

Synthesis of Sodium Salt of 3,6-Dibutanoic-1,2,4,5-Tetroxane

¹Eduardo A. Castro, Soledad Bustillo, Jorge M. Romero, Laura C. Leiva, Nelly L. Jorge
and Manuel E. Gómez Vara

Facultad de Ciencias Exactas y Naturales y Agrimensura, Área de Química-Física,
Universidad Nacional del Nordeste, Avda Libertad 5400, (3400) Corrientes, Argentina

¹División de Química Teórica, INIFTA, Suc.4, C.C. 16, La Plata 1900, Buenos Aires, Argentina

Abstract: We report the experimental preparation of the sodium salt of 3,6-dibutanoic-1,2,4,5-tetroxane by addition of saturated solution of sodium hydroxide to the 3,6-dibutanoic-1,2,4,5-tetroxane, synthesized following the method modified by Jorge *et al.* The UV and IR spectra were studied from the experimental standpoint. A rather complete vibrational assignment was performed and the nature of the electronic transitions was discussed in detail.

Key words: Sodium salt, tetroxane derivatives, synthesis, peroxide, UV and IR spectroscopy

INTRODUCTION

The study of organic peroxides comprehends a large number of chemical issues, from biological like themes (involving, for example, the metabolic oxidation processes), up to industrial applications (disinfections action and pigment manufacture) Kohler^[1], Adam y Cilento^[2].

In biological systems organic peroxides are specially important since they take part in cellular decaying transformations caused by enzymatic self-oxidation due to intermediate peroxidic chemical species. Malaria is one of the leading causes of morbidity and mortality in the tropics, with 300 to 500 million estimated clinical cases and 1.5 to 2.7 million deaths per year. Nearly all fatal cases are caused by *Plasmodium falciparum*. Because the parasite's resistance to conventional drugs such as chloroquine and mefloquine is growing at an alarming rate, new efficient drugs are urgently needed^[3].

For example, dispiro-1,2,4,5-tetroxanes, often prepared by the acid-catalysed peroxidation of cicloalkanones^[4,5], exhibit remarkable anti-malarial activity *in vitro* and *in vivo*^[6].

As a result of an apparent association between the peroxide functional group and antimalarial activity, a substantial effort has been devoted to developing new peroxide antimalarials^[7-10].

Even the importance of these compounds is well known in the chemistry area, several structural aspects and reactivity modeling need to be precisely defined. Low solubility is one of the pharmacological inconvenient of tetroxanes, ionic salt would facilitate this inconvenient.

The aim of this study is to report the synthesis of the sodium salt of 3,6-dibutanoic-1,2,4,5-tetroxane (SDPAG), as well as to present experimental results of the UV and IR spectra.

RESULTS AND DISCUSSION

In solid state SDPAG displayed bands at 3523 and 3539 cm^{-1} , that are assigned as stretching modes $\nu_{\text{O}_{11}\text{H}_{33}}$ and $\nu_{\text{O}_{18}\text{H}_{34}}$ disappears. (Table 1, Fig. 4)

Bands at 3448 and 3433 are assigned as an asymmetrical ring CH stretching mode, while the bands at 3255 and 3250 are assigned as a symmetrical ring CH stretching mode.

The band at 2819 cm^{-1} is assigned as a symmetrical CH_2 stretching mode. The asymmetrical CH stretching bands are located at 2848, 2860, 2878, 2909 and 2942 cm^{-1} .

The ion carboxilate asymmetrical and symmetrical stretching appear at 1659 and 1450 cm^{-1} . Bands calculated between 1212-1481 cm^{-1} correspond to different CH_2 bend, wag, rock and twisting modes. Experimental bands at 1481-1375, 1351, 1341, 1324, 1311, 1212, assigned as CH_2 wagging and CH bending; twist and wag CH_2 , δOCO , νCC and CH bending; CH bending and CH_2 twist, νCO ; CH bend, wag and twist CH_2 ; CH bend, twist CH_2 , $\nu\text{CC}(\text{O})\text{O}$; twisting CH_2 , CH bend, $\nu\text{CC}(\text{O})\text{O}$, respectively.

The C-O stretching bands appear at 1159 and 1165 cm^{-1} .

The OCO deformation mode at 1048 cm^{-1} is coupled with twist, wag, rocking CH_2 and asymmetrical stretching $\text{CC}(\text{O})\text{O}$; modes.

Table 1: Experimental frequency vibrational and assignments of the 3,6-dibutanoate disodium-1,2,4,5-tetroxane

Experimental Vibration	Assignments
441	τ OCCC, δ CCO
467	rocking CH ₂ , δ OCC, ν CO
496	τ OCOO, τ HCOO
527	τ HCOO, τ CCCH, rocking CH ₂ , bend CH, rocking CH ₂ , δ OOC, δ OCH
561	rocking CH ₂ , δ OCC
569	τ OCCH, rocking CH ₂
582	τ HCCO, ν OC, wag CH, wag CH ₂ , rocking CH ₂ , δ OCO, δ CCC
600	Sym ring def. O2,3,5,6, δ OOC
634	δ OCO, rocking CH ₂ , ν CO
662	δ OCO, rocking CH ₂ , δ CCC
705-706	Asym ring def. O2,6 \downarrow O3,5 \uparrow , rocking CH ₂ , bending CH
761	Rocking CH ₂
836	δ COO, bend CH, rocking CH ₂
837	δ COO, bending CH, rocking CH ₂ , δ OCC
924	ν OO, δ COO, twist CH ₂ , rocking CH ₂
992	ν OO, ring def., twist CH ₂ , rocking CH ₂
993	ν CO, ring def., rocking CH ₂ , wag CH ₂ , Asym ν CC(O)O
1044	ν CO, ν CC, wag CH ₂ , rocking CH ₂
1048	δ OCO, twist CH ₂ , wag CH ₂ , rocking CH ₂ , Asym ν CC(O)O
1093	Wag CH ₂ , bending CH ₂ , ν CC, wag CH ₂ , rocking CH ₂ , Sym ν CC(O)O
1095	ν CC, δ HCC, wag CH ₂ , rocking CH ₂ , ν CO
1131	ν CC, ν CO, twist CH ₂ , bend CH ₂
1158	ν CO, wag CH ₂ , δ COO, δ HCO
1165	ν CO, wag CH ₂ , δ CH ₂ , Sym ν CC(O)O
1212	Twist CH ₂ , twist CH ₂ , bend CH, Sym ν CC(O)O
1311	bend CH, twist CH ₂ , Sym ν CC(O)O
1324	Bend CH, wag CH ₂ , twist CH ₂
1341	Bend CH, twist CH ₂ , ν CO
1351	Twist CH ₂ , bend CH, δ OCO, wag CH ₂ , ν CC
1375	Bend CH, Sym ν carboxylate ion, ν CO
1411	Bend CH, wag CH ₂ , twist CH ₂ , twist CH ₂ , wag CH ₂ , ν CO, Sym ν carboxylate ion
1449	Wag CH ₂ , bend CH, Sym ν carboxylate ion
1450	
1481	δ HCH
1557	Asym ν carboxylate ion
1659	
2819	Sym ν CH ₂
2825	Sym ν CH
2848	Asym ν CH
2860	ν CH
2878	Asym ν CH
2909	Asym ν CH
2930	Asym ν CH
2942	
3250	Sym ring ν CH
3255	
3433	Asym ring ν CH
3448	

Bands at 1044-1095 cm^{-1} correspond to C-O and C-C stretching modes are coupled with twist, wag, rocking CH_2 and deformation HCC and OCO.

The corresponding O-O stretching modes of the ring are located at 992-924 cm^{-1} correspond to the asymmetric and symmetric O-O coupled stretching modes.

The bands at 837-836, 705 -600, 582 cm^{-1} , are assigned as COO deformation modes, asymmetric and symmetric O_4 ring deformation and OCO and CCC deformation modes, respectively.

Bands located between 582 and 441 cm^{-1} correspond to torsion angles coupled with wag, rock and twisting CH_2 modes.

Experimental

Synthesis of glutaraldehyde acid diperoxide (DPAG): The DPAG (Fig. 1) was synthesized by oxidation of glutaraldehyde with oxygen peroxide in presence of concentrated sulfuric acid, following the Bayer and Viller Method modified by Jorge *et al.*^[11].

Sixty eight percent H_2O_2 (0.102mol, 1.95g) and glutaraldehyde (35.4mmol, 4.02g) were added by consecutive dropwise addition to a stirred solution of water (12mL), EtOH (12 mL) and H_2SO_4 (12 mL) at -10°C . Stirring was continued for 1 h at -10°C . The resulting white precipitate was filtered, washed with water and air-dried to afford. The precipitate was recrystallized in methanol. The DPAG was analyzed via UV and IR Spectroscopic.

Synthesis of sodium salt of 3,6-dibutanoic-1,2,4,5-tetroxane (SDPAG): Solution of sodium hydroxide pH=9.5 (10 ml), was added to the DPAG (0,0117g), before obtained.

The DPAG, was maintained under agitation during 6 hours at room temperature. Progressive dissolution of the solid (DPAG) indicates conversion to the corresponding salt. Final pH value were 7.5.

Aqueous solution of the salt (SDPAG) was lyophilized in order to recover the product as a solid.

The SDPAG was analyzed via UV and IR Spectroscopic. The UV visible spectrum was carried out in the 200-700 nm range (the quartz cell was 1cm long, in a 0-2 absorbance range), in a trademark Camspec model M330 spectrophotometer. Standard solutions were employed. The IR spectrum was determined between 400-4000 cm^{-1} in an IR Nicolet infrared spectrometer using the diffuse refracting technique with KBr acting as solvent. These spectra are shown in Fig. 3 and 4.

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