Metal-assisted fragmentation of *N*-aryl- and -alkyl-*N*-trimethylsilylaminosulfur chlorides and *N*-aryl- and -alkyl-aminosulfur chlorides in the presence of conjugated dienes: synthesis and reactivity of 2-substituted-3,6-dihydro-1,2-thiazines

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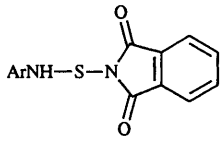
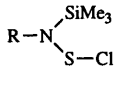
***N*-Alkyl- and -aryl-*N*-trimethylsilylaminosulfur chlorides 2 and *N*-aryl- and -alkyl-aminosulfur chlorides 8 fragment in the presence of silver ions and a conjugated diene to yield 2-substituted-3,6-dihydro-1,2-thiazines 6 as the major products, possibly *via* transient metal-coordinated thionitroso species. By judicious choice of the substituent on the nitrogen atom, the 1,2-thiazines 6 can be stabilised by an intramolecular non-bonded oxygen ··· sulfur or sulfur ··· sulfur interaction, *e.g.* structures 9 and 6j. Reactions of 1,2-thiazine derivatives 6g and 6i with butyllithium, followed by addition of methyl iodide, afforded the ring-opened products 21g and 21i, respectively. Reaction of transient pentacarbonyl-(tetrahydrofuran)chromium with compound 6b afforded the pentacarbonylchromium derivative 22 which was characterised by X-ray crystallography.**

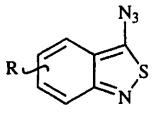
The first evidence for the intermediacy of thionitrosoarenes, Ar–N=S, was reported by Tavs, who demonstrated that thermolysis of thiodiamines, Ar–NH–S–NH–Ar, in the presence of dimethylbutadiene as solvent at *ca.* 70 °C led to the isolation of *N*-aryl-1,2-thiazine derivatives.[1] The subsequent literature contains scattered reports on the generation and trapping of organic thionitroso species. It has recently been established that compounds of general formulae **1**–**4** serve as efficient precursors of highly reactive thionitroso species which cannot be isolated, but which can be captured by reaction with conjugated dienes.[2] In the absence of a trap, sulfurdiimides, R–N=S=N–R, and azo compounds are formed. Compounds **1** fragment upon treatment with triethylamine at room temperature;[3] compounds **2** fragment thermally (typically at 70 °C);[4] the isothiazole ring of compounds **3** opens both thermally (20–70 °C) and photochemically;[5] and ylides **4** extrude R–N=S upon Diels–Alder reaction with an alkene.[6] For the generation of thionitrosoalkanes and thionitrosoarenes, compounds **2** are the most versatile precursors reported to date.[4b]



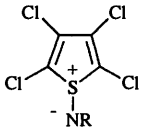
1 Ar = Ph, substituted aryl heteroaryl



2 R = aryl, alkyl

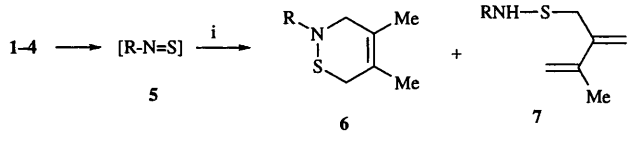


3 R = Cl, Br, NO_2

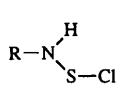


4 R = CO_2Et, CO_2Ph, tosyl

Meth-Cohn and van Vuuren first observed that the trapping of the electron-deficient thionitroso species derived from **4** with conjugated dienes, *e.g.* dimethylbutadiene and isoprene, resulted in competitive Diels–Alder and ene reactions (Scheme 1).[6] It is now clear that this is a widespread feature of the reactivity of thionitroso compounds, including aryl–,[3] heteroaryl–[3d] and alkyl–N=S derivatives.[4b] The ratio of adducts **6** and **7**, obtained by trapping **5** with dimethylbutadiene, is very sensitive to the electronic properties of the substituent attached to nitrogen, with electron-donating substituents favouring Diels–Alder reaction, while electron-withdrawing substituents result in a high proportion of the ene adduct.[3c,4b,5c] Whilst this is undoubtedly of mechanistic interest, as remarkably few dienophiles undergo competitive Diels–Alder and ene reactions with the same diene,[5c,6b] it has generally proved impossible to separate the isomeric adducts **6** and **7**, and it has, therefore, not been feasible to explore their properties or their reactions in any detail. We have sought to overcome this, and from this viewpoint we now report our studies on the fragmentation of precursors **2** and **8** in the presence of a range of metal salts. The key features of this work are: (i) in the presence of AgF (for precursors **2**) the formation of Diels–Alder adducts **6** is favoured over ene isomers **7** to the extent that the former compounds are readily obtained pure in good yields for the first time, thereby paving the way for the first systematic chemical and physico-chemical studies on ring system **6**; (ii) by judicious choice of substituents attached to nitrogen, the stability of adducts **6** is dramatically increased by virtue of non-bonded heteroatom ··· heteroatom interactions, represented by the general structure **9**; and (iii) sterically very demanding groups



Scheme 1 *Reagent:* i, dimethylbutadiene



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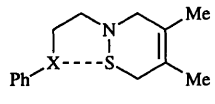


9 X = O,S

Table 1 Product isomer ratios and yields of compounds **6** and **7** obtained from compounds **2**. Data obtained in the absence of any added metal salt are shown in brackets[a]

2	R	Combined yield (%) 6 + 7	Product ratio 6:7
a	4-MeC_6H_4	78 (55)	>95:5 (60:40)
b	4-BrC_6H_4	87 (50)	>95:5 (25:75)
c	4-$NO_2C_6H_4$	77 (62)	>95:5 (20:80)
d	2-BrC_6H_4	80 (65)	>95:5 (15:85)
e	2-PrC_6H_4	60 (47)	>99:1 (50:50)
f	PhCH(Me)	30 (20)	>99:1 (92:8)
g	$PhOCH_2CH(Me)$	40 (40)	>99:1 (>99:1)
h	$PhOCH_2CH_2$	40 (40)	>99:1 (>99:1)
i	$PhSCH_2CH_2$	40 (40)	>99:1 (>99:1)

[a] Reaction conditions: AgF (1.0–1.1 equiv.), dimethylbutadiene (10 equiv.), MeCN, 20 °C, 16 h.

on nitrogen can be accommodated by using precursors **8** in the presence of KF.

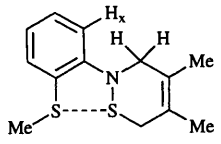
Results and discussion

Fragmentation of *N*-aryl- and -alkyl-*N*-trimethylsilylamino-sulfur chlorides 2

Compounds **2a–i** were readily prepared by reaction of the corresponding silylated amines with a mixture of triethylamine and sulfur dichloride in diethyl ether at between −10 and +20 °C. Due to their instability, compounds **2** were used in the next step within one hour of their preparation. A mixture of compounds **2a–i** and dimethylbutadiene (10 equiv.) dissolved in acetonitrile was stirred with silver fluoride (1.0–1.1 equiv.) for 16 h at 20 °C, and after removal of volatile materials *in vacuo* the crude product mixture was analysed by ^1H NMR spectroscopy, which showed the presence of Diels–Alder adducts **6a–i**, accompanied in some cases by a very small amount of the isomeric ene adduct **7** in the ratios shown (Table 1). For comparison, data from analogous reactions of **2a–i** in the absence of silver fluoride are also presented in Table 1 (these data are in brackets).

The most significant conclusion that can be drawn from the data in Table 1 is that the presence of AgF has a dramatic effect on the product isomer ratios and improves the overall yields of the reactions of the aryl derivatives **2a–e**, has a slight effect on 1-phenylethyl derivative **2f**, but has no effect on 1-methyl-2-phenoxyethyl, 2-phenoxyethyl- or 2-phenylsulfanylethyl derivatives **2g–i**. We have explored the effects of other metal salts in directly analogous reactions of **2b**, namely KF, CsF and $HgCl_2$ (1 equiv. in each case). The use of potassium fluoride instead of silver fluoride resulted in the formation of adducts **6b** and **7b** in a ratio of >95:5 (73% combined yield), while in the presence of caesium fluoride both **6b** and **7b** were formed in a ratio of >95:5 (40% combined yield). The presence of mercuric chloride had essentially no effect on the course of the reaction: the ratio of **6b**:**7b** was 30:70 (*cf.* 25:75 in the absence of any metal salt, Table 1). Of the reagents tried to date, silver fluoride is, therefore, the preferred reagent; other metal salts were not explored further in reactions of precursors **2**. For aryl systems **2a–e** two additional points are noteworthy. Firstly, the ratios of adducts **6a–d**:**7a–d** obtained from precursors **2a–d** in the *absence* of AgF, are the same as those reported previously using precursors **1**,[3c,5c] which provides compelling evidence that both routes proceed *via* the same intermediate, *viz.* the thionitroso species ArN=S. Secondly, adducts **6e** and **7e** have been obtained for the first time; previous attempts to synthesise precursor **1** (Ar = 2-PrC_6H_4) were unsuccessful, presumably for steric reasons.[7]

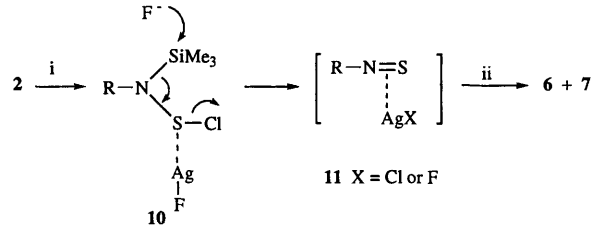
1,2-Thiazine derivatives **6a–i**, prepared in the presence of AgF (Table 1) were readily purified by flash chromatography. This is significant, as hitherto separation of the Diels–Alder and ene adducts obtained from trapping R–N=S species had proved to be extremely difficult, and in many cases, impossible to achieve.[3,6] After purification, the *N*-aryl- and *N*-(1-phenylethyl)-1,2-thiazines **6a–f** can be stored at 4 °C for *ca.* 6 days, before any decomposition is observed. In marked contrast to this instability of the *N*-aryl derivatives, adducts **6g–i** are stable at 20 °C for at least 6 months. We believe that the remarkable stability of **6g–i** (and **6j**, see below) arises from a non-bonded



6j

interaction between the oxygen or sulfur atom in the sidechain and the sulfur atom of the 1,2-thiazine ring, as represented by the general structure **9** (chemical evidence and ^1H NMR data discussed below support this claim).

A possible mechanism for the decomposition of precursors **2** in the presence of AgF is shown in Scheme 2. Fragmentation of



Scheme 2 *Reagents and conditions:* i, AgF, MeCN, 20 °C; ii, dimethylbutadiene

silver-coordinated species **10**, induced by attack of fluoride on the TMS group, would lead to thionitroso intermediate **11** in which silver is coordinated to the electron-rich N=S double bond. We believe that it is this species which reacts with dimethylbutadiene to afford adducts **6** and **7**. The low yield of ene adducts **7** in these reactions is consistent with reduced nucleophilicity of the S atom of **11**, compared to an intermediate R–N=S species in the absence of silver. This mechanism (Scheme 2) is akin to the AgF-induced generation of azomethine ylides by loss of TMS-cyanide from $PhN(CH_2TMS)CH_2CN$.[8] Metal coordination to the thionitroso intermediate **11** has the added benefit of hindering the formation of by-products such as sulfurdiimides (R–N=S=N–R) or azo compounds which arise from dimerisation of R–N=S species generated from other precursors.[2,3c]

Fragmentation of *N*-aryl- and -alkyl-aminosulfur chlorides 8

We have now demonstrated that compounds **8** are also suitable precursors for the formation of 1,2-thiazines **6**, although in general the product yields are considerably lower compared to those obtained from analogous silylated precursors **2**. Reaction of the appropriate arylamine or benzylamine derivative with triethylamine (1–1.1 equiv.) and sulfur dichloride (1–1.1 equiv.) at between −10 and +20 °C yielded compounds **8a,b,j** and **k** as unstable oils.[9] When compounds **8a,b** and **j** were stirred with dimethylbutadiene in the absence of a metal salt, no adducts were isolated; an intractable black residue was obtained. However, addition of either AgF, KF or CsF (1–1.1 equiv.) as a hydrohalide scavenger[10] to the reaction mixture resulted in the formation of both Diels–Alder and ene adducts **6** and **7**, respectively, in the ratios shown (Table 2). These data clearly show that precursors **8a** and **8b** are less suitable than the silylated analogues **2a** and **2b** for the preparation of 1,2-thiazine derivatives **6a** and **6b** (*cf.* Table 1). The main advantage of precursors **8** over compounds **2** is that the former can be

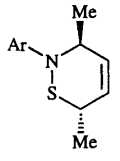
Table 2 Product isomer ratios and yields of compounds **6** and **7** obtained from compounds **8**[a]

8	R	M	Combined yield (%) 6 + 7	Product ratio 6:7
a	4-MeC_6H_4	Ag	64	>95:5
		K	50	>95:5
		Cs	40	>95:5
b	4-BrC_6H_4	Ag	50	>95:5
		K	40	>95:5
		Cs	76	>95:5
j	2-$MeSC_6H_4$	K	55	>95:5
k	Ph_2CH	K	30	>95:5

[a] Reaction conditions: MF (1.0–1.1 equiv.), dimethylbutadiene (5 equiv.), MeCN, 20 °C, 4 h.

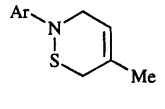
employed for bulky arylamines or benzylamines where silylation is inefficient, or does not occur at all, due to steric hindrance. However, compounds **8** are highly unstable and are difficult to manipulate. For fragmentation of the bulky systems **8j** and **8k**, KF is the metal fluoride of choice. For example, 2-methylsulfanylaniline derivative **8j** decomposed in the presence of potassium fluoride and dimethylbutadiene to afford the stable adduct **6j** in 55% yield. The inefficiency of this reaction in the presence of AgF is probably due to Ag coordination to the sulfur atom of the methylsulfanyl group of **8j**. Compound **6k** is notably more stable than other 1,2-thiazines **6** which do not possess a heteroatom in the side-chain, presumably due to the steric bulk of the diphenylmethyl group.

Previous work has shown that when thionitrosoarenes generated from precursors **1** react with *E,E*- and *E,Z*-hexadiene the stereochemistry of the diene is retained in the 1,2-thiazine Diels–Alder adducts, which is consistent with a concerted mechanism.[3b,c] In comparable experiments, precursors **2b** and **8b** were reacted with *E,Z*-hexadiene, in the presence of AgF, using the same conditions as shown in Tables 1 and 2, to yield adduct **12** exclusively (NMR evidence).



12 Ar = 4-BrC_6H_4

It is well known that the presence of a Lewis acid generally increases the regioselectivity of cycloaddition reactions.[11] We have examined the effect of silver fluoride on the ratio of regioisomers obtained from trapping ArN=S with isoprene. We had previously reported that 4-bromo- and 4-methoxy-thionitrosobenzene, generated from the corresponding phthalimido precursors **1**, reacted with isoprene to afford the regioisomeric adducts **13** and **14** in a 3:1 ratio, along with a small amount of the expected ene adduct.[3a,c] Fragmentation of the corresponding precursors **2b** and **2l** yielded adducts **13** and



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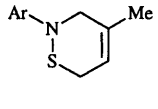


14

14 in a >14:1 ratio for both derivatives, with no ene adduct being detected (Table 3). This striking change in the isomer ratio, compared with the earlier experiments, can be explained by considering that the silver cation associates with the double bond of the thionitroso intermediate, structure **15** (Fig. 1, *cf.*

Table 3 Product isomer ratios and yields of compounds **13** and **14** obtained from compounds **2**[a]

2	Ar	Combined yield (%) 13 + 14	Product ratio 13:14
b	4-BrC_6H_4	20	>14:1
l	$MeOC_6H_4$	42	>14:1

[a] Reaction conditions: AgF (1.0 equiv.), isoprene (10 equiv.), MeCN, 20 °C, 16 h.

structure **11** in Scheme 2). This coordination would increase the electronegativity of the nitrogen atom, thus in the HOMO the coefficient on nitrogen will become larger. It follows, therefore, that in the LUMO the coefficient on sulfur is correspondingly larger (structure **16**) which will increase the driving force for the formation of isomer **13**.

Conformational studies on 1,2-thiazine derivatives 6f–k

The new methodology reported above provides expedient access to 1,2-thiazine derivatives **6**, which are obtained pure for the first time, enabling studies on the conformational properties of this ring system. Compounds **6** generally display two characteristic methylene singlets in the ^1H NMR spectrum at δ 3.9–3.2 (CH_2N) and 3.1–2.7 (CH_2S), both of which are slightly broadened at room temperature due to rapid ring flexing about the ring N and S atoms.[3c,d] The ^1H NMR spectrum of compound **6f** is unusual in that at 20 °C both the CH_2N and CH_2S methylene protons appear as doublets of doublets, due to the presence of two separate AB systems, *i.e.* all four hydrogens are different. We believe that this splitting pattern stems from the fact that the asymmetric substituent on nitrogen renders the protons in both methylene groups diastereotopic. The spectrum of compound **6g** at 20 °C is also noteworthy: whereas the CH_2N signal is, as usual, a broad singlet, the CH_2S signal appears as a distorted quartet, which is an incompletely resolved AB doublet of doublets. This is consistent with restricted inversion of this portion of the ring, which probably arises from a non-bonded intramolecular O···S interaction (structure **9**). For variable temperature ^1H NMR experiments we selected the stable derivatives **6g–j** and diphenylmethyl derivative **6k**, for which we anticipated the bulky substituent might slow the ring flip at higher temperatures. Upon lowering the temperature, the methylene signals for compounds **6g–k** collapsed, and on further cooling of compound **6j**, the CH_2S and CH_2N signals re-emerged as two doublets and a distorted quartet, respectively (the latter would also be expected to resolve into two doublets had lower temperatures been attainable). It was observed that the methylene signals of compounds **6g–j** became fully coalesced at −70 °C, while those of compound **6k** were unchanged upon cooling to −50 °C. These data are consistent with the increased rigidity of the 1,2-thiazine ring of **6g–j** which would result from an intramolecular O···S or S···S interaction (structure **9**). Further evidence to support this non-bonded interaction came from an observed NOE enhancement of one aromatic proton in compound **6j** (assumed to be H_x) when the CH_2N protons were irradiated. This is consistent with near coplanarity of the benzene ring and C–N–S fragment of the 1,2-thiazine ring of **6j**, which would be enforced by a S···S interaction. Similar experiments were performed on adducts for which a S···S or O···S interaction could not occur, and no NOE enhancement of the aromatic protons was observed.

Reactivity of 1,2-thiazine derivatives

Chemical evidence in support of an oxygen···sulfur interaction in compound **6g** was obtained by comparing the results of experiments on the oxidation of **6a** and **6g**. The reaction of **6a** with *m*-chloroperoxybenzoic acid (MCPBA) (2 equiv.) in dichloromethane at 20 °C, or with sodium periodate (2 equiv.) in aqueous THF at 20 °C, yielded an inseparable

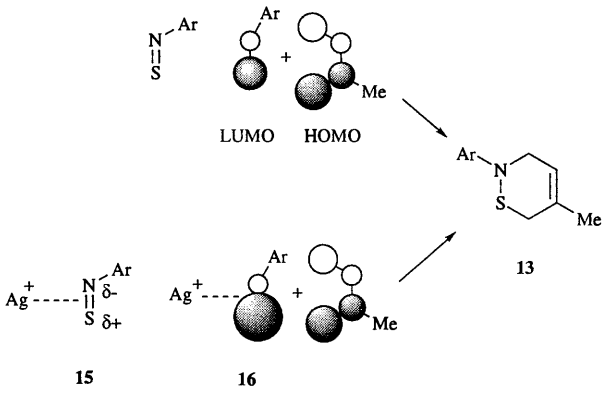
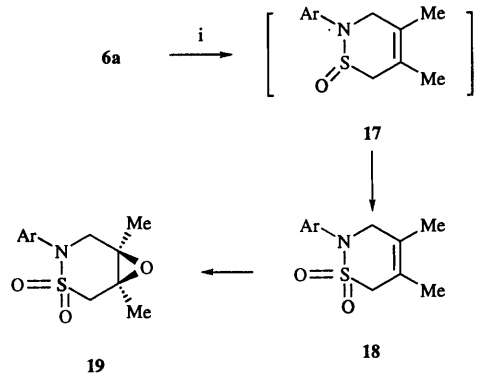


Fig. 1 Explanation for the enhanced regioselectivity in the formation of compound **13** from the reaction of ArN=S species with isoprene in the presence of AgF



Scheme 3 *Reagents and conditions:* i, MCPBA, dichloromethane, 20 °C

mixture of sulfone **18** and epoxy-sulfone **19**: sulfoxide **17** was not detected (GC–MS and ^{1}H NMR data) (Scheme 3). When MCPBA (1 equiv.) was used a mixture of unreacted thiazine **6a** and products **18** and **19** was obtained. The use of 4–5 equiv. of MCPBA yielded compound **19** as the sole product, although it could not be obtained analytically pure. In the ^{1}H NMR spectrum of **19** the CH_2 protons appear as AB systems (CH_2S and CH_2N centred at δ 3.28 and 3.99, respectively) due to the locked conformation of the ring. In compound **18** both the CH_2S and CH_2N protons appear as broad singlets (δ 3.45 and 4.11, respectively) with the former signals shifted downfield by 0.5 ppm, compared to **6a**,[3c] due to the deshielding oxygen atoms. In contrast to these results, compound **6g** was unreactive towards both MCPBA and sodium periodate under the same reaction conditions.

Reaction of compounds **6g** and **6i** with butyllithium at −78 °C, followed by addition of methyl iodide, afforded the ring-opened products **21g** and **21i**, respectively, presumably *via* intermediates **20g** and **20i** formed by initial nucleophilic attack of BuLi at sulfur of ring system **6** (Scheme 4). Reaction of compound **6a** under similar conditions produced a multitude of uncharacterised products. Diagnostic spectroscopic data for compounds **21** were the presence of an *N*-methyl peak in the ^{1}H and ^{13}C NMR spectra (δ 2.20–2.26 and 18.0–22.1, respectively) and a shift in the C=C stretching frequency in the IR spectrum from 1735 cm^{-1} for compounds **6** to 1730 cm^{-1} for compounds **21**, consistent with a relief of strain due to ring opening. Weinreb *et al.* noted that under similar reaction conditions analogous *N*-alkyl-1,2-thiazine-*S*-oxides underwent substitution at C(6) (adjacent to sulfur) whereas *N*-aryl derivatives gave ring-opened products.[12]

We have explored, for the first time, transition metal coordination to the 1,2-thiazine ring system. Reaction of photochemically generated pentacarbonyl(tetrahydrofuran)-

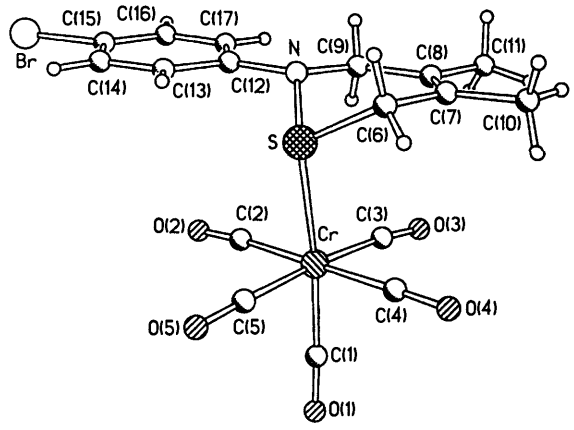
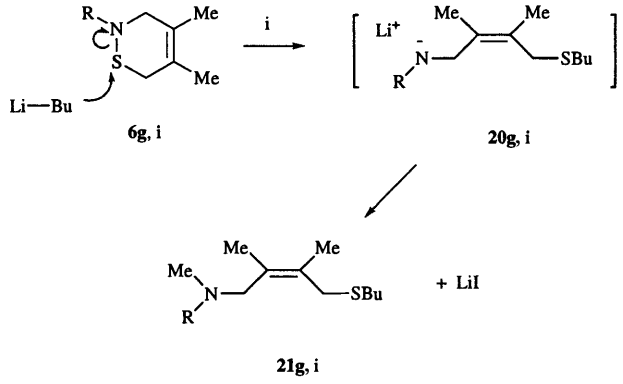
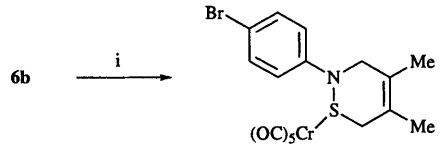


Fig. 2 Molecular structure of **22**. Selected bond distances (Å) at 293 and 150 K, respectively: S–N 1.725(6), 1.70(1); S–C(6) 1.784(10), 1.794(11); C(6)–C(7) 1.507(13), 1.49(2); C(7)–C(8) 1.29(1), 1.33(2); C(8)–C(9) 1.504(12), 1.48(2); C(9)–N 1.44(1), 1.46(1).



Scheme 4 *Reagents and conditions:* i, BuLi, MeI, THF, −78→20 °C



Scheme 5 *Reagents and conditions:* i, chromium hexacarbonyl, THF, UV light, −10→20 °C

chromium with compound **6b** (Scheme 5) yielded a yellow crystalline product in 45% yield, which was characterised as the chromiumpentacarbonyl species **22** by a single-crystal X-ray diffraction study (Fig. 2).

As far as we know, this is the first structural study of a 3,6-dihydro-1,2-thiazine ring, which in **22** adopts a sofa$_S$ conformation (Cremer–Pople parameters[13] Q = 0.611, φ = 2.5°, θ = 52.6°). The sulfur atom is displaced out of the C(6)C(7)C(8)C(9)N plane by 0.90 Å, while the benzene ring is coplanar with this plane to within 2°. The nitrogen atom has a pyramidal geometry, with the average bond angle (116.4°) intermediate between planar (120°) and tetrahedral (109.5°) geometry. The Cr–S and S–N distances [2.410(3) and 1.725(6) Å] are close to those found in $(OC)_5CrS(Ph)N(CH_2Ph)_2$ [Cr–S 2.402(2), S–N 1.702(6) Å],[14] where the nitrogen atom is even more profoundly pyramidal, with an average bond angle of *ca.* 113.2°. On the other hand, in $(OC)_5CrS(Ph)N(C_6H_{11})_2$, where the N atom is planar due to steric overcrowding,[15] the S–N bond is shortened to 1.668(5) Å and the Cr–S bond lengthened to 2.443(2) Å, thus indicating a substantial switch of the d_π-p_π interactions from the Cr–S to the S–N bond.

Experimental

General information

Details of instrumentation and techniques are the same as those reported previously.[3c] Variable temperature NMR spectra of compounds **6g–k** were obtained in the following solvents using a Varian 400 MHz instrument: **6g–j** (CD_2Cl_2) and **6k** ($CDCl_3$). All reactions and filtrations were performed using dry solvents under dry nitrogen.

General procedure for the preparation of *N*-trimethylsilyl-aminosulfur chlorides 2a–i

To a stirred solution of the appropriate silylated amine (obtained by stirring an equimolar amount of the amine and trimethylsilyl chloride in ether at 20 °C for 16 h, and used without purification) in diethyl ether at −10 °C was added dry triethylamine (1.1 equiv.) followed by dropwise addition of sulfur dichloride (1.1 equiv.). This mixture was stirred at −10 °C for 0.5 h, then the temperature was raised to 20 °C over 0.5 h. After removal of the precipitate of triethylamine hydrochloride by filtration, diethyl ether was removed as quickly as possible *in vacuo* at ≤20 °C to leave compounds **2a–i** as unstable red oils which were used within 1 h of their preparation.

General procedure for the preparation of compounds 6 and 7 from precursors 2

To a freshly prepared sample of compound **2a–i** (4.0 mmol) dissolved in acetonitrile (30 ml) at 20 °C was added 2,3-dimethylbuta-1,3-diene (40 mmol) and (when appropriate) the anhydrous metal fluoride (4.0–4.4 mmol). The resultant mixture was stirred in the dark at 20 °C for 16 h, after which time silver salts were removed by filtration and volatile materials were removed *in vacuo*. (Isomer ratios were obtained from the ^1H NMR spectra of this mixture at this stage. ^1H NMR and mass spectra of compounds **6a–c** and **7a–c** thereby obtained were identical with those reported previously.[3c,d]) The residue which remained was dissolved in hexane (15 ml) or a mixture of hexane and dichloromethane (15 ml, 9:1 v/v) which was flashed through a neutral alumina column, using hexane as the eluent to obtain pure adduct **6**. Data, which have not been reported previously, for compounds **6e–i** are given below.

2-(2-Propylphenyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 6e. (Found: M, 247.1394. $C_{15}H_{21}NS$ requires 247.1395); $\delta_H(CDCl_3)$ 7.2 and 6.9 (each 2 H, m, ArH), 3.8 (2 H, s, CH_2N), 2.9 (2 H, s, CH_2N), 2.7 (2 H, t, *J* 6 Hz, CH_2), 1.8 (2 H, sextet, *J* 6 Hz), 1.9 (6 H, s, 2 × Me) and 1.1 (3 H, t, *J* 6 Hz, Me); $\delta_C(CDCl_3)$ 136.6, 132.1, 130.5, 127.1, 127.0, 125.0, 121.7, 116.0, 58.4, 34.9, 34.1, 24.0, 23.5, 15.0 and 14.6. Also present in the reaction mixture (in the absence of AgF) was N-(2-propyl)-2-methylidenebut-3-ene-1-sulfenamide **7e**, which was identified by the diagnostic peaks[3c] in the ^1H NMR spectrum at δ 3.20 (2 H, s, CH_2S) and 1.90 (3 H, s, Me).

2-(1-Phenylethyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 6f. (Found: M, 233.0891. $C_{14}H_{19}NS$ requires 233.1239); $\delta_H(CDCl_3)$ 7.35–7.20 (5 H, m, ArH), 4.02 (1 H, q, *J* 7 Hz, CH), 3.53 and 3.03 (2 H, d, *J* 18 Hz, CH_2N), 3.25 and 2.57 (2 H, d, *J* 16 Hz, CH_2S), 1.79 and 1.59 (each 3 H, s, Me) and 1.55 (3 H, d, *J* 7 Hz, CH*Me*); $\delta_C(CDCl_3)$ 145.0, 128.4, 127.2, 126.3, 124.6, 122.6, 62.0, 56.0, 28.4, 23.2, 19.7 and 17.5. Also present in the reaction mixture (in the absence of AgF) was *N*-(1-phenylethyl)-2-methylidenebut-3-ene-1-sulfenamide **7f** which was identified by the diagnostic peaks[3c] in the ^1H NMR spectrum at δ 3.20 (2 H, s, CH_2S) and 1.90 (3 H, s, Me).

2-(1-Methyl-2-phenoxyethyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 6g. (Found: M, 263.0997. $C_{15}H_{21}NOS$ requires 263.1344); $\delta_H(CDCl_3)$ 7.10 (5 H, m, ArH), 4.00 (2 H, ABX, *J* 16 and 6 Hz, CH_2), 3.54 (2 H, s, CH_2N), 3.42 (1 H, sextet, CH), 2.95 (2 H, s, CH_2S), 1.69 and 1.62 (both 3 H, s, Me) and 1.27 (3 H, d, *J* 6 Hz, CH*Me*); $\delta_C(CDCl_3)$ 160.0, 129.4, 125.9, 123.8, 121.2, 115.1, 71.5, 60.4, 56.5, 31.5, 20.2, 17.8 and 17.5.

2-(2-Phenoxyethyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 6h. (Found: M, 249.1177. $C_{14}H_{19}NOS$ requires 249.1187); $\delta_H(CDCl_3)$ 7.2–6.8 (5 H, m, ArH), 4.10 (2 H, t, *J* 6 Hz, CH_2), 3.46 (2 H, s, CH_2N), 3.16 (2 H, t, *J* 6 Hz, CH_2), 2.94 (2 H, s, CH_2S) and 1.68 and 1.54 (both 3 H, s, Me); $\delta_C(CDCl_3)$ 159.0, 129.0, 124.0, 122.0, 121.0, 115.0, 66.6, 59.3, 55.9, 27.1, 19.7 and 17.4.

2-(2-Phenylsulfanylethyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 6i. (Found: M, 265.0946. $C_{14}H_{19}NS_2$ requires 265.0959); $\delta_H(CDCl_3)$ 7.30–7.10 (5 H, m, ArH), 3.39 (2 H, s, CH_2N), 3.17 (2 H, t, *J* 6 Hz, CH_2), 3.04 (2 H, t, *J* 6 Hz, CH_2), 2.90 (2 H, s, CH_2S) and 1.68 and 1.55 (both 3 H, s, Me); $\delta_C(CDCl_3)$ 153.6, 128.7, 125.8, 125.6, 124.0, 122.0, 59.1, 55.6, 32.1, 26.7, 18.6 and 17.2.

General procedure for the preparation of aminosulfur chlorides 8

The procedure was identical to the preparation of compounds **2**, using the amine instead of the silylated amine. Compounds **8a,b,j** and **k** were obtained as unstable yellow oils.

General procedure for the preparation of compounds 6 and 7 from precursors 8

The reaction procedure and work-up were the same as those described above using precursors **2**, except that the reaction time was reduced to 4 h. Data for the new compounds **6j**, **6k** and **7k** are given below.

2-(2-Methylsulfanylphenyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 6j. (Found: M, 251.0802. $C_{13}H_{17}NS_2$ requires 251.0646); $\delta_H(CDCl_3)$ 7.2–6.9 (4 H, m, ArH), 3.8 (2 H, s, CH_2N), 2.9 (2 H, s, CH_2S), 2.4 (3 H, s, SMe) and 1.8 and 1.7 (each 3 H, s, Me); irradiation at δ 3.8 resulted in an NOE enhancement of 7% of the proton at δ 6.9. $\delta_C(CDCl_3)$ 149.1, 127.1, 125.9, 125.1, 124.9, 124.2, 122.1, 120.6, 57.6, 29.9, 19.9, 16.6 and 15.2.

2-(Diphenylmethyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 6k. (Found: M, 295.1326. $C_{19}H_{21}NS$ requires 295.1395); $\delta_H(CDCl_3)$ 7.6–7.2 (10 H, m, ArH), 5.1 (1 H, s, CH), 3.45 (2 H, s, CH_2N), 2.9 (2 H, s, CH_2S) and 1.70 (6 H, s, 2 × Me); $\delta_C(CDCl_3)$ 143.9, 143.7, 129.0, 127.7, 124.7, 122.9, 72.6, 56.5, 28.5, 20.2 and 17.9. Also present in the crude reaction mixture was: *N*-(diphenylmethyl)-2-methylidenebut-3-ene-1-sulfenamide **7k**, which was identified by the ^1H NMR peaks[3c] at δ 3.20 (2 H, s, CH_2S) and 1.95 (3 H, s, Me).

Reactions of 1,2-thiazines 6a and 6g with *m*-chloroperoxybenzoic acid

The 1,2-thiazine (0.84 mmol) was dissolved in dichloromethane (30 ml) and cooled to 0 °C. MCPBA (1.7 mmol, 2 equiv.) was added, followed by potassium hydrogen carbonate (0.18 g, 1.7 mmol) and the mixture stirred for 2 h whilst allowing the temperature to rise to 20 °C. For compound **6g**, the colour was seen to change from yellow–orange to deep red then back to orange during the course of the reaction. After 2 h at 20 °C the mixture was washed with potassium hydrogen carbonate (2 × 20 ml) and the organic phase was dried over magnesium sulfate. Removal of the solvent *in vacuo* afforded an oil. Compound **6g** was recovered unchanged (^1H NMR evidence), whereas the product obtained from compound **6a** was an inseparable 1 : 3 mixture of compounds **18** and **19** in a combined yield of 80% (the ratio is based on integration of the ^1H NMR spectrum).

2-(4-Methylphenyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 1,1-dioxide 18. *m/z* 251 (M^+); δ_H 6.85–8.12 (4 H, m), 4.11 (2 H, br s, CH_2N), 3.45 (2 H, br s, CH_2S), 2.23, 1.70 and 1.67 (each 3 H, s, Me).

2-(4-Methylphenyl)-4,5-dimethyl-4,5-epoxy-3,6-dihydro-2*H*-1,2-thiazine 1,1-dioxide 19. *m/z* 267 (M^+); $\delta_H(CDCl_3)$ 6.85–8.12 (4 H, m), 3.99 [2 H, q, CH_2N, J_{HH} (AB) 16 Hz], 3.28 [2 H, q, CH_2S, J_{HH} (AB) 14 Hz], 2.25, 1.45 and 1.31 (each 3 H, s, Me).

General procedure for the reaction of 1,2-thiazines 6g and 6i with butyllithium and methyl iodide

The corresponding 1,2-thiazine (2.4 mmol) was dissolved in THF (10 ml) and the mixture cooled to −78 °C. Butyllithium (3 ml, 4.8 mmol; 1.6 M in hexane) was added dropwise, which led to a colour change from yellow to dark red. Upon completion of addition the mixture was stirred at −78 °C for 5 min, then methyl iodide (0.3 ml, 4.8 mmol) was added dropwise. A colour change from red to pale orange was observed. After stirring for a further 0.5 h at −78 °C the reaction was allowed to warm to 20 °C over 2 h and the excess base was then removed by quenching with distilled water (2 ml). The water was decanted from the mixture and extracted with dichloromethane (2 × 3 ml). The organic layer was then combined with the original THF solution and this mixture was evaporated *in vacuo* to afford a yellow oil which was purified by column chromatography on neutral alumina (dichloromethane) to yield compounds **21g** and **21i** as pale yellow oils which were stable in air but decomposed on heating.

***N*-Methyl-*N*-(1-methyl-2-phenoxyethyl)-4-butylsulfanyl-2,3-dimethylbut-2-enamine 21g.** Yield 42%; *m/z* (CI) 336 ($M^+ + 1$) (Found: M, 335.2282. $C_{20}H_{33}NOS$ requires 335.2283); $\delta_H(CDCl_3)$ 7.40–6.90 (5 H, m, aromatics), 4.10–3.80 (2 H, m, CH_2), 3.17 (3 H, m, CH + CH_2), 3.39 (2 H, br s, CH_2), 2.43 (2 H, t, CH_2, J_{HH} 7.5 Hz), 2.26 (3 H, br s, NMe), 1.79 (3 H, s, Me), 1.74 (3 H, s, Me), 1.60–1.20 (4 H, m, 2 × CH_2), 1.14 (3 H, d, Me, J_{HH} 6.2 Hz) and 0.90 (3 H, t, CMe, J_{HH} 6.2 Hz); $\delta_C(CDCl_3)$ 129.4, 121.0 (C2 butene), 120.8 (C3 butene), 114.5, 69.6, 55.9 (CH_2N), 37.2, 31.9, 31.8 (CH_2S), 30.1, 22.1 (MeN), 18.8, 18.0, 13.7 and 12.0; ν_{max}/cm^{-1} 3030, 2958, 2928 (CH), 1730 (C=C of butene), 1599, 1586 (C=C) and 1243 (C–O).

***N*-Methyl-*N*-(2-phenylsulfanylethyl)-4-butylsulfanyl-2,3-dimethylbut-2-enamine 21i.** Yield 20%; *m/z* (CI) 338 ($M^+ + 1$) (Found: 338.1574. $C_{19}H_{31}NS_2$ + H requires 338.1976); $\delta_H(CDCl_3)$ 7.34–7.26 (5 H, m, aromatics), 3.50 (2 H, t, J_{HH} 7.5 Hz), 3.23 (2 H, br s, CH_2), 3.01 (2 H, t, CH_2, J_{HH} 7.5 Hz), 2.96 (2 H, br s, CH_2), 2.57 (2 H, t, CH_2, J_{HH} 7.5 Hz), 2.20 (3 H, br s, NMe), 1.80 (3 H, s, Me), 1.72 (3 H, s, Me), 1.54–1.21 (4 H, m, 2 × CH_2) and 0.90 (3 H, t, Me, J_{HH} 7.5 Hz); $\delta_C(CDCl_3)$ 136.2, 129.4, 128.3, 125.2, 121.6 (C2 butene), 120.8 (C3 butene), 59.4, 55.6 (CH_2N), 41.5, 35.0 (CH_2S), 31.4, 31.1, 21.5, 18.0 (MeN), 17.3, 14.5 and 13.1; ν_{max}/cm^{-1} 3030, 2958, 2928 (CH), 1730 (C=C of butene), 1599, 1586 (C=C) and 1243 (C–O).

1-(Pentacarbonylchromium)-2-(4-bromophenyl)-4,5-dimethyl-3,6-dihydro-2*H*-1,2-thiazine 22

Freshly sublimed chromium hexacarbonyl (1.70 g, 7.5 mmol) was dissolved in dry THF (100 ml) under nitrogen and the solution was irradiated for 2 h with a 250 W mercury lamp. The resulting yellow solution containing pentacarbonyl(THF)chromium was cooled to −10 °C and stirred vigorously while compound **2b** (0.25 g, 0.88 mmol) dissolved in dry THF (10 ml) was added. The mixture was stirred at −10 °C for 0.5 h and then at 20 °C for 1 h, before solvent was removed *in vacuo* to leave a pale yellow solid which was chromatographed on a neutral alumina column (hexane) to afford *compound* **22** (190 mg, 45%) as amber crystals, mp 117–119 °C, obtained by very slow evaporation of a hexane solution of **22** at 0 °C (Found: C, 42.6; H, 2.8; N, 2.9. $C_{17}H_{14}BrCrO_5NS$ requires C, 42.9; H, 3.0; N, 2.9%); $\delta_H(CDCl_3)$ 7.4 (1 H, m), 7.25 (1 H, m), 7.0 (2 H, m), 3.75 (2 H, br s, CH_2N), 3.6–3.2 (2 H, very br s, CH_2S) and 1.90 and 1.81 (both 3 H, br s); $\delta_C(CDCl_3)$ 230.5, 146.5, 132.7, 130.5, 127.0, 123.0, 119.9, 51.0, 43.3, 20.6 and 19.6.

X-Ray structural determination of compound 22

Amber crystals of **22** were obtained from hexane solution. The experiment was performed on a Rigaku AFC6S four-circle diffractometer at room temperature (graphite-monochromated Mo-Kα radiation, λ = 0.710 73 Å, ω scan mode with Lehmann–Larsen profile analysis). Crystal data: $C_{17}H_{14}BrCrNO_5S$, M = 476.26, monoclinic, space group $C2/c$ (No.15), a = 23.684(5), b = 8.581(2), c = 19.137(4) Å, β = 90.11(3)°, V = 3889.3(15) Å^3 (from 18 reflections, 12 < θ < 14°), Z = 8, $F(000)$ = 1904, D_c = 1.63 g cm^{-3}, μ = 27.8 cm^{-1}, crystal size 0.16 × 0.2 × 0.3 mm, $2\theta \leqslant 50°$, 2664 total, 2576 unique and 1315 observed [$I \geqslant 2\sigma(I)$] data, R_{int} = 0.051, empirical absorption correction (72 ψ-scans of 2 reflections, TEXSAN software,[16] T_{min} = 0.80 and T_{max} = 1.00). The structure was solved by direct methods with SHELXS-86 programs[17] and refined (non-H atoms anisotropically, methyl groups as rigid bodies, other H atoms as 'riding'; 239 variables) by full-matrix least-squares (SHELXL-93 software[18]) against F^2 of all data, converging at w$R(F^2)$ = 0.164, $R(F$, obs. data) = 0.069, goodness-of-fit 0.931; residual electron density $\Delta\rho_{max}$ = 0.41, $\Delta\rho_{min}$ = −0.36 e Å^{-3}. A study (of another sample of **22**) at T = 150 K gave essentially the same stucture.

Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/32.

Acknowledgements

This work was funded by the EPSRC (A. C.) and Shell Research (Sittingbourne) (CASE Award to G. N. M.). M. R. B. thanks the University of Durham for the award of a Sir Derman Christopherson Research Fellowship.

References

1 P. Tavs, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 1048.
2 Reviews: (*a*) M. R. Bryce, J. Becher and B. Fält-Hansen, *Adv. Heterocycl. Chem.*, 1992, **55**, 1; (*b*) M. Takahashi and R. Okazaki, *Sulfur Rep.*, 1993, **13**, 293.
3 (*a*) M. R. Bryce and P. C. Taylor, *J. Chem. Soc., Chem. Commun.*, 1988, 950; (*b*) M. R. Bryce and P. C. Taylor, *Tetrahedron Lett.*, 1989, **30**, 3835; (*c*) M. R. Bryce and P. C. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1990, 3225; (*d*) M. R. Bryce, J. N. Heaton, P. C. Taylor and M. Anderson, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1935.
4 (*a*) L. N. Markovskii, A. V. Solov'ev, E. I. Kamanskaya, A. V. Borodin and Y. G. Shermolovich, *Zh. Org. Khim.*, 1990, **26**, 2083 (Engl. trans., 1990, **26**, 1799); (*b*) M. R. Bryce, A. Chesney, J. N. Heaton, G. N. McKelvey and M. Anderson, *Tetrahedron Lett.*, 1994, **35**, 5275.
5 (*a*) M. F. Joucla and C. W. Rees, *J. Chem. Soc., Chem. Commun.*, 1984, 374; (*b*) M. Takahashi, R. Okazaki, N. Inamoto, T. Sugawara and H. Iwamura, *J. Am. Chem. Soc.*, 1992, **114**, 1830; (*c*) M. R. Bryce and J. N. Heaton, *Tetrahedron Lett.*, 1991, **32**, 7459.
6 (*a*) O. Meth-Cohn and G. van Vuuren, *J. Chem. Soc., Chem. Commun.*, 1984, 1144; (*b*) O. Meth-Cohn and G. van Vuuren, *J. Chem. Soc., Perkin Trans. 1*, 1986, 245.
7 J. N. Heaton, Ph.D. Thesis, University of Durham, 1992.
8 A. Padwa, Y. Y. Chen, U. Chiacchio and W. Dent, *Tetrahedron*, 1985, **41**, 3529. See also E. Vedejs and G. R. Martinez, *J. Am. Chem. Soc.*, 1979, **101**, 6452.
9 R. Mayer, *Phosphorus Sulfur Relat. Elem.*, 1985, **23**, 277, postulated that the formation of sulfurdiimides in reactions of primary amines with disulfur dichloride proceeded *via* thionitroso intermediates. No details of reaction conditions were given.
10 P. Pevarello, R. Amici, M. Colombo and M. Varasi, *J. Chem. Soc., Perkin Trans. 1*, 1993, 2151.
11 I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, Wiley, London, 1976.
12 S. I. Bell, M. Parvez and S. M. Weinreb, *J. Org. Chem.*, 1991, **56**, 373.
13 D. Cremer and J. A. Pople, *J. Am. Chem. Soc.*, 1975, **97**, 1354.

14 M. L. Rodriguez, C. Ruiz-Perez, I. Brito, J. Cuevas, G. Gonzalez and V. Manriquez, *J. Organomet. Chem.*, 1989, **377**, 235.
15 M. L. Rodriguez, I. Brito, C. Diaz, G. Gonzalez and V. Manriquez, *J. Organomet. Chem.*, 1992, **425**, 49.
16 TEXSAN: Single Crystal Structure Analysis Software, Version 5.0, Molecular Structure Corporation, USA, 1989.
17 G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 1990, **46**, 467.
18 G. M. Sheldrick, SHELXL 93, Program for the Refinement of Crystal Structures, University of Göttingen, 1993.

Paper 6/00777E
Received 1*st February* 1996
Accepted 22*nd April* 1996