The reactions of phthalazinium-2-(unsubstituted)methanide and aryl(3-phenylprop-2-en-1-ylidene)ammoniomethanide 1,3-dipoles with some thioester and thioketone C=S dipolarophiles. Regio- and stereochemistry: substituted thiazolo-[4,3-*a*]- and -[2,3-*a*]-phthalazines and 2- and 4-styryl substituted tetrahydrothiazoles

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In cycloaddition reactions of phthalazinium-2-methanide and aryl(3-phenylprop-2-en-1-ylidene)ammoniomethanide 1,3-dipoles with thiobenzophenone, phenyl dithioacetate and methyl cyanodithioformate the regiochemistry was such that the nucleophilic methanide terminus of the dipole bonded to the sulfur atom, thus giving stereoisomeric substituted thiazolo[4,3-*a*]phthalazines and 4-styryl substituted tetrahydrothiazoles. With dicyclopropyl thioketone and thioadamantanone, steric effects caused a gradual reversal of this regiochemistry. Solvent polarity did not alter the distribution of regioisomers. X-Ray crystal structures are reported for 1,1-diphenyl[1,3]thiazolo[4,3-*a*]phthalazine **7** and 3-(*p*-bromophenyl)-4-[(*E*)-styryl]-5-*trans*-cyano-5-*cis*-methylthio-2,3,4,5-tetrahydrothiazole **15b**.

Results and discussion

There has been much recent interest in the 1,3-dipolar cyclo-additions of thiones, which have been classified as super dipolarophiles.[1–9] The regiochemistry of thione cycloadditions has provided added interest since it may vary quite dramatically. For nitrone 1,3-dipoles the nucleophilic oxygen terminus of the dipole invariably bonds to the thione carbon atom.[1–3] With substituted diazomethanes as 1,3-dipoles, mixtures of regioisomers are formed and the balance of these may vary with solvent polarity.[4–7] Thus in non-polar solvents the propensity is for the N-terminus of diazomethane to bond to the thione carbon, while in more polar alcoholic solvents the diazomethane nitrogen bonds to the sulfur atom.[7] Calculated dipole moments of the transition states have been implicated in these effects.[7] There are relatively few reports of the reactions of methanide (ylide) 1,3-dipoles with thiones but the most famous of these, the Schonberg reaction between thiobenzophenone and diazomethane, shows that the CH_2^- terminus of the intermediate thiobenzophenone *S*-methanide 1,3-dipole bonds to the sulfur atom of thiobenzophenone.[8,9] Following our recent work [10] on the reactions of phthalazinium-2-methanide 1,3-dipoles with alkene and alkyne dipolarophiles we have investigated herein the reactions of phthalazinium-2-methanide **2** with some thioesters and thioketones including thiobenzophenone. For comparison purposes the aryl(3-phenylprop-2-en-1-ylidene)-ammoniomethanide 1,3-dipole systems **13** have also been included. These contain the same reactive structural unit as in the rigid planar structure **2** but without the structural rigidity. In general the nucleophilic methanide terminus of the dipole added to the sulfur atom of the C=S bond but the regiocontrol is delicately balanced and a relatively small steric effect can alter it. Solvent polarity had no detectable influence on the synthetic outcome of these reactions.

Results and discussion

The dipoles **2** and **13** were generated at ambient temperatures in dichloromethane by desilylation of the trimethylsilylmethyl trifluoromethanesulfonate (triflate) salts **1** and **11–12** with CsF following a literature procedure.[11,12] With imine systems these types of salts have generally not been isolated prior to desilylation and the influence if any of their *E,E* or *E,Z* stereo-
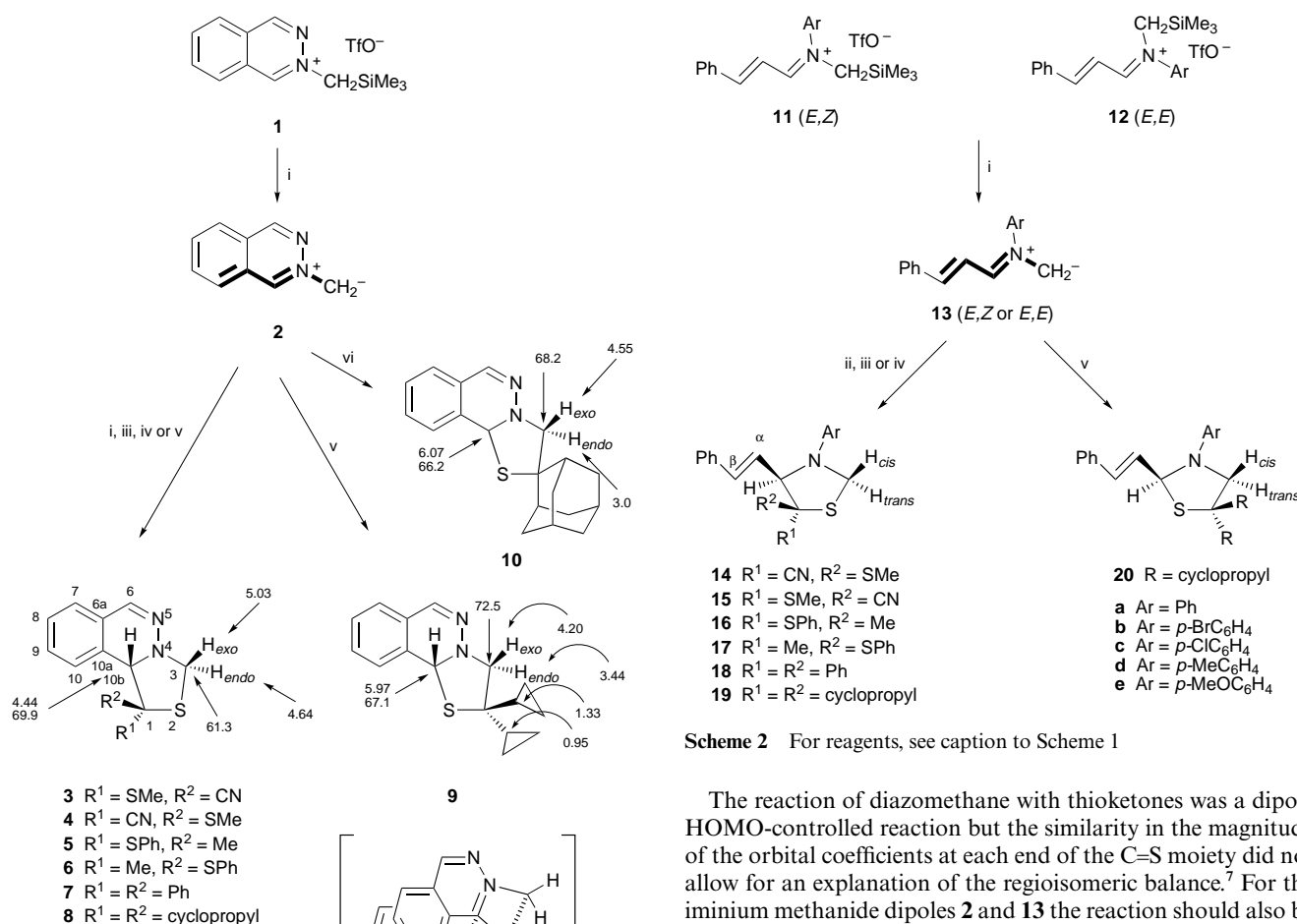
chemistry has not been commented on previously in the literature. Recently [13] and in the present case we have found that various proportioned mixtures of **11** and **12** were formed on quaternisation of the *N*-aryl imine, but the isomer distribution in the salt had no influence on the distribution of cycloaddition products, suggesting the generation of a single dipole **13** (*E,E* or *E,Z*) from either isomer.[13] The reaction of the dipoles **2** (Scheme 1) and **13** (Scheme 2) with methyl cyanodithioformate [N≡C–C(=S)–SMe] was regiospecific and gave in all cases 1:1 mixtures of the stereoisomer pairs **3,4** and the series **14,15** (Table 1). In these thiazolo[4,3-*a*]phthalazine products the methanide carbon atom has bonded to the thione sulfur atom.

The fused thiazolo[4,3-*a*]phthalazine ring system is not well known and is absent from some prominent ring indexes. We have found but one paper where a single derivative of the ring system is reported.[14] Use of the dipolarophile *S*-phenyl dithio-acetate (Scheme 1), in which a CN group has been replaced by Me at the C=S, resulted in a similar regiochemistry and gave the stereoisomeric product pairs **5,6** and **16b,17b** (from **13b**). In this case the isomer **6** with the larger SPh in the *exo* position dominated by 2:1 over product **5**, while for the more flexible dipole **13b** the dominant product was **17b** with the SPh group *endo* to the styryl group (Table 1, entry 11). There appears to be a larger steric influence operating in cycloaddition with the phthalazinium-2-methanide dipole **2**. When thiobenzophenone was the dipolarophile the regiochemistry was similar and gave the single products **7** from **2** and **18b** from **13b**. Thus the normal regiochemistry is such that the nucleophilic methanide end of the dipole bonds to the sulfur atom. An X-ray crystal structure of compound **7** (Fig. 1) shows that the *endo* phenyl group lies in a stacking-type position under the plane of the phthalazine ring. This suggests a planar transition state of type **I** with favourable secondary π-orbital interactions and no steric difficulties. Introduction of a steric effect by using dicyclopropyl thioketone as dipolarophile (Scheme 1) caused a major change in the regiochemistry and both regioisomeric pairs **8,9** and **19b,20b** (from **13b**) were obtained. For the structurally more rigid dipole **2** the product ratio **8:9** was 2:1 and a significant amount of the reversed regioisomer **9** was formed. For the more flexible dipole **13b** the ratio of the products **19b:20b** was 3:1.

Table 1 Cycloaddition products—stereo- and regio-isomers

Entry	Compound	Mp^a/°C	Yield^b (%)	δ_H	Compound	Mp^a/°C	Yield^b (%)	δ_H
1	**3**	118–119	31	4.95^c	**4**	116–118	31	4.43^c
2	**5**	128–130	29(7)	4.31^c	**6**	123–124	51(12)	4.32^c
3	**7**	152–154	90(40)	5.5^c	—	—	—	—
4	**8**	91–92	61(12)	4.44^c	**9**	89–90	25(5)	5.97^c
5	—	—	—	—	**10**	159–160	87(15)	6.07^c
6	**14a**	126–128	45	5.06^d	**15a**	66–68	45	4.77^d
7	**14b**	108–110	45	5.0^d	**15b**	102–104	45	4.65^d
8	**14c**	118–120	32	5.0^d	**15c**	78–82	32	4.65^d
9	**14d**	115–117	35	5.01^d	**15d**	88–90	35	4.64^d
10	**14e**	110–112	30	4.91^d	**15e**	84–86	30	4.48^d
11	**16b**^{e}	—^{f}	26(17)	4.88^d	**17b**^{e}	—^{f}	52(34)	4.44^d
12	**18b**	82–84	70	5.13^d	—	—	—	—
13	**19b**	95–97	59(18)	4.34^d	**20b**^{g}	—^{g}	20(6)	5.47^h

^{a} From EtOH. ^{b} Conversion (%) in parentheses. ^{c} δ_H for H-10b. ^{d} δ_H for H-4. ^{e} **16b** and **17b** could not be separated. ^{f} Mp of isomer mixture = 74–76 °C. ^{g} **20b** could not be fully separated from **19b**; mp of (3:1) isomer mixture = 78–80 °C. ^{h} δ_H for H-2.

Scheme 1 *Reagents*: i, CsF; ii, MeS–C(=S)CN; iii, PhS–C(=S)Me; iv, Ph$_2$C=S; v, dicyclopropyl thioketone; vi, thioadamantanone. Some ^{1}H and ^{13}C NMR shifts for **8**, **9** and **10** are shown.

3 R^1 = SMe, R^2 = CN
4 R^1 = CN, R^2 = SMe
5 R^1 = SPh, R^2 = Me
6 R^1 = Me, R^2 = SPh
7 R^1 = R^2 = Ph
8 R^1 = R^2 = cyclopropyl

Scheme 2 For reagents, see caption to Scheme 1

14 R^1 = CN, R^2 = SMe
15 R^1 = SMe, R^2 = CN
16 R^1 = SPh, R^2 = Me
17 R^1 = Me, R^2 = SPh
18 R^1 = R^2 = Ph
19 R^1 = R^2 = cyclopropyl

20 R = cyclopropyl

a Ar = Ph
b Ar = p-BrC$_6$H$_4$
c Ar = p-ClC$_6$H$_4$
d Ar = p-MeC$_6$H$_4$
e Ar = p-MeOC$_6$H$_4$

These regioisomeric ratios were not changed when the solvent was changed from dichloromethane to pentane, toluene or ethanol, and product distribution was not influenced by solvent polarity, as was the case for diazomethane as dipolarophile.[7] Increasing the steric effect in the thione by using thioadamantanone as dipolarophile (Scheme 1) totally reversed the regiochemistry and the product **10** was the exclusive cycloadduct with this dipolarophile.
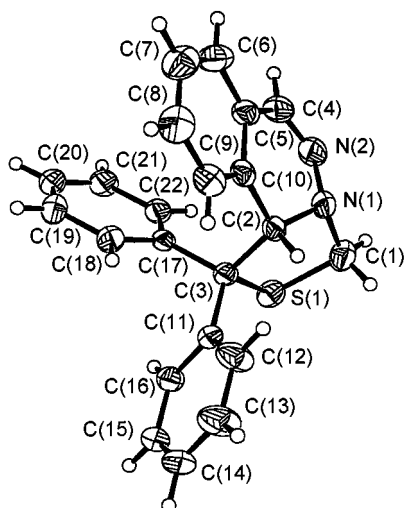
The reaction of diazomethane with thioketones was a dipole HOMO-controlled reaction but the similarity in the magnitude of the orbital coefficients at each end of the C=S moiety did not allow for an explanation of the regioisomeric balance.[7] For the iminium methanide dipoles **2** and **13** the reaction should also be dipole HOMO controlled and the largest orbital coefficient of the dipole HOMO should be at the methanide terminus. Previous *ab initio* calculations[15] of the coefficients at the S and C atoms of the LUMO ($\pi^*_{C=S}$) of methyl cyanodithioformate gave values of 0.719 and 0.674 respectively, suggesting a preference for bonding of the methanide at the S atom as observed. However the difference between the orbital coefficient at C and S is relatively small and this is the case also for the CH=S group.[16] The regiocontrol is therefore delicately balanced and a steric effect may reverse it with these iminium methanide dipoles.

The electronic effect of the substituents at C=S in the dipolarophiles used herein did not affect the regiochemistry of the products. It is of interest that replacement of a CN group (methyl cyanodithioformate) by a CH$_3$ group at the C=S of a thioester (phenyl dithioacetate) had no effect on regiochemistry when a similar change for thioaldehydes reversed the regiochemistry of Diels–Alder reactions with electron-rich dienes.[16] The major influence observed in the present reactions on

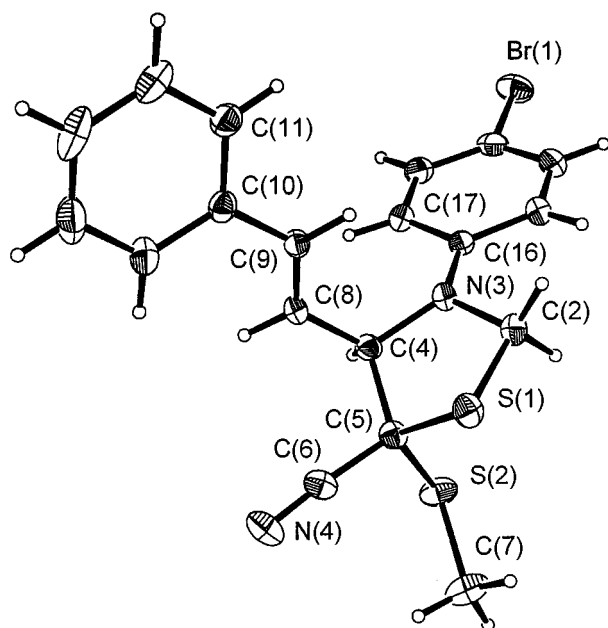**Fig. 1** X-Ray crystal structure of compound **7**

Fig. 2 X-Ray crystal structure of compound **15b**

changing the dipolarophile from methyl cyanodithioformate to *S*-phenyl dithioacetate (Scheme 1) was a reduction in the efficiency of the reaction (conversion yield) for identical reaction conditions (Table 1). This was accompanied by more extensive *in situ* decomposition of the unreacted labile dipoles and recovery of the thione. The CN substituent significantly lowers the energy of the $^*\pi_{C=S}$ orbital,[16] thereby enhancing a dipole HOMO controlled reaction, and conversion yields of 60–90% were obtained for methyl cyanodithioformate (Scheme 1) (Table 1, entries 1, 6–10). A methyl group causes a moderate rise in the energy of the $^*\pi_{C=S}$ orbital[16] and this, combined with the loss of the reaction-enhancing effect of the CN, caused a reduction in conversion yields which also occurred as expected with two aliphatic substituents on the C=S (for dicyclopropyl thioketone and thioadamantanone). In the cases with low conversion yields the reaction yields were in the range 78–96% when corrected for the recovery of starting materials.

Structures of products
The structures of the products were established by microanalyses and IR and ^{1}H and ^{13}C NMR spectra, which showed all of the expected signals. Assignments were bolstered by X-ray crystal structure determinations on compounds **7** (Fig. 1) and **15b** (Fig. 2). The proton NMR chemical shifts were particularly useful for distinguishing the stereoisomeric pairs.

Aliphatic protons in the *endo* orientations at C-1 in structures **3,6** and **8**, which lie under the face of the phthalazine π system, were shielded by 0.4–0.8 ppm relative to the *exo* orientation. Thus the *endo* methyl group in compounds **3** and **6** appeared at δ 1.96 and 1.23, respectively, while in the isomers **4** and **5**, where these methyl groups are in the *exo* position, the respective chemical shifts were δ 2.49 and 1.82. Similarly the shift of the *endo* cyclopropyl 1-CH in compound **8** was δ 0.66 while the 1-CH of the *exo* cyclopropyl of the same compound appeared at δ 1.26. Structures bearing a C≡N group *cis* to the vicinal H-atom, as at C-10b in **3** and C-2 in **14**, showed exceptional deshielding of this H which falls in the deshielding region of the nitrile bond. Thus the H atom at C-10b in **3** was deshielded to δ 4.95 while that in **4** was at δ 4.43. The regioisomers **8,9,19b** and **20b** were readily distinguished since the carbon bonded to sulfur was the more shielded while the H atoms on this carbon were the more deshielded (Scheme 1).

Experimental

Mps were measured on an Electrothermal apparatus. IR spectra were measured with a Perkin-Elmer 983G spectrophotometer. NMR spectra were measured on JEOL JNM-GX-270 and GXFT 400 instruments with tetramethylsilane as internal reference and deuteriochloroform as solvent. NMR assignments were supported by decoupled, off-resonance decoupled and DEPT spectra. Microanalyses were measured on a Perkin-Elmer model 240 CHN analyser. The salts **1** and mixtures of **11** and **12** were prepared as previously described.[10,13] The thione dipolarophiles (Scheme 1) were prepared by literature procedures.[17] The terms H$_o$, H$_m$, H$_p$ refer to *ortho*, *meta* and *para* H-atoms.

Fused thiazolophthalazines
1-*exo*-Cyano-1-*endo*-methylthio[1,3]thiazolo[4,3-*a*]phthalazine 3 and its stereoisomer 4 (Table 1, entry 1). A solution of the triflate salt **1** (0.45 g, 1.23 mmol) in dry CH$_2$Cl$_2$ (20 cm^3) was treated with methyl cyanodithioformate (0.29 g, 2.47 mmol) followed by excess CsF, stirred under anhydrous conditions at ambient temperature for 24 h, filtered and the filtrate (together with CH$_2$Cl$_2$ filter-cake washings) evaporated under reduced pressure to 4 cm^3, placed on a gravity column of silica gel (70–230 mesh ASTM) and eluted slowly with CH$_2$Cl$_2$. First eluted was **3** (31%) followed by **4** (31%).

3: mp 118–119 °C (EtOH) (Found: C, 55.3; H, 3.9; N, 16.1. C$_{12}$H$_{11}$N$_3$S$_2$ requires C, 55.1; H, 4.2; N, 16.1%); ν_{max}/cm^{-1} (mull) 2222 (C≡N); δ_H(CDCl$_3$) 1.96 (s, 3H, SMe), 4.94–4.96 (m, 2H, H-3*endo*, H-10b), 5.40 (d, 1H, H-3*exo*, *J* = 9.8 Hz), 7.42 (m, 1H, H-10), 7.52 (s, 1H, H-6), 7.56–7.57 (m, 3H, H-7–H-9); δ_C(CDCl$_3$) 17.0 (CH$_3$), 60.9 (C-1), 64.2 (C-3), 70.3 (C-10b), 118.0 (C≡N), 125.1 (C-10a), 126.5, 127.7 and 130.4 (C-8–C-10), 126.9 (C-6a), 140.4 (C-6).
4: mp 116–118 °C (EtOH) (Found: C, 55.1; H, 4.0; N, 15.7. C$_{12}$H$_{11}$N$_3$S$_2$ requires C, 55.1; H, 4.2; N, 16.1%); ν_{max}/cm^{-1} (mull) 2220 (C≡N); δ_H(CDCl$_3$) 2.49 (s, 3H, SMe), 4.43 (s, 1H, H-10b), 4.84 (d, 1H, H-3*endo*, *J* = 9.8 Hz), 5.39 (d, 1H, H-3*exo*), 7.43–7.45 (m, 1H, H-10), 7.49–7.55 (m, 3H, H7–H9), 7.67 (s, 1H, H-6); δ_C(CDCl$_3$) 16.8 (CH$_3$), 61.6 (C-1), 64.2 (C-3), 71.4 (C-10b), 117.0 (C≡N), 123.7 (C-10a), 126.8, 127.6 and 130.4 (C-8–C-10), 127.2 (C-6a), 131.3 (C-7), 142.3 (C-6).
1,1-Diphenyl[1,3]thiazolo[4,3-*a*]phthalazine 7 (Table 1, entry 3). A solution of the triflate salt **1** (0.45 g, 1.23 mmol) in dry CH$_2$Cl$_2$ (20 cm^3) was treated with thiobenzophenone (0.45 g, 2.26 mmol) followed by excess CsF, stirred under anhydrous conditions at ambient temperature for 24 h, filtered and the filtrate (together with CH$_2$Cl$_2$ filter-cake washings) evaporated under reduced pressure to 4 cm^3, placed on a gravity column of silica gel (70–230 mesh ASTM) and eluted slowly with CH$_2$Cl$_2$ to give **7** (40%); mp 152–154 °C (EtOH) (Found: C, 77.0; H, 5.2; N, 8.2. C$_{22}$H$_{18}$N$_2$S requires C, 77.2; H, 5.3; N, 8.2%); δ_H(CDCl$_3$) 4.96 (d, 1H, H-3*endo*, *J* = 9.3 Hz), 5.24 (d, 1H, H-3*exo*), 5.50

(s, 1H, H-10b), 6.56 (s, 1H, H-6), 6.78–6.85 (m, 3H, H_m and H_p of endo C_6H_5), 6.96–7.0 (t, 1H, H-10), 7.04 (d, 2H, $J = 7.3$ Hz, H_o of endo C_6H_5), 7.17–7.22 (m, 3H, H_m and H_p of exo C_6H_5), 7.26–7.36 (m, 3H, H-7–H-9), 7.43 (d, 2H, H_o of exo C_6H_5); δ_C(CDCl$_3$) 61.9 (C-3), 67.8 (C-10b), 73.4 (C-1), 125.7 (C-10a), 125.9 (1-endo C_6H_5, C-2′), 125.9 (1-exo C_6H_5, C-2′), 126.6, 126.9 and 129.9 (C-8–C-10), 126.8 (1-endo C_6H_5, C-4′), 128.3 (1-endo C_6H_5, C-3′), 128.3 (1-exo C_6H_5, C-3′), 128.5 (1-exo C_6H_5, C-4′), 131.0 (C-6a), 131.5 (C-7), 137.3 (C-6), 140.2 (1-endo C_6H_5, C-1′), 144.4 (1-exo C_6H_5, C-7′).

1,1-Dicyclopropyl[1,3]thiazolo[4,3-a]phthalazine 8 and its regioisomer 9 (Table 1, entry 4). A solution of the triflate salt **1** (0.80 g, 2.19 mmol) in dry CH$_2$Cl$_2$ (20 cm^3) was treated with dicyclopropyl thioketone (0.55 g, 4.36 mmol) followed by excess CsF, stirred under anhydrous conditions at ambient temperatures for 24 h, filtered and the filtrate (together with CH$_2$Cl$_2$ filter-cake washings) evaporated under reduced pressure to 4 cm^3, placed on a column of silica gel (230–400 mesh ASTM) and eluted slowly with CH$_2$Cl$_2$. First eluted was **9** (5%) followed by **8** (12%).

8: mp 91–92 °C (EtOH) (Found: C, 71.0; H, 6.6; N, 10.2. C$_{16}$H$_{18}$N$_2$S requires C, 71.1; H, 6.7; N, 10.4%); δ_H(CDCl$_3$), 0.02–0.41 (m, 4H, H-2′, endo cyclopropyl ring), 0.51–0.60 and 0.72–0.82 (m, 4H, H-2, exo cyclopropyl ring), 0.63–0.69 (m, 1H, H-1′, endo cyclopropyl ring), 1.24–1.28 (m, 1H, H-1′, exo cyclopropyl ring), 4.44 (s, 1H, H-10b), 4.64 (d, 1H, $J = 9.8$ Hz, H-3 endo), 5.03 (d, 1H, H-3 exo), 7.39–7.50 (m, 4H, H-7–H-10), 7.55 (s, 1H, H-6); δ_C(CDCl$_3$) 0.0, 2.6, 3.6 and 5.9 (C-2′, cyclopropyl rings), 16.3 and 18.7 (C-1′, cyclopropyl rings), 61.3 (C-3), 69.9 (C-10b), 71.5 (C-1), 125.6 (C-10a), 125.8, 126.9 and 128.6 (C-8–C-10), 130.1 (C-7), 131.3 (C-6a), 138.1 (C-6).

9: mp 89–90 °C (EtOH) (Found: C, 70.9; H, 6.5; N, 10.1. C$_{16}$H$_{18}$N$_2$S requires C, 71.1; H, 6.7; N, 10.4%); δ_H(CDCl$_3$) 0.35–0.66 (m, 8H, H-2′, cyclopropyl rings), 0.94–0.97 (m, 1H, H-1′, endo cyclopropyl ring), 1.31–1.35 (m, 1H, H-1′, exo cyclopropyl ring), 3.44 (d, 1H, $J = 12.2$ Hz, H-3 endo), 4.20 (d, 1H, H-3exo), 5.97 (s, 1H, H-10b), 7.16–7.36 (m, 4H, H-7–H-10), 7.49 (s, 1H, H-6); δ_C(CDCl$_3$) 0.0, 3.0, 3.5 and 5.2 (C-2′, cyclopropyl rings), 17.5 and 20.3 (C-1′, cyclopropyl rings), 65.4 (C-2), 67.1 (C-10b), 72.5 (C-3), 123.7 (C-10a), 126.1, 126.5 and 129.3 (C-8–C-10), 129.8 (C-6a), 130.7 (C-7), 137.5 (C-6).

Styryl substituted thiazoles (the terms cis and trans are relative to the styryl group)
3-(p-Bromophenyl)-4-[(E)-styryl]-5-cis-methylthio-5-trans-cyano-2,3,4,5-tetrahydrothiazole 14b and its stereoisomer 15b (Table 1, entry 7). A solution of the triflate salts **11b** and **12b** (0.50 g, 1.13 mmol) in dry CH$_2$Cl$_2$ (20 cm^3) was treated with methyl cyanodithioformate (0.26 g, 2.26 mmol) followed by excess CsF, stirred under anhydrous conditions at ambient temperature for 24 h, filtered and the filtrate (together with CH$_2$Cl$_2$ filter-cake washings) evaporated under reduced pressure to 4 cm^3, placed on a flash column of silica gel (230–400 mesh ASTM) and eluted with light petroleum (bp 40–60 °C)–CH$_2$Cl$_2$ having gradient variations of 5% from 10:0–6:4 (v/v). First eluted was **15b** (45%) followed by **14b** (45%).

14b: mp 108–110 °C (EtOH) (Found: C, 54.6; H, 3.9; N, 6.6. C$_{19}$H$_{17}$BrN$_2$S$_2$ requires C, 54.7; H, 4.1; N, 6.7%); ν_{max}/cm^{-1} (mull) 2216 (C≡N); δ_H(CDCl$_3$) 2.44 (s, 3H, SMe), 4.74–4.84 (dd, 2H, H-2 cis and trans), 5.0 (d, 1H, H-4, $J = 8.1$ Hz), 6.11–6.20 (dd, 1H, styryl H-α), 6.66–6.77 (m, 3H, styryl H-β and H_o of p-BrC$_6$H$_4$), 7.24–7.37 (m, 7H, remaining aromatics); δ_C(CDCl$_3$) 16.0 (CH$_3$), 52.4 (C-2), 56.7 (C-5), 72.5 (C-4), 116.3 (C≡N), 116.7 (p-BrC$_6$H$_4$, C-2′), 117.8 (p-BrC$_6$H$_4$, C-4′), 121.3 (styryl C$_6$H$_5$, C-2′), 127.0 (styryl C$_6$H$_5$, C-3′), 128.7 (styryl C$_6$H$_5$, C-4′), 128.8 (styryl, C-α), 132.2 (p-BrC$_6$H$_5$, C-3′), 135.4 (styryl C$_6$H$_5$, C-1′), 136.5 (styryl, C-β), 144.2 (p-BrC$_6$H$_4$, C-1′).

15b: mp 102–104 °C (EtOH) (Found: C, 54.5; H, 3.9; N, 6.7. C$_{19}$H$_{17}$BrN$_2$S$_2$ requires C, 54.7; H, 4.1; N, 6.7%); ν_{max}/cm^{-1} (mull) 2239 (C≡N); δ_H(CDCl$_3$) 2.47 (s, 3H, SMe), 4.65 (d, 1H, $J = 6.6$ Hz, H-4), 4.72 (s, 2H, H-2 cis and trans), 6.31–6.38

(dd, 1H, styryl H-α), 6.66 (d, 2H, H_o of p-BrC$_6$H$_4$, $J = 7.3$ Hz), 6.76 (d, 1H, $J = 15.4$ Hz, styryl H-β), 7.25–7.43 (m, 7H, remaining aromatics); δ_C(CDCl$_3$) 16.1 (CH$_3$), 52.0 (C-2), 58.7 (C-5), 72.7 (C-4), 115.2 (C≡N), 116.3 (p-BrC$_6$H$_4$, C-2′), 119.4 (p-BrC$_6$H$_4$, C-4′), 123.4 (styryl C$_6$H$_5$, C-2′), 127.1 (styryl C$_6$H$_5$, C-3′), 128.7 (styryl C$_6$H$_5$, C-4′), 128.8 (styryl C-α), 132.2 (p-BrC$_6$H$_4$, C-3′), 135.4 (styryl C$_6$H$_5$, C-1′), 136.2 (styryl C-β), 144.8 (p-BrC$_6$H$_4$, C-1′).

3-(p-Bromophenyl)-4-[(E)-styryl]-5,5-diphenyl-2,3,4,5-tetrahydrothiazole 18b (Table 1, entry 12)
A solution of the triflate salts **11b** and **12b** (0.50 g, 1.13 mmol) in dry CH$_2$Cl$_2$ (20 cm^3) was treated with thiobenzophenone (0.45 g, 2.26 mmol) followed by excess CsF, stirred under anhydrous conditions at ambient temperature for 24 h, filtered and the filtrate (together with CH$_2$Cl$_2$ filter-cake washings) evaporated under reduced pressure to 4 cm^3, placed on a column of silica gel (230–400 mesh ASTM) and eluted slowly with CH$_2$Cl$_2$ to give **18b** (70%); mp 82–84 °C (EtOH) (Found: C, 69.7; H, 4.6; N, 2.7. C$_{29}$H$_{24}$BrNS requires C, 69.9; H, 4.8; N, 2.8%); δ_H(CDCl$_3$) 4.07 (d, 1H, $J = 7.3$ Hz, H-2 trans), 4.53 (d, 1H, H-2, cis), 5.13 (d, 1H, H-4, $J = 5.9$ Hz), 5.62–5.68 (dd, 1H, styryl H-α), 6.31 (d, 1H, $J = 16.1$ Hz, styryl H-β), 6.60 (d, 2H, H_o of p-BrC$_6$H$_4$, $J = 8.8$ Hz), 7.03 (d, 2H, H_m of p-BrC$_6$H$_4$), 7.12–7.36 (m, 15H, remaining aromatics); δ_C(CDCl$_3$) 49.1 (C-2), 68.6 (C-4), 68.8 (C-5), 114.0 (p-BrC$_6$H$_4$, C-2′), 115.6 (p-BrC$_6$H$_4$, C-4′), 126.4 (styryl C$_6$H$_5$, C-2′), 126.5 and 126.8 (5,5-diphenyl, C-2′), 127.5 (styryl C$_6$H$_5$, C-3′), 128.0 (styryl C$_6$H$_5$, C-4′), 128.3 and 128.6 (5,5-diphenyl, C-3′), 128.4 and 128.5 (5,5-diphenyl, C-4′), 128.7 (styryl C-α), 132.1 (p-BrC$_6$H$_4$, C-3′), 132.5 (styryl C-β), 136.6 (styryl C$_6$H$_5$, C-1′), 140.6 and 144.4 (5,5-diphenyl, C-1′), 145.8 (p-BrC$_6$H$_4$, C-1′).

X-Ray crystal structure determination of compound 7
Good quality colorless crystals of compound **7** were grown from ethanol at ambient temperature. The crystal used for data collection had the approximate dimensions $0.43 \times 0.28 \times 0.25$ mm. The crystal was triclinic with space group $P\bar{1}$ and had unit cell parameters $a = 9.2930(10)$, $b = 9.466(2)$, $c = 10.838(2)$ Å, $\alpha = 82.470(10)$, $\beta = 65.740(10)$, $\gamma = 89.330(10)°$. Reflections were collected on an Enraf-Nonius CAD4F four circle diffractometer, using graphite monochromated Mo-Kα radiation, $\lambda = 0.710\ 69$ Å. The criterion which qualified a reflection for observation was $I > 2\sigma(I)$ and 2316 reflections satisfied this condition. The calculated density was 1.321 Mg m^{-3} and $Z = 2$. The absorption coefficient was 0.194 mm^{-1} and the theta range for data collection was 2.08 to 23.97°. The total number of independent reflections was 2706 [$R(\text{int}) = 0.270$]. The structure was solved by direct methods, SHELXS-86,[18] and refined by full-matrix least-squares using SHELXL-93.[19] SHELX operations were rendered paperless using ORTEX which was also used to obtain the drawings.[20] Data were corrected for Lorentz and polarization effects but not for absorption. Hydrogen atoms were included in calculated positions with thermal parameters 30% larger than for the atom to which they were attached. The non-hydrogen atoms were refined anisotropically. After full-matrix refinement the final R indices [$I > 2\sigma(I)$] were $R_1 = 3.73\%$ and $wR_2 = 12.55\%$, and R indices (all data) were $R_1 = 4.35\%$, $wR_2 = 13.04\%$. The maximum and minimum excursions in the final $F_o - F_c$ difference map were 0.239 and -0.209 e Å^{-3}. All calculations were performed on a Silicon Graphics R4000 computer.†

X-Ray crystal structure determination of compound 15b
Good quality yellow crystals of compound **15b** were grown from methanol at ambient temperature. The crystal used for data collection had the approximate dimensions $0.548 \times 0.52 \times 0.55$ mm. The crystal was orthorhombic with space group *Pbca* and had unit cell parameters $a = 10.5530(10)$, $b = 11.325(2)$, $c = 31.424(3)$ Å. Reflections were collected on an Enraf-Nonius CAD4F four circle diffractometer, using graphite monochromated Mo-Kα radiation, $\lambda = 0.710\,69$ Å. The criterion which qualified a reflection for observation was $I > 2\sigma(I)$ and 2325 reflections satisfied this condition. The calculated density was 1.476 Mg m^{-3} and $Z = 8$. The absorption coefficient was 2.414 mm^{-1} and the theta range for data collection was 2.32 to $27.97°$. The total number of independent reflections was 4508 [R(int) $= 0.0133$]. The structure was solved by direct methods, SHELXS-86,[18] and refined by full-matrix least-squares using SHELXL-93.[19] SHELX operations were rendered paperless using ORTEX which was also used to obtain the drawings.[20] Data were corrected for Lorentz and polarization effects but not for absorption. Hydrogen atoms were included in calculated positions with thermal parameters 30% larger than for the atom to which they were attached. The non-hydrogen atoms were refined anisotropically. After full-matrix refinement the final R indices [$I > 2\sigma(I)$] were $R_1 = 4.89\%$ and $wR_2 = 12.86\%$ and R indices (all data) were $R_1 = 10.73\%$, $wR_2 = 14.74\%$. The maximum and minimum excursions in the final F_o - F_c difference map were 0.670 and -0.647 e Å^{-3}. All calculations were performed on a Silicon Graphics R4000 computer.†

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