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THE CRYSTAL STRUCTURE OF N-(4-AMINO-2-METHYL-5-PYRIMIDYL)METHYL-N-4-HYDROXY-1-METHYL-2-(2,2,6,6-TETRAMETHYL-4-OXOPIPERIDINE)THIO-1-BUTENYL-FORMAMIDE

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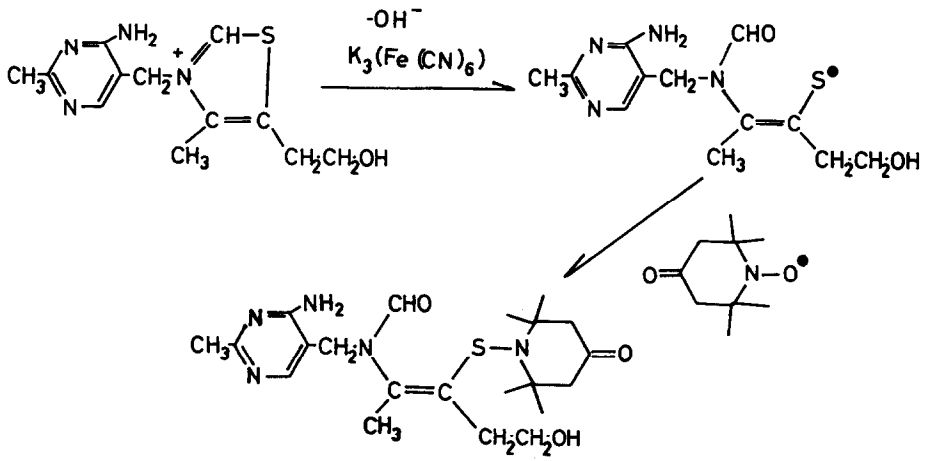
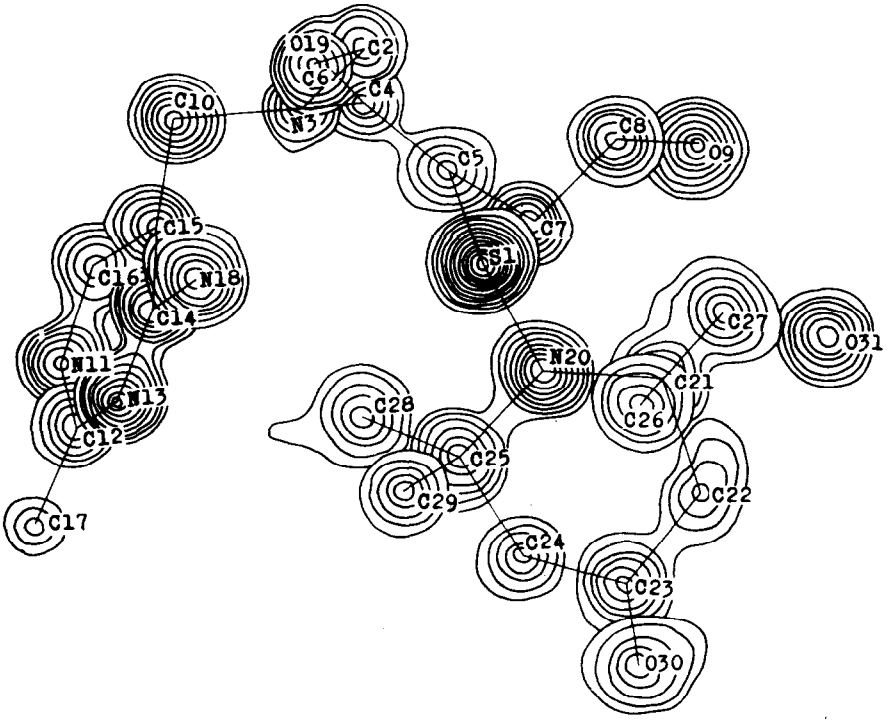
The structure of the radical reaction product between thiamine and 4-oxo-2,2,6,6-tetramethylpiperidine-1-oxyl has been investigated by X-ray crystallographic analysis. This structure had already been proposed by means of Mass-spectrometry and various chemical reactions.[1)]



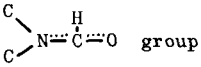
Interest was directed to the S(II)-N(sp^3) bond system which is uncommon in nature, and the 1,3-diaxial-tetramethyl groups of the piperidine ring which might exhibit hindrance around that moiety.[2)] We also examined the heavy atom method for sulfur as a heavy atom in such a big molecule. The parameter of the contribution of heavy atom, indicating r-value $= (\sum f_H^2 / \sum f_L^2)^{1/2}$, is 0.45. This suggested that the probability of correct phases was only 42%.[2)] Physical data for the crystals are : a = 10.92, b = 25.90, c = 9.02 Å and $\beta = 106°$. The space group was determined to be $P2_1/c$ by its extinctions. The observed

density is 1.252 g/cm^3 by floatation method and calculated value is 1.233 g/cm^3.

In a three dimensional sharpened Patterson synthesis, the reasonable heavy atom vectors for a monoclinic system are observed. At the first stage, the R-index of the structure factor calculation was 62.5% using the contribution of the sulfur atom only. The atomic coordinates were assigned to vitamin B_1 part which could be assumed from the first Fourier calculation using the Sim's weighting scheme[3]. By the two cycles of Fourier refinements, the all atoms including the water of crystallization were found. Several cycles of block diagonal least squares refinements, the R-index satisfactorily decreased to 13.5% including hydrogen atoms. Standard deviations of the bond lengths between these light atoms are within 0.025 Å and the sulfur to the light atoms are within 0.015 Å.



The molecular structure was confirmed as previously formulated, in which the oxygen atom of the N-oxide group has been eliminated and the nitrogen formed a rare S(II)-N(sp^3) bond, whose distance is 1.715 Å. The environment of sulfur is of particular interest, in

which the close proximity of sulfur to N(3) and C(2) is 2.90 Å in both cases in spite of the shortest predicted value of 3.5 Å based on van der waals radii. The reason of this interaction is not very clear, but from the fact that the bond angles of C(4)-N(3)-C(10) and C(2)-N(3)-C(10), and C(2)-N(3)-C(4) are 119.9, 119.9, and 120.4° respectively indicated the nitrogen has a more sp^2 like conformation. Thus, one can imagine the p-orbital of  group would have some association with the d-orbital electrons of sulfur. In addition the proximity of two equatorial methyl groups in piperidine ring to the sulfur is 3.02 and 3.05 Å respectively. The ideal atomic distance between 1,3 diaxial methyl groups in a piperidine ring is expected to be 2.35 Å, while the observed value between these methyl groups, C(26) and C(29), is 3.28 Å. Also, the value for the methylene, C(21) and C(25), in the piperidine ring is 2.57 Å. These are significantly greater than 2.35 Å and are due to the hindrance effect of the non bonded electron cloud of these methyl groups. The deviations of N(20) and C(23) from the plane through C(21), C(22), C(24) and C(25) in the piperidine ring are -0.55 Å and 0.61 Å respectively which indicated a chair conformation.

All intermolecular hydrogen bonds are observed in usual range of values, which are 2.79 Å for O(9) ...O(31) and O(9')....O(31), 2.89 Å for O(31)....N(11). A weak intramolecular hydrogen bond might be considered at N(18) to C(19) whose length is 3.06 Å.

Acknowledgements

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