The Effect of Intramolecular Hydrogen Bonding on Anion Induced Hydrolysis of Salicylidene Schiff Bases

DISSERTATION

Submitted in partial fulfilment for the award of the degree of M.Sc. in Inorganic Chemistry

Submitted by

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Roll No. CH-18-46

To

School of Chemical Sciences

Goa University

April 2020

STATEMENT

I hereby declare that the matter presented in this dissertation entitled **''*The Effect of Intramolecular Hydrogen Bonding on Anion Induced Hydrolysis of Salicylidene Schiff Bases*''** is based on the result of investigations carried out by me in the School of Chemical Sciences, Goa University under the supervision of **Dr. Sandeep Kumar Dey** and the same has not been submitted elsewhere for the award of a degree or diploma.

Ms. Rhea Mendes

CH-18-046 (Inorganic Chemistry)

CERTIFICATE

This is to certify that the dissertation entitled **‘‘*The Effect of Intramolecular Hydrogen Bonding on Anion Induced Hydrolysis of Salicylidene Schiff Bases*’’** is bonafide work carried out by **Ms. Rhea Mendes** under my supervision in partial fulfillment of the requirements for the award of the degree of Master of Science in Chemistry in the School of Chemical Sciences, Goa University.

Dr. Sandeep Kumar Dey

Project Supervisor

School of Chemical Sciences

CERTIFICATE

This is to certify that the dissertation entitled **‘‘*The Effect of Intramolecular Hydrogen Bonding on Anion Induced Hydrolysis of Salicylidene Schiff Bases*’’** is bonafide work carried out by **Ms. Rhea Mendes** under the supervision of **Dr. Sandeep Kumar Dey** in partial fulfillment of the requirements for the award of the degree of Master of Science in Chemistry in the School of Chemical Sciences, Goa University.

Dean

School of Chemical Sciences

Goa University.

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In writing a project of this kind, one incurs a mounting indebtedness to several writers on this subject. As I have drawn and assimilated a great amount of material from works of these well-known researchers, I acknowledge with gratitude, my debt to these authors and their publishers whose work I have referred to in the course of my project.

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1. INTRODUCTION

Anions play a crucial role in a wide variety of fields that are known to be present in many commonly used agricultural fertilisers as well as food additives. On one hand, anions such as phosphorylated species are essential in the human body to participate in a variety of fundamental processes such as genetic information storage, energy transduction, signal processing and membrane transport while on the other hand, a high level of anionic ions can do a lot of harm to biological systems. [1]

Anion recognition is an area of growing interest in supramolecular chemistry due to its important role in a wide range of environmental, clinical, chemical, and biological applications, and considerable attention has been focused on the design of artificial receptors that are able to selectively recognize and sense anion species. [2]

One of the frequently used strategies to design anion sensors involves the construction of optical receptors. Such systems are generally composed of anion binding sites and the chromogenic moieties. When anions interact with the sensor via electrostatic, hydrogen bonding, coordination to a metal centre, hydrophobic interaction, or a combination of any two or more of these interactions, the sensor can output binding information either by its altered fluorescence, absorption spectra or both behaviours. [3]

Over the past few years, great efforts have been dedicated for the development of optical and fluorescent chemosensors for the detection of halides (F^-, Cl^-, Br^-, I^-) and oxyanions of environmental and biological relevance (such as CH_3COO^-, $H_2PO_4^-$, HSO_4^-, HCO_3^-, NO_2^- and NO_3^-) as fluorimeters are cost-effective and highly sensitive which can detect an analyte (cations/anions) at the nanomolar (nM) concentration. Further, colorimetric detection of anions based on UV-VIS and VIS-NIR spectroscopy have gained comparatively faster attention than other techniques due to their simplicity, high sensitivity and cost effectiveness.

Over the past two decades, many excellent chemosensors have been reported for recognition and sensing of anions with high selectivity and sensitivity. However, there are certain disadvantages associated with those chemosensors due to their complicated structure, synthetic difficulties, or troublesome purification process and poor yields. On the other hand, chemosensors which are easy to synthesize with significantly good yield should be preferred over others. Along this line, Schiff bases have widely been employed as chemosensors. Mainly, the Schiff bases derived from salicylaldehyde, i.e. salicylidene Schiff bases exist in a tautomerization equilibrium in solution due to the presence of

intramolecular –O-H···N=C- type of hydrogen bonding. Therefore, action of strongly basic anions (such as F^- and CH_3COO^-) can easily deprotonate the acidic -OH proton and promote the formation of keto-enol tautomerism and hence, acts as an efficient optical sensor. Importantly, the acidity of the -OH proton also plays a key role for such H-bonding/acid–base type reaction. The acidity of -OH proton usually depends on the effect of substitution in the benzene ring, especially, with respect to the -OH group, in that case most electron withdrawing substituents (such as $-NO_2$ and -CN) get preference. The selectivity and sensitivity of the receptor clearly depends on the basicity and shape of the anions and definitely on the acidity of hydroxyl group which depends on the nature of the substituents in the benzene ring with respect to the -OH group i.e. more electron withdrawing substituents makes it more acidic. [4]

Examples of some reported salicylidene Schiff base chemosensors for anions are discussed below:

(A) 2-Hydroxyl-3-nitro-benzaldehyde 4-nitrophenylhydrazone:

This salicylaldehyde-based sensor designed for fluoride sensing has been investigated in DMSO and in 9:1 DMSO-H_2O (v/v) mixture. The sensor shows strong binding affinity as well as a good sensing ability and selectivity for fluoride ion in 9:1 DMSO-d_6/D_2O (v/v). Also, the colour changes induced by anions can provide a way of detection by 'naked-eye'. These results can be analysed by the spectrum changes upon the addition of 25 equiv. of anions to the sensor in the 9:1 DMSO-H_2O solution. The nature of interactions between the sensor and F^- were investigated by ^1H NMR titration and UV-Vis spectroscopy experiments in 9:1 DMSO-*d*6-D_2O (v/v).[5]

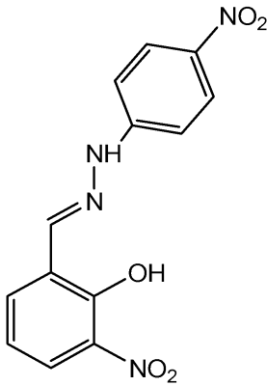


Figure 1: Molecular structure of 2-hydroxyl-3-nitro-benzaldehyde 4-nitrophenylhydrazone.

(B) 2-amino-4-nitrophenol-N-salicylidene

Butcher et al. reported a simple but interesting Schiff base receptor that exists in the solid state as keto-amine tautomeric form instead of phenol–imine tautomer due to the presence of highly acidic phenolic -OH proton and therefore enhances hydrogen bonding capability in presence of anions. The sensor shows yellow colour in acetonitrile but upon addition of considerable amount of F^-, AcO^- and $H_2PO_4^-$ anion in acetonitrile medium, the colour of the solution turns to deep yellow from light yellow. The selectivity and sensitivity of the receptor clearly depends on the basicity and shape of the anions and also on the acidity of hydroxyl group which depends on the nature of the substituents in the benzene ring with respect to the -OH group, i.e. more electron withdrawing substituents makes it more acidic. The selectivity of the receptor towards Y-shaped AcO^- anion has been proved by using 10% water–acetonitrile solution of AcO^-, where a detectable change in the colour and UV-Vis spectra has been observed unlike in the case of F^- and $H_2PO_4^-$. Colour change/UV–vis spectral change is reversible upon the addition of protic solvents, such as water and methanol as the anions can exit in the highly solvated form in those solvents, which support the concept of host–guest H-bonding interactions.[6]

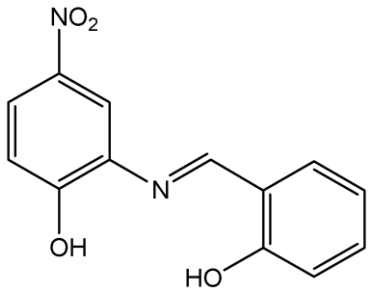


Figure 2: Molecular structure of 2-amino-4-nitrophenol-N-salicylidene.

(C) N-phenyl salicylidene imine:

This simple salicylidene Schiff based receptor is shown to be highly sensitive to fluoride ion which has been studied by colorimetric and UV–vis experiments in acetonitrile solvent. In presence of fluoride anion, the solution of receptor undergoes a naked-eye colour change from colourless to pale yellow. This colour change has also been reported in $CHCl_3$ and DMSO solvents. The reason for this colour change is probably due to the formation of hydrogen bond interactions between the –OH groups of the phenyl ring of salicylaldimine and fluoride ions. This is because, fluoride ions have higher electro

negativity and small size interacts with hydroxyl group through intermolecular hydrogen bond (O–H–F) which affects the optical properties of the receptor.[7]

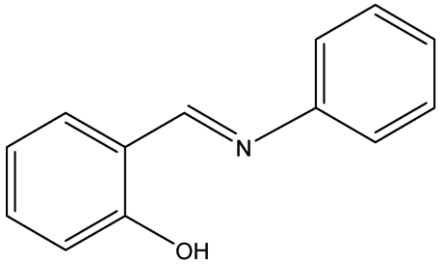


Figure 3: Molecular structure of N-phenyl salicylidene imine.

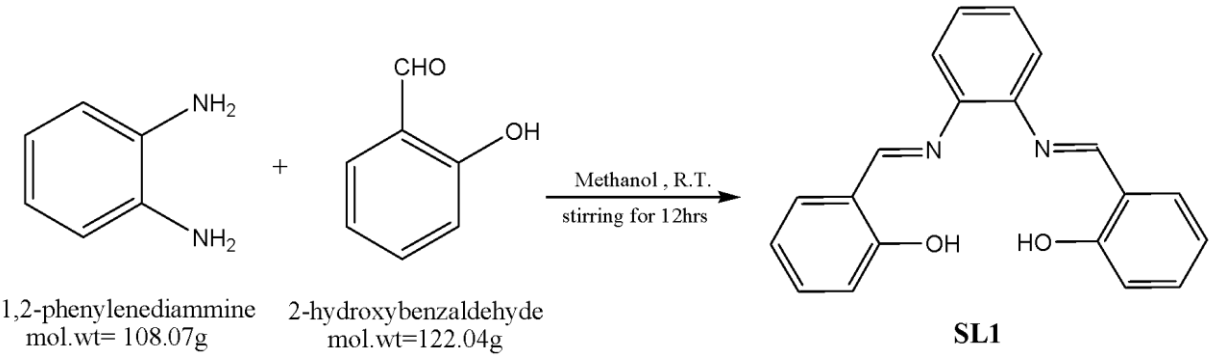
Salicylaldehyde is a popular substrate for nucleophilic addition reaction by virtue of its carbonyl group which is activated intramolecularly by the neighbouring phenolic hydroxyl group through hydrogen-bonding. Based on this concept, chemosensors with a salicylaldehyde functionality as the binding site has been developed recently for selective detection of anions. [8]

The mechanism of sensing can be explained by either the formation of $–OH^{\cdots}\ X^-$ hydrogen bonding or –OH deprotonation by the basic anion (X^-). Although, a lot of research has been done in the field of chemosensors, it is surprising to note that crystals of salicylidene based receptor-anion complex or deprotonated salicylidene receptor have not been reported and the probable reason for which has been studied in this work by analysing the mechanism of F^- sensing/binding by SL1 and NL1. The proposed mechanism suggests anion induced imine bond hydrolysis which results in regeneration of salicylaldehyde can also behave as a sensor. This implies that the optical properties shown by the regenerated salicylaldehyde in presence of a basic anion could be mistaken as anion sensing by salicylidene Schiff bases.

2. SYNTHESIS AND CHARACTERISATION

2.1. Synthesis of 1,2-(2-hydroxybenzylideneamino) benzene (SL1)

1 g of 1,2-phenylenediamine (9.25 mmol) was dissolved in 25 ml of methanol and 1.35 g (1.15 ml) of 2-hydroxybenzaldehyde (11.10 mmol) was added into the solution. The solution mixture was then stirred for about 12 hrs. and the yellow precipitate formed was then filtered and washed with 15 ml (3 x 5 ml) of methanol to obtain S**L1**. The compound was then air dried at room temperature and characterized by ^{1}H-NMR and HR-MS.



Scheme 1: Synthesis of **SL1**.

Chemical formula: $C_{20}H_{16}N_2O_2$

Molecular weight : 316.12 g

Isolated yield of **SL1**: 2.15 g

Percentage yield: 73%

Solubility: The compound is soluble in dimethylformamide, dimethyl sulfoxide, chloroform and tetrahydrofuran.

^{1}H-NMR: (400 MHz, DMSO-d_6) chemical shift in δ ppm: 2.51 (DMSO-CH_3), 3.35 (HOD), 6.98 (m, 4xCH), 7.42 (m, 6xCH), 7.68 (d, 2xCH), 8.94 (s, 2xN=CH), 12.95 (s, 2xOH).

HR-MS (+ ion mode): m/z 317.128 ($L1+H^+$), 318.131 ($L1+2H^+$), 319.134 ($L1+3H^+$)

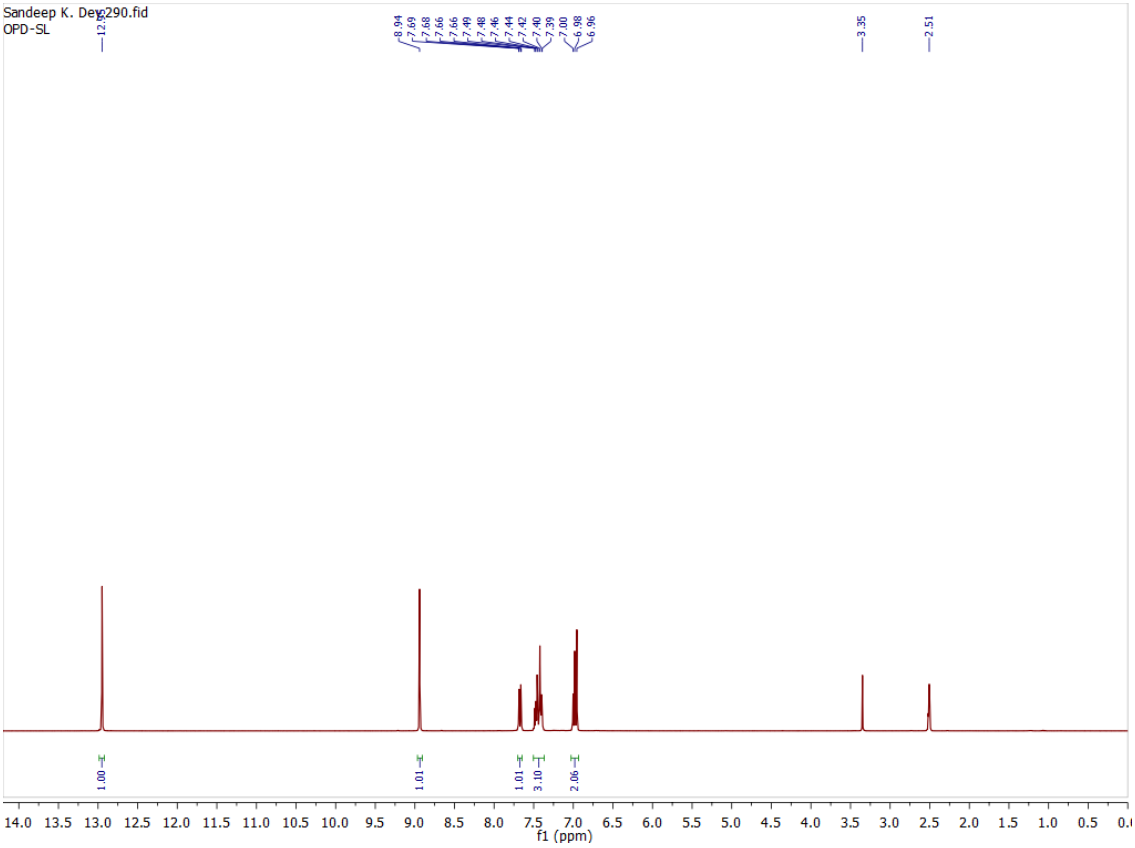


Figure 4: ^{1}H-NMR spectrum of **SL1** in DMSO-d_6.

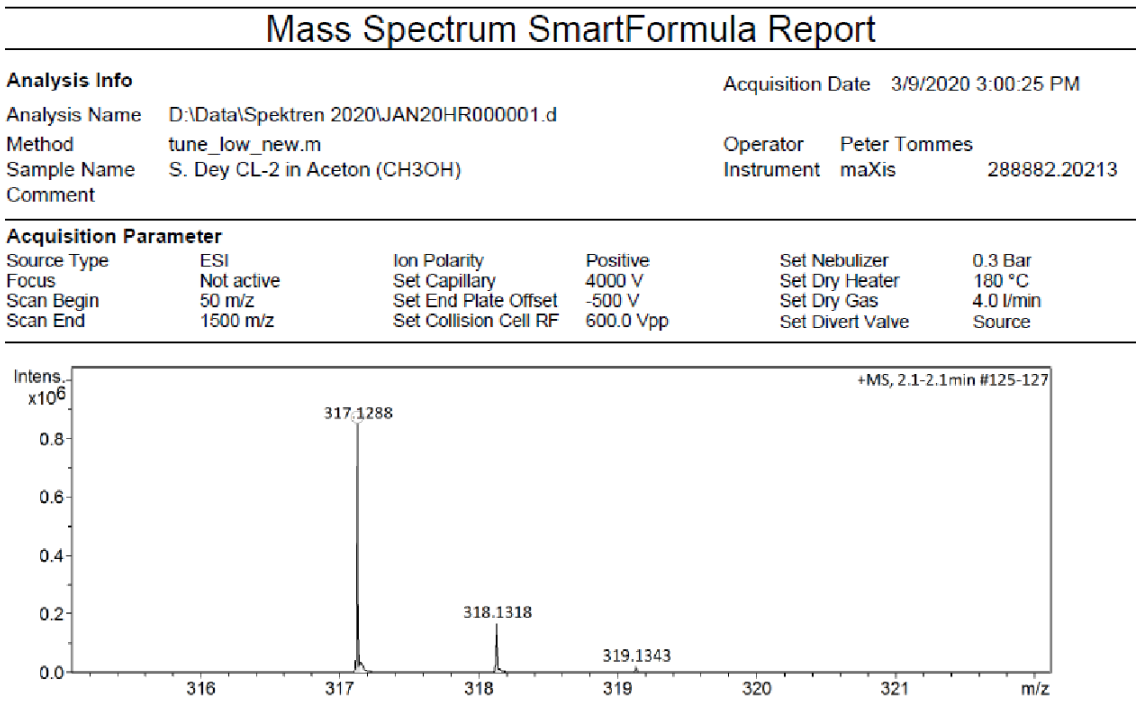


Figure 5: HR-MS of **SL1** in acetone. Peak at m/z 317.12 corresponds to (**SL1**+H^+).

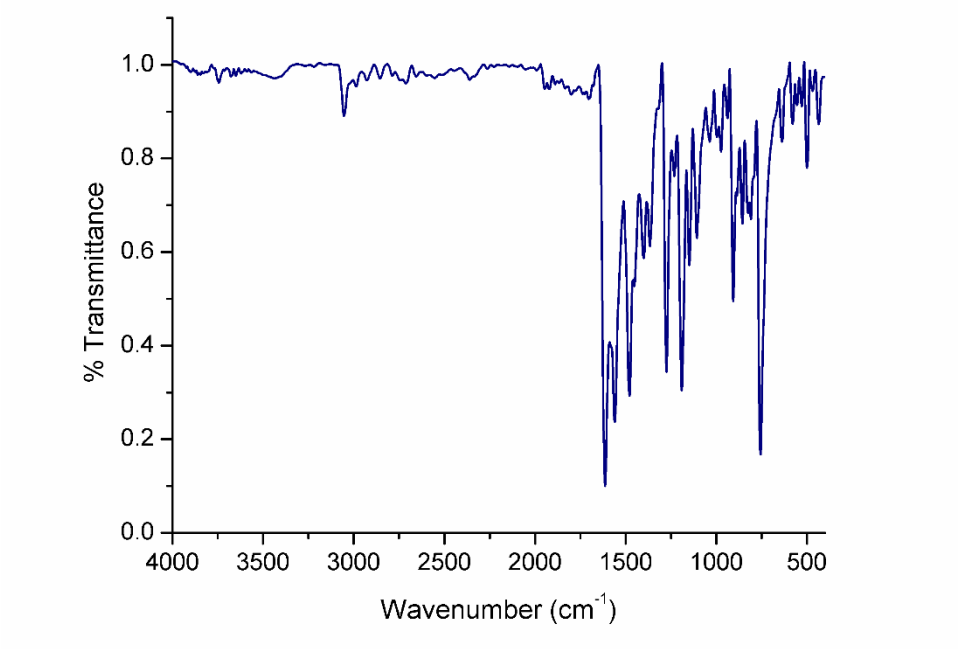
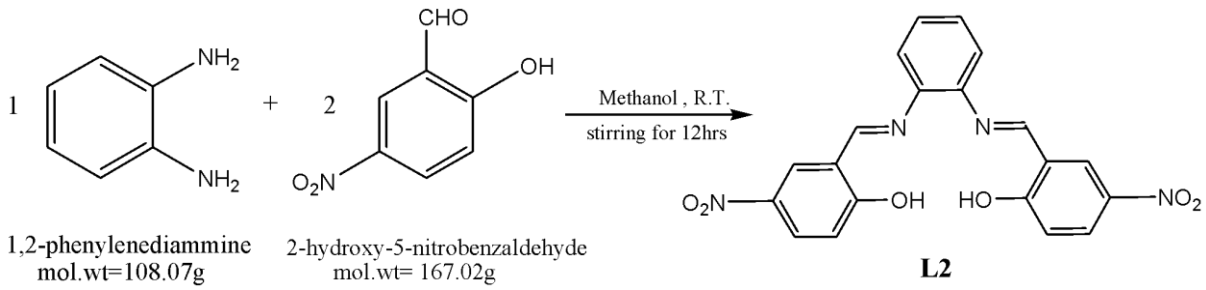


Figure 6: FT-IR spectrum of **SL1** (KBr).

2.2. Synthesis of 1,2-(2- hydroxy-5-nitrobenzylideneamino) benzene (SL2)

0.1 g of 1,2-phenylene diamine (0.925 mmol) was dissolved in 10 mL methanol and 0.31 g of 2-hydroxy-5-nitrobenzaldehyde (1.85 mmol) was added into the solution. The solution mixture was then stirred for about 12 hrs. and the orange-yellow precipitate formed was then filtered and washed with 15 mL (3×5 mL) of methanol to obtain **SL2**. The compound was then air dried at room temperature but due to its insolubility it could not be characterised by H-NMR and mass spectroscopy.



Scheme 2: Synthesis of **SL2**.

Chemical formula: $C_{20}H_{14}N_4O_6$

Molecular weight: 406.09 g

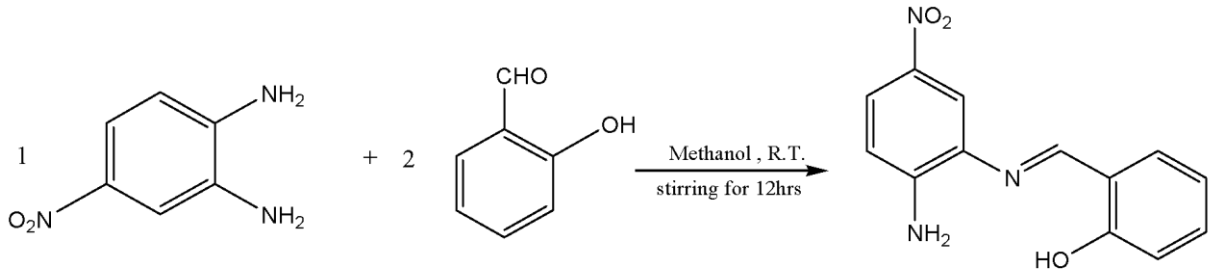
Isolated yield of **SL2**: 0.330 g

Percentage yield: 88 %

Solubility: The compound is insoluble in common organic solvents including DMSO.

2.3. Synthesis of 2-salicylidene-4-nitroaniline (NL1)

0.153 g of 4-nitro-1,2-phenylene diamine (1.0 mmol) was dissolved in 20 mL of methanol and 0.25 mL of salicylaldehyde (2.34 mmol) was added into the solution. The solution mixture was then stirred for about 12 hrs. and the yellow precipitate formed was then filtered and washed with 15 mL (3×5 mL) of methanol to obtain NL1. The compound was then air dried at room temperature and characterised by ^{1}H-NMR.



4-nitro-1,2-phenylenediammine
mol.wt=153.05g

2-hydroxybenzaldehyde
mol.wt=122.04g

NL1

Scheme 3: Synthesis of **NL1**.

Chemical formula: $C_{13}H_{11}N_3O_3$

Molecular weight: 257.08 g

Isolated yield of **NL1**: 0.150 g

Percentage yield: _____ %

Solubility: The compound is soluble in DMSO, acetonitrile.

^{1}H-NMR (400 MHz, DMSO-d_6) chemical shift in δ ppm: 2.5 (DMSO-CH_3), 11.85 (s, 1×OH), 8.97 (s, 1× -N=CH), 7.95 (d, 2×CH), 7.85 (s, 1×CH), 7.45(m, 1×CH), 7.0 (m, 2×CH), 6.8 (d, 1×CH), 6.7 (s, 1×NH_2)**.**

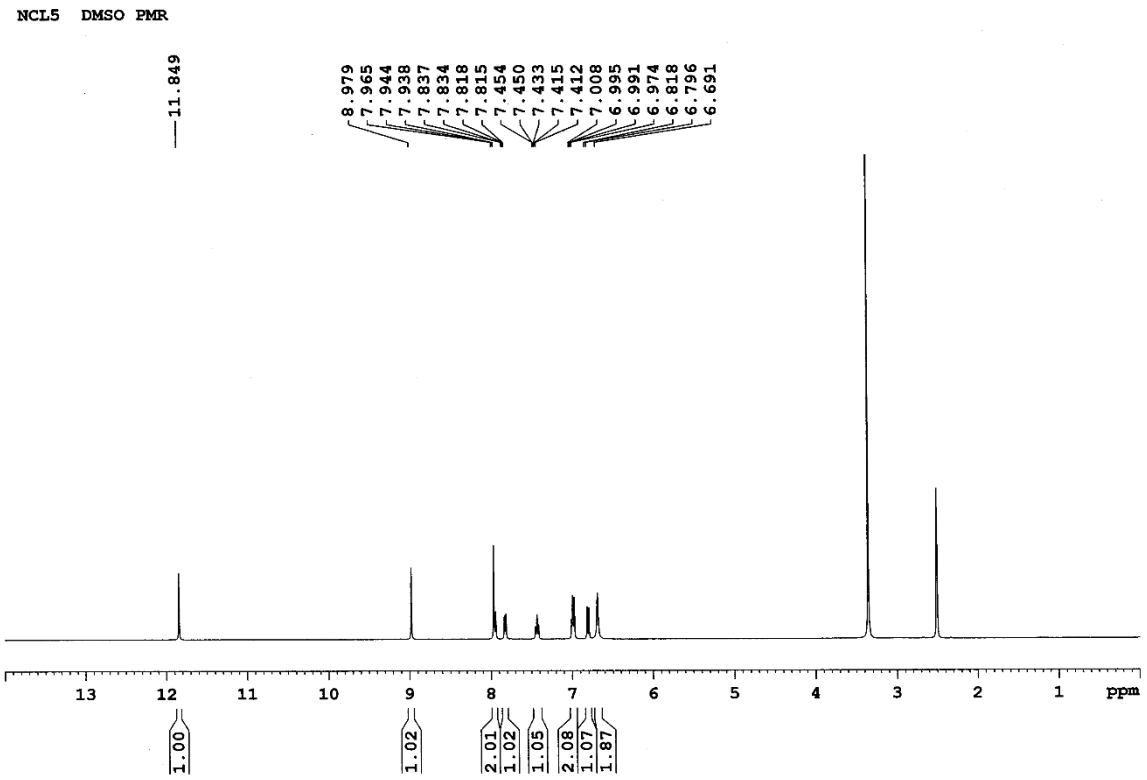
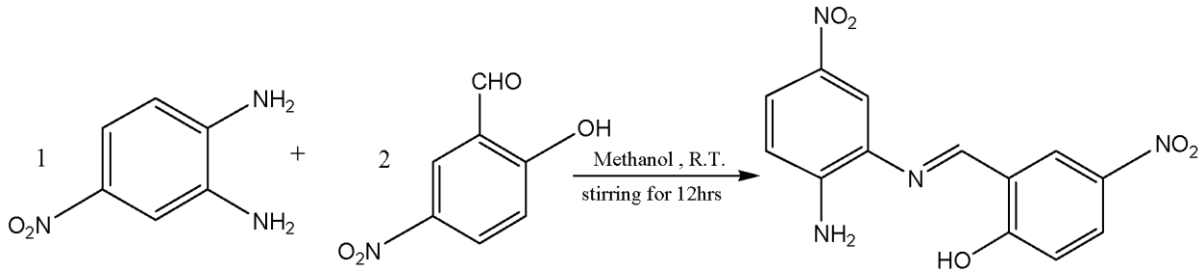


Figure 7: ^{1}H-NMR spectrum of **NL1** in DMSO-d_6.

2.4. Synthesis of 2-(5-nitrosalicylidene)-4-nitroaniline (NL2)

0.1 g of 4-nitro-1,2-phenylene diamine (0.65 mmol) was dissolved in 20 mL of methanol and 0.13 g of 2-hydroxy-5-nitrobenzaldehyde (0.77 mmol) was added into the solution. The solution mixture was then stirred for about 12 hrs. and the yellow precipitate formed was then filtered and washed with 15 mL (3×5 mL) of methanol to obtain **NL2**. The compound was then air dried at room temperature and characterised by ^{1}H-NMR.



4-nitro-1,2-phenylenediammine
mol.wt=153.05g

2-hydroxy-5-nitrobenzaldehyde
mol.wt=167.02g

NL2

Scheme 4: Synthesis of **NL2**.

Chemical formula: $C_{13}H_{10}N_4O_5$

Molecular weight: 302.07 g

Isolated yield of **NL2**: 0.190 g

Percentage yield: _____ %

Solubility: The compound is soluble in DMSO.

3. RESULTS AND DISCUSSIONS

^{1}H-NMR spectra of SL1 recorded in the presence of fluoride, chloride, hydrogenphosphate and acetate salts showed interesting results. The deprotonation of salicylidene –OH in SL1 followed by slow hydrolysis of an imine bond in the presence of (n-Bu_4N)F, (n-Bu_4N)Cl and (n-Bu_4N)H_2PO_4 was observed, which are in contrast to the several reported salicylidene Schiff bases studied as anion sensors over the years.

3.1. Fluoride ion induced hydrolysis of imine bond in SL1

SL1 has two imine linkages and addition of excess (n-Bu_4N)F (5 equiv.) resulted in the hydrolysis of only one imine bond which was confirmed by ^{1}H-NMR and HR-MS experiments. The ^{1}H-NMR spectrum of SL1 in DMSO-d_6 (0.6 mL) showed the –OH signal at 12.8 ppm and imine –N=CH signal at 8.9 ppm. An initial addition of 2 equiv. of (n-Bu_4N)F to a solution of SL1 (DMSO-d_6) resulted in the immediate disappearance of -OH signal indicating deprotonation of phenolic -OH and also showed the appearance of a new peak at 10.25 ppm indicating the formation of salicylaldehyde by hydrolysis of SL1 (D1 in Figure 8). The NMR solution mixture showed about 40% hydrolysis after 24 hrs (D2 in Figure 8) with peaks of –CHO and –NH_2 growing intense at 10.25 ppm and 5.1 ppm, respectively beyond which no further hydrolysis was observed. Addition of 3 more equivalents of (n-Bu_4N)F to the NMR solution mixture showed further hydrolysis of imine bonds showing 50% hydrolysis of SL1 within 5 days, beyond which no further hydrolysis was observed again (D3, D4 and D5 in Figure 8). The singlet peak of N=CH at 8.9 ppm splits into two closely spaced peaks in the presence of fluoride ion, due to the coexistence of both keto and enol forms of deprotonated SL1.

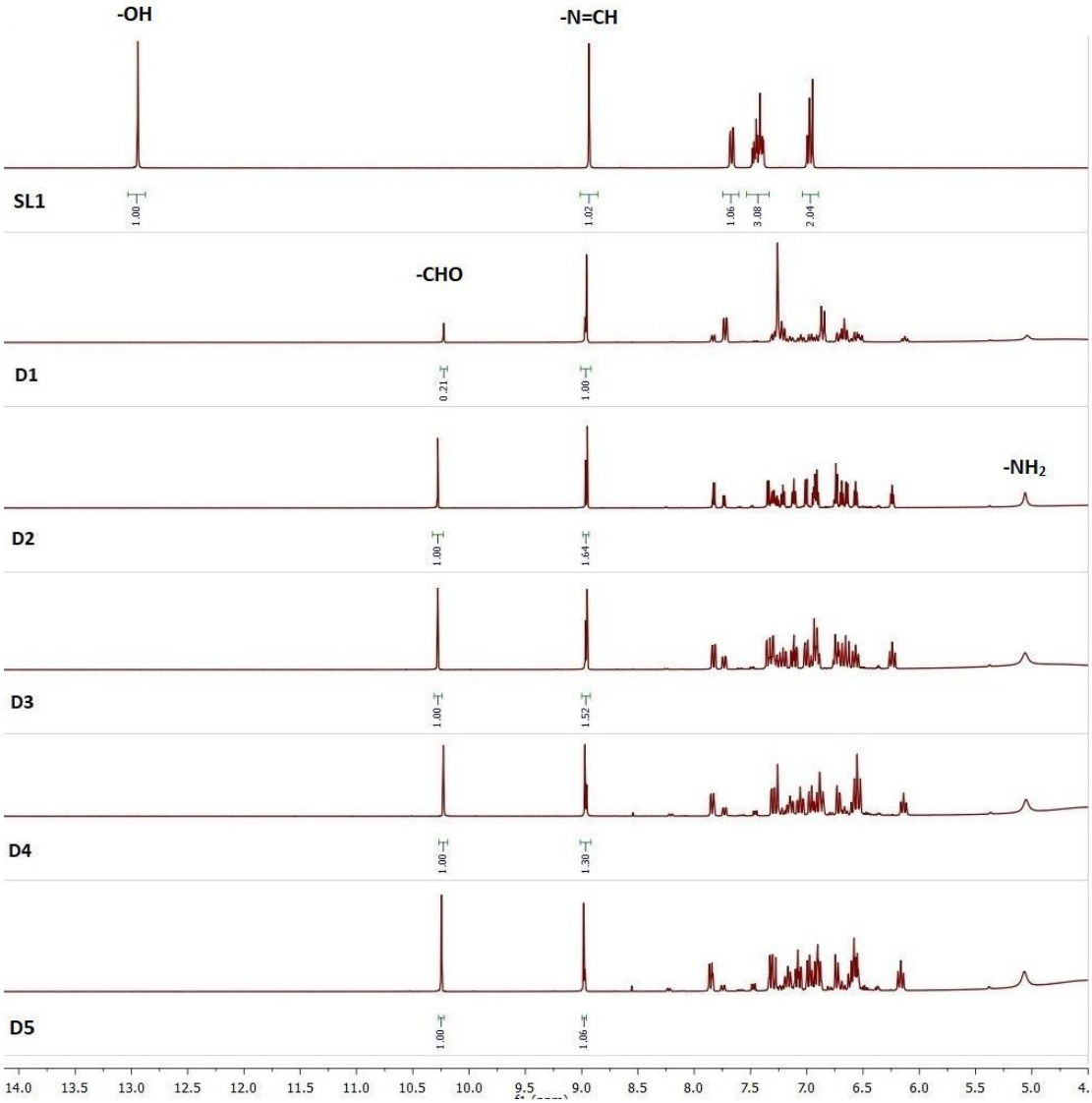


Figure 8: ^{1}H-NMR spectra (DMSO-d_6) showing hydrolysis of **SL1** in the presence of (n-Bu_4N)F (2 and 5 equiv.). D1, D2,…..D5 indicates spectrum of **SL1** mixed with (n-Bu_4N)F recorded on day1 (within 1 hr.), day2 (after 24 hrs.),…..day5, respectively. No more than 50% hydrolysis was observed in presence of excess (n-Bu_4N)F.

The HR-MS of the NMR solution mixture diluted with acetonitrile showed m/z at 213.10 (Figure 9), which indicates the partial hydrolysis of SL1 with the loss of only one salicylaldehyde molecule as shown in Scheme 5 below. The partial hydrolysis of SL1 is observed due to the hydrogen bonding between amine -NH_2 (donor) with the phenolate oxygen and imine nitrogen (acceptors) which possibly restricts complete hydrolysis of the partially hydrolysed product. Our efforts to obtain single crystals of partially hydrolysed product of SL1 was not successful.

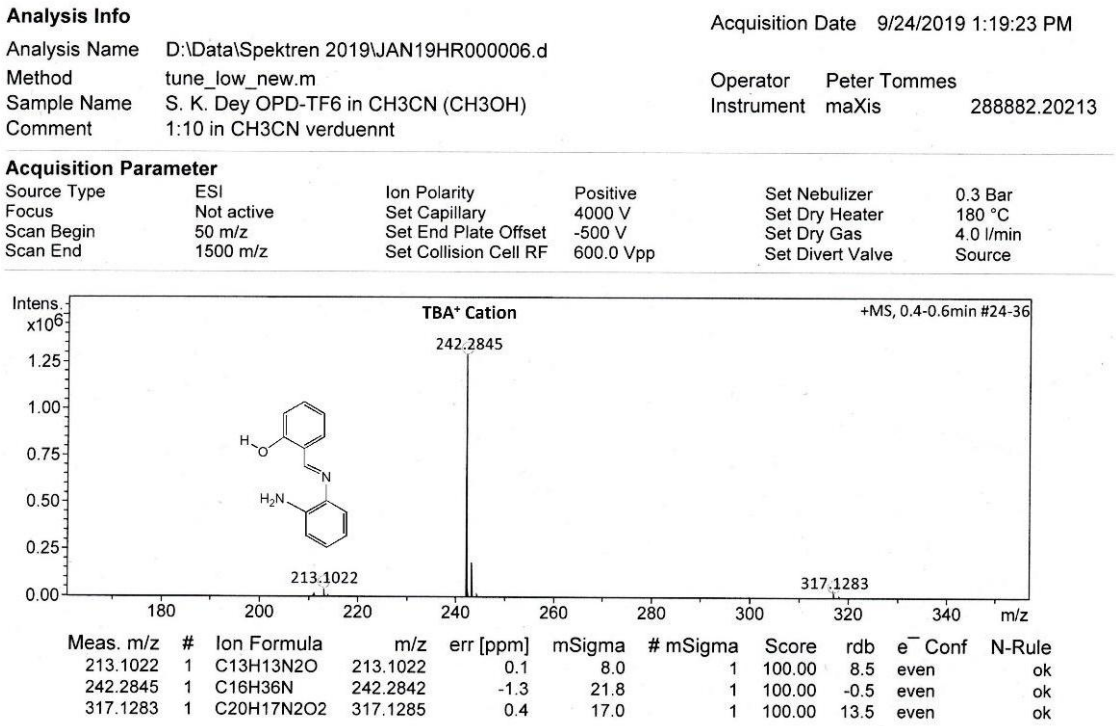
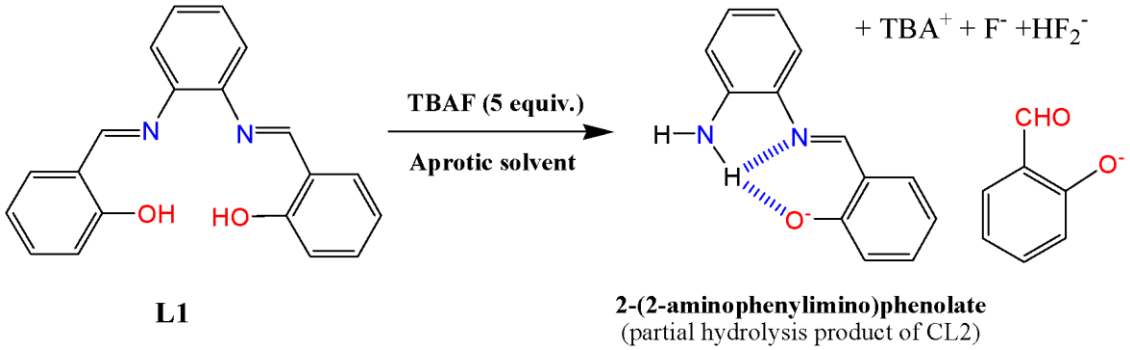


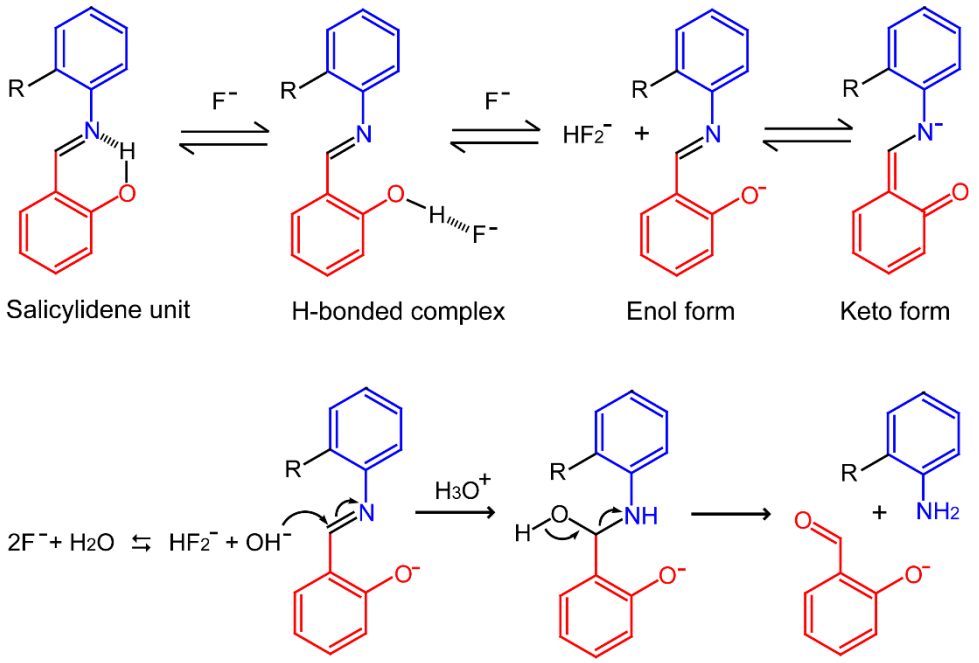
Figure 9: HR-MS spectrum of **SL1** in acetonitrile mixed with TBAF recorded after 6 days of mixing.



L1

2-(2-aminophenylimino)phenolate
(partial hydrolysis product of CL2)

Scheme 5: Partial hydrolysis of S**L1** to form 2-formyl phenolate and 2(2-aminophenylimino)phenolate as observed in ^{1}H-NMR and LC-MS experiments. Formation of intramolecular H-bond between -NH_2 and phenolate oxygen in 2(2-aminophenylimino)phenolate might resist the hydrolysis of the second imine bond in S**L1**. HF_2^- anion is formed in situ in the solution mixture of S**L1** and TBAF.



Scheme 6: Plausible mechanism for the fluoride ion induced hydrolysis of imine bond in SL1.

Formation of keto-enol tautomer of deprotonated SL1 and its hydrolysis in presence of (n-Bu_4N)F salt can be explained by the following mechanism (Scheme 6).

In the first step, a fluoride ion forms a transient hydrogen-bonded complex with the –OH group of the salicylidene unit followed by deprotonation of –OH (due to the basicity of F^- ion and acidic nature of the phenolic –OH) releasing HF which combines with another F^- to form HF_2^- and the deprotonated receptor (keto-enol forms).

In the second step, a nucleophilic attack of the in situ generated hydroxide ion, $2F^- + H_2O \leftrightharpoons OH^- + HF_2^-$ ((n-Bu_4N)F salts being hygroscopic in nature) on the imine carbon of the deprotonated enol form, followed by protonation of the imine nitrogen in the solution.

Finally, formation of the C=O double bond by the loss of the O-H proton results in the cleavage of C-N bond to give salicylaldehyde and respective aromatic amine.

3.2. Chloride ion induced hydrolysis of imine bond in SL1

A DMSO-d_6 solution of SL1 added with 5 equiv. of (n-Bu_4N)Cl when recorded after 24 hours (D2 in Figure 10) showed hydrolysis of imine bonds as exemplified from the appearance of salicylaldehyde -CHO peak at 10.3 ppm and -OH peak at 11.2 ppm in the NMR spectrum. Further, -NH_2 peak at 5.4 ppm could also be observed for the corresponding amine product confirming hydrolysis of SL1. The -OH signal of SL1 appearing at 13.0 ppm became significantly weaker and broad in presence of chloride indicative of gradual deprotonation of -OH groups. The singlet peak of –N=CH at 9.0 ppm (SL1 in Fig. 10) splits into two distinct peaks occurring at 8.9 and 9.0 ppm (D2 in Figure 10) due to the presence of keto (k) and enol (e) forms of SL1 in presence of chloride. In addition to the hydrolysis products of SL1, presence of hydrogen bonded adducts formed between -OH groups of SL1 and Cl^- could be observed in NMR spectra (Scheme 8). Two new peaks corresponding to two different types of hydrogen bonded O-H···Cl^- adducts appeared at 12.3 and 10.3 ppm. Due to the presence of two types of hydrogen bonded adducts in solution, two additional peaks have also appeared for imine N=CH proton at 8.4 and 10.0 ppm, each of which splits into two distinct peaks due to keto-enol tautomerism. The –N=CH peaks at 8.9(k)/9.0(e) ppm are associated with deprotonated SL1. Identical –N=CH peaks observed at 8.4(k)/8.5(e) and 9.9 (k)/10(e) ppm correspond to the O–H···Cl^- hydrogen bonded signals at 10.35 and 12.35 ppm.

The NMR solution mixture when recorded after 72 hrs. (D4 in Figure 10) showed disappearance of the -OH signal at 13.0 ppm and intensity of –N=CH peaks at 8.9(k)/9.0(e) ppm has been significantly reduced. Significant broadening of the hydrogen bonded -OH signal at 12.35 ppm was also observed indicating further deprotonation of -OH groups. However, no change in peak intensity and integral values were observed for the –N=CH peaks at 8.4(k)/8.5(e) and the corresponding hydrogen bonded -OH signal at 10.3 ppm that appears next to the -CHO peak. The percentage of hydrolysis of SL1 on D2 and D4 could not be determined accurately due to the presence of multiple complex species in the solution containing (n-Bu_4N)Cl. It has already been observed that, SL1 undergoes hydrolysis of only one imine linkage in the presence of 5 equiv. (n-Bu_4N)F (50% hydrolysis) due to stabilization of the partially hydrolysed product by hydrogen bonding between -NH_2 group with imine-N and phenolate-O. Thus, it is customary to assume that no more than 50% hydrolysis of SL1 is possible in presence of (n-Bu_4N)Cl since Cl^- is a weaker base than F^-. Due to the weaker basicity, free -OH peak and

hydrogen bonded -OH peaks in CL2 could be observed in presence of Cl^-, which were not observed in presence of F^-.

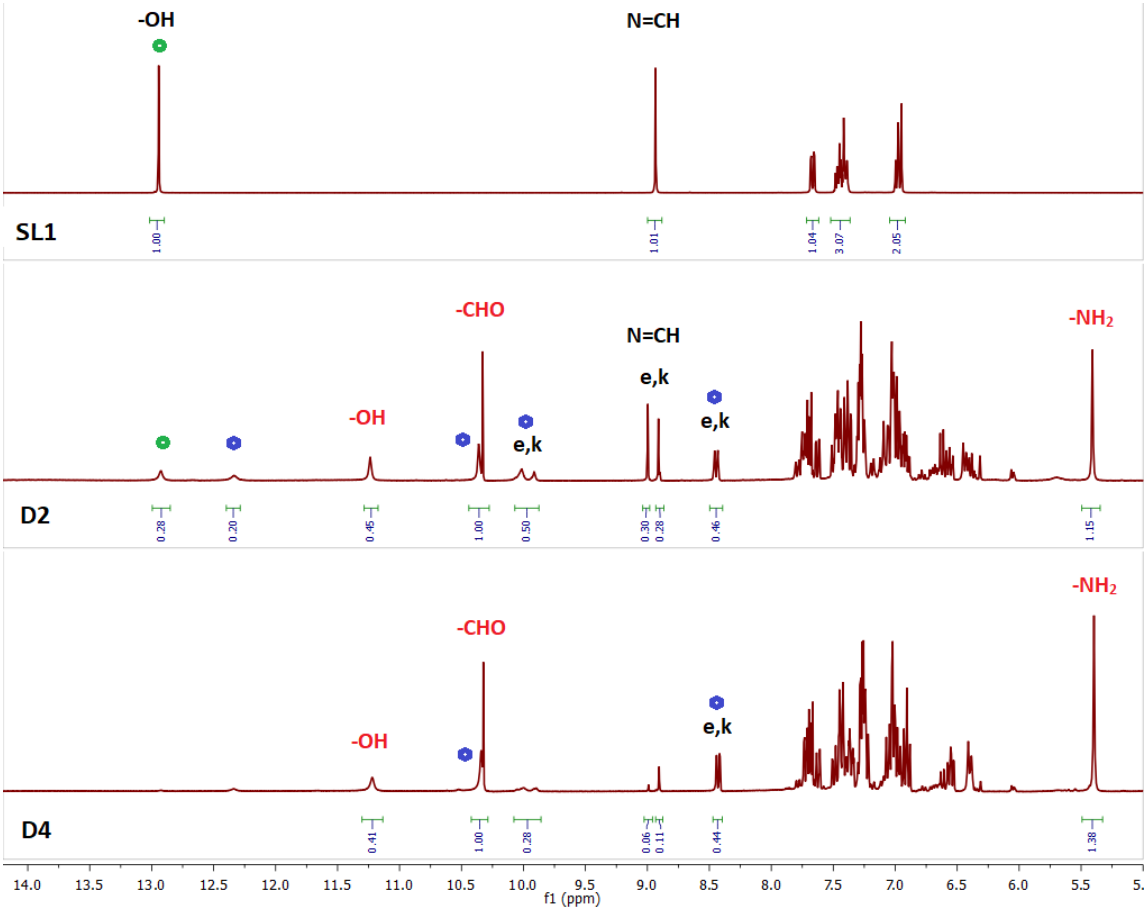
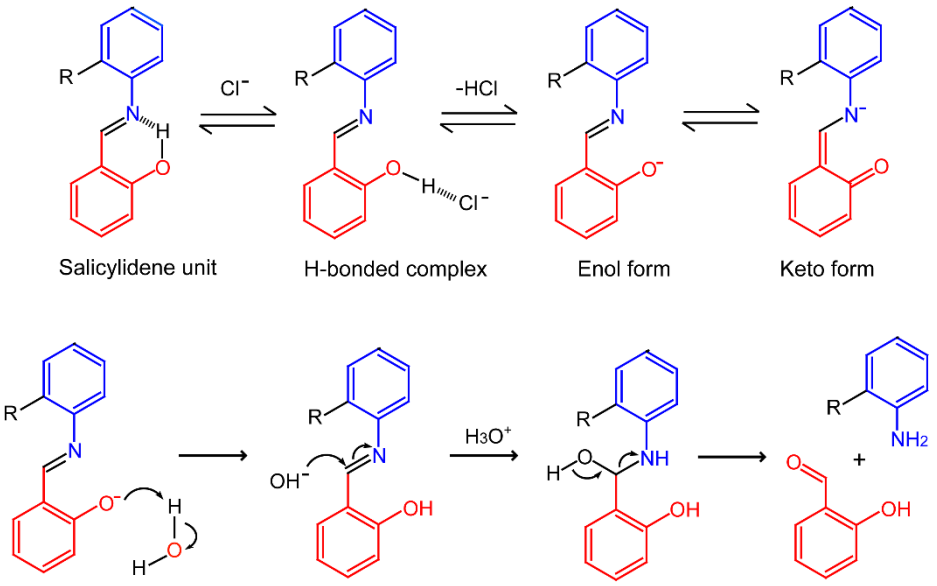


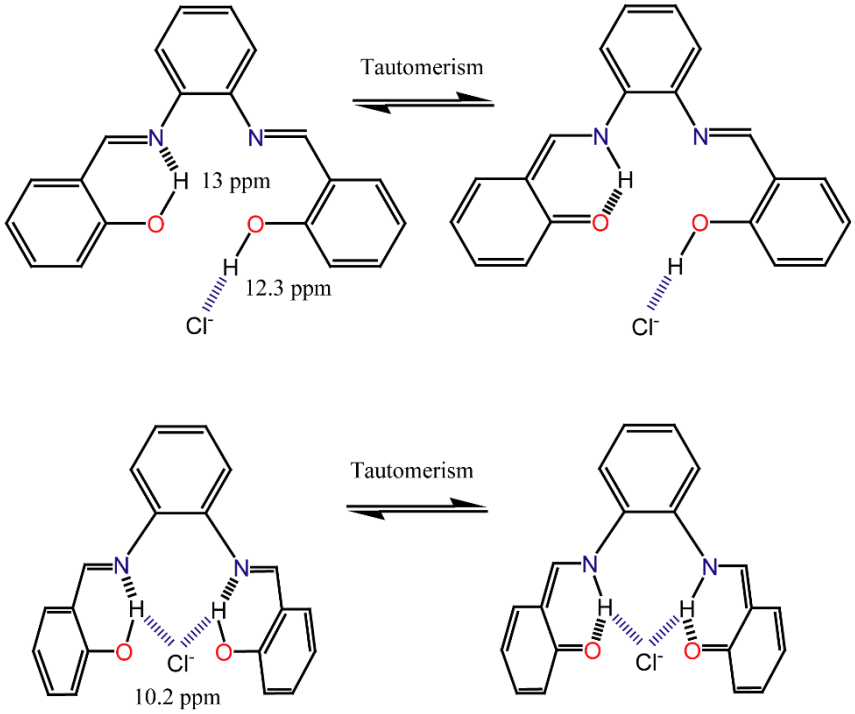
Figure 10: ^{1}H-NMR spectra (DMSO-d_6) showing hydrolysis of **SL1** in the presence of (n-Bu_4N)Cl.



Scheme 7: Plausible mechanism for the chloride ion induced hydrolysis of imine bond in **SL1**.

From the H-NMR experimental results, herein we propose a mechanism for the chloride ion induced hydrolysis of imine bond in **SL1**, which is different from fluoride ion induced hydrolysis **SL1** in many aspects, as depicted in Scheme 7. In the first step, a Cl^- ion forms transient hydrogen bonded complex with -OH group of SL1, which we have observed in the H-NMR spectrum of SL1 mixed with (n-Bu_4N)Cl (Figure 10). In the second step, deprotonation of –OH (due to the basicity of Cl^- ion and acidic nature of the phenolic –OH) resulted in negatively charged receptor which can exist either as keto or enol form as observed in the H-NMR spectrum showing two distinct peaks for N=CH proton. In the third step, the phenolate oxygen of deprotonated SL1 possibly abstracts hydrogen from a water molecule to generate hydroxide ion in solution. The in situ generated hydroxide nucleophile then attack on the imine carbon of SL1, followed by protonation of the imine nitrogen in the solution.

Finally, formation of the C=O double bond by the loss of the O–H proton results in the cleavage of C–N bond to give salicylaldehyde and respective aromatic amine.



Scheme 8. Two plausible hydrogen bonded O-H···Cl^- adducts formed between **SL1** and Cl^- as observed in the H-NMR spectra of Figure 10.

3.3. Hydrogenphosphate ion induced hydrolysis of imine bond in SL1

Hydrolysis of SL1 has also been observed in presence of hydrogenphosphate, however rather slowly as compared to fluoride which behaves as a stronger base in DMSO than hydrogenphosphate. Addition of 2 equiv. of $(n\text{-}Bu_4N)H_2PO_4$ to a solution of SL1 in DMSO-d_6 showed the disappearance of -OH signal at 12.8 ppm and appearance of a peak at 10.3 ppm for -CHO within an hour, indicating the hydrolysis of imine bond to generate salicylaldehyde. The NMR solution mixture when recorded on the next day after 24 hrs. showed 10 % hydrolysis (D2 in Figure 11) beyond which no further hydrolysis observed. Further addition of 3 more equivalents of $(n\text{-}Bu_4N)H_2PO_4$ to the NMR solution mixture showed 25% hydrolysis of SL1 in one week beyond which no further hydrolysis was observed again (D7 in Figure 11). Thus, it has been observed that the rate of hydrolysis of imine bond with hydrogenphosphate is significantly slower as compared to fluoride. While 50% hydrolysis was observed to be completed with 5 equiv. of fluoride, only 25% hydrolysis is achieved with 5 equiv. of hydrogenphosphate.

Interestingly, upon the addition of $(n\text{-}Bu_4N)H_2PO_4$ to SL1 solution, the singlet peak of –N=CH at 8.9 ppm, splits into two distinct peaks occurring at 8.8 and 8.9 ppm confirming the presence of both keto & enol forms of deprotonated SL1 in presence of hydrogenphosphate. The peak at 8.9 ppm is of enol form and the new peak at 8.8 ppm is of keto form of SL1. The enol form has been observed to be in excess as compared to keto form, but percentage of keto form slowly increases as hydrolysis progresses (Figure 11). The ratio of keto/enol tautomer after 25% hydrolysis in 7 days was 1:2.

The mechanism for the hydrolysis of SL1 by hydrogenphosphate is very much similar to that of chloride ion induced hydrolysis except that a proton accepted by the imine nitrogen in the third step of the mechanism comes from phenolic -OH and not from the solution (Scheme 9).

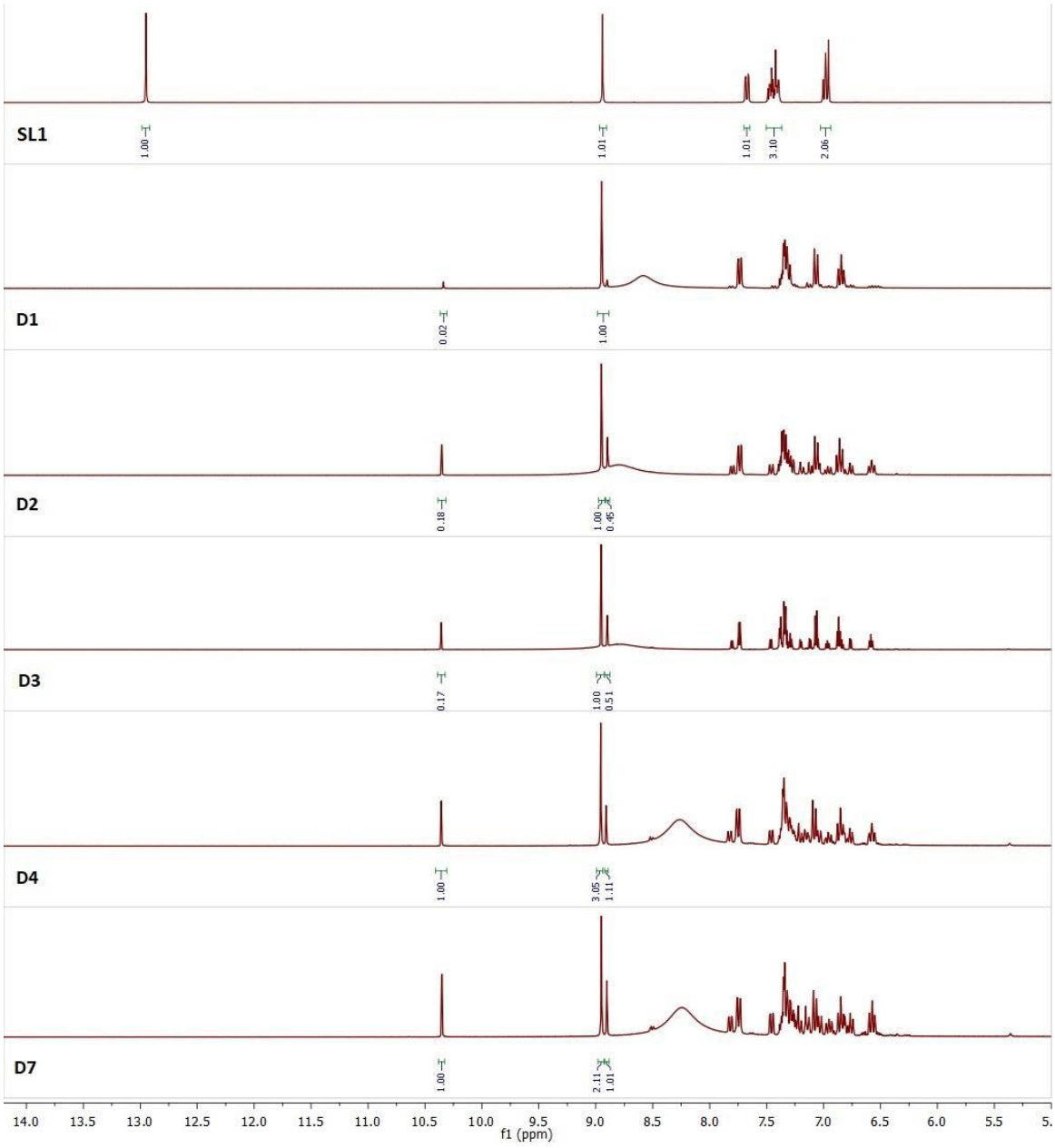
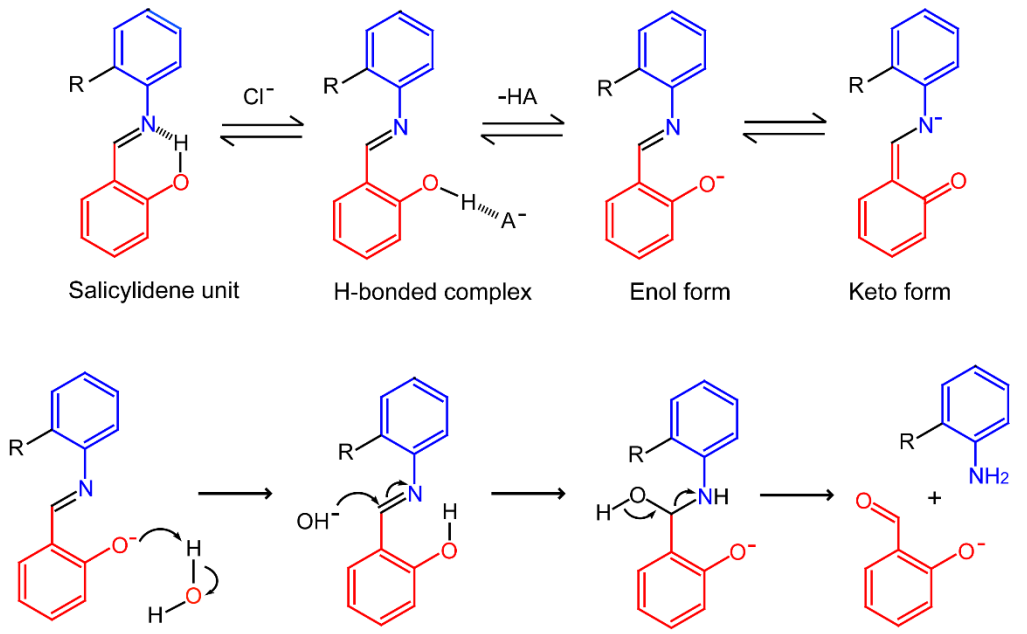


Figure 11: ^{1}H-NMR spectra (DMSO-d_6) showing hydrolysis of **SL1** in the presence of (n-$Bu_4N)H_2PO_4$ (2 and 5 equiv.) for 7 cosecutive days. No more than 25% hydrolysis was observed in presence of excess (n-$Bu_4N)H_2PO_4$.



Scheme 9: Plausible mechanism for the hydrogenphosphate ion induced hydrolysis of imine bond in **SL1** (A = hydrogenphosphate).

Hydrolysis of SL1 occuring in presence of 5 equiv. of hydrogenphosphate and fluoride, respectively occurs at different rates due to the difference in basicity of the anions. On comparing the behaviour of hydrolysis of SL1 in presence of these anions on day 7, it is observed that hydrogenphosphate hydrolyses SL1 relatively slower than fluoride indicated by the intensity and integral values of the –CHO and N=CH peaks. Rate of hydrolysis of the imine bond in SL1 in presence of hydrogenphosphate is 25% while in presence of fluoride is 50%. Another interesting behaviour observed in SL1 is the occurrence of keto-enol tautomerism in presence of anions which is in the ratio of 1:2 for hydrogenphosphate but is not distinctively observed in the case of fluoride.

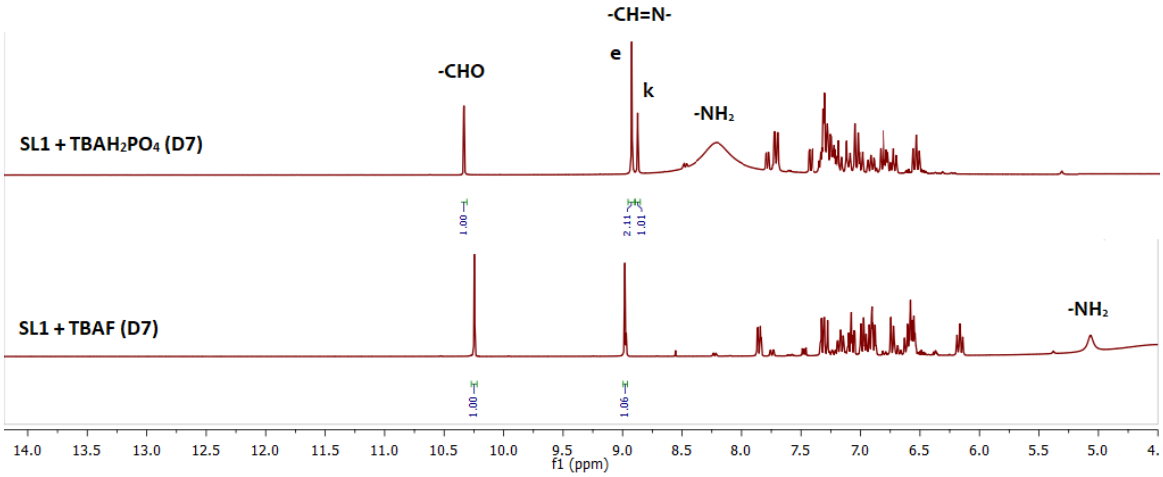


Figure 12: Comparison of the H-NMR spectra (DMSO-d_6) of **SL1** in presence of 5 equiv. of hydrogenphosphate and fluoride, recorded after 7 days.

3.4. Acetate ion induced hydrolysis of imine bond in SL1

Upon addition of 2 equiv. of LiAcO to SL1, deprotonation of the salicylidene –OH was observed indicated by disappearance of the –OH signal at 12.8 ppm with the hydrolysis of –N=CH bond occurring at a very slow rate (Figure 13).

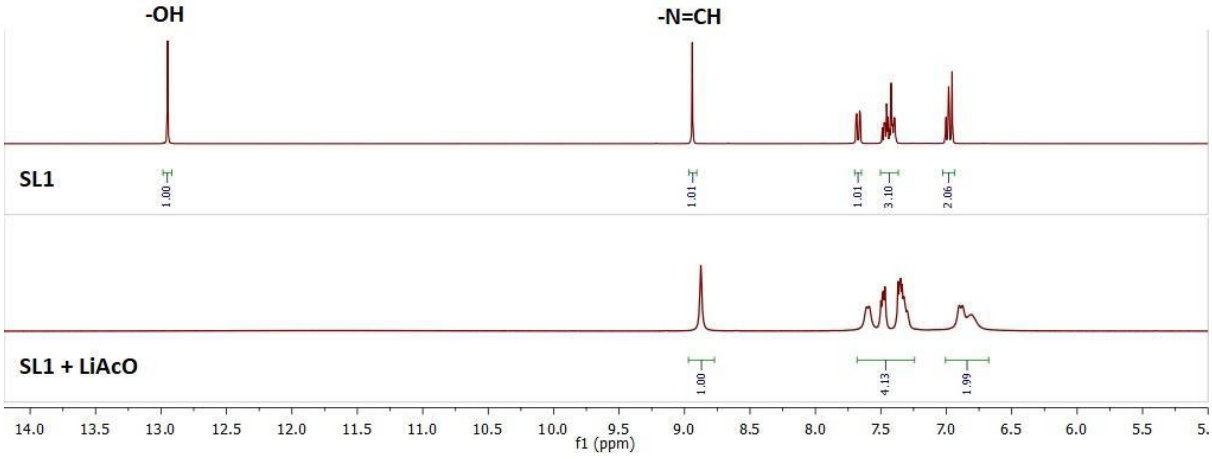


Figure 13: ^{1}H-NMR spectra (DMSO-d_6) of **SL1** in the presence of Lithium acetate (5 equiv.).

3.5. Anion induced UV-Visible spectral changes of NL1

NL1 having only one imine linkage is proven to be highly stable due to the intramolecular hydrogen bonding possibly occurring in the compound. For the UV-Vis experiment, 10^{-5} M solution was prepared from the stock solution of NL1 (10^{-3} M). Anion selectivity study was conducted by addition of 250 µL of various anions individually to 10^{-5} M solution of NL1 in organic medium (250µL in 2.5 mL DMSO) and measuring the absorbance value from 200-700nm. The changes in the absorption spectrum of SL1 in the presence of F^-, Br^-, Cl^-, $H_2PO_4^-$, HSO_4^-, CH_3COO^- & CN^- anions were recorded. The UV-Vis spectrum of NL1 showed two absorption bands at 275 nm and 380 nm. Addition of fluoride salt resulted in bathochromic shift (red shift) of 85 nm of the higher wavelength peak (at 380 nm) to 465 nm which tails till 600 nm. Addition of acetate salt resulted in red shift of 40 nm of the higher wavelength peak (at 380 nm) to 420 nm which tails till 550 nm. However, addition of other anions did not result in any observable changes in the UV-vis spectrum of NL1 except cyanide which showed an increase and a decrease in absorbances of peaks at 275 nm and 380 nm, respectively.

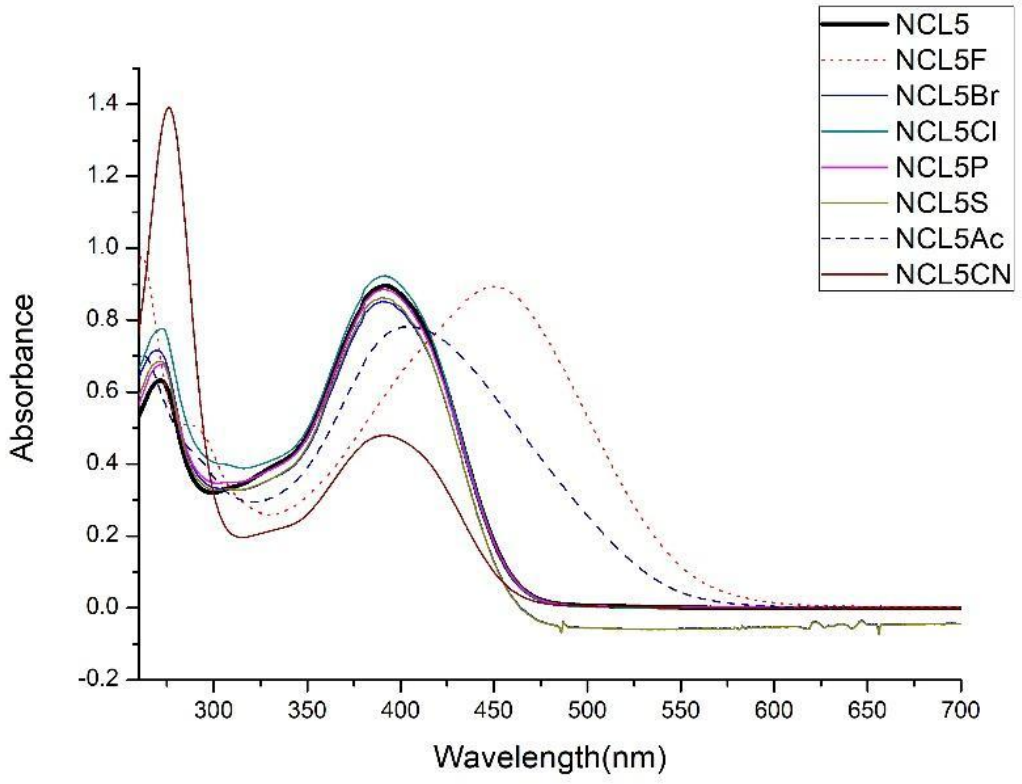


Figure 14: UV-vis spectral changes of **NL1** in presence of different anions in DMSO.

4. CONCLUSION

We have synthesised four salicylidene Schiff bases namely, SL1, SL2, NL1 and NL2, and characterised by ^{1}H-NMR, LC-MS/UV-Vis spectroscopy wherever possible. SL1 has two imine C=N linkages while NL1 has one imine C=N linkage. SL2 couldn't be characterised and studied due to its insolubility in organic solvents. The stability of the SL1 receptor was studied in the presence of anions like fluoride, chloride, acetate and hydrogenphosphate in solution state.

The experimental results of the salicylidene based compound SL1 shows that it is not stable in the presence of fluoride, chloride and hydrogenphosphate and undergoes hydrolysis of imine bond to generate salicylaldehyde and corresponding salicylidene-amine compounds. SL1 although being highly sensitive to basic anions undergoes partial hydrolysis i.e., only one imine linkage is hydrolysed. The hydrolysis of partially hydrolysed product is restricted due to the intramolecular hydrogen bonding occurring in the receptor molecule.

A similar behaviour has also been observed in salicylidene Schiff base NL1 which has only one imine linkage and is highly stable in presence of anions (fluoride/hydrogenphosphate). The stability of NL1 is also due the intramolecular hydrogen bonding occurring in the molecule similar to the partially hydrolysed product of SL1. Thus, the presence of a hydrogen bond donor group (-NH_2 and O=C-NH) at a position close to the salicylidene N=CH group is important to limit the hydrolysis of imine bond.

Upon understanding the effect of intramolecular hydrogen bonding, the second aspect of the studies of these salicylidene Schiff based receptors is whether it can be called a sensor. The question arises due to the fact that in presence of fluoride, chloride and hydrogenphosphate, the receptor molecule SL1 is hydrolysed and regenerates one of the starting materials. It can so happen that the receptor and the starting material may react in-situ to produce a new compound which may cause shift in the absorbance peaks thus making it a reactive sensor or chemodosimeter. Salicylaldehyde can sense fluoride by distinctive colour changes by the emergence of a peak above 400 nm which is in similar in comparison to salicylidene Schiff base sensors showing similar fluoride induced colour changes due to absorption at 400-450nm.

5. REFERENCES

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