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A chemosensor selection for the fluorescence identification of tryptophan (Trp) amino acids in aqueous solutions with nanomolar detection

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ABSTRACT

A new disulfide-based, imine-linked fluorescent receptor **1** has been synthesized for the highly selective gratitude of tryptophan (Trp) among the all amino acids investigated in aqueous solutions *via* synergistic effects of intermolecular hydrogen bonding and electrostatic interactions. The photophysical properties of the receptor 1 were evaluated by UV/Vis absorption and fluorescence spectroscopic methods. Receptor **1** selectively recognized tryptophan (Trp) amino acid in DMSO/water with a detection limit down to 47.6 nM. The mechanism of binding was fully validated by computational studies. The theoretical calculations revealed the role of π-π stacking as well as hydrogen bonding in binding of tryptophan with receptor.

1. Introduction

Chemosensors are molecules competent of connecting a given ionic and biomolecular species selectively such that the attaching occasion induces a measurable signal, mainly frequently a change in the spectral properties of a chromophore or fluorophore. In one meticulous plan, reported receptors live in the binding location for the goal of ionic and biomolecular species within the receptor and transitions occurs upon aggressive dislocation of this reporter molecule from the binding site by the guest molecules [1–5]. Even though some powerful analytical methods such as Gas chromatography, High Performance Liquid Chromatography, Gel permission chromatography are currently used to monitor low levels of these biomolecules, they have some drawbacks such as being time-consuming and expensive [6–8]. Thus, cheap and simple methods for monitoring these biomolecules are in high demand. Still, only a little fluorescent chemosensors for amino acids have been explained thus distant [9–11].

Amino acids, the input components of proteins, are small molecules with a variety of functional side chain groups, which consequence in different roles of amino acids in biochemical processes [12,13]. In this family unit, lysine is directly related to the Krebs–Henseleit cycle and polyamine synthesis, and an suitable amount of lysine in the diet is essential for the metabolic functions and weight gain of animals, histidine is necessary for the expansion and restore of tissue as well as for the organize of essential trace elements communication in biological bases, tryptophan participates a critical element in life development such as protein biosynthesis, animal growth, and plant development [14–16]. In addition, the lack of some amino acids causes various irregularities, for example, shortage of tryptophan results in slow growth, dry mouth, nausea, blurred, edema, hair depigmentation, lethargy, liver damage, muscle and fat loss [17,18]. As the effect of growing notice waged to human fitness, diagnosis and treatment of illness, a lot of attempts have been straighter to the growth of new processes toward amino acid investigation. Although there are many systems for their recognition [19–21], still there is scope for development of new fluorescent and colorimetric chemosensors that can operate able in semi aqueous or purely aqueous medium.

As a result, the curiosity in developing visual chemosensors purposely distinguishing an objective amino acid has developed progressively and the ability to easily and quickly obtain fingerprints for tryptophan amino acid by chemosensors will still comprise a get through. The amino acid containing aromatic rings such as Tryptophan, phenylalanine and tyrosine have affinity to interact with organic receptor through π-π stacking, which results in change in photo physical properties of receptor [22–24]. These types of non-covalent interactions

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are highly sensitive toward micro environment therefore can be used for development of highly sensitive sensors. Earlier Keeping these things in mind we have designed a disulphide based amine conjugated with 2,3-dihydroxybenzaldehyde through Schiff base linkage. Two hydroxyl groups provide hydrogen bonding interactions that can be used for selectively binding with suitable analyte. Here, we report the synthesis and characterization of a 3,3'-((1E,1'E)-((disulfanediylbis(2,1-phenylene))bis(azanylylidene))bis(methanylylidene))bis(benzene-1,2-diol) (**1**) and develop it for selective sensing of tryptophan. Further sensing of amino acids has been examined by using UV–vis and fluorescence titration experiments in aqueous solvent. The selective and sensitive nature of **1** toward tryptophan amino acid arises from the non-covalent interactions between imine, hydroxyl and sulphur containing functional groups.

2. Experimental section

2.1. General information

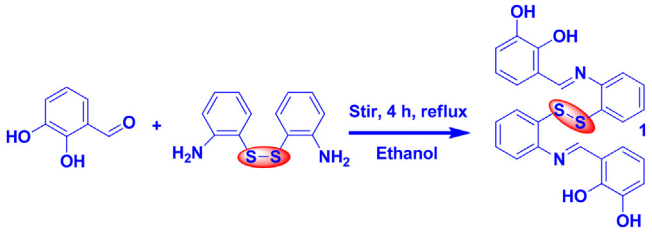
All reactions were carried out using oven-dried glassware beneath a slight positive pressure of nitrogen unless otherwise specified. Where necessary, solvents were purified prior to use. All chemicals were purchased from Sigma Aldrich, India. All reactions were magnetically stirred and monitored by thin-layer chromatography (TLC). ^{1}H NMR (400 MHz) and 13C NMR (100 MHz) spectra were determined on a Bruker AVANCE II 400 spectrometer. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm), calibrated to the solvent peak set. Fluorescence measurements were made with a HORIBA JOBIN YVON, Fluoromax-4 Spectrofluorometer equipped with a xenon lamp. UV–vis absorption spectra were recorded on a Shimadzu UV-2450 spectrophotometer.

2.2. Synthesis of receptor 1

Receptor **1** was synthesized by refluxing 2,2′-disulfanediyldianiline (0.248 g, 1 mmol) and 2,3-dihydroxybenzaldehyde (0.276 g, 2 mmol) in ethanolic medium (50 mL) for four hour. After cooling, the receptor **1** obtained as red crystal powder was collected by filtration and subsequently washed with cold ethanol, followed by recrystallization with ethanol. Crystals suitable for X-ray diffraction determination were obtained by slowly evaporating an ethanol solution of receptor **1** at room temperature. Yield 90%, mp > 250 °C. ^{1}H NMR (400 MHz, DMSO-d_6): d = 6.79 (t, 2H, Ar-H, J = 8 Hz), 6.97(d, 2H, Ar-H, J = 8 Hz), 7.08 (d, 2H, Ar-H, J = 8 Hz), 7.23 (d, 2H, Ar-H, J = 8 Hz), 7.29 (t, 2H, Ar-H, J = 8 Hz), 7.42 (d, 2H, Ar-H, J = 8 Hz), 7.56 (d, 2H, Ar-H, J = 8 Hz), 8.88(s, 2H, CH═N), 9.12(s, 2H, Ar-OH), 12.86 (s, 2H, Ar-OH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6,): δ = 117.8, 117.9, 118.9, 119.1, 119.4, 123.0, 126.2, 127.5, 127.7, 130.5, 145.5, 148.9, 163.6 ppm. LC–MS(ESI) ($C_{26}H_{20}N_2S_2O_4$) [M + H$^+$] m/z Calcd 489.09 found 489.40.

2.3. X-Ray structure description

Data of single crystal of receptor was collected on Bruker diffractometer. A suitable crystal was selected and mounted on a diffractometer. The crystal was kept at 298 K during data collection. The data collection crystal was an orange colour rectangular plate. The data collection strategy was set up to measure a quadrant of reciprocal space with a redundancy factor of 3.9, which means that 90% of these reflections were measured at least 3.9 times. Phi and omega scans with a frame width of 2.0° were used. Data integration was done with Denzo and scaling and merging of the data was done with Scalepack. Merging the data and averaging the symmetry equivalent reflections resulted in a R_{int} value of 0.036. Using Olex2, the structure was solved with the olex2.solve structure solution program using Charge Flipping and refined with the olex2.refine refinement package using Gauss-Newton minimization.



Scheme 1. Synthesis of receptor **1.**

2.4. Spectroscopic studies

The amino acids recognition studies of **1** were performed at ambient temperature. All solutions were shaken properly to ensure consistency before recording the absorption and emission spectra. The amino acids recognition ability was studied by adding a fixed amount of different amino acids (1 equivalent, 20 μL, 1×10^{-3} M, c = 1 mM, in H_2O) to the standard solution of receptor **1** (c = 0.01 mM, 1×10^{-5} M, 2 mL, in DMSO). The fluorescence titration experiment was carried out to determine the association constant (K_a) of the receptor **1** with the selective amino acids. The titration experiment was accomplished through a stepwise addition of amino acids solution (0.02 mL, 1 mM, guest in water) to a solution of receptor **1** (2 mL, 0.01 mM, host in DMSO) in the cell. The fluorescence intensity was recorded at $\lambda_{exc}/\lambda_{em}$ = 300/432 nm alongside a reagent blank. The excitation and emission slits were both set to 5.0 nm. All the experiments were repeated three times and mean of these values were taken, the variation of results has indicated using error bars (Fig. 6).

3. Results and discussion

3.1. Synthesis and characterization

Receptor**1** was synthesized by simple condensation reaction of 2,2′-disulfanediyldianiline with 2,3-dihydroxybenzaldehyde in the ethanolic medium under reflux condition (Scheme 1). The red coloured precipitate was separated out after filtration; the receptor was characterized by ^{1}H NMR, ^{13}C NMR and LC–MS spectroscopic methods (Fig. S1–3, SI). The spectral investigation gave consistent data along with the molecular structure of **1**. Finally, the structure of **1** was confirmed using single crystal X-ray crystallography shown in Fig. 1.The crystallographic data are listed in Table S1. The CIF file for receptor **1** was deposited in the Cambridge Structure Database with CCDC No 1470572.

Perspective views of the crystal structure of 1, with labelling and packing diagram are shown in Fig. 1 and S4, (SI). Crystal of receptor 1 suitable for X-ray diffraction was obtained by slow evaporation of an ethanol solution of compound responding to the formula $C_{26}H_{20}N_2O_4S_2$. The crystal was tetragonal in molecular setting with $I4_1/a$ space group and there were eight molecules present in a unit cell (Z = 8). Hydrogen bonding of the phenolic–OH was major advantageous feature in host-guest complexation. Invariability, phenolic hydrogen atom formed an intramolecular hydrogen bond to the N atom of the azomethine group, giving a six member ring. This interaction was usually characterized in terms of phenolic oxygen to imine nitrogen separation [25,26]. This distance varies little between the two molecules. In all free receptor structure, the molecular involvement was *via* intramolecular hydrogen bonding. The receptor **1** exhibits intramolecular hydrogen bond-