

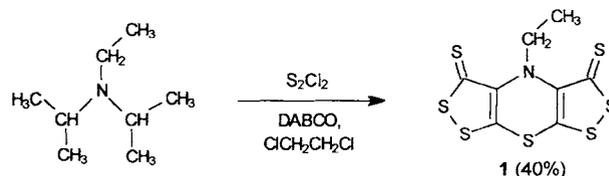
From Hünig's Base to Bis([1,2]dithiolo)-[1,4]thiazines in One Pot: The Fast Route to Highly Sulfurated Heterocycles**

Carlos F. Marcos, Cecilia Polo, Oleg A. Rakitin, Charles W. Rees,* and Tomás Torroba*

Dedicated to Professor Siegfried Hünig on the occasion of his 75th birthday

The chemistry of sulfur-containing heterocycles such as thio-phenes and 1,3-dithioles has been extensively studied since the discovery of their superconductivity^[1] and optical and electronic switching properties.^[2] Polysulfur–nitrogen heterocycles may be even better candidates, but few practical syntheses can be performed on a multigram scale. We have been studying the reactions of cyclic oximes with disulfur dichloride (sulfur monochloride), S_2Cl_2 , in the presence of *N*-ethyl-diisopropyl amine (Hünig's base) to produce suitable materials for electronic and/or optical applications, and have discovered a useful route to cyclopenta- and cyclohepta-1,2,3-dithiazoles,^[3] and some new heterocyclic pseudoazulenes.^[4] Several products from these reactions showed birefringence upon melting in a hot-stage polarizing microscope^[5] and this, together with the π -excessive nature of the sulfur–nitrogen rings has motivated the development of a new family of liquid-crystalline materials. A striking feature of these S_2Cl_2 reactions is the dependence of the nature of the products and their yields upon the experimental conditions. The best results were obtained when the reactions were conducted with a lengthy induction period (about 3 d) at 4 °C, in THF as solvent, and then heated at reflux for up to three hours. When we tried to shorten the induction period by performing the reactions at room temperature, we obtained an entirely new set of products, as shown by TLC. Furthermore we observed the same products from different starting oximes, indicating that the new products arose from a reaction between S_2Cl_2 and the "inert" Hünig's base. We now describe this reaction which affords, in one pot, the first three examples of a new multisulfur–nitrogen tricyclic system resulting from a multi-stage reaction sequence, the conditions that favor formation of each product, and a possible mechanistic explanation.

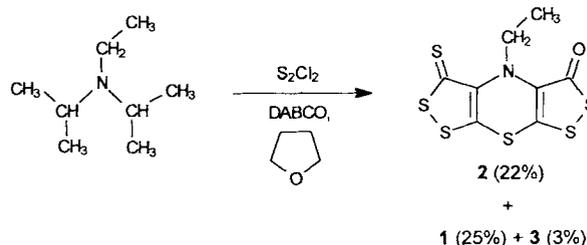
Hünig's base was treated with an excess of S_2Cl_2 in 1,2-dichloroethane in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) for three days at room temperature and the mixture was then heated at reflux for two hours. After purification by chromatography compound **1** (m.p. 202–203 °C, 40% yield) was obtained as black needles with a striking metallic luster. The mass spectrum of **1** supported the molecular formula $C_8H_5NS_7$,



which was also confirmed by HRMS and microanalysis; the 1H NMR spectrum indicated that the *N*-ethyl group was still present. Thus all the C–H bonds of the two isopropyl groups had been cleaved, and these groups had presumably been fully sulfurated ($EtNC_6H_{14} \rightarrow EtNC_6S_7$). If the carbon connectivity of Hünig's base is retained, only a few reasonable structures are possible for the product. The spectroscopic data all pointed to what we considered to be the most stable possible product **1**, and this was confirmed by X-ray crystallography.^[6]

In this one-pot conversion of Hünig's base into **1** the 14 isopropyl C–H bonds have been replaced by 10 C–S bonds and two C–C double bonds, whilst the ethyl group has been untouched. This provides a striking example of high selectivity between primary and secondary *N*-alkyl groups in a competitive reaction.

By variation of the solvent and reflux time, other derivatives of the bis(dithiolo)thiazine ring system could be obtained. Thus replacement of 1,2-dichloroethane by THF led to the formation of a small amount of compound **1** (25%) together with the new red compound **2** ($C_8H_5NOS_6$, m.p. 179–181 °C, 22% yield).



Mass spectrometry and microanalysis showed that one sulfur atom in **1** had been replaced by an oxygen atom in compound **2**, which had a carbonyl absorption at 1660 cm^{-1} in its IR spectrum. Signals for the *N*-ethyl group were observed in the 1H NMR spectrum and in the ^{13}C NMR spectrum, which also displayed the signals of six quaternary carbon atoms, proving that **2** does not have a symmetrical structure but rather a 3-oxo-5-thione structure. In addition, minor amounts of the orange product **3** ($C_8H_5NO_2S_5$, m.p. 191–193 °C, 3% yield) were obtained, in which two sulfur atoms in **1** are replaced by two oxygen atoms. Again the *N*-ethyl group was intact and the ^{13}C NMR spectrum now showed signals for three quaternary carbon atoms, indicating a symmetrical 3,5-dione structure. The source of the oxygen atoms in **2** and **3**, which both formed in THF but not in 1,2-dichloroethane, appears to be the solvent. The reaction was repeated several times in carefully dried THF under dry nitrogen, and compounds **1** and **2** always formed in comparable yields. Under the reaction conditions described, S_2Cl_2 reacts with THF to give 4-chlorobut-1-ene (confirmed by GC-MS), presumably by ring opening to 4-chlorobutanol and dehydration; the alcohol or the water formed could then be the oxygen nucleophile.

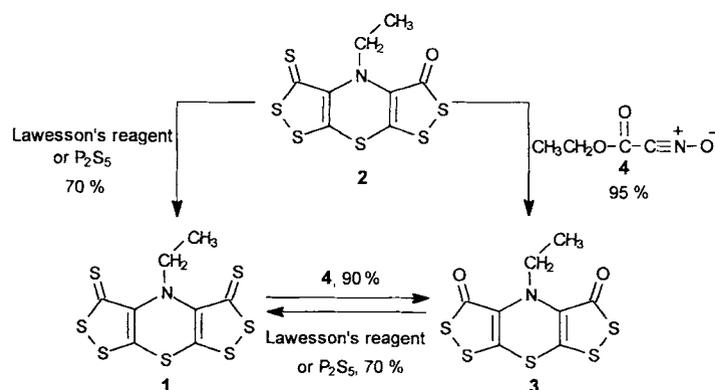
Application of the nitrile oxide method for converting thio-carbonyl into carbonyl groups^[7] readily gave the minor product **3** in 90% yield from **1** and in 95% from **2**. Solutions of the

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substrates in THF were treated at 0 °C for 15 min with an excess of the nitrile oxide **4** generated from ethyl chlorooximidoacetate and triethylamine. The reverse reactions, thiation of **2** and of **3**, were also readily achieved in about 70% yield by heating with Lawesson's reagent or phosphorus pentasulfide in THF for five hours. However, it was more difficult to convert the symmetrical compounds **1** and **3** into the unsymmetrical 3-oxo-5-thione **2**, and the only satisfactory way to obtain **2** was by the reaction of Hünig's base with S₂Cl₂ in THF with or without DABCO.

It is remarkable that **2** was the major product when Hünig's base was stirred in THF for three days with one equivalent of S₂Cl₂, without DABCO, and then refluxed for 5.5 h. Whilst the precise stoichiometry of this complex reaction is not known, we assume that in the absence of DABCO, Hünig's base is both the reactant and the base that neutralizes the hydrogen chloride formed. Since 14 C–H bonds are broken, up to 14 mol of HCl could be formed, and if the base hydrochloride does not react with S₂Cl₂, then 15 mol of Hünig's base should give 1 mol of product. On this basis the yield of **2** is 82%.

We propose that the first step in these reactions is oxidation of an isopropyl group in Hünig's base by S₂Cl₂ (or its more reactive complex with DABCO) to give the stable iminium ion **5**, as in the oxidation of tertiary amines generally.^[8] In agreement with this, electron-withdrawing substituents on nitrogen (as in *N,N*-diisopropylacetamide or *N,N*-diisopropylcyanamide) suppress the reaction with S₂Cl₂ even under more vigorous conditions. Deprotonation of iminium ion **5** gives enamine **6**, which reacts with S₂Cl₂ (or its DABCO complex) to give the 1,2-dithiole **7**. In turn, **7** would be expected to react further with S₂Cl₂ to give the chlorodithiolium salt **8**. The dithiolium ring in

this compound is expected to be stable and the whole sequence could then be repeated to transform the other isopropyl group similarly, giving the bis(dithiolium) salt **9**. This could cyclize to form the tricyclic species **10**, the key intermediate that reacts with sulfur and oxygen nucleophiles to form the three products identified. The isolated compounds **1** and **2** are perfectly stable in boiling aqueous THF in the presence of acidic amberlite IR-120H resin, which implies that the oxo groups in **2** and **3** are not formed from the thione groups during the reaction or on workup. Under milder conditions we have been able to isolate some intermediate salts, including a pale green solid which could be **9** and a deep green solid which could be **10**; both of these compounds are under investigation.

Whatever the precise mechanism, the transformation of Hünig's base into the bis([1,2]dithiolo)[1,4]thiazines must require some 15 or so separate steps, which must therefore proceed in an average yield of about 94% (for a 40% yield of **1**).

In summary, we have shown that Hünig's base is readily and extensively transformed in a one-pot process to give the first three examples (**1**–**3**) of the new bis[1,2]dithiolo[1,4]thiazine ring system. Because of the high reactivity of S₂Cl₂ and its complex with DABCO, the reaction conditions are very mild, in striking contrast to the very vigorous conditions typically required for the formation of 1,2-dithiolo-3-thiones (heating organic substrates with sulfur).^[9] Surprisingly, S₂Cl₂ does not appear to have been used before for the synthesis of 1,2-dithioles.

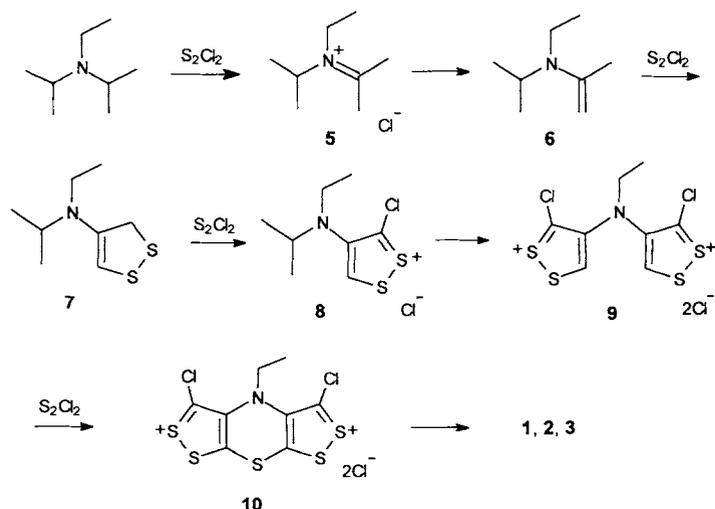
Experimental Section

1: Disulfur dichloride (4.6 mL, 57.6 mmol) was added dropwise to a solution of *N*-ethyl-diisopropylamine (1.0 mL, 5.76 mmol) and DABCO (6.44 g, 57.6 mmol) in dichloroethane (100 mL) at –40 °C. The mixture was stirred for 15 min at –40 °, for 3 d at room temperature, and then for 2 h at reflux. The reaction mixture was filtered through celite and the solvent removed under reduced pressure. The residue was subjected to medium-pressure liquid chromatography (MPLC) (Silicagel Merck 60, petroleum ether → CH₂Cl₂). Yield: 0.78 g, (40%).

Typical procedure for the reaction of **2** or **3**: A solution of **2** (0.19 g, 0.59 mmol) or **3** (0.18 g, 0.59 mmol) and Lawesson's reagent (1 g, 2.47 mmol) in anhydrous THF (50 mL) was heated at reflux under N₂ for 5 h; the transformation was followed by TLC. The solvent was removed under reduced pressure and the crude product purified by MPLC. Yield: 140 mg (70%); black metallic needles (petroleum ether/CH₂Cl₂), m.p. 202–203 °C (decomp); MS (EI, 70 eV): *m/z* (%): 339 (6) [*M*⁺], 307 (22) [*M*⁺–S], 274 (9) [*M*⁺–S₂H], 247 (7) [*M*⁺–S₂–C₂H₅+1], 174 (6) [*M*⁺–C₃S₂–C₂H₅], 160 (7) [*M*⁺–C₃S₂–NC(CH₃)₂H₅], 126 (8) [*M*⁺–C₃S₄–NC₂H₅], 112 (23) [*M*⁺–C₂S₅–NC₂H₅], 100 (38) [*M*⁺–C₂S₅–NC₂H₅], 76 (52) [*M*⁺–C₂S₅–NC₂H₅]; HRMS: calcd 338.8467, found 338.8450; IR (CCl₄): $\tilde{\nu}$ = 2964, 1551, 1314, 1254, 1057, 1000 cm^{–1}; ¹H NMR (400 MHz, CDCl₃): δ = 1.34 (t, *J* = 7.4 Hz, 3H, CH₃), 4.11 (q, *J* = 7.4 Hz, 2H, CH₂); ¹³C NMR (100 MHz, [D₅]pyridine): δ = 14.12 (CH₃, DEPT), 44.07 (CH₂, DEPT), 148.65 and 158.75 (quaternary C), 201.55 (C=S); Elemental analysis calcd for C₈H₉NS₇: C 28.30, H 1.48, N 4.12; found: C 28.02, H 1.18, N 3.96.

2: Disulfur dichloride (4.8 mL, 60 mmol) was added dropwise to a solution of *N*-ethyl-diisopropylamine (10.4 mL, 60 mmol) in THF (100 mL) at –40 °C. The mixture was stirred for 15 min at –40 °C, for 3 d at room temperature, and then for 5.5 h at reflux. The reaction mixture was filtered through celite and the solvent removed under reduced pressure. The residue was subjected to MPLC (Silicagel Merck 60, petroleum ether to CH₂Cl₂). Yield 1.06 g (82%) (based on 1/15 of the starting amine); red needles (petroleum ether/CH₂Cl₂); m.p. 179–181 °C (decomp); MS (EI, 70 eV): *m/z* (%): 323 (4) [*M*⁺], 291 (100) [*M*⁺–S], 276 (18) [*M*⁺–S–CH₃], 263 (13) [*M*⁺–S–CO], 231 (23) [*M*⁺–S₂CO], 198 (9) [*M*⁺–S₃–C₂H₅], 160 (11) [*M*⁺–C₂S₃–NC₂H₅], 126 (12) [*M*⁺–C₂S₃O–C₂H₅], 112 (27) [*M*⁺–C₂S₂O–NC₂H₅], 100 (29) [*M*⁺–C₃S₂O–NC₂H₅]; HRMS: calcd 322.8695, found 322.8671; IR (CCl₄): $\tilde{\nu}$ = 2922, 1660 (C=O), 1633, 1287 (C=S), 1080, 1009 cm^{–1}; ¹H NMR (400 MHz, CDCl₃): δ = 1.33 (t, *J* = 7.2 Hz, 3H, CH₃), 3.96 (q, *J* = 7.2 Hz, 2H, CH₂); ¹³C NMR (100 MHz, CDCl₃): δ = 14.42 (CH₃, DEPT), 42.97 (CH₂, DEPT), 137.46, 148.10, 148.18, and 155.24 (quaternary C), 182.29 (C=O), 201.81 (C=S); Elemental analysis calcd for C₈H₉NOS₆: C 29.72, H 1.55, N 4.33; found: C 29.78, H 1.57, N 4.31.

3: Triethylamine (0.42 mL, 3.0 mmol) was added dropwise to a solution of **1** (0.2 g, 0.59 mmol) and ethyl chlorooximidoacetate (0.36 g, 2.4 mmol) in dry THF (10 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C and a further 15 min at room temperature. The reaction mixture was filtered through celite and the solvent removed under reduced pressure. The residue was subjected to MPLC (Silicagel



Merck 60, petroleum ether → CH₂Cl₂/petroleum ether 5/1). Yield 163 mg (90%). By a similar procedure, triethylamine (0.21 mL, 1.5 mmol), **2** (0.19 g, 0.59 mmol), and ethyl chloroacetate (0.18 g, 1.2 mmol) afforded **3**. Yield 172 mg (95%); orange crystals (petroleum ether/CH₂Cl₂); m.p. 191–193 °C (decomp). MS (EI, 70 eV): *m/z* (%): 307 (75) [*M*⁺], 292 (25) [*M*⁺ – CH₃], 279 (62) [*M*⁺ – CO], 251 (32) [*M*⁺ – 2CO], 219 (39) [*M*⁺ – 2CO – S], 191 (27) [*M*⁺ – C₂S₂O], 175 (59) [*M*⁺ – C₃S₃O], 159 (48) [*M*⁺ – C₃S₃O], 126 (45) [*M*⁺ – C₂S₂ – C₂H₅], 114 (80) [*M*⁺ – C₃S₄ – C₂H₅], 100 (65) [*M*⁺ – C₂S₄ – NC₂H₅], 88 (100) [*M*⁺ – C₃ – S₄ – NC₂H₅]; HRMS: calcd 306.8926, found 306.8924; IR (CCl₄): $\tilde{\nu}$ = 2945, 1676, 1626, 1553, 1145, 1024 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 1.32 (t, *J* = 7.2 Hz, 3H, CH₃), 3.80 (q, *J* = 7.2 Hz, 2H, CH₂); ¹³C NMR (100 MHz, CDCl₃): δ = 14.57 (CH₃, DEPT), 42.42 (CH₂, DEPT), 136.83 and 146.57 (quaternary C), 182.16 (C=O); Elemental analysis calcd for C₈H₉NO₂S₅: C 31.27, H 1.63, N 4.56; found: C 31.07, H 1.59, N 4.51.

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New Surprises with Fischer Carbene Complexes: Formal [3 + 2] Cycloadditions with and without Preceding Carbene–Ligand Metathesis**

Matthias Hoffmann, Matthias Buchert, and Hans-Ulrich Reissig*

Dedicated to Professor Roland Mayer
on the occasion of his 70th birthday

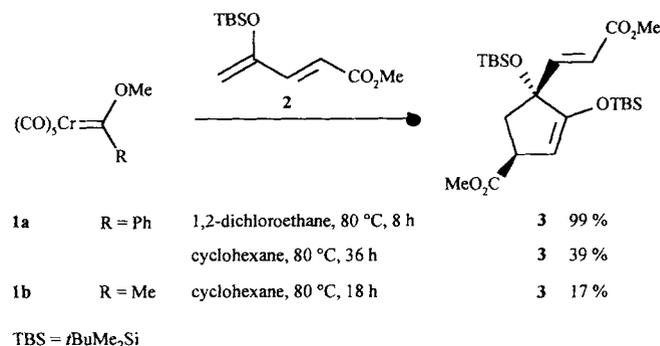
Fischer carbene complexes have proved to be versatile and interesting building blocks in organic synthesis.^[1] Widely applicable procedures have been developed based on their initially

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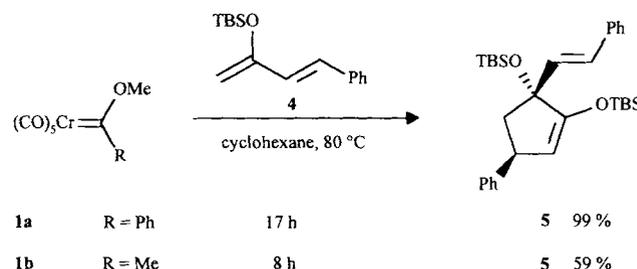
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surprising reactions with unsaturated substrates such as alkenes, alkynes, nitriles, isonitriles, and imines. Thermal reactions of carbene chromium complexes **1** with dienes provide the expected cyclopropane derivatives with high regio- and periselectivity.^[2] When α,β -unsaturated carbene complexes such as **1c** and **1d** are employed, the initially formed cyclopropane products rearrange to give cycloheptadienes.^[3] We have now found a new unexpected reaction sequence with dienes **2** and **4**: a carbene metathesis is followed by a formal [3 + 2] cycloaddition of the newly generated carbene ligands to dienes **2** and **4** to furnish highly functionalized alkenyl siloxycyclopentene derivatives **3** and **5**, respectively.



By heating complex **1a** with three equivalents of methyl 4-(*tert*-butyldimethylsiloxy)-2,4-pentadienecarboxylate (**2**)^[4] in 1,2-dichloroethane or cyclohexane, cyclopentene derivative **3** (diastereomeric ratio >95:5) was obtained in nearly quantitative yield after chromatographic workup. The product was also formed when **2** was treated with the less reactive methyl-substituted carbene complex **1b** (17% yield, one diastereomer (>90%)). Based on its ¹H NMR spectrum, a byproduct from the reaction of **1a** with **2** was identified as 1-methoxy-1-phenylethene (**8**).

Similar results were obtained from the reactions of siloxybutadiene **4** with complexes **1a** and **1b**. Both carbene complexes furnished the corresponding siloxycyclopentene **5** as a diastereomerically pure product. As in the previous case, the more reactive complex **1a** gave higher yields than **1b**. The constitution and relative configuration of the unexpected products **3** and **5**,



which do not incorporate the carbene ligand of the starting material, were determined by 1D- and 2D-INADEQUATE NMR spectra, which established the connectivity, and by 2D-NOESY NMR spectra.^[5]

These results can be explained by postulating the formation of new α,β -unsaturated carbene complexes from complexes **1a** and **1b** by an initial carbene ligand metathesis.^[6] Accordingly, the highly reactive donor–acceptor-substituted carbene complex **7** and enol ether **8** (which was indeed found) should be formed