Organic Heterocyclothiazenes. Part 9.[1] The Chemistry of a Mesoionic Bicyclic Imine and Its Oxides

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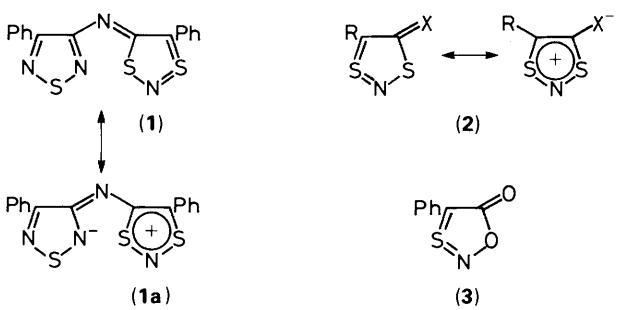
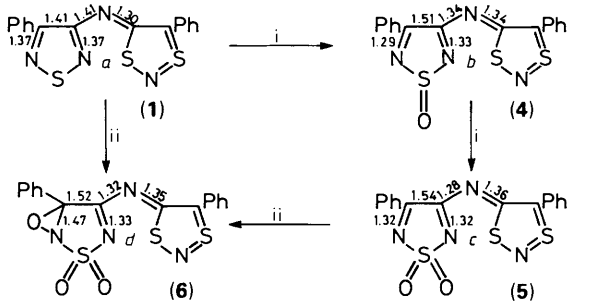
The mesoionic bicyclic imine (**1**) is stable to heat, light, and acids, and is resistant to cycloaddition. However it is readily oxidised, exclusively in the thiadiazole ring, to the mono-(**4**), di-(**5**), and tri-(**6**) oxides, the last being an unusual hetero fused oxaziridine. In the sequence of structures (**1**)→(**4**)→(**5**)→(**6**) the interannular N···S separation gets progressively smaller and the relative lengths of the bonds from the bridging N atom to the rings invert (Scheme 1). This is attributed to enhanced dipolar attraction between the rings as the dithiazolium contribution (**8b**) becomes increasingly important. Chemical consequences of this interaction are the unprecedented formation of a thiadiazole trioxide (**6**) and the very ready hydrolysis of the monoxide (**4**) to the dibenzoylthiadiazole (**7**) (Scheme 2) which involves cleavage of the original rings and complete formation of the incipient central 'ring'.

Part 2 of this series described the reaction of S_4N_4 with phenylacetylene to give the highly rearranged structure (**1**) in which both heterocyclic rings and the linking nitrogen atom are accurately coplanar in the crystalline state.[2] The 1,3,2-diathiazole ring is rare and the deep violet imine (**1**) was its first mesoionic[3] derivative (**2**). (These derivatives are subsequently written in the fully covalent form for simplicity.) However, the analogous mesoionic 4-phenyl-1,3,2-oxathiazol-5-one (**3**) has been quite well studied.[4]

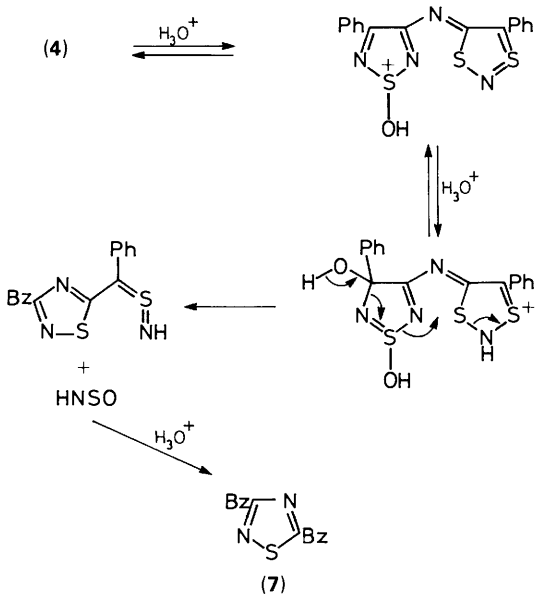
The bicyclic imine (**1**), very stable thermally, is only slowly decomposed by irradiation at 254 and 350 nm, and is inert to acids. It survived prolonged boiling with 4M hydrochloric acid in aqueous tetrahydrofuran, and the orange conjugate acid formed in concentrated hydrochloric acid was stable in this medium, or under strictly anhydrous conditions, but was readily hydrolysed back to the violet imine (**1**). The imine was also relatively stable to base and required heating at reflux in aqueous ethanolic potassium hydroxide (0.3M) for 20 h for hydrolysis to 3-amino-4-phenyl-1,2,5-thiadiazole (69%). The imine was resistant to cycloaddition with electron-deficient alkynes. It did not react with either dimethyl acetylenedicarboxylate or dibenzoylacetylene on prolonged boiling in bromobenzene, in striking contrast with the related oxathiazolone (**3**) which undergoes complete reaction with both alkynes in boiling benzene within 1 h.[4] These results suggest that the imine (**1**) is stabilised, presumably by delocalisation from the electron-donating dithiazole ring to the electron-withdrawing thiadiazole ring [*cf.* (**1a**)], a trend which was found to be greatly enhanced when the thiadiazole ring is oxidised.



Oxidation of the Dithiazolimine (**1**).—The imine (**1**) was reported[2] to be sensitive to oxidation, being completely consumed by *m*-chloroperbenzoic acid (MCPBA) (2 equiv.) at room temperature to give a mixture of four products; these have now been characterised and their structures confirmed by *X*-ray crystallography.[5] The milder oxidant, dinitrogen tetraoxide, in dichloromethane at −20 °C converted the imine (**1**) into the thiadiazole 1-oxide (**4**) (90%). Its i.r. spectrum had a peak at 1 110 cm^{-1} typical of an *S*-oxide and its mass spectrum showed ready loss of oxygen from the molecular ion. Treatment of the monoxide (**4**) with more N_2O_4 gave the 1,1-dioxide (**5**) (55%) together with a lower molecular weight product (*m*/*z* 294) (20%) which clearly required some sort of ring cleavage for its formation (see below). The major product, $C_{16}H_{10}N_4O_2S_3$, did not lose oxygen from its molecular ion, suggesting that it was an *S*,*S*-dioxide. This was supported by a strong i.r. absorption at 1 165 cm^{-1} and the thiadiazole 1,1-dioxide structure (**5**) was proved by *X*-ray analysis. This compound was inert to further reaction with N_2O_4 (50 equiv., 20 °C, 14 h) so we returned to the preliminary observation of extensive oxidation of the imine (**1**) with MCPBA.[2] With 2 equiv. of this reagent in dichloromethane at room temperature four products were formed. They were the monoxide (**4**) (18%), the dioxide (**5**) (16%), a very small amount of the *m*/*z* 294 product, and a new highly fluorescent product which, by analysis and mass spectrometry, was shown to be a trioxide (15%). When the oxidation of (**1**) was repeated with an excess of MCPBA the trioxide became the major product (55%)



Scheme 1. *Reagents:* i, N_2O_4; ii, MCPBA. Selected bond lengths in Å. Interannular N–S separations: *a* 2.70 Å, *b* 2.57 Å, *c* 2.53 Å, *d* 2.50 Å. Sum of van der Waals radii for S and N: 3.35 Å. S–N single bond length 1.74 Å



Scheme 2.

at the expense of the mono- and di-oxides, and it was formed in higher yield (80%) by direct oxidation of the dioxide (**5**). *X*-Ray analysis showed that the third oxygen was also attached to the thiadiazole ring to give, unexpectedly, the intriguing oxaziridine structure (**6**). Oxidation of imines to oxaziridines is well known,[6] but the trioxidation of thiadiazoles has not been reported, and the ready formation of (**6**) appears to be another consequence of electron release from the dithiazole to the thiadiazole ring. This is borne out by a comparison of the *X*-ray data.[5]

Reactions of the S-*Oxides*.—Of the three, the dioxide (**5**) proved to be the most stable thermally, followed by the monoxide (**4**), and then the trioxide (**6**). Heating the last in propionitrile (3 days) or bromobenzene (4 h) cleanly gave the dioxide (94 and 97% respectively). Oxaziridines normally rearrange to nitrones or amides on heating;[6] this loss of the oxaziridine oxygen atom, possibly *via* the *N*-oxide, is reminiscent of the thermal deoxygenation of heterocyclic *N*-oxides. The fate of the oxygen atom is unknown, but the reaction may be bimolecular, producing singlet O_2. Deoxygenation also occurred when the molten monoxide (**4**) was heated in a capillary tube at 250 °C; the violet imine (**1**) sublimed out in a very clean reaction. The dioxide (**5**) was unchanged after heating for 1 h at 280 °C.

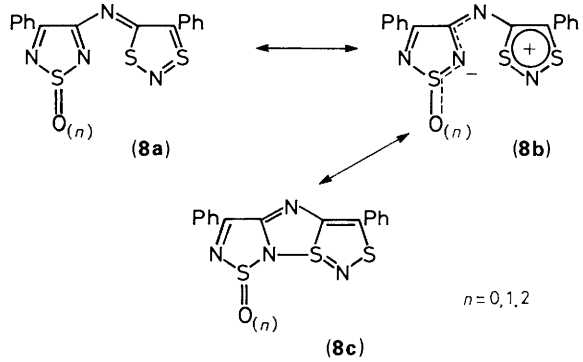
As noted above, a minor product (*m*/*z* 294) was isolated in the oxidation of the monoxide (**4**) with N_2O_4. Since this might have been a nitrosation product, we treated the monoxide with the more powerful reagent nitrosonium tetrafluoroborate. The reaction in acetonitrile was slow but was found to be accelerated by exposure to air; the same product was eventually formed in high yield (75%), thus permitting its identification as 3,5-dibenzoyl-1,2,4-thiadiazole (**7**). This was based upon the molecular formula, carbonyl absorptions at 1 683 and 1 653 cm^{-1}, two non-equivalent phenyl groups (^1H n.m.r.), and the mass spectral fragmentation and u.v. spectrum being very similar to those of 3,4-dibenzoyl-1,2,5-thiadiazole (obtained from the reaction of S_4N_4 with dibenzoylacetylene). This all pointed to an unsymmetrical dibenzoylthiadiazole, but structure (**7**) initially seemed so surprising that it was confirmed by *X*-ray crystallography.[7]

The formation of (**7**) from (**4**) became more understandable when we realised that it was a product of acid catalysed hydrolysis ($NO^+BF_4^-$ or N_2O_4 plus atmospheric moisture). Indeed treatment of (**4**) with cold dilute hydrochloric acid in THF gave the thiadiazole (**7**) in good yield (79%). In this unexpected reaction the thiadiazole and dithiazole rings are both destroyed and a new thiadiazole ring, incorporating the bridging nitrogen atom, is formed. A possible mechanism is proposed in Scheme 2. It is tempting to consider this unusual 1,2,4-thiadiazole ring formation as a chemical consequence of the close interannular N ··· S separation which is discussed below.

Structures of the Bicyclic Imine (**1**) *and Its Oxides*.—Several trends emerge when the bond lengths of the four bicyclic imines (**1**), (**4**), (**5**), and (**6**) are compared.[5] Disrupting the aromaticity in the thiadiazole ring results, as expected, in the localisation of bonds in that ring. More interesting are comparisons of the bond lengths between the 5-membered rings and the bridging nitrogen atom, and the shortest S ··· N atomic separations between the rings.

In the unoxidised imine (**1**) the bond lengths indicate that there is significant delocalisation in the dithiazole ring: although this suggests a contribution of type (**1a**), it is not a major contributor since the central nitrogen to dithiazole bond is significantly shorter than the central nitrogen to thiadiazole bond. In the monoxide (**4**), however, the analogous delocalisation is expected to be greater as the negative charge is delocalised onto oxygen as well as nitrogen, and the *X*-ray data show that the two ring-to-bridging nitrogen bonds are now of equal length. This trend is enhanced further in the dioxide (**5**) and the trioxide (**6**), as would be expected from the increased electron withdrawal; the central nitrogen to thiadiazole (formally single) bonds (1.28 and 1.32 Å) are now shorter than the (formally double) bonds to the dithiazole ring (1.36 and 1.35 Å). Using the experimental bond lengths as a measure of bond order, a neutral structure can only be drawn with a formal bond between the neighbouring annular nitrogen and sulphur atoms (**8c**). It is interesting to note that as the number of oxygens in the system increases the interannular separation gets progressively less (see Scheme 1). The major contraction, from 2.70 Å in (**1**) to 2.57 Å in (**4**), occurs when the aromaticity of the thiadiazole is first disrupted.

The structures of the bicyclic imines can be considered as hybrids of the three extreme canonical forms (or possibly valence isomers) (**8**). The heterocyclic rings will be held close together and coplanar by dipolar attraction (**8b**), the ultimate form resulting from this being the tricyclic structure (**8c**). From the *X*-ray data it appears that (**8a**) is most important for the unoxidised imine, but that the mesoionic (**8b**) and the tricyclic (**8c**) structures become increasingly important as the oxidation level increases.



Experimental

For general points see ref. 8. Light petroleum refers to the fraction, b.p. 40—60 °C.

4-(1-*Oxo*-4-*phenyl*-1,2,5-*thiadiazol*-3-*ylimino*)-5-*phenyl*-1,3,2-*dithiazole* (**4**).—The bicyclic imine (**1**)[2] (70.8 mg, 0.2 mmol) in dichloromethane (10 ml) was treated with N_2O_4 (27.2 mg, 0.296 mmol, in 0.7 ml of CCl_4) at 20 °C; eight such portions were added at 10 min intervals. The reaction mixture was preadsorbed onto silica and separated by dry flash column chromatography on silica (25 g) using gradient elution. Ethyl acetate (15 to 25%) in dichloromethane eluted the *title compound* (**4**) (68 mg, 92%) as bright orange plates, m.p. 247 °C (EtOAc–CH_2Cl_2) (Found: C, 51.7; H, 2.7; N, 14.9. $C_{16}H_{10}N_4OS_3$ requires C, 51.9; H, 2.7; N, 15.1%); $\lambda_{max.}$(EtOH) 236 (log ε 4.16), 271 (4.18), 380 (3.93), and 445 nm (3.84); $\nu_{max.}$($CHCl_3$) 1 470s, 1 445m, 1 405s, 1 300m, 1 110s (SO), and 910s cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.47 (2 H, td, *J* 7.8 and 1.9 Hz, 2 × ArH), 7.58–7.70 (4 H, m, 4 × ArH), 8.05 (2 H, dd, *J* 7.8 and 2.2 Hz, 2 × ArH), and 8.62 (2 H, dd, *J* 7.8 and 2.2 Hz, 2 × ArH); *m/z* (260 °C) 370 (M^+, 3%), 354 (M^+ − O, 29), 308 [M^+ − (O + NS), 3%], 219 (M^+ − PhCNSO, 5), 121 ($PhCS^+$, 100), and 77 (Ph^+, 12).

4-(1,1-*Dioxo*-4-*phenyl*-1,2,5-*thiadiazol*-3-*ylimino*)-5-*phenyl*-1,3,2-*dithiazole* (**5**).—The monoxide (**4**) (40 mg, 0.108 mmol) in dichloromethane (10 ml) was treated with eight portions of N_2O_4 (10 mg, 0.108 mmol in 0.1 ml of CCl_4), one portion being added every 10 min. When all the starting material had been consumed (t.l.c.) the reaction mixture was preadsorbed onto silica and separated by dry flash chromatography using gradient elution. Ethyl acetate (0—2%) in dichloromethane eluted 3,5-*dibenzoyl*-1,2,4-*thiadiazole* (**7**) (6 mg, 19%), m.p. 68—69 °C (Found: C, 65.35; H, 3.5; N, 9.60; M^+, 294.0474. $C_{16}H_{10}N_2O_2S$ requires C, 65.3; H, 3.4; N, 9.5%; *M*, 294.0463); $\lambda_{max.}$(EtOH) 267 nm (log ε 4.20); $\nu_{max.}$(CCl_4) 3 073w, 1 683s (CO), 1 653s (CO), 1 599m, 1 580w, 1 477w, 1 445m, 1 316m, 1 282m, 1 205m, 1 181m, 1 123w, 1 005m, 996m, 897m, 860s, 713s, 688s, and 664m cm^{-1}; δ_H(250 MHz; $CDCl_3$) 7.52—7.76 (6 H, m, 6 × ArH), 8.27 (2 H, dd, *J* 8.5 and 1.5 Hz, 2 × ArH), and 8.62 (2 H, dd, *J* 8.5 and 1.5 Hz, 2 × ArH); *m/z* (170 °C) 294 (M^+, 14%), 105 ($PhCO^+$, 100), and 77 (Ph^+, 44). Ethyl acetate (4 to 5%) in dichloromethane eluted the *title compound* (**5**) (23 mg, 55%) as pale yellow needles, m.p. 280 °C (dichloromethane) (Found: C, 49.5; H, 2.5; N, 14.3. $C_{16}H_{10}N_4O_2S_3$ requires C, 49.7; H, 2.6; N, 14.5%); $\lambda_{max.}$(EtOH) 238 sh (log ε 3.89), 270 (3.94), 305 sh (3.72), 372 (3.65), and 440 nm (3.71); $\nu_{max.}$($CHCl_3$) 1 516m, 1 490w, 1 449w, 1 417m, 1 347m, 1 301w, 1 165s (SO), 934m, 689w, 669w, 651m, 640w, and 616m cm^{-1}; δ_H(250 MHz; $CDCl_3$) 7.43 (2 H, ≈t, *J* 8.1 Hz, 2 × ArH), 7.58—7.70 (4 H, m, 4 × ArH), 7.97 (2 H, dd, *J* 7.7 Hz and 1.6 Hz, 2 × ArH), and 8.60 (2 H, dd, *J* 8.1 and 1.6 Hz, 2 × ArH); *m/z* (220 °C) 388 (M^+ + 2, 3.7%), 386 (M^+, 22), 219 [M^+ − (PhCN + SO_2), 100], 173 (12), 146 (62), 121 ($PhCS^+$, 83), and 77 (Ph^+, 23).

4-(3,3-*Dioxo*-5a-*phenyl*-5aH-*oxazirino*[2,3-b][1,2,5]*thiadiazol*-5-*ylimino*)-5-*phenyl*-1,3,2-*dithiazole* (**6**).—(i) *From the bicyclic imine* (**1**). The bicyclic imine (10 mg, 0.028 mmol), MCPBA (8.4 mg, 0.041 mmol), and dichloromethane (3 ml) were stirred together at 0 °C for 1 h. MCPBA (9 mg, 0.044 mmol) was added and the reaction mixture stirred for 3 h. A final portion of MCPBA (15 mg, 0.074 mmol) was added and the reaction mixture stirred for 24 h, preadsorbed onto silica, and separated by dry flash chromatography on silica (10 g) using gradient elution. Dichloromethane eluted the *oxaziridine* (**6**) as pale yellow needles, m.p. 240 °C (light petroleum–dichloromethane) (Found: C, 47.5; H, 2.4; N, 13.7. $C_{16}H_{10}N_4O_3S_3$ requires C, 47.75; H, 2.5; N, 13.9%); $\lambda_{max.}$(EtOH) 237, 297, and 440 nm; $\nu_{max.}$ 1 519m, 1 428w, 1 372w, 1 175s, and 930 cm^{-1}; δ_H(250 MHz; $CDCl_3$) 7.4—7.63 (6 H, m, 6 × ArH), 7.79 (2 H, dd, *J* 8.7 and 1.7 Hz, 2 × ArH), and 7.92 (2 H, dd, *J* 8.7 and 1.8 Hz, 2 × ArH); *m/z* (220 °C) 402 (M^+, 1) 386 (M^+ − O, 11), 219 (66), 149 (100), 146 (53), 121 ($PhCS^+$, 93), 103 ($PhCN^+$, 53), and 77 (Ph^+, 37).

(ii) *From the dioxide* (**5**). The dioxide (**5**) (5 mg, 0.013 mmol), MCPBA (85%; 5 mg, 0.025 mmol), and dichloromethane (2 ml) were stirred at 0 °C for 6 h. Purification by dry flash chromatography as above gave the oxaziridine (**6**) (4.1 mg, 79%) identical with that obtained above.

Hydrolysis of the Monoxide (**4**).—A mixture of the monoxide (**4**) (8 mg, 0.022 mmol) in THF (3 ml) was treated with hydrochloric acid (4M; 0.1 ml) and stirred for 6 h at 20 °C. Purification by flash chromatography gave 3,5-dibenzoyl-1,2,4-thiadiazole (5 mg, 79%) identical with that obtained above.

Thermolysis of the Oxaziridine (**6**).—The oxaziridine (**6**) (6 mg, 0.015 mmol) was heated in bromobenzene (3 ml) for 4 h. Purification by dry flash chromatography gave the dioxide (**5**) (5.6 mg, 97%), identical with that obtained above. Thermolysis in propionitrile (at reflux, 3 days) also gave the dioxide (**5**) (94%).

Acknowledgements

We thank the S.E.R.C. for a studentship to P. J. D. and Dr. D. J. Williams for the *X*-ray diffraction results.

References

1 Part 8, P. J. Dunn and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1405.
2 S. T. A. K. Daley and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1987, 207.
3 W. D. Ollis and C. A. Ramsden, *Adv. Heterocycl. Chem.*, 1976, **19**, 1.
4 H. Gotthardt, *Chem. Ber.*, 1972, **105**, 188, 196.
5 P. J. Dunn, C. W. Rees, A. M. Z. Slawin, and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1989, 1134.
6 E. Schmitz in 'Comprehensive Heterocyclic Chemistry,' eds. A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, ch. 5.08.
7 D. J. Williams, Department of Chemistry, Imperial College, unpublished results.
8 S. T. A. K. Daley and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1987, 203.

Received 1*st June* 1989; *Paper* 9/02281C