

Molecular Structure and Stereochemical Assignment of 3-phenyl-5-(2-naphthyl)-1,2,4-trioxolane-3-carbonitrile

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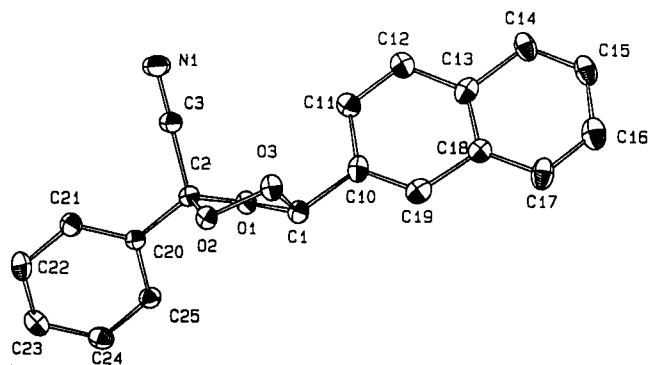
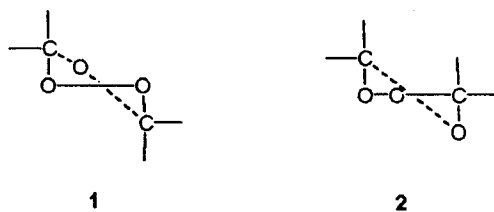


Figure 1. A molecular conformation with the atomic labelling scheme of 3-phenyl-5-(2-naphthyl)-1,2,4-trioxolane-3-carbonitrile (7).

The mechanism of the formation of ozonides in the ozonolysis of alkenes in inert solvents was first proposed by Criegee^{1,2} and later extended by others^{3,4} in order to include stereochemical effects. More recently, attention was focused on conformational and stereochemical assignments of ozonides. Few experimentally determined ozonide conformations have been reported, and only those of simple ozonides have been elucidated in detail by microwave spectroscopy.^{5,6} The conclusion was reached both from experimental results and theoretical calculations that for ozonides bearing small substituents, the most stable conformation is an oxygen-oxygen half-chair of type 1. By contrast, several ozonides derived from cyclic and bicyclic olefins were shown to have symmetrical ether-O-envelope conformations of type 2.



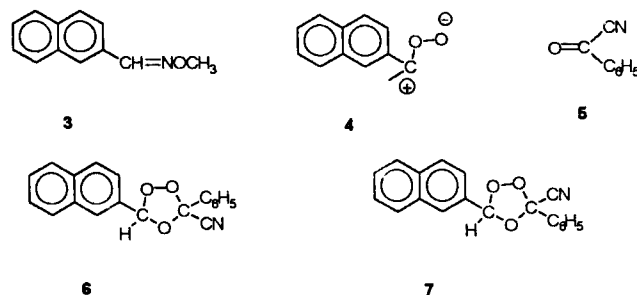
Formula 1.

Stereochemical assignments for *cis-trans*-isomeric ozonides, bearing H-atoms at the ozonide rings, have been made with the help of ¹H NMR spectroscopy: It was reported that in many cases the signals of the CH groups in *trans*-ozonides appear in higher field positions than those of the corresponding *cis*-ozonides.⁷ More equivocal stereochemical assignments of *cis-trans*-ozonides have been made based on the partial resolutions of the racemates of *trans*-isomers,^{8,9} on deuterium isotope effects¹⁰ and particularly on X-ray diffraction analysis.

Recently, we have found that ozonolyses of O-methyl oximes like **3** generate predominantly the corresponding carbonyl oxides like **4** are formed.¹¹ The latter can be trapped with dipolarophiles like acyl cyanides to give cyano substituted ozonides.

Thus, ozonolysis of **3** in the presence of **5** was done to generate two isomeric ozonides which showed ¹H NMR signals for the CH groups in the ozonide rings at $\delta=6.52$ and $\delta=6.91$.¹¹ Here, only the ozonide absorbing at $\delta=6.52$ could be isolated, whereas the other isomer decomposed over the

separation process.



Formula 2.

The isolated ozonide was a colorless crystalline material which melted at 100-101 °C without decomposition.¹¹ We have now obtained single crystals of this ozonide (from pentane-ether) and determined its structure by X-ray diffraction.¹⁴ This analysis showed (Figure 1) that the naphthyl and the phenyl group adopt a *trans*-arrangement, i.e. the crystalline material is isomer **7**. This is in line with the above mentioned result⁷ that in the ¹H NMR spectra the CH signals of *trans*-ozonides appear upfield as compared to those of *cis*-ozonides. Depending on this, the structure of the elusive second ozonide which was obtained in the ozonolysis of **3** in the presence of **5** can be assigned as shown in **6**.

The X-ray analysis of **7** revealed the following additional salient features: The atoms C(1), O(1), C(2) and O(2) of the ozonide ring are in a plane, whereas the second peroxidic oxygen atom O(3) is displaced from the plane by 70.1 pm. This half-chair conformation has been shown to be adopted by many ozonides¹² in the absence of specific steric effects. By contrast, in ozonides of norbornenes the O-atom of the ether bridge adopts an out-of-plane position.¹³ The O-O distance of 147.3 pm and the C(1)-O(1)-C(2) angle of 107.1° in **5** correspond well with those of unstrained ozonides.¹²

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- Data for crystallographic studies were measured on a MAC sciences MXC3 fourcircle diffractometer. The unit cell and other related parameters of compounds (5) are as follows; F.W=303.32; Colorless polyhedral; Crystal demension=1.80×0.80×0.40 mm³; Space group C_{2h}⁵-P2₁/n; a=18.214(5) Å, b=7.416(2) Å, c=12.037(3) Å, β=108.49(2) Å, V=1542.1(2) Å³; Z=4; D_{calc}=1.337 g/cm³; Radiation=Mokα, λ=0.71073 Å; Temperature=293(2)K; Final R=0.0539; Number of unique reflections=1982.

The Relationship between the C2 Proton NMR Signals of Coordinated Imidazole Rings of Cytochrome c₃ and Their Redox Properties

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Cytochrome c₃ are a unique class of heme protein which contains four hemes in a single polypeptide.¹ Crystal structures of cytochrome c₃ from *Desulfovibrio vulgaris* Miyazaki F (*Dv*MF) and *Desulfovibrio vulgaris* Hildenborough (*Dv*H) have been reported.^{2,3} All of the 5th and 6th ligands of the four hemes are histidyl imidazoles. One of the remarkable features of these proteins are the extremely low redox potentials of the four hemes in comparison with other c-type cytochromes. The crystal structure, however, did not give a clue to the extremely low redox potentials. The assignment of the C2 proton signals of ¹H NMR spectrum of cytochrome

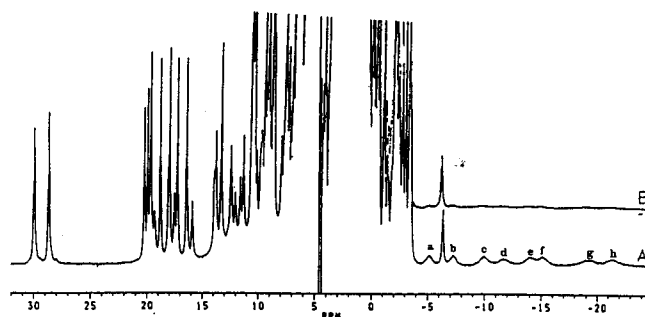


Figure 1. 400 MHz ¹H NMR spectra of *Dv*MF cytochrome c₃ at pH 7.0 and 30 °C. (A) Non-deuterated. (B) Specifically deuterated at the C2 position of histidyl imidazole.

c₃ carried out in this work, which suggested the role of the imidazole rings in realizing the low redox potentials.

Desulfovibrio vulgaris Miyazaki F and *Desulfovibrio vulgaris* Hildenborough were cultured in medium C¹ and in a minimal medium⁴ to obtain non-deuterated and deuterated cytochrome c₃ from *Desulfovibrio vulgaris* Miyazaki F, respectively. In the latter case, the C2 proton of the histidyl imidazole of cytochrome c₃ was specifically deuterated by replacing L-histidine of the minimal medium with deuterated L-histidine. Cytochrome c₃ were purified according to the reported procedure.⁴ The purity was checked by the purity index (A₅₅₂(red)/A₂₈₀(ox)) and SDS-PAGE. 400 MHz ¹H NMR spectra were measured with a Bruker AM-400 NMR spectrometer. Chemical shifts are presented in parts per million (ppm) to the internal standard 2,2-dimethyl-2-silapentane-5-sulfonate (DSS).

There are nine histidine residues in the cytochrome c₃ from *Dv*MF, eight of which are ligands of the four hemes. ¹H NMR spectra of non-deuterated and deuterated ferricytochrome c₃ from *Dv*MF are presented in Figure 1.

In the spectrum of non-deuterated ferricytochrome c₃ from *Dv*MF (Figure 1A), eight extremely broad signals were observed in the region higher than 0 ppm, which disappeared on the deuteration of the C2 position of the imidazole rings (Figure 1B). Thus, they can be assigned to the C2 protons of the histidyl imidazoles coordinated to the heme irons. This means that all of the coordinated histidines could be detected as separate signals. They were designated as a-h from the low to high field. A sharp peak at about 8.9 ppm also disappeared. This can be ascribed to the C2 proton of non coordinated histidine (His-67), which agrees with the earlier assignment.⁴

The formal potentials of each heme (the microscopic redox potentials) of *Dv*MF and *Dv*H cytochrome c₃ were estimated by the use of NMR.^{5,6} Macroscopic redox potentials of cytochrome c₃ are reported to be -240, -297, -315 and -357 mV for *Dv*MF, and -263, -321, -329 and -381 mV for *Dv*H, respectively.⁷ The macroscopic redox potentials of *Dv*H cytochrome c₃ are lower than those of *Dv*MF by about 24 mV except for the third redox potential. But, the crystal structure did not give a clue to the difference redox potential between both protein. The C2 proton signals of the coordinated imidazole groups were identified in a very high field region of the ¹H NMR as shown in Figure 2.

It scattered in a wide range from -5 to -22 ppm. The