Regio-isomerism in tetradentate Schiff bases and their copper(II) complexes

A. M. Maitra*
CSIRO, Division of Coal Technology, P. O. Box 136, North Ryde, NSW 2113 (Australia)

S. Dilli
School of Chemistry, University of New South Wales, P.O. Box 1, Kensington, NSW 2033 (Australia)

and **E. Patsalides**
School of Chemistry, University of Sydney, Sydney, NSW 2006 (Australia)

(Received July 16, 1990)

Abstract

Tetradentate Schiff bases obtained from the condensation of hexane-2,4-dione or heptane-2,4-dione with 1,2-diaminoethane have been found to consist of mixtures of three regio-isomers. Procedures for the separation of isomeric ligands and the properties of the pure isomeric ligands and copper(II) complexes are reported for the first time. The constitutional structure of each isomer has been determined from ^{1}H NMR and electron-impact mass spectral data. For the corresponding ligands derived from 1,2-diaminopropane, in which four regio-isomers are possible, only two pure isomeric forms were isolated in each case. The third and fourth isomers were obtained as a 1:1 mixture but could not be resolved chromatographically. Spectroscopic data and structures for these ligands and their copper(II) complexes are also reported.

Introduction

Schiff bases formed in condensation reactions between unsymmetrical β-diketones and 1,2-diaminoethane can, in principle, exist in three isomeric forms [1]. However, in the literature such condensation reactions have been depicted as occurring exclusively at the more electrophilic or less sterically hindered carbonyl group of the β-diketone molecule. Thus, benzoylacetone [2], isobutyrylacetone [3], pivaloylacetone [4] and trifluoroacetylacetone [5] apparently all condense with 1,2-diaminoethane at the carbonyl group adjacent to the methyl substituent rather than at the carbonyl adjacent to a phenyl, isobutyl, t-butyl or trifluoromethyl substituent, respectively. The result is that only one of three possible isomers is formed. In these cases it appears that kinetic control in the condensation reaction is responsible for the formation of only one isomer [6, 7]. To date, the isolation of regio-isomers for this class of ligands has been confined to those obtained between pivaloyltrifluoroacetone and 1,2-diaminoethane [1, 7]. However, in the latter case only two of three possible isomers have been found, with the major product of the reaction being a dihydrodiazepin.

As a continuation of the study of isomerism in this class of ligands [8, 9] we have extended our studies to reactions of 1,2-diamines with unsymmetrical β-diketones containing similar n-alkyl substituents (Me, Et and n-Pr). Isomeric Schiff bases I–VII derived from the condensation of hexane-2,4-dione or heptane-2,4-dione with 1,2-diaminoethane or 1,2-diaminopropane are reported as well as the corresponding copper(II) complexes. Detailed ^{1}H NMR and mass spectral analyses are presented in support of the proposed structures (Fig. 1).

Experimental

Synthesis and separation of the isomeric ligands

Hexane-2,4-dione and heptane-2,4-dione were prepared by a Claisen condensation of acetone with ethyl n-propionate and ethyl n-butyrate, respectively, utilizing lithium hydride as condensing agent. The

*Author to whom correspondence should be addressed.

0020-1693/91/$3.50

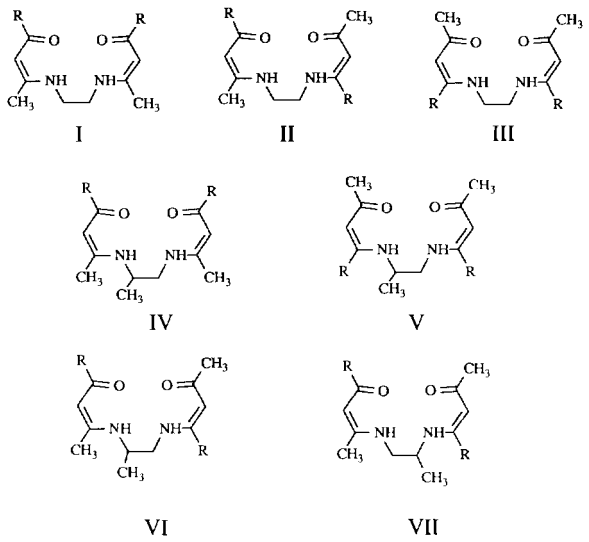


Fig. 1. Regio-isomers (**I–III**) of Schiff base ligands derived from 1,2-diaminoethane, corresponding to isomers **1**, **2** and **3**, respectively, and regio-isomers (**IV–VII**) derived from 1,2-diaminopropane, corresponding to isomers **1**, **3**, **2a** and **2b**, respectively. R is either Et or n-Pr.

pure β-diketones were obtained by vacuum fractional distillation following the preparation and acid decomposition of the copper(II) complexes [10].

The isomeric Schiff bases were prepared as mixtures in yields of 60–80% by the addition of 0.050 mol of 1,2-diaminoethane or 1,2-diaminopropane (approx. 20% vol./vol. in ethanol) to an ethanolic solution of β-diketone (0.20 mol) followed by heating on a steam bath for 30–60 min. The cooled reaction mixture was diluted with water, extracted with chloroform and the extract dried over anhydrous sodium sulfate. Solvent and excess β-diketone were removed on a rotary evaporator. The copper(II) complexes were synthesized from the crude solid or liquid ligands and separated on a silica gel column (see below). Individual isomeric ligands were recovered from the corresponding complexes by bubbling hydrogen sulfide into an approximately 10% solution of complex in ether. Bubbling was continued until the originally deep violet solution became colorless (approx. 5–10 min). The precipitated copper sulfide was removed by filtration with the aid of activated charcoal and ether removed under vacuum. The recovered ligand was then purified by one of three procedures (a) eluting through a short column of silica gel with 5–10% ethyl acetate in benzene, (b) recrystallization from hexane or (c) vacuum sublimation at 50–58 °C/0.05 torr. Data for the purified isomeric ligands are summarized in Table 1. Names, abbreviations and structures are as follows (refer to Fig. 1 for structures **I–VII**).

5,10-Dimethyl-6,9-diazatetradeca-4,10-diene-3,12-dione, H_2hed(1) (**I**, R = Et); 4-ethyl-9-methyl-5,8-diazatrideca-3,9-diene-2,11-dione, H_2hed(2) (**II**, R = Et); 4,9-diethyl-5,8-diazadodeca-3,9-diene-2,11-dione, H_2hed(3) (**III**, R = Et); 5,7,10-trimethyl-6,9-diazatetradeca-4,10-diene-3,12-dione, H_2hpd(1) (**IV**, R = Et); 4-ethyl-6,9-dimethyl-5,8-diazatrideca-3,9-diene-2,11-dione, H_2hpd(2a) (**VI**, R = Et); 4-ethyl-7,9-dimethyl-5,8-diazatrideca-3,9-diene-2,11-dione, H_2hpd(2b) (**VII**, R = Et); 4,9-diethyl-6-methyl-5,8-diazadodeca-3,9-diene-2,11-dione, H_2hpd(3) (**V**, R = Et); 6,11-dimethyl-7,10-diazahexadeca-5,11-diene-4,13-dione, H_2sed(1) (**I**, R = n-Pr); 4-n-propyl-9-methyl-5,8-diazatetradeca-3,9-diene-2,11-dione, H_2sed(2) (**II**, R = n-Pr); 4,9-di-n-propyl-5,8-diazadodeca-3,9-diene-2,11-dione, H_2sed(3) (**III**, R = n-Pr); 6,8,11-trimethyl-7,10-diazahexadeca-5,11-diene-4,13-dione, H_2spd(1) (**IV**, R = n-Pr); 4-n-propyl-6,9-dimethyl-5,8-diazatetradeca-3,9-diene-2,11-dione, H_2spd(2a) (**VI**, R = n-Pr); 4-n-propyl-7,9-dimethyl-5,8-diazatetradeca-3,9-diene-2,11-dione, H_2spd (2b) (*VII*, R = n-Pr); 4,9-D-n-propyl-6,-methyl-5,8-diazadodeca-3,9-diene-2,11-dione, H_2spd(3) (**V**, R = n-Pr).

Synthesis and separation of the isomeric copper(II) complexes

The appropriate crude ligand (0.070 mol) in ethanol (80 ml) was stirred with copper(II) acetate monohydrate (14 g, 0.09 mol) in a similar volume of aqueous ethanol made strongly alkaline by the addition of concentrated ammonia (10 ml). The mixture was heated on a steam bath for 20 min. On cooling, the solution was diluted with water (50 ml), extracted with dichloromethane and the extract dried over anhydrous sodium sulfate then solvent removed on a rotary evaporator. The residue of isomeric complexes (obtained in ~80% yield based on crude ligand) was dissolved in a small volume of dichloromethane and the isomers separated by slow elution from a silica gel (TLC grade) column (30 cm × 7 cm ID) with 0–10% vol./vol. ethyl acetate in benzene. For each crude chelate, three distinct violet bands were separated. Isomer **1** was always obtained as a discrete band requiring no further column purification. Isomers **2** and **3** were separated from a second column (20 cm × 5 cm ID) under conditions similar to those described above. Isomer **2** was often contaminated with the corresponding β-diketonate and this necessitated additional column clean-up. Fractions which gave single spots on silica gel TLC plates were evaporated under vacuum to give the pure chelates. Data for the complexes are given in Table 2. Note that the designation of isomers (**1**, **2**, **3**) in Fig. 1 is based on the relative order of elution of

TABLE 1. Characterization of the purified isomeric tetradentate Schiff bases. Refer to 'Experimental' for GC column and conditions

Ligand	Melting point (°C)	Analyses calc. (found) (%)			Molecular ion (*m/z*)[e]	GC retention (min)
		C	H	N		
H_2hed(1)	84–85	66.7 (66.1)	9.5 (9.7)	11.1 (10.9)	252	13.3
H_2hed(2)	64–66	66.7 (66.3)	9.5 (9.6)	11.1 (11.1)	252	12.9
H_2hed(3)	[d]	66.7 (66.4)	9.5 (9.3)	11.1 (10.8)	252	12.0
H_2hpd(1)[b]	~50	67.7 (66.8)	9.8 (10.0)	10.5 (10.1)	266	10.9
H_2hpd(2)[a]	[c]	67.7 (66.5)	9.8 (9.6)	10.5 (10.0)	266	10.5
H_2hpd(3)	[c]	67.7 (66.9)	9.8 (9.8)	10.5 (9.5)	266	9.9
H_2sed(1)	72–74	68.6 (69.4)	10.0 (10.3)	10.0 (10.1)	280	23.8
H_2sed(2)	35–36	68.6 (68.7)	10.0 (10.3)	10.0 (9.8)	280	21.3
H_2sed(3)	90–96	68.6 (69.0)	10.0 (10.4)	10.0 (9.8)	280	18.6
H_2spd(1)	[c]	69.4 (68.6)	10.2 (10.3)	9.5 (9.0)	294	19.7
H_2spd(2)[a]	[c]	69.4 (68.5)	10.2 (10.4)	9.5 (9.0)	294	17.1
H_2spd(3)[f]	[c]				294	15.0

[a]Consists of a mixture of isomers **2a** and **2b** (see Fig. 1). [b]Yellowish liquid, solidified after several weeks in a vacuum desiccator. [c]Yellowish brown oil. [d]Not recorded. [e]Molecular ion was only 2–10% of most intense ion. [f]Insufficient quantity for elemental analysis, however GC and ^{1}H NMR indicated a single chemical species.

TABLE 2. Characterization of the purified isomeric copper(II) complexes

Copper(II)[a] complex of	Melting point (°C)	Analyses: calc. (found) (%)			Molecular ion[c] (*m/z*)	GC retention (min)
		C	H	N		
H_2hed(1)	95–97	53.6 (53.2)	7.1 (7.1)	8.9 (8.5)	313, 315	26.5
H_2hed(2)	63–65	53.6 (53.4)	7.1 (6.9)	8.9 (8.8)	313, 315	28.2
H_2hed(3)	100–101	53.6 (53.3)	7.1 (7.0)	8.9 (8.3)	313, 315	30.4
H_2hpd(1)	80–82	55.0 (54.7)	7.3 (7.6)	8.6 (8.5)	327, 329	20.7
H_2hpd(2)	[b]	55.0 (54.5)	7.3 (7.6)	8.6 (8.4)	327, 329	22.6
H_2hpd(3)	74–77	55.0 (55.4)	7.3 (7.5)	8.6 (8.6)	327, 329	24.9
H_2sed(1)	119–120	56.3 (55.9)	7.6 (7.7)	8.2 (8.1)	341, 343	43.8
H_2sed(2)	112	56.3 (56.2)	7.6 (7.6)	8.2 (7.7)	341, 343	48.7
H_2sed(3)	89–92	56.3 (56.8)	7.6 (7.9)	8.2 (7.8)	341, 343	55.1
H_2spd(1)	[b]	57.5 (57.6)	7.9 (8.1)	7.9 (7.8)	355, 357	31.3
H_2spd(2)	[b]	57.5 (57.9)	7.9 (8.1)	7.9 (7.9)	355, 357	35.2
H_2spd(3)	[b]	57.5 (57.0)	7.9 (7.9)	7.9 (7.6)	355, 357	40.9

[a]Deep violet solids or tars. [b]Liquid. [c]Molecular ions corresponding to Cu^{63} and Cu^{65} isotopes, respectively, in approx. 2:1 ratio.

the corresponding copper(II) complexes from the silica gel column. Thus H_2hed(1) corresponds to Cuhed(1), H_2hed(2) corresponds to Cuhed(2) and so on.

Chromatography

For thin layer chromatography (TLC) examination of the isomeric ligands or complexes, silica gel (Merck, Kieselgel G) layers (20 cm×10 cm×0.5 mm) were prepared and air-dried for several days before use Development utilized 0–10% vol./vol. ethyl acetate in benzene. No visualizing reagent was necessary for the complexes as these were intensely coloured, however, ligands were visualized by exposure to iodine vapor or by spraying with 0.5% aqueous copper(II) acetate and heating in the oven at 80 °C for 5 min.

Gas chromatography (GC) data were obtained utilizing a Packard Becker model 417 gas chromatograph equipped with a flame ionization detector. Ligands and complexes were prepared as approximately 1% wt./vol. solutions in dichloromethane and 1 μl of solution (corresponding to 10 μg of compound) injected onto the column. The chromatographic column (1.2 m×4 mm ID) was of borosilicate glass and was packed with 5% wt./wt. SE 30 on Chromosorb

W (80/100 mesh). Isothermal column conditions were used with a column temperature of 190 °C for the ligands (or as described in the text) and 200 °C for the complexes. The injector and detector temperatures were both 230 °C. Nitrogen was utilized as carrier gas and was maintained at a flow rate of 35 ml min^{-1}.

Other instrumentation

Elemental analyses for carbon, hydrogen and nitrogen were performed by Dr H.P. Pham of the University of New South Wales microanalytical service. Proton NMR spectra were obtained in deuterochloroform or hexadeuterobenzene as approximately 20% wt./vol. solutions and the chemical shifts measured relative to tetramethylsilane on the δ scale at 25 °C. The spectra were recorded on a JEOL JNM FX-100 FT spectrometer equipped with a Digital Quadrature Detection system and 5 mm proton probe. For the data summarized in Tables 4–7 the following abbreviations are used; d = doublet, t = triplet, q = quartet, s = sextet, m = complex multiplet. Coupling constants (J) are in Hertz for the frequency indicated (100 MHz). No significant shifts in the signals were observed for infinite dilution of the ligands in $CDCl_3$ or C_6D_6.

Electron impact (70 eV) mass spectra were obtained on a GEC-AEI-MS12 single focussing mass spectrometer. Compounds were introduced in borosilicate glass capillaries using a heated direct insertion probe. Operating conditions were: accelerating voltage (8 kV), electron energy (70 eV) and source pressure (10^{-6} torr).

Results and discussion

Chromatographic data

The formation of isomeric ligands in condensation reactions between hexane-2,4-dione or heptane-2,4-dione and diamines was observed on chromatographic examination (TLC, GC or column) of the crude ligands or complexes. Characterization of recrystallized product has, in the past, led to the erroneous conclusion that only one isomeric species is formed for these compounds [4]. In 'Experimental' it was indicated that three distinct bands were separated by column chromatography for crude copper(II) complexes of each ligand. Mass spectrometric and elemental analyses of the purified complexes established these to be constitutional isomers (Table 2), while TLC and GC examination of the crude products indicated the absence of other complexes, apart from the corresponding β-diketonates which sometimes occurred as contaminants. These Schiff base complexes do not readily undergo dehydrogenation/oxidation reactions typical of the corresponding nickel(II) complexes. Indeed, examination of the nickel(II) complexes which were also synthesized but not studied in detail, revealed that these consisted of numerous species comprising the isomeric Schiff base complexes as well as dehydrogenated and oxidized derivatives of each [10]. For this reason, our study of isomeric complexes was confined to the more stable copper(II) complexes. Crude ligand preparations similarly displayed isomeric species when examined by TLC or GC. Three distinct peaks I–III corresponding to isomeric species were observed by GC in each case as illustrated in Fig. 2. In addition, peaks due to unreacted β-diketone (R), dihydrodiazepin (D) and other by-products were obtained although Schiff base ligands were the main products in each case. Peak identification was established by comparison of retention data for the crude ligands with those of the pure isomeric ligands.

The relative proportion of isomers I, II and III obtained (Fig. 2) were for H_2sed approximately 51%,

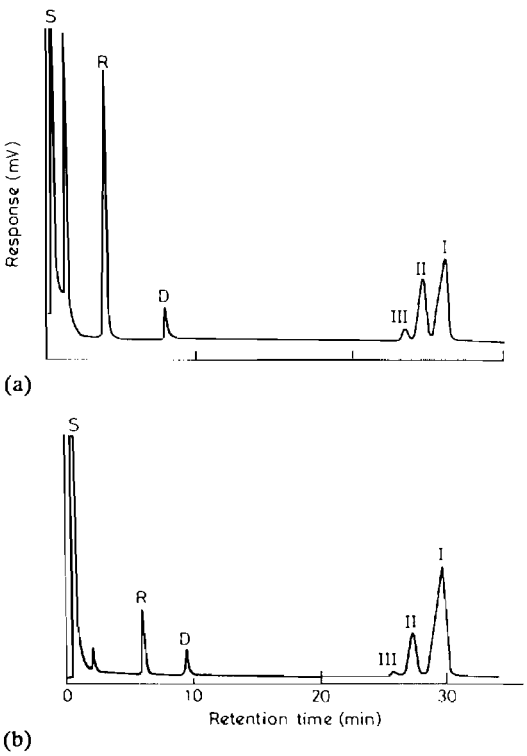


Fig. 2. Gas chromatogram showing the separation of the isomers of (a) H_2sed and (b) H_2spd in crude reaction mixtures. I, II and III correspond to isomers **1**, **2**, **2a/2b** and **3**, respectively, in each case. R represents unreacted β-diketone and D the corresponding dihydrodiazepin. Refer to 'Experimental' for column description. Column temperature: 70 °C (hold 5 min), scan 10 °C/min to 200 °C (hold 20 min).

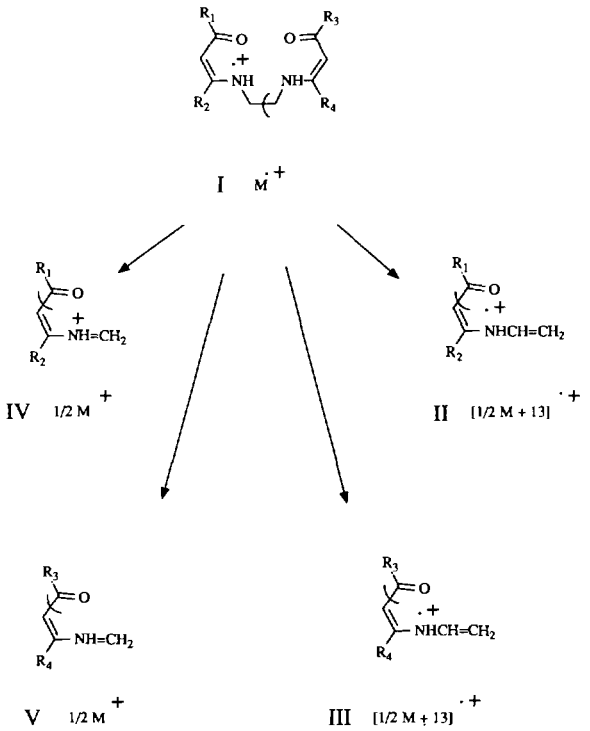
40% and 9%, respectively, with other ligands giving similar ratios. This compares to calculated ratios of 25%, 50% and 25%, respectively, assuming a random condensation of diamine and β-diketone. Thus, in this reaction a significant preference is shown for condensation at carbonyl groups adjacent to a methyl substituent rather than an ethyl or n-propyl substituent. It is, therefore, understandable why in β-diketones containing i-Pr, t-Bu, CF_3 or C_6H_5 substituent on one side and CH_3 on the other, only one isomeric species is formed. In such cases, the synthesis of more than one isomeric species may require the use of different reaction conditions (e.g. elevated temperatures) or a different synthetic route.

Retention data for the isomeric ligands and complexes on packed GC columns are given in Tables 1 and 2. In the chromatographic separations (GC, TLC and column) carried out, no evidence for more than three isomers in H_2hpd or H_2spd, nor for the corresponding copper(II) complexes was ever found. This is not surprising in view of the close similarity of isomers **2a** and **2b** (see Fig. 1) and is not a separation likely to be achieved other than on an open-tubular GC column of high selectivity and plate number. Indeed, for each of H_2hpd and H_2spd a total of eight isomers (four pairs of enantiomers) are formed and it should be possible to separate these on a suitable chiral column. It will be shown spectroscopically (see below) that bands II in Fig. 2(a) and (b) represent 1:1 mixtures of the **2a** and **2b** isomeric forms.

Mass spectral data

Detailed analyses of the electron impact (EI) mass spectra of the Schiff base ligands and complexes are given in ref. 10 and only data of direct relevance to structural analysis will be examined. Furthermore, the mass spectra of the copper(II) complexes will be omitted as these are less useful for structure analysis.

General features of the EI mass spectra of the Schiff base ligands include the primary fragment ions $\frac{1}{2}M^+$, $[\frac{1}{2}M+13]^{\cdot+}$ and daughter ions of these species (Scheme 1). Molecular ions **I** are of low relative abundance, being 10% or less of the base peak, and do not fragment directly such that structural assignments can be made (for example, loss of terminal acyl radical or ketene molecule). It is the characteristic fragmentation of daughter ions **II**–**V** shown in Scheme 1 which allows such assignments to be made. As shown, odd-electron ions **II** and **III** undergo simple fragmentation to $[\frac{1}{2}M-R_1CO]^+$ and $[\frac{1}{2}M-R_3CO]^+$ while even-electron ions **IV** and **V** undergo fragmentation/rearrangement involving loss of ketene to produce $[\frac{1}{2}M-(R_1-H)CO]^+$ and



Scheme 1. Primary daughter ions formed from the Schiff base molecular ion.

$[\frac{1}{2}M-(R_3-H)CO]^+$, respectively. In both fragmentation paths the identity of R_1 and R_3, and therefore of R_2 and R_4, can be deduced. Table 3 gives the relevant fragment ions and intensities for the H_2hed isomers and allows the constitutional structure of each isomer to be determined. For example, isomer **1** contains significant peaks at $[\frac{1}{2}M+13-CH_3CH_2CO]^+$ and $[\frac{1}{2}M-CH_3CHCO]^+$ but not at $[\frac{1}{2}M+13-CH_3CO]^+$ or $[\frac{1}{2}M-CH_2CO]^+$ which in structure **I** (Scheme 1) indicates that $R_1=R_3=CH_3CH_2$ and, therefore, that $R_2=R_4=CH_3$. Conversely, isomer **3** contains significant peaks at $[\frac{1}{2}M+13-CH_3CO]^+$ and $[\frac{1}{2}M-CH_2CO]^+$ but not at $[\frac{1}{2}M+13-CH_3CH_2CO]^+$ and $[\frac{1}{2}M-CH_3CHCO]^+$ indicating that $R_1=R_3=CH_3$ and $R_2=R_4=CH_3CH_2$. Isomer **2** must, therefore, have the constitutional structure in which $R_1=R_4=CH_3$ and $R_2=R_3=CH_3CH_2$. Indeed, the data in Table 3 is consistent with these conclusions.

Acyl ions RCO^+ in the mass spectra can also indicate ligand constitutional structure. For example, a fragment ion $CH_3CH_2CO^+$ was identified in the spectrum of isomer **1**, and CH_3CO^+ for that of isomer **3**, while both fragments, as expected, were identified for isomer **2**. Although such acyl ions can be formed directly from the molecular ion they may also form from the fragmentation of odd-electron ions such as $[\frac{1}{2}M+13]^+$ (which still bear structural

TABLE 3. Significant fragment ions for determining the constitutional structure of the isomers of H_2hed. Detailed mass spectral data are given in ref. 10

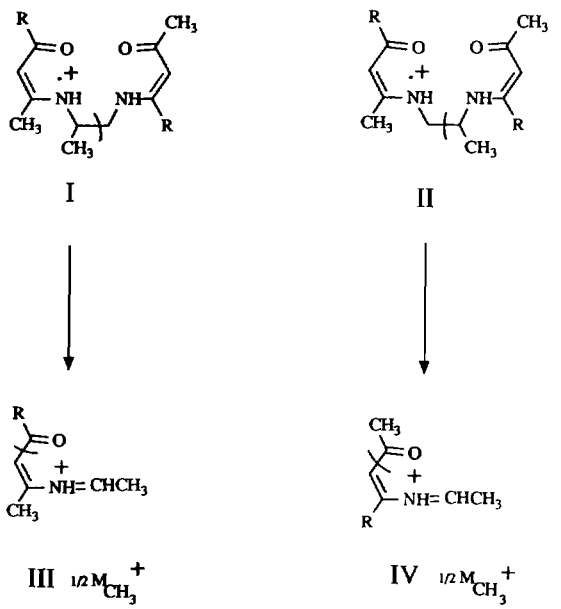
Ion	*m/z* (relative abundance (%)		
	H_2hed(1)[a]	H_2hed(2)	H_2hed(3)
$M^{\cdot+}$	252 (10)	252 (8)	252 (2)
$[\frac{1}{2}M+13]^{\cdot+}$	139 (77)	139 (87)	139 (68)
$\frac{1}{2}M^+$	126 (91)	126 (100)	126 (100)
$[\frac{1}{2}M+13-CH_3CO]^+$		96[b] (19)	96 (19)
$[\frac{1}{2}M+13-CH_3CH_2CO]^+$	82[b] (21)	82[b] (16)	
$[\frac{1}{2}M-CH_3CHCO]^+$	70 (10)	70 (7)	
$[\frac{1}{2}M-CH_2CO]^+$		84[b] (15)	84 (15)
$CH_3CH_2CO^+$	57 (24)	57 (13)	
CH_3CO^+		43 (35)	43 (38)

[a]Most intense ion at $m/z=98$ is assigned to $[\frac{1}{2}M-CO]^+$ or $[\frac{1}{2}M+H-R]^+$ ion. [b]Indicates that a metastable ion for the transition from the parent ion was observed.

information), as well as other ions which may not bear such information. The identification of acyl fragments thus serves as a quick but less reliable method of establishing isomer structure.

Similar analyses for the isomers of H_2sed indicated that for H_2sed(1) $R_1=R_3=$ n-Pr with $R_2=R_4=CH_3$; for H_2sed(2) $R_1=R_4=$ n-Pr with $R_2=R_3=CH_3$ and for H_2sed(3) $R_1=R_3=CH_3$ with $R_2=R_4=$ n-Pr as indicated in Fig. 1.

For H_2hpd and H_2spd, the major fragments and most intense ions in the spectra were the even electron ions $\frac{1}{2}M_{CH_3}{}^+$ formed as shown in Scheme 2. Odd electron fragments were of greatly reduced abundance (<10%). Mass spectral analyses similar to



Scheme 2. Fragmentation of isobaric $\frac{1}{2}M_{CH_3}{}^+$ ions of isomers **2a** and **2b**.

those performed for H_2hed established that for isomer **1** of each ligand the *terminal substituents* (those adjacent to the carbonyl group) were both Et or both n-Pr, respectively, while *proximal substituents* (those adjacent to the carbon bearing the imino group) were Me in both cases. Conversely, for isomer **3** of each ligand both terminal substituents are Me while, as shown in Fig. 1, the proximal substituents are Et and n-Pr in H_2hpd(3) and H_2spd(3), respectively.

H_2hpd and H_2spd contain two closely similar constitutional isomers (isomers **2a** and **2b**). It is possible to determine the structure of each isomer from differences in the fragmentation of the two isobaric fragment ions $\frac{1}{2}M_{CH_3}{}^+$ (Scheme 2). However, since the isomers were not physically separated and individual spectra obtained, the distinction was not achieved. Nonetheless, it is possible to tentatively establish that both isomeric forms are present in this fraction. Thus, the mass spectrum of H_2hpd(2) contains fragment ions assigned as $[\frac{1}{2}M_{CH_3}-CH_2CO]^+$ and $[\frac{1}{2}M_{CH_3}-CH_3CHCO]^+$ while the mass spectrum of H_2spd(2) contains fragment ions assigned as $[\frac{1}{2}M_{CH_3}-CH_2CO]^+$ and $[\frac{1}{2}M-CH_3CH_2CHCO]^+$. From the preceding analyses this suggests that both species **I** and **II** in Scheme 2 (corresponding to **VII** and **VI**, respectively, in Fig. 1) occur in Schiff base fraction 2. Although it is risky to make conclusions based on the mass spectra alone it turns out that the NMR data is entirely in agreement with these conclusions.

NMR data

A general feature of the NMR spectra of the Schiff base ligands is that, in contrast to β-diketones [11], they exist in solution exclusively as one tautomeric form [12–14]. The discussion of isomerism

presented here is, therefore, not further complicated by tautomeric equilibria. Evidence that these ligands occur in a hydrogen-bonded ketoenamine form includes (i) the acidic proton signal appears at low field near 11 ppm and shows both quadrupole broadening and splitting characteristic of an AX_2 pattern, (ii) the absence of free carbonyl group bands in the infrared spectra [15, 16], (iii) concentration-independent NMR and electronic spectra and (iv) X-ray structural data [17].

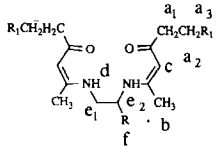
Proton NMR spectra of the isomers of H_2hed, H_2sed, H_2hpd and H_2spd, summarized in Tables 4–7 are similar to the representative ligands H_2aaed and H_2aapd included here as reference compounds (Table 4). The spectra of the isomeric species are complicated only by additional resonances and couplings due to the longer alkyl substituents, asymmetry in the molecules and, in two cases, by the presence of unresolved isomeric species. As a representative ligand of the ethylenediamine-derived Schiff bases, H_2aaed ($R = CH_3$ in structure **I**, Fig. 1) has a proton NMR spectrum in $CDCl_3$ consisting of two methyl singlets near 1.9 ppm, a singlet for the methine (CH) group near 5.0 ppm, a broadened triplet for the NH group protons near 11 ppm and a curious multiplet for the bridge CH_2 protons near 3.4 ppm. The pattern for this CH_2 signal is attributed to coupling to non-equivalent NH protons [18] as the multiplet alters to a singlet after D_2O exchange of the NH protons. The spectrum for H_2aapd ($R = CH_3$ in structure **IV**, Fig. 1), the representative model for the propylenediamine-derived ligands, is more complicated than that of H_2aaed and has been studied in some detail [19]. In $CDCl_3$ the signals for the bridge-protons of this ligand consist of two closely spaced multiplets near 3.2 and 3.7 ppm for the CH_2 and CH protons, respectively, and a doublet for the bridge CH_2. On D_2O exchange the resonances for the CH_2 and CH group protons alter to appear as doublets and sextets, respectively. A feature of the spectrum of this unsymmetrical ligand is the distinct signals for non-equivalent methine protons near 4.9 ppm. Again, the spectra of H_2hpd(1), H_2hpd(3), H_2spd(1) and H_2spd(3) are closely similar to that of H_2aapd except for additional signals and couplings.

The spectra for H_2hpd(2) and H_2spd(2) were more complicated due to the presence of (i) two distinct types of proximal and two distinct types of terminal substituents and (ii) the presence of unseparated isomers (isomers **2a** and **2b**) in each sample. Nonetheless, the signals were sufficiently resolved in most cases for assignments to be made (see Table 6).

We now examine how aromatic solvent induced shifts can be utilized to make structural assignments. A feature of the proton NMR spectra of Schiff base ligands is the characteristic aromatic solvent induced shifts (Δ) observed in hexadeuterobenzene and other aromatic solvents [7, 8, 12]. This shift is defined as $\Delta = \delta_S - \delta_B$ where δ_S is the chemical shift in an 'inert' solvent such as tetrachloromethane and δ_B is the corresponding shift in the aromatic solvent, typically hexadeuterobenzene. Aromatic solvent induced shifts can generally be represented by the summation of at least five solvent screening terms [20, 21]. However, when chemical shifts are measured relative to an inert internal standard such as tetramethylsilane only one term (σ_C) contributes significantly to the aromatic solvent induced shift Δ so that $\Delta \cong \sigma_C$. Aromatic solvent induced shifts are due to weak complex formation between solute and solvent and have been examined and analyzed in some detail in the literature [20, 21]. The contribution of terms other than σ_c to Δ is usually less than 0.1 ppm [20]. Variations significantly larger than this (~ 1 ppm) are largely associated with σ_C. These variations are due to a combination of two effects: (i) the formation of charge-transfer complexes between aromatic solvents and polar solutes and (ii) large shielding/deshielding effects produced by aromatic solvent molecules as a result of ring currents set up in these molecules by the strong magnetic field of the NMR probe [21]. The result is a set of Δ values that can be interpreted in terms of preferred solvation in each region of the solute molecule. Furthermore, these effects are fairly predictable for dipolar solutes [22–24] with shielding usually observed for protons in the electron-deficient (positive) regions of the solute molecule and smaller deshielding effects observed in the electron-rich (negative) regions. An empirical rule which has been proposed to predict the sign of Δ values for protons about a carbonyl group is the 'carbonyl plane rule'. This rule has also been extended to stereochemical and conformational studies of carbonyl and related compounds [21].

In this paper we have used a similar empirical rule to determine the position of substituents in the Schiff base ligands. For the latter, Δ values for proton groups are indicated as differences between the chemical shifts in $CDCl_3$ and C_6D_6 (Tables 4–7). The set of Δ values obtained vary between 0 and 0.7 ppm and are consistent with the known dipolar nature of the ligands. As conjugated analogs of amides these ligands have significant resonance structures with electron delocalization from the nitrogen and ring carbon atoms to the carbonyl oxygen. Thus in the conformational structures **VIII** and **IX** (Scheme 3) shielding interactions (i)–(v) between hexadeuterobenzene and the polar solute molecules are thought to predominate over the H-bonded (deshielding) interactions (vi) and stacking (planar)

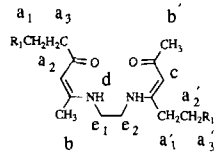
TABLE 4. ^{1}H NMR chemical shifts for H_2aaed, H_2aapd, H_2hed(1), H_2hpd(1), H_2sed(1) and H_2spd(1) in $CDCl_3$ and C_6D_6



Compound	Solvent	Proton chemical shifts (ppm)							
		a_1	a_2	a_3	b	c	d[a]	e_1e_2	f
H_2aaed ($R=CH_3$ in I of Fig. 1)	$CDCl_3$	1.98			1.90	4.98	10.86	3.42[b]	
	C_6D_6	1.97			1.44	4.80	10.99	2.56[b]	
H_2aapd ($R=CH_3$ in IV of Fig. 1)	$CDCl_3$	1.99			1.87, 1.90	4.97, 4.95	10.92	3.27, 3.73[c]	1.26d
	C_6D_6	1.97			1.52, 155	4.84, 4.82	11.10	2.60, 3.03[c]	0.71d
H_2hed(1) ($R_1=R=H$)	$CDCl_3$	2.24q ($J=7.5$)	1.07t ($J=7.5$)		1.90	4.97	10.90	3.41[b] ($J=3.1$)	
	C_6D_6	2.24q ($J=7.5$)	1.16t ($J=7.3$)		1.40	4.82	10.97	2.45[b] ($J=3.2$)	
H_2hpd(1) ($R_1=H$, $R=CH_3$)	$CDCl_3$	2.24q ($J=7.6$)	1.08t ($J=7.5$)		1.90, 1.87	4.97, 4.94	10.92	3.27[c], 3.70[c] ($J=6.5$)	1.27[d] ($J=6.4$)
	C_6D_6	2.24q ($J=7.4$)	1.16t ($J=7.6$)		1.55, 1.50	4.86, 4.84	11.10	2.55m, 2.98m	0.71d ($J=6.4$)
H_2sed(1) ($R_1=CH_3$, $R=H$)	$CDCl_3$	2.20t ($J=7.6$)	1.60s ($J=7.2$)	0.91t ($J=7.2$)	1.90	4.95	10.94	3.41[b] ($J=3.1$)	
	C_6D_6	2.24t ($J=7.4$)	1.73s ($J=7.1$)	0.93t ($J=7.2$)	1.43	4.84	11.06	2.51[b] ($J=3.2$)	
H_2spd(1) ($R_1=R=CH_3$)	$CDCl_3$	2.20t ($J=7.6$)	1.59s ($J=7.3$)	0.91t ($J=7.1$)	1.89, 1.86	4.95, 4.92	10.96	3.26[c], 3.70[c]	1.27d ($J=6.4$)
	C_6D_6	2.23t ($J=7.2$)	1.72s ($J=7.6$)	0.92t ($J=7.3$)	1.54, 1.50	4.87, 4.85	11.15	2.53m, 2.97m	0.67d ($J=6.3$)

[a]A broad signal with hyperfine splitting; disappears after D_2O exchange. [b]An inverted triplet which reverts to a singlet after D_2O exchange. [c]e_1 triplet changes to a doubet upon D_2O exchange; e_2 appears as a complex multiplet which appears as a sextet after D_2O exchange.

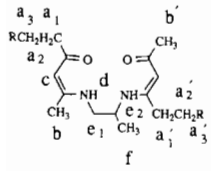
TABLE 5. ^{1}H NMR chemical shifts for H_2hed(2) and H_2sed(2) in $CDCl_3$ and C_6D_6

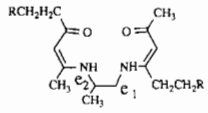


Compound	Solvent	Proton chemical shifts (ppm)						
		a_1a_1'	a_2a_2'	a_3a_3'	bb'	c	d[b]	e_1e_2[c]
H_2hed(2) (R_1=H)	$CDCl_3$	2.26q, 2.20q (J=7.5)	1.12t, 1.08t (J=7.5)		1.93, 2.02	5.01, 5.00	10.93	3.42
	C_6D_6	2.26q, 1.71q (J=7.5)(J=7.6)	1.18t, 0.79t (J=7.6)(J=7.5)		1.43, 2.01	4.89, 4.86	11.07	2.50
H_2sed(2) (R_1=CH_3)	$CDCl_3$	2.20t, 2.13t (J=7.1)	1.59s (J=7.2)	0.95t, 0.90t (J=7)(J=7.1)	1.92, 2.0	4.96	10.95	3.41
	C_6D_6	2.23t[a] (J=7.5)	1.77[a], 1.27s (J=7.2)	0.93t, 0.78t (J=7.1)(J=6.7)	1.50, 1.99	4.86	11.09	2.66

[a]Approximate values only as a_1' and a_2 signals overlap. [b]Broad signal, disappears after D_2O exchange. [c]Inverted triplet, alters to a singlet after D_2O exchange.

TABLE 6. ^{1}H NMR chemical shifts for H_2hpd(2a and 2b) and H_2spd(2a and 2b) in $CDCl_3$ and C_6D_6

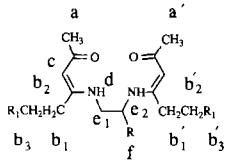




Compound[a]	Solvent	Proton chemical shifts (ppm)							
		a_1a_1'	a_2a_2'	a_3a_3'	bb′	c	d[g]	e_1e_2[h]	f
H_2hpd(2) (R=H)	$CDCl_3$	2.25q, 2.18q (J=7.5)	1.10t(J=7.5), 1.08(J=7.6)		1.92, 1.89; 2.02	4.97[c]	10.85 (J=9)	3.28, 3.71	1.28d (J=6.6)
	C_6D_6	2.26[b], 2.24[b]; 1.81[b]	1.17t, 1.16t (J=7.5); 0.86t(J=7.5), 0.83t(J=7.4)		1.57, 1.52; 2.01, 2.00	4.88[c]	11.14 (J=9)	~2.6, ~3.00	0.72d(J=6.3), 0.71(J=6.4)
H_2spd(2) (R=CH_3)	$CDCl_3$	2.19[b], 2.17[d]	1.59[e], 1.51[e]	0.94t(J=7.1), 0.9t(J=7.4)	1.87, 1.91; 2.00	4.97, 4.95, 4.94	10.98	3.27, 3.73	1.27d (J=6.7)
	C_6D_6	2.22t, ~1.8m	1.31s[d] (J=7.2)	1.00–0.70[f]	1.54, 1.58; 1.98, 1.99	4.91, 4.88, 4.87	11.19	~2.61, 3.08	1.00–0.70[f]

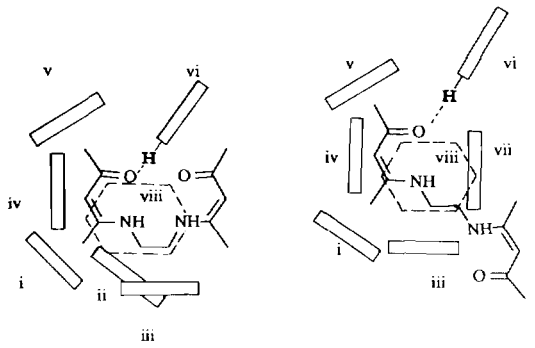
[a]Consists of a 1:1 mixture of isomers **2a** and **2b** (left and right in Table heading, respectively). [b]Two slightly non-equivalent quartets a_1 and a_1' (J=7.5). [c]Three non-equivalent singlets in $CDCl_3$ and C_6D_6. [d]Consists of two overlapping triplets. [e]Consists of two overlapping sextets. [f]Only range given. [g]Distorted triplet or quartet which disappears after D_2O exchange. [h]e_1 and e_2 have complex multiplets which appear as a doublet and sextet, respectively, after D_2O exchange.

TABLE 7. ^{1}H NMR chemical shifts for H_2hed(3), H_2hpd(3), H_2sed(3) and H_2spd(3) in $CDCl_3$ and C_6D_6



Compound	Solvent	Proton chemical shifts (ppm)							
		aa′	b_1b_1'	b_2b_2'	b_3b_3'	c	d[b]	e_1e_2[c]	f
H_2hed(3) (R_1=R=H)	$CDCl_3$	2.02	2.20q (J=6.8)	1.13t (J=7.4)		5.01	10.92	3.43	
	C_6D_6	2.02	1.65q	0.79t		4.89	11.10	2.50	
H_2hpd(3) (R_1=H, R=CH_3)	$CDCl_3$	2.02	2.19q (J=7.8)	1.12t, 1.10t (J=7.6), (J=7.5)		4.99, 4.98	10.95	3.28, 3.69	1.29d
	C_6D_6	2.02, 2.00	1.81q, 1.79q	0.86t, 0.83t (J=7.5)		4.89, 4.88	11.10	2.35–3.15	0.70d
H_2sed(3) (R_1=CH_3, R=H)	$CDCl_3$	2.01	2.15t[a] (J=7.6)	1.55s[a] (J=6.8)	0.97t (J=7.1)	5.00	10.95	3.42	
	C_6D_6	2.02	1.79t[a] (J=7.4)	1.27s[a]	0.80t (J=7.2)	4.90	11.17	2.61	
H_2spd(3) (R_1=R=CH_3)	$CDCl_3$	2.01, 2.00	2.01t, 2.08t (J=7.5)	1.50s (J=7)	0.96t (J=7)	4.96, 4.94	10.98	3.25 3.85–3.50	1.26d (J=6.3)
	C_6D_6	2.02, 2.00	~1.80t	1.30m	0.83t, 0.80t	4.87, 4.86	11.29	2.40–3.25	0.73d (J=6.5)

[a]Hyperfine splitting evident. [b]Broad singlet which disappears after D_2O exchange. The singlet is split into a distorted doublet in H_2hpd(3) and H_2spd(3). [c]In $CDCl_3$, e_1 protons appear as a triplet which alters to a doublet after D_2O exchange. The e_2 proton appears as a complex multiplet which appears like a sextet after D_2O exchange.



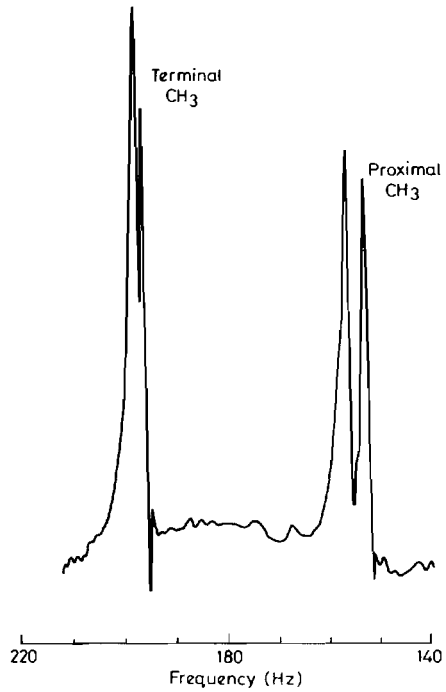
VIII IX

Scheme 3. Proposed solvent–solute interactions between a Schiff base solute molecule and benzene as solvent.

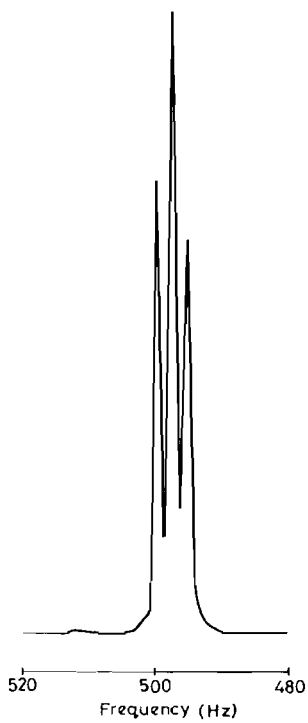
interactions (viii). The preferred interactions (i)–(v) are proposed on the basis of the Δ values observed which are +0.5 ppm for the bridge CH_2, bridge CH_3 and proximal CH_3 groups but ~zero for the terminal CH_3 group protons (Tables 4–7). The absence of a large positive Δ for the NH protons indicates that interactions (vii) and (viii) are not preferred in collision complexes. Substituents in the proximal position have Δ values of +0.5 to +0.7 ppm while those at the terminal positions are approximately zero. This has been established from data for a variety of Schiff base ligands of known structure [2–5] and can be utilized for structural/diagnostic purposes.

From the above rule, the constitutional structure of the Schiff base isomers can be determined*. As an example of the use of this method of structure determination, consider the spectrum of H_2hed(1). In the $CDCl_3$ this consists of a quartet, a triplet and a singlet at 2.27, 1.07 and 1.90 ppm, corresponding to CH_2, CH_3 (of the ethyl substituent) and the CH_3 substituent, respectively (Table 4). The corresponding resonances in C_6D_6 were 2.24, 1.16 and 1.40 ppm, respectively. Since only the methyl singlet had shifted upfield by more than 0.1 ppm in C_6D_6 it was inferred that in H_2hed(1) both methyl substituents are in the proximal positions and therefore both ethyl substituents must be in the terminal positions (i.e. R = Et in structure I). Conversely, in H_2hed(3) upfield chemical shifts of approximately 0.5 ppm occur for both the CH_3 and CH_2 groups of the ethyl substituent, while those for the methyl substituents were close to zero. This indicates that in this isomer both the ethyl substituents are in the proximal position and both methyl substituents are in the terminal positions.

*An alternative procedure utilizing lanthanide shift reagents [25] gives much larger shifts but the use of aromatic solvent induced shifts is more general and convenient and avoids the use of water-sensitive reagents.



(a)



(b)

Fig. 3. ^{1}H NMR spectrum of a mixture of H_2spd(2a) and H_2spd(2b) in C_6D_6 showing the signals for (a) the methyl group hydrogens b, b′ (four in all) and (b) the methine hydrogens. The relative intensities of the signals indicate a 1:1 ratio of isomers.

Finally, the structure of H_2hed(2) must correspond to structure **II** in Fig. 1. Indeed, Δ values obtained for this isomer (Table 5) are entirely consistent with this structure. Thus the spectrum, H_2hed(2) consists of a pair of non-equivalent signals for each of the quartets, triplets and singlets observed in isomers **1** and **3**. Only one of each pair of signals shifts significantly to higher field in C_6D_6 so only one of the methyls and only one of the ethyls occupy proximal positions, as expected. Similar analyses for H_2sed(1), H_2sed(2) and H_2sed(3) and for H_2hpd(1), H_2hpd(3), H_2spd(1) and H_2spd(3) gave the structures indicated in **I–VIII**.

The NMR spectra of H_2hpd(2) and H_2spd(2) were more complex than those of the previous isomers and could only be satisfactorily explained if it was assumed that two isomeric species were present in each case. For these fractions, four singlets corresponding to protons b, b′ (see Table 6) were observed only two of which moved upfield in C_6D_6. In fact, it is only in the latter solvent that four distinct signals for the methyl substituents b, b′ are clearly seen (Fig. 3(a)). Similar trends were seen with resonances a_1, a_1', a_2, a_2' and c although here the juxtaposition of slightly non-equivalent multiplets complicated the interpretation (see Fig. 3(b)). Proton counts for the clearly separated peaks of H_2hpd(2) and H_2spd(2) in Fig. 3 indicated that a mixture of the isomeric pairs H_2hpd(2a)/H_2hpd(2b) and H_2spd(2a)/H_2spd(2b) were present in a 1:1 ratio.

Finally, it can be stated that the structures proposed here are entirely consistent with those assigned previously form the mass spectra.

Conclusions

Regio-isomeric Schiff base ligands are formed in condensation reactions between hexane-2,4-dione or heptane-2,4-dione with 1,2-diamines, the number of such isomers being three or four depending on the symmetry of the diamine involved. The structure of the separated isomers can be determined by mass spectrometry or by ^{1}H NMR employing aromatic solvent induced shifts. The proportion of isomers formed appears sensitive to the steric effects of β-diketone substituents with condensation greatly favoured at carbonyl groups adjacent to a methyl substituent rather than an ethyl or n-propyl substituent.

References

1 S. Dilli and E. Patsalides, *J. Chromatogr., 134* (1977) 477.
2 S. H. H. Chaston, S. E. Livingstone, T. N. Lockyer and J. S. Shannon, *Aust. J. Chem., 18* (1965) 1539.
3 S. Dilli and E. Patsalides, *Aust. J. Chem., 34* (1981) 1579.
4 L. F. Lindoy, W. E. Moody and D. Taylor, *Inorg. Chem., 16* (1972) 1962.
5 S. E. Livingstone and J. H. Mayfield, *Aust. J. Chem., 28* (1975) 1517.
6 E. Patsalides, *Diss. Abstr. Int., B, 42* (1981) 1449.
7 S. Dilli and E. Patsalides, *Aust. J. Chem., 31* (1978) 765.
8 S. Dilli and A. M. Maitra, *J. Chromatogr., 358* (1986) 337.
9 S. Dilli, A. M. Maitra and E. Patsalides, *J. Chromatogr., 358* (1986) 359.
10 A. M. Maitra, *Doctoral Dissertation, Diss. Abstr. Int. B, 43* (1983) 422.
11 L. W. Reeves, *Can. J. Chem., 35* (1957) 1351.
12 G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc., 83* (1961) 2099.
13 H. J. Harris, G. Parry and J. Burgess, *J. Inorg. Nucl. Chem., 40* (1978) 194.
14 K. Ueno and A. E. Martell, *J. Phys. Chem., 61* (1957) 257.
15 H. F. Holtzclaw, J. P. Collman and R. M. Alire, *J. Am. Chem. Soc., 80* (1958) 1100.
16 K. Ueno and A. Martell, *J. Phys. Chem., 59* (1955) 998.
17 E. Larsen, S. Larsen, S. Roen and K. J. Watson, *Acta Chem. Scand., Ser. A, 30* (1976) 125.
18 E. Patsalides, unpublished data.
19 E. Larsen and K. Schaumberg, *Acta Chem. Scand., 25* (1971) 962.
20 J. Ronayne and D. H. Williams, in E. F. Mooney (ed.), *Annual Reviews of NMR Spectroscopy,* Academic Press, London, 1969.
21 L. M. Jackson and S. Sternhell, *Applications of Nuclear Magnetic Resonance in Organic Chemistry,* Pergamon, London, 1969.
22 R. J. W. LeFevre, D. V. Radford, G. L. O. Ritchie and P. J. Stiles, *J. Chem. Soc. B,* (1968) 148.
23 R. S. Armstrong, M. J. Aroney, R. K. Duffin, H. J. Stootman and R. J. W. LeFevre, *J. Chem. Soc., Perkin Trans., 2* (1973) 1272.
24 M. J. Aroney, E. Patsalides and R. K. Pierens, *Aust. J. Chem., 38* (1985) 507.
25 L. F. Lindoy and W. E. Moody, *J. Am. Chem. Soc., 97* (1975) 2275.