The Effect of Methyl Substitution on the Ferroin and Cuproin Reactions in Pyridyl Substituted Pyrazines and Dihydropyrazines

M.Y. KHUHAWAR* AND W.I. STEPHEN

Department of Chemistry, The University, P.O. Box 363, Birmingham B15, U.K.

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Summary: In the present work 14 pyrazines and dihydropyrazine ligands have been examined and their absorptiometric properties are compared. An attempt has been made to correlate the effect of single and multiple methyl substitution on molar absorptivity, wavelength of maximum absorbance and solution stability of their iron(II) and copper(I) complexes. The effect of the aromatic ring and the replacement of the pyridyl group by a phenyl group in the pyrazine ring is also established.

Introduction

The colour reactions formed by ferroin and cuproin type ligands find a number of applications, which signify their analytical importance and provide a good example of group action towards copper(I) and iron(II).

Goodwin and Lions[1] have synthesized a number of bidentate and tridentate pyridyl substituted pyrazines and quinoxalines and have reported their complex formation abilities towards transition metal ions. Pflaum et, al[2,3] and Stephen[4,5] and his coworkers[6,12] have synthesized more ligands of this class and have extended the analytical applications of these compounds to the quantitative determination of copper and nickel. In the present work the absorptiometric properties of 14 ligands are compared and the effects of methyl substitution on their reactions towards copper(I) and iorn(II) are correlated.

Experimental

The ligands I through XIV were synthesized by reported methods[5,6,11]. Solutions and solvent extraction procedures were the same as reported earlier[11]. All the spectrophotometric studies were carried out on Unicam SP-800 and Cecil CE505 spectrophotometrers.

Results and Discussion

The dihydropyrazine ligands (I to VII) react with copper(I) to form purple-red complexes, reagents (I,III,V,VII) react with iron(II) to show greenish to blue colour reactions of significant sensitivity. The absorptiometric data from the Table 1 indicate that single or multiple alkyl substitution increases the basicity of the donor nitrogen atoms by an inductive effect. Hence the molar absorptivity and stability of the copper(I) complexes are enhanced. The copper(I) complex of reagent IV shows higher molar absorptivity and chromphoric stability than II because of the presence of a methyl group in the former ligands at position 5 in the pyrazine ring. The reagent IV also forms the copper(I) complex at a comparatively lower pH and the copper(I) complex is stable over a broader pH range (pH 3.5 - 6.5) than II (pH 4 - 6), as might be expected.

The effect of single and multiple alkyl substitution on pyridyl- substituted dihydropyrazine copper(I) complexes upon the wavelength of maximum absorbance shows that there is a bathochromic shift with alkyl substitution in the pyridyl or dihydropyrazine ring. This shift in λ-max on the multiple alkyl substitution is not observed as additive.

The copper(I) complexes of reagents I, II and V absorb maximally at 528nm, 538nm & 541nm respectively in aqueous ethanolic solution. Hence the bathochromic shifts of 10nm and 13nm are observed because of a methyl group in each pyridyl aromatic ring and two methyl groups in a dihydropyrazine ring respectively. The reagent VI could be expected to absorb at 551nm (528 + 10

*Institute of Chemistry, University of Sind, Jamshoro, Pakistan.

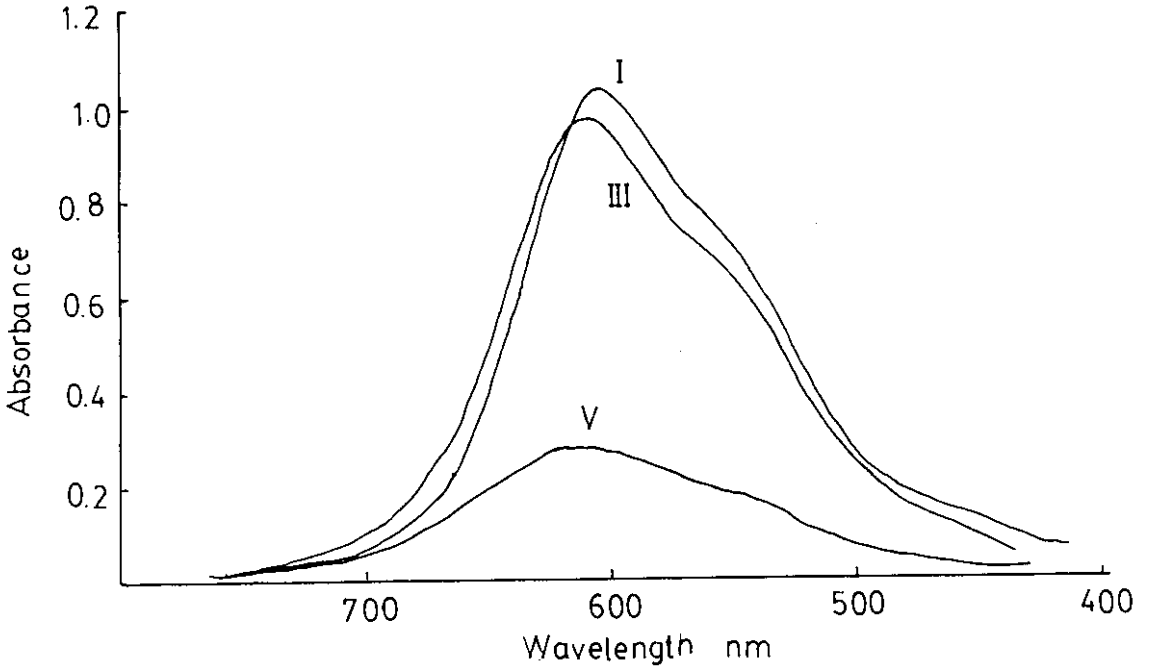

Fig. 1: Comparison of Absorptiometric Properties of Iron(II) Complexes in aqueous solution at a final concentration of 4υg/ml with;
I. 2,3-Bis (2'-pyridyl)-5,6-dihydropyrazine.
III. 2,3-Bis (2'-pyridyl)-5 methyl-5,6-dihydropyrazine and
V. 2,3-Bis (2'-pyridyl)-5,6-dimethyl-5,6-dihydropyrazine.

+ 13 = 551nm) if the shift in λ-max due to methyl substitution is additive. Actually it absorbs at 543nm in the same solvent system. Therefore, it is difficult to correlate the shift in λ-max with alkyl substitution. Similarly no simple relationship seems to exist between molar absorptivity and methyl substitution, although some enhancement is observed.

Methyl group substitution in pyridyl or dihydropyrazine rings leads to a decrease rather than an increase in the sensitivity of the ligands towards iron(II) (Table 1). Presumably, methyl substitution introduces a measure of steric hindrance or disturbs the coplanarity of the heterocyclic ring, where III is less sensitive than I for iron(II), in spite of expected higher basicities of the donor nitrogen atoms in the former ligand arising from alkyl substitution (Fig. 1). The iron(II) complex of VII is more sensitive but less stable than I because of the replacement of a pyridyl group by a phenyl group in the dihydropyrazine ring.

The present work confirms earlier work, which emphasises that substituents ortho to the donor nitrogen can cause sufficient steric hindrance to inhibit completely or partially the coordination with iron(II). The reaction of II is completely inhibited because of methyl substitution in the pyridyl ring adjacent to the imine nitrogen, but the reaction of V with iron(II) is partially inhibited because of the methyl groups present near to the donor nitrogen atoms in the dihydropyrazine ring. This is indicated by the low colour intensity of the iron(II) complex in aqueous ethanolic solution (Table 1), but when this complex is extracted into 1,2-dichlorethane as the perchlorate ion-association complex, it obeys Beer's Law and indicates strong complex formation, contrary to the experience with tris (2-methyl-1,10-phenanthroline) iron(II) perchlorate a weak complex where solution deviates from Beer's law. This difference in behaviour could be because the methyl group in 1,10-phenanthroline is present in an aromatic ring, whereas in ligand V it is present in a ring which is not aromatic, one bond of the pyrazine ring being saturated with two hydrogen atoms. Therefore, it could be that the said hydrogen atoms in the less regid, more flexible and possibly puckered dihydropyrazine ring are pushing the methyl groups from direct exposure to iron(II) in order to accommodate three molecules around the iron(II) ion to form an octahedral complex. Moreover, the reagent

Table 1: Quantitative absorptiometric data for copper(I) and iron(II) complexes of dihydropyrazine ligands

	Reagent	Solvent	Copper (I)		Chromoph-ore stability	Iron (II)		
			λ – max nm	ε^{-1}. mole cm^{-1}		λ-max nm	ε-1. mole^{-1} cm^{-1}	Chromophore stability
I	2,3-Bis (2'-pyridyl)-5,6-dihydropyrazine	Ethanol	528	$8.1x10^3$	30 min	610	$1.28x10^4$	15 min
		Chloroform	523	$8.1x10^3$	30 min	600	$1.49x10^4$	2 hr
II	2,3-Bis [2'-(6'-methyl-pyridyl)]-5,6-dihydro-pyrazine	Ethanol	538	$1.09x10^3$	30 min	-	-	-
		1,2-dich-loroethane	534	$1.1x10^4$	24 hr	-	-	-
III	2,3-Bis (2'-pyridyl)-5-methyl-5,6-dihydro-pyrazine	Ethanol	535	$9.6x10^3$	30 min	617	$1.08x10^4$	15 min
		1,2-dichl-croe thane	530	$9.2x10^3$	30 min	600	$1.39x10^4$	2 hr
IV	2,3-Bis [2'-(6-methyl-pyridyl)]-5-methyl-5, 6-dihydropyrazine	Ethanol	540	$1.15x10^4$	4 hr			
		1,2-dichl-oroethane	537	$1.6x10^4$	2 hr			
V	2,3-Bis (2'-pyridyl)-5,6-dimethyl-5,6-dihydropyrazine	Ethanol	541	$1.05x10^4$	1 hr	640	$2.3x10^3$	-
		1,2-dichl-oroethane	536	$9.8x10^3$	20 min	600	$1.2x10^4$	30 min
VI	2,3-Bis [2'(6'-methyl-pyridyl)]-5,6-dimethyl-5,6-dihydropyrazine	Ethanol	543	$1.16x10^4$	6 hr	-	-	-
		1,2-dichl-oroethane	539	$1.15x10^4$	6 hr	-	-	-
VII	2-Phenyl-3-(2'-pyridyl-5,6-dihydropyrazine	Ethanol	520	$7.9x10^3$	30 min	635	$1.4x10^4$	-
		1,2-dichl-oroethane	522	$8.1x10^3$	30 min	593	$1.52x10^4$	10 min

XIII formed after dehydrogenation of V shows no reactivity towards iron(II) as expected.

The effect of methyl group substitution in pyridyl-substituted pyrazine ligands also shows a positive effect on the molar absorptivity (Table 2) and the stability of the copper(I) complexes. The copper(I) complex of IX is only stable for a short time, but the ligand XIV forms a copper(I) complex which shows no sign of the slightest change in absorbance for up to one week after its formation. This confirms that the ligands containing the =N-C-C=N- grouping are able to react with copper(I), but two substituents ortho to each of the donor nitrogen atoms are necessary for sensitive and stable chromogenic reagents for copper to be obtained.

The effect of symmetrical methyl substitution in IX upon the λ-max of copper(I) complexes shows that the ligands X and XIII absorb maximally at 465nm and 450nm respectively compared to IX at 455nm in the same solvent (1,2-dichloroethane) as the perchlorate ion- association complex. Therefore, a bathochromic shift of 10nm in λ-max due to two methyl groups, one in each pyridyl ring, and a hypsochromic shift of 5nm for methyl groups in a pyrazine ring is observed. Hence XIV is expected to absorb at 460nm, if the shift in λ-max is the result of methyl substitution being additive. Actually it absorbs at 453nm in the same solvent system. Thus the shift in λ-max is not additive and an increase in the molar absorptivity on multiple alkyl substitution is not observed to be additive either.

The effect of methyl group substitution is IX in the pyrazine ring to give XI results in an iron(II) complex which shows a hypsochromic shift of 10nm with a remarkable increase in chromophoric stability, compared to the parent ligand IX, but without a significant change in the molar absorptivity. The replacement of the pyridyl group in IX by a phenyl group results in ligand VIII, which forms an iron(II) complex with a higher molar ab-

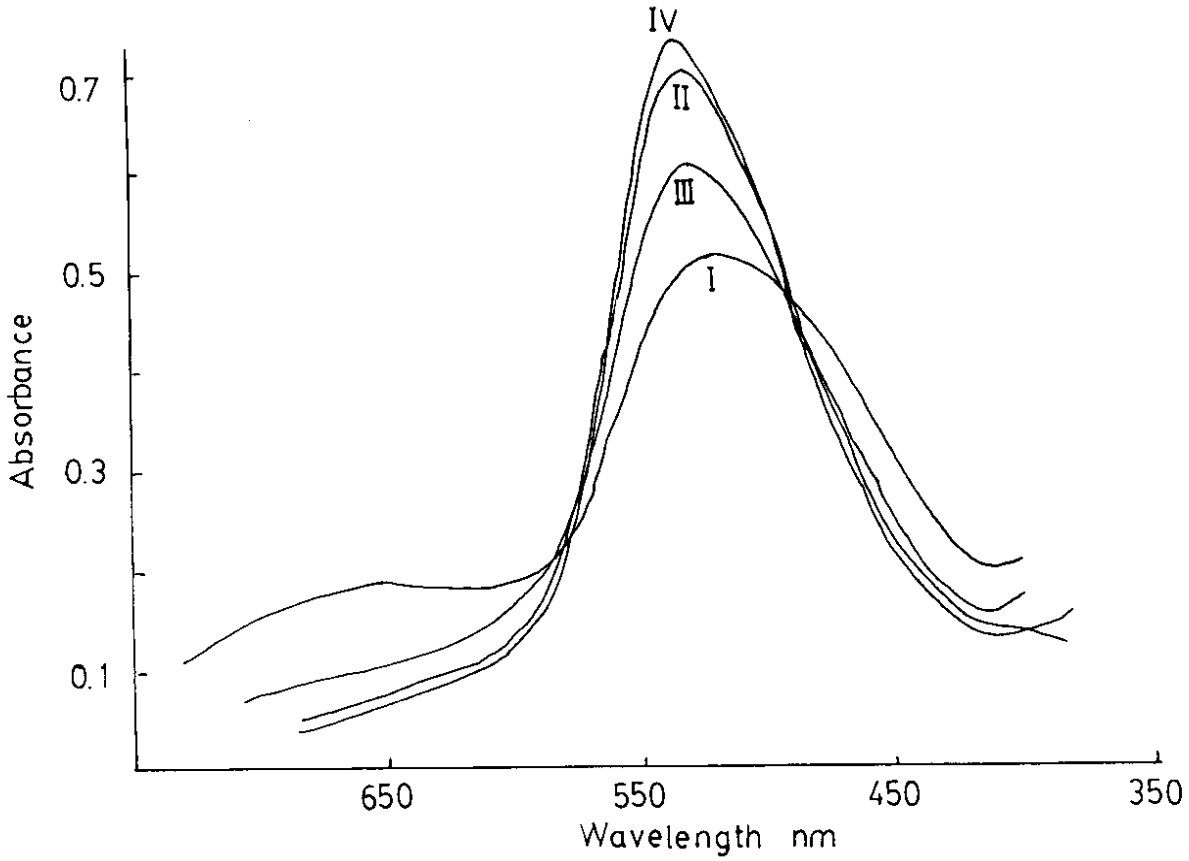

Fig. 2: Comparison of Absorptiometric Properties of Copper(I) complexes in 1,2-Dichloroethane as perchlorate at a final conc. of 4 υg/ml of cation.

I. 2,3-Bis (2'-pridyl)-5,6-dihydropyrazine.
III. 2,3-Bis(2'-pyridyl)-5,6-dihydropyrazine.
II. 2,3-Bis (2'-(6'-methylpyridyl))-5,6-dihydropyrazine
IV. 2,3-Bis (2'-(6'-methylpyridyl))-5-methyl-5,6-dihydropyrazine.

sorptivity and hypsochromic shift of 4nm relative to the parent ligand. This increase in molar absorptivity can be explained as resulting from an increase in the electron density of the donor nitrogen atoms because of the greater tautomeric effect of a phenyl group as compared to a pyridyl group.

The wavelength of maximum absorbance in the visible region shifts towards the violet for both copper(I) and iron(II) complexes as the dihydropyrazine ring is changed to the aromatic pyrazine ring in the free ligand (Tables I & II). Bailer[9] et al have also noticed the shift in λ-max in the visible towards the violet end of the spectrum as the number of aromatic rings in the free ligand is increased. Therefore, the explanation of the present phenomenon may be based on the concept of crossed resonance suggested by Bailer et al[9]. The increase in the number of aromatic rings leads to a condition of greater cross resonance which facilitates back-coordination and a shift of the absorption towards the violet.

Another significant observation in the present work is the decrease in molar absorptivity of iron(II) and copper(I) complexes when the free pyridyl-substituted dihydropyrazine ligands are dehydrogenated to pyridyl-substituted pyrazine ligands. It is generally known that the basicity of the chelate ligand determines the molar absorptivity of the complex. It is also known that quinoline is weaker in base strength than is pyridine because of the decrease in negative charge caused by the extended conjugated double bonds of the benzene ring to nitrogen atom. It may be that the donor nitrogen atoms in the pyrazine ring are less basic

Table 1: Quantitative absorptiometric data for copper(I) and iron(II) complexes of pyrazine ligands

	Reagent	Solvent	Copper (I) complex λ-max nm	ε-1. mole cm^{-1}	Chromoph-ore stability	Iron (II) complex λ-max nm	ε-1. $mole^{-1}$ cm^{-1}	Chromophore stability
VIII	2-phenyl-3-(2'-py-ridyl) pyrazine	1,2-dichl-oroethane over anhye Na2SC4	455	$5.6x10^3$	30 min	528	$1.07x10^4$	5 days
IX	2,3-Bis (2'-pyridyl)-pyrazine	1,2-dichl-oroethane	454	$5.1x10^3$	30 min	532	$1x10^4$	24 hr
X	2,3-Bis [2'-(6'-methyl pyridyl)] pyrazine	Ethanol 1,2-dichl-oroethane	465 465	$7.1x10^3$ $6.6x10^3$	1 hr 3 hr	- -	- -	- -
XI	2,3 Bis(2'-pyridyl)-5-methylpyrazine	1,2-dichl-oroethane	459	$6.3x10^3$	1 hr	522	$9.8x10^3$	2 days
XII	2,3-Bis [2'-(6'-methyl-pyridyl)]-5-methyl-pyrazine	Water 1.2-dichl-oroethane	473 461	$7.5x10^3$ $7.3x10^3$	1 hr 16 hrs	-	-	-
XIII	2.3-Bis (2'-pyridyl)-5.6-dimethylpyrazine	Ethanol 1,2-dichl-oroethane	450 450	$6.4x10^3$ $6.4x10^4$	6 hrs 2 days	- -	- -	- -
XIV	2,3-Bis [2'-(6'.methyl-pyridyl)]-5.6-dimethyl--pyrazine.	Ethanol 1,2-dichl-oroethane	455 453	$7.2x10^3$ $7.1x10^3$	24 hrs 4 days	- -	- -	- -

than the corresponding nitrogens in the dihydropyrazine ring. The former contains a conjugated double bond system extended to nitrogen atoms in the pyrazine ring, but the latter does not. This may be responsible for the decrease in the molar absorptivity, but the data for the basicities of the donor nitrogen atoms in the ligands under investigation are not available to support the claim.

Lastly it is significant during these studies that there is an increase in chromophoric stability when the dihydropyrazine ligand is dehydrogenated to the pyrazine ligand. The iron(II) complex of VIII in 1,2-dichloroethane as its perchlorate ion-association complex, when stored over anhydrous sodium sulphate does not show any decrease in absorbance upto 4 days, whereas the corresponding iron(II) perchlorate complex of VII is stable for only a few minutes in the same solvent system. This observation is also in line with the observation of previous workers, which emphasises that the stability of the metal chelate is enhanced by resonance energy contribution if the methine chromophoric group is incorporated in an aromatic ring system.

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