Model Studies Related to the Cofactor of Oxomolybdoenzymes. Part 2[1]. Quinoxalin-2-yl-ethane- and -ethene-1,2-dithiols

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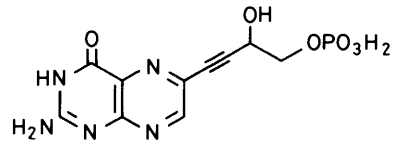
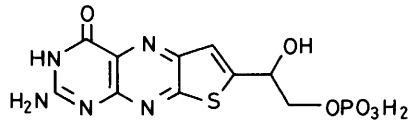
2-Hydroxy-2-phenylethyl and -2-quinoxalin-2-ylethyl *N,N*-dimethyldithiocarbamates are cyclised to 4-aryl-1,3-dithiolane-2-thiones, (**8b**) and (**10**), and these could be dehydrogenated to the corresponding dithioles, (**7b**) and (**11**), from which the arylethene-1,2-dithiolates could be released by alkaline hydrolysis. MCPBA then TFAA treatments of cyclohexanone, acetophenone, and quinoxalin-1-yl methyl ketone ethane-1,2-dithiol thioacetals and of cyclohexanone 1,2-diphenylethane-1,2-dithiol thioacetal produces the corresponding rearranged dihydro-1,4-dithiins (**14a**), (**17**), (**19**), and (**14b**) respectively. Only in the cases of (**14a**) and (**14b**) could the desired reductive cleavages to generate 1,2-dithiolate, be achieved. Under reductive methylation conditions the pyrazine ring of (**19**) was selectively reduced, release of 1,2-dithiolate from the product (**20b**) now proving possible. 2-Acetylquinoxaline gave a 1,3,2-oxaphospholane 2-sulphide on treatment with Lawesson's reagent.

The oxomolybdoenzymes, xanthine oxidase, aldehyde oxidase, sulphite oxidase, and nitrate reductase, but not nitrogenase, contain a common cofactor, known as Moco. There is now a considerable body of evidence[2] which has shown that the molybdenum in Moco is complexed by an organic component, known as molybdopterin. Oxidative chemical degradations of Moco produced the pteridinylalkyne (**1**) and the thiophenopteridine (**2**); these, taken with urothione (**3**), a metabolic breakdown product of Moco, provided evidence for the carbon skeleton of molybdopterin, and for the location of the two sulphur atoms which are considered to ligand the metal. In the most recently published[3] work on Moco, the organic component was trapped by alkylation of the sulphurs with iodoacetamide; in this way (**4**) was isolated and spectroscopically characterised. Partial structure (**5**) then, is believed to represent Moco; no comment has yet been made on the relative or absolute stereochemistry at the two asymmetric carbon atoms nor on the nature of the other ligands attached to the metal. Further, we believe that neither the oxidation level of the pyrazine ring nor that of the sulphur-bearing carbons, has been fully established for the native enzymes.

The catalyses achieved by the oxomolybdoenzymes involve the molybdenum undergoing 2-electron redox changes between Mo^{VI} and Mo^{IV} and this ability may well be linked to changes in the pyrazine ring oxidation level. Further, it is possible that an important function of the pyrimidine ring of Moco is for linking to the protein, presumably *via* hydrogen bonding interactions; however, a study[4] of molybdenum/pterin complex formation, using xanthopterin and molybdate, did demonstrate binding to the metal *via* hetero-atoms from *both* rings. Xanthopterin, however, has no side chain, nor of course associated sulphur atoms. Also, the possible role of phosphate/molybdenum interaction in Moco has been discussed.[5] However, molybdenum K-edge Extended *X*-ray Absorption Fine Structure (EXAFS) of the Mo^{VI} and Mo^{IV} centres of the oxomolybdoenzymes,[6] and electron spin resonance (ESR) of the Mo^{V} counterparts,[7] demonstrate sulphur co-ordination to molybdenum. Therefore, we have directed our efforts towards the synthesis of quinoxaline relatives of Moco which, though simpler than pteridines, would nevertheless possess those features of molybdopterin which are probably crucial to its operation, *i.e.* the pyrazine ring and the side-chain sulphurs. Further, because of uncertainties alluded to above, we also felt it relevant to develop syntheses which would make available varying oxidation levels of both side chain and



(**1**)



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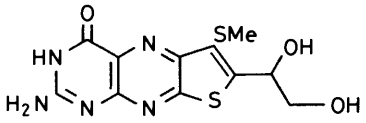
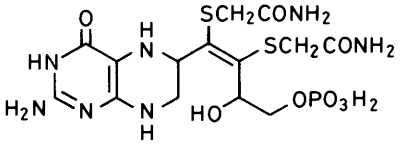
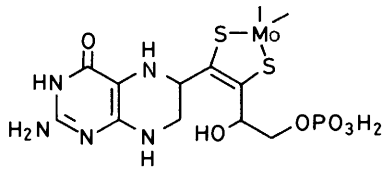


(**3**)



(**4**)

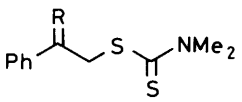


(**5**)

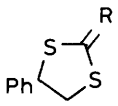
pyrazine ring. We have already reported[8] on a method for the synthesis of 1-aryl- and 1-heteroaryl-alkene-1,2-dithiolates and on some metal complexes produced[9] using these substances. We describe here further work on the formation of phenyl- and quinoxalin-2-yl-C_2-side-chain ethene-1,2-dithiolates and also methods for the formation of the corresponding ethane-1,2-dithiolates, and for their dehydrogenation to the former, and make comment on the interconversion of quinoxaline, *versus* 1,2,3,4-tetrahydroquinoxaline oxidation levels.

Results

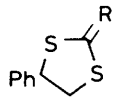
The expected relative instability of ethene-1,2-dithiols and ethane-1,2-dithiols necessitated a synthetic strategy where these entities were produced in protected form, for later release of the potential ligand. In our previous work,[8] for example, the α-keto-dimethyldithiocarbamate (**6a**) was converted into the salt (**7a**) from which an ene-1,2-dithiolate dianion could be generated by alkaline hydrolysis. We have now utilised (**6a**) as the starting material for a new method for the synthesis of an alkali-cleavable, protected ethane-1,2-dithiol—a cyclic trithiocarbonate. Borohydride reduction of (**6a**) gave alcohol (**6b**), from which, by successive treatments with methanesulphonyl chloride and then hydrogen sulphide, the trithiocarbonate (**8b**)[10] could be obtained *via* presumed intermediates (**6c**) and (**8a**). We found that this side-chain oxidation level could be easily raised by reaction of (**8b**) with *m*-chloroperbenzoic acid (MCPBA) and then trifluoroacetic anhydride (TFAA), producing (**7b**).[11]



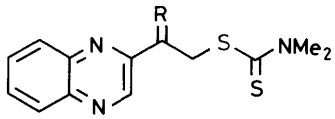
(**6**) R
a; O
b; H,OH
c; H OMes



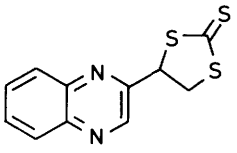
(**7**) R
a; $N^+Me_2\ HSO_4^-$
b; S



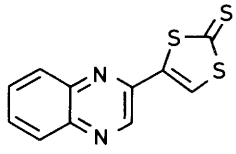
(**8**) R
a; $N^+Me_2\ MesO^-$
b; S



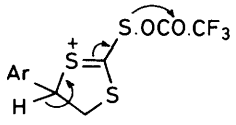
(**9**) R
a; O
b; H,OH



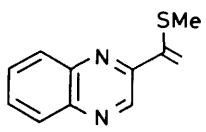
(**10**)



(**11**)



(**12**)



(**13**)

Extending the approach to quinoxalines proved straightforward, thus the α-keto-dimethyldithiocarbamate (**9a**)[8] was reduced with borohydride, at 0 °C in this case to avoid reduction of the pyrazine ring, giving the alcohol (**9b**) which was cyclised and converted into the side-chain saturated trithiocarbonate (**10**) and this, in turn, dehydrogenated to the unsaturated trithiocarbonate (**11**), using MCPBA and then TFAA in essentially the same way as that described above for the phenyl analogue.

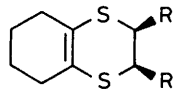
These dehydrogenations must involve an S-oxidation, at the exocyclic sulphur we suggest and, subsequently, the intermediates (**12**). It is important from the viewpoint of our further synthetic endeavours on more complex quinoxalines, and subsequently, pteridines, that this now establishes a simple, mild method for the conversion of side chain- alkane-1,2-dithiol to -alkene-1,2-dithiol oxidation level, and that therefore future work aimed ultimately at the latter can, if necessary, aim first at the former.

In analogy with previous work, an ene-1,2-dithiolate dianion could be liberated from (**11**) by alkaline hydrolysis. However, attempts to liberate the corresponding saturated dithiolate from (**10**) by reaction with sodium hydroxide in methanol followed by trapping with iodomethane led to the formation of the thioenol ether (**13**), presumably *via* a 1,2-elimination promoted by deprotonation at the benzylic and further sulphur-acidified position, and then loss of carbon disulphide before trapping.[12] The usually efficient lithium aluminium hydride cleavage of a cyclic trithiocarbonate to 1,2-dithiol[13] is, of course, not relevant in the present case because of the presence of the pyrazine ring.

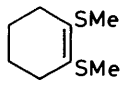
As an alternative to forming an hydrolytically cleavable protected ethene-1,2-dithiol we have examined the production and reductive cleavage of *S*-alkyl-protected derivatives, the basis for this line of approach being the known preferential cleavage of sulphur-saturated- *versus* sulphur-unsaturated-carbon bonds.[14]

It seemed that dihydro-1,4-dithiins might serve as alkyl-protected ene-1,2-dithiols in that metal–ammonia reductive selective cleavage of the two sulphur-saturated-carbon bonds would provide a convenient entry to dilithium (sodium) salts of ethene-1,2-diols. As a means of obtaining such protected ene-dithiols, we turned to a number of reports of dithiolane rearrangements[15] which produce dihydro-1,4-dithiins. We began by showing that the *S*-oxide of the ethane-1,2-dithiol ketal of cyclohexanone could be smoothly converted into the bicyclic dithiin (**14a**) on reaction with TFAA at 0 °C, conditions considerably milder than those previously employed.[15] Further, this line of approach was vindicated when the reaction of (**14a**) with lithium–ammonia did indeed result in the required product, the resultant ene-1,2-dithiol dilithium salt being then trapped with iodomethane, generating (**15**).

Thus encouraged, we converted the dithiolane (**16**)[15b] into (**17**), using identical methodology, however, the alkyl-protection could not now be reductively removed; the result of metal–ammonia treatment was a complex mixture, which we suggest may be associated with reduction of the conjugated, side-chain double bond with subsequent unselective C–S cleavages. The conversion of 2-acetylquinoxaline into its ethane-1,2-dithiol ketal could not be made efficient, the cleanest catalyst was zinc triflate, but a conversion of only 28% could be achieved and that after 5 days; boron trifluoride effected a better conversion, but in a less clean process; *N,N*-bis-trimethylsilylethane-1,2-dithiol[16] produced no dithioketal at all. The TFAA-promoted rearrangement proceeded well, however, and the quinoxalin-2-yl-5,6-dihydro-1,4-dithiin (**19**) was thus obtained. Unfortunately, as in the phenyl-substituted case, all attempts to bring about the desired reductive deprotection led to complex mixtures, the failure almost certainly being associated with reduction of the quinoxaline-conjugated double bond, with associated subsequent non-selective C–S bond cleavages.



(14) R
a; H
b; Ph



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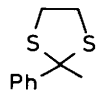
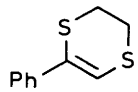
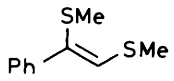


(16)



(17)



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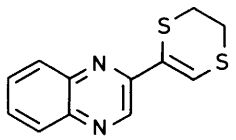
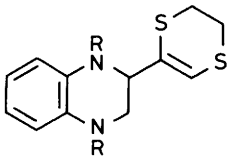
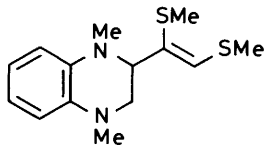


(19)



(20) R
a; H
b; Me



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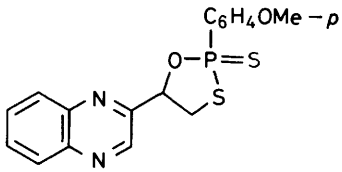


(22)

Arguing that the cleavage of a benzylic C–S bond might be possible under sufficiently mild conditions to provide selectivity in a deprotection, we next turned to the use of *meso*-1,2-diphenylethane-1,2-dithiol,[17,18] dithioketals from which would have two benzylic C–S bonds as the bonds to be cleaved during deprotection.

Reaction of the solid diphenylethanedithiol with cyclohexanone proceeded normally and TFAA-promoted rearrangement then gave (**14b**); finally, the release of the ene-1,2-dithiol unit from (**14b**) could be straightforwardly achieved. Unfortunately, all attempts to effect reaction of *meso*-1,2-diphenylethane-1,2-dithiol with 2-acetylquinoxaline which, in any case, reacted only sluggishly with ethane-1,2-dithiol itself, met with failure.

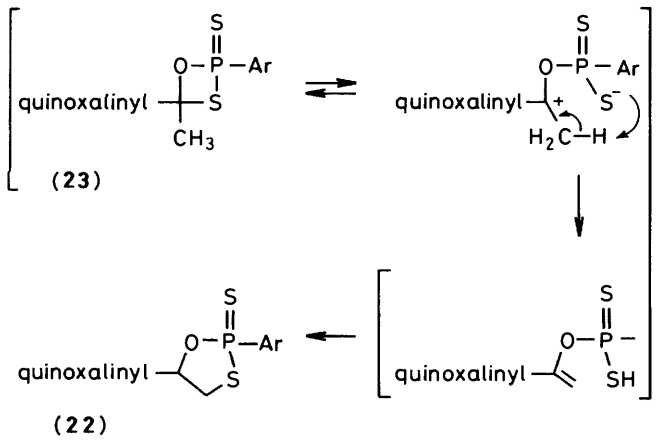
Reduction of the pyrazine ring in (**19**) proceeded easily with sodium borohydride at room temperature, despite literature suggestions[19] to the contrary; however, the expected tetrahydro derivative (**20a**) could not be isolated; t.l.c. and mass spectroscopic and n.m.r. analyses suggesting that rearomatisation was a major complicating factor. A pyrazine-ring-reduced derivative *could* be obtained by reductive alkylative trapping using formaldehyde and sodium cyanoborohydride, giving (**20b**). Reductive cleavage of the protection in (**20b**), now having neither a reduceable pyrazine ring, nor a conjugated double bond, proceeded smoothly, as proved by trapping in the usual way furnishing (**21**).

Finally, we record what appears to be the first report of the formation of a 1,3,2-oxathiaphospholane, using Lawesson's reagent[20] and a simple ketone. In an attempt to convert 2-acetylquinoxaline into its thio analogue, it was heated with 2,4-bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulphide (Lawesson's reagent) in refluxing toluene. The only characterisable product was shown to have structure (**22**), ^{1}H n.m.r. signals for the 5-ring CH_2CH unit together with those for the reagent-derived methoxy-aromatic ring, leaving no doubt as to the presence of a residue from the reagent and a five-membered ring. Major mass spectroscopic fragment ions corresponding to quinoxalinyl-C_2H_3S and quinoxalinyl-C_2H_3O confirmed the hetero-substitution of the five-membered ring. We view this product as having been formed from an expected 'normal' Lawesson's intermediate (**23**), by carbon–sulphur heterolytic cleavage, intramolecular deprotonation and then intramolecular addition[21] of the dithiophosphonate to the quinoxaline-conjugated double bond. The formation, using Lawesson's reagent, of the oxathiaphospholane ring system has been previously reported from epoxides,[22] α-hydroxy ketones,[23] allyl alcohols,[24] and acetylenic carbinols.[25]

Experimental

General.—M.p.s were determined on a Kofler hot-stage microscope and are uncorrected. Wet organic solutions/extracts were dried with anhydrous $MgSO_4$, Na_2SO_4, or K_2CO_3 and evaporated at *ca.* 20 mmHg at *ca.* 40—70 °C using a rotary evaporator. Unless otherwise stated, u.v./vis. spectra (reported in nm) were measured in ethanol using a Shimadzu UV/VIS 260 instrument; i.r. spectra (in cm^{-1}) were measured using Pye-Unicam SP3-200 or Perkin-Elmer 1710 FT spectrometers. ^{1}H N.m.r. spectra of deuteriochloroform solutions, reported as δ values in p.p.m. with respect to internal $SiMe_4$ (0 p.p.m.) with coupling constants, *J*, given in Hz, were measured on Perkin-Elmer R12B (60 MHz), Perkin-Elmer R34 (220 MHz), Varian SC300 (300 MHz), or Varian XL300 (300 MHz) spectrometers. Unless otherwise stated, mass spectra were determined by the electron impact method on an AEI MS30 instrument coupled to a DS55 data system. Chemical ionisation (c.i.) mass spectra, using NH_3, were obtained with a Kratos MS25 instrument, coupled to a DS55 data system. For ^{1}H n.m.r. spectra, only signals which are clearly distinguished and unambiguously identifiable are assigned to particular protons. For i.r. spectra, only those absorptions of obvious structural relevance are detailed. Only ions of >10% of base peak are given for mass spectra, except where a less intense ion is of importance for structure establishment.

2-*Hydroxy*-2-*phenylethyl* NN-*Dimethyldithiocarbamate* (**6b**).—To a solution of the ketone (**6a**) (5 g) in methanol (100 ml) at 0 °C, was added sodium borohydride in portions (1 g) with stirring over a period of 1 h. The mixture was then brought to room temperature, stirred for a further 1 h, after which aqueous ammonium chloride and dichloromethane were added. The organic phase was separated, dried, and evaporated under reduced pressure to give the crude alcohol as a white crystalline solid. Recrystallisation from dichloromethane–hexane gave the pure *alcohol* (**6b**) (4.5 g, 89%), m.p. 121—123 °C; $\nu_{max.}$(film) 3 100; δ_H 7.48 (2 H, d, *J* 7, ArH), 7.37 (2 H, t, *J* 7, ArH), 7.29 (1 H, m, ArH), 5.03 (1 H, dd, *J* 3, 8, 2-H), 3.85 (1 H, dd, *J* 3, 14, 1-H), 3.60 (1 H, dd, *J* 8, 14, 1-H), 3.58 (3 H, s, NMe), and 3.40 (3 H, s, NMe); *m/z* 241 ($M^{\cdot+}$, 0.1%), 223 (1), 135 (18), 121 (40), 104 (19), and 88 (100) (Found: C, 54.9; H, 6.4; N, 5.8; S, 26.6. $C_{11}H_{15}NOS_2$ requires C, 54.8; H, 6.2; N, 5.8; S, 26.6%).



4-*Phenyl*-1,3-*dithiolane*-2-*thione* (**8b**).—To a solution of the alcohol (**6b**) (1 g) in pyridine (5 ml) at 0 °C was added methanesulphonyl chloride (0.42 g). The mixture was brought to room temperature, heated on a steam-bath for 5 min and then cooled and hydrogen sulphide bubbled through it for 10 min. After a further 30 min at room temperature, nitrogen was bubbled through the mixture to remove any residual hydrogen sulphide after that water and dichloromethane were added. The organic layer was separated, dried, and evaporated under reduced pressure to give the crude material which was purified by recrystallisation from dichloromethane–hexane and gave the pure trithiocarbonate (**8b**) (0.71 g, 81%), m.p. 85—87 °C (lit,[10a] m.p. 87—88 °C).

4-*Phenyl*-1,3-*dithiole*-2-*thione* (**7b**).—To a stirred solution of the trithiocarbonate (**8b**) (100 mg) in dry chloroform (5 ml) at 0 °C was added MCPBA (60 mg). The mixture was brought to room temperature and stirred for 3 h. The chloroform solution was then washed with aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure to give a residue which was redissolved in dry chloroform (5 ml). TFAA (90 mg) was then added with stirring at 0 °C to this solution. The mixture was brought to room temperature and stirred for a further 2 h, after which the mixture was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give an orange gum. Crystallisation of this from dichloromethane–hexane gave the 1,3-dithiole (**7b**) as yellow crystals (79 mg, 80%), m.p. 116—118 °C (lit,[26] m.p. 117—118 °C).

2-*Hydroxy*-2-(*quinoxalin*-2-*yl*)*ethyl* NN-*Dimethyldithiocarbamate* (**9b**).—A solution of the ketone (**9a**) (5 g) in dry methanol (150 ml) at 0 °C was stirred while sodium borohydride was added in portions (6 × 0.5 g) over 2 h. A solution of ammonium chloride (10 g) in water (200 ml) was added dropwise at 0 °C followed by dichloromethane (200 ml); the organic layer was then separated, dried, and evaporated under reduced pressure to give the crude alcohol. Recrystallisation of this from dichloromethane–hexane gave the pure *alcohol* (**9b**) (4.4 g, 87%), m.p. 152—154 °C; $\nu_{max.}$ 3 320; δ_H 9.21 (1 H, s, quinoxalin-2-yl-H), 8.15 (1 H, m, ArH), 8.08 (1 H, m, ArH), 7.78 (2 H, m, ArH), 5.40 (1 H, dd, *J* 4, 7, 2-H), 4.62 (1 H, br s, OH), 4.22 (1 H, dd, *J* 4, 15, 1-H), 3.74 (1 H, dd, *J* 7, 15, 1-H), 3.58 (3 H, s, NMe), and 3.40 (3 H, s, NMe); *m/z* (c.i.) 294 (MH^+, 7%), 260 (3), 189 (20), 173 (80), 157 (90), 90 (74), and 46 (100) (Found: C, 50.3; H, 6.1; N, 13.8; S, 20.7%; MH^+, 294.0731. $C_{13}H_{15}N_3OS_2$ requires C, 50.2; H, 5.5; N, 13.5; S, 20.6%; $C_{13}H_{16}N_3OS_2$ requires 294.0735).

4-(*Quinoxalin*-2-yl)-1,3-*dithiolane*-2-*thione* (**10**).—To a solution of the alcohol (**9b**) (1 g) in dry pyridine (5 ml) at 0 °C was added methanesulphonyl chloride (2 ml) and the mixture allowed to come to room temperature. After 3 h ether (50 ml) was added to give a precipitate. The ether was decanted and acetic acid (15 ml) followed by sodium hydrogen sulphide (1 g) in water (10 ml) were added dropwise at 0 °C. After 30 min dichloromethane (50 ml) and water (50 ml) were added and the organic layer separated, dried, and evaporated under reduced pressure to leave the trithiocarbonate as a yellow solid. Purification of this by column chromatography over silica gel eluting with dichloromethane gave the pure *quinoxalinyldithiolane* (**10**) as a yellow crystalline solid (0.6 g, 67%), m.p. 136—138 °C (from dichloromethane–hexane); $\lambda_{max.}$ 238, 300 sh, 321, and 395; δ_H 9.02 (1 H, s, quinoxalin-2-yl-H), 8.14 (2 H, m, ArH), 7.84 (2 H, m, ArH), 5.89 (1 H, dd, *J* 6, 7, 4-H), 4.70 (1 H, dd, *J* 7, 12, 5-H), and 4.34 (1 H, dd, *J* 6, 12, 5-H); *m/z* 264 ($M^{\cdot+}$, 1%), 236 (1), 214 (1), 187 (13), 156 (84), 129 (33), 103 (32), and 76 (100) (Found: C, 49.6; H, 2.9; N, 10.3; S, 36.2; *M*, 263.9840. $C_{11}H_8N_2S_3$ requires C, 50.0; H, 3.1; N, 10.6; S, 36.2%; *M*, 263.9850).

4-(*Quinoxalin*-2-*yl*)-1,3-*dithiole*-2-*thione* (**11**).—To a stirred solution of the trithiocarbonate (100 mg) in dry chloroform (5 ml) at 0 °C was added MCPBA (70 mg); the mixture was then brought to room temperature and stirred for 3 h. After this the solution was washed with aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure to give a residue which was redissolved in dry chloroform (5 ml). TFAA (100 mg) was added with stirring at 0 °C to the solution which was then brought to room temperature and stirred for a further 2 h; after this it was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give an orange gum. Crystallisation of this from dichloromethane–hexane gave the *quinoxalinyldithiole* (**11**) (83 mg, 84%) as yellow crystals, m.p. 253—254 °C, $\lambda_{max.}$(EtOH) 242, 323, 387, and 400; δ 9.12 (1 H, s, quinoxalin-2-yl-H), 8.11 (2 H, m, ArH), 7.84 (1 H, s, C=CH), and 7.81 (2 H, m, ArH); *m/z* 262 ($M^{\cdot+}$, 54%), 186 (100), 159 (31), 129 (12), 102 (22), and 76 (50) (Found: C, 50.2; H, 2.2; N, 10.7; S, 36.8. $C_{11}H_6N_2O_3$ requires C, 50.4; H, 2.3; N, 10.7; S, 36.6%).

Hydrolysis of (**11**) *and Trapping of the Ene*-1,2-*dithiolate*.—Saturated methanolic potassium hydroxide (1 ml) was added to the trithiocarbonate (**11**) (100 mg) in methanol (10 ml) and the whole refluxed for 10 min to produce a purple solution. This was evaporated under reduced pressure after which methyl iodide (2 ml) was added to the residue; the mixture was then stirred for 2 h after which the purple colour had completely disappeared. Methylene dichloride was added and the mixture washed with water, dried, and evaporated to afford an orange gum. This was purified by chromatography over silica gel, with methylene dichloride as eluant to afford the bismethylthioethene, identical with material prepared previously.[8]

1-*Methylthio*-1-(*quinoxalin*-2-*yl*)*ethene* (**13**).—To a solution of the trithiocarbonate (**10**) (50 mg) in methanol (5 ml) was added aqueous sodium hydroxide (3M; 1 ml). The mixture was refluxed for 1 min, cooled, and then methyl iodide (1 ml) added. After 5 min the solvent was evaporated under reduced pressure and dichloromethane and water added. The organic phase was separated and evaporated under reduced pressure to give an orange gum. Purification of this by column chromatography over silica gel eluting with dichloromethane gave the *thioenol ether* (**13**) as an orange gum (12 mg, 31%), followed by a mixture of many other more polar products; δ_H 9.19 (1 H, s, quinoxalin-2-yl-H), 8.12 (2 H, m, ArH), 7.76 (2 H, m, ArH), 6.22 (1 H, d, *J* 1, C=CH_2), 5.42 (1 H, d, *J* 1, C=CH_2), and 2.43 (3 H, s, SMe); *m/z* 202 ($M^{\cdot+}$, 78%), 187 (24), 156 (100), 144 (33), 129 (69), 102 (59),

and 76 (48) (Found: M^+, 202.0549. $C_{11}H_{10}N_2S$ requires M, 202.0565).

2,3,5,6,7,8-*Hexahydro*-1,4-*benzodithiin* (**14a**).—To a stirred solution of cyclohexanone ethane-1,2-dithiol acetal (100 mg) in dry dichloromethane (5 ml) at 0 °C was added MCPBA (60 mg) and then the mixture was stirred for 15 min. The solution was washed with aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure. The residue was then redissolved in dry dichloromethane (5 ml) and, with stirring at 0 °C, TFAA (90 mg) was added. The mixture was stirred for a further 30 min, after which the solution was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give the dithiin[27] as an orange gum (82 mg, 81%); δ_H 3.12 [4H, s, $S(CH_2)_2S$], 2.09 (4 H, m, $CH_2C{=}CCH_2$), and 1.70 (4 H, m, $(CH_2)_2$); *m/z* 172 ($M^{\bullet+}$, 55%), 144 (28), 131 (14), and 111 (16).

Reductive Cleavage of (**14a**) *and Trapping of the Ene*-1,2-*dithiolate*.—A solution of the dithiin (**14a**) (50 mg) in dry THF (5 ml) was added with stirring to a solution of sodium metal (50 mg) in liquid ammonia (20 ml). The mixture was stirred for a further 30 min after which the ammonia was allowed to evaporate to leave a white solid. Methyl iodide (2 ml) was added and the mixture stirred for 1 h. Dichloromethane and water were then added and the organic phase was separated, dried, and evaporated under reduced pressure to give a pale brown gum. Purification of this by column chromatography over silica gel eluting with dichloromethane–hexane gave pure 1,2-dimethylthiocyclohexene[28] (**15**) (32 mg, 63%); δ_H 2.29 (4 H, m, $CH_2C{=}CCH_2$), 2.21 (6 H, s, 2 × SMe), and 1.70 [4 H, m, $(CH_2)_2$]; *m/z* 174 ($M^{\bullet+}$, 80%), 159 (49), 127 (64), 111 (80), 91 (17), 79 (84), and 40 (100).

2,3-*Dihydro*-5-*phenyl*-1,4-*dithiin* (**17**).—To a stirred solution of the dithioacetal (**16**) (100 mg) in dry dichloromethane (5 ml) at 0 °C was added MCPBA (60 mg). The mixture was stirred for 30 min after which it was washed with aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure to give a residue. This was redissolved in dry dichloromethane (5 ml) and, with stirring at 0 °C, TFAA (90 mg) was added. The mixture was stirred for a further 30 min, after which it was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give a pale yellow gum. Purification of this column chromatography over silica gel, eluting with dichloromethane–hexane gave the pure phenyl-dithiin (**17**) (85 mg, 86%) as a crystalline solid, m.p. 54—56 °C (lit.,[13a] m.p. 57—58 °C).

2-*Methyl*-2-(*quinoxalin*-2-*yl*)-1,3-*dithiolane*.—A mixture 2-acetylquinoxaline[29] (5 g), ethanedithiol (3 g), and boron trifluoride–diethyl ether (1 ml) in dry chloroform (100 ml) was refluxed for 4 h. The mixture was cooled and saturated aqueous sodium hydrogen carbonate (100 ml) was added. The organic layer was separated, dried, and evaporated under reduced pressure to give a brown oil, purification of which by column chromatography over silica gel, eluting with dichloromethane gave the *dithioacetal* as an off-white crystalline solid (1 g, 14%), followed by recovered starting material (2.6 g, 52%), m.p. 140—142 °C (from dichloromethane–hexane); δ_H 9.27 (1 H, s, quinoxalin-2-yl-H), 7.96 (2 H, m, ArH), 7.65 (2 H, m, ArH), 3.56 (4 H, s, $S(CH_2)_2S$), and 2.30 (3 H, s, CMe); *m/z* 248 ($M^{\bullet+}$, 6%), 233 (3), 189 (100), 155 (15), 144 (11), 129 (16), and 119 (33) (Found: C, 57.7; H, 4.8; N, 11.3; S, 25.9. $C_{12}H_{12}N_2S_2$ requires C, 58.0; H, 4.9; N, 11.3; S, 25.8%).

2,3-*Dihydro*-5-(*quinoxalin*-2-*yl*)-1,4-*dithiin* (**19**).—To a stirred solution of 2-acetylquinoxaline ethanedithioacetal (0.5 g) in dry dichloromethane (10 ml) at 0 °C was added MCPBA (0.4 g). The mixture was then brought to room temperature and stirred for 3 h after which it was washed with aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure. The residue was redissolved in dry dichloromethane (10 ml) and, with stirring at 0 °C, TFAA (0.45 g) was added. The mixture was brought to room temperature and stirred for a further 14 h, after which it was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give a yellow solid. Purification of this by column chromatography over silica gel, eluting with dichloromethane gave the pure *quinoxalinyl-dithiin* (**19**) (0.42 g, 85%) as yellow crystals, m.p. 135—138 °C (from dichloromethane–hexane), $\lambda_{max.}$(EtOH) 227, 258, 295, and 393; δ_H 8.92 (1 H, s, quinoxalin-2-yl-H), 7.90 (2 H, m, ArH), 7.65 (2 H, m, ArH), 7.37 (1 H, s, C=CH), and 3.26 [4 H, s, $S(CH_2)_2S$]; *m/z* 246 ($M^{\bullet+}$, 86%), 218 (100), 189 (14), 174 (56), 129 (31), and 102 (31) (Found: C, 58.6; H, 4.1; N, 11.2; S, 25.8. $C_{12}H_{10}N_2S_2$ requires C, 58.5; H, 4.1; N, 11.4; S, 26.0%).

cis-4′,5′-*Diphenylcyclohexanespiro*-2′-(1,3-*dithiolane*).—Dry hydrogen chloride was bubbled through a solution of *meso*-1,2-diphenylethane-1,2-dithiol[15] (100 mg) in cyclohexanone (200 mg) at room temperature for 30 min. Aqueous sodium hydrogen carbonate and dichloromethane were added, and the organic phase separated, dried, and evaporated under reduced pressure to give a colourless liquid. Purification of this by column chromatography over silica gel eluting with dichloromethane–hexane gave the pure *dithioacetal* (56 mg, 42%) as a white crystalline solid, m.p. 89—91 °C (from dichloromethane–hexane); δ_H 7.20 (10 H, m, ArH), 4.91 [2 H, s, SCH(Ph)CH(Ph)S], 2.23—1.45 (10 H, m, cyclohexyl-H_{10}); *m/z* 326 ($M^{\bullet+}$, 14%), 303 (1), 283 (4), 204 (100), 180 (78), 121 (24), and 91 (74) (Found: C, 73.3; H, 6.9; S, 19.7. $C_{20}H_{22}S_2$ requires C, 73.6; H, 6.7; S, 19.6%).

cis-2,3,5,6,7,8-*Hexahydro*-2,3-*diphenyl*-1,4-*benzodithiin* (**14b**).—To a stirred solution of the dithioacetal (15 mg) in dry dichloromethane (3 ml) at 0 °C was added MCPBA (12 mg). The mixture was then stirred for 30 min after which it was washed with aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure. The residue was redissolved in dry dichloromethane (3 ml) and, with stirring at 0 °C, TFAA (10 mg) was added. The mixture was stirred for 30 min, after which it was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give a pale yellow gum. Purification of this by column chromatography over silica gel, eluting with dichloromethane–hexane gave the *diphenyl-dithiin* (**14b**) (11 mg, 74%) as an off-white gum, δ_H 7.30 (10 H, m, ArH), 4.75 [2 H, s, SCH(Ph)CH(Ph)S], 2.37 (4 H, m, $CH_2C{=}CCH_2$), and 1.98—1.91 (4 H, m, $(CH_2)_2$); *m/z* 324 ($M^{\bullet+}$, 57%), 293 (23), 275 (7), 204 (47), 179 (100), and 165 (50) (Found: *M*, 324.1006. $C_{20}H_{20}S_2$ requires *M*, 324.1007).

Reductive Cleavage of (**14b**) *and Trapping of the Ene*-1,2-*dithiolate*.—The diphenyldithiin (**14b**) (10 mg) in solution in dry THF (2 ml) was added with stirring to a solution of lithium metal (10 mg) in liquid ammonia (10 ml). The mixture was stirred for 30 min after which the ammonia was allowed to evaporate to leave a white solid. Methyl iodide (1 ml) was added to this and the mixture was stirred for 1 h; dichloromethane and water were then added and the organic phase separated, dried, and evaporated under reduced pressure to give a pale brown gum. Purification of this by column chromatography over silica gel eluting with dichloromethane–hexane gave pure 1,2-dimethylthiocyclohexene[28] (3 mg, 61%).

2,3-*Dihydro*-5-(1,2,3,4-*tetrahydro*-1,4-*dimethylquinoxalin*-2-*yl*)-1,4-*dithiin* (**20b**).—To a solution of the quinoxalinyl-dithiin (**19**) (20 mg) in acetonitrile (3 ml) containing formaldehyde (37% in water, 15 μl), was added sodium cyanoborohydride (40

mg). Glacial acetic acid (1 μl) was added over 10 min, after which the reaction mixture was stirred for a further 3 h. A second portion of glacial acetic acid (1 μl) was added and the mixture stirred for a further 30 min. The mixture was then evaporated under reduced pressure and water and dichloromethane were added. The organic layer was separated, dried, and evaporated under reduced pressure to give an orange gum. Purification of this by column chromatography over silica gel eluting with dichloromethane gave the pure *tetrahydroquinoxalinyldithiin* (**20b**) (6 mg, 27%) as a pale yellow gum, followed by recovered starting material (12 mg, 60%); δ_H 6.74 (1 H, m, ArH), 6.68 (1 H, m, ArH), 6.58 (2 H, d, *J* 7, ArH), 6.06 (1 H, s, C=CH), 3.92 (1 H, m, 2-H), 3.24 (2 H, m, 3-H_2), 3.15 [4 H, s, $S(CH_2)_2S$], 2.89 (3 H, s, NMe), and 2.84 (3 H, s, NMe); *m/z* 278 ($M^{\bullet+}$, 66%), 161 (100), and 145 (27) (Found: *M*, 278.0911. $C_{14}H_{18}N_2O_2$ requires *M*, 278.0911).

Reductive Cleavage of (**20b**) *and Trapping of the Ene-1,2-dithiolate.*—A solution of the tetrahydroquinoxalinyl-dithiin (15 mg) in dry THF (2 ml) was added to a solution of lithium (10 mg) in liquid ammonia (5 ml). The mixture was stirred for 30 min after which the ammonia was allowed to evaporate. Methyl iodide (3 ml) was added to the residue and the mixture stirred for a further 3 h. Dichloromethane and water were then added and the organic phase was separated, dried, and evaporated under reduced pressure to give a pale yellow gum. This was purified by column chromatography over silica gel eluting with dichloromethane to give the *dimethyldithio ether* (**21**) (10 mg, 66%) as a pale yellow gum; δ_H 6.76 (1 H, m, ArH), 6.69 (1 H, m, ArH), 6.57 (2 H, d, *J* 7, ArH), 6.23 (1 H, s, C=CH), 4.03 (1 H, br s, 2-H), 3.31 (1 H, br d, *J* 10, 3-H), 3.16 (1 H, br d, *J* 10, 3-H), 2.88 (3 H, s, SMe), 2.82 (3 H, s, SMe), 2.30 (3 H, s, NMe), and 2.25 (3 H, s, NMe); *m/z* 280 ($M^{\bullet+}$, 68%), 186 (19), 171 (11), 161 (100), and 145 (46) (Found: M^+, 280.1071. $C_{14}H_{20}N_2S_2$ requires *M*, 280.1072).

2-(4-*Methoxyphenyl*)-5-(*quinoxalin-2-yl*)-1,3,2-*oxathiaphospholane 2-Sulphide* (**22**).—A solution of the 2-acetylquinoxaline[29] (100 mg) and Lawesson's reagent (100 mg) were refluxed together, with stirring, in dry toluene (25 ml). After 2 h the solvent was removed to leave a black tar. Purification of this by column chromatography over silica gel eluting with dichloromethane gave the pure oxathiaphospholane (**22**) (10 mg, 5%) as a pale brown crystalline solid, m.p. 128—130 °C (from methylene dichloride–hexane), together with some unchanged starting material (25 mg, 25%); $\nu_{max.}$ 1593; δ_H 9.48 (1 H, s, quinoxalin-2-yl-H), 8.20 (1 H, m, ArH), 8.07 (3 H, m, ArH), 7.83 (2 H, m, ArH), 7.06 (2 H, d, *J* 7, ArH), 5.95 (1 H, dd, *J* 6,7, 5-H), 4.17 (1 H, dd, *J* 7, 12, 4-H), 4.03 (1 H, dd, *J* 6, 12, 4-H), and 3.91 (3 H, s, OMe); *m/z* 374 ($M^{\bullet+}$, 24%), 235 (2), 218 (5), 202 (4), 187 (100), 172 (64), 156 (65), 129 (61), 102 (54), and 76 (69) (Found: M^+, 374.0311. $C_{17}H_{15}N_2O_2PS_2$ requires *M*, 374.0312).

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