

Significance of Intermolecular S \cdots C(π) Interaction Involving M–S and –C=O Centers in Crystal Structures of Metal Thiolate Complexes

Janusz Lewiński,^{*[a]} Wojciech Bury,^[a] and Iwona Justyniak^[b]

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The database analysis of intermolecular S \cdots C(π) distances involving a metal-bonded thiolate sulfur atom and various C(π)-centered Lewis acid domains provided evidences for M–S \cdots C(π) contacts as resulting from specific noncovalent interactions.

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Introduction

A plethora of noncovalent interactions account for a number of known binding and structural motifs in biological systems, synthetic catalysis and supramolecular chemistry.^[1] In this regard hydrogen bonding plays a dominant role,^[2] but many other less conventional noncovalent forces like the C–H \cdots π ,^[3] cation \cdots π ,^[4] and anion \cdots π interactions,^[5] π – π aromatic stacking,^[6] halogen bonding,^[7] or chalcogen–chalcogen^[8] interactions have been identified and extensively explored recently. Nevertheless, some structural and functional aspects of biomolecular or catalytic functions remain an active problem which partly results from the fact that less obvious specific forces involving different chemical entities are only rarely encountered. In this regard, studies on identifying and characterizing noncovalent interactions are essential for a more complete understanding of biochemical processes and could provide useful tools in the field of molecular recognition. One of such emerging areas of research are interactions between divalent sulfur centers and electron-deficient π -systems. It is over 30 years since the seminal work of Dunitz et al. revealed that a large number of the close contacts between an electrophilic carbonyl group and a nucleophilic group exist in the crystal structures of small organic molecules, and based on the correlation analysis the authors mapped out reaction pathways of the nucleophilic addition to a carbonyl group.^[9] More recently, it has been found that the nucleophilic attack by an amino acid S-terminal side chain on a peptide carbonyl atom is the crucial step in the mechanism of self-catalyzed

peptide bond rearrangement.^[10] An attractive intramolecular interaction between the thiolate group of a metal-bound cysteine and a carbonyl carbon atom of a peptide group is also essential in the determination of metalloprotein structures.^[11–13] Nevertheless, the chemistry of specific weak interactions involving a thiolate center in metal complexes and metalloproteins has been so far explored only fleetingly.^[14] Very recently, we have revealed that the intermolecular S \cdots C(π) interaction between an M–S thiolate unit and the π -surface of an ester functionality can compete with the potential sulfur–metal dative bond of group 13 metal–alkyl compounds derived from methyl thiosalicylate, Me₂M(SC₆H₄-2-CO₂Me) (cf. structures **I** and **II**; Figure 1).^[15] In order to verify the significance of the M–S \cdots C(π) interaction between the M–S–C thiolate sulfur atom and the carbonyl carbon atom as an intermolecular force, we have performed detailed structural analysis of intermolecular contacts for various types of metal thiolate complexes retrieved from the Cambridge Structural Database (CSD).

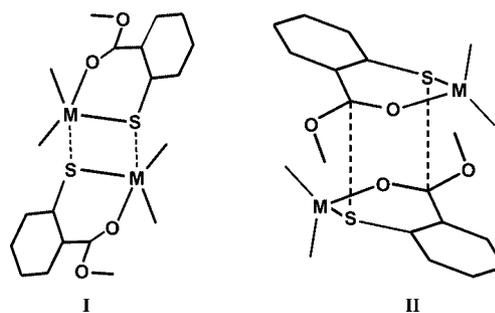


Figure 1. Coordination mode variation of the group 13 organometallic derivatives of methyl thiosalicylate: five-coordinate dimer [Me₂In(μ -SC₆H₄-2-CO₂Me)₂] (**I**) and four-coordinate non-covalently bonded dimer Me₂Al(SC₆H₄-2-CO₂Me) (**II**).

[a] Department of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00-664 Warsaw, Poland, E-mail: lewin@ch.pw.edu.pl

[b] Institute of Physical Chemistry, Polish Academy of Sciences, Kasprzaka 44, 01-224 Warsaw, Poland

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Results and Discussion

The collection of structural data was obtained through the systematic search of the CSD using CCDC software (version 5.25).^[16] The searches were performed for structures containing a sulfur atom bonded to any metal atom and carbonyl group moieties of the type X-C=O (where X = C, N, O, S). Only the intermolecular contacts between the sulfur atom and the carbonyl carbon atom were examined (the S...C=O intermolecular contact). The coordinate system, the atom labeling scheme and the resulting geometric parameters used in our analysis are sketched in Figure 2.

The position of the sulfur atom relative to the carbonyl group plane is specified in spherical polar coordinates by two angles, φ and θ and the distance r . The carbonyl group lies in the xy plane and the vector C=O defines the direction of the X axis. The search was subjected to the following criteria: S...C intermolecular contacts up to 4.0 Å, R -factor less than 0.075 and error free, the position of the sulfur atom was specified relative to the π -phase of C=O moieties in spherical polar coordinates. The restricted searches revealed 101 compounds and the total data set used for the correlation analysis was 141 data points. In our analysis were excluded all intermolecular contacts between the sulfur atom and a carbonyl group corresponding to the S...O=C interaction between a C-S-C unit and a carbonyl oxygen atom.^[8b] A survey of available crystal structures shows several types of functional groups acting as the C(π)-centered Lewis acid domains. In total 27 contacts were found in which the sulfur lone pair is directed to the carbon atom of the carboxylate group bonded to a metal center, 48 contacts involve metal-bonded thiocarboxylates, 23 amides, 21 esters, and 22 ketones. The corresponding histogram plots of the S...C=O distances for various type of X-C=O carbonyl moieties are offset essentially regularly (Figure 2). This observation is consistent with the expectation taking into account that the functional groups in question are both bound (or not bound at all) to various metal centers and with various coordination modes, and thus the metal-ligand interactions have a different character which affects the Lewis acidity of the X-C=O carbon center. Not surprisingly, the effect is most pronounced for the carboxylate

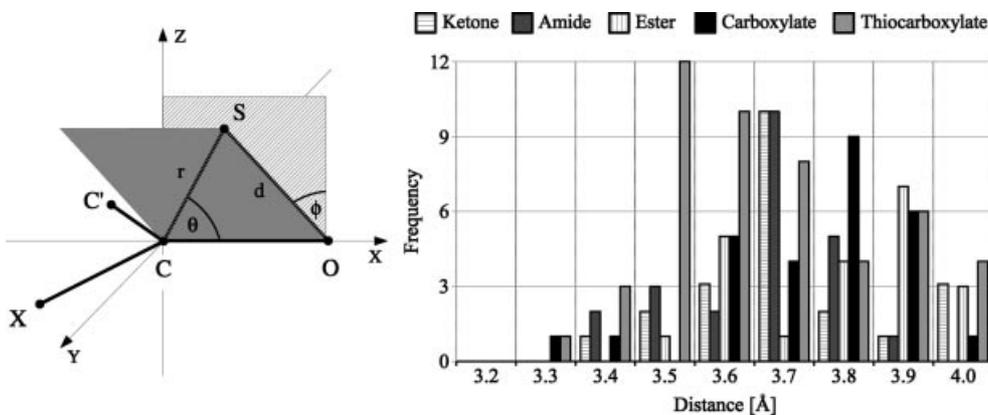


Figure 2. Geometrical parameters and histogram of S...C=O distances involving metal thiolates and various types of X-C=O carbonyl moieties (where X = C, N, O, S).

groups which exhibit the greatest metal-ligand bonding diversity.^[17] Interestingly, it appears from the considered data set that in the short range of contacts (i.e., below 3.5 Å) there are interactions involving essentially all types of functional groups except the ester group. Thus, this fact suggests that the ester group Lewis acid domain is one of the weakest acidity. On the other hand, the S...C(π) distance recently found by us for Me₂Al(SC₆H₄-2-CO₂Me) is one of the shortest intermolecular contacts observed to date between the M-S center and the carbon atom of the ester group. Furthermore, the analysis of angular attributes of the S...C(π) interactions clearly show the directional nature of this novel noncovalent force, Figure 3 (see also Figures S3 and S4 of the Supporting Information).

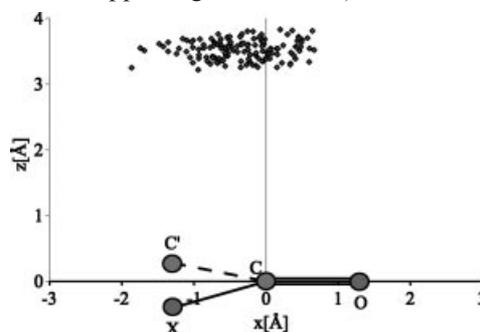


Figure 3. Distribution of the axial positions for the sulfur atom of a metal thiolate unit position relative to the X-C=O π -face projected on the xz plane.

In conclusion, detailed structural analysis was performed for crystal structures of metal thiolate complexes retrieved from the CSD which demonstrates that the intermolecular S...C(π) interactions involving a metal-bonded thiolate sulfur atom and various C(π)-centered Lewis acid domains appear very frequently and play a crucial role in the molecular assembly of these compounds in the solid state {cf. the crystal structures of [Co(SC₆H₄-2-CO₂)N(C₂H₄NH₂)₃]ClO₄ (**III**)^[18] and Zn(SC₆F₅)₂(C₅H₄N-2-COCH₃) (**IV**)^[19] see Figure 4}.

There are already more than 100 crystal structures deposited in the CSD and surprisingly the S...C(π) interaction as well its role on the supramolecular structure of various

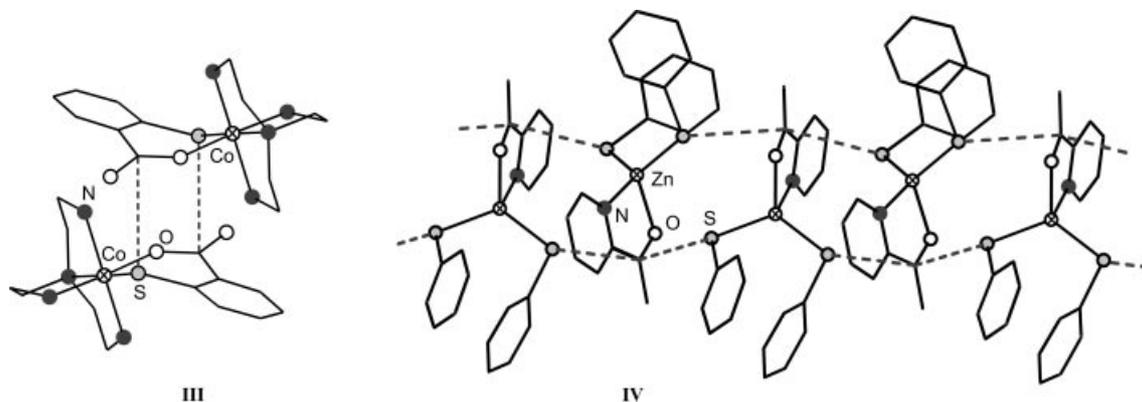


Figure 4. Structures of non-covalently bonded dimer $[\text{Co}(\text{SC}_6\text{H}_4\text{-2-CO}_2)\text{N}(\text{C}_2\text{H}_4\text{NH}_2)_3]\text{ClO}_4$ (**III**) and polymer chain of $\text{Zn}(\text{SC}_6\text{F}_5)_2\text{-(C}_5\text{H}_4\text{N-2-COCH}_3\text{)}$ (**IV**).

complexes has not been recognized in any case by the original authors. Furthermore, it is reasonable that the $\text{M-S}\cdots\text{C}=\text{O}$ interactions may be expected to be responsible for the high bioactivity of sulfur, because such an interaction may occur at an early stage along the reaction coordinate or stabilize the folded protein structure as well as it might be a controlling factor in regulating the reactivity and specificity of metal–thiolate bonds.^[20] The fact that the chemistry of specific weak interactions involving a thiolate center in metalloenzymes has been often underestimated in model studies is well expressed by the investigation involving the above-mentioned complex **IV**.^[19] Further studies on both the relationship between dative bonds in metal complexes and secondary interactions, and the significance of the intermolecular $\text{S}\cdots\text{C}(\pi)$ interaction between M-S thiolate units and the π -surface of a carbonyl functionality in various systems are in progress.

Supporting Information (see footnote on the first page of this article) is available online for this manuscript, including parameterization data, histograms, scatter plots based on analyzed datasets and CCDC reference codes used in the database analysis can be found there.

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