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Stereochemistry at Iron of the Sulfur Dioxide Insertion Reaction of Iron Alkyls. Crystallographic Determination of the Absolute Configuration at Iron of a Chiral Iron Sulfinate

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Abstract: The absolute configuration of (-)₅₇₈-CpFe(CO)(PPh₃)S(O)₂CH₂CH(CH₃)₂ has been shown by X-ray anomalous dispersion techniques to be *S* (nomenclature based on the sequencing rules recently formulated by Stanley and Baird). The compound crystallizes in the orthorhombic space group *P*2₁2₁2₁, with *a* = 13.800 (4), *b* = 13.523 (5), *c* = 13.649 (5) Å. Refinement of the structure with two Friedel-related sets of data (3059 reflections) yielded *R* = 6.4% for the *S* configuration, as opposed to *R* = 7.0% for the *R* configuration. The structure of this compound, which was prepared from the isoconfigurational alkyl complex (+)₅₇₈-(*S*)-CpFe(CO)(PPh₃)CH₂CH(CH₃)₂, confirms prevailing beliefs that the stereochemistry of the SO₂-insertion reaction involves retention of configuration at iron.

Introduction

Since its discovery in 1964 by Bibler and Wojcicki,² the reaction of sulfur dioxide with metal-carbon σ bonds has been the object of intense scrutiny.^{3,4} This is presumably not because the reaction itself is of especial synthetic importance, but rather it seemed to be another well-defined member of the class of reactions often called "insertions",⁵ of which carbon monoxide insertion is probably the best known example. It was assumed at first by many that all of these reactions proceed by essentially the same mechanism, so that thorough investigation of the SO₂ insertion should yield more insight into this class of reactions which is important generally in metal-catalyzed transformations of organic molecules.

The reactions of metal alkyls with SO₂ and CO are now known to be very different.³⁻⁵ The most striking dissimilarity is that insertion of SO₂ into the Fe-C bond of *threo*- or

erythro-CpFe(CO)₂CHDCHDC(CH₃)₃ (Cp = η^5 -C₅H₅) proceeds with inversion of configuration at carbon, while insertion of CO proceeds with retention.⁶ Only half of the stereochemical information necessary for a detailed mechanistic understanding resides at carbon, so we⁷ and others^{8,9} have undertaken to examine the stereochemical outcome at iron of these insertions in molecules of types **1**^{7,8b,9} (where R is a variety of alkyl groups) and **2**.⁸

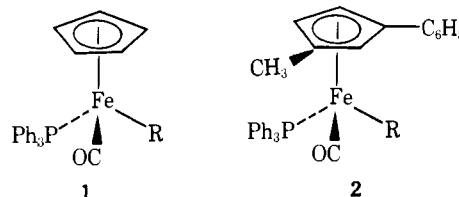
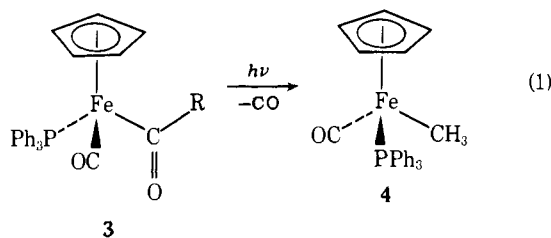


Table I. Crystal Data for $(-)_578$ -(*S*)-CpFe(CO)(PPh₃)S(O)₂-CH₂CH(CH₃)₂

space group = $P2_12_12_1$ (no. 19)
$a = 13.800$ (4) Å
$b = 13.523$ (5) Å
$c = 13.649$ (5) Å
$V = 2547.5$ Å ³
$Z = 4$
$\rho(\text{exp})^a = 1.38$ g/cm ³
$\rho(\text{calcd}) = 1.39$ g/cm ³
$\mu = 11.2$ cm ⁻¹ (for Mo K α X-rays)

^a Obtained by flotation in an aqueous zinc chloride solution.

In an elegant study, Davison and Martinez⁹ found that (*S*)-**3** undergoes photochemical decarbonylation to form **4** which is predominantly *R* (eq 1).¹⁰ Attig and Wojcicki found



that **2** underwent SO₂ insertion with high stereospecificity,^{8a} and simultaneously we have found that **1**, independent of the alkyl group, similarly undergoes stereospecific SO₂ insertion.⁷ Based on an empirical argument using circular dichroism spectra,^{7b,11} it was suggested that this reaction, unlike the CO insertion, proceeds with retention of configuration at iron.⁷ In order to unequivocally establish the stereochemical course of the SO₂ insertion, and to contribute to the empirical basis for the use of CD spectra in configurational assignments in these iron systems,¹¹ we have determined the molecular structure and absolute configuration of $(-)_578$ -CpFe(CO)(PPh₃)S(O)₂CH₂CH(CH₃)₂ (**5**) by X-ray crystallographic methods.

Experimental Section

Crystals of $(-)_578$ -(*S*)-CpFe(CO)(PPh₃)S(O)₂CH₂CH(CH₃)₂ (**5**), prepared from the corresponding alkyl complex using published procedures,^{7a} are bright red parallelepipeds. A specimen with dimensions 1.00 × 0.385 × 0.308 mm was obtained via fractional recrystallization from a dichloromethane solution under an inert atmosphere. This crystal, of the $(-)_578$ -**5** enantiomeric form, was mounted on a glass fiber. Precession photographs indicated an orthorhombic crystal system with systematic absences consistent with space group $P2_12_12_1$ (no. 19). The unit cell parameters, which are given in Table I together with other crystallographic details, were obtained by carefully measuring the setting angles of 25 reflections on a Nonius CAD-3 automated diffractometer.

A full hemisphere of data was collected by the $\theta/2\theta$ scan technique up to a 2θ limit of 45°. A scan speed of 10°/min was used with a scan width of 1.2° and a take-off angle of 4°. Each reflection was scanned between two and six times, depending on its intensity, and background counts were taken at the beginning and end of each scan. Zirconium filters were automatically inserted between the crystal and the detector to prevent the counting rate from exceeding 2500 counts/s. As a check on the stability of the crystal and the diffractometer, three check reflections were measured at 60-reflection intervals during the collection of data; no significant variation in these monitor intensities was observed.

The four octants of data (8243 reflections, including 148 check reflections) were merged to yield a data set consisting of two octants ($hkl, \bar{h}\bar{k}\bar{l}$) of Friedel-related reflections (3059 reflections; data set A). This was further merged to give a smaller data set (1781 reflections of the type hkl ; data set B), which was used in the initial structural analysis. The full data set ($hkl-\bar{h}\bar{k}\bar{l}$) was used in the final stages of

Table II. Ratios^a of the Largest Bijvoet Differences for CpFe(CO)-(PPh₃)S(O)₂CH₂CH(CH₃)₂

<i>h</i>	<i>k</i>	<i>l</i>	$F_{hkl}/F_{\bar{h}\bar{k}\bar{l}}$ (obsd)	$F_{hkl}/F_{\bar{h}\bar{k}\bar{l}}$ (calcd)	
				<i>S</i>	<i>R</i>
1	7	12	1.17	1.24	0.80
1	6	10	1.04	1.06	0.95
8	5	10	1.04	1.06	0.95
7	5	8	1.10	1.06	0.94
5	5	8	1.10	1.07	0.94
3	5	8	1.22	1.26	0.79
1	9	7	1.08	1.07	0.94
7	8	3	1.18	1.15	0.87
3	5	2	1.04	1.08	0.93
2	5	2	1.10	1.14	0.89
3	2	1	1.14	1.17	0.86
4	2	14	0.88	0.93	1.07
4	5	13	0.78	0.89	1.02
3	1	12	0.95	0.92	1.08
6	5	11	0.84	0.91	1.10
5	2	11	0.90	0.90	1.10
6	3	10	0.91	0.91	1.10
5	5	9	0.98	0.94	1.06
7	3	9	0.98	0.94	1.06
5	8	7	0.99	0.93	1.08
2	5	6	0.94	0.93	1.08
6	7	5	0.92	0.92	1.09
1	2	5	0.97	0.94	1.06
7	11	4	0.91	0.91	1.09
4	5	4	0.86	0.92	1.09

^a For example see ref 16.

refinement and determination of absolute configuration. Only those reflections having intensities greater than 3 σ were included in these data reductions. The standard deviation of each intensity reading, $\sigma(I)$, was estimated using the expression $\sigma(I) = [(\text{peak} + \text{background counts}) + (0.04)^2(\text{net intensity})^2]^{1/2}$. The intensities were corrected for Lorentz and polarization effects; an empirical absorption correction was also applied,¹² with transmission factors (normalized to unity) varying between 0.943 and 1.030. The scattering factors for Fe, S, P, O, C, and H were taken from the "International Tables for X-ray Crystallography". The effects of anomalous dispersion ($\Delta f'$ and $\Delta f''$) for Fe, S, and P were included in the calculated structure factors.

Using the hkl data set (set B), the coordinates of the Fe, S, and P atoms were obtained from a three-dimensional Patterson map and other nonhydrogen atoms were located from successive difference Fourier maps.¹³ Four cycles of full-matrix anisotropic refinement resulted in agreement factors of $R = 6.7\%$ and $R_w = 8.3\%$.¹⁴ The atomic coordinates at this stage corresponded to the *S* configuration.

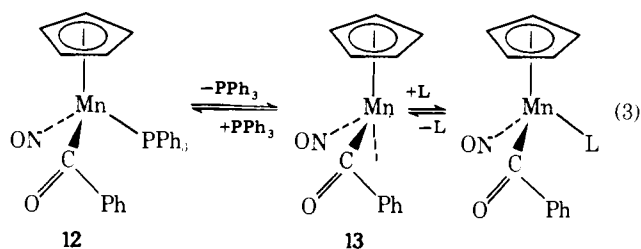
To determine the absolute configuration of the molecule, the signs of the x , y , and z coordinates obtained by the above method were reversed to generate the opposite configuration (*R*). Both these sets of coordinates, the new (*R*) and the original (*S*) forms, as well as their anisotropic thermal parameters, were then subjected to four cycles of full-matrix refinement in the full $hkl-\bar{h}\bar{k}\bar{l}$ data set (set A). The final agreement factors were ($R = 7.0\%$, $R_w = 8.9\%$) and ($R = 6.4\%$, $R_w = 8.1\%$) for the *R* and the *S* sets, respectively. This difference, according to Hamilton's *R* factor significance test,¹⁵ indicates that the probability of the *S* form being the correct configuration is well over 99.5%.

Additional support to this assignment is provided by a comparison of the largest Bijvoet differences, listed in Table II. In each case the ratio of $F_{hkl}/F_{\bar{h}\bar{k}\bar{l}}$ (obsd) more closely matches the corresponding ratio of calculated structure factors of the *S* form.¹⁶

Results and Discussion

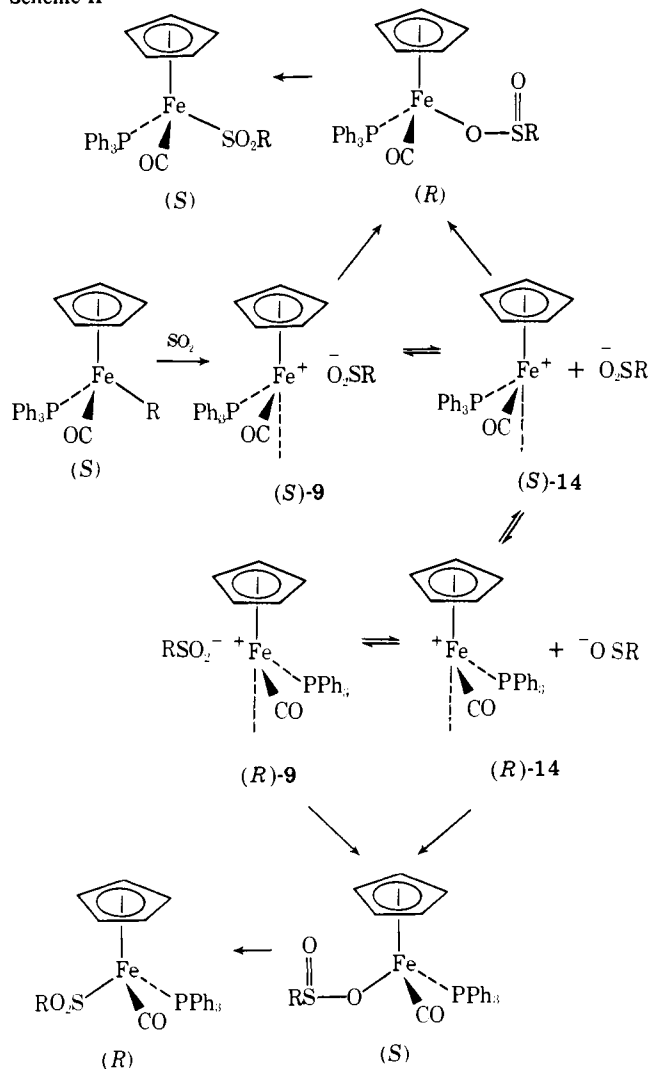
Interatomic distances and bond angles and their estimated standard deviation (esd's) of **5** are shown in Table III. The final atomic parameters and a table of observed and calculated structure factors are available.¹⁷ The overall geometry and absolute stereochemistry of $(-)_578$ -**5** are shown in Figures 1 and 2. As described in the Experimental Section, the absolute

However, the extent of the optical stability of these ions is noteworthy. In this regard, the recent reports by Brunner and co-workers²⁵ that **12** undergoes S_N1 ligand exchange with net retention of configuration (eq 3) is important since all of his

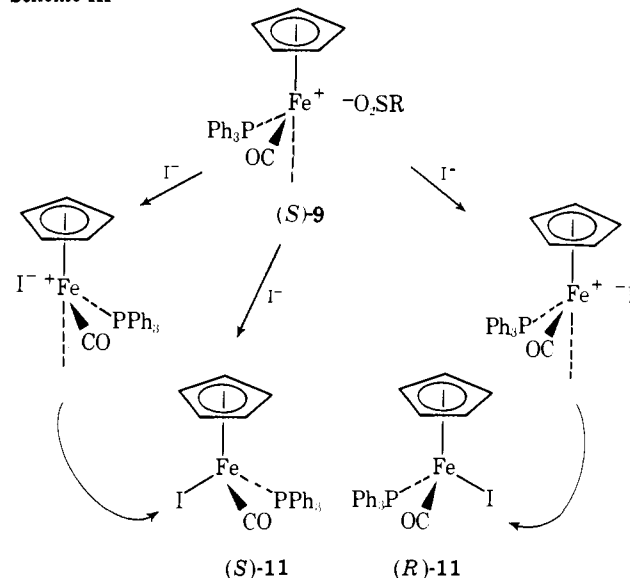


data taken together strongly suggest that the unsaturated intermediate **13** is nonplanar. Furthermore, extended Hückel calculations by Hofmann²⁶ are in accord with "16-electron" species CpMLL' being nonplanar. If this is indeed a general phenomenon, then [CpFe(CO)(PPh₃)]⁺ should also be pyramidal and chiral, and the detailed stereochemistry of the reaction would presumably resemble that shown in Scheme II. Any barrier to inversion could go a long way toward assisting in maintaining the configuration of ion pair **9**. The racemic portion of methyl sulfinate **10** which is formed from methyliron **4** in liquid SO₂ would arise from the dissociated ions **14**. When iodide ion is present it presumably efficiently traps **14** and also traps some of the tight ion pair **9** since iron iodide product **11** is net inverted in configuration while **14**, in analogy with Brunner's results (eq 3), should be trapped with

Scheme II



Scheme III



net retention. As depicted in Scheme III, one might expect any range for the extent of preference for inversion since arguments have been made in organic systems for efficient trapping of tight ion pairs with inversion, and solvent-separated ion pairs with retention of configuration.²⁷ The extent of preference for inversion upon reaction of **9** with iodide cannot be determined since the rate of inversion of **14** is unknown and therefore any preference for **14** to react with retention of configuration is unknown.

In any event, the hypothesis that "16-electron" molecules of the type (Cp or arene)MLL' are nonplanar has profound implications for interpretation of stereochemical observations for reactions of pseudotetrahedral organometallics, and points out the fact that highly stereospecific reactions of these neutral molecules, carried out in low polarity solvents in which they tend to be soluble, must be interpreted with great care lest ionic or electron transfer reactions be mistaken for concerted processes.

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Supplementary Material Available: Listings of the observed and calculated structure factors and final atomic parameters for **5** (21 pages). Ordering information is given on any current masthead page.

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- (17) See paragraph at end of paper regarding supplementary material.
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Studies on the Ferric Forms of Cytochrome P-450 and Chloroperoxidase by Extended X-ray Absorption Fine Structure. Characterization of the Fe-N and Fe-S Distances

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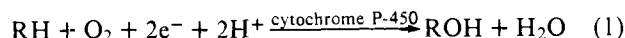
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Abstract: Cytochrome P-450 and chloroperoxidase are Fe-heme proteins with similar spectroscopic properties, which catalyze respectively the hydroxylation and halogenation of organic substances. The nature of and distances to the nonporphyrin (axial) ligands in these proteins are clearly of importance in understanding their catalytic cycles on a molecular level. This paper reports the first use of extended X-ray absorption fine structure (EXAFS) spectroscopy to study the iron environment in the ferric resting states of these two enzymes. First, analysis methods were developed for model iron porphyrin systems. Least-squares curve fits to the EXAFS data, using empirical phase and amplitude functions, led to the determination of interatomic distances in Fe porphyrins of known structure; Fe-N_P distances were determined to within ± 0.007 Å and the Fe-C _{α} and Fe-X (where X = O, S, N) to better than ± 0.025 Å. Second, visual comparison of the protein data with that for the models allowed classification of the chloroperoxidase as high spin (iron out of plane) and P-450-LM-2 as low spin (iron in plane). The data for both oxidized enzymes demonstrate the presence of an axial sulfur ligand. Finally, detailed curve fitting analysis of the EXAFS revealed that the chloroperoxidase distances were Fe-N_P = 2.05 Å, Fe-C _{α} = 3.09 Å, and Fe-S = 2.30 Å. These are strikingly similar to the corresponding distances found in Fe^{III}(PPIXDME)(SC₆H₄-*p*-NO₂). The distances from EXAFS analysis for P-450-LM-2 were 2.00, 3.07, and 2.19 Å for the Fe to N_P, C _{α} , and axial S ligands, respectively. The use of EXAFS for determining accurate interatomic distances, atomic types, and coordination numbers in these types of iron-heme proteins is clearly demonstrated.

Introduction

Cytochrome P-450 and chloroperoxidase are heme proteins with unusual catalytic and spectral properties. The P-450 enzymes,² which have been isolated from numerous sources including mammalian tissues, catalyze the hydroxylation of substrates, RH (see reaction 1), by dioxygen. One oxygen atom of dioxygen is incorporated into the substrate while the other is reduced to water, thus placing the P-450 enzymes in the monooxygenase or mixed-function oxidase classification of oxygen metabolizing enzymes. The two electron equivalents utilized in this process are provided physiologically by either a flavin or iron-sulfur protein reductase. Only one other heme

protein³ is normally capable of activating dioxygen for insertion into organic substrates.⁴ Clearly, a structural and mechanistic understanding of the activation of dioxygen by P-450 will be of considerable use in the design of comparable nonenzymatic catalysts.



Chloroperoxidase is an enzyme isolated from the fungus *Caldarcomyces fumago*.⁷ In addition to classical peroxidase and catalase activities exhibited by other peroxidases,⁸ chloroperoxidase catalyzes the formation of carbon-halogen bonds between I⁻, Br⁻, Cl⁻, and halogen acceptors such as β -keto