be forbidden for some of them, but allowed with high activation energy for others. This state of affairs has been recognized by Dewar and Kirschner.[3,4] They have shown that the difference in activation energy between "allowed" and "forbidden" bicyclobutane → butadiene reactions is only 2.7 kcal/mol which nicely illustrates our point. They also concluded that there are no correlation diagram arguments for an allowed or forbidden designation to either the bicyclobutane → butadiene reactions or the benzvalene → benzene transformation.

We now turn to the six-electron case. The correlation diagram to which the later literature invariably refers has been given by Haller.[5] This diagram shows a correlation between an excited state of benzene and the ground state of benzvalene. However, as we have remarked earlier,[6] the diagram is in error. The $\pi$ orbitals of benzvalene have the wrong symmetry labels ($C_2$ axis) and the correct labels would give a correlation between the ground state of benzene and that of benzvalene. The analogy with butadiene → bicyclobutane is notable. Bryce Smith[1] states on p 1312 "Note that disregarding the electronic symmetry properties of the intermediate would have produced the misleading conclusion that the thermal rearomatization of benzvalene is a symmetry allowed process". This statement clearly shows the problem that is manifest in these reactions: the rules have been stretched beyond their limits. The mere fact that the thermal rearomatization of benzvalene does not occur spontaneously does not make this process forbidden. The words forbidden and allowed are really useful only in those cases where we have a choice between two stereochemically different modes of a reaction. The fact that the rules are not directly applicable in cases where we do not have this choice in no way diminishes their value. The proof of the rules[6,11] only allows for the distinction between two pathways, one having a higher activation energy than the other.

Continuing the argument, Bryce Smith describes the reaction as proceeding from $S_2$ benzene via "a species formally resembling *cis-,cis-,trans*-cyclohexatriene, the so-called 'Möbius-benzene' ".[7,8] Now benzvalene has the correct symmetry labeling of the orbitals. The "intermediate" can only correlate with excited states of benzene as well as benzvalene. Benzvalene is produced from $S_1$ benzene as well as from $S_2$ benzene. In the former process there is evidence for thermal (vibrational) activation, in the latter this phenomenon is absent. Whereas the "Möbius-benzene" is invoked in the $S_2$ reaction, it is the "prefulvene" meta-bonded intermediate in the $S_1$ process.

A relation between $S_1$ benzene and "Möbius-benzene" was first put forward by Farenhorst[9] who showed that the two systems would be equienergetic in the Hückel approximation. This fact was—erroneously—repudiated by Bryce Smith.[10] Careful consideration shows that Farenhorst did take into account the difference in $\beta$ between the normal and the Möbius ring. $E_{S_1}$ benzene $= 6.00\,\beta$; $E_{\text{Möbius-benzene}} = 4\sqrt{3}\,\beta'$ with $\beta' = \beta \cos \pi/6 = \sqrt{3}/2\,\beta$; so $E_{\text{Möbius-benzene}} = 6.00\,\beta$. This point would not be mentioned were it not that it is exactly the antiaromatic $S_1$ state of benzene which would have the tendency to adopt an out-of-phase overlap to give the Möbius ring.[11] Therefore in our opinion the "Möbius-benzene intermediate" should correspond to a maximum in the ground-state potential energy surface and to a minimum on the surface of the first excited ($S_1$) state. Conceivably this minimum can be reached directly from $S_2$ benzene, but starting from $S_1$ the favorable out-of-phase overlap can only come into play after an energy requiring deformation of the six-membered ring.

In conclusion the following two statements seem appropriate: (i) the use of correlation diagrams, which offer the opportunity to approximate potential energy curves or surfaces, should be distinguished from the application of the Woodward-Hoffmann rules, which were developed to deduce stereochemistry; (ii) intended correlation of ground state of reactant with excited state of product or vice versa does not per se predict a high activation energy, nor does a low activation energy necessarily follow from a ground state to ground-state correlation.

## References and Notes

(1) D. Bryce Smith and A. Gilbert. *Tetrahedron.* **32,** 1309 (1976).
(2) R. B. Woodward and R. Hoffmann. "The Conservation of Orbital Symmetry". Verlag Chemie. Academic Press. New York. N.Y.. 1970.
(3) M. J. S. Dewar and S. Kirschner. *J. Am. Chem. Soc.*. **97**. 2931 (1975).
(4) M. J. S. Dewar and S. Kirschner. *J. Am. Chem. Soc.*. **97**. 2932 (1975).
(5) I. Haller. *J. Chem. Phys.*. **47**, 1117 (1967).
(6) W. J. van der Hart. J. J. C. Mulder. and L. J. Oosterhoff. *J. Am. Chem. Soc.*. **94**. 5724 (1972).
(7) E. Heilbronner. *Tetrahedron Lett.*. 1923 (1964).
(8) H. E. Zimmerman. *J. Am. Chem. Soc.*. **88**. 1564 (1966).
(9) E. Farenhorst. *Tetrahedron Lett.*. 6465 (1966).
(10) D. Bryce Smith. *Pure Appl. Chem.*. **16,** 58 (1968).
(11) J. J. C. Mulder and L. J. Oosterhoff. *Chem. Commun.*. 305. 307 (1970).

**J. J. C. Mulder**

*Department of Theoretical Organic Chemistry*
*Gorlaeus Laboratories. P.O. Box 75. Leiden. The Netherlands*

*Received August 20. 1976*

---

## On the Size of the Singlet–Triplet Energy Gap in Trimethylenemethanes[1]

*Sir:*

Some of the organic biradical reactive intermediates, notably carbenes[2-7] and trimethylenemethanes,[8] can be intercepted in two electronic states of differing multiplicity. Although electron spin resonance (ESR) spectroscopy of immobilized samples is capable of determining the singlet or triplet nature of the molecular ground state from the temperature dependence of the signal intensity,[9,10a] in many cases this method is inapplicable to the determination of $\Delta E$ ($= E_S - E_T$) when $\Delta E$ is more positive than ~0.2 kcal/mol (triplet ground state) or more negative than ~2 kcal/mol (singlet ground state). Hence, the estimation of the singlet–triplet energy gap remains as one of the stubbornly difficult problems of biradical chemistry. By demonstrating that it is possible to trap singlet **1** (**1**-S) from a spin-equilibrated triplet–singlet mixture of **1**-T and **1**-S, the present work determines an upper limit of 3.5 kcal/mol for $\Delta E$ of a trimethylenemethane derivative, 2-isopropylidenecyclopentane-1,3-diyl.

A spin-equilibrated **1**-S-**1**-T diyl mixture can be prepared by irradiation of the diazene **2** in a rigid glassy or polycrystalline matrix containing an olefinic trapping agent, M. Warming the matrix permits diffusion and reaction according to Scheme I. The ratio of products from singlet and triplet diyls, $X_s/X_t$, is given by eq 1.

$$X_S/X_T = K(k_4 + k_4')/(k_3 + k_3') \tag{1}$$

where

$$K = [\mathbf{1}\text{-S}]_{eq}/[\mathbf{1}\text{-T}]_{eq} = (1/3)\exp(-\Delta E/RT) \tag{2}$$

Since **1** has a triplet ground state,[10a] products of capture of the singlet will be formed in detectable amounts under these conditions only if the ratio $(k_4 + k_4')/(k_3 + k_3')$ of the singlet and triplet trapping rates is large. When M = $CH_2{=}CHCN$ or $CH_2{=}CHCO_2Me$, this requirement is not satisfied, and products are formed in the typical triplet distribution.[10b] We now find, however, that such molten matrix experiments with dimethyl fumarate and dimethyl maleate give substantial quantities of singlet products.

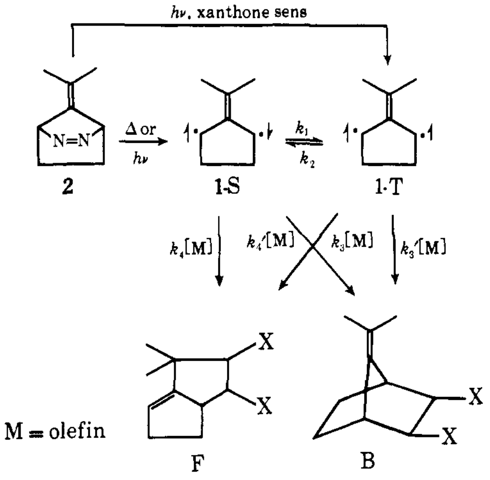
The recognition of the singlet products is based upon criteria justified previously:[8,10b] regiospecificity favoring a high fused-to-bridged ratio ($F/B$), stereospecificity for cis addition, and effect of added oxygen in increasing both forms of specificity (Table I).[11]

Table I. Product Distributions[a] from Molten Matrix Experiments

| Olefin (M), X = $CO_2Me$ | [M], $M/1$ | $P_{O_2}$, Torr | $F/B$ | % cis $F$ | Yield, %[e] |
|---|---|---|---|---|---|
|  | 0.22[c] | 0 | 9.5 ± 1 | | 36 ± 3 |
| | 0.22[c] | 500 | 32.0 ± 3 | | 30 ± 3 |
| | 0.14[c] | 0 | 10.4 ± 0.2 | | 13.3 ± 0.2 |
| | 0.14[c] | 500 | 92 ± 30 | | 12 ± 3 |
| | "pure triplet" reaction | | 0.8[b] | | |
|  | 7.8[d] | 0 | 1.8 | 41 | |
| | 7.8[d] | 460 | 2.6 | 49 | |
| | "pure triplet" reaction | | 0.7–1.5[b] | 5–13[b] | |

[a] Analyses by gas chromatography on 1% packing, 3-mm-i.d. columns. Dimethyl fumarate runs analyzed on XE-60 column, dimethyl maleate on TCEP column (temperature programmed). The XE-60 column did not permit analysis for cis $F$ separately. [b] References 8 and 10b. [c] In benzene polycrystalline matrix. [d] Neat. [e] Relative to diphenyl ether internal standard.

Scheme I



The fractional contributions of singlet and triplet products, $X_s$ and $X_t$, can be calculated from eq 3[8]

$$(F/B)_{\text{obsd}} = (X_sF_s + X_tF_t)/(X_sB_s + X_tB_t) \qquad (3)$$

where the fractions of the singlet ($F_s$, $B_s$) and triplet ($F_t$, $B_t$) products that are, respectively, fused and bridged are indicated. Application of the values determined previously,[8] $F_s = 0.987$, $B_s = 0.013$, $F_t = 0.410$, and $B_t = 0.590$, to the oxygen-free fumarate data of Table I gives $X_s = 0.87$, $X_t = 0.13$.[12] The corresponding "spin-pure" $F/B$ ratios are known with somewhat lower accuracy for maleate,[8] but the high proportion of fused adduct with cis-related $CO_2Me$ functions (cis $F$, Table I) makes it clear that at least a third of the product is singlet derived.

To calculate $K$ and $\Delta E$, we note that the total rate of capture of the triplet ($k_t = k_3 + k_3'$) as measured by kinetic ESR methods is $\sim 10^{-4}$ of the bimolecular diffusive encounter rate ($k_d$) in moderately viscous propanolic medium at 143.8 K.[13] Although both $k_t$ and $k_d$ will depend on temperature and viscosity, their ratio should be relatively insensitive, and we may estimate from the activation energy difference for the $k_d$ and $k_t$ processes that $k_d/k_t \sim 2.3 \times 10^2$ to $10^4$ under the conditions of Table I.[14] Since the singlet capture rate constant ($k_s = k_4 + k_4'$) cannot exceed $k_d$, $k_s/k_t \leq 2.3 \times 10^2$ to $10^4$. From eq 1 and 2, we calculate $K \geq 6.7 \times 10^{-4}$ to $2.9 \times 10^{-2}$, and $\Delta E \leq$ 1.4 to 3.5 kcal/mol.[15]

Several sophisticated quantum mechanical calculations of the singlet-triplet gap in unsubstituted TMM predict $\Delta E$ in the range 18–21 kcal/mol.[16-23] Although the constricted internal C-C-C bond angle[24] in the TMM system of our diyl **1**-T should narrow the S-T gap,[20] the effect as estimated by a zero-differential overlap calculation[25] should be small. If this is correct, the low $\Delta E$ value found here by chemical methods for **1**-T is in serious disagreement with the theoretical predictions. Similar conclusions have been reached recently for TMM itself, where $\Delta E \leq 7$ kcal/mol.[26] These discrepancies are reminiscent of and perhaps related to the still unexplained disagreement among the values for the S-T gap in $CH_2$, where chemical,[3,5,6] theoretical,[27] and spectroscopic[28] methods give 7.5–9, 15, and 19.5 kcal/mol, respectively.

**Acknowledgment.** We thank Professor W. T. Borden for helpful criticisms and comments.

## References and Notes

(1) The support of this work by the National Science Foundation (Grant No. CHE-76-00416) is gratefully acknowledged.

(2) M. Jones, Jr., and K. R. Rettig, *J. Am. Chem. Soc.*, **87**, 4015, 4613 (1965).
(3) (a) H. M. Frey, *J. Chem. Soc., Chem. Commun.* 1024 (1972), and references cited therein; (b) H. M. Frey and G. J. Kennedy, *ibid.*, 233 (1975).
(4) P. P. Gaspar and G. S. Hammond in "Carbenes", Vol. II, R. A. Moss and M. Jones, Jr., Ed., Wiley, New York, N.Y., 1975, Chapter 6.
(5) J. W. Simons and R. Curry, *Chem. Phys. Lett.*, **38,** 171 (1976).
(6) F. Lahmani, *J. Phys. Chem.*, **80,** 2623 (1976).
(7) G. L. Closs and B. E. Rabinow, *J. Am. Chem. Soc.*, **98,** 8190 (1976).
(8) J. A. Berson, L. R. Corwin, and J. H. Davis, *J. Am. Chem. Soc.*, **96**, 6177 (1974).
(9) R. J. Baseman, D. W. Pratt, M. Chow, and P. Dowd, *J. Am. Chem. Soc.*, **98,** 5726 (1976), and references cited therein.
(10) (a) M. S. Platz, J. M. McBride, R. D. Little, J. J. Harrison, A. Shaw, S. E. Potter, and J. A. Berson, *J. Am. Chem. Soc.*, **98**, 5725 (1976); (b) J. A. Berson, C. D. Duncan, G. C. O'Connell, and M. S. Platz, *J. Am. Chem. Soc.*, **98,** 2358 (1976).
(11) If the benzene matrices contained high local concentrations of dimethyl fumarate, one might imagine that entrapment of the singlet **1**-S could occur in the cascade from photoexcited diazene **2**, before spin equilibration. However, continuous irradiation of diazene **2** in a benzene matrix at 98 K leads to a rapid buildup of the triplet ESR signal followed by a slow decay due to a secondary photoreaction of the triplet. Control experiments show that the intensity of the maximum signal and the time needed to achieve it are independent of whether the matrix contains 0.23 M dimethyl fumarate. This behavior is inconsistent with the hypothetical intracascade singlet trapping. Capture of at least 30% (Table I) of the photolyzed material in this manner should have decreased the intensity or retarded the buildup of the triplet ESR signal markedly.
(12) We assume for the purpose of this calculation that the $F_s$, $B_s$, $F_t$, and $B_t$ values are temperature independent. The assumption is experimentally substantiated in the case of the triplet values, which do not change between 60 and 0 °C, as established from "infinite dilution" studies in pyrolysis experiments and from xanthone photosensitization at 0 and 22 °C. We have no direct experimental verification that the assumption is true for the singlet values, but this has no effect upon the conclusions, since a value of $F_s$ >0.987 will have a negligible effect on $X_s$, and a smaller value of $F_s$ can only make $X_s$ larger. The calculated $X_s = 0.87$ therefore should be taken as a minimum value.
(13) M. S. Platz and J. A. Berson, *J. Am. Chem. Soc.*, **98**, 6743 (1976).
(14) It is reasonable to assume that reaction occurs at a temperature between −70 °C (203 K), where the ESR signal of the benzene matrices of Table I begins to decay, and the melting point of benzene, 5 °C (278 K). The factor of $10^4$ at 143.8 K in propanols[13] corresponds to $\Delta\Delta G^{\ddagger} \sim 3$ kcal/mol. Assuming $\Delta\Delta H^{\ddagger} = \Delta\Delta G^{\ddagger}$, we obtain $k_d/k_t = 1.8 \times 10^3$ and $2.3 \times 10^2$ for the 203 and 278 K runs. Assuming $\Delta\Delta H^{\ddagger} = 0$, we obtain $k_d/k_t = 10^4$. Even if the estimate were inaccurate by three orders of magnitude, and $k_d/K_T = 10^7$, $\Delta E$ would rise only to ~7 kcal/mol.
(15) (a) Even if the $X_s/X_t$ ratio were only half the 87/13 value deduced above, $\Delta E$ still would be ≤4.0 kcal/mol. The bicyclic ring-closure products, isopropylidenebicyclo[2.1.0]pentane and dimethylbicyclo[3.1.0]hexene, are not formed in the cascade mechanism from diazene **2**.[15b] They could be the singlet species that we now detect in the molten matrix experiments only if they are intermediate in energy between the triplet and singlet diyls, are formed from the triplet, and have chemistry indistinguishable from that of the singlet diyl. (b) M. Platz, D. R. Kelsey, J.A. Berson, N. J. Turro, and M. Mirbach, *J. Am. Chem. Soc.*, **99,** 2009 (1977).
(16) M. J. S. Dewar and J. S. Wasson, *J. Am. Chem. Soc.*, **93,** 3081 (1971).
(17) W. W. Schoeller, *Tetrahedron Lett.*, 2043 (1973).
(18) W. T. Borden and L. Salem, *J. Am. Chem. Soc.*, **95**, 932 (1973).
(19) W. T. Borden, *J. Am. Chem. Soc.*, **97**, 2906 (1975).
(20) W. T. Borden, *Tetrahedron Lett.*, 259 (1967).
(21) W. J. Hehre, L. Salem, and M. R. Willcott, *J. Am. Chem. Soc.*, **96,** 4328 (1974).
(22) J. H. Davis and W. H. Goddard, III, *J. Am. Chem. Soc.*, **98,** 303 (1976).
(23) D. R. Yarkony and H. F. Schaefer, *J. Am. Chem. Soc.*, **96,** 3754 (1974).
(24) J. A. Berson, R. J. Bushby, J. M. McBride, and M. Tremelling, *J. Am. Chem. Soc.*, **93,** 1544 (1971).
(25) B. K. Carpenter, R. D. Little, and J. A. Berson, *J. Am. Chem. Soc.*, **98,** 5723 (1976).
(26) P. Dowd and M. Chow, *J. Am. Chem. Soc.*, submitted for publication. We

thank Professor Dowd for an advance copy of his paper and for permission to cite it.
(27) J. H. Meadows and H. F. Schaefer, III, *J. Am. Chem. Soc.*, **98**, 4384 (1976), and references cited therein.
(28) P. F. Zittel, G. B. Ellison, S. V. O'Neill, E. Horbst, N. C. Lineberger, and W. P. Reinhardt, *J. Am. Chem. Soc.*, **98**, 3731 (1976).

**Matthew S. Platz, Jerome A. Berson***
*Department of Chemistry, Yale University*
*New Haven, Connecticut 06520*
*March 8, 1977*

# Molecular Dynamics in the Solid State. A Dynamic Model of the Low-Spin Iron(III) to High-Spin Iron(III) Transformation in P450 Enzymes

*Sir:*

Substrate binding by the cytochrome P450$_{cam}$[1] enzyme isolated from *Pseudomonas putida* has been shown to promote a change of the iron(III) protoporphyrin IX prosthetic group from a low-spin to a high-spin electronic configuration.[2] A change in coordination number from six to five is believed to accompany this transformation.[3] The nature of the axial ligands in the two forms has been the subject of intensive investigation and there is growing evidence that the axial ligand in the five-coordinate ferric form and one of the axial ligands in the six-coordinate ferric form is a deprotonated cysteine (cysS$^-$) residue.[4-6] Although the identity of the second ligand in the six-coordinate form has not been established, histidine, lysine, cysteine (cysSH), and methionine have been suggested as possibilities.

Recently a number of ferrous and ferric complexes have been synthesized that mimic the physical and spectroscopic properties of the active site of P450 at various stages of its catalytic cycle.[5b] Among these is iron(III) tetraphenylporphyrinatobenzenethiolate benzenethiol, FeTPP($C_6H_5S$)($C_6H_5SH$),[5] for which EPR, Mossbauer, and magnetic susceptibility measurements performed on crystalline samples indicate the presence of both low-spin and high-spin iron(III).[10] At room temperature, this compound is predominantly high spin and, at 4.2 K, primarily low spin. Employing the aforementioned physical techniques, we have found that the populations of the two spin states change continuously as a function of the temperature. Similar spin equilibria have been observed is several complexes of the ferric forms of myoglobin and hemoglobin[11] and in the substrate bound ferric form of P450$_{cam}$.[2,12] A multiple-temperature crystallographic investigation of FeTPP($C_6H_5S$)($C_6H_5SH$) has been undertaken to examine the structural changes associated with the spin transition. A preliminary phase of this investigation has resulted in the first crystallographic resolution of an equilibrium mixture of spin isomers and has produced a *dynamic* model for the low-spin to high-spin transformation in oxidized P450 enzymes.

Crystallographic data were obtained at 115 K with a Syntex P$\bar{1}$ diffractometer equipped with a locally constructed low-temperature device.[13] Experimental and data-handling techniques were analogous to those described previously.[14] Experimental parameters are summarized in Table I. Standard Patterson, Fourier, and least-squares techniques led to the identification of all nonhydrogen atoms expected from the empirical formula. Full matrix least-squares refinement converged to an acceptable $R$ value, but gave large and highly anisotropic thermal parameters for the iron and sulfur atoms as well as several chemically unreasonable interatomic distances. These problems were eventually overcome by refinement of a model which included two alternate configurations for the iron atom and both sulfur-containing ligands. On the basis of independently refined iron and sulfur occupations it was possible to identify two compatible sets of iron atoms and ligand positions. In further refinements the total population in the two molecular configurations was constrained to unity, and all phenyl groups were constrained to an idealized geometry.

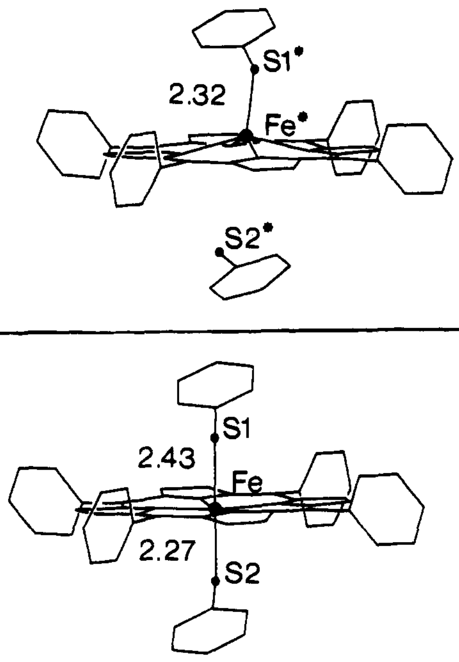


**Figure 1.** The high-spin and low-spin forms of Fe$^{III}$TPP($C_6H_5S$)($C_6H_5SH$).

**Table I.** Crystal Data

Space group $P1$; $Z = 1$
Lattice parameters (115 K)
$a = 10.678\ (3)$, $b = 11.463\ (3)$, $c = 12.305\ (5)$ Å
$\alpha = 58.37\ (2)$, $\beta = 57.04\ (2)$, $\gamma = 72.12\ (2)°$
Radiation Mo K$\alpha$, monochromatized
Crystal dimensions, 0.29 × 0.21 × 0.09 mm
Scan range, 1.0° below $K_{\alpha 1}$ to 1.0° above $K_{\alpha 2}$
Scan rate, 2.0°/min
Scan mode, $\theta/2\theta$
Background time = scan time
$2\theta_{max} = 45°$
Observed reflections ($h > 0, I > 3\sigma I$), 1754
$R = 0.054$, $R_w = 0.056$
Error in observation of unit weight, 1.6

The final model consists of a disordered mixture of a six-coordinate, low-spin complex[15] and a five-coordinate, high-spin complex in which the iron atom is displaced significantly from the plane of the four nitrogen atoms. The ligand lost in the transition is retained in the lattice but is not coordinated. Figure 1 shows the two structural forms identified in this investigation. At 115 K the ratio of the high-spin form to the low-spin form is 0.37/0.63. No attempt has been made to resolve alternate configurations for the porphyrin ligand, but temperature factors in the range 1.0-2.0 Å$^2$ indicate that the displacements of the porphyrin atoms in the course of the transition are very small.

Structural parameters of the high-spin, five-coordinate complex do not differ significantly from those obtained for iron(III) protoporphyrin IX dimethyl ester *p*-nitrophenylthiolate.[4] In particular, the Fe*-S1* distance of 2.32 (2) Å and the Fe*-S1*-C* angle of 103° [16] correspond to the values of 2.324 (2) Å and 100° in the previously reported structure.[4] On the basis of these observations as well as on electrostatic grounds, it is reasonable to infer that the uncoordinated species