One-pot synthesis and chemistry of bis[1,2]dithiolopyrroles

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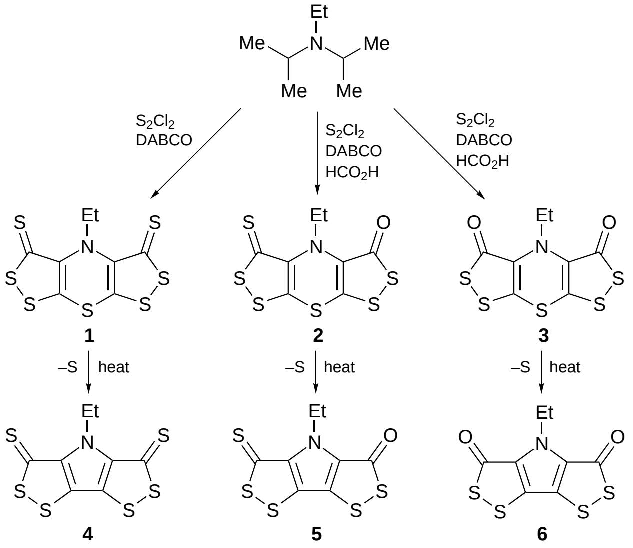
Hünig's base and S_2Cl_2 give the fused 1,4-thiazines 1 and (in the presence of formic acid) 2 and 3, each of which readily extrudes sulfur, selectively and quantitatively, to give the fused pyrroles 4, 5 and 6 respectively; at higher temperatures Hünig's base and S_2Cl_2 can be converted into the pyrroles in one pot, and the cycloadducts 8 and 10 are thus readily available in two steps.

The formation of C–C bonds by thermal or catalytic sulfur extrusion reactions[1] has proved to be valuable in the synthesis of a wide range of organic structures, most notably that of Vitamin B_{12} and the corrins.[2] We describe here the selective and quantitative desulfurisation of some polysulfur–nitrogen heterocyclic compounds which provides a new route to highly substituted fused pyrroles. Derivatives of sulfur heterocycles such as thiophene and 1,3-dithiole have been widely explored as new materials because of their superconducting[3] and optical and electronic switching properties.[4] We have synthesised sulfur–nitrogen systems with potentially similar properties, such as cyclopenta- and cyclohepta-dithiazoles[5] and liquid crystalline pseudoazulene 1,2-dithioles and 1,2-thiazines.[6]

During this work we discovered that ethyldiisopropylamine (Hünig's base), initially added as an inert base, reacted with disulfur dichloride in 1,2-dichloroethane or THF to give the first examples (**1**, **2** and **3**, Scheme 1) of the bis[1,2]dithiolo[5,4-*b*][5′,4′-*e*][1,4]thiazine ring system, in a one-pot process in which all 14 isopropyl C–H bonds of Hünig's base were replaced by C–S, C–O and C–C bonds.[7] The ready availability of these new 1,4-thiazines from commercial reagents, and their potential for sulfur extrusion[1,8] led us to study their thermal behaviour. We found that all three thiazines, **1**, **2** and **3**, underwent very clean and selective thermal extrusion of one sulfur atom only to give the first examples (**4**, **5** and **6**) of the bis[1,2]dithiolo[4,5-*b*][5′,4′-*d*]pyrroles. Furthermore the Hünig's base–S_2Cl_2 reaction and the sulfur extrusion could be combined to give immediate access to the new pyrrole ring system which, in turn, could be extended to polyheterocyclic pyrroles by cycloaddition reactions.



Scheme 1

Refluxing bisdithiolothiazine-3,5-dithione **1** in xylene for 0.5 h gave a deep purple solution from which **4** ($C_8H_5NS_6$, mp 242–243 °C) was obtained as black needles in quantitative yield.† All spectroscopic data agreed with the formation of a symmetrical structure, which requires the selective extrusion of the central ring sulfur atom to give the bisdithiolopyrrole-3,5-dithione **4**. The same product (42% after purification) was also obtained directly from Hünig's base when treated with an excess of S_2Cl_2 (10 equiv.) in chlorobenzene in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO, 10 equiv.) for 3 days at room temperature, followed by refluxing for 2 h. In these conditions none of the thiazine **1** survived. It is notable that in this overall reaction a carbon–carbon bond is formed between two (formally) unreactive methyl groups in Hünig's base, whilst the ethyl group is unchanged.

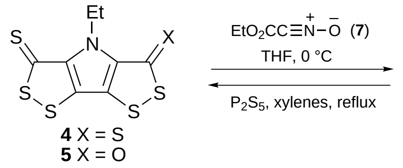
The mono-and bis-oxo thiazines **2** and **3** were equally good substrates for selective sulfur extrusion. Thus, when the 3-oxo 5-thione **2** or the 3,5-dione **3** were refluxed in xylene for 1 and 3 h, respectively, the 3-oxobisdithiolopyrrol-5-thione **5**,† light red crystals, mp 175–176 °C, and the bisdithiolopyrrole-3,5-dione **6**,† yellow crystals, mp 199–200 °C, respectively, were obtained in quantitative yield. All spectroscopic data, notably the ^{13}C NMR spectra, agreed with the unsymmetrical structure **5** and the symmetrical structure **6** for these products. Just as the fully sulfurated pyrrole **4** could be prepared directly from Hünig's base and S_2Cl_2 in chlorobenzene, so too could the mono- and bis-oxo pyrroles, **5** and **6**, in the presence of an oxygen donor. Thus, treating Hünig's base with S_2Cl_2 (10 equiv.) and DABCO (8 equiv.) in chlorobenzene for 3 days at room temperature, followed by addition of formic acid (20 equiv.) and refluxing for 7.5 h, gave the dione **6** (42%) as the only reaction product; TLC monitoring showed the intermediacy of the 1,4-thiazine **3**. If the period of refluxing were restricted to 2 h [with DABCO (10 equiv.) and formic acid (10 equiv.)] the oxo thione **5** (25%) was the main product, together with minor amounts of **4** and **6**.

Compounds **4**, **5** and **6** could be readily interconverted. Thiation of **5** or **6** with excess of P_2S_5 in refluxing xylene for 1 h gave the dithione **4** in almost quantitative yield. Similar thiation of the 1,4-thiazines **2** and **3**, under the same conditions, was accompanied by sulfur extrusion to give compound **4**, again in very high yield. Oxidation of **4** with mercuric acetate gave the dione **6** (35%). Nitrile oxides are known to convert 1,2-dithiolo 3-thiones into the 3-keto compounds;[9] treatment of dithione **4** or oxo thione **5** in THF at 0 °C for 15 min with an excess of ethoxycarbonyl nitrile oxide **7**, generated *in situ* from ethyl chlorooximidoacetate and triethylamine, gave the dione **6** (70–75%) (Scheme 2). Lowering the reaction temperature or reducing the amount of the reagent **7** led to mixtures of **5** and **6** with unchanged **4** and thus did not provide a satisfactory route to oxo thione **5**.

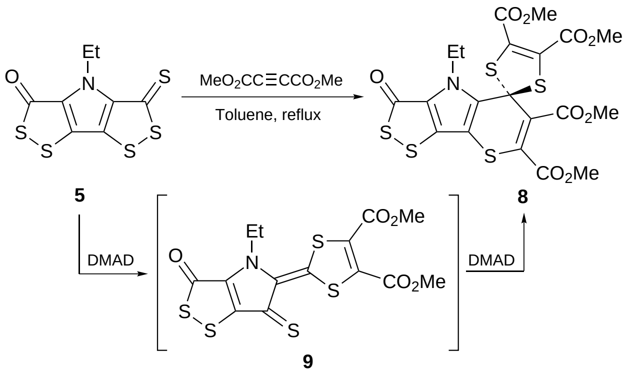
1,2-Dithiolo 3-thiones can also act as 1,3-dipoles.[10] Treatment of compound **5** with dimethyl acetylenedicarboxylate

(DMAD) (5 equiv.) in refluxing toluene for 2 h gave yellow crystals of the 1 : 2 adduct **8**,† mp 219–220 °C (65%), as the only recognisable product (Scheme 3). ^{1}H NMR spectroscopy showed the presence of the *N*-ethyl group and four ester methyl groups, two of which were identical; ^{13}C NMR showed four methoxycarbonyl groups (two identical), the carbonyl group, eight alkenyl carbons and one quaternary carbon corresponding to S–CR$_2$–S. Since the 1,2-dithiolo 3-one ring was still intact, both DMAD molecules had added to the 1,2-dithiolo 3-thione moiety to give the spiro[1,3-dithiolo-thiopyran] structure **8**, *via* the intermediate **9**.[11] In an exactly analogous manner dithiole **4** gave the 1 : 4 adduct ($C_{32}H_{29}NO_{16}S_6$), bis-spiro[1,3-dithiolo-thiopyran]pyrrole **10**† as yellow crystals, mp 224–225 °C, in 77% yield (Scheme 4). This symmetrical structure followed, as above, from spectroscopy, particularly ^{1}H and ^{13}C NMR and mass spectrometry; the fully substituted pentacyclic molecule was obtained from commercial Hünig's base in two steps in 32% overall yield.

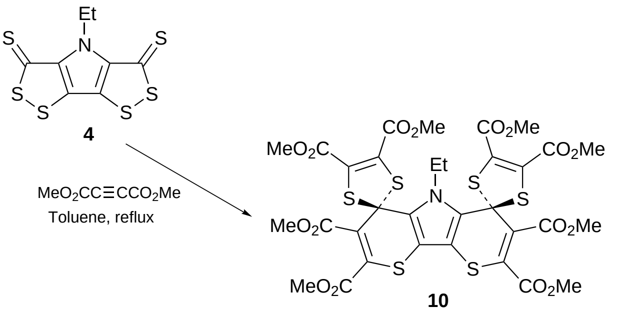
Thus new tricyclic (**4**, **5**, **6**), tetracyclic (**8**) and pentacyclic (**10**) systems, with pyrroles fused to 5- and 6-membered sulfur rings, are now readily available for assessment as new materials of the 1,2-dithiole type[12] and for biological screening.[13]



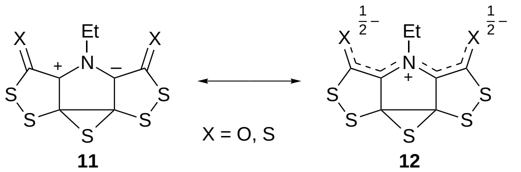
Scheme 2



Scheme 3



Scheme 4



Scheme 5

The quantitative, uncatalysed conversion of thiazines **1**, **2** and **3** into the respective pyrroles **4**, **5** and **6** occurs under much milder conditions than for other annelated 1,4-thiazines,[8] such as phenothiazines which require strong heating with copper to yield carbazoles.[14] This can be explained by stabilization of the key thiirane intermediates **11** (*cf*. refs. 8 and 14) by electron release from nitrogen and electron withdrawal by the carbonyl and thiocarbonyl groups, giving highly delocalised (**12**) intermediates on the way to the aromatic products (Scheme 5). The ene-thiolate contribution, for X = S, will be more stable than the enolate contribution, for X = O, in agreement with the observed rate of sulfur extrusion (**1** > **2** > **3**).

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Footnote

† All new compounds were fully characterized by spectroscopy and elemental analysis.

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