Resonance-Induced Hydrogen Bonding at Sulfur Acceptors in $R_1R_2C{=}S$ and $R_1CS_2^-$ Systems

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Abstract

The hydrogen-bond acceptor ability of sulfur in C=S systems has been investigated using crystallographic data retrieved from the Cambridge Structural Database and *via ab initio* molecular orbital calculations. The $R_1R_2C{=}S$ bond lengths span a wide range, from 1.58 Å in pure thiones ($R_1 = R_2 = Csp^3$) to 1.75 Å in thioureido species ($R_1 = R_2 = N$) and in dithioates $-CS_2^-$. The frequency of hydrogen-bond formation at =S increases from 4.8% for C=S $\simeq$ 1.63 Å to more than 70% for C=S > 1.70 Å in uncharged species. The effective electronegativity of S is increased by conjugative interactions between C=S and the lone pairs of one or more N substituents (R_1R_2): a clear example of resonance-induced hydrogen bonding. More than 80% of S in $-CS_2^-$ accept hydrogen bonds. C=S···H—N,O bonds are shown to be significantly weaker than their C=O···H—N,O analogues by (*a*) comparing mean S···H and O···H distances (taking account of the differing non-bonded sizes of S and O and using neutron-normalized H positions) and (*b*) comparing frequencies of hydrogen-bond formation in 'competitive' environments, *i.e.* in structures containing both C=S and C=O acceptors. The directional properties and hydrogen-bond coordination numbers of C=S and C=O acceptors have also been compared. There is evidence for lone-pair directionality in both systems, but =S is more likely (17% of cases) than =O (4%) to accept more than two hydrogen bonds. *Ab initio* calculations of residual atomic charges and electrostatic potentials reinforce the crystallographic observations.

1. Introduction

Sulfur compounds are relatively common in biological systems: the amino acids methionine, cysteine and the S—S bridged cystine, together with thiamine (vitamin B_1) and penicillin, are obvious examples. Sulfur compounds are effective as therapeutic agents, particularly derivatives of thiourea and thionucleosides, and also find applications as agrochemicals. To date, however, the molecular recognition properties of sulfur as observed

in crystal structures have seen relatively little systematic study, either in its divalent (*Y*—S—*Z*) state or terminally bonded to C in $R_1R_2C{=}S$ or $R_1CS_2^-$ systems.

Most existing work has centred around the interactions of divalent sulfur with nucleophiles and electrophiles (see *e.g.* Rosenfield, Parthasarathy & Dunitz, 1977; Burling & Goldstein, 1992, 1993). However, to our knowledge, little recent attention has been paid to the most fundamental molecular recognition mechanism: that of hydrogen-bond formation involving C=S or *Y*—S—*Z* sulfurs as acceptors. Many reports of individual crystal structures record the presence of N,OH···S hydrogen bonds and they are noted, at the individual structure level, in early monographs (Pimentel & McClellan, 1960; Hamilton & Ibers, 1968). However, the only reference to a systematic study of the geometrical characteristics of these interactions is by Srinivasan & Chacko (1967). It is, perhaps, this lack of published systematic information that led to minimal coverage of N,OH···S bonds in a recent monograph on hydrogen bonding in biological systems (Jeffrey & Saenger, 1991).

In this paper we use the Cambridge Structural Database system (CSD: Allen *et al.*, 1991) to analyse the geometrical characteristics of inter- and intramolecular N,OH···S=C bonds formed by terminal sulfur. These results are compared with crystallographic data for the analogous N,OH···O=C bonds and results for both systems are related, where relevant, to *ab initio* calculations of residual atomic charges and electrostatic potentials. A similar study of hydrogen-bonded interactions involving divalent sulfur will be presented later (Allen, Bird, Rowland & Raithby, 1997).

2. Methodology

2.1. Database analyses

The October 1994 and April 1995 releases of the Cambridge Structural Database (Releases 5.08 and 5.09: 126,353 and 140,236 entries, respectively) were used in this work. Searches for bonded substructures and for inter- and intramolecular non-bonded contacts were

carried out using the program *QUEST3D* (Cambridge Structural Database, 1994). Data analyses were performed with *VISTA* (Cambridge Structural Database, 1995).

The chemical constitutions of individual search fragments are fully defined in subsequent sections. However, the *total coordination number(s)* is frequently used to define specific atom(s) in search queries. Thus, the nomenclature, *e.g.* N^3, to indicate a three-coordinate nitrogen (inclusive of terminal H atoms where appropriate) is used throughout this paper.

Substructures were only located in CSD entries that satisfied the secondary search criteria: (*a*) organic compounds within CSD chemical class definitions, (*b*) error-free coordinate sets in CSD check procedures, (*c*) no disorder present in the structure, (*d*) contained no polymeric (*catena*) bonds and (*e*) had a crystallographic $R \leq 0.10$. All H atoms involved in non-bonded contact searches were placed in normalized positions, *i.e.* they were positioned on the X-ray determined N—H or O—H vectors at a distance from N,O equal to the appropriate mean bond length established from neutron studies (Allen *et al.*, 1987).

Geometrical analyses for a generalized non-bonded contact C=S···H—D (D = donor) were carried out using the parameters d(CS), the C=S bond length, d(SH), the S···H hydrogen-bond distance, d(SD), the S···D (N,O) distance, and ρ_H, the S···H—D valence angle. For hydrogen bonds to R_1R_2C=S acceptors, the directionality parameters θ and φ were also calculated as illustrated in Fig. 1. Assuming that the S lone pairs lie in the R_1R_2C=S plane, θ measures the angle of elevation of the S···H vector from that plane, while φ represents the angle of rotation from the C=S bond of the projection of the S···H vector onto that plane. In this study there are no stereochemical considerations and absolute values of θ and φ are used throughout. Thus, $|\theta| \simeq 0$ and $|\varphi| \simeq 120°$ describe an S···H vector in which H approaches S close to the lone-pair plane
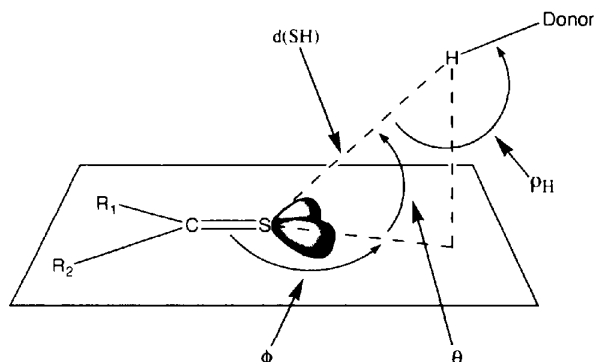

Fig. 1. Definition of geometrical parameters describing hydrogen-bonded fragments. angles θ (angle of elevation from sp^2 lone-pair plane) and φ (angle of rotation from the C=S vector in that plane) are H···· lone-pair directionality parameters (see text).

and at an sp^2 angle of 120° to the C=S bond, *i.e.* close to a putative lone-pair direction. Comparison data for oxygen acceptors have similar mnemonics. For all non-bonded contact searches, the primary distance constraint was placed on S···H (normalized) or O···H (normalized) and required d(SH) or d(OH) to be less than the appropriate sum of van der Waals radii [$v_s = 1.80$, $v_o = 1.52$ (Bondi, 1964); $v_H = 1.10$ Å (Rowland & Taylor, 1996)]. Other constraints required that $90 \leq \rho_H \leq 180°$ and $60 \leq |\varphi| \leq 180°$.

2.2. *Statistical descriptors of geometrical parameter distributions*

Mean values (*m*) of geometrical parameters cited in the text and tables throughout this paper are cited with the e.s.d. (σ) of that mean in parentheses, together with the number of observations (N_{obs}) that contribute to these statistics. The sample standard deviation (*S*) is simply derived as $\sigma N_{obs}^{1/2}$ and limiting values of *ca* $m \pm 3.0S$ may then be used as a guide to the numerical spread in the underlying parameter distribution.

2.3. *Ab initio molecular orbital (MO) calculations*

Ab initio MO calculations for model compounds were carried out to obtain residual atomic charges using the *GAMESS-UK* package (Guest *et al.*, 1993). Closed-shell self-consistent field (restricted Hartree–Fock) calculations were performed using the 6-31G* basis set, with full geometry optimization. Point charges, q_j, were obtained by Mulliken population analysis. Local software was used to compute the electrostatic potential (ep_i kJ mol^{-1}) at various points, *i*, around the S acceptors as

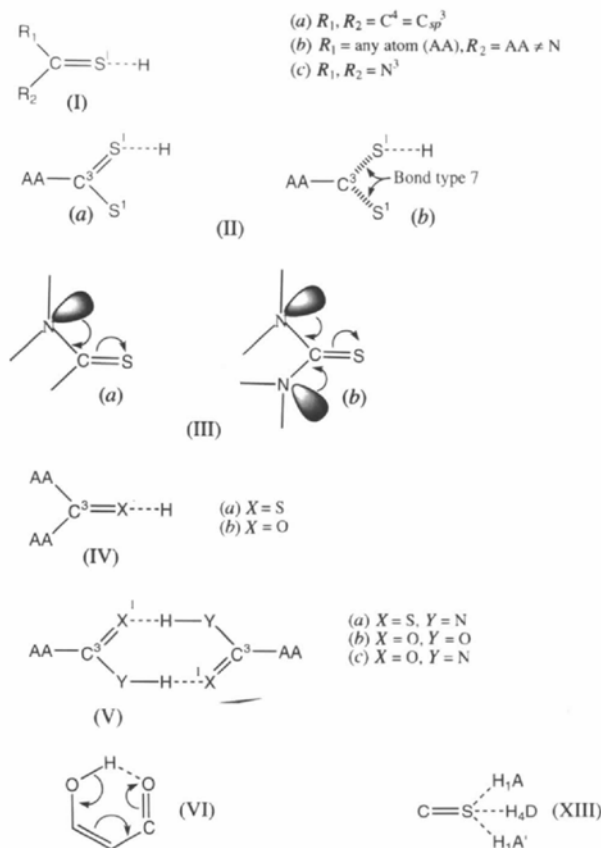$$ep_i = C \sum_{j=1}^{N} q_j/r_{ij},$$ (1)

where the summation is over all *j* atoms of the model compound, r_{ij} is the distance of each atom from the point *i* and the unit conversion constant *C* is 1388.47.

All computations involved in database searches, data analysis and *ab initio* studies were carried out on SUN SparcStations and Silicon Graphics computers on the CCDC Unix Network.

3. C=S bond lengths

The incidence of terminal S is dominated by its occurrence in substructures of the general formula R_1R_2C=S (I) or in dithioates RCS_2^- (II). The σ and π components of the C=S bond are weaker than those in the analogous C=O bond. Further, the electronegativity of S [2.41, 2.58, 2.44: Mulliken (1934, 1935), Pauling (1960), Allred & Rochow (1958), respectively] is much lower than for O (3.17, 3.44, 3.50) and is very similar to that of C (2.63, 2.55, 2.50). For these reasons, the C=S bond

(a) is known to span a much broader distance range than C=O (Abrahams, 1956; Allen *et al.*, 1987) and (b) is likely to be less polar than $>C^{\delta+}=O^{\delta-}$ and, hence, the =S atom is likely to be a weaker hydrogen-bond acceptor than =O.

(a) $R_1, R_2 = C^4 = C_{sp^3}$
(b) R_1 = any atom (AA), $R_2 = AA \neq N$
(c) $R_1, R_2 = N^3$

character; C=S bond lengths of *ca* 1.74 Å are cited as representing *ca* 50% double-bond character. Given the lack of X-ray results for pure thioketones, a value of 1.61 Å is a reasonable baseline from which to assess the effects of conjugation on C=S in other substructures of Table 1. The comparable baseline for C=O in ketones $(Csp^3)_2$ C=O is taken as 1.210 (1) Å (Table 1).

In all but one of the major R_1R_2C=S subgroups of Table 1 the two R substituents are associated with either lone-pair or π density. Three-coordinate nitrogen (N^3) is a substituent in five of the six major subgroups and appreciable conjugative shortening is observed for N^3—C single bonds in N^3C=S systems, by comparison with N^3C=O analogues. This comparative shortening (Δ_2, Table 1) is also remarkably constant at 0.024 (four times) and 0.029 Å (in the N^3, C^4 class). The comparative shortening of R_2—C single bonds for $R_2 = C^3$ or O^2 in N^3R_2C=S systems is negligible in light of the e.s.d.'s obtained, but is appreciable (0.017 Å) for the $R_2 = S^2$, $R_1 = N^3$ system. However, when $R_1 = R_2 = C^3$ the extended conjugated system yields a C^3—C=S single bond shortening of 0.016 Å by comparison with C=O analogues.

The mean C=S bond length itself is remarkably constant [1.654 (2)–1.665 (2) Å], with the exception of the thiourea and thioureido system (I*c*), where the bond length increases to 1.681 (1) Å. Nevertheless, all these bond lengths are from 0.04 to 0.07 Å longer than the pure C=S baseline value of 1.61 Å. For the C=O systems all the mean double-bond lengths lie within the narrow range 1.209 (2)–1.231 (1) Å, a maximum lengthening of only 0.02 Å from the baseline C=O value of 1.210 Å. Unsurprisingly, the spread of C=S bond lengths, defined in terms of the difference between upper and lower deciles of each distribution, is as high as 0.08 Å and is always larger than for C=O bond lengths (Δ_1, Table 1).

Point (a) is clearly illustrated by the composite histogram (Fig. 2) of C=S bond lengths observed in substructures (I) and (II). There is overlap between data from the two classes and the small dithioate area is highlighted. The overall distribution of Fig. 2 is near normal with a mean C=S distance of 1.670 (1) Å. We now analyse the chemical constitution of substructures that contribute to Fig. 2 to provide experimental evidence for point (b).

3.1. *Mean bond lengths in R_1R_2C=S systems*

Table 1 compares mean geometries for X = S or O variants of R_1R_2C=X substructures. There are very few thioketones (I*a*) and a mean C=S of 1.59 (2) Å is obtained for only three contributors. Gas-phase data for thioformaldehyde, H_2C=S, gives C=S as 1.61 Å (Johnson, Powell & Kirchoff, 1971), while a value of 1.597 Å is given by *ab initio* calculations (6-31G* level: Fausto, Batista da Carvalho, Teixeira-Dias & Ramos, 1989). A C=S bond length of 1.61 Å is also cited by Abrahams (1956) as representing 100% double-bond
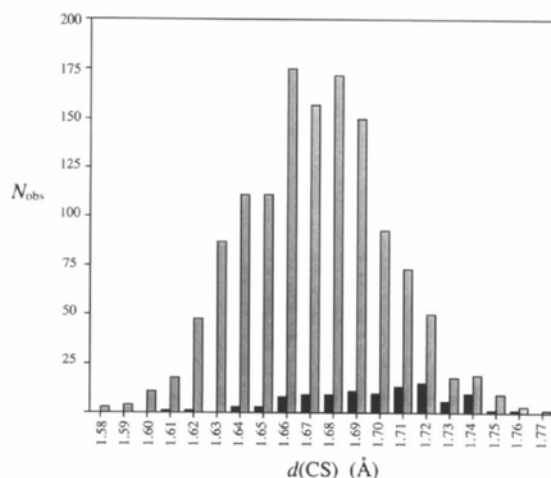

Fig. 2. Histogram of C=S bond lengths, d(CS) for >C=S (thiones and thioureido systems, hatched bars) and —CS_2^- (diothiolates, black bars).

Table 1. *Comparative mean bond lengths [Å, e.s.d.'s in parentheses (see Methodology)] in $R_1R_2C{=}X$ systems for $X = S$ or O*

Data are given for major R_1, R_2 subgroups located in the CSD. Substituents R_1, R_2 are denoted by e.g. C^n, where n is the 'total coordination number' (including H) of the C atom; thus C^3 is sp^2 carbon. N_{obs} is the number of observations. When $R_1 = R_2$, the mean $C{-}R_1, R_2$ distance is averaged over $2N_{obs}$ contributors. Lower and upper decile values (l.d. and u.d.) are given for the $C{=}X$ distributions, thus the spread, $Q = $ u.d. $-$ l.d., encompasses 80% of the observations in each case. Parameter Δ_1 is Q(sulfur) $- Q$(oxygen). Parameter Δ_2 is the difference between the mean $N^3{-}C$ single bond lengths for $X = S$ and $X = O$.

X	R_1	R_2	N_{obs}	$\langle C{-}R_1\rangle$	$\langle C{-}R_2\rangle$	$\langle C{=}X\rangle$	l.d.	u.d.	Q	Δ_1	Δ_2
S	C^4	C^4	3	1.534 (10)		1.59 (2)	—	—	—	—	—
O	C^4	C^4	3180	1.512 (1)		1.210 (1)	1.095	1.122	0.027	—	—
S	N^3	N^3	323	1.349 (1)		1.681 (1)	1.651	1.708	0.057	0.017	−0.024
O	N^3	N^3	1774	1.373 (1)		1.221 (1)	1.204	1.244	0.040	—	—
S	N^3	S^2	171	1.346 (2)	1.758 (2)	1.658 (1)	1.633	1.681	0.048	0.011	−0.024
O	N^3	S^2	42	1.370 (3)	1.775 (3)	1.209 (2)	1.190	1.227	0.037	—	—
S	N^3	C^3	184	1.346 (2)	1.471 (3)	1.665 (2)	1.638	1.690	0.052	0.009	−0.024
O	N^3	C^3	3797	1.370 (1)	1.473 (1)	1.226 (1)	1.205	1.248	0.043	—	—
S	N^3	C^4	77	1.322 (2)	1.516 (2)	1.654 (2)	1.628	1.678	0.050	0.010	−0.029
O	N^3	C^4	6739	1.351 (1)	1.518 (1)	1.224 (1)	1.202	1.242	0.040	—	—
S	C^3	C^3	29	1.459 (5)		1.655 (5)	1.610	1.691	0.081	0.029	—
O	C^3	C^3	2876	1.475 (1)		1.231 (1)	1.208	1.260	0.052	—	—
S	N^3	O^2	42	1.331 (4)	1.339 (3)	1.658 (3)	1.622	1.679	0.057	0.020	−0.024
O	N^3	O^2	1178	1.355 (1)	1.345 (1)	1.208 (1)	1.190	1.227	0.037	—	—

We also note that there is a clear relationship between the lengths, d(CN) and d(CS), of the formally single and double bonds in $N^3C{=}S$ systems. The linear relationship between the N—C and C=O bond lengths in urea and ureido systems, $(N^3)_2C{=}O$, is well known (Blessing, 1983) and, in Fig. 3, we show this relationship for (a) $(N^3)_2C{=}S$ and (b) $(N^3)_2C{=}O$ systems using currently available CSD data. In these plots C=O or C=S distances are plotted against the mean N^3—C single-bond length, d(CN), from each available substructure. Correlation coefficients linking N^3—C and C=X are relatively high (−0.752 for X = O, −0.771 for X = S).

In summary, then, the data of Table 1 indicate three distinct subsets of C=S bonds in $R_1R_2C{=}S$ systems, for which overall mean values are collected in Table 2(a). These subsets are denoted as thioketones (Ia): short (pure) C=S bonds at 1.59 (2) Å; thiones (Ib): intermediate bonds at 1.659 (1) Å, in which $(N^3)_2C{=}S$ systems are excluded; thioureido species (Ic): long bonds in $(N^3)_2C{=}S$ systems at 1.681 (1) Å. A single R_1 = N^3 substituent is ubiquitous in the thione subset (Ib) and the positive mesomeric influence of N^3 (see IIIa,b) illustrates the increasing delocalization in passing from bonds in subset (Ia) to those in subset (Ic). Thus, C=S bonds appear to rely on the +M influence of substituents R_1, R_2 to generate a $\delta-$ charge on S. This contrasts with the analogous C=O systems where resonance effects simply reinforce an existing $\delta-$ charge on O that is primarily induced by its electronegativity difference with carbon.

3.2. Mean bond lengths in dithioates

A total of 76 dithioates R_1—CS_2^- (II) were located within the CSD search criteria given above. The sample is dominated by R_1 = N^3 systems (42 examples) and
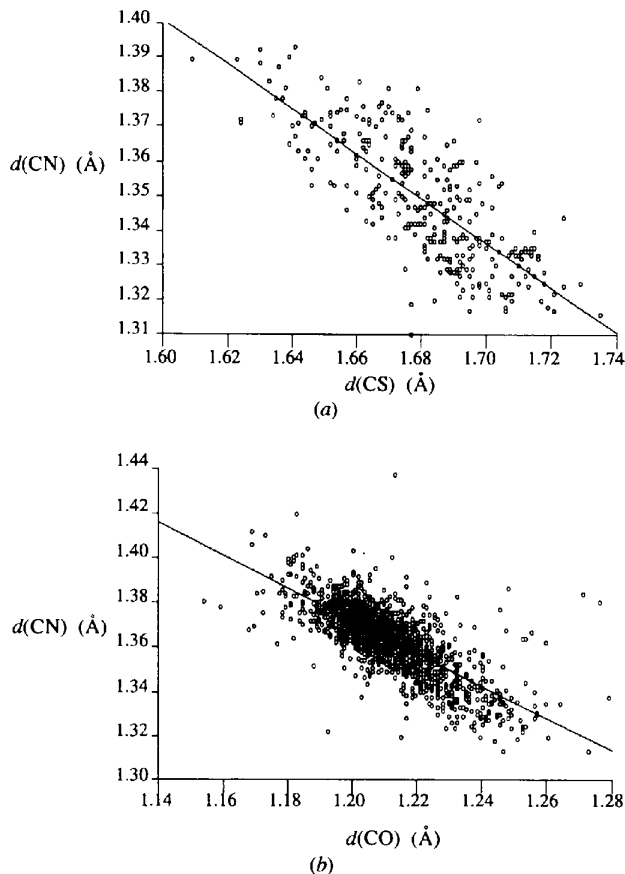

Fig. 3. Scatterplots of C—N bond lengths [d(CN)] *versus* C=S or C=O bond lengths [d(CS) or d(CO)] in (a) thiourea and thioureido compounds, $(N^3)_2C{=}S$, and (b) urea and ureido compounds, $(N^3)_2C{=}O$. The least-squares regression line is shown on both plots.

Table 2. *Summary of mean C=S bond lengths [d(CS) in Å, e.s.d.'s in parentheses (see Methodology)] in various chemical environments*

Lower and upper decile values (l.d., u.d.) and the spread of each distribution, $Q = $ u.d. $-$ l.d., are also given (in Å).

Bond	N_{obs}	$\langle d(CS) \rangle$	l.d.	u.d.	Q
(a) C=S in R_1R_2C=S systems					
In thioketones (I*a*)	3	1.59 (2)	—	—	—
In thiones (I*b*)	980	1.659 (1)	1.623	1.691	0.068
In thioureido species (I*c*)	322	1.681 (1)	1.651	1.708	0.057
(b) C=S in dithioates, CSS⁻ (II)					
In C³—CSS⁻	20	1.685 (4)	1.662	1.707	0.045
In N³—CSS⁻	84	1.708 (3)	1.658	1.727	0.069
Overall	152	1.694 (3)	1.657	1.725	0.068

$R_1 = C^3$ (ten examples), for which mean bond lengths for the 84 and 20 partial C=S double bonds are given in Table 2(*b*). For comparison with Table 1, the R_1 single bonds have mean values of 1.354 (5) Å for $R_1 = N^3$ and 1.493 (5) Å for $R_1 = C^3$. The mean C=S bond in C^3 systems is almost identical to that in the thioureido subset (I*c*). However, it is 0.030 Å longer than the mean value in $(C^3)_2$C=S systems, a more appropriate comparator. Similarly, the mean C=S bond length in N^3—CS_2^- systems exceeds that in $(N^3)_2$C=S systems by 0.027 Å.

4. Intermolecular hydrogen bonding to C=S acceptors

4.1. *Searches and geometrical results for hydrogen-bonded systems*

Mean values of the geometrical descriptors (defined in Fig. 1 and in the *Methodology*) for hydrogen bonds to terminal sulfur are collected in Table 3. Here, the C=S acceptors are subdivided as (*a*) thiones, as defined in substructure (I*b*), (*b*) thioureido compounds (I*c*) and (*c*) the dithioates of substructure (II). Superscripts against element symbols in (I) and (II) are the total coordination numbers (see *Methodology*) required in the search. Variable bond-type coding is required in (II) so as to locate dithioates encoded either as (a) S—C=S or (*b*) S⋯C⋯S (CSD bond type 7 represents a delocalized double bond).

In Table 4, (*a*) and (*b*), we compare overall hydrogen-bond geometries for C=S and C=O acceptors using the substructure search fragment (IV). This formulation will include all hydrogen bonds to thiones (ketones), together with those to the C=S (C=O) bonds of dithioates (carboxylates) that are encoded as (O)S—C=S(O) in the CSD. Thus, hydrogen bonds to dithioates (carboxylates) encoded with delocalized double bonds (O)S⋯C⋯S(O) are not included in Table 4. Table 4 also includes data for subsets of hydrogen bonds that are [Table 4, (*c*) and (*d*)] and are not [Table 4, (*e*) and (*f*)] involved in the common hydrogen-bonded motifs depicted in (V).

4.2. *The C=S bond length in C=S⋯H—N,O systems*

Table 3 gives mean values of $d(CS)$, the length of C=S bonds that are actually involved in hydrogen bonding. Comparison of these values with the overall mean C=S bond lengths cited in Tables 1 and 2 indicate that only the longer C=S bonds appear to be involved in hydrogen bonding. This observation is examined in more detail in Table 5, which subdivides hydrogen-bonded C=S⋯H—N,O systems according to some of the major subgroups of Table 1 and in Table 6 which presents hydrogen-bond frequency data for the complete C=S bond-length range. Distributions n_2 and n_3 of Table 6 are also presented in the histogram in Fig. 4 for visualization purposes. Table 5 shows that mean values of the C=S bond length in hydrogen-bonded systems ($<$C=S$>_3$) significantly exceed the overall mean values ($<$C=S$>_1$) for all the substructural subdivisions. Indeed, values of $\Delta = <$C=S$>_3 - <$C=S$>_1$ increase over the three basic classes of C=S bonds identified in Table 2, *i.e.* Δ increases as the C=S bond length increases. Further, the percentage of C=S acceptors that form hydrogen bonds (n_3/n_2, Table 5) also increases significantly for each of these major subdivisions. Thus, Δ:$<$C=S$>_1$:n_3/n_2 (%) triplets for (*a*) thiones, (*b*) thioureido compounds and (*c*) dithioates are: (*a*) 0.014:1.659:51.9; (*b*) 0.017:1.681:61.1; (*c*) 0.023:1.694:82.7.

These points are further reinforced by the data of Table 6 and Fig. 4, in which n_3 represents numbers of unique C=S bonds that are involved in hydrogen bonding. This number is lower than the number of hydrogen bonds actually formed, since C=S sulfurs are often coordinated by more than one donor H atom, as described later. Table 6 and Fig. 4 clearly show (i) that the percentage of hydrogen bonds formed by C=S sulfurs increases systematically from 5 to 75% as the C=S bond length increases from 1.63 to 1.75 Å and (ii) that the mean C=S bond length in C=S⋯H—N,O systems, $<$C=S$>_3$, exceeds the overall mean $<$C=S$>_1$ by 0.019 Å and exceeds $<$C=S$>_2$, the overall mean value in structures that also have O—H or N—H donors, by 0.011 Å. In Table 6, however, both $<$C=S$>_1$ and $<$C=S$>_2$ include the hydrogen-bonded subset. If these $\Sigma n_3 = 453$ bonds are removed from these averages, we obtain 'corrected' values of $<$C=S$>_1$ and $<$C=S$>_2$, *i.e.* C=S that are *not* involved in hydrogen bonding, of 1.663 (1) and 1.667 (1) Å, respectively. The $<$C=S$>_3$ (hydrogen-bonded) value now exceeds these values by more than 0.02 Å, a very significant elongation in view of the large number of contributors and the low e.s.d.'s obtained for these means.

4.3. *N—C bond lengths in $>$N—C=S acceptors*

We have already discussed (see Table 1) the greater importance of resonance forms (III*a,b*) in the structures of thioamides and thioureido compounds by comparison with their oxygen analogues: there is a significant

Table 3. *Mean values ($\mathring{A}$, °) of geometrical descriptors (Fig. 1), with e.s.d.'s in parentheses (see Methodology) for intermolecular [(a)–(c)] and intramolecular [(d)] hydrogen bonds to terminal sulfur*

N_{obs} is the number of observations, r is the correlation coefficient linking d(SH) and ρ_H.

Donor	N_{obs}	$\langle d(SH) \rangle$	$\langle d(SD) \rangle$	$\langle d(CS) \rangle$	$\langle \rho_H \rangle$	$\langle |\theta| \rangle$	$\langle |\varphi| \rangle$	$r[d(SH),\rho_H]$
(a) Thione acceptors: $R_1R_2C{=}S$ [substructure (Ib)]								
O—H	71	2.42 (2)	3.32 (1)	1.682 (2)	156 (2)	40 (3)	112 (3)	−0.718
N—H	492	2.50 (1)	3.43 (1)	1.690 (1)	157 (1)	28 (1)	110 (1)	−0.665
Major N—H donor subgroups								
—NH$_2$	71	2.53 (2)	3.46 (2)	1.683 (2)	158 (2)	24 (3)	113 (3)	−0.623
>NH	146	2.46 (1)	3.40 (1)	1.676 (2)	158 (1)	24 (2)	111 (1)	−0.720
N$^+$—H	40	2.51 (3)	3.36 (2)	1.699 (3)	147 (3)	27 (4)	98 (4)	−0.889
N—NH	89	2.56 (2)	3.48 (1)	1.687 (1)	154 (2)	30 (2)	114 (2)	−0.450
(b) Thioureido acceptors: $(N^3)_2$—C$=$S [substructure (Ic)]								
O—H	35	2.42 (3)	3.31 (2)	1.687 (2)	155 (3)	45 (4)	111 (4)	−0.723
N—H	340	2.51 (1)	3.44 (1)	1.698 (1)	158 (1)	30 (1)	111 (1)	−0.702
(c) Dithioate acceptors: —CSS$^-$ [substructure (II)]								
O—H	106	2.38 (1)	3.31 (1)	1.725 (2)	162 (1)	42 (2)	113 (2)	−0.704
N—H	56	2.51 (2)	3.40 (1)	1.701 (3)	152 (2)	21 (3)	102 (4)	−0.764
(d) Intramolecular hydrogen bonds to thiones and dithioates								
N,O—H	86	2.30 (3)	2.98 (2)	1.675 (2)	127 (2)	8 (1)	79 (1)	—

Table 4. *Comparison of mean values ($\mathring{A}$, °) of geometrical descriptors (Fig. 1, e.s.d.'s in parentheses, see Methodology) for intermolecular hydrogen bonds to C$=$S and C$=$O acceptors*

N_{obs} is the number of observations.

Donor	N_{obs}	$\langle d(SH) \rangle$ or $\langle d(OH) \rangle$	$\langle d(SD) \rangle$ or $\langle d(OD) \rangle$	$\langle \rho_H \rangle$	$\langle |\theta| \rangle$	$\langle |\varphi| \rangle$
(a) All C$=$S acceptors [substructure (IVa)]						
O—H	119	2.41 (1)	3.32 (1)	157 (1)	41 (2)	112 (2)
N—H	530	2.51 (1)	3.43 (1)	157 (1)	28 (1)	111 (1)
(b) All C$=$O acceptors [substructure (IVb)]						
O—H	5861	1.884 (2)	2.790 (2)	158.2 (2)	18.3 (2)	135.3 (2)
N—H	7014	2.011 (2)	2.931 (2)	156.2 (2)	20.0 (2)	139.9 (2)
(c) C$=$S in hydrogen-bonded motif [substructure (Va)]						
N—H	216	2.43 (7)	3.40 (1)	167 (1)	15 (9)	109 (1)
(d) C$=$O in hydrogen-bonded motifs [substructures (Vb,c)]						
O—H	607	1.692 (3)	2.220 (1)	169.1 (4)	5.2 (2)	123.2 (2)
N—H	1023	1.918 (4)	2.266 (1)	166.7 (3)	9.5 (2)	124.6 (2)
(e) C$=$S acceptors (IVa) not in hydrogen-bonded motifs						
O—H	119	2.41 (1)	3.32 (1)	157 (1)	41 (2)	112 (2)
N—H	132	2.54 (1)	3.44 (1)	151 (1)	34 (2)	113 (2)
(f) C$=$O acceptors (IVb) not in hydrogen-bonded motifs						
O—H	5101	1.909 (3)	2.808 (2)	156.9 (3)	20.1 (2)	136.9 (3)
N—H	5358	2.028 (3)	2.936 (2)	154.1 (2)	22.0 (2)	143.3 (3)

Table 5. *Comparison of C$=$S bond lengths in hydrogen-bonded and non-hydrogen-bonded examples of $R_1R_2C{=}S$ substructures (Ib,c) and (II)*

AA in substructure definitions means any non-H atom; element symbol superscripts are defined in Table 1. n_x are, respectively: n_1 the total number of CSD entries in the class, n_2 the number that also contain N—H or O—H donor groups and n_3 the number having C$=$S$\cdots$H—N,O hydrogen bonds. $\langle C{=}S \rangle_x$ and $\langle N{-}C \rangle_x$ (where relevant) are mean bond lengths in $\mathring{A}$ (e.s.d.'s in parentheses) for entries in group x.

Class	R_1	R_2	n_1	n_2	n_3	n_3/n_2 (%)	$\langle C{=}S \rangle_1$	$\langle C{=}S \rangle_3$	$\langle N{=}C \rangle_1$	$\langle N{=}C \rangle_3$
(II)	AA	S$^-$	76	52	43	82.7	1.694 (3)	1.717 (2)	—	—
(Ic)	N^3	N^3	295	247	153	61.1	1.681 (1)	1.698 (1)	1.349 (1)	1.335 (1)
(Ib):1	N^3	S^2,O^2	174	62	38	61.3	1.658 (1)	1.674 (1)	1.343 (1)	1.327 (1)
(Ib):2	N^3	C^3	145	110	53	48.2	1.665 (2)	1.676 (1)	1.346 (2)	1.346 (3)
(Ib):3	N^3	C^4	62	44	22	50.0	1.654 (2)	1.665 (3)	1.322 (2)	1.322 (3)
(Ib):4	C,O	C,O	63	15	7	46.7	1.651 (3)	1.674 (7)	—	—
(Ib):1–4	—	—	444	231	123	51.9	1.659 (1)	1.673 (2)	—	—

Table 6. *$C=S$ bond frequencies for 0.01 Å ranges of the $C=S$ bond length*

n_1 includes all $C=S$ bonds, n_2 is the number of $C=S$ bonds in entries that contain O—H or N—H donors, n_3 is the number of unique $C=S$ bonds that form hydrogen bonds. In the summary statistics l.d. and u.d. are the lower and upper decile limits. All bond lengths are in Å with e.s.d.'s in parentheses for mean values (see *Methodology*). N_{obs} is the total number of observations in each distribution.

Range	n_1	n_2	n_3	n_3/n_2 (%)
1.58–1.59	7	1	0	0.0
1.59–1.60	6	1	0	0.0
1.60–1.61	13	3	0	0.0
1.61–1.62	37	13	0	0.0
1.62–1.63	78	26	0	0.0
1.63–1.64	120	42	2	4.8
1.64–1.65	130	68	16	23.5
1.65–1.66	187	90	33	36.7
1.66–1.67	194	111	52	46.8
1.67–1.68	216	139	75	54.0
1.68–1.69	165	127	77	60.6
1.69–1.70	137	102	57	55.9
1.70–1.71	89	69	48	69.6
1.71–1.72	74	62	45	72.6
1.72–1.73	35	31	23	74.2
1.73–1.74	17	14	10	71.4
1.74–1.75	18	16	12	75.0
1.75–1.76	11	9	3	33.3
1.76–1.77	5	3	0	0.0

Summary statistics (all data)

N_{obs}	1539	927	453	48.9
$\langle C=S \rangle$	1.670 (1)	1.678 (1)	1.689 (1)	—
Median	1.669	1.678	1.686	—
l.d.	1.630	1.640	1.658	—
u.d.	1.710	1.716	1.722	—

foreshortening of >N—C single bonds in >N—C=S systems compared with >N—C=O systems. At the same time (Table 1) the associated $C=S$ bonds are considerably elongated, with the >N—C and $C=S$ bonds in thioureido species showing the linear dependency of Fig. 2(a).

Given these facts, together with the observation that $C=S\cdots H$ hydrogen bonds tend to form to the longer $C=S$ bonds, it is of interest to see if there is a further foreshortening of >N—C bonds in >N—C=S$\cdots$H systems. Table 5 compares mean values of >N—C bonds in hydrogen-bonded systems, <N—C>$_3$, with overall mean values, <N—C>$_1$, for four chemical subgroups of substructure (I). In two classes in Table 5, additional foreshortenings of 0.014 and 0.016 Å are observed, while for two further classes the two means are identical. Because of the ubiquity of N^3 as a >C=S substituent, we have further examined all >N—C=S systems within an R-factor limit of 0.075: (a) those systems that do form S$\cdots$H—N,O hydrogen bonds and (b) those that do not. For 545 instances of (a) the mean >N—C distance of 1.341 (1) Å is 0.010 Å shorter than the mean of 1.351 (1) Å for 726 instances of (b). The mean $C=S$ distances, 1.684 (1) for (a) and 1.665 (1) Å for (b), differ by 0.019 Å in this sample.

4.4. *Resonance-induced hydrogen bonding at* >$C=S$ *acceptors*

Gilli, Bellucci, Ferretti & Bertolasi (1989) and Bertolasi, Gilli, Ferretti & Gilli (1991) have drawn attention to the crucial importance of resonance in the formation of strong homonuclear (*e.g.* O—H$\cdots$O and N—H$\cdots$N) hydrogen bonds and have pointed out that resonance is also important in heteronuclear systems (*e.g.* N—H$\cdots$O). Specifically, their detailed study of enolones (VI) and related substructures shows that resonance enhances the δ^- charge on $=$O and the δ^+ charge on H, leading to a strengthening of the hydrogen bond O$\cdots$H.

Mechanism (VI) is termed resonance-assisted hydrogen bonding and these authors (Gilli, Bellucci, Ferretti & Bertolasi, 1989) generalize their findings to heteroconjugated systems, such as amides $R_1NH(R_2)C=O$. These are, of course, the oxy analogues of the $R_1NH(R_2)C=S$ and $(RNH)_2C=S$ systems (I*b*,*c*) that dominate our subsets of $C=S$ acceptors. The data on N—C and $C=S$ bond lengths in N—C=S$\cdots$H hydrogen-bonded systems (Tables 5 and 6; Fig. 6) indicate that resonance mechanisms (III*a*,*b*) do not merely assist hydrogen-bond formation: given the minimal electronegativity difference between S and C, the resonance effects alone are primarily responsible for inducing the δ negativity at S in $C=S$ bonds in these systems. It is reasonable, then, to describe hydrogen bonding to $C=S$ sulfur centres as being resonance-induced rather than resonance-assisted. To check the validity of this description, we have carried out *ab initio* molecular orbital calculations for a variety of model compounds containing >$C=S$ or >$C=O$ bonds in appropriate environments.
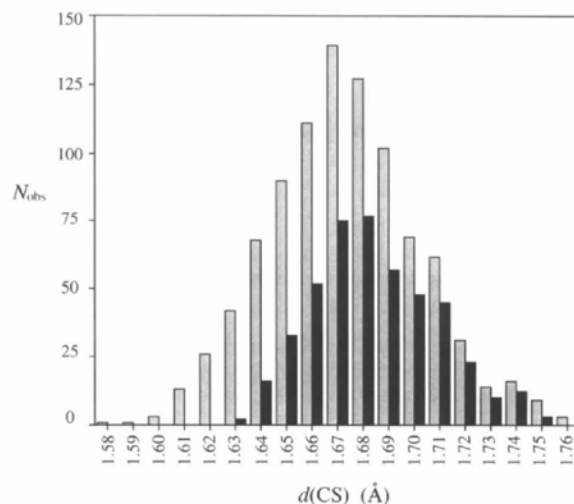

Fig. 4. Comparative histogram of >$C=S$ bond lengths for $C=S$ bonds in potential hydrogen-bonding environments (hatched bars) and $C=S$ bonds that take part in $C=S\cdots H$—(N or O) hydrogen bonds (black bars).

4.5. Molecular orbital calculations for >C=S and >C=O systems

Ab initio molecular orbital calculations (see *Methodology*) were carried out for six pairs of model compounds [Fig. 5, (VII)–(XII): denoted as (*a*) for the C=S compounds and (*b*) for the C=O analogues]. The models extend from (thio) formaldehyde (VII*a*,*b*) to (thio) urea (XII*a*,*b*). Between these symmetrical extremes, we have chosen four models of general formula $NH_2(R)C=S,O$, where R is successively —H, —OCH$_3$, —SCH$_3$ and —C(sp^2)CH$_3$. Residual atomic charges for all model compounds are given in Fig. 5. From these data, and using equation (1), we have also calculated the electrostatic potential (*ep*) that is encountered by a donor H atom approaching =S or =O along the assumed S,O-lone-pair vectors. These vectors are taken as lying in the >C=S,O plane and at C—(S,O)—(lone pair) angles of 120°, as indicated for (VIII*a*,*b*) (Fig. 5). Values of ep_i were calculated at points (*i*) along these vectors that were 2.4 Å from S and 2.2 Å from O. For the unsymmetrical model compounds (VIII)–(XI) values of ep_i will differ for the H-atom approach to the lone pairs that are *syn* or *anti* to the C—NH$_2$ substitutent bond. Values of ep_i are reported in Table 7, together with the C=S or C=O, C—N and C—R bond lengths given by the *ab initio* optimization at the 6-31G* level.

Despite the use of simple model compounds, the results of Fig. 5 and Table 7 are in good agreement with the crystallographic observations that are obtained from a wide spectrum of chemical environments. Thus, Fig. 5 shows that =S in (VII*a*) is almost neutral, in contrast to the –0.416e for the more electronegative =O in (VII*b*). However, the addition of an amino group in (VIII*a*)–(XI*a*) induces a negative charge on =S of between –0.270 to –0.322e. The effect of —NH$_2$ substitution in (VIII*b*)–(XI*b*) also induces an increased negative charge on =O, but not to the extent exhibited in the =S analogues. Nevertheless, the =O compounds are significantly better H acceptors than the =S analogues. The addition of a second —NH$_2$ substituent in (XII) induces further negativity at (*a*) =S (to –0.390e), but has a less noticeable effect at (*b*) =O.

The resonance effects are clearly reflected in the *ab initio* optimized bond lengths of Table 7, which agree well with the crystallographic results of Table 1. The pure C=S double bond in (VII) (1.597 Å) increases for monoamines $NH_2(R)C=S$ to 1.641 Å in (VIII) (R = H) and 1.658–1.668 Å for (IX)–(XI) (R = O, S, Csp^2). There is a further increase in thiourea (XII*a*) to 1.681 Å, a value that is almost identical to the crystallographic mean of 1.683 (1) Å (Table 1). Values of the C—N bond length show similar agreement between *ab initio* and crystallographic results.
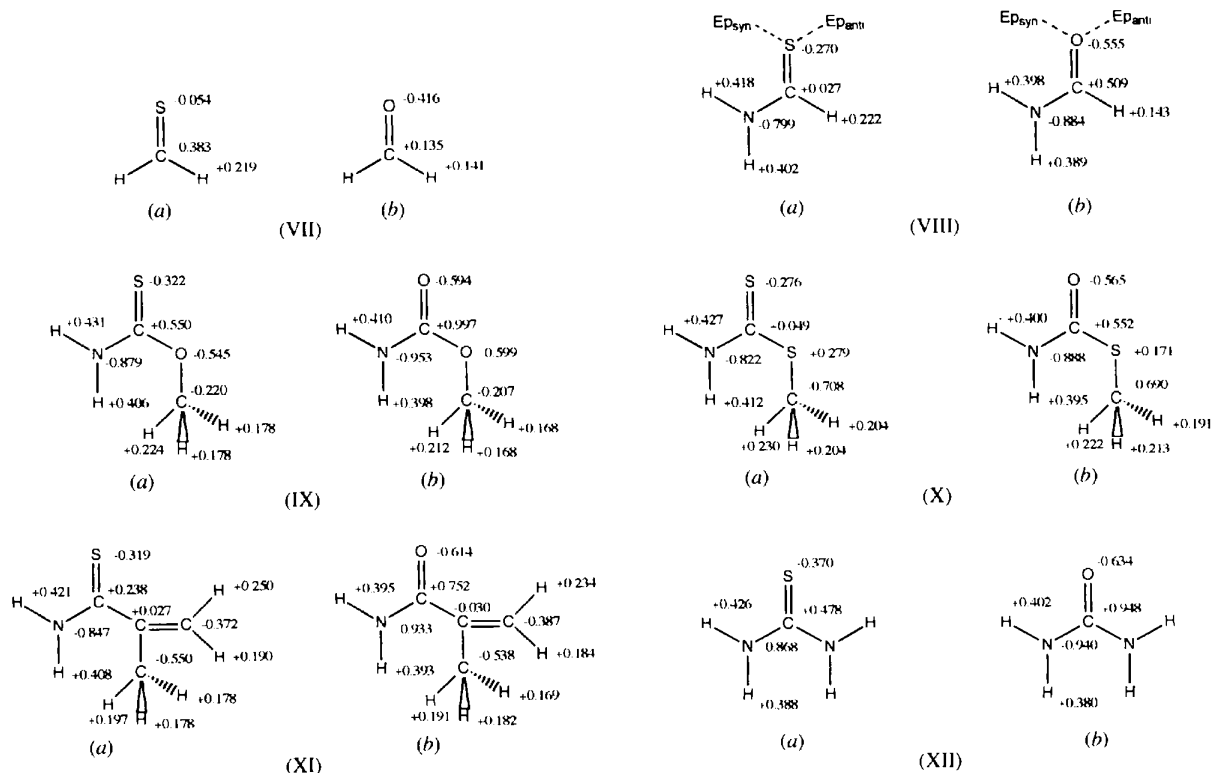

Fig. 5. Residual atomic charges (*ab initio* MO calculations, Mulliken population analysis) for a series of model molecules containing (*a*) >C=S systems and (*b*) their >C=O analogues.

Values of the electrostatic potential (ep_i, Table 7) are, as expected, always lower for the $=S$ analogues (VIIa–XIIa). Indeed, it is only for the monoamines (Xa), (XIa) and for thiourea (XIIa) that ep_i values for S begin to approach those for the O atom of formaldehyde (VIIb): only when $>C=S$ is involved in an extended conjugated system can the S atom exhibit a hydrogen-bonding potential that approaches that attained by $=O$ simply as a result of its inherent high electronegativity relative to C.

4.6. Hydrogen-bond ($H \cdots S$) distances to $C=S$ acceptors

A histogram of the 649 normalized intermolecular $d(SH)$ values of Table 4(a) is shown in Fig. 6. Some 85% of these values fall within a major peak in the histogram that spans the range 2.28–2.72 Å, an upper limit that is 0.18 Å shorter than the sum of van der Waals radii (2.90 Å). Values of $d(SH)$ for OH donors are consistently shorter than for NH donors [Table 3, (a), (b) and (c)] and $d(SH)$ attains its shortest values for the dithioates of Table 3(c). For the thiones of Table 3(a) it is possible to further subdivide the data for N—H donors. The mean $d(SH)$ for $>NH$ donors at 2.46 (1) Å is significantly shorter than for —N(H)H donors [2.53 (2) Å], in agreement with a variety of studies of N—H$\cdots$O hydrogen-bond geometry (Jeffrey & Maluszynska, 1986; Taylor, Kennard & Versichel, 1984; Jeffrey & Saenger, 1991). Data for N^+—H$\cdots$S are sparse and cannot be further
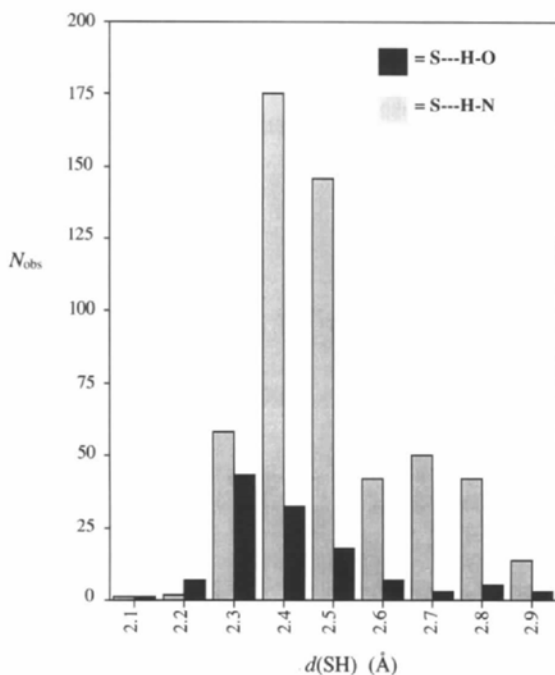
Table 7. *Optimized bond lengths in Å in (VII)–(XII) from ab initio molecular orbital calculations (GAMESS-UK: Guest et al., 1993), together with electrostatic potentials along the presumed S or O lone-pair vectors (ep_i, kJ mol^{-1}, see text)*

$ep_i(syn)$ and $ep_i(anti)$ refer to the lone pairs that are *syn* or *anti* to the —NH$_2$ substituent in (VIII)–(XI). Values that are equal in symmetric molecules are in square brackets.

Molecule	C=S/O	C—N	C—R	$ep_i(syn)$	$ep_i(anti)$
(VIIa)	1.597	—	—	−31.9	[−31.9]
(VIIb)	1.184	—	—	−86.1	[−86.1]
(VIIIa)	1.641	1.324	—	−74.9	−77.8
(VIIIb)	1.193	1.348	—	−111.1	−108.3
(IXa)	1.663	1.335	1.314	−68.0	−126.4
(IXb)	1.189	1.357	1.333	−90.3	−166.6
(Xa)	1.658	1.329	1.759	−81.9	−84.7
(Xb)	1.190	1.358	1.787	−111.1	−115.2
(XIa)	1.668	1.330	1.498	−80.5	−55.5
(XIb)	1.200	1.357	1.507	−111.1	−54.2
(XIIa)	1.683	1.337	[1.337]	−84.7	[−84.7]
(XIIb)	1.202	1.360	[1.360]	−106.9	[−106.9]

subdivided in the manner described by Taylor, Kennard & Versichel (1984) for $C=O$ acceptors. The only other major subgroup involves N—NH donors, where a mean $d(SH)$ of 2.56 (2) Å might imply a reduction in partial positive charge on H, perhaps due to resonance effects.

The comparative $d(SH)/d(OH)$ data of Table 4, (a) and (b), gives some indication of the relative strengths of $C=S\cdots H$ and $C=O\cdots H$ hydrogen bonds. We may compare mean values of $d(SH)$ and $d(OH)$ with the appropriate sums of van der Waals radii [$v_s = 1.80$, $v_o = 1.52$: Bondi, 1964; $v_H = 1.1$ Å: Rowland & Taylor, 1996] *via*

$$\Delta_Y^X = v_X + v_H - d(XH), \qquad (2)$$

where superscript X refers to the acceptor atom (S or O) and subscript Y refers to the H-donor atom (O or N). Thus, $\Delta_o^s = 0.49$ and $\Delta_o^o = 0.74$ Å, while $\Delta_N^s = 0.39$ and $\Delta_N^o = 0.61$. It is clear that hydrogen bonds to $C=O$ acceptors are shorter, relative to van der Waals radii sums, than they are for $C=S$ acceptors. The additional relative shortening, given by $\Delta_o^o - \Delta_o^s = 0.25$ Å or by $\Delta_N^o - \Delta_N^s = 0.22$ Å, is closely consistent for both O—H and N—H donors.

4.7. Donor ($N,O \cdots S$) distances to $C=S$ acceptors

The $d(SD)$ values ($S\cdots O$, $S\cdots N$) of donor N or O atoms from $C=S$ acceptors [Tables 3 and 6(a)] follow the same trends exhibited by the $d(SH)$ values. Again, the relative mean values of $d(SD)$ ($C=S$ acceptors) and $d(OD)$ ($C=O$ acceptors) may be used to assess the relative strengths of $C=S\cdots H$ and $C=O\cdots H$ hydrogen bonds. Here we define

$$\delta_Y^X = v_X + v_Y - d(XY), \qquad (3)$$

Fig. 6. Histogram of $S\cdots H$ distances in the hydrogen-bonded systems $>C—S\cdots H—N$ (hatched bars) and $>C=S\cdots H—O$ (black bars).

where superscript X refers to the acceptor atom (S or O) and subscript Y refers to the donor atom (O or N). Taking $v_s = 1.80$, $v_o = 1.52$, $v_N = 1.55$ Å as van der Waals radii (Bondi, 1964), we obtain $\delta_o^s = 0.0$ and $\delta_N^s = -0.08$, and $\delta_o^o = 0.25$ and $\delta_N^o = 0.14$ Å from the data of Table 6, (a) and (b). Thus, the additional shortening of $d(OD)$ (C=O···O,N systems) relative to $d(SD)$ (C=S···O,N systems) is given by $\delta_o^o - \delta_o^s = 0.25$ or by $\delta_N^o - \delta_N^s = 0.22$ Å, values that are closely consistent with one another and with the Δ-based values obtained above from the $d(SH)/d(OH)$ comparison. Indeed, the near identical relative shortenings obtained from the $d(SD)/d(OD)$ and $d(SH)/d(OH)$ comparisons give confidence to the overall effectiveness of the 'neutron-normalized' H-atom positions used throughout these studies.

4.8. Linearity of C=S···H—N,O hydrogen bonds

The mean hydrogen-bond angle (ρ_H, Fig. 1) for C=S···H—N,O hydrogen bonds is remarkably consistent across the various subsets of Table 3, (a), (b) and (c). The overall mean of $157 (1)°$ [Table 4(a)] is almost identical to values obtained for the C=O acceptor [Table 4(b)]. A histogram of the 649 observed ρ_H values of Table 4(a) is given in Fig. 7(a) and this distribution is replotted in Fig. 7(b) after correction for geometrical factors (Kroon et al., 1975) to show the strong tendency to linearity in C=S···H—N,O systems.

Table 3 also shows that ρ_H is, as expected, highly correlated with the hydrogen-bond distance $d(SH)$. Apart from the small N—NH donor subset, all correlation coefficients $r[d(SH),\rho_H]$ have absolute values that exceed 0.62 and show a mean value of 0.723. The scattergram derived from the data of Table 4(a), with regression line fitted, is shown in Fig. 7(c). The high negative linear correlation coefficient confirms that the hydrogen-bond length decreases (strength increases) as ρ_H moves towards linearity: an observation that is typical of systems involving medium and strong hydrogen bonds.

4.9. Hydrogen-bond directionality at >C=S acceptors

Mean values of the hydrogen-bond directionality parameters, $|\theta|$ and $|\varphi|$ (see Fig. 1), are included in Tables 3 and 4. Mean values of $|\theta|$ for the various C=S···H subgroups of Table 3 range from $21 (3)$ to $45 (4)°$, considerably different from the $|\theta|$ of ca 0 that corresponds to H approach to S in the lone-pair plane. In view of this result, it is perhaps surprising that the mean $|\varphi|$ values are consistently in the narrow range $98 (4)–114 (2)°$, some 10–20° below the $|\varphi| = 120°$ that might be considered to correspond to the position of an idealized S(sp^2) lone pair.

The comparative overall mean $|\theta|$ and $|\varphi|$ values for C=S and C=O acceptors [Table 4, (a) and (b)] show some interesting differences and circular histograms of the complete (symmetrized) distributions are compared

in Figs. 8(a) and 8(b) (θ for C=S, C=O, respectively) and Figs. 8(c) and 8(d) (φ for C=S, C=O, respectively). The θ values for the C=O acceptor show a normal distribution around 0, while the φ distribution for C=O···H systems shows two clear peaks either side of the $\varphi = 180°$ symmetry axis. The overall mean $|\varphi| = 137.8 (2)°$ is some 18° higher than the $|\varphi| = 120°$ that corresponds to the expected position of an O(sp^2)
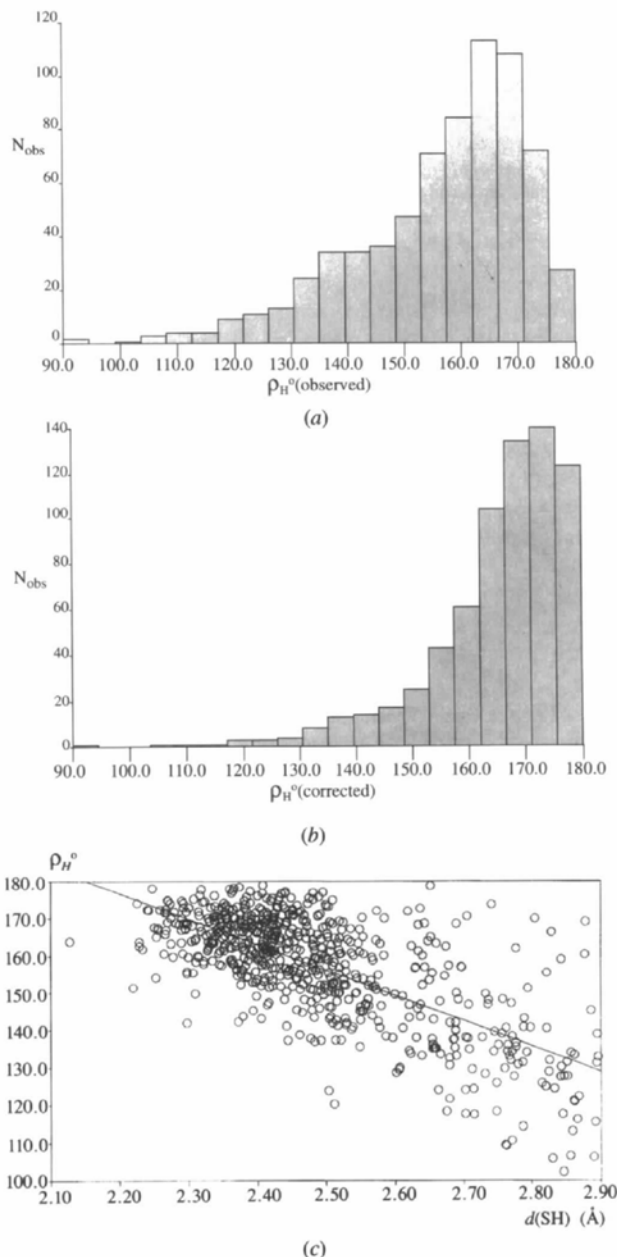

(a)

(b)

(c)

Fig. 7. The hydrogen-bond angle $\rho_H = $ S···H—(N or O): (a) histogram of observed values; (b) the distribution after correction for geometrical factors (Kroon et al., 1975). In frame (c) ρ_H is plotted against the hydrogen bond length [d(SH) in Å].

lone pair. These results are not new, they mirror very closely the results of Murray-Rust & Glusker (1984) and of Taylor, Kennard & Versichel (1984), who cite mean values of $|\theta|$ and $|\varphi|$ of 19.7 and 135.0°, respectively, for 1509 C=O···H—N hydrogen bonds. All these results are accepted as indicating a clear preference for donor H to approach C=O acceptors in a direction that is close to the lone-pair plane and to the positions of expected O lone-pair density in that plane.

The θ and φ distributions for C=S acceptors (Figs. 8a and 8c) appear to be somewhat different to those for C=O acceptors, despite the considerable difference in the number of observations in each case. The symmetrized φ histogram for C=S (Fig. 8a) does show maximum density around 0, but has a very broad population spread out to ~70° with additional small peaks at $|\theta| > 45°$. By contrast, the symmetrized φ distribution for

C=S (Fig. 8c) appears much less diffuse than its C=O counterpart with two very sharp peaks and a mean $|\varphi|$ of 111 (1)°, indicative of lone-pair directions.

We have investigated the effect on hydrogen-bond directionality of two major factors: (a) the presence of common cyclic hydrogen-bonded motifs (V) that involve both C=O and C=S acceptors and (b) our observation that C=S often accepts more than two D—H···S interactions.

4.10. Directionality in cyclic hydrogen-bonded motifs (V)

The carboxylic acid and amido motifs (Vb,c) involving C=O acceptors are commonly observed in crystal structures, while the thioamide motif (Va) is the C=S analogue of (Vc). We do not observe many examples of
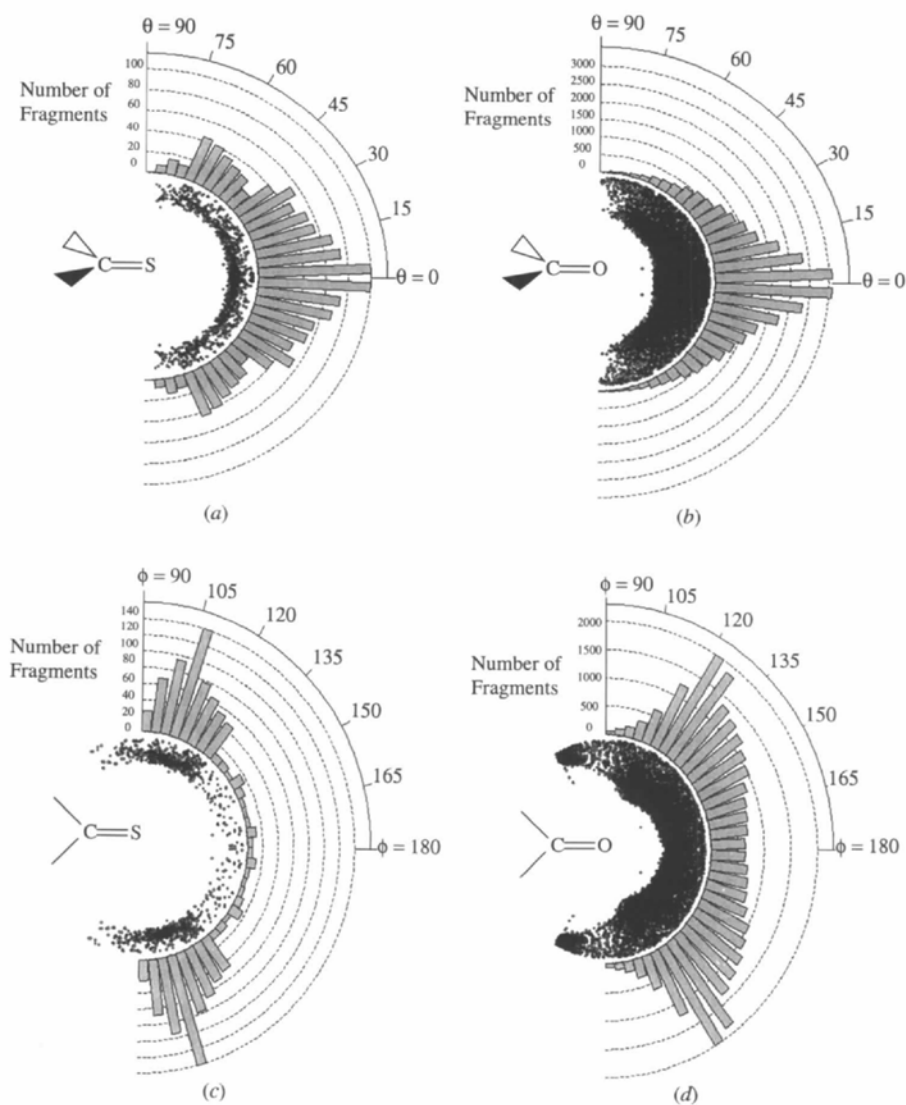

Fig. 8. Symmetrized polar scattergrams of the directionality parameters θ and φ (see Fig. 1) for >C=S···H—(N or O) hydrogen bonds: (a) for θ and (c) for φ. Comparison data for >C=O···H—(N or O) systems are in (b) for θ and (d) for φ.

the S analogue of (V*b*) and many of the C=S···H—O bonds involve H atoms from water molecules.

The geometrical data of Table 4, (*c*) and (*d*), indicate that mean |θ| values, even for the thioamide motifs, are some 10–12° lower than the overall means of Table 4, (*a*) and (*b*). Motif formation, taken to indicate an energetically favourable cooperative arrangement, leads to a H-atom approach that is close to the lone-pair planes of both O and S acceptors. As a result, the mean |θ| value for C=S···H—N bonds that do not occur in the thioamide motif (V*a*) is considerably higher [see Table 4(*e*)] than the overall mean at 34 (2)°, a value which is now much closer to the mean |θ| value in C=S···H—O bonds. This increase in |θ| values is only marginal [(Table 4(*f*)] for non-motif C=O···H—N,O bonds.

The mean |φ| values in motifs [Table 4, (*c*) and (*d*)] are also lower than their corresponding overall means, but this difference is only marginal for the C=S···N—H motif system (V*a*). The decrease in |φ| for the C=O···H—N,O motifs (V*b,c*) is, however, highly significant. The |φ| (motif) mean is 124.0 (2)°, some 16° less than the |φ| (non-motif) mean of 140.2 (2)° [Table 4(*f*)]. Obviously, these shifts in |φ| (and |θ|) permit the C=O motifs (V*b,c*) to adopt a near-planar, elongated hexagonal conformation that best preserves linearity of both O···H—N,O angles (ρ_H). Indeed, we note that ρ_H (Fig. 1*a*) is more closely linear in all three motifs [Table 4, (*c*) and (*d*)] than it is in the non-motif hydrogen bonds [Table 4, (*e*) and (*f*)].

In the light of this analysis, it is possible to see why |φ| in the thioamide motif (V*a*) would adopt a lower value than in the C=O motifs (V*b,c*). In (V*a*) the C=S bond is some 0.04 Å longer than the C=O bond in (V*b,c*) and, in a near planar system, the angle between the C=S and S···H vectors becomes equivalent to φ. Thus, in order to maximize the linearity of the S···H—N system, the near-planar hexagon of (V*a*) must distort about the S···S diagonal to accommodate the longer C=S bond. This, in turn, leads to a small reduction in the C=S···H angle and also in φ by comparison to the C=O motifs (V*b,c*). However, we note that |φ| in non-motif C=S···H—N,O bonds [113 (2)°, Table 4(*c*)] is not significantly larger than in motif structures and conclude that this is, indeed, the preferred direction of H-atom approach to C=S acceptors.

4.11. *Hydrogen-bond coordination numbers for* >C=S *acceptors*

A visual scan of the graphical output of CSD searches for hydrogen-bonded fragments showed that C=S acceptors frequently interact with three, four and, on rare occasions, more than four donor N,O—H atoms. Obviously, this has a significant effect on the direction of approach of H to the >C=S 'plane' of Fig. 1(*b*) and, for steric reasons, has a greater effect on |θ| than on |φ|, a fact confirmed by a scan of the geometry listings.

We performed a detailed analysis of hydrogen-bond coordination by C=S acceptors and, in so doing, had to consider the symmetry of the coordination sphere as follows. The default action of the non-bonded contact searches *via* the CSD system program *QUEST3D* is to locate all symmetry-independent contacts, here S···H, within the geometrical criteria supplied to the program. Thus, in (XIII) the default search would locate S···H1*A* and S···H4*D*, where the alphabetic atom-label terminators (*A,D*) refer to specific symmetry operators. The contact S···H1*A'* would be checked geometrically, found to be equivalent to S···H1*A* and rejected. This default procedure ensures that only symmetry-unique hydrogen bonds are included in summary statistics. For the coordination study, however, it was necessary to switch off the symmetry checking (a standard switch in *QUEST3D*) and also include all intramolecular C=S···H—N,O hydrogen bonds that passed the geometrical criteria detailed in the *Methodology*. Separate local code was then written to postprocess the resultant geometry table (containing all parameters shown in Fig. 1) to obtain mean values for the various coordination numbers (Table 8), but taken over symmetry-unique instances only. For C=S acceptors, we have used all available data (within the general criteria of the *Methodology*) from the April 1995 release of the CSD. For C=O acceptors, the analysis was limited to 3859 hydrogen-bonded C=O acceptors (from 2000 CSD entries) occurring in the first 58,626 entries of that release.

The results of Table 8 provide one immediate explanation for the high mean |θ| values for C=S acceptors in Tables 3 and 4 and for the broad θ distribution of Fig. 8(*a*): the S atom forms hydrogen bonds to three or more donor H atoms in 17% of cases, whereas only 4.1% of C=O acceptors have hydrogen-bond coordination numbers (N_c) $\geq$ 3. However, the |θ| distributions for C=S (Fig. 9, left) and C=O (Fig. 9, right) for N_c = 1, 2, 3 or 4 show that this is not a complete explanation. Even for N_c = 1 or 2 the C=S distributions show much more variation than the corresponding distributions for C=O. A more satisfactory explanation of these effects is prompted by the mean |θ| values of Tables 3 and 4, which show much higher values for OH donors than for NH: $<\theta>_{O—H} - <\theta>_{N—H} = 12°$ for thiones, 15° for thioureido fragments and 19° for dithioates [Table 3, (*a*), (*b*) and (*c*)]. We have examined the chemical origins of these donor groups and find that O—H from water molecules is the donor in 46% of thioureido—S···H—O bonds and in a massive 80% of dithioato—S···H—O bonds. The overall percentage ratio of O—H (water) donors to C=S groups is 57%, but it is only 25% for donation to C=O. By contrast, 56% of N—H donors to C=S originate from self:self interactions in (H)N—C=S···H(N) systems, while virtually all N—H donors are further bonded to sterically bulky systems.

In Fig. 10 we show separate symmetrized polar scatterplots of θ and φ for N—H and O—H donation to

Table 8. *Hydrogen-bond coordination of C=S and C=O acceptors*

Mean values (Å, °) of geometrical descriptors (see Fig. 1) together with mean C=[O or S]···H angles (CXH) for the observed coordination numbers N_c. E.s.d.'s are in parentheses (see *Methodology*). N_H is the number of unique hydrogen bonds in each group, N_x is the number of unique C=S or C=O bonds in each group and $N\%$ is the percentage of all C=S or C=O acceptors having coordination number N_c.

N_c	N_H	N_x	$N\%$	$\langle d(\text{SH})\rangle$ or $\langle d(\text{OH})\rangle$	$\langle d(\text{SD})\rangle$ or $\langle d(\text{OD})\rangle$	$\langle C X H\rangle$	$\langle \rho_H\rangle$	$\langle|\theta|\rangle$	$\langle|\varphi|\rangle$
(a) For C=S acceptors									
1	277	277	54.2	2.41 (1)	1.676 (1)	101 (1)	153 (1)	20 (2)	104 (2)
2	289	147	28.8	2.46 (1)	1.693 (1)	102 (2)	156 (1)	28 (2)	107 (2)
3	124	42	8.2	2.50 (2)	1.702 (3)	104 (3)	151 (3)	37 (3)	113 (4)
4	136	42	8.2	2.50 (2)	1.713 (2)	103 (3)	157 (4)	37 (4)	107 (3)
5,6	17	3	0.6	2.62 (6)	1.725 (7)	110 (6)	149 (6)	38 (7)	117 (6)
(b) For C=O acceptors									
1	2192	2192	74.0	1.909 (4)	1.223 (1)	127 (1)	156.3 (5)	16.3 (6)	132.3 (8)
2	1291	649	21.9	2.002 (6)	1.236 (1)	121 (1)	148.2 (7)	19.4 (7)	126.9 (8)
3	333	111	3.7	2.05 (1)	1.249 (1)	116 (2)	148 (1)	27 (2)	126 (2)
4,5	43	11	0.4	2.20 (3)	1.243 (2)	115 (3)	144 (2)	31 (3)	122 (3)

>C=S, which should be compared with the composite (N—H and O—H) distributions of Figs. 8(a) and 8(c). The θ plot (Fig. 10b) for C=S···H—O bonds is remarkably different from its C=S···H—N counterpart (Fig. 10a). The latter shows a reasonably normal distribution about $\theta = 0°$, which is comparable to the >C=O···H—N,O θ plot of Fig. 8(b). By contrast, Fig. 10(b) (O—H donors) shows a small peak at $\theta = 0°$ and larger peaks at $\theta \simeq 30$, 55–60°. Interestingly, the separate φ plots for N—H and O—H donation to >C=S
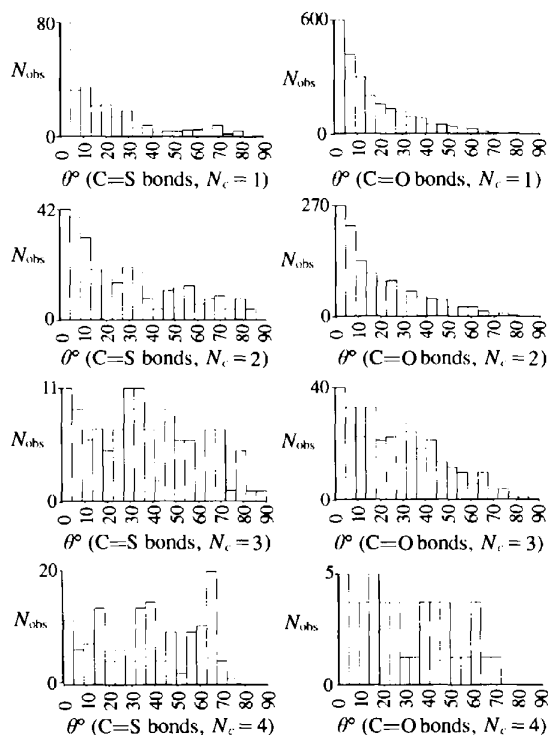

Fig. 9. Histograms of directionality parameter |θ| (Fig. 1) for C=S bonds (left column) and C=O bonds (right column) that accept N_c = 1–4 hydrogen bonds from N—H or O—H donors.

(Figs. 10c and 10d) both show the clear preference for approach to S at $\varphi \simeq 105$–115° as exhibited in the composite-donor φ plot of Fig. 8(c). The separate θ and φ plots for N—H and O—H donation to >C=O (not shown here) are almost identical in form to the composite donor plots of Figs. 8(b) and 8(d).

It would appear that the small steric bulk of water permits the multiple approach of this strong donor towards >C=S, since it is the water donor that is involved in the majority of high (N_c >2) hydrogen-bond coordination geometries. This, in turn, implies that the lone-pair density at =S is diffuse and wraps around the S atom, such that an appreciable electrostatic interaction is still effective, even at higher |θ| values. However, the φ plots of Figs. 8(c), 10(c) and 10(d) would indicate that the lone-pair density is localized in 'planes' that are perpendicular to the >C=S plane and make angles of *ca* 110° with the C=S bond. Very few hydrogen bonds form along the continuation of the C=S vector, *i.e.* at |φ| $\simeq$ 180°.

Table 8(a) also shows that, while the angles CXH and ρ_H are also closely consistent over N_c for C=S, there is a very significant increase in d(CS) and also in d(SH), as N_c increases. Only the longest C=S bonds, with the largest resonance contributions, appear to form multiple hydrogen bonds and these hydrogen bonds appear to weaken with increasing coordination number. This trend [increasing d(OH), d(CO)] is also shown for C=O acceptors [Table 8(b)]. Here, however, the distance increases are accompanied by decreases in both ρ_H and CXH. A more complete analysis of hydrogen-bond coordination of C=O oxygens is now being performed.

4.12. *Comparison of hydrogen-bond acceptor abilities of C=S and C=O*

In an earlier section we assessed the relative strengths of C=S···H—N,O and C=O···H—N,O bonds in terms of their lengths relative to sums of van der Waals radii. Another way of assessing relative

hydrogen-bond strengths is to quantify hydrogen-bond formation in structures that contain both acceptors. Such competitive studies are fraught with problems since, ideally, we would wish to compare acceptor abilities in equivalent environments, *i.e.* where the accessibilities of both acceptors are similar and donor:acceptor ratios are not hugely divergent. In practice, the concept of environmental equivalence is not easy to attain and corrections for environmental diversity are not easy to formulate. Nevertheless, information on the relative hydrogen-bonding ability of acceptors is important, particularly in modelling ligand interactions at active

sites, and we have treated the $C\!\!=\!\!S/C\!\!=\!\!O$ acceptor pair as follows.

The CSD system software has been coupled with local code to obtain statistics on hydrogen-bond formation in three subgroups of CSD entries containing: (*a*) one $C\!\!=\!\!S$ group and no $C\!\!=\!\!O$ groups, (*b*) one $C\!\!=\!\!O$ group and no $C\!\!=\!\!S$ groups, and (*c*) one $C\!\!=\!\!S$ group and one $C\!\!=\!\!O$ group. The analysis proceeded in five stages for each subgroup: (i) A basic substructure search for $C\!\!=\!\!O$ and/or $C\!\!=\!\!S$ acceptors in the presence of N,O—H donors was performed, followed by a tabulation of $C\!\!=\!\!S$ and/or $C\!\!=\!\!O$ distances. Secondary search criteria
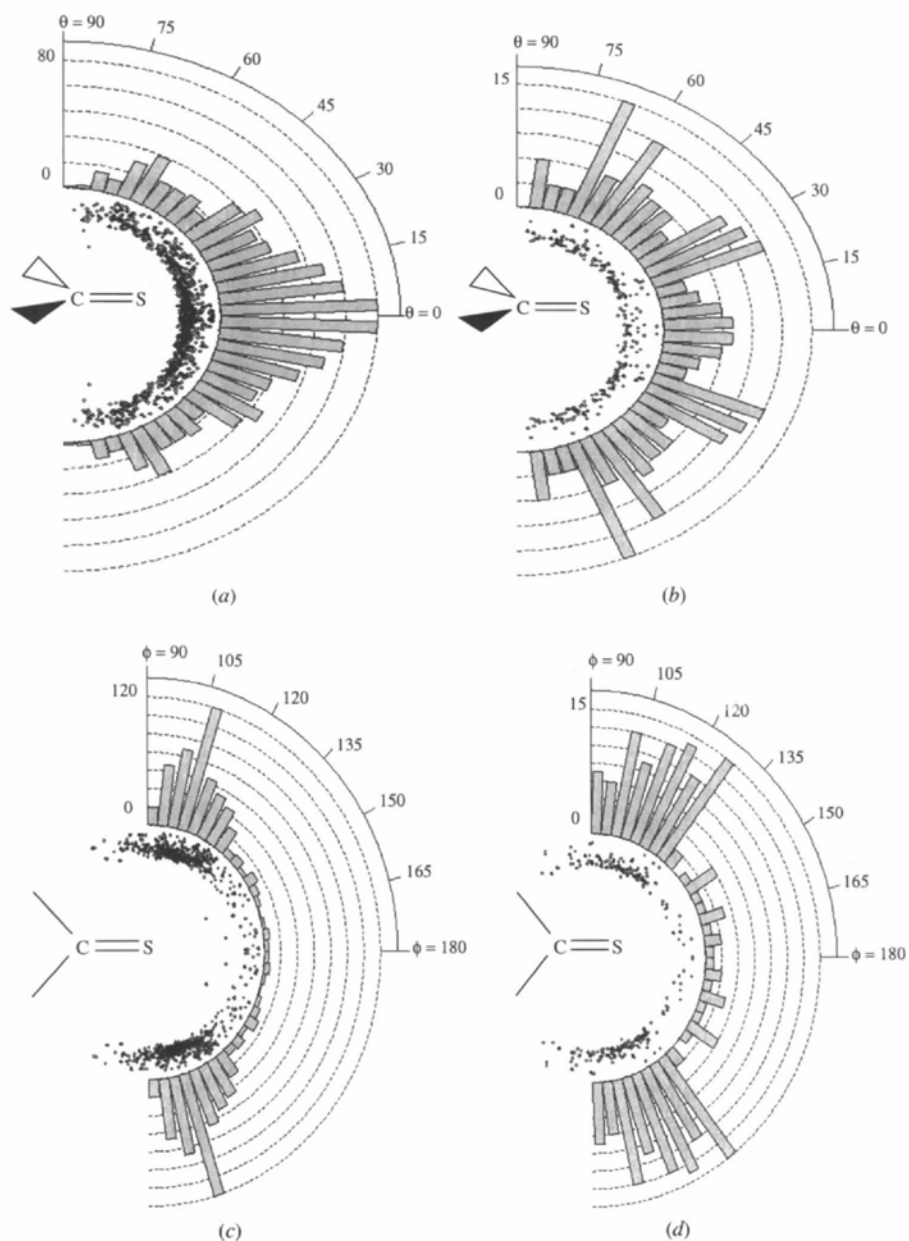

Fig. 10. Symmetrized polar scattergrams of the directionality parameters θ and φ (see Fig. 1): (*a*) θ for $>\!C\!\!=\!\!S\cdots H\!\!-\!\!N$, (*b*) θ for $>\!C\!\!=\!\!S\cdots H\!\!-\!\!O$, (*c*) φ for $>\!C\!\!=\!\!S\cdots H\!\!-\!\!N$ and (*d*) φ for $>\!C\!\!=\!\!S\cdots H\!\!-\!\!O$.

described in the *Methodology* were employed and the unitary presence of C=O and/or C=S groups was enforced in the chemical structures retrieved. (ii) Local code was used to ensure the unitary presence of acceptor(s) in the crystal structures, *i.e.* to eliminate instances of more than one chemical entity in any crystal structure. (iii) Local code was also used to eliminate duplicate structure determinations, retaining only the most precise example on the basis of the R factor. (iv) A non-bonded contact search was performed for structures that survived steps (ii) and (iii) to locate intermolecular hydrogen bonds within the criteria noted elsewhere in this paper. (v) An exhaustive geometric search was performed to determine the numbers of N,O—H donors present in each entry surviving steps (ii) and (iii).

Final results of these procedures are given in Table 9. For the subsets chosen, the unitary C=S and C=O groups both form hydrogen bonds with near-identical percentage frequencies, although we note that more N,O—H donors are available, on average, to each C=S group. In the competitive environment of subgroup (c), however, the percentage frequency of C=O⋯H formation actually rises slightly, while that for C=S⋯H formation falls significantly from 65.8 to 42.0%. Fortuitously, the fact that D—H for subset (c) is approximately double that for the unitary subsets (a) and (b) does provide some similarity in the potential donor environments of each acceptor. Although obviously in need of refinement, the current method provides results that agree with expectation: >C=S is a weaker hydrogen-bond acceptor than >C=O.

Table 9. *Comparison of hydrogen-bond acceptor abilities of* > C=S *and* > C=O *groups*

n_p is the number of potential hydrogen-bond acceptors (S or O) in each subgroup. n_b is the number of acceptors that actually form intermolecular hydrogen bonds with n_b as a percentage of n_p in parentheses. D—H is the average number of N,O—H donors in each structure of each subgroup.

Subgroup	n_p	n_b (%)		D—H
		C=S	C=O	
(a) One C=S only	202	133 (65.8)	—	1.97
(b) One C=O only	3549	—	2342 (66.0)	1.62
(c) One C=S + one C=O	81	34 (42.0)	58 (71.6)	3.37

a result, =O seldom accepts more than two hydrogen bonds. The situation at =S is significantly different and the lone-pair density is obviously more diffuse: values of θ extend to ±60–65° and hydrogen-bond coordination numbers greater than two are observed much more frequently.

The relative strengths of hydrogen bonds to =S and =O are revealed in a qualitative manner by comparisons of O⋯H (normalized) distances, in which the differing van der Waals radii are taken into account. Conclusions based on distance criteria are reinforced by the studies of competitive hydrogen-bond formation reported in Table 9. The overall conclusion is that univalent =S in a conjugative environment acts as an effective, but not potent, acceptor of hydrogen bonds.

5. Conclusions

This study shows conclusively, using both crystallographic and *ab initio* results, that S in R_1R_2C=S systems is an effective acceptor only when R_1,R_2 can form an extended delocalized system with C=S. Only then can the resonance-induced electronegativity of =S approach the natural electronegativity of ketonic =O in $(Csp^3)_2$C=O, an electronegativity that can be further enhanced by resonance in other R_1R_2C=O systems. Our results indicate that >C=S⋯H—N,O bonds are unlikely to form when C=S < *ca* 1.65 Å. It is this resonance that also promotes the formation of the cyclic hydrogen-bonded motif (V*a*) by enhancing the residual positive charge on the amino H atoms in H_2N(R)C=S systems.

The comparative analyses of hydrogen-bond directionality and hydrogen-bond coordination numbers at =S and =O show that both acceptors exhibit consistent, but different, values of φ (Fig. 1*b*), but that θ (Fig. 1*b*) for =S is far more variable than for =O. In the latter, θ tends to be within 20, indicative of H approach to localized lone-pair density in the >C=O plane. As

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