112. Directional Preferences of Approach of Nucleophiles to Sulfonium Ions

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Summary

An analysis of the crystal environments of sulfonium ions shows that short non-bonded contacts (secondary bonds) to sulfur tend to occur along the extensions of the C–S primary bonds. Non-bonded contacts to the C(α)-atoms of sulfonium ions are not especially short and do not show any striking directional preference, except in sulfonium ions derived from methionine where a specific intramolecular interaction between a carboxyl O-atom and the C(γ)-atom may represent an incipient stage of the internal nucleophilic displacement leading to formation of homoserine and mercaptan.

How does a nucleophilic center approach a sulfonium ion? To answer this question we made a search of the Cambridge Crystallographic Database [1] (19 September 1979 version with 24813 entries in the bibliographic file). This yielded 32 crystal structures containing the R_3S^+ grouping (sulfur with three carbon substituents). We have analyzed the environments of the sulfonium ion in 22 of these listed in the *Table*[2]).

The questions we ask are: (1) in what directions do neighbouring atoms, X, occur in the vicinity of the sulfur atom? (2) how do S···X distances compare with the *van der Waals* distances for the atoms involved? Our main conclusions are based on the analysis of 17 of the 22 sulfonium ions or ylids in the *Table*. The remaining five (marked with an asterisk in the *Table*) are omitted for reasons that will be discussed later.

The S–C bond lengths *(Table A)*[3]) show little variation. Excluding the ylid bonds the average (omitting TMSGHI, which is of low accuracy) is 1.813 Å (standard deviation 0.035 Å). The ylid bonds with average length 1.720 (0.017) Å

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[2]) Of the remainder, two structures involve organometallic compounds with a metal atom bonded to the π-system of a ring that either includes the sulfur atom or is adjacent to it; for eight structures atomic coordinates are not listed in the file.

[3]) Tables designated by a letter rather than a number give numerical information that is contained in the Cambridge Crystallographic Database, either directly or indirectly. These Tables can be obtained from the authors on request.

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Table. *Sulfonium compounds included*

Cambridge reference code	Compound	Ref.
	Category I: Sulfonium ions without special features	
ACTHCO	1-Acetonyl-1-thionia-5-thiacyclooctane perchlorate	[a]
CXMETN	*S*-Carboxymethylmethionine trinitrobenzene sulfonate	[b]
CXMPSP	(Carboxymethyl)methyl(1-methylpropyl)sulfonium perchlorate	[c]
MEPSOP	Dimethylphenylsulfonium perchlorate	[d]
MNSISZ	Methyl-di(neopentyl)sulfonium tri-iodo-di(neopentyl)sulfonium-methylzincate	[e]
MTBTIR	1-Methyl-2,3-di(*t*-butyl)thi-irenium tetrafluoroborate	[f]
MTHCXI	1-Methyl-1-thionia-cyclohexane iodide	[g]
NBOIPS	*N*-(*p*-Nitrobenzoyl)-2-iminophenyldimethylsulfur (IV)	[h]
SFONBS	(2,3-Dimethyl-2-butenyl)-(1,1,2-trimethylpropyl)-methylsulfonium 2,4,6-trinitrobenzenesulfonate	[i]
SMMETC	*S*-Methyl-1-methionine chloride hydrochloride	[j]
THBDEC	*trans*-1-Thionia-bicyclo[4.4.0]decane bromide	[k]
TMETSI	Trimethylsulfonium iodide	[l]
TMSCHG	(Trimethylsulfonium)trichloromercury (II)	[m]
TMSHGI	(Trimethylsulfonium)triiodomercury (II)	[n]
	Category II: S-Atom in ring with π-bonding	
CPYBZT*	7-Chloro-1,3,5-trimethyl-5*H*-pyrimido[5,4-b]-1,4-benzothiazine-2,4(1*H*,3*H*)-dione	[o]
PSUOXI*	*S*-Phenyl-phenoxathiinium iodide	[p]
	Category III: Ylids (MSULIN and THMCMY in category IV are also ylids)	
CIMESY	4,5-Dicyano-2-imidazolyl(diethyl)sulfonium ylide	[q]
DMSCPY	Cyclopentadienylidene-dimethyl-sulfur	[r]
MSMNIT	2-Dimethylsulfuranylidene-malononitrile	[s]
	Category IV: Steric hinderance determines interactions	
AFMSCY*	2,2'-Anhydro-1β-D-arabinofuranosyl-5-dimethylsulfonio-6-oxo-cytosine chloride	[t]
MSULIN*	2-Dimethylsulfuranylidene-indan-1,3-dione	[u]
THMCMY*	Thiophenium bis(methoxycarbonyl)methylide	[v]

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[s] *A.T. Christensen & W.G. Witmore,* Acta Cryst. *B25*, 73 (1969).
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are decidedly shorter. The average C–S–C angle (excluding MTBTIR with S in a three-membered ring, THBDEC with S in a fused ring system, and TMSGHI, as before) is 102.4 (2.2)°.

Δd, the observed S···X distance minus the *van der Waals* distance, is plotted *vs.* all three C–S···X angles in *Figure 1* (numerical data in *Table A*). The *van der Waals* radii (Å) used are F, 1.35; O, 1.40; N, 1.50; C, 1.60; Cl, 1.80; S, 1.85; Br, 1.95; I, 2.15. All distances with $\Delta d \leq 0.40$ Å are shown. The distribution is far from random. The largest C–S···X angle is always near 180 (±30)° for each X; *i.e.* short contacts tend to occur along the extension of one of the C–S bonds. As usual, intramolecular X···S contact distances tend to be shorter than intermolecular ones, but even the shortest (O···S, 2.8 Å in ACTHCO with synperiplanar O=C–C–S side chain) corresponds only to weak secondary bonding. There is no discernible relationship between the S···X distances and the opposing S–C distances. Nevertheless, the marked directional preference evident in *Figure 1* suggests that some kind of specific interaction is at work.

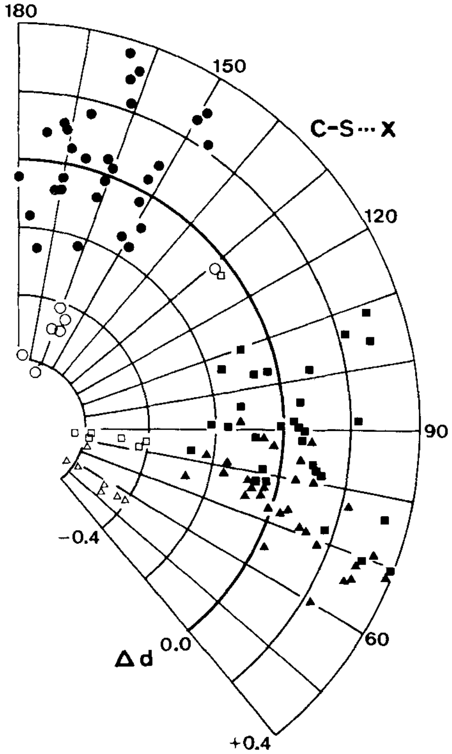


Fig. 1. *S···X distances* vs. *C–S···X angles.* Circles indicate the largest C–S···X angle for each X, squares the intermediate C–S···X angle, and triangles the smallest. Open points show intramolecular S···X contacts.

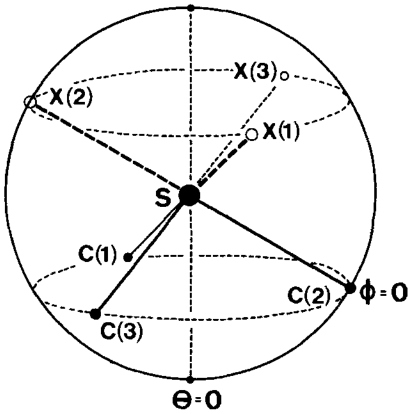


Fig. 2. *The SC_3 group in a polar coordinate system.* The two poles are on the line equi-inclined to the three S–C vectors, so that $\theta(C(1)) = \theta(C(2)) = \theta(C(3))$. C(2) is placed at $\varphi = 0$ and C(1) near $\varphi = 120°$. The expected positions for nucleophilic approach, opposite the S–C directions, are shown as X(1),X(2),X(3).

This preference is seen even more strikingly when the directions of the C and X atoms are plotted in spherical polar coordinates θ and φ (numerical data in *Table B*)[3]). The coordinate system is shown in *Figure 2;* the origin is at S, the z-axis is equi-inclined to the three S–C bond directions, and the x-axis is as near the direction of the S–C(2) bond as possible after the z-axis has been fixed. If the molecule contains a mirror-plane or a pseudo-mirror-plane, the C(2)-atom is placed in this plane. The distribution of θ and φ for the S–C and S···X directions is shown as a *Mercator* projection in *Figure 3;* the points representing the S–C directions cluster tightly around $\theta = 64.3$ (1.1)°, and $\varphi = 90$, 120, and 240°, those representing the S···X directions cluster loosely around $\theta = 120$ (13)° and $\varphi = 60$, 180, and 300°. There are only three sets of points that lie outside these clusters, one where the S-atom is in a three-membered ring, one where it is in a five-membered ring, and one where the light atom coordinates are of very low accuracy. The avoidance of approach along or close to the direction of the ternary axis of the sulfonium ion is strikingly evident from the barrenness of the polar regions in *Figure 3.*

We are now in a position to answer the question posed at the start: *nucleophilic centers tend to approach sulfonium ions along the directions opposite to the primary bonds.* A similar tendency occurs in the approach of nucleophilic centers to divalent S-atoms [2-5]. Our present survey shows no apparent preference for any particular number of secondary bonds. We have one example of a S-atom with no secondary bonds, six examples with one secondary bond, seven examples with two, four examples with three, and one example with four secondary bonds (the count has 19 S-atoms because two of the 17 crystal structures each contain two independent molecules).

A single S···X^- contact opposite a primary bond can be regarded as an incipient stage of an addition reaction leading to a sulfurane or of a nucleophilic

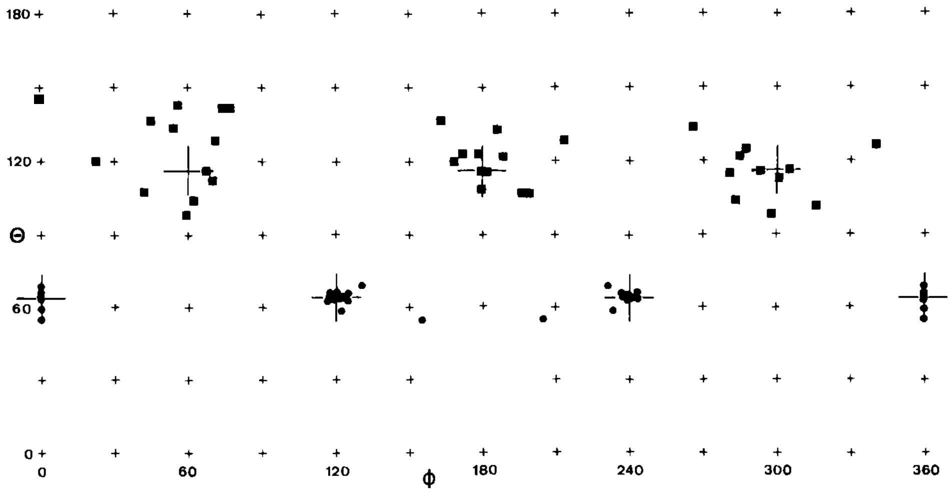


Fig. 3. *Mercator projection of the S–C* (●) *and S···X* (■) *directions.* The large crosses show the average S–C directions and the diametrially opposed directions.

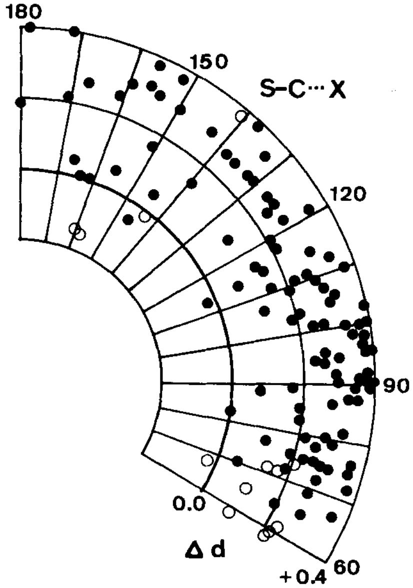


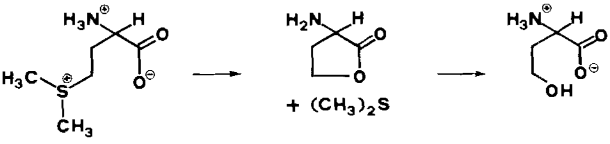
Fig. 4. *C(S)···X distances* vs. *S–C···X angles.* Open points show intramolecular S···X contacts.

displacement reaction at sulfur. Neither process can be expected to proceed very far along the reaction path: sulfuranes with three carbon substituents are unlikely to be stable; carbon substituents are generally poor leaving groups.

If we examine the X···C–S contacts in the same fashion as in *Figure 1,* we find *(Fig. 4)* that the X···C distances are equal to or larger than the *van der Waals* distances and also that the distribution of S–C···X angles between 70 and 180° corresponds roughly to a random distribution on the surface of a sphere (numerical data for *Fig. 4* are taken from *Table C*)[3]). There is thus no general tendency for nucleophilic centers to approach the α-carbon atoms in any particular direction.

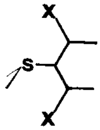
However, there are a few examples of what appears to correspond to a specific and chemically relevant type of intramolecular nucleophilic approach. In the two crystallographically independent CXMETN molecules (*S*-carboxymethylmethionine trinitrobenzenesulfonate), intramolecular O···C distances of 2.86 and 2.87 Å occur with S–C···O angles of 159 and 160°, respectively. In both cases the O···C secondary bond completes a five-membered (S)C-C–C–C-O ring with torsion angles close to +60 and −60° for the two central bonds. In SMMETC (*S*-methylmethionine chloride hydrochloride) the corresponding O···C distance is 2.97 Å and the S–C···O angle is 143°.

In basic solution *S*-methylmethionine is readily converted to homoserine lactone with expulsion of the mercaptan [6].



The short O···C contact observed in these crystal structures can be regarded as an incipient stage of this type of internal nucleophilic displacement reaction.

Exceptions to normal S···X directions. - As mentioned earlier five compounds were excluded from *Figures 1* and *3*. For each of the five at least one intramolecular S···X contact occurs in an unusual direction because of steric constraints. In CPYBZT and PSUOXI *(Table)* the S-atom is in a nearly planar π-bonded ring and makes a *trans*-annular S···X contact which would lie near $\theta = 30°$, $\varphi = 180°$ in *Figure 3*. In AFMSCY, MSULIN, and THMCMY the molecule is sterically hindered in the vicinity of the S-atom as shown:



where the group to the right of the S-atom is planar. This causes the directions to the X-atoms to be near $\theta = 20$ or 120° and $\varphi = 0°$ in *Figure 3*.

Miscellaneous comments. - The compounds TMSCHG and TMSGHI (trimethyl sulfonium trichloro- and triiodo-mercurate, respectively) are isomorphous. This relationship appears to have been overlooked by the original authors. The transformation $\bar{1}0\bar{1}/010/\bar{1}00$ converts the space group of TMSGHI to that of TMSCHG with similar lattice translations and atomic coordinates.

The crystal structure of TMSCHG is reported to be disordered. The S-atom occurs on either side of the plane of the three methyl groups with occupancies of 62 and 38%. The 62% position is similar to that in the isomorphous iodo compound, and has the normal type of contacts as shown in *Figure 3*. The 38% position makes one S···Cl contact of 3.49 Å, but the C–C···Cl angles are 118, 119, and 80°, which does not fit the pattern of *Figure 2*. This disorder should be investigated further.

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