Synthesis of Biologically Active 3-Hydroxy-3-Phenyl-1-(5-Chloro-2-Methyl) Phenyltriazene and Application in the Spectrophotometric Study of Iron Complex

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ABSTRACT

In the present study synthesis, characterization and activity prediction of 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene has been done. The spectrophotometric behaviour of complex of Fe (III) with 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene was also studied. It was observed that 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene forms 1:3 complex with Fe (III) between pH 2.8-3.8.

Keywords: 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene, spectrophotometric determination of Fe (III), PASS, CADD.

INTRODUCTION

Hydroxytriazenes have attracted attention due to their chelating ability as revealed by reviews appearing on them during last few years [1-8]. Hydroxytriazenes and their transition metal complexes have also been found to possess biological activities [9-11] in recent years [12-18]. In the present paper, the spectrophotometric determination [19-21] of Fe (III) was done using 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene. The reagent 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene was synthesized by using standard method[22-24], duly characterized by IR, elemental analysis(CHN), $^1$HNMR, and m.p. determination. Biological activity has been screened by using computer aided program PASS [25-26] for synthesized 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl)phenyltriazene. PASS provides large no. of possible biological activities with their per cent activity and per cent inactivity to design drug which would pave a way to CADD.

MATERIALS AND METHODS

All the materials and solvents used were of analytical grade and used as such without purification. All the chemicals were purchased from Aldrich. Melting points were recorded on an open capillary tube in Sigma Melting point apparatus and are uncorrected. The synthesized hydroxytriazenes were analysed for C, H, N by micro analytical techniques. The IR spectra were recorded using Bruker (4000-400 cm$^{-1}$). NMR spectra were obtained from a 400 MHz spectrometer in DMSO-$d_6$ and tetramethylsilane (TMS) was used as an internal standard and recorded in ppm. 3-Hydroxy-3-phenyl-1-mchlorophenyltriazene was subjected to
four spot tests as described by Purohit [27-29] viz. α-naphthylamine test, picric acid test, sulphuric acid test, N, N-dimethylaniline test.

**Synthesis:** Hydroxytriazene was synthesized as per standard method [16-18]. The general method is described below. The synthesis was done in three steps.

**Preparation of aryl hydroxylamine:** 0.05 mol of nitrobenzene compound, 3 g of NH₄Cl and 35 mL of alcohol and 35 mL of water were mixed and stirred mechanically at 40°C and then 10 g of Zn dust was added in the small lots. The temperature of the reaction mixture remained between 45-60°C. The reaction mixture was filtered, washed with ice-cold water and used for coupling.

**Preparation of aryl diazonium salts:** 0.025 mol of 2-methyl-5-chloroaniline was dissolved in mixture containing 7 mL of HCl and 7 mL of water. In another beaker 2.5 g of sodium nitrite was dissolved in minimum quantity of water. The temperature of the aryl amine hydrochloride solution was maintained between 0-5°C. To this solution, sodium nitrite solution was added drop by drop with stirring. The diazotised product so obtained was directly used for coupling.

**Coupling:** The temperature of aryl hydroxylamine prepared in step-1 and diazotised product obtained from step-2 was maintained between 0-5°C. Step-2 solution was added drop-by-drop to the solution obtained in step-1 and pH of solution was maintained between 5 to 6°C by adding sodium acetate buffer. The resultant product was filtered, washed with cold water and dried. Evaporation of solvent and recrystallized from ethanol afforded respective product.

The tentative mechanism (Scheme-1) has been proposed for the formation of hydroxytriazene.

**Characterization**

**3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene:** Light yellow needle shape shining crystal. The product was recrystallised in ethanol and dried in air. m.p. 110°C, found (%): C, 59.60, H, 4.49, N, 15.96. C₁₃H₁₂N₁O₁Cl (261.70), calculated (%): C, 59.65, H, 4.58, N, 16.06. IR (cm⁻¹) 3417 (νO-H), 3189 (νN-H), 1461 (νN=N), 1325 (νN-O), 1166 (νN,N); ¹HNMR (400MHz, DMSO-d₆, δ) 10.85 (1H,S,OH), 2.30 (3H,S,CH₃), 7.01-8.10 (8H,M,ArH).
Spectrophotometric Study Of Fe (III) With 3-Hydroxy-3-Phenyl-1-(5-Chloro-2-Methyl) Phenyltriazene: Following set of experiment were carried out for the spectrophotometric study of Fe(III).

Preparation of solutions
Reagent Solution: A fresh stock solution of 1.0 X 10^{-2} M of the reagent 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene was prepared by dissolving requisite quantity of the reagent in ethanol. Dilute solution was prepared from this solution as used when required.

Standard Solution of Fe (III): A 1.0 X 10^{-2} M stock solution of Fe(III) was prepared by dissolving the requisite quantity of ferric nitrate in double distilled water. A few drops of dilute HNO_{3} added to prevent hydrolysis. It was standardized by using 1.0 X 10^{-2} M EDTA solution using sulfosalicylic acid as an indicator.

Tris-buffer solution-An aqueous solution of 1% tris buffer was prepared by dissolving it in double distilled water.

Perchloric Acid-A 1% solution of perchloric acid was prepared in double distilled water and used to adjust the desired lower pH.

Instrument: The spectrophotometric study was carried out using Elico SL 210 UV-VIS spectrophotometer.

Determination of working wavelength-The spectrum of the complex formed with reagent (M): (R) was obtained in wavelength range 350 nm to 650 nm against reagent blank. Further spectrum of reagent was also measured in the same wavelength region against ethanol. The working wavelength was chosen such that there was maximum difference between the absorbance of the complex and reagent.

Effect of pH on absorbance-Absorbance of the solution at various pH in the range 2.8-3.8 containing Fe (III) and hydroxytriazene solutions in the ratio of 1:10 were taken at corresponding working wavelength against respective reagent blank. The optimum pH range for maximum absorption selected.

Composition of the Fe (III) complex-The composition of the Fe(III) complex with was determined using Job’s method, mole ratio method of Yoe and Jones method.

Job’s method- The composition of Fe(III) complex with 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl)phenyltriazene was determined using Job’s method. In this method, set of solutions was prepared by varying the volume of equimolar Fe (III) and reagent solution from 0 to 3 mL. After pH adjustment, the solutions were marked (10 mL) with ethanol. The absorbance of solution was measured at working wavelength against reagent blank. by this method the composition was found to be 1:3. (Fe: R)

Mole ratio of Fe: R. Yoe and Jones method- In this method, the composition of binary complex Fe(III) with 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl)phenyltriazene was determined and M to L ratio was taken
in 1:10 ratio. In this a series of solutions were prepared keeping the Fe(III) concentration values constant and varying the concentration of hydroxytriazenes.

Sandell's sensitivity - The molar absorbivity of ternary complex of Fe (III) complex with hydroxytriazone calculated from the Beer's law graph and the value thus obtained was used for determining Sandell's sensitivity of the complex.

<table>
<thead>
<tr>
<th>Table-1 Spectrophotometric determination of Fe(III) with 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl)phenyltriazene</th>
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<tbody>
<tr>
<td>Fe(III) complex with reagent</td>
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<tr>
<td>3-hydroxy-3-phenyl-1-(5-chloro-2-methyl)phenyltriazene</td>
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</tbody>
</table>

RESULTS AND DISCUSSION

As described above, 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene forms 1:3 complex. 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene act as bidentate ligand which indicates hexacoordinated Fe(III) complex with a probable octahedral geometry. The result of PASS prediction for 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene is presented in table 2. PASS is based on structure activity relationship.

APPLICATIONS

Prediction Of The Biological Activities (Brief Description of PASS): The computer program for the prediction of biological activity according to structural formula which was used to predict the biological activity of 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl)phenyltriazene. The PASS system provides the following basic elements: description of the chemical structure, representation of the biological activity and structure activity relationship. In PASS system, biological activity is predicted qualitatively. PASS involves more than 400 pharmacological effects and mechanism of action as well as carcinogenicity, teratogenicity, embryoxicity and mutagenicity.

Activity Prediction: The biological activity spectra of 3-hydroxy-3-phenyl-1-(5-chloro-2-methyl) phenyltriazene was obtained by PASS. Pa and Pi of compound have been represented in table 2.

<table>
<thead>
<tr>
<th>Table 2 - Prediction of percent activity(Pa) and inactivity(Pi) of compound</th>
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<tbody>
<tr>
<td>Pa</td>
</tr>
<tr>
<td>0.791</td>
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<td>0.632</td>
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<td>0.612</td>
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</table>
CONCLUSIONS

The present compound has been developed as an analytical reagent for Fe (III) and is biologically active compound. Thus, it will be useful drug candidate if explored further.

REFERENCES


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