

New reactions of Hünig's base with S₂Cl₂: formation of monocyclic 1,2-dithioles

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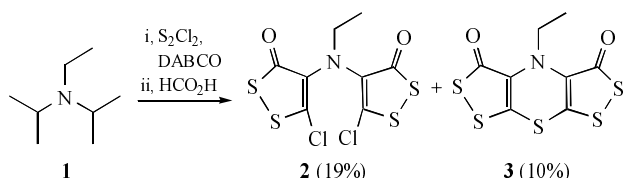
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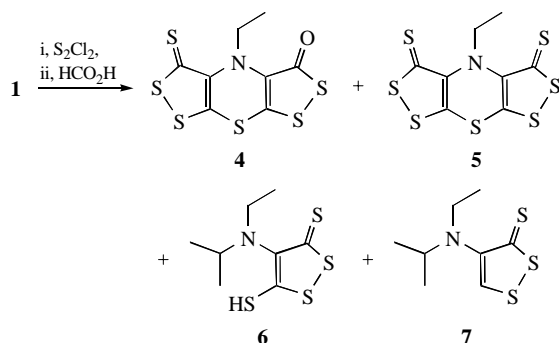
Systematic variation of the ratio of Hünig's base **1** to S₂Cl₂ in their reactions in chloroform shows that, in addition to known tricyclic bisdithiolothiazine thiones **4** and **5**, monocyclic dithiole-3-thiones **6** and **7** can be isolated; when the inert base DABCO is added the extent of sulfuration of the products is reduced and thiones are replaced by their oxo analogues, and diisopropylamines **15** are converted into monocyclic dithiol-3-ones **16**; an overall mechanistic rationalisation of the results, extending earlier work, is presented.

We have shown that *N*-ethyldiisopropylamine (Hünig's base) **1** and other *N*-alkyldiisopropylamines are converted in one-pot reactions by disulfur dichloride, S₂Cl₂, and 1,4-diazabicyclo-octane (DABCO) into fully unsaturated tricyclic bis[1,2]dithio-[3,4-*b*][4',3'-*e*][1,4]thiazines such as **3**, **4** and **5**.^{1–3} We proposed a mechanism for this transformation, which involves the conversion of isopropyl groups into 3-chlorodithiolium salts followed by formation of the central 1,4-thiazine ring and final nucleophilic displacement of the reactive 3-chloro groups.¹ If the S₂Cl₂ is in molar excess over DABCO the dithiole rings are chlorinated further to give tricyclic *N,N*-bis(chlorodithioly)amines, such as **2**, as well as tricyclic products, such as **3** (Scheme 1).⁴



Scheme 1

In all of these reactions, both isopropyl groups have been transformed into 1,2-dithiole rings. If only one isopropyl could be so transformed, we would have a new synthesis of monocyclic 3*H*-1,2-dithioles under unusually mild conditions.⁵ We therefore systematically investigated the reaction of Hünig's base **1** with S₂Cl₂, varying the ratio of the reactants, initially in the absence of another base such as DABCO. The two reactants were mixed in chloroform for 3 days at 0 °C and then quenched by brief heating with formic acid, which gives cleaner reactions by converting the intermediate 1,2-dithiolium salts into 1,2-dithiol-3-ones.¹ The four products shown in Scheme 2 were isolated in the yields given in Table 1.



Scheme 2

When the molar quantities of **1** and S₂Cl₂ are in ratio 0.9 to 1.2 (Table 1, entries 1–4), the main products are tricyclic bisdithiolothiazines **4**¹ and **5**.¹ As the ratio of **1** to S₂Cl₂ increases, there is insufficient S₂Cl₂ to react with the second isopropyl group in **1** and monocyclic 1,2-dithiole-3-thiones **6**[†] and **7** are

indeed formed. In **6** the dithiole has been sulfurated at the 3- and 5-positions but as the relative amount of S₂Cl₂ decreases further, product **7** of mono-sulfuration appears. Separate experiments showed that **6** and **7** are converted into **4** and **5** in high yield by S₂Cl₂ (in the presence of DABCO or triethylamine to neutralise the hydrogen chloride liberated).

It is striking that all the products in Scheme 2 have thiono groups, in spite of the final quench with formic acid, which usually converts chlorodithiolium intermediates into the keto compounds (see, for example, Scheme 1). This suggests that in the DABCO-free reactions the 3-chlorodithiolium ions are further chlorinated by S₂Cl₂ to give 3,5-dichloro salts and that both the mono- and dichlorodithiolium salts are attacked by some reactive sulfur nucleophile,[‡] which is present in the Hünig's base reactions without added DABCO, but not in those

[†] General procedure for the reactions of tertiary amines with S₂Cl₂. Disulfur dichloride was added dropwise to a stirred solution of a corresponding amine and DABCO (in the case of *N*-ethyldiisopropylamine without DABCO) in chloroform at –15–20 °C. The mixture was stirred at 0 °C for 72 h. Formic acid (3.75 ml, 100 mmol) was added; the mixture was refluxed for 1.5 h, and filtered, and the solvents were evaporated. The residue was separated by column chromatography (Merck 60 Silica Gel, light petroleum and then light petroleum–CH₂Cl₂ mixtures).

All new compounds were fully characterised by elemental analysis, ¹H and ¹³C NMR, IR and mass spectra and HMRS.

15a: obtained from the commercial hydrochloride (Aldrich).

15b: an oil prepared from **15a** and sodium azide in DMSO at room temperature in 88% yield.

6: yellow crystals, mp 128–130 °C. ¹H NMR (CDCl₃) δ: 1.24 (t, 6H, 2Me, *J* 6.5 Hz), 1.61 (d, 3H, Me, *J* 6.5 Hz), 3.55 and 4.78 (2m, 2H, CH₂), 4.93 (septet, 1H, CH, *J* 6.5 Hz), 8.70 (br. s, H, SH). ¹³C NMR (CDCl₃) δ: 198.73 (C=S), 193.71 (=C–SH), 133.83 (*sp*² tertiary C), 57.75 (CH), 46.32 (CH₂), 20.27, 18.97 and 10.76 (3Me). MS, *m/z*: 251 (M⁺, 100%), 236 (15), 218 (19), 208 (39).

7: yellow oil. ¹H NMR (CDCl₃) δ: 0.99 (t, 3H, Me, *J* 7.2 Hz), 1.11 (d, 6H, 2Me, *J* 6.5 Hz), 3.06 (q, 2H, CH₂, *J* 7.2 Hz), 3.96 (septet, 1H, CH, *J* 6.5 Hz), 7.71 (s, 1H, CH). ¹³C NMR (CDCl₃) δ: 211.89 (C=S), 154.69 (*sp*² tertiary C), 141.07 (CH), 51.29 (CH), 40.35 (CH₂), 20.15 and 13.43 (2Me). MS, *m/z* (%): 219 (M⁺, 69%), 204(36), 176 (38), 142 (31), 128 (28).

16a: yellow oil. ¹H NMR (CDCl₃) δ: 1.11 (d, 6H, 2Me, *J* 6.5 Hz), 3.31 (m, 1H, CH), 3.39 (s, 4H, 2CH₂). ¹³C NMR (CDCl₃) δ: 187.96 (C=O), 155.37 and 137.92 (2*sp*² tertiary C), 54.65 (CH), 48.89 and 43.71 (2CH₂), 22.45 (Me). IR, *ν*/cm^{–1}: 2980 (CH), 1660 (C=O). MS, *m/z* (%): 275 (M⁺, 4%), 273 (M⁺, 16), 271 (M⁺, 23), 236 (20), 222 (22), 182 (23), 180 (64).

16b: yellow oil. ¹H NMR (CDCl₃) δ: 1.12 (d, 6H, 2Me, *J* 6.5 Hz), 3.17 and 3.29 (2m, 4H, 2CH₂), 3.35 (m, 1H, CH). ¹³C NMR (CDCl₃) δ: 187.43 (C=O), 154.87 and 137.02 (2*sp*² tertiary C), 54.33 (CH), 50.80 and 44.98 (2CH₂), 21.50 (Me). IR, *ν*/cm^{–1}: 2970 (CH), 2120 (N₃), 1660 (C=O). MS, *m/z* (%): 278 (M⁺, 10%), 222 (69), 180 (100).

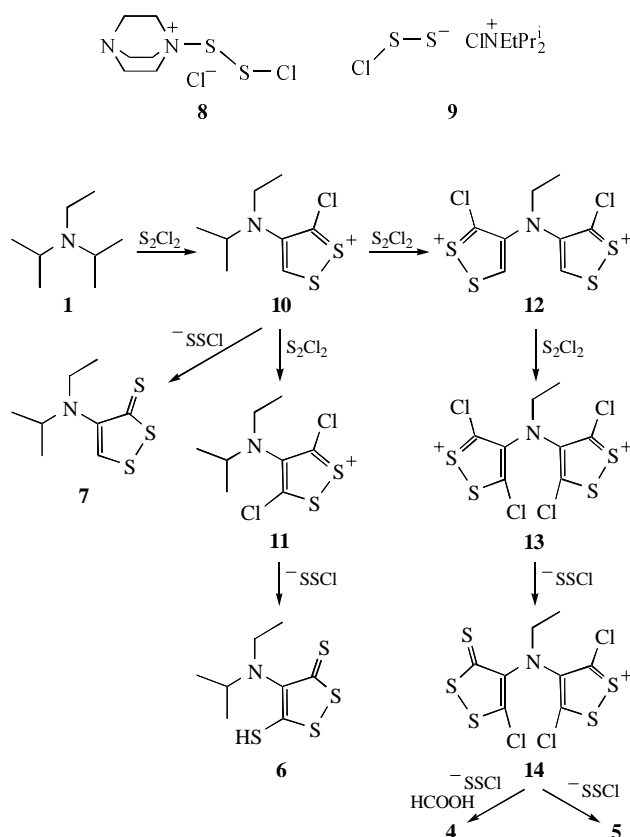
16c: yellow oil. ¹H NMR (CDCl₃) δ: 1.15 (d, 6H, 2Me, *J* 6.5 Hz), 3.51 (septet, 1H, CH, *J* 6.5 Hz), 4.01 (s, 2H, CH₂). ¹³C NMR (CDCl₃) δ: 187.17 (C=O), 155.97 and 136.12 (2*sp*² tertiary C), 117.15 (CN), 53.59 (CH), 35.92 (CH₂), 21.17 (Me). IR, *ν*/cm^{–1}: 2980 (CH), 2140 (CN), 1660 (C=O). MS, *m/z* (%): 248 (M⁺, 57%), 233 (43), 212 (32), 206 (55), 179 (36).

[‡] This nucleophile is not S₈ formed in the reaction since addition of S₈ to the initial reaction mixture made no significant difference to the product distribution.

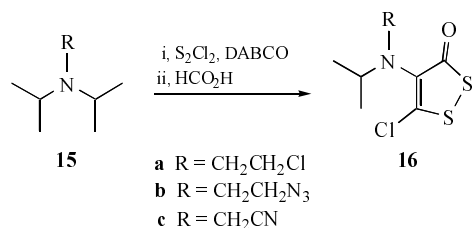
Table 1 Reaction of Hünig's base **1** (*x* mmol) with S₂Cl₂ (10 mmol) in CHCl₃ (25 ml).

Entry	Quantity of Hünig's base 1 (<i>x</i> mmol)	Product yield, mmol (%) ^a			
		4	5	6	7
1	9	0.20 (33)	0	0	0
2	10	0.14 (21)	0.01 (1.5)	0	0
3	11	0.11 (15)	0.03 (4)	0.04 (2.5)	0
4	12	0.08 (10)	0.06 (7.5)	0.06 (3.5)	0
5	13	0	0.13 (15)	0.12 (6.5)	0
6	15	0	0.12 (12)	0.12 (5.5)	0
7	18	0	0	0.38 (15)	0.08 (3)
8	20	0	0	0.72 (25)	0.23 (8)
9	22	0	0	0.68 (22)	0.32 (10)

^aYields are calculated on the basis that 15 mol of Hünig's base **1** should give 1 mol of **4** or **5**¹ together with 14 mol of the Hünig's base hydrochloride, and analogously 7 mol of the Hünig's base should give 1 mol of **6** or **7**.



with DABCO. This difference could arise from the greater nucleophilicity of DABCO over Hünig's base. DABCO could attack S₂Cl₂ at sulfur to give salt **8**, whilst the much more sterically demanding Hünig's base is more likely to attack S₂Cl₂ at a terminal chlorine atom to give **9**. The latter generates the Cl-S-S⁻ anion, which could rapidly convert a 3-chlorodithiolium salt into the corresponding 3-thione and SCl₂. An outline mechanism for the formation of **4** to **7** is suggested in Scheme 3. Some of the early steps have been given in more detail before.¹



In the DABCO-containing reaction, electrophilic species **8** could act as a chlorinating agent to give ultimately tetrachloro compound **13**, which, in the absence of a strong sulfur nucleophile like Cl-S-S⁻, would be converted by formic acid into bis-keto compound **2**.

The formation of monocyclic products **6** and **7** and their conversion into tricyclic products **4** and **5** lends support to our overall mechanism¹ in which the dithiole rings are formed first, followed by completion of the central 1,4-thiazine ring to give tricyclic bisdithiolothiazines **3–5**.

Having established (Scheme 2) that treatment of Hünig's base with S₂Cl₂ could provide a route to monocyclic 1,2-dithiole-3-thiones **6** and **7**, we tried to enhance the utility of the reactions by replacing that part of starting amine **1** which is acting simply as a base by another more inert tertiary amine, DABCO. Furthermore, the reactions were conducted at 0 °C to minimise conversion of the second isopropyl group. Under these conditions, a new reaction, which involved an attack at the ethyl rather than isopropyl group of Hünig's base, was observed; however, other substituted diisopropylamines gave monocyclic 1,2-dithioles in low to modest yields among other products. Thus, the treatment of amines **15a**, **15b** and **15c**⁶ with S₂Cl₂ (7 equiv.) and DABCO (7 equiv.) in chloroform at 0 °C for 3 days followed by addition of formic acid and heating under reflux for 1.5 h gave 5-chloro-1,2-dithiol-3-ones **16a** (32%), **16b** (12%) and **16c** (20%), respectively (Scheme 4).

In agreement with the proposed mechanism (Scheme 3), the combination of an excess of S₂Cl₂ over tertiary amine **15** and the presence of DABCO is expected to yield dichlorodithiolium salt (*cf.* **11** in Scheme 3), which, in the absence of a strong sulfur nucleophile, gives 5-chlorodithiol-3-one **16** rather than dithiole-3-thione.

In summary, these experiments throw further light on the likely mechanism of the complex reactions between Hünig's base and S₂Cl₂, which have now produced no less than 13 different products. Furthermore, they show that monocyclic 1,2-dithiol-3-ones and 3-thiones can be added to the bicyclic and tricyclic products already reported for these simple one-pot reactions.^{1–4}

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