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Synthesis, characterization and biological studies of a charge transfer complex: 2-Aminopyridinium-4-methylbenzenesulfonate

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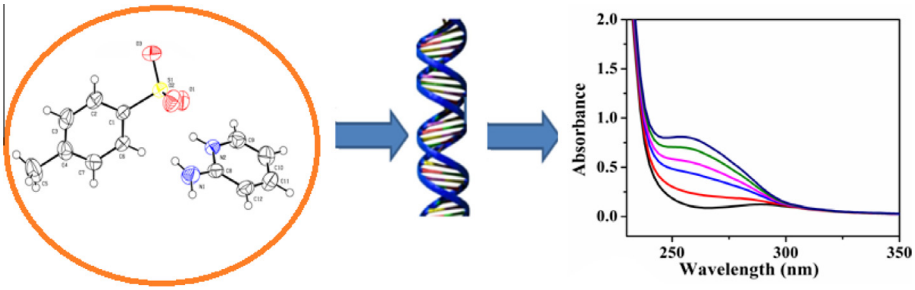
HIGHLIGHTS

- The single crystals were grown via solution growth technique at room temperature.
- The charge transfer complex is characterized through elemental, IR, UV–vis spectra and thermal analysis.
- DNA-binding studies of CT complex have been performed.
- The CT complex is also screened for its antioxidant activity.

GRAPHICAL ABSTRACT



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ABSTRACT

A single crystal charge transfer (CT) complex, 2-aminopyridinium-4-methylbenzenesulfonate (APTS) was synthesized and recrystallized by slow solvent evaporation solution growth method at room temperature. The complex has been characterized with the elemental analysis, UV–visible, infrared (IR), ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra. Thermogravimetric (TG) and differential thermal analysis (DTA) were reported the thermal behaviour of the complex. Single crystal XRD studies showed that the orthorhombic nature of the crystal with space group Pbca. The biological activities of CT complex, such as DNA binding and antioxidant activity has been carried out. The results indicated that the compound could interact with DNA through intercalation and show significant capacity of scavenging with 2,2-diphenyl-2-picryl-hydrazyl (DPPH).

Introduction

Crystal lattice plays vital role in the formation of organic crystals by the formation of proton or charge transfer complexes. CT complexes act as intermediate in wide variety of reactions involving electron rich and electron deficient molecules [1–4]. CT complexes are well-known to have a wide range of application such as optoelectronic, photorefractive and light emitting materials. In addition CT complexes are also used in biological field [5–9]. Aminopyridine constitute an important group of electron donor (or) proton acceptors and the study of their charge transfer complex help to elucidate many chemical phenomena [10]. The compound 4-methylbenzenesulfonic acid has a methyl group which act as an electron donor and a sulfonate group as an electron acceptor [11]. Generally, CT interactions between 4-methylbenzenesulfonic acid electron acceptor and electron donor containing nitrogen, oxygen (or) sulfur atoms have been reported over the past three decades. This type of interactions play an important role in the field of drug–receptor binding mechanism [12,13], surface chemistry [14], solar energy storage [15], organic superconductors [16] and in biological field as antibacterial and antifungal agent [17–20]. The study of interaction between drug and DNA is one of the most important aspects in biological investigation aimed

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at discovering and developing new type of antiproliferative agent [21] since, DNA is the molecular target in the design of anticancer compound [22–24].

This paper focuses on the synthesis of CT complex 2-aminopyridinium-4-methylbenzenesulfonate from 2-aminopyridine and 4-methylbenzenesulfonic acid and study of its properties such as DNA binding ability and antioxidant activity. The molecular structure, charge transfer interaction and thermal stability of complex has been established with the help of NMR, single crystal XRD, IR, UV–vis spectra and TG/DTA thermal analyses.

Experimental section

Materials and methods

All the chemicals were used chemically pure and AR grade. Solvents were purified and dried according to the standard procedures [25]. Calf-thymus (CT-DNA) was purchased from Bangalore Genei, Bangalore, India. Tetracycline, Nystatin and Agar were purchased from Hi-Media, Mumbai. Micro analyses (C, H and N) were performed on a Vario EL III CHNS analyzer at STIC, Cochin University of Science and Technology, Kerala, India. The IR spectrum was recorded as KBr pellet method in the 400–4000 cm^{-1} region using a Perkin Elmer FT-IR 8000 spectrophotometer. Electronic spectrum was recorded in methanol solution with a Systronics Double Beam UV–vis spectrophotometer 2202 in the range 200–800 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV III 500 MHz instrument using TMS as an internal reference and DMSO as solvent, Indian Institute of Technology, Madras, Chennai. Melting points were recorded with Veego VMP-DS heating table and are uncorrected. The thermal analyses (TG and DTA) were carried out under nitrogen atmosphere with a heating rate of 20 °C/min by NETZCHSTA 409C analyzers.

Synthesis of APTS complex

APTS crystals were grown by using slow solvent evaporation solution growth technique. The 2-aminopyridine in methanol and 4-methylbenzenesulfonic acid in water were dissolved and mixed together. The solution was stirred well using a magnetic stirrer to get homogenous mixture and filtered using Whatmann filter paper. The clear filtrate obtained was kept aside unperturbed in a dust-free room for the growth of single crystals. A good transparent needle shaped crystals were harvested in a growth period of 20–25 days. The purity of the synthesized crystals were further improved by repeated recrystallization process by using methanol as solvent. The reaction scheme and the chemical structure of APTS was shown in Fig. 1.

DNA binding – titration experiments

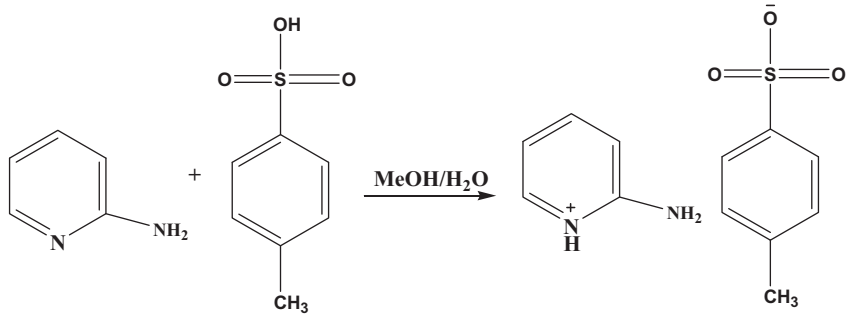
The binding affinity of the compound with CT-DNA were carried out in double distilled water with tris(hydroxymethyl)-aminomethane (Tris, 5 mM) and sodium chloride (50 mM). The pH was adjusted to 7.2 using hydrochloric acid. A solution of CT-DNA in the buffer gave a ratio of UV absorbance of about 1.8–1.9 at 260 and 280 nm, indicating that the DNA was sufficiently free of protein. The DNA concentration per nucleotide was determined by absorption spectroscopy using the molar extinction coefficient value of 6600 $dm^3\ mol^{-1}\ cm^{-1}$ at 260 nm. The compound was dissolved in a mixed solvent of 5% DMSO and 95% Tris–HCl buffer for all the experiments. Stock solutions were stored at 4 °C and used within 4 days. Adsorption titration experiments were performed with a fixed concentration of the compound (25 μM) with varying concentration of DNA (0–50 μM). While, measuring the absorption spectra an equal amount of DNA was added to all the test solutions and reference solution to eliminate the absorbance of DNA itself.

Antioxidant behaviour

The 2,2-diphenyl-2-picryl-hydrazyl radical scavenging activity of the compound was measured according to the method of Elizabeth and Rao et al. [26]. The DPPH is a free radical having a stable λ_{max} at 517 nm. A fixed concentration of the experimental compound (100 μL) was added to a solution of DPPH in methanol (0.3 mM, 1 mL) and the final volume was made up to 4 mL with double distilled water. DPPH solution with methanol was used as a positive control and methanol alone acted as a blank. The solution was incubated at 37 °C for 30 min in darkness. The decrease in absorbance of DPPH was measured at 517 nm. The tests were run in triplicate and various concentrations (20–100 μg/mL) of the compound was used to fix a concentration at which the compound showed 50% activity. In addition, the percentage of activity was calculated by using the formula, % of suppression ratio = $[(A_0 - A_c)/A_0] \times 100$. Where, A_0 and A_c are the absorbance in the absence and presence of the tested compound respectively. The minimum inhibitory concentration of the compound (IC_{50}) was 50% with DPPH.

X-ray crystal structure determination

The crystallographic data of the complex has been measured at 298 K on a Bruker SMART APEX CCD, area detector system [λ (MoKα) = 0.71073 Å]. A graphite monochromator, 2400 frames were recorded with an ω scan width of 0.3°, each for 10 s, crystal-detector distance 60 mm, collimator 0.5 mm. Data reduction was carried out by SAINPTUS [27] and absorption correction was made using an empirical method SADBS [28]. The structure was



2- Aminopyridine **4-Methylbenzenesulfonic acid** **2-aminopyridinium-4-methylbenzenesulfonate**

Fig. 1. Reaction scheme and chemical structure of APTS.