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Synthesis and Fluorescence study of Novel Schiff Bases of Isoniazide

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ABSTRACT

Isoniazide can be synthesized by the known literature method. Nicotin-4-carboxylic acid ***(1)*** *was converted into methyl ester by using methanol in presence of catalytic amount of sulphuric acid. The methyl nicotin-4-carboxylate* ***(2)*** *is converted into isoniazide* ***(3)*** *by the condensation with hydrazine hydrate in DMF. The isoniazide is then condensed with various aldehydes* ***(4a-d)*** *in absolute alcohol in presence of catalytic amount of acetic acid and final product N[(1E)-alkylidene]pyridine-4-carbohydrazide* ***(5a-d)*** *is subjected for further fluorescence study.*

Key Words: Isoniazide, Aldehydes, Schiff Bases, fluorescence, Imines.

INTRODUCTION

The compounds containing azomethine (-C=N-) group are know as Schiff bases, are formed by the condensation of a primary amines with a carbonyl compounds such as aldehydes or ketones. Schiff bases are characterized by the –N=CH– (imine) group which is important in elucidating the mechanism of transamination and racemisation reactions in biological systems.[1,2] Schiff bases play an important role in inorganic chemistry as they easily form stable complexes with most transition metal ions in the periodic table. Schiff base ligands are very important in the development of coordination chemistry as they can readily form stable complexes with most metal ions[3-6]. Schiff base complexes of transition metals have been extensively investigated for many years[7-9]. Their ready syntheses and excellent properties have contributed greatly to their popularity as well as to the development of inorganic chemistry[10-12].

The remarkable biological activity of acid hydrazides R-CO-NH-NH_2, a class of Schiff base, their corresponding aroylhydrazones, R-CO-NH-N=CH-R' and the dependence of their mode of chelation with transition metal ions present in the living system have been of significant interest in the past[13-16]. Isoniazide were treated with different substituted aromatic aldehydes to produce Schiff's base[24]. The coordination compounds of aroylhydrazones have been reported to act as enzyme inhibitors[17] and are useful due to their pharmacological applications[18−20]. Isonazide (INH) is a drug of proven therapeutic importance and is used against a wide spectrum ofbacterial ailments, e.g., tuberculosis[21]. Hydrazones derived from condensation of isoniazide with pyridine aldehydes have been found to show better antitubercular activity than INH[22]. In the past Agarwal et al.[23] have investigated the coordinating ability of INH-derivatives with metal ions.

The word phosphor was invented in the early 17th century. There are some characteristics of typical phosphor as- must survive hazardous chemical environment, cannot be water soluble, durable, easy to apply, not easily detected or noticed without specialized equipment, etc. Phosphors become technologically and industrially important with the introduction of fluorescent lamps in 1938. Thermometry was suggested in the German patent in 1938. First peer-reviewed article, to our knowledge appeared in 1949. Between 1950 to 1980, it was not widely used. Its most common use was aerodynamic applications. Advances in lasers, microelectronics, and other supporting technologies enable additional commercial as well as scientific use. The physics and chemistry of luminescence materials and their applications become and still is the core area covered by Luminescence symposia.

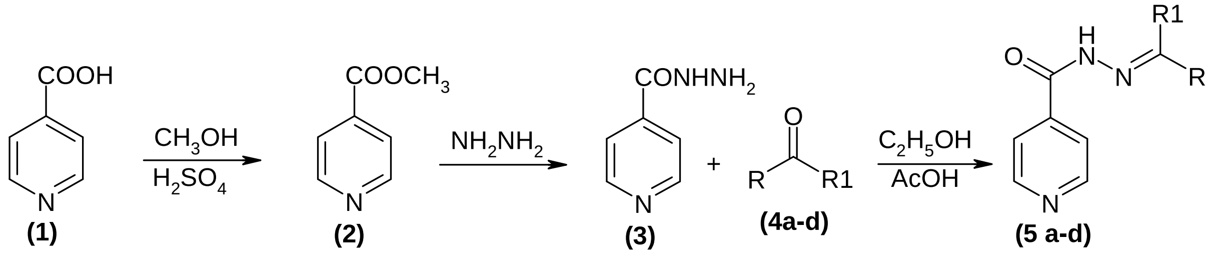
In the small molecules organic light emitting diodes, the family of carbazoles(25) could be extended to be suitably fit for red(26-28), green(29-31), and blue light(32-34) triplet emitters and therefore, they can be used in full color displays(35-38, 40-43). More recently studies of Thompson, Forrest and co-workers shows that the use of electron blocking layers (EBLs) consisting of Ir^{III} complexes with picolinate ligands(44) produced improved color purities in the case of blue light emitting device(35). Some of the organic molecules are used as EBLs as- fluorinated phenylenes(39), and oxadiazole as well as triazole containing molecules such as trimer of N-arylbenzimidazoles (TPBi)(45,46), 2-tert-butylphenyl-5-biphenyl-1,3,4-oxadiazole (PBD)(47), 3-phenyl-4-(1'-naphthyl)-5-phenyl-1,2,4-triazole (TAZ)(48,49), 1,8-Naphthalimides(50), polyquinolines(51), or carbon nanotubes doped in PPV(52) were also found to be useful as hole blocking layers (HBLs).

Searching for highly efficient fluorescence organic compounds (Schiff bases) is a topic of current interest. The aromatic based ligand having electron donating or withdrawing groups has been increased or decreased the intensity of absorption or shifted absorption wavelength on either side. Luminescence properties of the various Schiff bases of isonizide and aromatic aldehydes has been checked by using Spectrofluorometer model number RF5301. A Xe laser lamp was used for excitation and emission spectra were scanned from the range 220nm to 750 nm.

In this paper we tried to synthesis of various Schiff bases of isonizide and various aldehydes which has general name as N-[(1E)-alkylidene]pyridine-4-carbohydrazide **(5a-d)** study their fluorescence study.

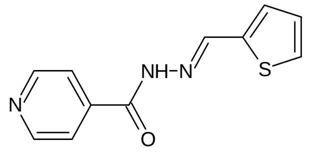
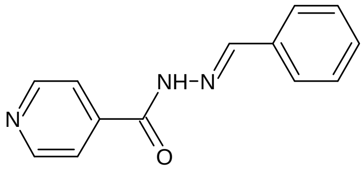
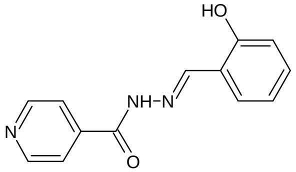
MATERIALS AND METHODS

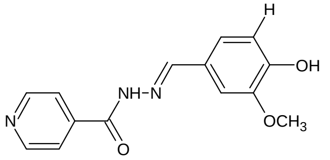
Isoniazide can be synthesized by the known literature method. Nicotin-4-carboxylic acid **(1)** was converted into methyl ester by using methanol in presence of catalytic amount of sulphuric acid. The methyl nicotin-4-carboxylate **(2)** is converted into isoniazide **(3)** by the condensation with hydrazine hydrate in DMF. The isoniazide is then condensed with various aldehydes.



	4a / 5a	**4b / 5b**	**4c / 5c**	**4d / 5d**
R	2-Thiophene	Phenyl	2-Hydroxy phenyl	4-Hydroxy-3-methoxy Phenyl
R1	H	H	H	H

Synthesis of Schiff bases {N'-[(1E)-alkylidene]pyridine-4-carbohydrazide (5a-h)}:
Dissolve 500 mg of isoniazide (3.65 mmol) **(3)** in 15 ml of absolute alcohol. Add 3.70 mmol of aldehyde **(4a-d)** in with constant stirring and finally add catalytic amount of acetic acid. Reflux the reaction mixture with stirring for about 4 – 6 hrs and check the completion of reaction with help of TLC (in pet ether and ethyl acetate). Cool the reaction mixture and filter the resulting solid on Buckner funnel, wash with cold ethanol. Record the yield, M.P and recrystallized from absolute ethanol.

Starting Aldehyde or ketone	Name and structure of Product	Yield	M.P. ^{0}C	NMR data (δ in ppm)
Thiophene-2-carbaldehyde	 *N*'-[(*E*)-thiophen-2-ylmethylidene]pyridine -4-carbohydrazide (5a)	68%	190	**12.05** (bs, NH); **8.44** (t, 2H); 7.79 (m, 1H); **7.75** (t, 2H); 7.72 (m, 1H), 7.66 (m, 1H); 7.45 (s, 1H).
Benzaldehyde	 *N*'-[(*E*)-phenylmethylidene]pyridine-4-carbohydrazide (5b)	84%	132	**12.00** (bs, NH); **8.75** (t, 2H); **7.74** (t, 2H); 7.51-7.80 (m, 5H); 7.14 (s, 1H).
Salicylaldehyde	 *N*'-[(*E*)-(2-hydroxyphenyl)methylidene]pyridine -4-carbohydrazide (5c)	83%	238	**12.26** (bs, 1H); 11.04 (bs, 1H); **8.77** (t, 2H); 8.65 (s, 1H); **7.81-7.83** (t, 2H); 7.56-7.60 (d, 1H); 7.26-7.33 (t, 1H); 6.87-6.94 (m, 2H).

Vaniline	 *N'*-[(*E*)-(4-hydroxy-3-methoxyphenyl)methylidene] pyridine-4-carbohydrazide (5d)	84%	196	**11.87** (bs, NH); 9.76 (bs, OH), **8.76** (t, 2H); 8.30 (s, 1H); **7.78** (t, 2H); 7.31 (d, 1H), 7.10 (d, 1H); 6.83 (d, 1H), 3.82 (s, 3H).

Luminescence Properties:

Luminescence properties of the schiff bases of isoniazide with various various aromatic aldehydes has been checked by using Spectrofluorometer model number RF5301. A Xe laser lamp was used for excitation and emission spectra were scanned from the range 220 nm to 750 nm. For fluorescence study of the Schiff bases, dimthylsulfoxide is used as solvent and reference material. The excitation of the molecule is occurred due to the n→π* and π→π* transitions.

The fluorescence data can be shown in following data:
Slit width: Excitation and emission is 5 mm; Concentration of solution is 500 ppm; Solvent used is DMSO.

Sample Name	Excitation wavelength (nm)	Emission wavelength (nm)
N'-[(E)-thiophene-2-ylmethylidene] pyridine -4-carbohydrazide	370 (ε 125.314) **399** (ε **485**.823) 736 (ε 95.903)	371 (701.30), 421 (288.9), 742 (39.49) **401** (648.84), 444 (77.41), 454 (78.91) 370 (410.7), 417 (226.56), 740 (36.24), 820 (5.76)
N'-[(E)-phenylmethylidene] pyridine-4-carbohydrazide	**399** (ε **216**.38) 750 (ε 2.322)	**401** (259), 454 (23.54) 477 (295.24), 493 (5.537), 554 (6.35)
N'-[(E)-(2-hydroxyphenyl) methylidene] pyridine-4-carbohydrazide	**400** (ε **114**.573) 667 (ε 0.430)	**403** (124.89), 496 (71.24) 669 (20.25)
N'-[(E)-(4-hydroxy-3-methoxyphenyl) methylidene] pyridine-4-carbohydrazide	**399** (ε **265**.391) 458 (ε 3.083) 473 (ε 3.138)	**401** (269.36), 503 (229.17) 460 (351.30), 512 (157.112) 475 (354.83), 511 (155.78)

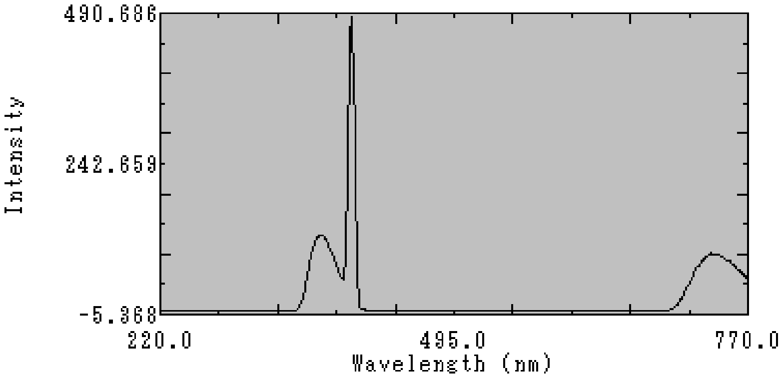
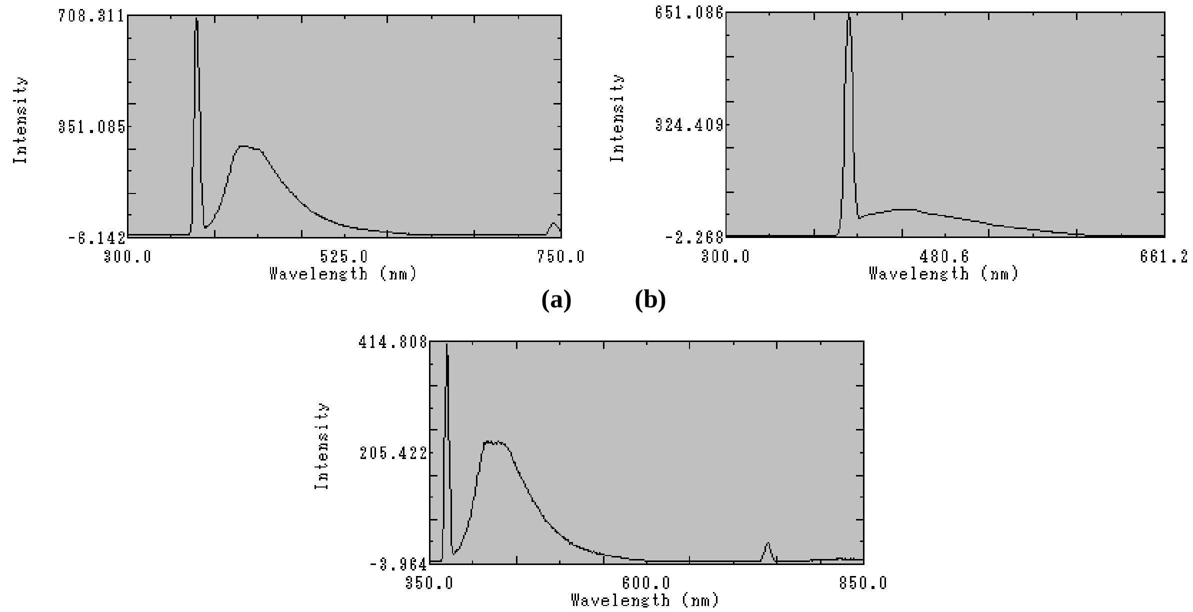


Fig: 1 Excitation spectra of N'-[(E)-thiophene-2-ylmethylidene]pyridine-4-carbohydrazide



(a) (b)

(c)

Fig: 2 Emission spectra of N’-[(E)-thiophene-2-ylmethylidene]pyridine-4-carbohydrazide at (a) 370 nm (b) 399 nm (c) 736 nm

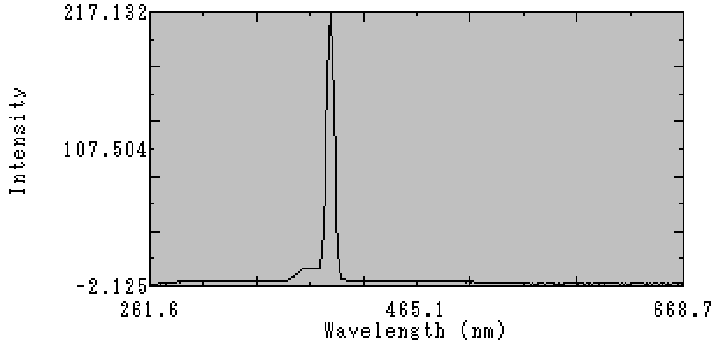
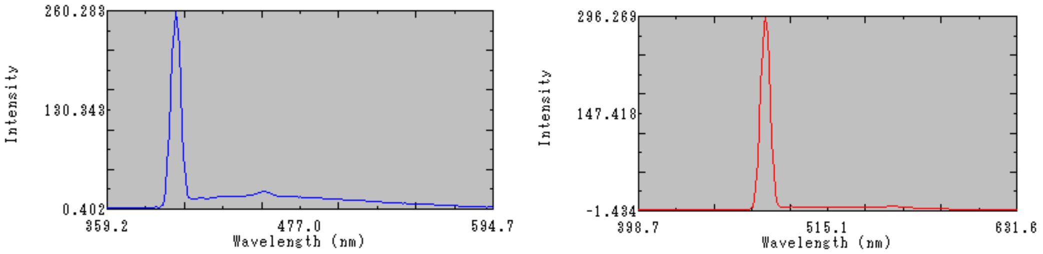


Fig: 3 Excitation spectra of N’-[(E)-phenylmethylidene]pyridine-4-carbohydrazide



(a) (b)

Fig. 4 Emission spectra of N’-[(E)-phenylmethylidene]pyridine-4-carbohydrazide at (a) 399 nm (b) 475 nm

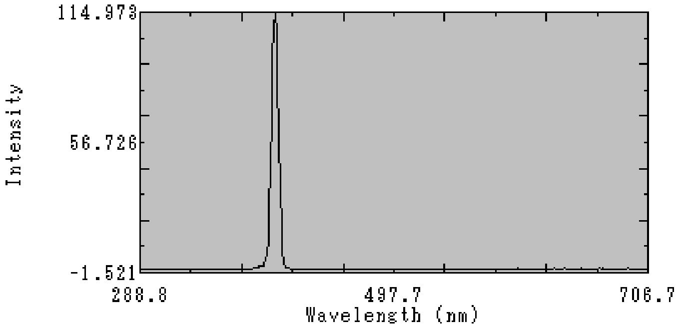
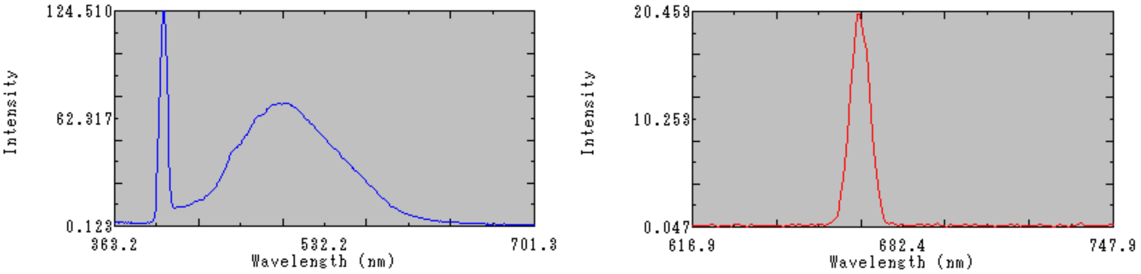


Fig: 5 Excitation spectra of N'-[(E)-(2-hydroxyphenyl) methylidene]pyridine-4-carbohydrazide



(a) (b)

Fig: 6 Emission spectra of N'-[(E)-(2-hydroxyphenyl) methylidene]pyridine-4-carbohydrazide at (a) 400 nm (b) 667 nm

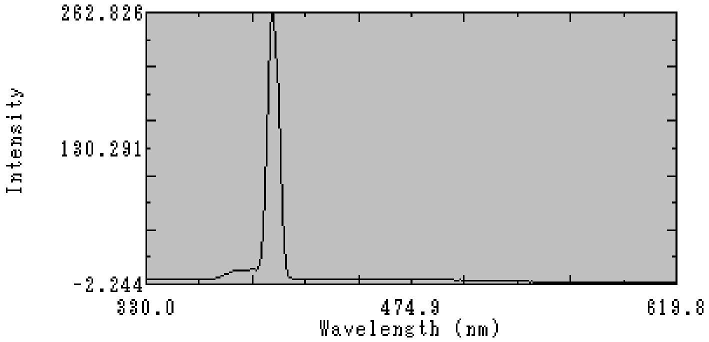
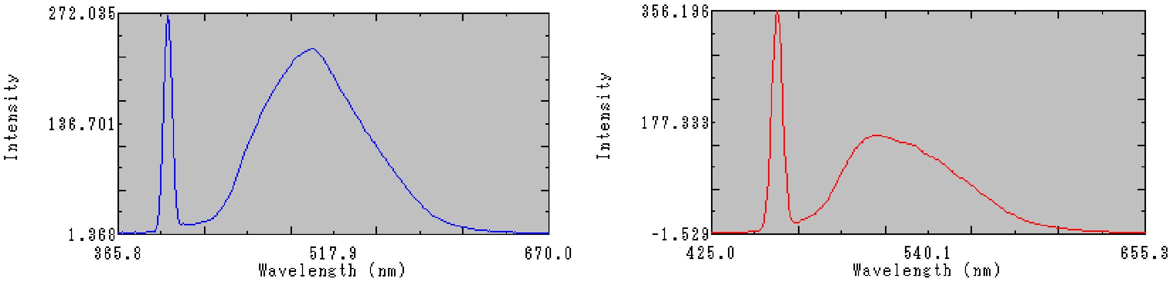
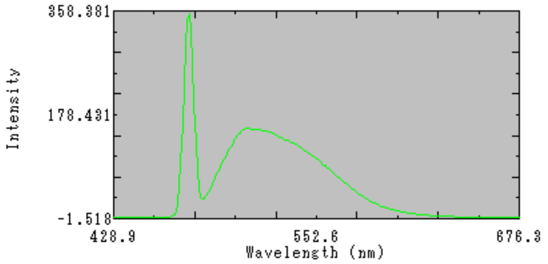


Fig: 7 Excitation spectra of N'-[(E)-(4-hydroxy-3-methoxyphenyl) methylidene]pyridine-4-carbohydrazide



(a) (b)



(c)

Fig: 8 Emission spectra of N'-[(E)-(4-hydroxy-3-methoxyphenyl) methylidene]pyridine-4-carbohydrazide at (a) 399 nm (b) 458nm (c) 473 nm

RESULT AND DISCUSSION

Isoniazide was synthesized by the sequence of reaction and purified by successive recrystallization using aq. ethanol. It is further condensed with variety of aldehyde such as thiophen-2-aldehyde, benzaldehyde, salicyladehyde and vanillin. The purity of the synthesized compounds was checked by performing TLC. The structures of the synthesized compounds were confirmed from their 1H-NMR data. The broad single of the –NH- group of hydrazone in the range of **12.26 to 11.87** (δ in ppm) confirm the formation of imine linkage. The two set of protons of 4-substituted pyridine ring shows two triplets at **8.75** and **7.74** (δ in ppm). The yield of the product depending on the nature of aldehyde. The aldehydes with electron withdrawing groups (active aldehydic functional group) are more reactive and give good yield of product.

The Schiff bases of isoniazide and aromatic aldehydes shows shifting of some absorption bands (wavelengths) towards lower (in case of chloro and bromo) and in some cases towards higher wavelengths. The effect of shifting is considerable in case of para-substitution rather than meta-substitution. N'-[(E)-(2-chloroquinolin-3-yl)methylidene]4-chloroaniline (**2c**) shows absorption and emission at higher wavelength as compared to N'-[(E)-(2-chloroquinolin-3-yl)methylidene]3-chloroaniline (**2e**) but intensity of meta-substituted Schiff base is higher than para-substituted Schiff base.

The Schiff bases of isoniazide shows absorption in the range of **390 – 401** nm and shows emission at **400-403** nm wavelengths due to excitation at same it indicates that, isoniazide skeleton is responsible for that absorption. Some other emissions (at different wavelength) which are different for different Schiff bases are also reported which are due to aromatic imine in conjugation to isoniazide skeleton. Other absorption wavelengths are also reported by changing the nature of aldehyde.

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