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FLUORESCENCE STUDIES OF 2–PHENOXYPYRIMIDINE, 2–PHENOXYPURINE, 5–PHENOXY[1,2,5]THIADIAZOLO[3,4–*d*] PYRIMIDINE AND 5–PHENOXYTHIAZOLO[5,4–*d*]PYRIMIDINE

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ABSTRACT

2–Phenoxypyrimidine, 2–phenoxypurine, 5–phenoxy[1,2,5]thiadiazolo[3,4–*d*] pyrimidine and 5–phenoxythiazolo[5,4–*d*]pyrimidine were prepared from 2–fluoropyrimidine, 2–fluoropurine, 5–chloro[1,2,5]thiadiazolo[3,4–*d*]pyrimidine and 5–chlorothiazolo[5,4–*d*]pyrimidine, respectively. The fluorescence characteristic of these compounds were studied in ethanol and 2–phenoxypyrimidine gave the highest fluorescence intensity followed by 2–phenoxypurine, 5–phenoxy [1,2,5] thiadiazolo[3,4–*d*]pyrimidine and 5–phenoxythiazolo[5,4–*d*]pyrimidine.

Kew words : Flourescence, Phenoxypyrimidine, Phenoxypurine.

INTRODUCTION

The fluorescence of heterocyclic compounds is not very well understood and less researched into. However, a wide variety of heterocyclic compounds are known to be fluorescent, even though relatively very few studies have been made on their structure–fluorescence relationship. Investigations on these compounds are made difficult because their fluorescence characteristics are often solvent dependent. Generally, heterocyclic compounds tend to be more fluorescent in polar solvents, whilst others are fluoresced in acidic medium.

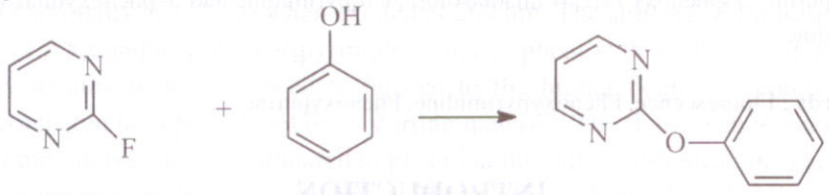
The structure–fluorescence relationships of heterocyclic compounds, particularly those containing nitrogen are poorly understood at present and therefore it is very difficult to generalize. It appears that those heterocyclic where the longest absorption wavelength correspond to $n \longrightarrow \pi^*$ transition are likely to be non–fluorescent, whereas those correspond to a $\pi \longrightarrow \pi^*$ transition are likely to fluoresce. It has been reported that pyridine, six–membered ring containing a single nitrogen atom and its derivatives, are non–fluorescent[1,2] and when the conjugation is increased by the fusion of a benzene ring as in the case of quinoline, weak fluorescence was observed[3]. Derivatives of quinoline had been studied[4,5] and fluorescence was observed in acidic medium.

In this study, the work started with the study of the effect of a phenoxy group to a pyrimidine system, followed by purine system; a system that was formed when pyrimidine ring is fused with a five–membered ring with two nitrogen atoms as part of the 5–membered ring. When one nitrogen atom in five–membered ring was replaced by a sulphur atom, thiazolopyrimidine system was formed, whereas in thiadiazolopyrimidine system, two nitrogen atoms and one sulphur atom are part of the five–membered ring. The substituent, phenoxy group is choosen in this study because phenols and its derivatives are toxic compounds. Phenol can be obtained from domestic and industrial waste, present either in water, sediment or soils.

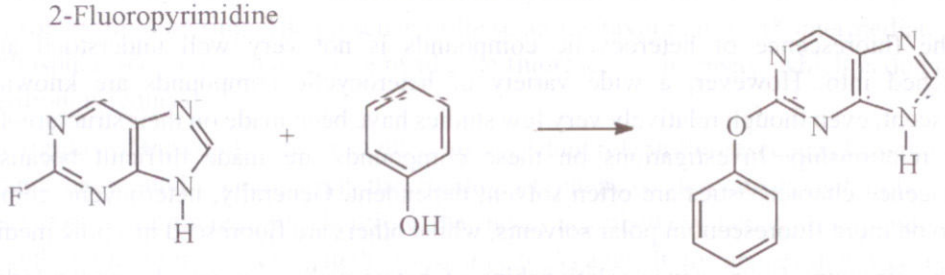
It is hoped that the finding of this study will later be used to design a fluorogenic reagent which will be used to detect the presence of phenols using fluorescence spectroscopy. The fluorescence spectroscopy can be used not only to detect phenols but also to speciate phenols.

RESULTS AND DISCUSSION

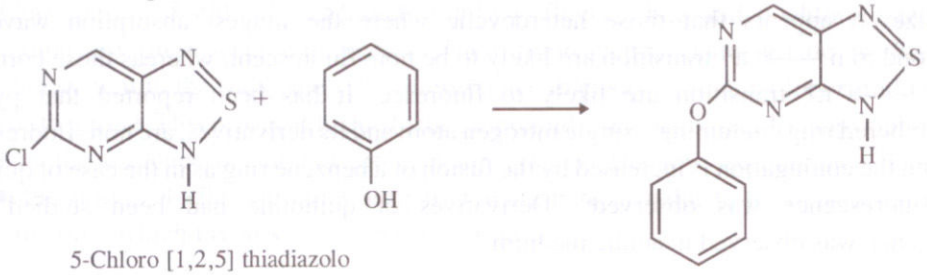
Treatment of 2–fluoropyrimidine, 2–fluoropurine, 5–chloro[1,2,5]thiadiazolo[3,4–*d*] pyrimidine and 5–chlorothiazolo[5,4–*d*]pyrimidine with phenol formed phenoxy derivatives respectively as shown below:–



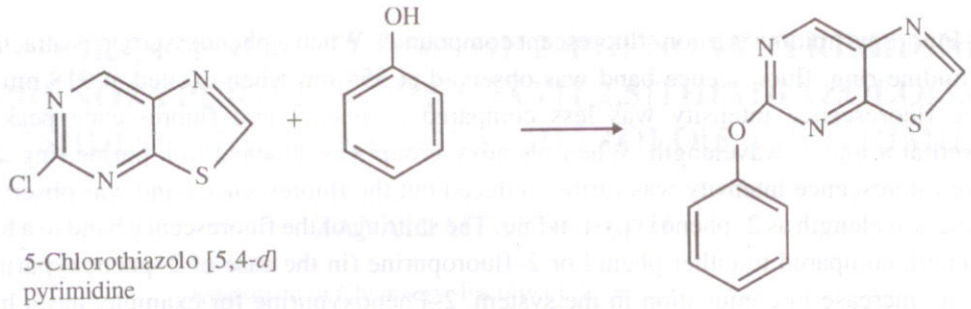
2-Fluoropyrimidine



2-Fluoropurine



5-Chloro [1,2,5] thiadiazolo
[3,4-*d*] pyrimidine



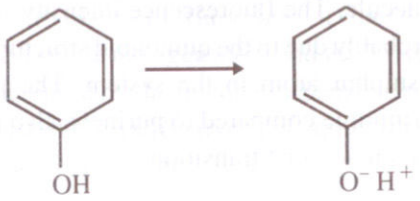
5-Chlorothiazolo [5,4-*d*] pyrimidine

The fluorescence characteristics of the compounds studied in ethanol are as shown in Table 1.

Table 1. Fluorescence characteristic of phenoxy derivatives

Compounds	Solvent	Excitation wavelength/nm	Fluorescence wavelength/nm	Relative intensity
2–Fluoropyrimidine	Ethanol	–	–	–
2–Fluoropurine	75% ethanol	250	330	0.321
5–Chlorothiadizolo[3,4–*d*] pyrimidine	Water	338	369	0.242
5–Chlorothiazolo[5,4–*d*] pyrimidine	Ethanol	270	380	0.015
Phenol	Ethanol	281	297	0.218
2–Phenoxypyrimidine	Ethanol	318	354	0.437
2–Phenoxypurine	Ethanol	308	355	0.215
5–Phenoxythiadizolo[3,4–*d*] pyrimidine	Ethanol	384	452	0.126
5–Phenoxythiazolo[5,4–*d*] pyrimidine	Ethanol	260	412	0.133

Earlier studies have shown that phenol fluoresced at 297 nm when excited at 281 nm in ethanol. The fluorescence of phenol was pH dependent and its fluorescence intensity maximized at pH 1[6].The higher fluorescence intensity observed at pH 1 is probably due to phenol in its unionized form. When pH was increased, phenol undergoes ionization process forming phenoxide ion[6,7]. The fluorescence intensity at higher pH is due to the phenoxide ion which is lower than that of the fluorescence intensity of phenol molecule.



2–Fluoropyrimidine is a non–fluorescent compound[8]. When a phenoxy group is attached to a pyrimidine ring, fluorescence band was observed at 354 nm when excited at 318 nm. The relative fluorescence intensity was less compared to phenol and fluorescence peak was observed at a higher wavelength. When phenoxy group was attached to a purine ring at C_2, relative fluorescence intensity was further reduced but the fluorescence band was observed at the same wavelength as 2–phenoxypyrimidine. The shifting of the fluorescence band to a higher wavelength compared to either phenol or 2–fluoropurine (in the case of 2–phenoxypurine) is due to an increase in conjugation in the system. 2–Phenoxypurine for example, has a higher degree of conjugation compared to either purine or phenol. An introduction of two nitrogen atoms in the pyrimidine ring reduced the fluorescence intensity and the fluorescence intensity was further reduced as more nitrogen atoms present in the system, as shown by purine system. The introduction of nitrogen atoms in the ring favours the low lying $n \longrightarrow \pi^*$ which allows phosphorescence to occur. As a result, fluorescence intensity is reduced.

Similar phenomenon was observed when phenoxy group is attached to thiadiazolo and thiazolo ring where the fluorescence peak of 5–phenoxy[1,2,5]thiadiazolo[3,4–*d*] pyrimidine was observed at 452 nm when excited at 384 nm and 5–phenoxythiazolo[5,4–*d*]pyrimidine fluoresced maximally at 412 nm when excited at 260 nm. The shifting of fluorescence peak of 5–phenoxy[1,2,5]thiadiazolo[3,4–*d*]pyrimidine and 5–phenoxythiazolo[5,4–*d*] pyrimidine to higher wavelengths is also believed to be due to the higher degree of conjugation in the molecule compared to either phenol or its starting material. The fluorescence intensity of these phenoxy compounds is less as compared to phenol at the same concentration. The reduction in fluorescence intensity is due to the presence of heavy atoms, N and S in thiadiazolopyrimidine and thiazolopyrimidine ring. The presence of these atoms favours $n \rightarrow \pi^*$ intermediate which cause phosphorescence to occur[9]. As a result, the fluorescence intensity, which is due to $\pi \rightarrow \pi^*$ transition, is reduced.

The rigidity of the compounds also plays an important role in fluorescence characteristic of an organic compound[7]. Comparing the rigidity of phenoxy derivatives with phenol, the molecule of phenol is more rigid. Therefore, the energy absorbed by phenoxy compounds is lost through vibration of the molecules in the form of heat. As a result, the energy that was absorbed to promote fluorescence becomes less, and low fluorescence intensity is observed.

2–Fluoropurine, 5–chloro[1,2,5]thiadiazolo[3,4–*d*]pyrimidine and 5–chlorothiazolo[5,4–*d*]pyrimidine are fluorescent compounds. Their fluorescence characteristic is due to the conjugated system in the molecule. The fluorescence intensity of thiadizolopyrimidine is less compared to purine. This is probably due to the quinonoid structure of thiadizolopyrimidine ring as well as the presence of sulphur atom in the system. The low fluorescence intensity of 5–chlorothiazolo [5, 4–*d*] pyrimidine compared to purine is also due to the presence of sulphur atom in the ring, which favours $n \longrightarrow \pi^*$ transition.

EXPERIMENTAL

Synthesis

General

The phenoxy derivatives were obtained as below. The fluorescence studies were carried out using Fluorescence Spectroscopy Model F–2000 Hitachi. All measurements were carried out at room temperature using ethanol as the solvent in a quartz cell, and quinine sulphate was used as the standard. ^{1}H NMR were recorded using JEOL 60MHZ JNM–PMX60SI, Bruker WP–80 and Bruker AM 250 instruments. Mass spectra were recorded using Kratos MS 50TC with DS 90 Data system and infrared spectra were recorded using FTIR Perkin Elmer 1600 Spectrophotometer.

2–Phenoxypyrimidine

Phenol (0.2 g) was dissolved in absolute alcohol (3 mL) and added to a solution of sodium ethoxide (0.05 g sodium metal in 5 mL absolute alcohol), and an ethanolic solution of 2–fluoropyrimidine (0.2 g in 3 mL alcohol) was added dropwise. The mixture was refluxed for one hour. The mixture was filtered and cooled and solvent evaporated off. A minimum volume of chloroform (25 mL) was added and the chloroform layer was shaken thoroughly with 5% sodium hydroxide solution (10 mL) and water, dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave crude product, which further recystallised from hexane giving pure 2–phenoxypyrimidine.

% Yield: 80%, m.pt: 82–83 ^oC (85–88 ^oC[10]), ir (cm^{-1}): 1200.7; ^{1}H NMR (d_6–acetone): 8.70, d, 2H,H–4, H–6 (pyrimidine ring), 7.56, t, 1H, H–5 (pyrimidine ring)), 7.30–7.39, m, 5H, H–2', H–3', H–4', H–5', H–6' (benzene ring)); Mass : M^+ = 172.211, $C_{10}H_8N_2O$ requires M^+ =172.064

2–Phenoxypurine

Phenol (60 mg) was dissolved in 2M sodium hydroxide solution (3 mL) and the pH was adjusted to pH 10.6. The solution was added to 2–fluoropurine (66 mg) in 75% ethanol (10 mL). The mixture was refluxed for one hour with constant stirring. The solvent was removed under *vacuo* and water (5 mL) was added and the pH was adjusted to pH 7, extracted with chloroform (3 x 10 mL). The organic layer was washed with water and dried. Removal of chloroform followed by recrystallisation with alcohol gave the product.

Yield: 30%, m.pt: decomposed above 219^oC; ir (cm^{-1}): 1675, 1625, 1080; ^{1}HNMR (d_6–DMSO) δ : 8.70, s, 1H, H–6 (purine ring)), 8.00, s, 1H, H–8 (purine ring)), 6.80, m, 5H, H–2', H–3', H–4', H–5', H–6' (benzene ring), 5.50–5.70, bR,1H, NH of purine ring; Mass : not done; but structure confirmed by comparing data with literature[11–12].

5–Phenoxy[1,2,5]thiadiazolo[3,4–*d*]pyrimidine

Phenol (35 mg) was dissolved in sodium hydroxide (1M, 2 mL) and the pH was adjusted to pH 10.3. 5–Chloro[1,2,5]thiadiazolo[3,4–*d*]pyrimidine (52 mg) was dissolved in ethanol (5 mL) and added slowly to the alkaline solution of phenol and refluxed for two hours. The mixture was cooled and solvent evaporated off. Water (5 mL) was added to the residue, pH adjusted to pH 7, and extracted three times with ether (18 mL). Ethereal layer was washed with water and dried. Evaporation of ether followed by recrystallisation with dichloromethane gave the product.

Yield:30%, m.pt 213°C, ir (cm^{-1}):1680, 1625, 1425,1150; ^1H NMR ($CDCl_3$ & d_6–DMSO), δ : 7.35, s, 1H, H–7, 7.10, t, 2H, H–2', H–6' (benzene ring)), 6.72, m, 3H, H–3', H–4',H–5' (benzene ring)); Mass : M^+: 230.026, $C_{10}H_6N_4OS$ requires M^+ = 230.026

5–Phenoxythiazolo[5,4–*d*]pyrimidine

Phenol (60 mg) was dissolved in sodium hydroxide (0.1M, 2 mL) and the pH was adjusted to pH 10. 5–Chloro [1,2,5]thiazolo[5,4–*d*]pyrimidine (90 mg) was dissolved in absolute ethanol (3 mL) and added to the alkaline solution of phenol and refluxed for one and half hours. The mixture was cooled and solvent evaporated off. Water (5 mL) was added to the residue, pH adjusted to pH 7, and extracted three times with ether (18 mL). Ethereal layer was washed with water and dried. Evaporation of ether followed by recrystallisation from chloroform gave the product, yellowish crystals.

Yield:35%; darkens above 200°C; ir (cm^{-1}):1670, 1620, 1750; ^1H NMR ($CDCl_3$ & d_6–DMSO), δ : 9.20, s, 1H, H–2, 9.00, s, 1H, H–7, 6.85–6.65, m, 5H, H–2', H–3', H–4', H–5', H–6' (benzene ring), Mass : M^+: 229.031, $C_{11}H_7N_3OS$ requires M^+ = 229.031

Fluorescence studies (General)

2–Phenoxypyrimidine, 2–phenoxypurine, 5–phenoxy[1,2,5] thiadiazolo[3,4–*d*]pyrimidine and 5–phenoxythiazolo[5,4–*d*]pyrimidine of the same concentration were prepared. The fluorescence measurement was carried out using Fluorescence Spectroscopy Model F–2000 Hitachi. All measurements were carried out at room temperature using ethanol as the solvent and quinine sulphate was used as the standard.

CONCLUSION

2–Fluoropyrimidine is a non–fluorescent compound but formed fluorescence product when treated with phenol. 2–Phenoxypurine, 5–phenoxy[1,2,5]thiadiazolo[3,4–*d*]pyrimidine and 5–phenoxythiazolo[5,4–*d*]pyrimidine are fluorescent compounds but their fluorescence intensity is less than phenol. The low fluorescence intensity observed with these four phenoxy derivatives is believed to be due to the presence of heavier atoms, the presence of N and S as part of the ring and the rigidity of the compounds.

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