

Synthesis and Spectroscopic Studies of $\text{Na}_2[\text{PCl}_3(\text{O}_2)]$ and $\text{Na}_2[\text{PCl}_3(\text{S}_2\text{O}_3)]$ as Anti-cancer Agent

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Abstract: Two new organophosphorus compounds, Sodium trichloroperoxophosphate (STFPOB) and Sodium trichlorotiosolphatophosphate (STCTSP) were synthesized from the reaction between Na_2O_2 and $\text{Na}_2\text{S}_2\text{O}_3$ with PCl_3 respectively. Their chemical composition is characterized obviously by spectroscopic methods such as IR and UV/Vis techniques. Also one of these new compounds (STFPOB) has showed excellent anti cancer activity against 742 (Colon adenocarcinoma) cell lines.

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1. Introduction

In the past five decades, numerous structurally different Organ phosphorous compounds have been synthesized and characterized [1 – 3]. The chief commercial source is phosphate rock, an impure massive form of carbonate-bearing apatite. Estimates of the total phosphate rock in the Earth's crust average about 50,000,000,000 tones, of which North Africa contains two-thirds, and Russia and the United States most of the remaining third. This estimate includes only ore sufficiently rich in phosphate for conversion to useful product by present methods. Vast quantities of material lowering in phosphorus content also exist.

Because the P:N ratio found in manure is much higher than P:N ratio required by plants, excessive P application has occurred resulting in elevated soil P concentrations [4]. The phosphorus chemistry has been developed in recent years as one of the most important branches of science [5]. Many biological processes such as energy transfer, bone synthesis, amino acid synthesis, and metabolism require phosphorus and phosphate esters [6 – 7].

Organophosphorous chemistry is the corresponding science of the properties and reactivity of Organophosphorous compounds [8 – 9]. Also they have been used as pesticides and chemical warfare nerve agents. [10]. Phosphorus sorption is the process of precipitation of P from dissolved to

solid forms [11]. Presently, more than 100 different OP's are used worldwide as insecticides. [12].

Chemotherapeutic agents are cytotoxic drugs used to treat cancer that function by targeting fast growing cells and by blocking some critical element of the cell division process impairing mitosis as well as promoting apoptosis. Because of the similarity of the structures of the synthesized ligand and complexes to the compounds used as chemotherapeutic drugs, their in vitro cytotoxicity effects were carried out using MTT assay method. Therefore in this investigation, two novel organophosphorous compounds with formula $\text{Na}_2[\text{PCl}_3(\text{O}_2)]$ and $\text{Na}_2[\text{PCl}_3(\text{S}_2\text{O}_3)]$ were synthesized and characterized by IR and UV-Vis techniques. Because of mentioning reasons the anticancer activity of STFPOB is discussed clearly.

Material and Methods:

All of the materials used in this study were prepared from Merck company. They include: Na_2O_2 and $\text{Na}_2\text{S}_2\text{O}_3$ and PCl_3 and hexane with 99% purity. Solvent that was used for reactions were purified and dried by standard procedures. Infrared spectra were recorded as KBr disks on a Bruker Tensor model 450 spectrometer and UV/Vis spectra were recorded by CamSpec Company Wpabio Wave, model 350.

Both of these compounds were prepared by dissolving powdered Na_2O_2 (0.32gr/1.41mmol) and $\text{Na}_2\text{S}_2\text{O}_3$ (0.26gr/1.04mmol) in proportional amount of PCl_3 (0.4, 0.14ml).

Sodium trichloroperoxophosphate (STFPOB)UV-Vis in CH_2CN , λ/nm : 280,227.**Sodium trichloroperoxophosphate (STCTSP)**IR (KBr) (cm^{-1}): 640.26(vp-cl),552.51(vp-s) 449.11(vp-s),1118.78(vs-o).UV-Vis in CH_2CN , λ/nm : 279,229.**Cell culture**

The 742(Colon adenocarcinoma)cell lines is used for treatment with the dugs,It was grown at 37° C in at atmosphere containing 5% CO_2 , with RPMI-1640 MEDIUM HEPES Modification with L-glutamine and 25mM HEPES (SIGMA-ALDRICH CHEMIE GmbH)supplemented with 10% heat-inactivated fetal bovine serum (FBS) (Gibco), 2.7% sodium bicarbonate and 500mg/L ampicillin.

Antitumor activity

In chemotherapy,when a tumor is exposed to anticancer agents,the percentage of tumor cells which are killed would be proportional to drug dosage (20%-90%).Some specific anticancer drugs destruct cell reproduction via cellular tools.Researches indicate indicate that the maximum effect occurs during the S phase of DNA and RNA synthesis or during the mitosis process for some herbal alkaloidal anticancer drugs. agents which directly effect on cell cycle stages are called cell-cycle nonspecific anticancer agents.They usually have a long-term effect on cell which ends up in cell destructions.

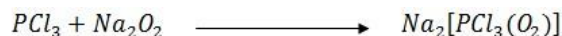


Table 1: IR information of synthesized compounds

ν	Intensity	Vibrational mod	ν	Intensity	Vibrational mod
$Na_2[PCl_3(O_2)]$			$Na_2[PCl_3(SO_2O_4)]$		
666.12	m	P-Cl	640.26	w	P-Cl
1193.60	s	P-O	552.51	m	P-S
1487.83	s	O-O	449.11	m	P-S
			1118.78	w	S-O

Because of the similarity of the structures of the synthesized ligand and complexes to compounds used as chemotherapeutic drugs, they're in vitro cytotoxicity effects were carried out using MTTmethod. Assay method.Results is absolutely novel. Studied cell lines including 724 (colon cancer cells).they were dissolved in DMSO in three different concentrations.

Toxicity of ligand and complexes were different.some were cytotoxic in high concentrations while the others showed cytotoxic effects in low concentrations.Also in some cases,the complexes showed higher cytotoxic effects in comparison with ligand.The result may be due to the presence of metal in the complexes.Apparently,the complexes prevented cellular proliferation and thus to lead this death (Figure 5-7).Therefore,this compound (STFPOB) is suggested as suitable models for novel antitumor drug designs.

Result and Discussion:

The present contributions aim to build experimental data for preparation two novel phosphorus compounds with formula $Na_2[PCl_3(O_2)]$ and $Na_2[PCl_3(SO_2O_4)]$. These products could be easily prepared in good yield by combination of mentioned components with phosphorus trichloride as follows:

Table 2: UV/Vis features of synthesized compounds

Wave length ($\epsilon, M^{-1}cm^{-1}$)	Kind of transitions
$Na_2[PCl_3(O_2)]$	
280(76)	$A_1 \longrightarrow A_1'$
227(174)	$A_1 \longrightarrow E$
$Na_2[PCl_3(SO_2O_4)]$	
279(78)	$A_1 \longrightarrow A_1'$
229(170)	$A_1 \longrightarrow E$

Table 3: Solubility of synthesized compounds in some common solvents

Solvent	$Na_2[PCl_3(O_2)]$	$Na_2[PCl_3(SO_2O_4)]$
Hexane	imisc	imisc
Ether	imisc	imisc
Toluene	imisc	imisc
Chloroform	imisc	imisc
Ethanol	imisc	imisc
Acetonitrile	low dissolved	imisc
Methanol	low dissolved	low dissolved
H ₂ O	misc	misc
DMSO	imisc	imisc

Listed compounds were characterized by IR,UV/Visible techniques (Figure 1-4).in vibrational spectrum of them all of the expectable bands have been seen.The most important of these bands are related to tensile motion of P-Cl and P-O links (in 666 and 1193cm^{-1} for (STFPOB) and tensile motion of P-Cl and P-S links (in $640,550$ and 449cm^{-1} for STCTSP).

All data of vibrational spectrum of these compounds are given in Table completely.

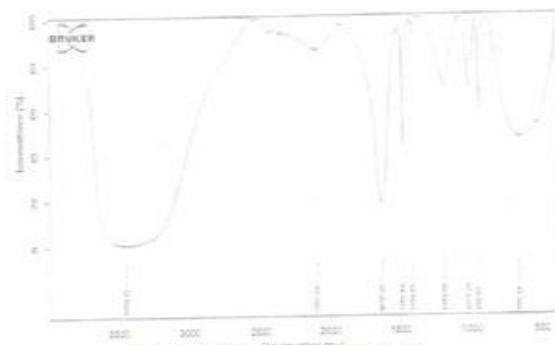


Fig. 1: IR Spectrum of STFPOB

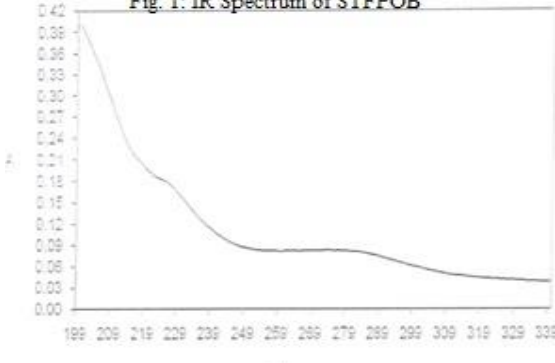


Fig 3: UV/V is spectrum of STFPOB

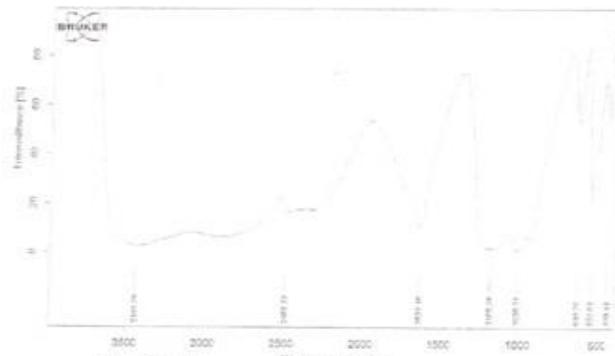


Fig. 2: IR Spectrum of STCTSP

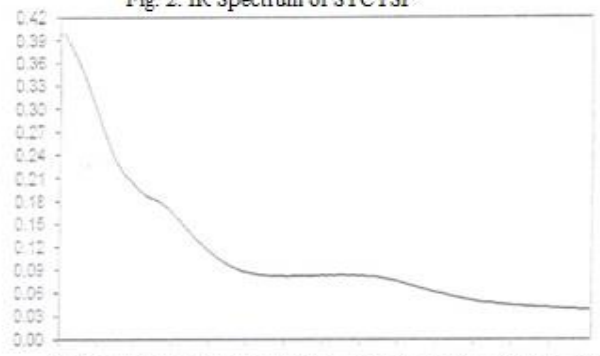


Fig. 4: UV/V is spectrum of STCTSP

As its observable in 2,UV/Visible spectru of STFPBO and STCTSP has 2 transitions.

There are two $\pi \rightarrow \pi^*$ transitions in wave length 280 and 279 nm respectively that link to charge transitions.

For the solubility of these synthesized compound there are no many data,as it shown in Table 3 both of them are soluble in H_2O but they are in hexane,ether,,toluene,chloroform and DMSO.

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