullet}$ 314.1402. $C_{13}H_{22}N_4O_3S$ requires C 49.7, H 7.1, N 17.8%; $M^{+\bullet}$ 314.1407). δ_H (500 MHz, $CDCl_3$) 3.57 (2H, q, *J* 7, NCH_2), 3.49 (2H, q, *J* 7, NCH_2), 2.43 (3H, s, CH_3), 1.61 (9H, s, $C(CH_3)_3$), 1.27 (6H, t, *J* 7, 2 × CH_3). δ_C (125 MHz, $CDCl_3$) 147.4, 145.0, 141.3, 100.0, 60.5, 44.8, 42.4, 29.1, 13.9, 13.4, 12.4. *m/z* (EI) 314 (54%, $M^{+\bullet}$), 216 (43), 99 (35), 67 (100). Crystals suitable for X-ray analysis were obtained by slow evaporation of an ethyl acetate/dichloromethane solution.

3-Dimethylamino-1,1-dioxo-5-methyl-7-trifluoromethyl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine ***5g***

Obtained as a cream-coloured solid solid in 59% yield. Recrystallized from methanol/chloroform (~4:1) giving small, white, woolly needles, mp 280–282°C. (Found: C 32.4, H 3.0, N 18.6%; $M^{+\bullet}$ 298.0336. $C_8H_9F_3N_4O_3S$ requires C 32.2, H 3.0, N 18.8%; $M^{+\bullet}$ 298.0342). δ_H (400 MHz, $CDCl_3$) 3.91 (3H, s, 5-NCH_3), 3.23 (6H, s, NMe_2). δ_H (400 MHz, [D_6]DMSO) 3.87 (3H, s, 5-NCH_3), 3.19 (3H, s, NCH_3), 3.09 (3H, s, NCH_3). δ_F (188 MHz, $CDCl_3$) −57.01. δ_C (100 MHz, [D_6]DMSO) 147.9, 147.4, 132.8 (q, J_{CF} 40.6), 120.2 (q, J_{CF} 269.3), 99.9, 38.8, 36.9, 36.0. *m/z* (EI) 298 (100%, $M^{+\bullet}$).

3-Diethylamino-1,1-dioxo-5-methyl-7-trifluoromethyl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine ***5h***

Obtained as colourless crystals in 34% yield; mp 231–233°C. (Found: C 36.9, H 4.2, N 17.0%; $M^{+\bullet}$ 326.0651. $C_{10}H_{13}F_3N_4O_3S$ requires C 36.8, H 4.0, N 17.2%; $M^{+\bullet}$ 326.0655). δ_H (400 MHz, $CDCl_3$) 3.89 (3H, s, NCH_3), 3.57 (2H, q, *J* 7, NCH_2), 3.55 (2H, q, *J* 7, NCH_2), 1.32 (3H, t, *J* 7, CH_3), 1.28 (3H, t, *J* 7, CH_3). δ_F (188 MHz, $CDCl_3$) −62.99. δ_C (50 MHz, $CDCl_3$) 146.4, 146.0, 135.3 (q, J_{CF} 41.7), 119.4 (q, J_{CF} 270.2), 100.2, 45.1, 42.8, 35.3, 13.8, 12.2. *m/z* (EI) 326 (66%, $M^{+\bullet}$), 98 (100).

1,1-Dioxo-5-methyl-3-piperidin-1-yl-7-trifluoromethyl-1λ^6-pyrazolo[4,3-e][1,4,3]oxathiazine ***5i***

Obtained as a very pale pink solid in 50% yield. Recrystallized from methanol/chloroform (~4:1); small, colourless needles, mp 276–277°C. (Found: C 39.1, H 4.1, N 16.8%; $M^{+\bullet}$ 338.0649. $C_{11}H_{13}F_3N_4O_3S$ requires C 39.1, H 3.9, N 16.6%; $M^{+\bullet}$ 338.0655). δ_H (500 MHz, $CDCl_3$) 3.90 (3H, s, NCH_3), 3.73 (2H, br s, NCH_2), 3.68 (2H, br s, NCH_2), 1.72 (6H, br s, 3 × CH_2). δ_F (188 MHz, $CDCl_3$) −62.99. δ_C (125 MHz, $CDCl_3$) 146.4, 145.4, 135.5 (q, J_{CF} 41.8), 119.3 (q, J_{CF} 270.2), 100.2, 47.7, 45.7, 35.4, 25.7, 24.9, 23.7. *m/z* (EI) 338 (45%, $M^{+\bullet}$), 110 (100).

X-ray Crystallography

General methods were described previously.[1] Crystals of **5f** have two independent molecules in the unit cell. Both molecules are essentially identical, differing only in orientation of the Et groups on the NEt_2 fragment. CCDC 755592–755596 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.CCDC.cam.ac.uk/data_request/cif.

Acknowledgements

We thank Ms Katarina Johansson and Mrs Ruth Woodgate for technical assistance, Dr Roger Mulder and Dr Jo Cosgriff for assistance with NMR spectroscopy, and Mr Carl Braybrook and Dr Jo Cosgriff for mass spectrometry.

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