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N,*N*-Dialkyl-*N*′-Chlorosulfonyl Chloroformamidines in Heterocyclic Synthesis. Part VIII.* Novel Pyrazolo-Fused Oxathiadiazines and Thiatriazoles

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N,*N*-dialkyl-*N*′-chlorosulfonyl chloroformamidines **1** reacted with pyrazol-3-ones **2** tunder a variety of conditions to give pyrazolo[2,3-*e*][1,2,3,5]oxathiadiazine dioxides **3** and pyrazolo[3,2-*b*][1,4,3,5]oxathiadiazine dioxides **5**, and frequently, one or both of pyrazolo[1,2-*b*][1,2,3,5]thiatriazole 1,1,5-trioxides **4** and 1,1,7-trioxides **6**. In all reactions, the pyrazolo[3,2-*b*][1,4,3,5]oxathiadiazine **5** was the major product, with the pyrazolo[2,3-*e*][1,2,3,5]oxathiadiazine **3** being a significant product in the absence of base. Prior to our recent work, the core ring systems of compounds **3** and **5** had not been reported and compounds **4** and **6** are new derivatives of a rare ring system.

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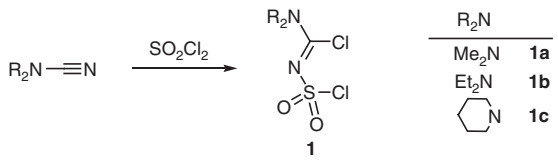
Introduction

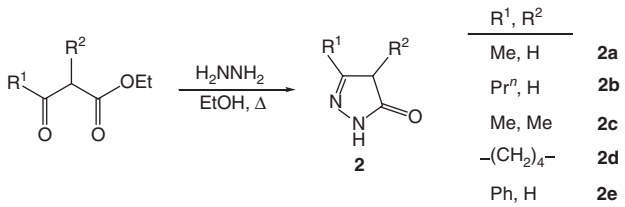
In a series of recent reports, we have demonstrated the facility with which *N*,*N*-dialkyl *N*′-chlorosulfonyl chloroformamidines **1** provide uncommon or new heterocyclic ring systems. For example, **1** reacted with hydrazine derivatives to afford novel [1,2,3,5]thiatriazole dioxides.[1] Various 2-amino-1-azaheterocycles provided a range of fused [1,2,4,6]thiatriazine dioxides[2–4] and 2-mercapto-1*H*-azaheterocycles gave fused [1,4,2,6]dithiadiazine dioxides.[5] A logical extension of the above methodology for creating six-membered rings would be to employ 2-hydroxy-1*H*-azaheterocycles in similar reactions to produce fused oxathiadiazine derivatives. We envisaged that pyrazol-3-ones **2** would represent a suitable candidate 2-hydroxy-1*H*-azaheterocyclic system, because these compounds have been shown to act as 1,3-NCO dinucleophiles in reactions with dielectrophiles to produce cyclic products.[6,7] However, these known ambident nucleophiles can also react as 1,2-NN dinucleophiles with dielectrophiles to produce fused heterocycles.[8,9] We were interested in studying the ability of pyrazol-3-ones **2** to condense with the dichloro compounds **1** and determining the mode(s) of that reaction. This paper reports the results from our examination.

Results and Discussion

The dichlorides **1a**–**c** were readily prepared[10] from sulfuryl chloride and the corresponding dialkyl cyanamide (Scheme 1).



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



Scheme 2. General synthesis of pyrazolones **2**.

Pyrazol-3-ones **2a**–**e** were synthesized from cyclocondensation of appropriate β-ketoesters and hydrazine according to a well-established literature procedure (Scheme 2).[11]

The reaction of dichlorides **1** with pyrazol-3-ones **2** was examined under a variety of conditions: (A) at 80°C in 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (dimethylpropylene urea, DMPU); (B) at ambient temperature in DMPU with *N*,*N*-diisopropylethylamine (Hünig's base); (C) at ambient

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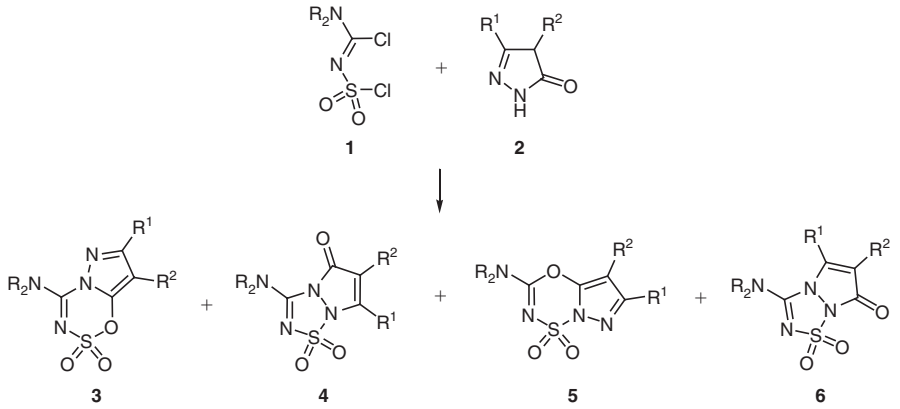

Scheme 3.

Table 1. Synthesis of the fused heterocycles 3, 4, 5, and 6
Method A: dimethylpropylene urea (DMPU)/80°C; Method B: Pr^i_2NEt/DMPU; Method C: $KHCO_{3(aq)}/C_6H_6/Bu^n_4NHSO_4$; Method D: Et_3N/CH_2Cl_2

R_2N	R^1	R^2	Method	Products (yields [%])			
				3	**4**	**5**	**6**
Me_2N (**1a**)	Me	H (**2a**)	A	**3a** (22)	–	**5a** (29)	–
N (**1c**)	Me	H (**2a**)	A	**3b** (14)	**4b**[A] (3)	**5b** (22)	–
Me_2N (**1a**)	Pr^n	H (**2b**)	B	**3c** (24)	**4c** (2)	**5c** (34)	–
Et_2N (**1b**)	Pr^n	H (**2b**)	C	**3d** (8)	**4d** (2)	**5d** (60)	–
N (**1c**)	Pr^n	H (**2b**)	B	**3e**[A][12] (2)	**4e** (2)	**5e** (13)	–
Me_2N (**1a**)	Me	Me (**2c**)	B	**3f**[A] (7)	–	**5f**[A] (52)	**6f** (11)
Et_2N (**1b**)	Me	Me (**2c**)	A	**3g** (13)	–	**5g**[A][13] (26)	–
Me_2N (**1a**)	–$(CH_2)_4$– (**2d**)		A	**3h**[A] (17)	**4h**[A] (6)	**5h**[A] (23)	**6h**[A][14] (17)
			C	–	–	**5h**[A] (40)	–
Et_2N (**1b**)	–$(CH_2)_4$– (**2d**)		B	**3i**[A] (2)	–	**5i**[A] (37)	**6i**[A] (17)
Et_2N (**1b**)	Ph	H (**2e**)	B	**3j** (1)	–	**5j**[A] (47)	–
			C	**3j** (1)	–	**5j**[A] (58)	–
N (**1c**)	Ph	H (**2e**)	D	**3k** (2)	–	**5k**[A] (16)	–

[A]X-ray crystal structure obtained.

temperature in benzene/aqueous potassium bicarbonate/tetrabutylammonium hydrogen sulfate; and (D) at ambient temperature in dichloromethane with triethylamine (see Table 1). Usually, these reactions provided 4-dialkylamino-2,2-dioxo-2λ^6-pyrazolo[2,3-*e*][1,2,3,5]oxathiadiazines **3** and 3-dialkylamino-1,1-dioxo-1λ^6-pyrazolo[3,2-*b*][1,4,3,5]oxathiadiazines **5**, and frequently, one or both of 3-dialkylamino-1,1,5-trioxo-1λ^6-pyrazolo[1,2-*b*][1,2,3,5]thiatriazoles **4** and 3-dialkylamino-1,1,7-trioxo-1λ^6-pyrazolo[1,2-*b*][1,2,3,5]thiatriazoles **6** (Scheme 3, Table 1). The isomeric reaction products were separated by chromatography over silica gel.

Under all conditions employed, the pyrazolo[3,2-*b*][1,4,3,5] oxathiadiazine **5** was the major product, with the pyrazolo[2,3-*e*] [1,2,3,5]oxathiadiazine **3** usually appearing as a significant product in the absence of base. The other two products, pyrazolo [1,2-*b*][1,2,3,5]thiatriazoles **4** and **6**, were only isolated in minor amounts on some occasions.

The new fused, bicyclic products **3**, **4**, **5**, and **6** described above were stable, colourless, crystalline solids, unaffected by recrystallization from alcohols. Compounds **4d** and **5d** were stable, colourless oils.

Owing to the lack of contiguous NMR-responsive nuclei in the core heterocyclic systems of products **3**, **4**, **5**, and **6**, X-ray structural studies of several representative compounds were critical in confirming the exact connectivity of the atoms constituting the heterocyclic cores. Some of the structures obtained from the X-ray studies are shown in Figs 1–4. Crystal data and structure refinement for all compounds studied by X-ray diffraction can be found in Table 2 in the Experimental section, except for **3e**,[12] **5g**,[13] and **6h**,[14] which were published previously.

Prior to our work in this area,[12–14] the pyrazolo[2,3-*e*] [1,2,3,5]oxathiadiazine and pyrazolo[3,2-*b*][1,4,3,5] oxathiadiazine ring systems of compounds **3** and **5** had not been reported. The minor products, 3-dialkylamino-pyrazolo[1,2-*b*] [1,2,3,5]thiatriazole trioxides **4** and **6**, are new derivatives of a rare ring system.[15–17]

The structural assignments were aided by consistent trends in physical and spectral properties. The order of elution of the isomers during normal-phase silica gel chromatography was consistently **3**, **4**, **5**, and then **6**. The pyrazolo[2,3-*e*] [1,2,3,5]oxathiadiazines **3** were always the most soluble, the most mobile in TLC and gave strongly absorbing spots under UV

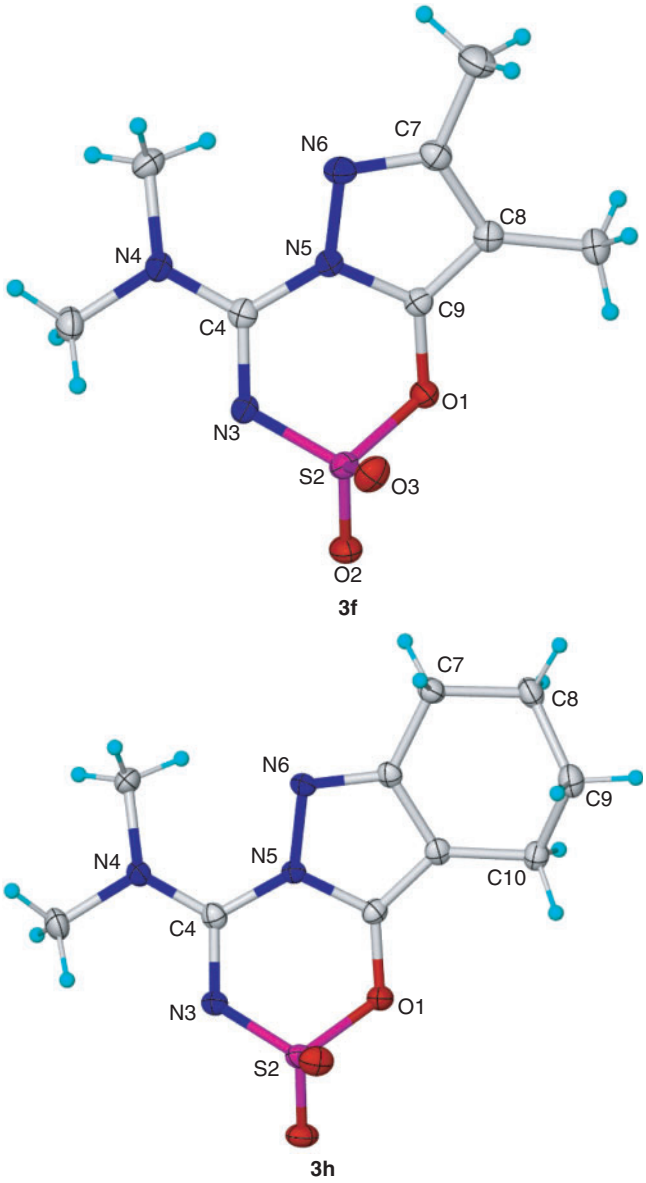

Fig. 1. *ORTEP* diagrams of **3f** and **3h**.

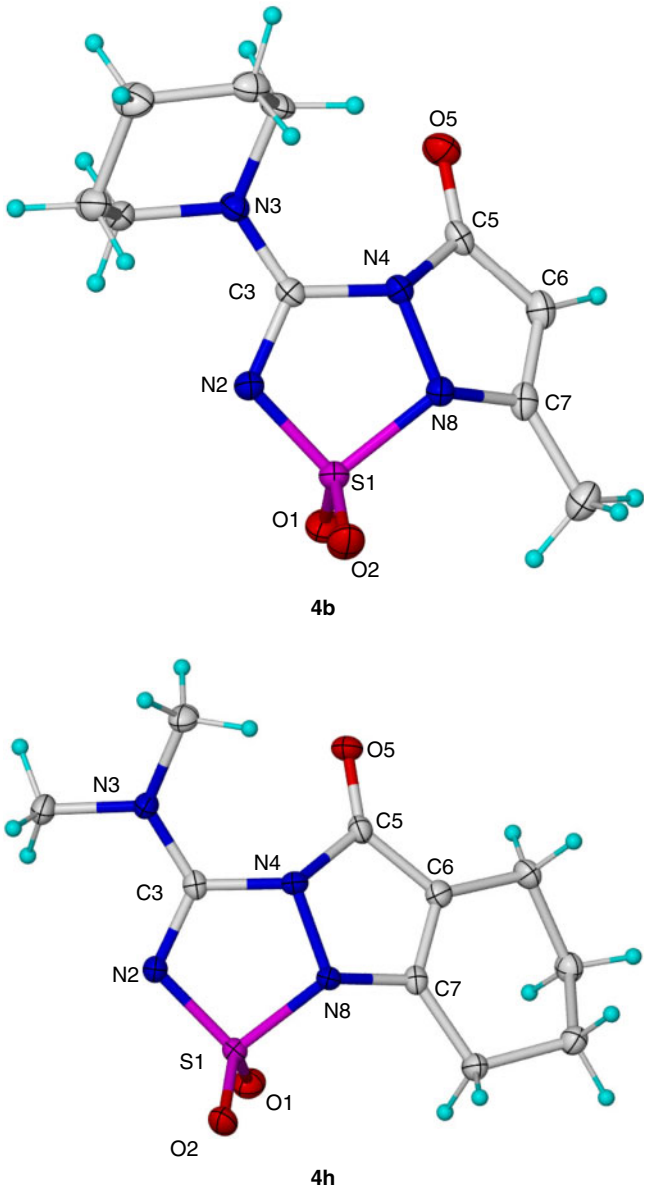

Fig. 2. *ORTEP* diagrams of **4b** and **4h**.

light. The pyrazolo[1,2-*b*][1,2,3,5]thiatriazole 1,1,5-trioxides **4** were also visualized satisfactorily under UV light, but most of the major products **5** (and the other minor products **6**) were not easily seen using this method or other common TLC visualization agents including potassium permanganate and anisaldehyde (vanillin) dips. Interestingly, some of compounds **5** responded to ninhydrin to give pink or purple coloured products following TLC, although they contain only tertiary amino groups.

In addition to the characteristics described above, there were consistent trends in ^{1}H NMR spectral properties that distinguished each of pyrazolo[2,3-*e*][1,2,3,5]oxathiadiazines **3** and pyrazolo[1,2-*b*][1,2,3,5]thiatriazoles **6** from the other isomers. The methyl or methylene groups immediately adjacent to the nitrogen atom of the amine function were non-equivalent in all derivatives **3** by ~0.4–0.6 ppm, whereas for all other isomers, the difference was <0.15 ppm. The reasons for this difference are unclear; however, the phenomenon allowed clear distinction of products **3**. In 500-MHz gradient-selected nuclear Overhauser effect correlation spectroscopy (NOESY) 2D ^{1}H NMR experiments with all compounds **6**, a relatively strong nuclear Overhauser effect (NOE) was observed between the methyl or methylene groups immediately adjacent to the nitrogen atom of the dialkylamino substituent and the nearest hydrogen-bearing substituent on C5. In similar experiments with compounds **3**, **4**, and **5**, no such NOEs were observed. The relatively close proximity of these hydrogen atoms in compound **6i** can be seen in Fig. 4 (C5 and C12).

Ring formation to produce the major products **5** proceeds such that the oxygen atom of **2** bonds with the amidine carbon atom of **1** and N2 reacts with the sulfamoyl chloride moiety. The other significant reaction product **3** results from N2 of the pyrazolone bonding with the amidine carbon atom of **1** and the oxygen reacting with the sulfamoyl chloride moiety.

The *N*-unsubstituted pyrazol-3-ones **2** provide a plethora of opportunities for tautomerism, with no fewer than eight tautomers being possible, but in fact four tautomers **2A**–**D** predominate (Fig. 5).[7,18–21] In non-polar solvents, there is mainly an equilibrium between the CH and the OH tautomers, in dipolar

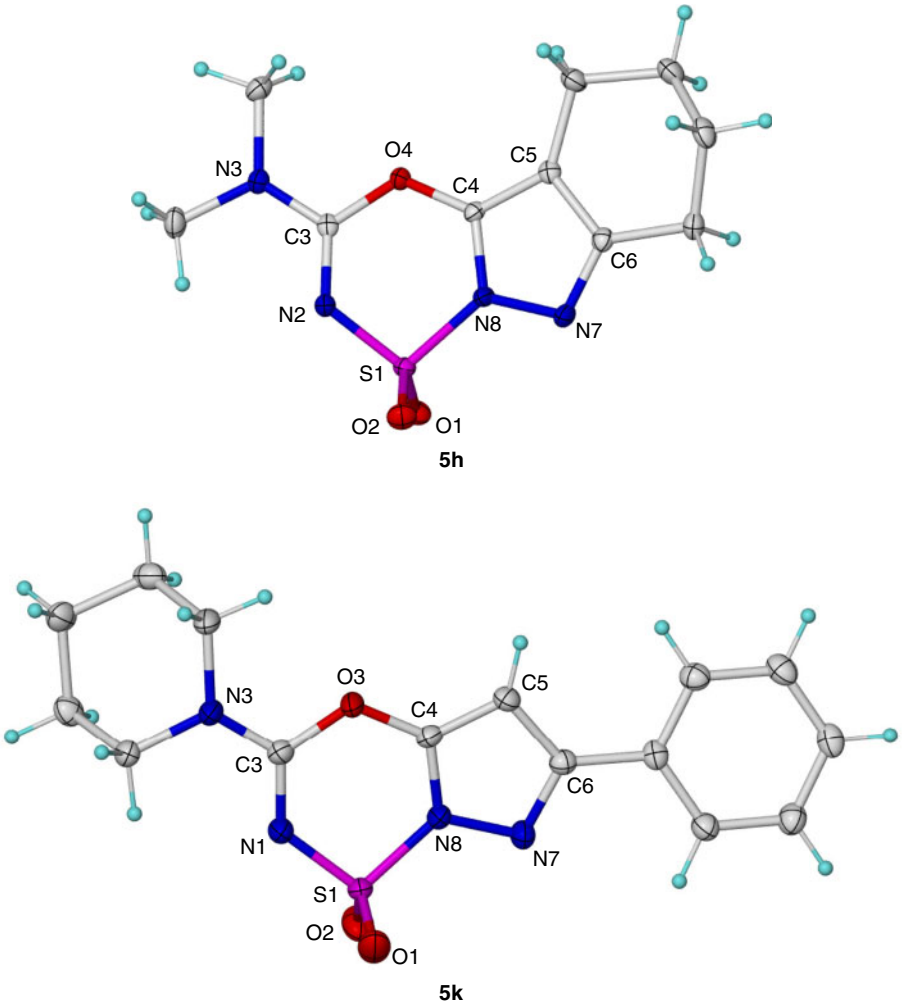

Fig. 3. *ORTEP* diagrams of **5h** and **5k**.

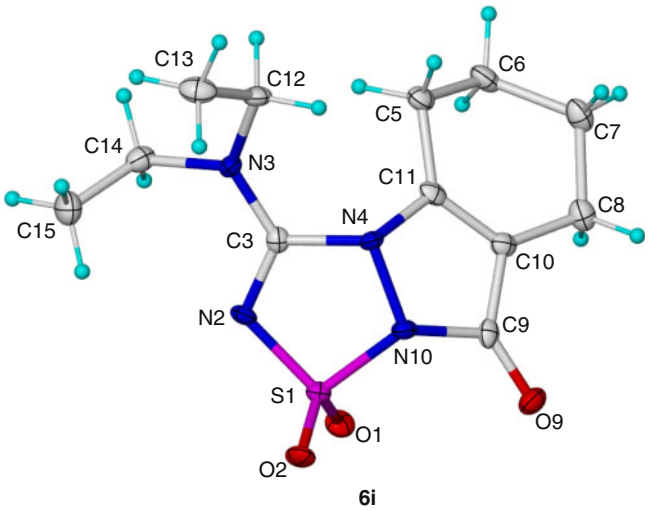

Fig. 4. *ORTEP* diagram of **6i**.

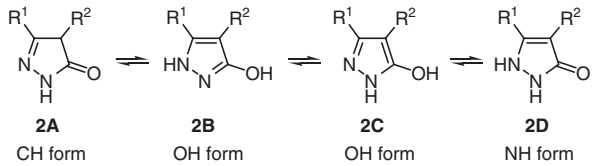

Fig. 5. Tautomers of *N*-unsubstituted pyrazolones **2**.

aprotic solvents, the OH tautomers predominate, whereas protic solvents favour a mixture of the OH and the NH tautomers.[19]

A recent report[21] described the formation of all four possible cyclic products that resulted when pyrazol-3-ones **2a**–**d** reacted as either a 1,3-NCO dinucleophile or as a 1,2-NN dinucleophile in reactions with some 1-alkynyl Fischer carbene complexes. The formation of the four products was attributed to the dominant tautomeric forms available to the *N*-unsubstituted pyrazolones.[21]

Nevertheless, the tautomers are rapidly interchangeable and according to the literature, the outcome of acylation of the ring atoms of pyrazol-3-ones with acid chlorides depends on the type of substitution on the pyrazol-3-one ring; *C*-, *N*-, and *O*-acylation are all observed.[18,22,23] Acylation of *N*-unsubstituted pyrazolones with such agents as acetyl chloride, benzoyl chloride and arylsulfonyl chlorides occurs readily to give 1-acyl-2-pyrazolin-5-ones as the usual products.[18]

The results obtained during this study are largely consistent with outcomes that could have been predicted based on literature precedents. However, our earlier papers in this

series[1–5,24] demonstrated the greater electrophilicity of the amidinyl chloride moiety relative to the sulfamoyl chloride group in dichlorides **1**, and this factor guides regiochemical selectivity during cyclization reactions. Thus, with *N*-unsubstituted pyrazolones **2**, it would have been expected that reactions with **1** would afford fused oxathiadiazines **3** as the major products. Therefore, it was somewhat surprising to find that the major cyclization pathway seemingly included an initial reaction by the sulfamoyl chloride, leading to the isomeric products **5**. The reason for this apparent reversal of selectivity is unclear, although an alternative explanation may also apply. There may still be a preference for the amidinyl chloride in all cases, but the nucleophilicity of the ambident nucleophile changes from nitrogen (to give **3**) to oxygen (to give **5**).

Conclusion

The dichloro compounds **1**, versatile 1,3-dielectrophiles, have been shown to react with readily available pyrazol-3-ones **2** to afford dioxo derivatives of the pyrazolo[2,3-*e*][1,2,3,5]oxathiadiazine and pyrazolo[3,2-*b*][1,4,3,5] oxathiadiazine ring systems, compounds **3** and **5**, respectively. Prior to our work in this area, these ring systems had not been reported. Basic reaction conditions favoured formation of the pyrazolo[3,2-*b*][1,4,3,5]oxathiadiazine product **5**. The minor products, 3-dialkylamino-pyrazolo[1,2-*b*][1,2,3,5]thiatriazole trioxides **4** and **6**, are new derivatives of a rare ring system.

Experimental

Methods and Materials

Melting points were determined using a Reichert hot-stage microscope or a Gallenkamp MPD350.BM2.5 apparatus and are uncorrected. Analytical TLC was carried out on Merck Kieselgel 60 F_{254} silica aluminium-backed sheets. Developed plates were visualized with either UV light (254 nm), cold 5% (w/v) aqueous $FeCl_3$ dip (good for pyrazolones, which gave a red, brown, or purple immediate colouration), ninhydrin dip (0.75 g ninhydrin, 2.5 mL acetic acid, 250 mL of 95% ethanol), or a solution of 10% (w/v) phosphomolybdic acid in ethanol followed by heating. Radial chromatography was performed on a Harrison Research Chromatotron (Model 7924T) using 1-, 2-, or 4-mm-thick silica plates (Merck silica gel 60 PF_{254} containing gypsum). ^{1}H NMR spectra were recorded on a Varian Gemini 300 at 300 MHz or a Bruker AV400 at 400 MHz. ^{13}C NMR spectra were recorded at room temperature on a Bruker AC-200 at 50 MHz, a Varian Gemini 300 at 75 MHz, a Bruker AV400 at 100.6 MHz, or a Bruker DRX500 at 125.75 MHz. Deuterochloroform was used as solvent and also as an internal lock. Electron impact (EI) mass spectra were recorded on a ThermoQuest MAT95XL mass spectrometer using ionization energy of 70 eV. Only the major fragments are given with their relative abundances shown in parentheses. Accurate mass measurements were obtained with a resolution of 5000–10000 using perfluorokerosene as the internal reference. Microanalyses were performed at the Campbell Microanalytical Laboratory, University of Otago, Dunedin, New Zealand.

The pyrazolones **2a**,[11,25,26] **2b**,[11] **2c**,[26] **2d**,[26] and **2e**[11,26] were all prepared from the appropriate β-ketoester and hydrazine using the procedure of Taylor and McKillop.[11] Other materials were obtained from commercial sources. Light petroleum refers to a fraction with boiling range 60–80°C.

N,N-*Dialkyl*-N′-*chlorosulfonyl Chloroformamidines* ***1a–c***

Prepared essentially by literature procedures.[1,10] Thus, the appropriate dialkylcyanamide (0.1 mol) was added dropwise to cooled (ice/water external bath) and stirred sulfuryl chloride (0.2 mol). The mixture was stirred overnight (ice bath replenished) and the excess of sulfuryl chloride was removed by rotary evaporation (2 h, 60°C, NaOH trap). The crude products were stored under nitrogen and used without further purification. The deterioration of these compounds and substantial losses during attempted purification outweighed the benefits of increased purity.

N,N-*Dimethyl*-N′-*chlorosulfonyl Chloroformamidine* ***1a***

Obtained as a pale yellow, low-mp solid (92% crude yield). δ_H (300 MHz) 3.40 (3H, s, NCH_2), 3.33 (3H, s, NCH_2). δ_C (75 MHz) 151.5, 41.9, 41.6.

N,N-*Diethyl*-N′-*chlorosulfonyl Chloroformamidine* ***1b***

Obtained as a yellow, sticky, low-mp solid (92% crude yield). δ_H (300 MHz) 3.71 (2H, q, *J* 4.7, NCH_2), 3.69 (2H, q, *J* 4.7, NCH_2), 1.36 (3H, t, *J* 7.4, CH_3), 1.30 (3H, t, *J* 7.4, CH_3). δ_C (75 MHz) 152.6, 47.9, 47.4, 13.0, 12.0.

N,N-*Pentamethylene*-N′-*chlorosulfonyl Chloroformamidine* ***1c***

Obtained as a pale yellow, low-mp solid (99% crude yield). δ_H (300 MHz) 3.88 (4H, q, *J* 5.8, 2 × NCH_2), 1.73 (6H, br s, 3 × CH_2). δ_C (75 MHz) 152.0, 51.0, 50.8, 26.0, 25.4, 23.4.

General Synthesis Procedures for 4-Dialkylamino-2,2-dioxo-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazines ***3****, 3-Dialkylamino-1,1,5-trioxo-1λ^6-pyrazolo[1,2-b][1,2,3,5] thiatriazoles* ***4****, 3-Dialkylamino-1,1-dioxo-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazines* ***5****, and 3-Dialkylamino-1,1,7-trioxo-1λ^6-pyrazolo[1,2-b][1,2,3,5]thiatriazoles* ***6***

Method A

A stirred mixture of pyrazolone **2** (5 mmol) and dichloro compound **1** (6.5 mmol) in DMPU (4 mL) was heated to 80°C for 4–9 h (reaction progress monitored using TLC (cold 5% aq. $FeCl_3$ dip)). The reaction mixture was allowed to cool, diluted slowly with water (20 mL), stirred for several hours and the resulting precipitate was filtered under suction, washed with water, and dried under vacuum. The mother liquor was allowed to stand overnight and any additional precipitate was treated as described above. If no precipitate formed, an extractive workup was carried out with dichloromethane. The crude product mixture was chromatographed over silica gel and the products were recrystallized.

Method B

A stirred solution of pyrazolone **2** (5 mmol) and dichloro compound **1** (6.5 mmol) in DMPU (4 mL) was warmed gently to dissolve the dichloro compound. The resulting mixture was cooled with an ice/water bath and *N*,*N*′-diisopropylethylamine (13 mmol) was added dropwise. Stirring was continued overnight (reaction progress monitored using TLC (cold 5% aq. $FeCl_3$ dip)). The mixture was diluted slowly with water (20 mL), stirred for several hours and the resulting precipitate was collected, washed with water and dried under vacuum. The mother liquor was adjusted to pH 3 by dropwise addition of HCl (conc.), allowed to stand overnight and any additional precipitate was

treated as described above. If no precipitate formed, an extractive workup was carried out with dichloromethane. The crude product mixture was chromatographed over silica gel and the products were recrystallized.

Method C

The dichloro compound **1** (6.5 mmol) was added to a stirred mixture of pyrazolone **2** (5 mmol), $KHCO_3$ (4 g), water (10 mL), $Bu^n_4NHSO_4$ (0.1 g), and benzene (10 mL). The reaction mixture was warmed gently to dissolve the dichloro compound and stirred overnight at room temperature. The aqueous layer was removed. The precipitate and benzene layer were washed with 5% aq. NaOH (2 × 10 mL) and water (2 × 10 mL) and then evaporated under reduced pressure. The pH of the aqueous layer was adjusted to pH 3 by dropwise addition of HCl (conc.) and allowed to stand overnight. Any additional precipitate was treated as above. The crude product mixture was chromatographed over silica gel and the products were recrystallized.

Method D

A stirred mixture of pyrazolone **2** (5 mmol) and dichloro compound **1** (6.5 mmol) in dichloromethane (5 mL) was warmed gently to dissolve the dichloro compound and then cooled in an ice/water bath. Triethylamine (13 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 5 h (reaction progress monitored using TLC (cold 5% aq. $FeCl_3$ dip)). The reaction mixture was diluted slowly with water (20 mL) and treated as for Method B.

The following compounds were prepared by the above procedures.

4-Dimethylamino-2,2-dioxo-7-methyl-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3a*** *and 3-Dimethylamino-1,1-dioxo-6-methyl-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5a***

Method A. Column chromatography mobile phase: 5% ethyl acetate/dichloromethane.

3a (22% yield): Recrystallized from isopropanol; colourless crystals, mp 134–136°C. (Found: C 36.6, H 4.4, N 24.6; $M^{+\bullet}$ 230.0466. $C_7H_{10}N_4O_3S$ requires C 36.5, H 4.4, N 24.3%; $M^{+\bullet}$ 230.0468). δ_H (300 MHz) 5.83 (1H, s, C=CH), 3.63 (3H, br s, NCH_3), 3.22 (3H, s, NCH_3), 2.26 (3H, s, CH_3). δ_C (75 MHz) 153.1, 150.7, 147.8, 93.1, 41.9, 40.2, 14.5. *m/z* (EI) 230 (95%, $M^{+\bullet}$), 166 (49), 123 (43), 111 (45), 110 (57), 70 (55), 69 (100), 68 (92).

5a (29% yield): Recrystallized from methanol; small, colourless, flat needles, mp 224–226°C. (Found: C 36.8, H 4.5, N 24.6; $M^{+\bullet}$ 230.0471. $C_7H_{10}N_4O_3S$ requires C 36.5, H 4.4, N 24.3%; $M^{+\bullet}$ 230.0468). δ_H (300 MHz) 5.74 (1H, s, C=CH), 3.22 (3H, s, NCH_3), 3.21 (3H, s, NCH_3), 2.32 (3H, s, CH_3). δ_C (75 MHz) 152.18, 149.6, 147.5, 89.5, 38.7, 36.9, 14.5. *m/z* (EI) 230 (100%, $M^{+\bullet}$), 123 (26).

2,2-Dioxo-7-methyl-4-piperidin-1-yl-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3b****, 7-Methyl-3-piperidin-1-yl-1,1,5-trioxo-1λ^6-pyrazolo[1,2-b][1,2,3,5]thiatriazole* ***4b****, and 1,1-Dioxo-6-methyl-3-piperidin-1-yl-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5b***

Method A. Column chromatography (50–100% dichloromethane in light petroleum, then 0–5% ethyl acetate in dichloromethane) gave three products.

3b (14% yield): Recrystallized from ethanol; colourless crystals, mp 106–107°C. (Found: C 44.6, H 5.2, N 20.9; $M^{+\bullet}$ 270.0777. $C_{10}H_{14}N_4O_3S$ requires C 44.4, H 5.2, N 20.7%; $M^{+\bullet}$ 270.0781). δ_H (300 MHz) 5.83 (1H, s, C=CH), 4.30 (2H, br s, NCH_2), 3.74 (2H, br s, NCH_2), 2.26 (3H, s, N=CCH_3), 1.72 (6H, br s, 3 × CH_2). δ_C (75 MHz) 153.1, 150.9, 146.6, 93.3, 50.9, 48.4, 26.0, 25.3, 23.7, 14.6. *m/z* (EI) 270 (1%, $M^{+\bullet}$), 206 (67), 109 (86), 84 (100).

4b (3% yield): Recrystallized from isopropanol; colourless crystals, mp 171–173°C. (Found: C 44.5, H 5.3, N 20.9; $M^{+\bullet}$ 270.0781. $C_{10}H_{14}N_4O_3S$ requires C 44.4, H 5.2, N 20.8%; $M^{+\bullet}$ 270.0781). δ_H (300 MHz) 5.48 (1H, s, C=CH), 3.67 (2H, t, *J* 5.4, NCH_2), 3.61 (2H, t, *J* 5.1, NCH_2), 2.39 (3H, s, N=CCH_3), 1.72 (6H, br s, 3 × CH_2). δ_C (75 MHz) 163.9, 160.5, 149.0, 106.0, 51.9, 48.8, 25.9, 24.9, 23.4, 13.5. *m/z* (EI) 270 (2%, $M^{+\bullet}$), 206 (67), 109 (85), 84 (100).

5b (22% yield): Recrystallized from isopropanol; colourless needles, mp 166–168°C. (Found: C 44.5, H 5.4, N 20.3; $M^{+\bullet}$ 270.0780. $C_{10}H_{14}N_4O_3S$ requires C 44.4, H 5.2, N 20.7%; $M^{+\bullet}$ 270.0781). δ_H (300 MHz) 5.71 (1H, s, C=CH), 3.66 (4H, br s, CH_2NCH_2), 2.26 (3H, s, N=CCH_3), 1.67 (6H, br s, 3 × CH_2). δ_C (75 MHz) 151.9, 147.9, 147.3, 89.4, 47.1, 45.8, 25.3, 24.7, 23.3, 14.3. *m/z* (EI) 270 (100%, $M^{+\bullet}$), 149 (19), 135 (16), 111 (54), 110 (58), 68 (92).

4-Dimethylamino-2,2-dioxo-7-propyl-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3c****, 3-Dimethylamino-7-propyl-1,1,5-trioxo-1λ^6-pyrazolo[1,2-b][1,2,3,5]thiatriazole* ***4c****, and 3-Dimethylamino-6-propyl-1,1-dioxo-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5c***

Method B. No precipitate after addition of ethyl acetate (6 mL) to the stirred reaction mixture followed by ether (20 mL) and pH correction to 3. The aqueous layer was extracted with dichloromethane. The combined organic phases were washed with water, dried, and concentrated under reduced pressure to yield a dark red, viscous oil. Purification by column chromatography (50–100% dichloromethane in light petroleum, then 0–5% ethyl acetate in dichloromethane) afforded three products:

3c (24% yield): Recrystallized from isopropanol; colourless needles, mp 78–80°C. (Found: C 42.0, H 5.4, N 21.9; $M^{+\bullet}$ 258.0773. $C_9H_{14}N_4O_3S$ requires C 41.9, H 5.5, N 21.7%; $M^{+\bullet}$ 258.0781). δ_H (300 MHz) 5.85 (1H, s, C=CH), 3.65 (3H, br s, NCH_3), 3.25 (3H, br s, NCH_3), 2.58 (2H, t, *J* 7.5, $CH_2CH_2CH_3$), 1.67 (2H, tq, *J* 7.5, 7.5, $CH_2CH_2CH_3$), 0.97 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 157.4, 150.8, 148.0, 92.4, 42.0, 40.4, 31.0, 21.4, 13.7. *m/z* (EI) 258 (100%, $M^{+\bullet}$), 194 (23), 151 (24), 139 (64), 138 (57).

4c (2% yield): Recrystallized from isopropanol; colourless crystals, mp 66–67°C. (Found: C 42.0, H 5.6, N 21.6; $M^{+\bullet}$ 258.0778. $C_9H_{14}N_4O_3S$ requires C 41.9, H 5.6, N 21.7%; $M^{+\bullet}$ 258.0781). δ_H (300 MHz) 5.48 (1H, s, C=CH), 3.32 (3H, br s, NCH_3), 3.17 (3H, br s, NCH_3), 2.68 (2H, t, *J* 7.5, $CH_2CH_2CH_3$), 1.76 (2H, tq, *J* 7.4, 7.4, $CH_2CH_2CH_3$), 1.04 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 165.1, 164.6, 150.8, 105.0, 42.0, 39.6, 29.7, 20.7, 13.5. *m/z* (EI) 258 (99%, $M^{+\bullet}$), 194 (26), 166 (20), 152 (23), 139 (70), 138 (62), 69 (100), 67 (77).

5c (34% yield): Recrystallized from isopropanol; colourless woolly needles, mp 87.5–88.5°C. (Found: C 42.0, H 5.5, N 22.0; $M^{+\bullet}$ 258.0772. $C_9H_{14}N_4O_3S$ requires C 41.9, H 5.6, N 21.7%; $M^{+\bullet}$ 258.0781). δ_H (400 MHz) 5.76 (1H, s, C=CH), 3.22 (3H, br s, NCH_3), 3.21 (3H, br s, NCH_3), 2.63 (2H, t, *J* 7.5, $CH_2CH_2CH_3$), 1.68 (2H, tq, *J* 7.4, 7.4, $CH_2CH_2CH_3$), 0.97 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 156.0, 149.4, 147.1, 88.4,

38.3, 36.6, 30.5, 21.5, 13.4. *m/z* (EI) 258 (8%, $M^{+\bullet}$), 243 (2), 230 (100).

4-Diethylamino-2,2-dioxo-7-propyl-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3d****, 3-Diethylamino-7-propyl-1,1,5-trioxo-1λ^6-pyrazolo[1,2-b][1,2,3,5]thiatriazole* ***4d****, and 3-Diethylamino-6-propyl-1,1-dioxo-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5d***

Method C. No precipitate after stirring vigorously overnight, addition of diethyl ether (15 mL) and pH adjustment to 3. The organic phase was washed with water, dried, and the solvent was removed under reduced pressure to give a deep red, viscous oil. Purification by column chromatography (50–100% dichloromethane in light petroleum, then 0–5% ethyl acetate in dichloromethane) afforded three products:

3d (8% yield): Recrystallized from isopropanol; colourless crystals, mp 59–60°C. (Found: C 46.0, H 6.4, N 19.3; $M^{+\bullet}$ 286.1087. $C_{11}H_{18}N_4O_3S$ requires C 46.1, H 6.3, N 19.6%; $M^{+\bullet}$ 286.1094). δ_H (400 MHz) 5.84 (1H, s, C=CH), 4.02 (2H, br q, *J* 6.6, NCH_2), 3.63 (2H, br q, *J* 6.6, NCH_2), 2.58 (2H, t, *J* 7.5, $CH_2CH_2CH_3$), 1.69 (2H, tq, *J* 7.4, 7.4, $CH_2CH_2CH_3$), 1.38 (3H, br t, *J* 6.6, NCH_2CH_3), 1.33 (3H, br t, *J* 6.6, NCH_2CH_3), 0.98 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 157.2, 150.8, 147.1, 92.2, 46.4, 45.5, 30.9, 21.0, 13.7, 13.6, 11.8. *m/z* (EI) 286 (4%, $M^{+\bullet}$), 271 (5), 222 (38), 194 (29), 179 (30), 152 (21), 97 (100).

4d (2% yield): Colourless oil. (Found: C 46.1, H 6.5, N 19.8; $M^{+\bullet}$ 286.1099. $C_{11}H_{18}N_4O_3S$ requires C 46.1, H 6.3, N 19.6%; $M^{+\bullet}$ 286.1094). δ_H (300 MHz) 5.48 (1H, s, C=CH), 3.70 (2H, q, *J* 7, NCH_2), 3.55 (2H, q, *J* 7, NCH_2), 2.68 (2H, t, *J* 7.7, $CH_2CH_2CH_3$), 1.75 (2H, tq, *J* 7.4, 7.4, $CH_2CH_2CH_3$), 1.36–1.26 (6H, br m, $2 \times NCH_2CH_3$) 1.04 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 164.7, 163.9, 149.9, 105.1, 46.7, 44.0, 29.6, 20.7, 13.5, 11.9. *m/z* (EI) 286 (5%, $M^{+\bullet}$), 271 (2), 222 (24), 207 (9), 194 (19), 179 (22), 97 (100), 72 (71).

5d (60% yield): Colourless oil. (Found: C 45.9, H 6.6, N 19.6; $M^{+\bullet}$ 286.1087. $C_{11}H_{18}N_4O_3S$ requires C 46.1, H 6.3, N 19.6%; $M^{+\bullet}$ 286.1094). δ_H (400 MHz) 5.75 (1H, s, C=CH), 3.533 (2H, q, *J* 7, NCH_2), 3.526 (2H, q, *J* 7, NCH_2), 2.59 (2H, t, *J* 7.5, $CH_2CH_2CH_3$), 1.64 (2H, tq, *J* 7.4, 7.4, $CH_2CH_2CH_3$), 1.27 (3H, t, *J* 7, NCH_2CH_3), 1.25 (3H, t, *J* 7, NCH_2CH_3), 0.93 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 155.9, 148.8, 147.2, 88.4, 44.5, 42.9, 30.6, 21.6, 13.4, 13.3, 11.9. *m/z* (EI) 286 (10%, $M^{+\bullet}$), 258 (100).

2,2-Dioxo-4-piperidin-1-yl-7-propyl-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3e****, 3-Piperidin-1-yl-7-propyl-1,1,5-trioxo-1λ^6-pyrazolo[1,2-b][1,2,3,5]thiatriazole* ***4e****, and 1,1-Dioxo-6-propyl-3-piperidin-1-yl-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5e***

Method B. No effective precipitation on dilution with water. The mixture was extracted with dichloromethane (10 mL). The organic phase was washed with water and the solvent was removed under reduced pressure affording a viscous red oil. Purification by column chromatography (50–100% dichloromethane in light petroleum followed by 0–5% ethyl acetate in dichloromethane) provided three products:

3e (2% yield): Recrystallized from isopropanol; colourless prisms, mp 80–82°C. (Found: C 48.4, H 6.1, N 19.0, S 10.8; $M^{+\bullet}$ 298.1088. $C_{12}H_{18}N_4O_3S$ requires C 48.3, H 6.1, N 18.8, S 10.8%; $M^{+\bullet}$ 298.1094). δ_H (300 MHz) 5.85 (1H, s, C=CH), 4.32 (2H, br s, NCH_2), 3.77 (2H, br s, NCH_2), 2.58 (2H, t, *J* 7.7, $N{=}CCH_2$), 1.75 (6H, br s, $3 \times CH_2$), 1.68 (2H, tq, *J* 7.5, 7.5, $CH_2CH_2CH_3$), 0.96 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 157.3, 151.0, 146.8, 92.5, 51.0, 48.5, 31.0, 26.1, 25.4, 23.9, 21.3, 13.7. *m/z* (EI) 298 (3%, $M^{+\bullet}$), 258 (3), 234 (68), 206 (22), 109 (86), 84 (100).

4e (2% yield): Obtained as an off-white powder, mp 65–67°C. (Found: $M^{+\bullet}$ 298.1087. $C_{12}H_{18}N_4O_3S$ requires $M^{+\bullet}$298.1094). δ_H (300 MHz) 5.47 (1H, s, C=C*H*), 3.67 (2H, t, *J* 5.3, NCH_2), 3.61 (2H, t, *J* 5.4, NCH_2), 2.67 (2H, t, *J* 7.7, $N{=}CCH_2$), 1.74 (6H, br s, $3 \times CH_2$), 1.65–1.55 (2H, m, $CH_2CH_2CH_3$), 1.03 (3H, t, *J* 7.4, $CH_2CH_2CH_3$). δ_C (75 MHz) 164.9, 163.9, 149.2, 105.0, 51.9, 48.7, 29.6, 25.9, 24.9, 23.4, 20.7, 13.5. *m/z* (EI) 298 (3%, $M^{+\bullet}$), 234 (52), 206 (18), 127 (13), 109 (81), 84 (100).

5e (13% yield): Recrystallized from isopropanol; colourless crystals, mp 92–93°C. (Found: C 48.4, H 6.2, N 18.9; $M^{+\bullet}$ 298.1084. $C_{12}H_{18}N_4O_3S$ requires C 48.3, H 6.1, N 18.8%; $M^{+\bullet}$298.1094). δ_H (300 MHz) 5.73 (1H, s, C=CH), 3.67 (4H, br s, CH_2NCH_2), 2.59 (2H, t, *J* 7.7, $N{=}CCH_2$), 1.67 (6H, br s, $3 \times CH_2$), 1.66–1.58 (2H, m, $CH_2CH_2CH_3$), 0.93 (3H, t, *J* 7.5, $CH_2CH_2CH_3$). δ_C (75 MHz) 156.2, 148.1, 147.3, 88.4, 47.2, 45.8, 30.8, 25.4, 24.8, 23.4, 21.9, 13.6. *m/z* 298 (12%, $M^{+\bullet}$), 270 (100).

7,8-Dimethyl-4-dimethylamino-2,2-dioxo-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3f****, 5,6-Dimethyl-3-dimethylamino-1,1-dioxo-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5f****, and 5,6-Dimethyl-3-dimethylamino-1,1,7-trioxo-1λ^6-pyrazolo[1,2-b][1,2,3,5]thiatriazole* ***6f***

Method B. Column chromatography (50–100% dichloromethane in light petroleum) provided three compounds:

3f (7% yield): Recrystallized from isopropanol; colourless crystals, mp 105–106°C. (Found: C 39.4, H 5.0, N 23.2; $M^{+\bullet}$ 244.0621. $C_8H_{12}N_4O_3S$ requires C 39.3, H 5.0, N 22.9%; $M^{+\bullet}$ 244.0625). δ_H (300 MHz) 3.62 (3H, br s, NCH_3), 3.22 (3H, br s, NCH_3), 2.21 (3H, s, $N{=}CCH_3$), 1.92 (3H, s, $C{=}CCH_3$). δ_C (75 MHz) 153.8, 148.0, 147.0, 101.3, 41.7, 40.2, 12.8, 5.7. *m/z* (EI) 244 (64%, $M^{+\bullet}$), 180 (4), 137 (21), 125 (15), 124 (32), 54 (100).

5f (52% yield): Recrystallized from ethanol; colourless needles, mp 226.5–228.5°C. (Found: C 39.4, H 5.0, N 22.9; $M^{+\bullet}$ 244.0622. $C_8H_{12}N_4O_3S$ requires C 39.3, H 5.0, N 22.9%; $M^{+\bullet}$ 244.0625). δ_H (300 MHz) 3.23 (3H, s, NCH_3), 3.19 (3H, s, NCH_3), 2.21 (3H, s, $N{=}CCH_3$), 1.93 (3H, s, $C{=}CCH_3$). δ_C (75 MHz) 152.7, 149.9, 144.6, 97.5, 38.7, 36.7, 12.7, 6.0. *m/z* (EI) 244 (100%, $M^{+\bullet}$), 137 (11).

6f (11% yield): Obtained as an off-white powder, mp 210–211°C. (Found: C 39.5, H 5.0, N 22.6; $M^{+\bullet}$ 244.0622. $C_8H_{12}N_4O_3S$ requires C 39.3, H 5.0, N 22.9%; $M^{+\bullet}$ 244.0625). δ_H (300 MHz) 3.13 (6H, s, $2 \times NCH_3$), 2.32 (3H, s, $N{=}CCH_3$), 1.79 (3H, s, $C{=}CCH_3$). NOE observed between δ 3.13 and δ 2.32. δ_C (75 MHz) 154.5, 152.3, 149.6, 88.8, 41.5, 13.5, 7.2. *m/z* (EI) 244 (53%, $M^{+\bullet}$), 137 (10), 54 (100).

7,8-Dimethyl-4-diethylamino-2,2-dioxo-2λ^6-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3g*** *and 5,6-Dimethyl-3-diethylamino-1,1-dioxo-1λ^6-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5g***

Method A. Column chromatography (50–100% dichloromethane in light petroleum, then 0–5% ethyl acetate in dichloromethane) afforded two products:

3g (13% yield): Recrystallized from isopropanol; colourless crystals, mp 91–92°C. (Found: C 44.2, H 6.1, N 20.8; $M^{+\bullet}$ 272.0934. $C_{10}H_{16}N_4O_3S$ requires C 44.1, H 5.9, N 20.6%; $M^{+\bullet}$

272.0938). δ_H (300 MHz) 4.00 (2H, br q, *J* 6, NCH_2), 3.59 (2H, br q, *J* 5.7, NCH_2), 2.20 (3H, s, N=CCH_3), 1.92 (3H, s, C=CCH_3), 1.32 (6H, br s, $N(CH_2CH_3)_2$). δ_C (75 MHz) 153.8, 147.1, 147.0, 101.1, 46.1, 45.4, 13.7, 12.9, 11.9, 5.8. *m/z* (EI) 272 (37%, $M^{+\bullet}$), 208 (57), 180 (21), 165 (48), 139 (16), 138 (41), 137 (32), 97 (90), 72 (100).

5g (26% yield): Recrystallized from isopropanol; colourless crystals, mp 167–168°C. (Found: C 44.4, H 6.0, N 20.5; $M^{+\bullet}$ 272.0936. $C_{10}H_{16}N_4O_3S$ requires C 44.1, H 5.9, N 20.6%; $M^{+\bullet}$ 272.0938). δ_H (300 MHz) 3.54 (4H, q, *J* 7.2, CH_2NCH_2), 2.22 (3H, s, N=CCH_3), 1.91 (3H, s, C=CCH_3), 1.29 (3H, t, *J* 6.5, NCH_2CH_3), 1.25 (3H, t, *J* 6.5, NCH_2CH_3). δ_C (75 MHz) 152.7, 148.9, 144.3, 97.2, 44.4, 42.9, 13.3, 12.4, 11.9, 5.7. *m/z* (EI) 272 (72%, $M^{+\bullet}$), 165 (5), 152 (11), 151 (16), 98 (22), 83 (34), 54 (100).

4-Dimethylamino-2,2-dioxo-7,8,9,10-tetrahydro-2λ⁶-[1,2,3,5]oxathiadiazino[5,6-b]indazole ***3h****, 3-Dimethylamino-6,7,8,9-tetrahydro-1,1,5-trioxo-1λ⁶-[1,2,3,5]thiatriazolo[2,3-a]indazole* ***4h****, 3-Dimethylamino-1,1-dioxo-5,6,7,8-tetrahydro-1λ⁶-[1,4,3,5]oxathiadiazino [3,2-b]indazole* ***5h****, and 3-Dimethylamino-5,6,7,8-tetrahydro-1,1,9-trioxo-1λ⁶-[1,2,3,5]triatriazolo [3,2-a]indazole* ***6h***

Method A. Column chromatography (50–100% dichloromethane in light petroleum, then 0–5% ethyl acetate in dichloromethane) provided four products:

3h (17% yield): Recrystallized from isopropanol; colourless crystals, mp 134–135°C. (Found: C 44.6, H 5.4, N 21.0; $M^{+\bullet}$ 270.0779. $C_{10}H_{14}N_4O_3S$ requires C 44.4, H 5.2, N 20.7%; $M^{+\bullet}$ 270.0781). δ_H (300 MHz) 3.60 (3H, br s, NCH_3), 3.21 (3H, br s, NCH_3), 2.61 (2H, t, *J* 5.9, C=CCH_2), 2.45 (2H, t, *J* 5.9, N=CCH_2), 1.79–1.72 (4H, m, 2 × CH_2). δ_C (75 MHz) 154.9, 148.0, 145.5, 102.4, 41.8, 40.1, 23.8, 22.2, 21.8, 18.0. *m/z* (EI) 270 (98%, $M^{+\bullet}$), 163 (37), 151 (26), 150 (59), 108 (22), 79 (100).

4h (6% yield): Recrystallized from isopropanol; large, colourless prisms, mp 148–150°C. (Found: C 44.6, H 5.3, N 20.9; $M^{+\bullet}$ 270.0781. $C_{10}H_{14}N_4O_3S$ requires C 44.4, H 5.2, N 20.7%; $M^{+\bullet}$ 270.0781). δ_H (300 MHz) 3.30 (3H, s, NCH_3), 3.14 (3H, s, NCH_3), 2.63 (2H, t, *J* 5.2, CH_2C=C), 2.25 (2H, t, *J* 5.2, N=CCH_2), 1.86–1.83 (2H, m, CH_2), 1.75–1.72 (2H, m, CH_2). δ_C (100 MHz) 164.9, 158.7, 151.4, 116.4, 41.9, 39.5, 22.9, 21.05, 21.04, 19.0. *m/z* (EI) 270 (100%, $M^{+\bullet}$), 163 (36), 151 (26), 150 (57), 80 (44), 79 (96).

5h (23% yield): Recrystallized from dichloromethane/ethyl acetate; colourless, flat needles, mp 227–229°C. (Found: C 44.5, H 5.3, N 20.9, S 11.9; $M^{+\bullet}$ 270.0779. $C_{10}H_{14}N_4O_3S$ requires C 44.4, H 5.2, N 20.7, S 11.9%; $M^{+\bullet}$ 270.0781). δ_H (400 MHz) 3.22 (3H, s, NCH_3), 3.21 (3H, s, NCH_3), 2.72 (2H, t, *J* 6.3, CH_2C=C), 2.47 (2H, t, *J* 6.3, N=CCH_2), 1.86–1.78 (2H, m, CH_2), 1.78–1.71 (2H, m, CH_2). δ_C (125 MHz) 154.0, 149.9, 143.1, 99.1, 38.8, 36.8, 23.9, 22.6, 22.2, 18.5. *m/z* (EI) 270 (100%, $M^{+\bullet}$), 177 (8), 163 (6), 150 (22), 108 (51), 80 (34), 79 (67).

6h (17% yield): Recrystallized from dichloromethane/acetonitrile (1:2); colourless needles, mp 248–249°C. (Found: C 44.4, H 5.3, N 20.9; $M^{+\bullet}$ 270.0783. $C_{10}H_{14}N_4O_3S$ requires C 44.4, H 5.2, N 20.7%; $M^{+\bullet}$ 270.0781). δ_H (500 MHz) 3.13 (6H, s, NMe_2), 2.60 (2H, tt, *J* 6.1, 1.9, CH_2C=C), 2.32 (2H, tt, *J* 6.2, 1.9, C=CCH_2), 1.91–1.83 (2H, m, CH_2), 1.77–1.69 (2H, m, CH_2). NOE observed between δ 3.13 and δ 2.60. δ_C (125 MHz) 167.0, 157.8, 154.0, 116.2, 41.2 (2C), 25.2, 21.8, 20.6, 19.0. *m/z* (EI) 270 (71%, $M^{+\bullet}$), 177 (9), 163 (8), 150 (25), 110 (31), 108 (56), 80 (52), 79 (100).

Method C resulted in isolation of only **5h** in 40% yield.

4-Diethylamino-2,2-dioxo-7,8,9,10-tetrahydro-2λ⁶-[1,2,3,5]oxathiadiazino[5,6-b]indazole ***3i****, 3-Diethylamino-1,1-dioxo-5,6,7,8-tetrahydro-1λ⁶-[1,4,3,5]oxathiadiazino [3,2-b]indazole* ***5i****, and 3-Diethylamino-5,6,7,8-tetrahydro-1,1,9-trioxo-1λ⁶-[1,2,3,5]thiatriazolo[3,2-a]indazole* ***6i***

Method B. Column chromatography (dichloromethane) afforded three isomers:

3i (2% yield): Recrystallized from isopropanol; colourless crystals, mp 128–130°C. (Found: C 48.4, H 6.1, N 18.8; $M^{+\bullet}$ 298.1086. $C_{12}H_{18}N_4O_3S$ requires C 48.3, H 6.1, N 18.8%; $M^{+\bullet}$ 298.1094). δ_H (300 MHz) 4.02 (2H, br s, NCH_2), 3.63 (2H, br s, NCH_2), 2.64 (2H, t, *J* 6, CH_2C=C), 2.50 (2H, t, *J* 6, N=CCH_2), 1.82–1.74 (4H, m, 2 × CH_2), 1.33 (6H, br s, 2 × NCH_2CH_3). δ_C (75 MHz) 155.1, 152.5, 147.3, 102.5, 46.2, 45.5, 24.1, 22.5, 22.1, 18.3, 13.9, 12.1. *m/z* (EI) 298 (24%, $M^{+\bullet}$), 234 (36), 191 (46), 164 (43), 163 (27), 138 (46), 97 (60), 79 (64), 72 (100).

5i (37% yield): Recrystallized from acetonitrile; small, colourless needles, mp 178–180°C. (Found: C 48.4, H 6.2, N 19.0; $M^{+\bullet}$ 298.1086. $C_{12}H_{18}N_4O_3S$ requires C 48.3, H 6.1, N 18.8%; $M^{+\bullet}$ 298.1094). δ_H (400 MHz) 3.57 (2H, q, *J* 7, NCH_2), 3.53 (2H, q, *J* 7, NCH_2), 2.72 (2H, t, *J* 6.2, CH_2C=C), 2.47 (2H, t, *J* 6.2, *N*=CCH_2), 1.86–1.70 (4H, m, 2 × CH_2), 1.31 (3H, t, *J* 7, NCH_2CH_3), 1.29 (3H, t, *J* 7, NCH_2CH_3). δ_C (100 MHz) 153.8, 149.2, 143.2, 99.0, 44.7, 43.0, 23.9, 22.6, 22.1, 18.4, 13.6, 12.2. *m/z* (EI) 298 (100%, $M^{+\bullet}$), 178 (30), 177 (52), 163 (22), 108 (79), 80 (59), 79 (82).

6i (17% yield): Recrystallized from acetonitrile; colourless needles, mp 229–231°C. (Found: C 48.4, H 6.2, N 19.0; $M^{+\bullet}$ 298.1090. $C_{12}H_{18}N_4O_3S$ requires C 48.3, H 6.1, N 18.8%; $M^{+\bullet}$ 298.1094). δ_H (500 MHz) 3.51 (4H, q, *J* 7.2, NCH_2), 2.58 (2H, tt, *J* 6.1, 1.9, CH_2C=C), 2.31 (2H, t, *J* 6.1, 1.9, N=CCH_2), 1.90–1.83 (2H, m, CH_2), 1.76–1.69 (2H, m, CH_2), 1.28 (6H, t, *J* 7.2, NCH_2CH_3). NOE observed between δ 3.51 and δ 2.58. δ_C (50 MHz) 167.2, 157.9, 153.3, 115.9, 44.8, 25.1, 21.8, 20.6, 18.9, 12.4. *m/z* (EI) 298 (88%, $M^{+\bullet}$), 178 (25), 177 (45), 163 (22), 108 (72), 80 (65), 79 (100).

4-Diethylamino-2,2-dioxo-7-phenyl-2λ⁶-pyrazolo [2,3-e][1,2,3,5]oxathiadiazine ***3j*** *and 3-Diethylamino-1,1-dioxo-6-phenyl-1λ⁶-pyrazolo[3,2-b][1,4,3,5] oxathiadiazine* ***5j***

Method B. Column chromatography (dichloromethane) provided two products: **3j** (1% yield) and **5j** (47% yield).

Method C. Column chromatography (50–100% dichloromethane in light petroleum) afforded two products: **3j** (1% yield) and **5j** (58% yield).

3j: Recrystallized from ethanol; colourless crystals, mp 181–183°C. (Found: C 52.6, H 5.1, N 17.6; $M^{+\bullet}$ 320.0936. $C_{14}H_{16}N_4O_3S$ requires C 52.5, H 5.0, N 17.5%; $M^{+\bullet}$ 320.0938). δ_H (300 MHz) 7.80–7.77 (2H, m, ArH), 7.47–7.45 (3H, m, ArH), 6.36 (1H, s, C=CH), 4.10 (2H, q, *J* 7, NCH_2), 3.68 (2H, q, *J* 7, NCH_2), 1.52 (3H, t, *J* 6.8, NCH_2CH_3), 1.37 (3H, t, *J* 6.9, NCH_2CH_3). δ_C (75 MHz) 154.1, 151.6, 147.2, 130.7, 130.1, 128.9, 126.2, 90.6, 46.6, 45.8, 13.9, 11.9. *m/z* (EI) 320 (5%, $M^{+\bullet}$), 256 (39), 160 (39), 103 (11), 102 (100).

5j: Recrystallized from isopropanol; large, colourless rhombs, mp 191–192°C. (Found: C 52.4, H 5.0, N 17.7; $M^{+\bullet}$ 320.0935. $C_{14}H_{16}N_4O_3S$ requires C 52.5, H 5.0, N 17.5%; $M^{+\bullet}$

Table 2a. Crystal data and structure refinement for 3f, 3h, 3i, 4b, 4h, and 5f

	3f	3h	3i	4b	4h	5f
CCDC no.	752406	752405	752408	752411	752414	752407
Empirical formula	$C_8H_{12}N_4O_3S$	$C_{10}H_{14}N_4O_3S$	$C_{12}H_{18}N_4O_3S$	$C_{10}H_{14}N_4O_3S$	$C_{10}H_{14}N_4O_3S$	$C_8H_{12}N_4O_3S$
Formula weight	244.28	270.31	298.36	270.31	270.31	244.28
Crystal system	Monoclinic	Monoclinic	Orthorhombic	Monoclinic	Orthorhombic	Triclinic
Space group	$P2_1/c$	$P2_1/c$	$Pbca$	$P2_1/c$	$Pbca$	$P\bar{1}$
Unit cell dimensions						
a [Å]	11.7385(2)	10.8594(3)	10.1488(1)	8.7518(1)	11.3202(2)	7.9492(8)
b [Å]	11.6488(2)	10.8458(2)	11.4196(1)	11.1197(2)	13.2699(2)	8.6774(11)
c [Å]	8.5485(1)	10.1386(1)	23.8679(4)	11.9908(2)	15.3511(3)	8.7656(11)
α [°]	90	90	90	90	90	85.978(6)
β [°]	109.752(1)	91.765(1)	90	91.570(1)	90	74.283(7)
γ [°]	90	90	90	90	90	66.742(6)
Volume [Å^3]	1100.14(3)	1193.55(4)	2766.18(6)	1166.48(3)	2306.01(4)	534.27(11)
Z	4	4	8	4	8	2
ρ (calc.) [mg m^{-3}]	1.475	1.504	1.433	1.539	1.557	1.518
μ [mm^{-1}]	0.294	0.279	0.248	0.285	0.289	0.302
Crystal size [mm]	0.25 × 0.25 × 0.25	0.25 × 0.13 × 0.13	0.25 × 0.13 × 0.10	0.25 × 0.25 × 0.25	0.30 × 0.25 × 0.2005	0.25 × 0.25 × 0.25
θ range [°]	1.84 to 27.49	1.88 to 27.49	1.71 to 27.50	2.33 to 27.50	2.65 to 27.50	2.42 to 25.00
N_{total}	10921	12411	27230	12001	21682	4594
N (R_{int})	2487 (0.045)	2739 (0.055)	3177 (0.50)	2676 (0.037)	2651 (0.053)	1816 (0.055)
N_{obs} [$I > 2\sigma(I)$]	2007	1810	2418	2107	1999	1505
R indices [$I > 2\sigma(I)$]						
R_1	0.0408	0.0458	0.0407	0.0432	0.0433	0.0506
wR_2	0.1047	0.0961	0.0985	0.1045	0.1098	0.1392
R indices (all data)						
R_1	0.0537	0.0866	0.0605	0.0602	0.0646	0.0610
wR_2	0.1128	0.1107	0.1116	0.1152	0.1231	0.1494
GoF (on F^2)	1.059	1.057	1.032	1.067	1.046	1.107

Table 2b. Crystal data and structure refinement for 5h, 5i, 5j, 5k, and 6i

	5h	5i	5j	5k	6i
CCDC no.	752413	752409	752410	752412	752415
Empirical formula	$C_{10}H_{14}N_4O_3S$	$C_{12}H_{18}N_4O_3S$	$C_{14}H_{16}N_4O_3S$	$C_{15}H_{16}N_4O_3S$	$C_{12}H_{18}N_4O_3S$
Formula weight	270.31	298.36	320.37	332.38	298.36
Crystal system	Monoclinic	Orthorhombic	Monoclinic	Orthorhombic	Triclinic
Space group	$P2_1/c$	$P2_12_12_1$	$P2_1/n$	$Pbca$	$P\bar{1}$
Unit cell dimensions					
a [Å]	7.4680(2)	8.7345(2)	9.1977(1)	11.5588(2)	8.313(2)
b [Å]	12.2561(4)	9.2597 (2)	11.1893(2)	14.9942(2)	8.7490(11)
c [Å]	13.2592(5)	17.2306(3)	14.6360(2)	17.1453(3)	9.972(2)
α [°]	90	90	90	90	76.606(10)
β [°]	101.085	90	106.409(1)	90	75.215(10)
γ [°]	90	90	90	90	88.831(10)
Volume [Å^3]	1190.95(7)	1393.59(5)	1444.92(4)	2971.54(8)	681.6(2)
Z	4	4	4	8	2
ρ (calc.) [mg m^{-3}]	1.508	1.422	1.473	1.486	1.454
μ [mm^{-1}]	0.279	0.246	0.243	0.240	0.252
Crystal size [mm]	0.30 × 0.10 × 0.10	0.25 × 0.10 × 0.10	0.25 × 0.25 × 0.25	0.25 × 0.25 × 0.10	0.15 × 0.10 × 0.05
θ range [°]	2.28 to 27.50	2.36 to 27.50	2.33 to 27.50	2.52 to 27.50	2.17 to 27.50
N_{total}	14809	13694	17656	30620	4783
N (R_{int})	2730 (0.057)	3193 (0.055)	3277 (0.056)	3402 (0.059)	2328 (0.043)
N_{obs} [$I > 2\sigma(I)$]	2244	2406	2603	2480	1720
R indices [$I > 2\sigma(I)$]					
R_1	0.0432	0.0449	0.0440	0.0463	0.0643
wR_2	0.0940	0.0972	0.1062	0.1166	0.1145
R indices (all data)					
R_1	0.0605	0.0744	0.0608	0.0729	0.0953
wR_2	0.0999	0.1099	0.1182	0.1332	0.1252
x_{abs}		−0.04(10)			
GoF (on F^2)	1.053	1.051	1.038	1.059	1.070

320.0938). δ_H (300 MHz) 7.87–7.83 (2H, m, ArH), 7.46–7.38 (3H, m, ArH), 6.24 (1H, s, C=CH), 3.59 (2H, q, *J* 7, NCH_2), 3.57 (2H, q, *J* 7, NCH_2), 1.33 (3H, t, *J* 7, NCH_2CH_3), 1.31 (3H, t, *J* 7, NCH_2CH_3). δ_C (75 MHz) 153.1, 148.9, 147.8, 131.2, 129.5, 128.7, 126.2, 86.8, 44.8, 43.1, 13.7, 12.2. *m/z* (EI) 320 (48%, $M^{+\bullet}$), 272 (4), 199 (10), 103 (11), 102 (100).

2,2-Dioxo-7-phenyl-4-piperidin-1-yl-2λ⁶-pyrazolo[2,3-e][1,2,3,5]oxathiadiazine ***3k*** *and 1,1-Dioxo-6-phenyl-3-piperidin-1-yl-1λ⁶-pyrazolo[3,2-b][1,4,3,5]oxathiadiazine* ***5k***

Method D. Column chromatography (dichloromethane/light petroleum, 1:1) provided two products:

3k (2% yield): Recrystallized from isopropanol; colourless crystals, mp 189–191°C. (Found: C 54.1, H 4.9, N 16.7; $M^{+\bullet}$ 332.0933. $C_{15}H_{16}N_4O_3S$ requires C 54.2, H 4.9, N 16.9%; $M^{+\bullet}$ 332.0938). δ_H (300 MHz) 7.80–7.77 (2H, m, ArH), 7.47–7.45 (3H, m, ArH), 6.37 (1H, s, C=CH), 4.41 (2H, br s, NCH_2), 3.83 (2H, br s, NCH_2), 1.82 (6H, br s, 3 × CH_2). δ_C (75 MHz) 154.3, 151.8, 147.1, 130.9, 130.5, 129.2, 126.5, 91.2, 51.5, 49.1, 26.5, 25.8, 24.2. *m/z* (EI) 332 (3%, $M^{+\bullet}$), 269 (12), 268 (75), 161 (11), 160 (52), 109 (48), 102 (100), 84 (68).

5k (16% yield): Recrystallized from ethanol; colourless crystals, mp 254–256°C. (Found: C 54.4, H 4.9, N 16.8; $M^{+\bullet}$ 332.0936. $C_{15}H_{16}N_4O_3S$ requires C 54.2, H 4.9, N 16.9%; $M^{+\bullet}$ 332.0938). δ_H (300 MHz) 7.86–7.84 (2H, m, ArH), 7.43–7.41 (3H, m, ArH), 6.23 (1H, s, C=CH), 3.73 (4H, br s, 2 × NCH_2), 1.73 (6H, br s, 3 × CH_2). δ_C (75 MHz) 153.2, 148.0, 147.7, 131.2, 129.5, 128.7, 126.2, 86.8, 47.5, 46.0, 25.6, 24.9, 23.5. *m/z* (EI) 332 (48%, $M^{+\bullet}$), 239 (11), 110 (9), 103 (11), 102 (100).

X-Ray Crystallography

Single crystals suitable for X-ray analysis were covered in viscous oil and mounted on a glass fibre. Data ($2\theta_{max}$ 50–55°) were collected at 123(1) K using either a Nonius KAPPA or Bruker X8 Apex CCD diffractometer and MoKα (λ 0.71073 Å) radiation. After integration and scaling, datasets (N_{total}) were merged to *N* unique reflections (R_{int} as quoted) with N_{obs} considered 'observed' with $I > 2\sigma(I)$. The structures were solved using conventional methods and refined by full matrix least-squares using the *SHELX-97* software,[27] in conjunction with the *X-Seed* interface.[28] Non-hydrogen atoms were refined with anisotropic thermal parameters and hydrogen atoms were placed in calculated positions. Molecular diagrams (Figs 1–4) are shown with 50% thermal ellipsoids and hydrogen atoms as spheres of arbitrary size. Data were corrected for absorption using either *SORTAV*[29a] or *SADABS*.[29b] For structure **5i**, the Flack parameter x_{abs} was refined (see Table 2). CCDC 752405–752415 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.

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