SYNTHESIS AND FLUOROMETRIC ANALYSIS OF SELECTED DIAZINE DERIVATIVES AND THEIR METAL COMPLEXES

(Sintesis dan Analisis Pendarfluor Terbitan Diazina dan Kompleks Logamnya)

Edura Badaruddin[1], Zaharah Aiyub[2], Zanariah Abdullah[2], Shah Bakhtiar Nasir[2]

[1]*Chemistry Division, Centre for Foundation Studies In Science,*
[2]*Department of Chemistry, Faculty of Science,*
University of Malaya, 50603 Kuala Lumpur, Malaysia

Abstract

2-N-anilinopyrimidine, 2-N-methylanilinopyrimidine and 2-N-ethylaminopyrimidine were obtained when commercially available 2-chloropyrimidine was refluxed with aniline, N-methylaniline and ethylamine respectively. Each ligand was then reacted with Cr(II) acetate to give their respective complexes. The structures of the ligands and complexes were confirmed by spectroscopic analysis. Fluorometric analysis of metal complexes of pyrimidine derivatives and the ligand itself were carried out in a quartz cell using methanol as the solvent. The compounds each exhibited fluorescence characteristic with the ligands. The ligands, in general, showed a high relative intensity and the fluorescence peak were also shifted to the lower wavelength compared to their metal complexes.

Keywords: fluorescence, pyrimidine derivatives, metal complexes

Abstrak

2-N-anilinopirimidina, 2-N-metilanilinopirimidina dan 2-N-etilaminopirimidina diperoleh apabila 2-kloropirimidina direfluks dengan anilina, N-metilanilina dan etilamina. Setiap ligan kemudiannya ditindak balaskan dengan Cr(II) asetat untuk mendapatkan kompleks logam. Struktur sebatian–sebatian ini kemudiannya dikenalpasti secara analisis spektroskopi. Kajian pendafluoran bagi setiap kompleks logam dan ligannya dilakukan dengan menggunakan sel kuartz dan metanol sebagai pelarut. Setiap sebatian menunjukkan ciri–ciri pendafluoran dengan setiap ligan, secara amnya menunjukkan peningkatan keamatan dan teranjak kepada jarak gelombang yang lebih rendah berbanding dengan kompleks logamnya.

Kata kunci: pendarfluor, terbitan pirimidina, kompleks logam

Introduction

Diazine refers to a group of organic compounds having the molecular formula $C_4H_4N_2$. Each contains a benzene ring in which two of the carbon atoms have been replaced by nitrogen. One of the isomers is pyrimidine (Figure 1). It is the parent heterocycle of a very important group of compounds which play a significant role in many biological systems [1]. The pyrimidine ring system, present in nucleic acids, several vitamins, coenzymes and antibiotics, provides potential binding sites for metal ions, and any information on their coordinating properties is important as a means of understanding the role of the metal ions in biological systems. Since pyrimidine bases are minor constituents of nucleic acids, the chemistry of pyrimidine has been the subject of much research owing to their applications in molecular biology and medicine [2]. Moreover, some divalent transition metal complexes of pyrimidine play an important role in the maintaining of functionality of DNA, as well as being used in the preparation of pesticides.

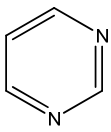


Figure 1

In general, fluorescence is the result of the rapid emission of light energy from a molecule which has been excited by light absorption. Moreover, molecular fluorescence spectrometry can be used for quantification of aromatic, or highly unsaturated, organic molecules present at trace concentrations, especially in biological and environmental

samples. It also can be extended to a wide variety of organic and inorganic compounds via chemical labeling and derivatization procedure [3].

The usefulness of fluorescence and absorption spectra of organic molecules is universally recognized and much progress has been made in investigating these molecules. However, the fluorescence-structure relationship is less investigated although it is known that some heterocyclic compounds are fluorescent. The fluorescence of crystals is especially prone to quenching even by trace amounts of impurities, due to energy transfer mechanisms, somehow made investigations on the fluorescence of these compounds difficult [4].

In general, metal ions, especially paramagnetic ions, are able to quench the fluorescence of organic ligands by enhancing the rate of same non-radiative processes that compete with fluorescence, such as intersystem crossing. Diamagnetic non-transition metal ions are usually poor quenchers and hence form good fluorescent chelates [4–5].

Quenching of fluorescence of a ligand by transition metal ions during complexation is a rather common phenomenon which is explained by processes such as magnetic perturbation, redox-activity, electronic energy transfer and etc. [6 – 7].

This paper will report on the preparation of 2-*N*-anilinopyrimidine, 2-*N*-methylanilinopyrimidine and 2-*N*-ethylaminopyrimidine and their metal complexes and a study of their fluorescence behavior.

Experimental

Synthesis

2-N-anilinopyrimidine

The compound 2-chloropyrimidine (0.5160 g , 0.0045 mol) was added to aniline (5.00 cm^3 , 0.0045 mol) and heated in an oil bath at 140^oC for about 3 hours. The mixture was then cooled and dissolved in a minimum volume of water. The aqueous layer was then extracted with ether (3 x 10 cm^3). The ether layer was washed with water and dried over anhydrous sodium sulphate. Evaporation of ether gave the product, a yellow powder. Yield 0.4740 g, 70 %, IR (cm^{-1}) : 3258.06, 3054.45, 1578.10, 1537.26, 1449.50; ^{1}H-NMR δ_H ppm (400MHz, $CDCl_3$) : 8.40, d, 2H (H-4, H-6), 7.59, d, 2H (H-2', H-6'), 7.34, t, 3H (H-3', H-5', N-H), 7.03, t, 1H (H-4'), 6.69, t, 1H (H-5); ^{13}C-NMR δ_C ppm (100.4MHz, $CDCl_3$) : 160.193 (C-2), 157.980 (C-4, C-6), 139.329 (C-1'), 128.921 (C-2', C-6'), 122.743 (C-4'), 119.575 (C-3', C-5'), 112.475 (C-5)

2-N-methylanilinopyrimidine

The compound N-methylaniline (5.00 cm^3, 0.05 mol) and 2-chloropyrimidine (5.3983 g , 0.05 mol) were heated in an oil bath at 140^oC - 160^oC for about 2 hours. The mixture was then cooled and dissolved in a minimum volume of water. The mixture was then extracted with ether. The aqueous layer was then extracted with ether (3 x 10 cm^3). The ether layer was washed with water and dried over anhydrous sodium sulphate. Evaporation of ether gave the product, a yellowish brown liquid. Yield 3.5634g, 66%, IR (cm^{-1}) : 3036.45, 2943.74, 1581.81, 1550.79, 1498.06, 1398.45; ^{1}H-NMR δ_H ppm (400MHz, $CDCl_3$) : 8.30, d, 2H (H-4, H-6), 7.20 – 7.42, m, 5H (H-2', H-3', H-4', H-5', H-6'), 6.53, t, 1H (H-5), 3.07, s, 3H (-CH_3); ^{13}C-NMR δ_C ppm (100.4MHz, $CDCl_3$) : 154.18 (C-2), 141.45 (C-1'), 130.48 (C-4, C-6), 129.04 (C-2', C-6'), 109.85 (C-5), 126.29 (C-3', C-4', C-5'), 41.20 (-CH_3)

2-N-ethylaminopyrimidine

The compound 2-chloropyrimidine (0.7915 g) was added to ethylamine (15.00 cm^3) and heated under reflux with continuous stirring for 4 hours. The mixture was then cooled and extracted with ether. The ether layer was washed with water and dried over anhydrous sodium sulphate. Evaporation of solvent gave the crude product, which was then recrystallised from chloroform to furnish the light yellow crystals. Yield 0.6765 g, 86%, IR (cm^{-1}) : 3258.34, 2970.57, 1595.76, 1534.05, 1450.85; ^{1}H-NMR δ_H ppm (400MHz, $CDCl_3$) : 8.24, d, 2H (H-4, H-6), 6.47, t, 1H (H-5), 5.17, s, 1H (N-H), 3.45, q, 2H (H-α), 1.21, t, 3H (H-β); ^{13}C-NMR δ_C ppm (100.4MHz, $CDCl_3$) : 162.29 (C-2), 158.01 (C-4, C-6), 110.37 (C-5), 36.23 (C-α), 14.89 (C-β)

Cr(II) Metal Complexes

The acetate salts of Cr(II) in acetic acid was refluxed and stirred for about an hour. Each ligand was then added to the metal ion solution in ratio 1 : 2 (metal : ligand), the mixture was then stirred and refluxed for another 8 hours. The resultant solution was evaporated to dryness. Coloured complexes of pale brown for Cr(II):2-*N*-anilinopyrimidine complex (0.3217 g, 67%), dark brown for Cr(II):2-*N*-methylanilinopyrimidine (0.2394 g, 58%) and dark brown for Cr(II):2-*N*-ethylaminopyrimidine complex (0.3914 g, 73%) were obtained.

Spectroscopic Analysis

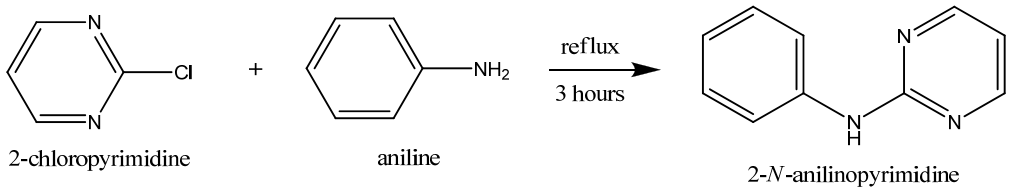
Infrared spectra were recorded as KBr discs(solids) on a Perkin Elmer 298 Infrared Spectrometer and FTIR Perkin Elmer 1600 Series. ^{1}H-NMR and ^{13}C-NMR spectra were measured on JEOL JNM-LA400FT NMR System in $CDCl_3$ with TMS as internal standard at 25 ^{o}C.

Fluorescence Studies

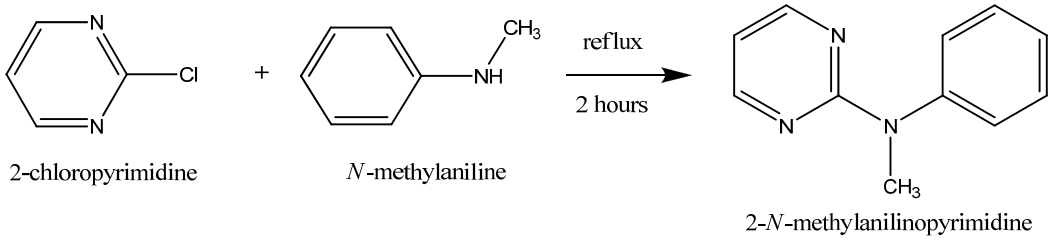
Each ligand and their metal complexes were prepared in methanol. The fluorescence measurement was carried out in a quartz cell, using Fluorescence Spectrometer Model F-2000 Hitachi at room temperature with the same instrument setting.

Results and Discussion

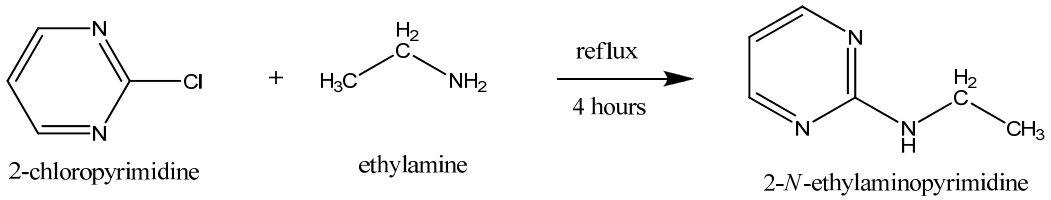
2-*N*-Anilinopyrimidine, 2-*N*-methylanilinopyrimidine and 2-*N*-ethylaminopyrimidine were obtained when commercially available 2-chloropyrimidine was reacted with aniline, *N*-methylaniline and ethylamine respectively as shown in Scheme 1, 2 and 3. Each ligand was then used as specific binder towards the transition metal ion, Cr(II) in a 1 : 2 ratio (metal : ligand) to give their respective complexes.



Scheme 1



Scheme 2



Scheme 3

The ^{1}H-NMR spectrum of 2-*N*-anilinopyrimidine showed a doublet at δ 8.40, which was due to H_4 and H_6 of pyrimidine ring. A doublet at δ 7.59 was due to $H_{2'}$ and $H_{6'}$ of the benzene ring. A triplet was recorded at δ 7.34, was due to proton resonance at $H_{3'}$, $H_{5'}$ and N-H group. A triplet peak was observed at δ 7.03 was due to $H_{4'}$ of the benzene ring and another triplet was recorded at δ 6.69 was due to proton resonance at H_5 of the pyrimidine ring. The ^{13}C-NMR spectrum showed a relatively low intensity absorption peak at δ 160.193, which was due to C_2 of the pyrimidine ring. A peak at δ 157.980 was assigned to C_4 and C_6 of pyrimidine ring. One absorption peak at δ 139.329 was due to $C_{1'}$ of benzene ring. A strong absorption peak at δ 128.921 was assigned to $C_{2'}$ and $C_{6'}$ of benzene ring. One peak at δ 122.743 was due to $C_{4'}$ of benzene ring. A medium absorption peaks at δ 119.575 and δ 112.475 were assigned to $C_{3'}$ and $C_{5'}$ of the benzene ring and C_5 of pyrimidine ring.

The ^{1}H-NMR spectrum of 2-*N*-methylanilinopyrimidine showed a doublet at δ 8.30, which was due to H_4 and H_6 of pyrimidine ring. A multiplet at δ 7.20 – 7.42 was due to $H_{2'}$, $H_{3'}$, $H_{4'}$, $H_{5'}$ and $H_{6'}$ of the benzene ring. A triplet was recorded at δ 6.53, was due to proton resonance at H_5 of pyrimidine ring. A singlet peak was observed at δ 3.07 was due to protons of the $–CH_3$ group. The ^{13}C-NMR spectrum showed a relatively low intensity absorption peak at δ 154.18, which was due to C_2 of the pyrimidine ring. A peak at δ 141.45 was due to $C_{1'}$ of benzene ring. One absorption peak at δ 130.48 was assigned to C_4 and C_6 of pyrimidine ring. A strong absorption peak at δ 129.04 was assigned to $C_{2'}$ and $C_{6'}$ of benzene ring. One peak at δ 109.85 was due to C_5 of the pyrimidine ring. A medium absorption peaks at δ 126.29 and δ 41.20 were assigned to $C_{3'}$, $C_{4'}$ and $C_{5'}$ of the benzene ring and C of the methyl group.

The ^{1}H-NMR spectrum of 2-*N*-ethylaminopyrimidine showed a doublet at δ 8.24, which was due to H_4 and H_6 of pyrimidine ring. A triplet at δ 6.47 was due to H_5 of the pyrimidine ring. A broad peak at δ 5.17 was assigned to proton of the N-H group. A quintet was recorded at δ 3.45 and a triplet at δ 1.21, were due to proton resonance at H_α and H_β of the ethyl group. The ^{13}C-NMR spectrum showed an absorption peak at δ 162.29, which was due to C_2 of the pyrimidine ring. A peak at δ 158.01 was assigned to C_4 and C_6 of pyrimidine ring. One absorption peak at δ 110.37 was due to C_5 of pyrimidine ring. An absorption peak at δ 36.23 and δ 14.89 were assigned to C_α and C_β of the ethyl group.

The fluorescence characteristic of 2-*N*-anilinopyrimidine, 2-*N*-methylanilinopyrimidine and 2-*N*- ethylamino-pyrimidine and their metal complexes are summarized in Table 1.

Table 1: Fluorescence characteristic of ligands and their metal complexes in methanol.

Compound	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-*N*-anilinopyrimidine	376	420	0.196
Cr(II):2-*N*-anilinopyrimidine	347	430	0.221
2-*N*-methylanilinopyrimidine	331	399	0.389
Cr(II):2-*N*-methylanilinopyrimidine	362	402	0.149
2-*N*-ethylaminopyrimidine	320	376	58.71
Cr(II):2-*N*-ethylaminopyrimidine	316	378	8.81

It can be seen in Table 1 that, 2-*N*-ethylaminopyrimidine fluoresced at 376 nm when excited at 320 nm while 2-*N*-methylanilinopyrimidine emitted at higher wavelength, 399 nm when excited at 331 nm. It is also noted that, 2-*N*-anilinopyrimidine had shown the highest wavelength, 420 nm when excited at 376 nm. This can be explained due to conjugation of anilino ring which allows the free mobility of electron within the system [4]. The same trend goes to their metal complexes, with Cr(II):2-*N*-anilinopyrimidine complex was shifted to the higher wavelength, 430 nm when excited at 347 nm compared to Cr(II):2-*N*-methylanilinopyrimidine complex, 402 nm and Cr(II):2-*N*-ethylaminopyrimidine complex, 378 nm when excited at 362 nm and 316 nm respectively.

Generally, the intensities of the ligands are higher than their metal complexes except for Cr(II):2-*N*-anilinopyrimidine complex. The fluorescence intensity decreased when the ligand is bound to metal. This is probably due to quenching effect of the transition metal, which bound to the ligand during complexation whereby the charge transfer transition occurred between ligand and metal ion [8]. In metal complexes, there are a charge transfer from the ligand to metal ions, thus decreased the relative fluorescence intensity [9].

However, Cr(II):2-*N*-anilinopyrimidine complex showed an increased in fluorescence intensity compared to its ligand as shown in Table 1. Usually, metal complexes showed a decreased in fluorescence intensities compared to the ligand due to the delocalization of π electrons within the system. The increase in fluorescence intensity can be explained by metal to ligand charge transfer when 2-*N*-anilinopyrimidine complexes with the metal [10].

The spectra for each of the ligand and its metal complex is given in Figure 2, 3 and 4.

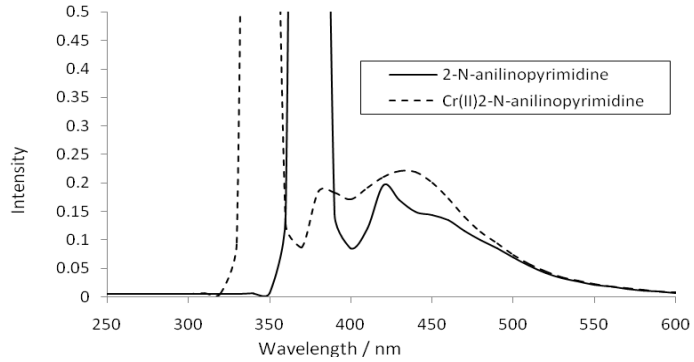


Figure 2: Fluorescence spectrum of 2-*N*-anilinopyrimidine and its metal complex

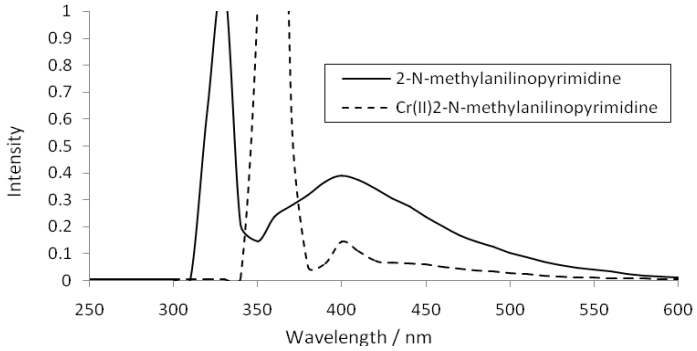


Figure 3: Fluorescence spectrum of 2-*N*-methylanilinopyrimidine and its metal complex

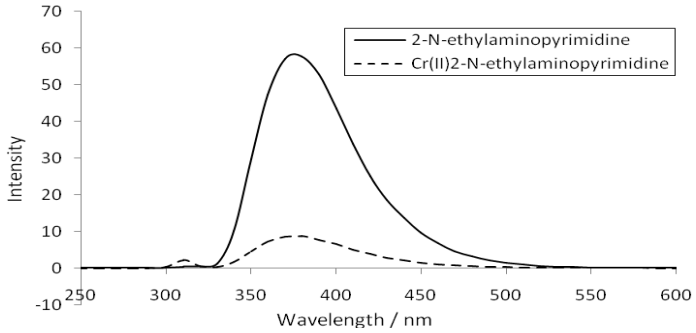


Figure 4: Fluorescence spectrum of 2-*N*-ethylaminopyrimidine and its metal complex

The fluorescence intensity for the ligands decreases in order, 2-*N*-ethylaminopyrimidine > 2-*N*-methylanilinopyrimidine > 2-*N*-anilinopyrimidine whilst for the metal complexes, the fluorescence intensity decreases in order, Cr(II):2-*N*-ethylaminopyrimidine > Cr(II):2-*N*-anilinopyrimidine > Cr(II):2-*N*-methylanilinopyrimidine. Figure 5 and 6 show a comparison for the fluorescence spectra of ligands and metal complexes respectively.

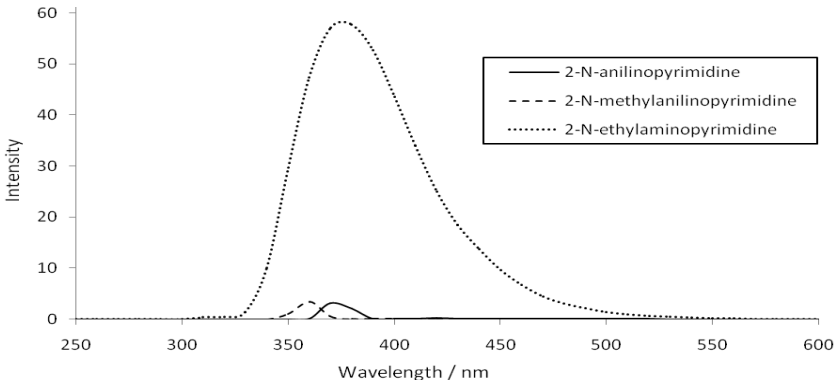


Figure 5: Fluorescence spectrum of the ligands

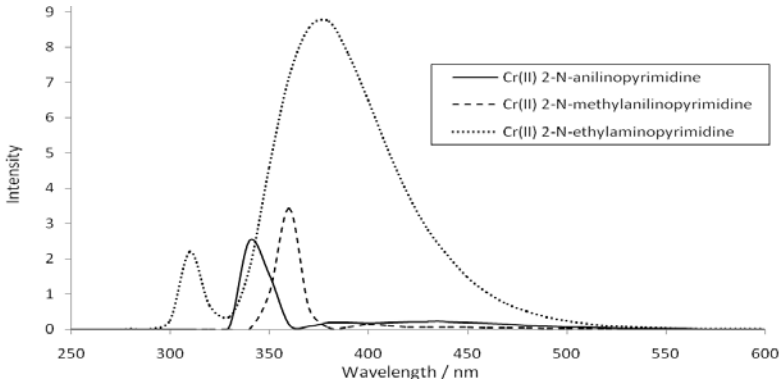


Figure 6: Fluorescence spectrum of the metal complexes

Conclusion

The compounds each exhibited characteristics fluorescence, with the ligands, in general showed a high relative intensity and the fluorescence peak were also shifted to the lower wavelength compared to their metal complexes. The relative intensities for complexes decreases in order, Cr(II):2-*N*-ethylaminopyrimidine > Cr(II):2-*N*-anilinopyrimidine > Cr(II):2-*N*-methylanilinopyrimidine whilst for the ligands, the intensities decreases in order, 2-*N*-ethylaminopyrimidine > 2-*N*-methylanilinopyrimidine > 2-*N*-anilinopyrimidine. Further study on the pyrimidine derivatives is in progress before any concrete conclusion can be made on complex–fluorescence relationship.

Acknowledgement

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