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Design of chiral picen-based metal complexes for molecular recognition of α-aminoacids and nucleic acids

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Contents

Abstract

Molecular design features which determine the enantio- and stereoselective behaviour of metal complexes derived from chiral linear N_4-tetradentate ligands with terminal α-pyridyl groups are described. Examples are provided of the ability of these complexes to recognise

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the molecular structures of biologically interesting molecules (α-aminoacids and nucleic acids). Noncovalent binding and steric factors which influence these molecular recognition processes are analysed and assessed. These include discriminatory interactions which occur at the *intra*ligand, *inter*ligand (*intra*molecular) and *inter*molecular levels. © 1997 Elsevier Science S.A.

Keywords: Molecular recognition; Chiral discrimination; Noncovalent binding; Molecular design; N_4-tetradentates; α-aminoacidates; Asymmetric synthesis; DNA metallointercalators

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Abbreviations

*R**-aa	generic representation of a chiral α-aminoacidate bidentate
*R**-ala	*R**-alaninate
ABMAH$_2$	2-amino-2-benzylpropandioic acid (α-amino-α-benzylmalonic acid)
ABuTMAH$_2$	2-amino-2-butylpropandioic acid (α-amino-α-(*n*-butyl)malonic acid)
AMMAH$_2$	2-amino-2-methylpropandioic acid (α-amino-α-methylmalonic acid)
APMAH$_2$	2-amino-2-propylpropandioic acid (α-amino-α-propylmalonic acid)
ARMAH$_2$	generic representation of an α-substituted-α-aminomalonic acid
bipy	2,2′-bipyridine
*R***R**-chxn	1*R**,2*R**-diaminocyclohexane
dmso	dimethylsulphoxide
dppz	dipyrido[3,2-*a*:2′,3′-*c*]phenazine
dppzMe$_2$	dipyrido[3,2-*a*:2′,3′-*c*]-7,8-dimethylphenazine
dpq	dipyrido[3,2-*d*:2′,3′-*f*] quinoxaline
dpqMe$_2$	dipyrido[3,2-*d*:2′,3′-*f*]-2,3-dimethylquinoxaline
gly	glycinate
hpm	hydroxy(2-pyridyl)methanol
S-α-Me-trp	α-methyl-*S*-tryptophanate
phdi	9,10-phenanthrenequinonediimine
*R**-phe	*R**-phenylalaninate
phen	1,10-phenanthroline
*R***R**-picbn	3*R**,4*R**-dimethyl-1,6-bis(2-pyridyl)-2,5-diazahexane
*R***R**-picchxn	*N*,*N*′-bis(2-picolyl)-1*R**,2*R**-diaminocyclohexane
*R***R**-picchxnmi	*N*,*N*′-bis(2-picolyl)-1*R**-amino-2*R**-iminocyclohexane
*R***R**-picchxnMe$_2$	*N*,*N*′-dimethyl-*N*,*N*′-bis(2-picolyl)-1*R**,2*R**-diaminocyclohexane
picen	1,6-bis(2-pyridyl)-2,5-diazahexane
picen*	generic representation of substituted homologues of picen
picenBz$_2$	2,5-dibenzyl-1,6-bis(2-pyridyl)-2,5-diazahexane
picenMe$_2$	2,5-dimethyl-1,6-bis(2-pyridyl)-2,5-diazahexane
*R**-picpn	3*R**-methyl-1,6-bis(2-pyridyl)-2,5-diazahexane
*R**-picpnMe$_2$	2,5-dimethyl-3*R**-methyl-1,6-bis(2-pyridyl)-2,5-diazahexane

R*-picpyrrMe	N,N′-bis(2-picolyl)-N′-methyl-2R*-aminomethylpyrrolidine
R*R*-picstien	3R*,4R*-diphenyl-1,6-bis(2-pyridyl)-2,5-diazahexane
R*R*-picstyen	3R*-phenyl-1,6-bis(2-pyridyl)-2,5-diazahexane
R*-pro	R*-prolinate
pro-2H	1,2-dehydroprolinate
S*R*R*S*-pychxn	N,N′-bis(2S*-pyrrolyd-2-yl)-1R*,2R*-diaminocyclohexane
tap	1,2,3-triaminopropane
tmp	3,4,7,8-tetramethyl-1,10-phenanthroline

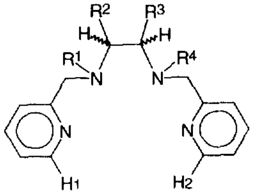
1. Introduction

Molecular recognition, defined in its broadest sense, is a discriminatory process in which a selection is made by a host molecule, through a thermodynamically preferred interaction, for one of a number of potential guest molecules. For this process to be discriminatory the different mechanisms involved in each intermolecular association must necessarily be reversible and noncovalent, thereby allowing subsequent displacement of a poorly matched guest molecule from an unfavourable host–guest complex. If the energetic preference for one guest molecule is sufficiently large then this discrimination process becomes specific and the ensuing recognition of one molecule by the other becomes unambiguous.

There are many examples of such discriminatory processes in the fields of chemistry and biology, determined by noncovalent intermolecular bonding and shape complementarity. An elegant molecular recognition process ensues when both the host and quest molecules are chiral, with the one hand of the host being able to discriminate between the enantiomeric forms of the guest. These fundamental concepts are employed by all living systems at the molecular level and are the basis for the inherent chirality of biological matter. An excellent example is the pivotal role played by DNA in orchestrating transcription and replication processes through its various molecular recognition functions.

The field of coordination chemistry provides ready application to this highly active and rapidly expanding area of scientific research. As a result, chiral metal complexes are finding potential uses ranging from that of auxiliaries in asymmetric synthesis reactions to their functioning as agents for molecular biology and pharmacology through an ability to selectively recognise, or be recognised by, naturally occurring molecules. In doing so the initial reversible molecular recognition process often may lead to subsequent irreversible covalent binding reactions involving the metal ion.

In this paper attention is paid to work undertaken in our laboratories on the abilities of chiral metal complexes containing ligands with terminal α-pyridyl groups to discriminate α-aminoacids and nucleic acids. Lead experiments involving complexes based on the common oligopyridyl bidentate ligands bipy and phen have resulted in our use of *C*- and/or *N*-substituted forms of the linear N_4-tetradentate 1,6-bis(2-pyridyl)-2,5-diazahexane, picen (**I** with R^1, R^2, R^3 and $R^4 = H$), a ligand which has been a subject for general study by coordination chemists for almost forty years. An assessment is made of design factors which influence the stereochemistries adopted by these ligands upon coordination and the use of such species for the asymmetric synthesis or optical enrichment and resolution of α-aminoacids, and of their use as components of metalloprobes of DNA conformational and base-sequence structures.



(I)

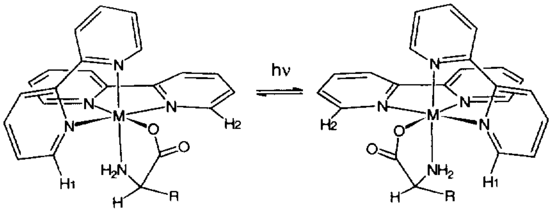
2. Intramolecular discrimination involving ligands with α-pyridyl groups

Examples of contributions made by noncovalent interligand interactions to the chiroptical properties, stereoselectivities and thermodynamic stabilities of metal complexes have been reviewed by Okawa [1]. Although coordination chemists commonly pay attention to the effects of unfavourable interligand steric interactions on the stereochemistries adopted by metal complexes, the significant favourable contributions made by electrostatics or hydrogen bonding or by interactions between hydrophobic groups on different ligands often receive less consideration. As a particular example, the influence of π-stacking interactions between aromatic rings on the stereochemistries adopted by metal complexes is often overlooked or not recognised. An evaluation of all of these possible contributions is important when considering the design features required for the molecular recognition capabilities of metal complexes or when attempting to interpret their observed discriminatory behaviour.

The thermodynamic stabilities of ternary complexes often are considerably enhanced by the occurrence of interligand π-stacking between molecular components of different ligands. Examples particularly relevant to this review are those between the purine moieties of simple nucleotide ligands and coordinated aromatic ligands [2–5], between α-aminoacidate aromatic substituents and nucleotide bases [6,7], between the aromatic substituents of two different α-aminoacidate ligands on a metal ion [6], and between aromatic α-aminoacidate substituents and aromatic components of other ligands [8–13]. Further, the propensity for such interactions to occur between pairs of complex ions containing coordinated phen ligands alone also has been demonstrated. The self-association of $[M(phen)_3]^{2+}$ cations (M = divalent Ru or Zn) has been identified from ^1H NMR studies [14,15]. In aqueous media these species give rise to NMR spectra which are significantly concentration dependent and display features consistent with π-stacking interactions between the cations to form dimers. In the case of the Ru(II) complexes an intermolecular chiral recognition process is apparent in which the associative mechanism is enantioselective, with shape complementarity occurring only between racemic pairs [15].

2.1. Chiral discrimination in [Ru(diimine)$_2$(R^*-aa)]$^+$ complexes

Our foundation work on a set of bivalent ruthenium complex cations of general form Δ,Λ-[Ru(diimine)$_2$(R^*-aa)]$^+$ (where diimine represents the oligopyridyl bidentates bipy or phen or their substituted homologues) provided evidence for the use of α-pyridyl groups as ligand components for intramolecular chiral discrimination purposes. These diastereoisomeric cations may be resolved using chromatographic methods. However, their photolability at the metal ion centres results in isomeric equilibrations which reflect the chiral discriminatory energy difference within each diastereoisomeric pair [16–22]. The steric bulk of the α-carbon aminoacid substituents was observed to play a significant role in determining the position of each equilibrium upon visible light irradiation. In general, a significant Λ preference is observed in equilibrated solutions of bulky *S*-aminoacidate complexes, ascribed to the existence of a primary repulsive interligand steric interaction involving an α-pyridyl proton of one diimine ligand (represented as H1 in **II**) and the aminoacidate α-substituent (R in **II**) in the less-favoured Δ propeller [16,19,20,23]. The consequent higher steric strain in this diastereoisomer therefore is able to be relieved by inversion of absolute configuration at the metal centre upon irradiation to give predominantly the Λ complex at equilibrium.



Λ-(*S*-aa) Δ-(*S*-aa)

(II)

The steric nature of this discrimination process was exploited to provide a means for the kinetically controlled stereospecific synthesis of some Co(III) analogues [24,25]. Additional alkyl or aryl substitution on the α-carbon atom [23] or on the α-aminoacidate N atom [22,26] was shown to enhance the overall steric contribution to the determination of the position of these intramolecular equilibrations. However, changes in the nature of the *S*-aminoacidate ligands demonstrate that unfavourable steric interactions are only one form of determinant of the diatereoisomeric balance existing after photoequilibration is achieved. Diastereoisomers with *S*-aminoacidates containing α-substituent groups capable of intramolecular hydrogen bonding commonly show a thermodynamic preference for the Δ complex cation [17,18,20,21], and the relative thermodynamic stabilities of such pairs also may be affected by changes in pH and the nature of the solvent [18,20,21]. It is clear that the simple achievement of a better steric fit is basic to each of the diastereoisomeric systems that these complexes represent, but intramolecular hydrogen bonding and hydrophobic interactions nonetheless may be predominant factors.

These diastereoisomeric equilibration processes represent an example of intramolecular recognition, occurring because of interligand discriminatory interactions, with the metal–bisdiimine and α-aminoacidate moieties playing host–guest roles. The photolability of these diastereoisomeric systems has allowed a unique opportunity to quantify and compare the thermodynamic contributions made by the different determinants of this type of discriminatory recognition process [16,17,19,22]. Moreover, the identification of the nature of these individual discriminatory factors allows them to be incorporated into other complex cations with similar structural features which may be designed for molecular recognition purposes. For example, the sterically-based discriminatory effect resulting from the disposition of the two pyridyl groups in these $[M(diimine)_2(R^*\text{-aa})]^{n+}$ species could similarly be achieved if their two diimine bidentate ligands were to be replaced by a single tetradentate ligand containing equivalent α-pyridyl groups. For this reason tetradentates based on substituted forms of picen have been selected for study and ternary complexes of general form $[M(picen^*)(R^*\text{-aa})]^{n+}$ have been synthesised. Our investigations on these compounds are described in more detail in Section 3 below. Similar discriminatory principles allow complexes of this type to be designed as metalloprobes of nucleic acid structures. This aspect of our investigations is elaborated upon in Section 4.

2.2. *Stereochemical aspects of picen-based tetradentates*

Complexes derived from picen* tetradentates have a number of potential advantages over bisdiimine-based compounds when used for discriminatory purposes. One important advantage is that an appropriate choice of optically active precursor allows such a tetradentate ligand to be readily constructed in a chiral form, thereby facilitating the study of enantioselectivity in its coordination behaviour. Through synthetic design, steric bulk and rigidity also may be incorporated intentionally into such a tetradentate so as to enhance its selectivity functions. Complexes of these ligands also would not allow the relief of steric strain achieved through optical inversion which is available to the photolabile bisdiimine compounds, thereby enhancing their enantiodiscriminatory abilities.

Additional advantages derive from the increased geometric selection allowed for study by the different stereoisomeric products which are possible when a linear tetradentate binds to an octahedral metal ion. These are the *trans* (planar), the dissymmetric (C_2) *cis*-α and the asymmetric (C_1) *cis*-β isomeric forms [27]. Moreover, if the remaining two coordination sites on the metal ion in a *cis*-β complex are occupied by two different monodentates, or by an unsymmetrical bidentate, then those sites are diastereotopic and it becomes necessary to distinguish further between the possible *cis*-β_1 or *cis*-β_2 forms [1,27]. If the tetradentate is unsymmetrical then *cis*-α_1 or *cis*-α_2 forms also are possible [28,29]. Further, the asymmetry of each of the individual *cis* forms of these complexes provides a foundation for control of metal ion absolute configuration and consequent enantioselective recognition abilities of complexes derived from these ligands.

The intramolecular parameters which determine the choice between these geometries have been comprehensively studied. Asperger and Liu [30–32], Bosnich *et al.* [33–35] and Brubaker *et al.* [36–38] have investigated and reported on the effects of *C*-substitution on the basic framework of picen. In particular, various defined forms of inherent intramolecular steric and torsional strain were identified and analysed in an extensive experimental study [39]. The existence of an important unfavourable intramolecular steric interaction between the α-protons of the terminal pyridyl groups (H1 and H2 in **I**) in *trans* complexes, defined as B-strain [39], was identified as the reason for the dominant preference for *cis* geometries observed with these ligands on octahedral metal ions. These same protons remain important when considering likely interligand and intermolecular steric interactions which could influence molecular recognition functions (*vide infra*).

2.3. *Synthetic aspects of picen-based metal complex precursors*

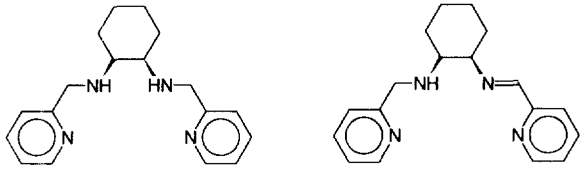
The synthesis of the archetypal ligand picen (**I** with R^1, R^2, R^3, $R^4 = H$) was first described by Goodwin and Lions [40], following reduction of the Schiff's base diimine formed between 1,2-diaminoethane and pyridine-2-carboxaldehyde. Modified forms of this general method have been utilised successfully with a selection of diamines to produce a broad set of substituted homologues, as summarised in Table 1.

The simplest *C*-substituted derivative is the chiral ligand *R**-picpn (**I** with $R^2 = CH_3$), which may be obtained in either enantiomeric form depending upon the choice of optically resolved 1,2-diaminopropane precursor [41–43]. A phenyl-substituted analogue, *R**-picstyen (**I** with $R^2 = C_6H_5$), also has been synthesised [44]. Selection of various 1,2-disubstituted diamines as precursors has provided for a set of tetradentates which may be obtained in enantiomeric or *meso* forms, depending on the nature and chosen configurations of the central *vicinal* substituent groups

Table 1
Picen-type N_4-tetradentate ligands synthesised

Ligand	Substituent group R^n of (**I**), *n* =				Ref.
	1	2	3	4	
Picen	H	H	H	H	[62]
PicenMe$_2$	CH_3	H	H	CH_3	[44]
PicenBz$_2$	$CH_2C_6H_5$	H	H	$CH_2C_6H_5$	[63]
*R**-picpn	H	CH_3	H	H	[41–43]
*R**-picpnMe$_2$	CH_3	CH_3	H	CH_3	[28]
*R***R**-picbn	H	CH_3	CH_3	H	[55]
*R***S**-picbn	H	CH_3	CH_3	H	[50]
*R***R**-picstien	H	C_6H_5	C_6H_5	H	[51]
*R***S**-picstien	H	C_6H_5	C_6H_5	H	[50]
*R**-picstyen	H	C_6H_5	H	H	[44]
*R***R**-picchxn	H	$-CH_2CH_2CH_2CH_2-$		H	[46]
*R***R**-picchxnMe$_2$	CH_3	$-CH_2CH_2CH_2CH_2-$		CH_3	[47]
*R**-picpyrrMe	$-CH_2CH_2CH_2$		H	CH_3	[29]

(**I**, R^2 and R^3). The facile optical resolution of the enantiomers of *R*R**-chxn [45] allows ready access to synthetic precursors for the *RR* or *SS* forms of picchxn (**III(a)**) [46]. The inherent inflexibility and chirality of this tetradentate, and *N*-substituted derivatives [47], have proven to be important determinants of its stereo- and enantioselective coordination behaviour and much of our work has concentrated on the use of this ligand.



(**a**) *RR*-picchxn (**b**) *RR*-picchxnmi

(III)

A series of Pd(II) complexes of these various tetradentates has been synthesised and the products structurally characterised by NMR, X-ray diffraction and circular dichroism methods [44,48]. Factors which determine the varying degrees of stereoselectivity which these ligands exhibit in an enforced square-planar geometry were assessed.

In the main, trivalent cobalt and bivalent ruthenium have been chosen for our study of the coordination behaviour of these ligands with octahedral metal ions. Normally, metal complex precursors of general form $[Co^{III}(picen^*)Cl_2]^+$ have been readily obtained either by aerial or peroxide oxidation of a $Co^{II}(picen^*)$ species *in situ* [28,29,41,46,47,50–52] or by reaction of the chosen tetradentate with either *trans*-$[Co^{III}(py)_4Cl_2]^+$ [51] or $Na_3[Co(CO_3)_3].3H_2O$ and hydrochloric acid [53]. The two chloro monodentates of these precursor complexes are readily substituted by other ligands such as nitro, oxalato or α-aminoacidates under relatively mild aqueous conditions. Appropriate $Ru^{II}(picen^*)$ precursor species are not so readily obtained, although a general method employing *cis*-$[Ru^{II}(dmso)_4Cl_2]$ as a starting material often has provided cationic products of general form *cis*-$[Ru^{II}(picen^*)(dmso)Cl]^+$ under normal reaction conditions [54,55]. The two monodentates in these cations may be replaced by other common ligands (e.g. bipy, phen), usually with retention of stereochemistry. However, *cis*-β complexes of this general type have proven to be photoactive, with one of the coordinated secondary picen* amine groups readily being oxidatively dehydrogenated to produce monoimine forms (e.g. **III(b)**) [54–57]. This Ru–amine photoactivity therefore complicates the use of α-aminoacidates as ligands in the formation of ternary complexes of these species [54].

Although *cis* geometries have been observed to result invariably with both of these metal ions, flexible and less-substituted derivatives such as picen and picpn, show very little stereoselectivity in their binding, and *R**-picpn demonstrates little enantioselectivity [41,58–60]. This lack of selectivity is also observed with related chiral tetradentates in which the picolyl methylene hydrogen atoms are substituted by methyl groups [49]. Complexes of this type which have been studied most extensively are those of R^*-picpn. Complicated patterns of stereoselectivity are noted for Co(III) complexes of this ligand. For example, the dichloro complex $[Co(R\text{-picpn})Cl_2]^+$ has been isolated in all four possible *cis* geometries Λ-α, Δ-α, Λ-β and Δ-β [33,36,37,41,42], and strain energy minimization calculations have been carried out for all of these stereochemistries. A thorough understanding of the system and kinetic *versus* thermodynamic control of isomer distributions was assisted by the realization [41,42] that the Δ-α-$[Co(R\text{-picpn})Cl_2]ClO_4$ salt is isolated as the least soluble diastereoisomer from a complex mixture of different species. Reaction of this latter salt with oxalate in water gives four disastereoismers, Δ,Λ-α,β-$[Co(R\text{-picpn})(ox)]^+$, with the Δ-α disastereoisomer being predominant (this represents a new kind of octahedral inversion [41]). Reaction with NO_2^- ion, however, produced only two isomers, Λ-α- and Δ-β-$[Co(R\text{-picpn})(NO_2)_2]^+$, the latter of which was shown to be the more thermodynamically stable [58].

Because of the single methyl substituent in the central chelate ring of R^*-picpn a further source of isomerism exists for *cis*-β complexes. These are the *exo* and *endo* forms, named according to the disposition of the methyl group relative to the fold in the tetradentate. Remarkably, the β-*exo* nitro complex forms stereospecifically, only Δ-β-*exo*-$[Co(R\text{-picpn})(NO_2)_2]^+$ being ultimately obtained, as confirmed by a single-crystal X-ray study [61].

In contrast to the mono-substituted ligands, the optically active forms of the *vicinal* *C,C′*-disubstituted ligands (**I** with both R^2 and $R^3 \neq H$) exhibit high stereo- and enantioselectivity in their coordination behaviour, the latter being determined by the choice of chirality of the diamine synthetic precursor. In particular, this holds for the N_4-tetradentates based on $2R^*,3R^*$-diaminobutane (R^*R^*-picbn) [8,34,55], $1R^*,2R^*$-diphenyl-1,2-diaminoethane (R^*R^*-picstien) [51,52] and $1R^*,2R^*$-diaminocyclohexane (R^*R^*-picchxn) [46]. Each is observed to be both stereo- and enantiospecific when bound to Co(III), the *RR* form of each, for example, producing exclusively Λ-*cis*-β complexes. The common stereochemical characteristics of these three *vicinal* ligands have been established by single-crystal X-ray studies (Table 2), circular dichroism and NMR measurements [8,34,46,51,52,54].

The choice between the formation of either *cis*-α or *cis*-β complexes is governed by the stereochemical requirements of the inner secondary N atoms of these tetradentates. The minor torsional requirements of the H substituents of these atoms facilitate the necessary meridional arrangement of three of the nitrogen donors in the *cis*-β forms. The central of these three has the choice of adopting either an *R* or *S* absolute configuration, whereas the N atom at the fold of the tetradentate is constrained such that its configuration is determined by that adopted by the metal ion. It was recognised that, similar to alkylpolyamine ligands [69,70], alkyl substitution at these secondary nitrogen atoms should enforce *cis*-α geometries on the Co(III) complexes, and experiment has shown this to be correct.

Substitution by methyl or benzyl groups on the secondary amine N atoms of several of these ligands has been achieved in high synthetic yields (>80%). The choice of *N*-substituents (**I**, R^1 and R^4) provides control of coordination stereoselectivity, with the *N,N′*-dialkylated forms picenMe$_2$, picpnMe$_2$, picchxnMe$_2$ and picpyrrMe, for example, yielding solely complexes with *cis*-α topologies with Co(III)

Table 2
Ternary Co(III)-aminoacidate complexes of picen-type ligands which have been structurally characterized by single-crystal X-ray methods

Complex	Ref.
Λ-β_1-[Co[*RR*-picchxn)(*R*-ABMA)]$ClO_4.1.5H_2O$	[8]
Λ-β_1-[Co[*RR*-picchxn)(*S*-APMA)]$ClO_4.2NaClO_4.5H_2O$	[9]
Λ-β_2-[Co[*RR*-pichxn)(pro-2*H*)]$Cl.ClO_4.H_2O$	[64]
Λ-β_2-[Co[*RR*-picchxn)(*R*-pro)]$(ClO_4)_2$	[64]
Λ-β_2-[Co[*RR*-picchxn)(*S*-pro)]$(ClO_4)_2.H_2O$	[64]
Λ-β_1-[Co[*RR*-picchxn)(*S*-α-Me-trp)]$(ClO_4)_2$	[10]
Λ-β_1-[Co{*RR*-picstien)(AMMA)]$ClO_4.2H_2O$	[52]
Δ-β_1-*endo*-[Co(*S*-picpn)(*S*-ala)]$(ClO_4)_2$	[65][a]
Δ-β_1-*exo*-[Co(*S*-picpn)(*S*-ala)]$(ClO_4)_2$	[65][a]
Λ-β_1-*endo*-[Co(*R*-picpn)(*S*-ala)]$(ClO_4)_2$	[65][a]
Λ-β_1-*exo*-[Co(*R*-picpn)(*S*-ala)]$(ClO_4)_2$	[65][a]
Δ-β_1-*exo*-[Co(*R*-picpn)(*S*-pro)]$(ClO_4)_2$	[60]
Δ-β_1-[Co(*S,RR,S*-pychxn)(*S*-ala)]$(ClO_4).H_2O$	[66]
Δ-β_1-[Co(*SSSS*-pychxn)(gly)]$(ClO_4)_2.2H_2O$	[67]
Δ-β_2-[Co(*SSSS*-pychxn)(*R*-ala)]$(ClO_4)_2.2H_2O$	[67]
Λ-α-[Co(*SS*-picchxnMe_2)(*R*-ala)]$(ClO_4)_2$	[47]
Λ-α-[Co(*SS*-picchxnMe_2)(*S*-pro)]$(ClO_4)_2.H_2O$	[68]
Λ-α-[Co(*SS*-picchxnMe_2)(*S*-phe)]$(ClO_4)_2$	[11]
Δ-α_1,α_2-[Co(*R*-picpnMe_2)(*S*-ala)]$(ClO_4)_2$	[28]
Λ-α_1-[Co(*S*-picpyrrMe)(*S*-ala)]$(ClO_4)_2.0.5H_2O$	[29]
Λ-α_1-[Co(*S*-picpyrrMe)(*R*-ala)]$(ClO_4)_2$	[29]

[a] Four diastereoisomers exist in a disordered crystal structure.

[11,28,29,47,68]. A similar stereochemistry has been observed in dinuclear Mn(III/IV) complexes of such ligands [71–73]. This stereospecificity is not retained for Ru(II), however, with these tertiary amine ligands. Although synthetic reactions are enantiospecific with both Co(III) and Ru(II), complex products often are obtained as mixtures of *cis*-α and *cis*-β forms with Ru(II), which require separation [57,63,74,75]. The problem of the photoactivity of the secondary amine groups observed with this metal ion and the unsubstituted picen* species is, however, overcome with these *N*-substituted ligands.

3. Recognition of α-aminoacid molecular structures

3.1. Chiral discrimination in ternary [Co^{III}(picen)(R*-aa)]$^{2+}$ complexes*

The stereochemistries of ternary Co(III) complexes formed with picen-type ligands and α-aminoacidates have been extensively explored and these studies have revealed the geometric preferences which are adopted. No *cis*-α isomers of ternary complexes of the type [Co(*R**-picpn)(*R**-aa)]$^{n+}$ are known, but all eight Δ,Λ-$\beta_{1,2}$-*exo*, *endo*-[Co(*R**-picpn)(*R**-aa)]$^{2+}$ diastereoisomers have been isolated for various α-aminoacids and these have been studied by NMR and spectroscopic (including circular dichroism) methods [59,60]. Five *R**-picpn complexes of this type have been characterised using single-crystal X-ray methods (Table 2), with the simultaneous co-crystallization of four diastereoisomers being identified with *S*-alanine [65]. Possible steric reasons for the observed isomeric preferences or predominances displayed by these *R**-picpn ternary complexes are outlined in Section 3.3. However, it is believed that at least in some of these ternary systems the isomer distributions found are kinetic in origin.

Substantial crystallographic information has been accumulated on ternary complexes of this type with *R***R**-picchxn. Table 2 lists those which have been studied by single-crystal X-ray methods. This crystallographic work is complemented by extensive NMR studies [8–10,46,53,76]. In all cases the α-aminoacidate products derived from *RR*-picchxn have been observed to retain the Λ-*cis*-β geometry of the dichloro precursor species enantio- and stereospecifically. This overwhelming stability of *cis*-β diastereoisomers for Co(III) complexes of *R***R**-picchxn is not confined to complexes containing α-aminoacids or their dichloro synthetic precursors. Single-crystal X-ray structures have revealed the same geometry in the species Λ-β-[Co(*RR*-picchxn)$(NO_2)_2]^+$ [61], Λ-β_2-[Co(*RR*-picchxn)(tap)$]^{3+}$ [62] and Λ-β_2-[Co(*RR*-picchxn)(hpm)$]^{3+}$ [77].

Evidence is available to confirm that this is the thermodynamically favoured geometry at room temperature [9]. When α-amino-α-(*n*-butyl)malonic acid ($ABuTMAH_2$) is reacted with Λ-β-[Co(*RR*-picchxn)$Cl_2]^+$ in aqueous media the main product formed is Λ-β_1-[Co(*RR*-picchxn)(*R*-ABuTMAH)]$(ClO_4)_2$. However, small quantities of a Δ-*cis*-α diastereoisomer intermediate, formed under kinetic control, were able to be isolated as a diperchlorate salt. This species appears to be relatively stable in aqueous solutions under ambient conditions, but epimerises at a rate conveniently followed by ^1H NMR methods to the Λ-*cis*-β_1 diastereoisomer when dissolved in dmso [9]. When the reaction is complete, no trace of the Δ-*cis*-α intermediate is detectable by NMR measurements and hence it is estimated that the equilibrium constant at room temperature relating the Δ-*cis*-α and Λ-*cis*-β_1 isomers is greater than 10^2 in favour of the latter. Thus the chiral discrimination energy preference for the β form is greater than 12 kJ mol^{-1}.

The same pattern of thermodynamic stability has been observed in asymmetric synthesis experiments employing Co^{III}-picen* complexes as chiral auxiliaries in the formation of α-aminoacidates. These include experiments involving decarboxylation of complexes containing various $ARMAH_2$ derivatives, these being precursors of α-aminoacids. Such work was based on the pioneering study of Asperger and Liu [31] and elaborations by other workers [78,79]. Thermodynamic rather than kinetic control with respect to a number of α-aminoacids was established for these reactions, which give mixes of two diastereoisomeric products containing opposite hands of the α-aminoacidates [8,9,52,76]. In the cases of *R*,*S*-phenylalaninate, and its coordinated α-amino-α-benzymalonic acid precursor, significant π-bonding interactions are evident between a pyridyl ring of the tetradentate and the phenyl ring of the pro-*S* aminoacidate ligand [8] (Fig. 1). Similar ring stacking is observed in the structure of the α-methyl-*S*-tryptophanate complex [10] (Fig. 2). Such interactions are important in other related complexes (*vide infra*). Complementing this asymmetric synthetic

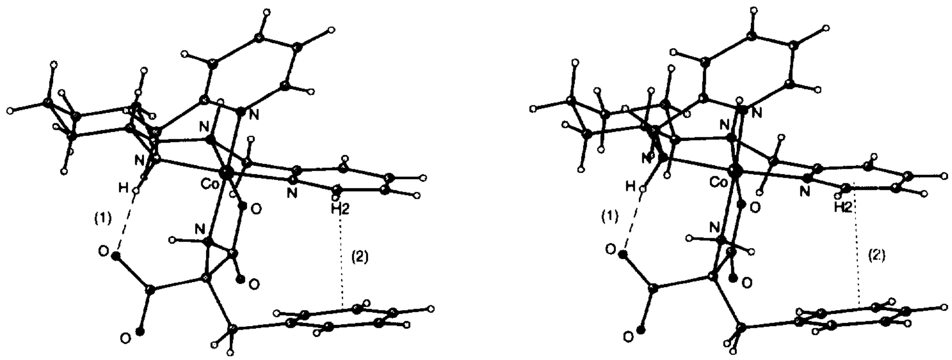


Fig. 1. A stereoview [110] of the molecular structure of the Λ-β_1-[Co[*RR*-picchxn)(*R*-ABMA)]$^{+}$ cation (atomic coordinates obtained from crystallographic data [8]). The two favourable noncovalent interactions indicated between the picchxn and ABMA ligands are (1) a hydrogen bond involving the amine NH and unbound carboxylate group, and (2) π-stacking of the aromatic pyridyl and phenyl ring components. A close structural relationship exists with that shown Fig. 2.

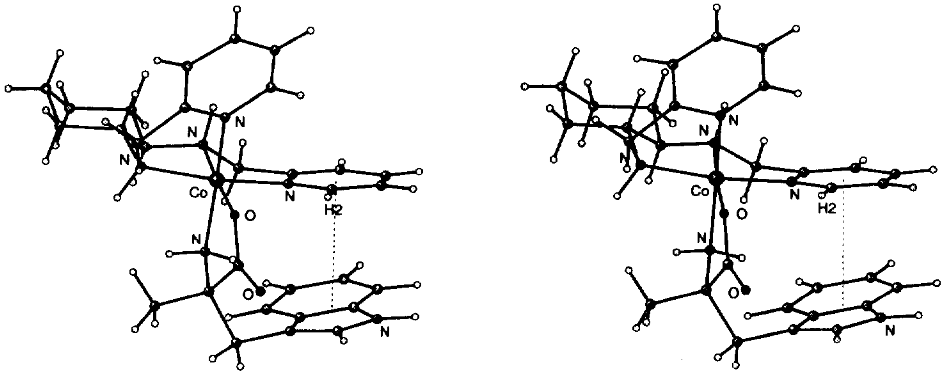


Fig. 2. A stereoview [110] of the molecular structure of the Λ-β_1-[Co[*RR*-picchxn)(*S*-α-Me-trp)]$^{2+}$ cation (atomic coordinates obtained from crystallographic data [10]). A favourable π-stacking interaction between one pyridyl ring of *RR*-picchxn and the aromatic indole substituent of the *S*-aminoacidate ligand is indicated. The structure may be related to diagram (**IV**(e)).

chemistry is that concerning the stereospecific hydrogenation of coordinated 1,2-dehydroproline (pro-2H) in a related complex (Table 2) to give *R*- and *S*-prolinate products [53,64]. These observations and measurements of chiral discrimination energies are a result of molecular design in the various systems studied based generally upon non-bonded steric interactions in this class of complexes. Such interactions are discussed in the structural papers (references in Table 2) and are analysed in further depth in Section 3.3.

Finally, in this section, we note that variations in the stereoselectivities displayed by these complexes which accompany different substitution patterns on the central chelate ring of the tetradentate are parallelled by similar effects occasioned by replacement of the pyridyl groups by saturated analogues. Thus, a tetradentate based on *RR*-picchxn but with the pyridyl groups replaced by 2*S*-pyrrolyd-2-yl groups (*SRRS*-pychxn) is not at all stereospecific in ternary complexes of Co(III) with α-aminoacidates [66]. The corresponding *SSSS* tetradentate demonstrates a higher degree of stereoselectivity [67], but these observations contrast with others reported in the literature [80,81]. Three complexes containing these ligands also have been characterized crystallographically (Table 2).

3.2. *Stereochemical effects of ligand N-alkylation*

Alkyl substitution on the central N atoms of *R***R**-picchxn is observed to have a dramatic effect on its coordination behaviour. With Co(III) its stereospecificity changes from *cis*-β to *cis*-α, and the absolute configurations at the metal ion centres are opposite to those obtained with the unsubstituted forms. The Δ-*cis*-α stereochemistry which *RR*-picchxnMe$_2$ enforces stereospecifically at Co(III) has been established by spectroscopic techniques [11,47,68] and confirmed by single-crystal X-ray studies on several of its ternary α-aminoacidate complexes (Table 2). This same stereochemistry is adopted by Ni(II) [82]. It is worth noting also that the synthesis of α-aminoacids *via* decarboxylation of coordinated α-aminomalonic acid precursors gives rise to much lower enantiomeric excesses in the *cis*-α complexes than is observed in the corresponding less symmetrical *cis*-β species [68]. The same kind of intramolecular hydrophobic interaction found in the α-amino-α-benzylmalonicacidate (Fig. 1) and α-methyl-*S*-tryptophanate (Fig. 2) complexes with *RR*-picchxn is also observed in the structure of the *S*-phe Λ-complex of *SS*-picchxnMe$_2$ (Fig. 3), and its stability in solution has been measured in terms of rotamer populations by NMR methods [11].

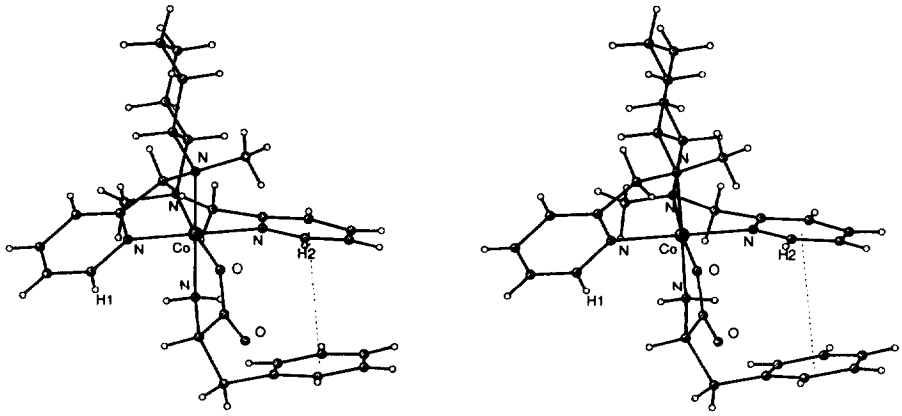


Fig. 3. A stereoview [110] of the molecular structure of the Λ-α-[Co(*SS*-picchxnMe$_2$)(*S*-phe)]$^{2+}$ cation (atomic coordinates obtained from crystallographic data [11]). A favourable π-stacking interaction between one pyridyl ring of *SS*-picchxnMe$_2$ and the phenyl substituent of the *S*-phe aminoacidate ligand is indicated. The structure may be related to diagram (**IV(c)**).

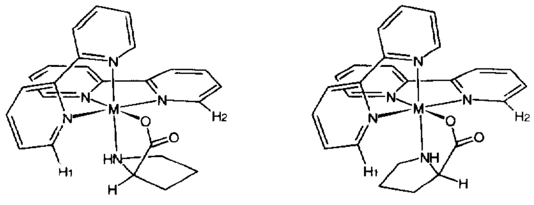
Of some interest with respect to stereospecificity considerations is the fact that the same pattern of geometric preference is found for *R*-picpnMe$_2$ in that *R* substitution in the picen backbone enforces exclusively a Δ-*cis*-α configuration. This was confirmed in a single-crystal X-ray study of Δ-α_1, α_2-[Co(*R*-picpnMe$_2$)(*S*-ala)](ClO$_4$)$_2$, where the α_1/α_2 nomenclature refers to the sense of coordination positioning of the aminoacid carboxylic oxygen atom, either *cis* or *trans* to the amine N atom closest to the tetradentate methyl group [28]. The above considerations appear to be general in the sense that other related but more exotic tetradentates (Table 1) give rise to the same stereospecifics. For example, the rigidity of the *R**-picpyrrMe ligand has been demonstrated by the structures of the two compounds Λ-α_1-[Co(*S*-picpyrrMe)(*R**-ala)](ClO$_4$)$_2$.1/2H$_2$O for both hands of the *R**-ala ligand [29]. A related Pd(II) complex also has been structurally characterised with this ligand [44].

3.3. *A structural analysis of α-aminoacidate discrimination*

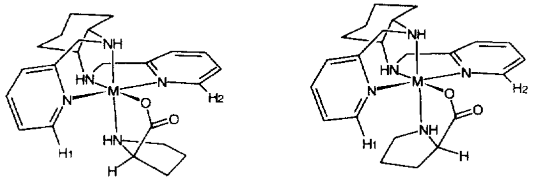
The distinction between the different topological forms of a *cis*-M(picen*) moiety when discriminating an α-aminoacidate bidentate is illustrated in (**IV**). Here the α-aminoacidate represented is *R**-prolinate and the tetradentate is *RR*-picchxn. Similar to the [Ru(diimine)$_2$(*R**-aa)]$^+$ species, a distinction may be made between the different steric environments on the two sides of the α-aminoacidate chelate ring, again best identified in each diastereoisomer represented in (**IV**) by the positioning of the α-pyridyl protons H1 and H2 relative to that ring. The *cis*-α structures (**IV(c)** and **(d)**) alone would produce steric environments analogous to those of the bisdiimine complexes (**IV(a)** and **(b)**), and hence similar discriminatory behaviour might be expected. In the *cis*-β_1 forms (**IV(e)** and **(f)**), however, the predominant steric interaction which would derive from proton H1 is absent, and hence so also would be any chiral discrimination based on this interaction. In contrast, this structural feature still exists in the *cis*-β_2 isomers (**IV(g)** and **(h)**) and therefore in these forms this steric source of potential discrimination remains.

Hence, for discriminatory functions based on chirality recognition there are very important structural distinctions between these three *cis* diastereoisomeric forms. These sterically based discriminations would not exist for an achiral α-aminoacidate ligand such as glycine, discrimination should be minor between the enantiomeric forms of a flexible and less bulky ligand such as *R**-alanine, but they should become quite pronounced for bulky α-aminoacids with limited torsional flexiblity such as *R**-proline, as represented in (**IV**). This is consistent with results obtained both for the photolabile Ru-bisdiimine compounds [22,23] and for the Co^{III}-picen* systems. Hence in the set of Λ complexes represented by **IV(b)**, **(d)** and **(h)** the *R*-prolinate ligand might be expected to be discriminated against by its metal-tetradentate hosts, its *S* enantiomeric form being the more welcome guest. Conversely, preferential recognition of the *R*-prolinate enantiomer would be achievable, if desired, through use of Δ-*cis*-α or Δ-*cis*-β_2 tetradentate complex fragments as hosts.

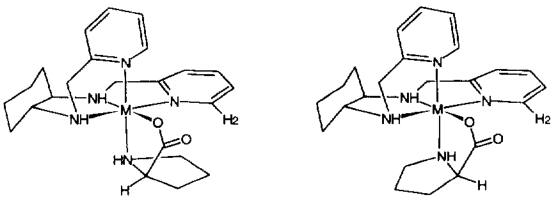
Other potential sources of discrimination through noncovalent interactions also may be identified in these different structures. The secondary amine NH group in



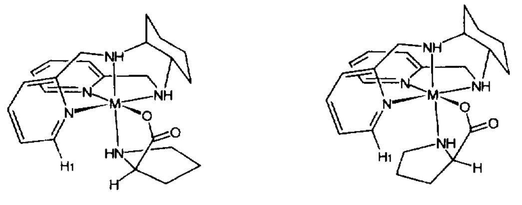
(a) Λ-*(S-pro)* **(b)** Λ-*(R-pro)*



(c) Λ-α-*(S-pro)* **(d)** Λ-α-*(R-pro)*



(e) Λ-β1-*(S-pro)* **(f)** Λ-β1-*(R-pro)*



(g) Λ-β2-*(S-pro)* **(h)** Λ-β2-*(R-pro)*

(IV)

the fold of the tetradentate is a potential H-bond donor. It adopts a *fac* relationship with the O and N donors of the aminoacidate ligands in the *cis*-β isomers but not in the *cis*-α forms. As a result, for aminoacids with α-substituents containing H-bond acceptor groups the potential exists for discriminatory contributions due to interligand H-bonding in the Λ-β_1-(*R*-aa), (**IV(f)**), and Λ-β_2-(*S*-aa) (**IV(g)**) diastereoisomers alone. Conversely, the pyridyl groups would have the potential for interligand hydrophobic interactions through π-stacking involving aromatic aminoacid substituents in the *cis*-β_1-(*S*-aa) (**IV(e)**), *cis*-β_2-(*R*-aa) (**IV(h)**) and both *cis*-α-(*R**-aa) forms (**IV (c)** and (**d**)). This suggests that π-stacking may make a more significant contribution to enantioselectivities exhibited in the *cis*-β systems than in those based on a *cis*-α geometry.

The analysis provided above is consistent with the stereoselectivities displayed in experiments involving optical resolutions or the syntheses of the α-aminoacidate complexes. The [Co(picen*)(*R**-aa)]$^{2+}$ products are readily obtained by reaction of an α-aminoacid with the respective [Co(picen*)Cl$_2$]$^+$ species as precursors in aqueous solutions and under mild conditions. The Λ-β-[Co(*RR*-picchxn)Cl$_2$]$^+$ precursor, for example, demonstrates little discrimination in reactions with *R**-alanine under such conditions and both *S*-alaninate and *R*-alaninate ternary products may be readily obtained [46]. It is of interest that, consistent with steric arguments presented above, both Λ-*cis*-β_1 and Λ-*cis*-β_2 forms of the *S*-alaninate complex are isolated, but the Λ-*cis*-β_1 form alone may be obtained with *R*-alanine. Similar behaviour is observed with the other tetradentates studied [52,59,60] and to date no Λ-*cis*-β_2 product containing an *R*-aminoacidate guest molecule has been obtained from a reaction involving a Λ-β-Co^{III}-picen* host moiety and an α-aminoacid as synthetic precursors. Furthermore, such synthetic reactions involving the less flexible *R**-proline as a precursor are observed to be enantiospecific. Each Co^{III}-picen* moiety studied has demonstrated an ability to distinguish the two hands of this more sterically demanding ligand and no *R*-prolinate complex has been isolated under these conditions as either a Λ-*cis*-α or a Λ-*cis*-β product.

It must be noted that this discriminatory behaviour is in complete contrast to that observed when the Λ-β-Co^{III}-*RR*-picchxn moiety is used as a template for the asymmetric synthesis of *R**-proline. The ternary complex formed with the prochiral 1,2-dehydroproline bidentate has a Λ-β_2 geometry [53] (allowed by the bidentate's lack of chirality) and its reduction by aqueous sodium borohydride yields a Λ-β_2-[Co(*RR*-picchxn)(*R**-pro]$^{2+}$ mix in which the *R*-pro species is in the higher diastereoisomeric proportion [53,64]. This result is quite remarkable in the context of the other synthetic chemistry and predictions based on steric factors, as described above. However, the two sets of synthetic conditions are distinctly different. In one case the Co^{III}(*RR*-picchxn) moiety discriminates against *R*-prolinate as an incoming ligand entering the coordination sphere. In the second, discrimination likely is governed by steric access to the already bound iminoacidate precursor for the incoming reducing agent. In this mechanism other factors such as selective hydrogen bonding or electrostatics involving reaction intermediates may play dominent roles. In each case, however, the molecular recognition process between the two reagents would be controlled by the stereochemical features established by the bound chiral tetradentate ligand.

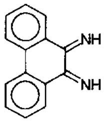
Indeed, the results of the α-aminoacidate asymmetric syntheses experiments based on decarboxylation of coordinated α-substituted-α-aminomalonate precursors confirm that likely products cannot be predicted solely from simple steric considerations. Decarboxylation experiments on Λ-β_1-[Co(picen*)(ARMA)]$^+$ species generally result in diastereoisomeric product mixtures which have a significant excess of the *R*-aminoacidate forms [8,9,52,76]. The *AMMA*-based precursors, for example, consistently give *R*-:*S*-alaninate product ratios of around 9:1 for the *RR*-picchxn [76], *RR*-picbn [8] and *RR*-picstien [52] complexes. There is no obvious steric reason for enantiopreferences in *cis*-β_1 isomers (**IV** (**e**) and (**f**), *vide supra*) and these consistent and high selectivities in favour of the *R*-handed products demonstrate the importance of the overall common molecular architecture of the complexes. An important comparison of the different discriminatory abilities of the *cis*-α and *cis*-β geometries is allowed by the observation that decarboxylation of the more symmetrical Λ-α-[Co(*SS*-picchxnMe$_2$)(AMMA)]$^+$ analogue under the same conditions results in no detectable enantiodiscrimination in the *R**-alaninate products [68].

When the *ARMA*-based precursors in these experiments have aromatic substituent groups, however, the enantiopreference observed in the products is reversed such that *S*-aa products are obtained in significant excess [8,9]. This behaviour has been attributed to stabilisation of the pro-*S* configuration by interligand H-bonding and to the existence also of π-stacking interactions involving the aminoacidate side-chain and the adjacent pyridyl ring in the Λ-β_1 isomeric forms. The presence of these structural features in the ABMA synthetic intermediate has been confirmed by X-ray analyses [8] (Fig. 1). Moreover, the π–π interaction would appear to play a dominant role in determining the chirality of the products, since similar interligand H-bonding is apparent also in the crystal structure of the non-aromatic pro-*S* AMMA analogue, decarboxylation of which results nonetheless in a significant *R*-alaninate preference [52]. Similar hydrophobic π-stacking interactions have been shown to exist in each of the [Co(picen*)(*R**-aa)]$^{2+}$ crystal structures obtained thus far for α-aminoacidates containing aromatic α-substituents [10,11,83] (Figs. 1–3). In addition, intermolecular π–π interactions between pyridyl rings alone have been observed in a related Pd(II) structure [44]. The indications are that this type of noncovalent interaction is a source of discrimination which is at least as significant as interligand steric effects.

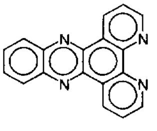
4. Recognition of nucleic acid molecular structures

4.1. Simple tris-bidentate metallointercalators

The development and use of chiral metal complexes as molecular probes of nucleic acid structures has been the subject of intense research over the last decade and the topic has been well reviewed recently [84]. Much of this work has been initiated by early reports of the enantiomeric recognition of duplex DNAs by simple tris-chelate octahedral cations derived from oligopyridyl bidentates and of general type [M(diimine)$_3$]$^{n+}$ [85–89]. Both Yamagishi [88] and Barton *et al.* [89] initially ascribed the observed enantiopreference for Δ-[Ru(phen)$_3$]$^{2+}$ to be due to a selective intercalative form of binding. In that model, one coordinated phen ligand of the Δ cation was proposed to be involved in positive hydrophobic bonding through π-stacking with the nucleobases of the duplex whilst the other two ancillary ligands make steric contacts with the surface of the helical groove [89]. It was proposed that the enantiopreference observed arises due to the more pronounced steric clashes that would exist between the two ancillary phen blades of the Λ isomer and the ribophosphate backbone of the duplex. The emergence of evidence against this intercalative model for the tris-phen complexes [90–93] led to the development and use of several modified derivatives. In particular, complexes containing diimine bidentates such as phdi (**V**), dppz (**VI**), ppz (**VII**) or dpq (**VIII**), which provide enhanced aromatic surface areas for intercalation, have been shown unambiguously to intercalate into DNA [74,94–96].



(V)



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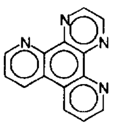

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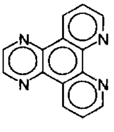


(VIII)

Both enantiomers of the $[Ru(phen)_2(dppz)]^{2+}$ cation, for example, have been shown to bind to calf-thymus DNA [95–97], to alternating GC and AT homo-polymer duplexes [96], and to $d(CGCGATCGCG)_2$ [90] and $d(GTCGAC)_2$ [99] duplex fragments *via* intercalation. From NMR analyses it is concluded that the Δ enantiomer intercalates selectively into the central CG base sequence of $d(GTCGAC)_2$ from the major groove of the duplex [95,99]. Similar intercalative behaviour has been observed for homologues based on phdi. The interaction of $[Ru(diimine)_2(phdi)]^{2+}$ complexes (diimine represents phen or bipy) with calf-thymus DNA and homo-polynucleic acids has been investigated. A study employing electric dichroism and photolysis methods [100] shows all ions to bind with enantio-meric discrimination *via* intercalation of the phdi fragment, and a Z-DNA conformer is transformed to B-DNA as a result of this intercalative interaction. Analogues of Rh(III) derived from bulky substituted forms of the ancillary diimine ligands show enantioselective base-sequence recognition [101]. The complex based on 4,4′-diphenyl-2,2′-bipyridine specifically targets 5′-CTCTAGAG-3′ sites. We have demonstrated that a correlation exists between the degree of aromatic area available for intercalation and chromatographic retention times on immobilised DNA for $[Ru(diimine)_3]^{2+}$ complexes of phen, dppz, dppzMe$_2$, dpq and dpqMe$_2$ [74]. Nonetheless, the enantioselectivity exhibited by simple complexes of this tris-bidentate type for interaction with calf-thymus DNA has been shown to be quite unpredictable [94].

4.2. *Ternary* $[Ru^{II}(picen^*)(bidentate)]^{2+}$ *ions designed as DNA metallointercalators*

The basic structural description of this intercalative model now has been proven to be substantially correct, at least for probe molecules containing bidentates with extended aromatic surface areas [95,96]. Hence the discriminatory abilities of complexes of this type, which are determined predominantly by intermolecular contacts between the DNA-groove surfaces and the ancillary bis-diimine components of the different $[M(diimine)_2(bidentate)]^{n+}$ enantiomers, should be controlled by stereochemical factors similar to those discussed above for the recognition of α-aminoacidates by $M(diimine)_2^{n+}$ species. That is, the unsymmetrical environment provided by the bis-diimine moieties which can assist in the discrimination of α-aminoacidates should be a common factor if applied to their recognition of nucleic acids. Once again, important advantages could be achieved if the two diimine ligands of these metalloprobes were to be replaced by picen-based tetradentates. Hence we have synthesised ternary complex cations of general form $[Ru(picen^*)(bidentate)]^{2+}$ and are evaluating them for this recognition purpose [54,56,57,63,74,75,102,103]. It is of interest that the only previously reported species of this general type is the elemental $[Ru(picen)(bipy)](ClO_4)_2$ complex described by Goodwin and Lions with the original synthesis of picen [40].

Ternary metallointercalators of this type would have a number of advantages over probe molecules based on a tris-bidentate geometry. Flexibility in their synthetic design again would allow for more facile control of chirality and for the ready incorporation of steric bulk and selective secondary-binding sites. Moreover, (1) since they contain only one intercalating bidentate any ambiguity as to which molecular fragment intercalates can be avoided; (2) their inherent chirality, determined through tetradentate design (*vide supra*), can provide optically pure metalloprobes which are not subject to racemisation at the metal centre and which do not require development of individual optical resolution methods; (3) the tetradentate non-aromatic components provide well-dispersed NMR resonances, of major assistance in solution structural analyses of interactions with oligonucleotide targets [82]; and (4) the existence of *cis*-α and *cis*-β stereoisomerism allows the opportunity for a study of discriminatory effects based on molecular shape which are unavailable to the structurally less-sophisticated tris-bidentate probe molecules.

We have synthesised a variety of Ru(II) complexes of this general type and, where necessary, have resolved the diastereoisomeric products into their pure *cis*-α and *cis*-β forms. (The distinction between β_1 and β_2 geometries does not exist with the symmetrical oligopyridyl bidentates.) The various complexes obtained with picen demonstrate little stereoselectivity in their formation, although the phen and tmp ternary derivatives have only been obtained with *cis*-α geometry [55]. The crystal structure [104] of the simplest potential metallointercalator of this type, the *cis*-α-$[Ru(picen)(phen)]^{2+}$ cation, is shown in Fig. 4.

The use of *vicinal* disubstituted picen derivatives provides the control over stereoselectivity which is lacking in the unsubstituted forms, and their structural chemistry parallels that of the Co(III) compounds described earlier. Complexes containing *R***R**-picchxn, for example, display the same stereo- and enantiospecificity found for Co(III). That is, *RR*-picchxn again forms solely Λ-*cis*-β products with Ru(II) [54,56,102]. Similar stereospecifics are observed with *R***R**-picbn [55]. The molecular structure of the *cis*-Λ-β-$[Ru(RR\text{-picchxn})(phen)]^{2+}$ cation [104] is shown in Fig. 5, where a comparison of its *cis*-β geometry may be made with that of the *cis*-α picen homologue (Fig. 4).

Photo-oxidation of complexes of this type [54–56] leads to products containing the tetradentate in a monoimine form (**III(b)**), and the crystal structure of such a complex has been determined [56]. The *cis*-Λ-β-$[Ru(RR\text{-picchxnmi})(phen)]^{2+}$ cation crystallises in an unusual solvate form with one molecule of unbound phen, and its molecular structure (Fig. 6) demonstrates two highly significant features. The parallel

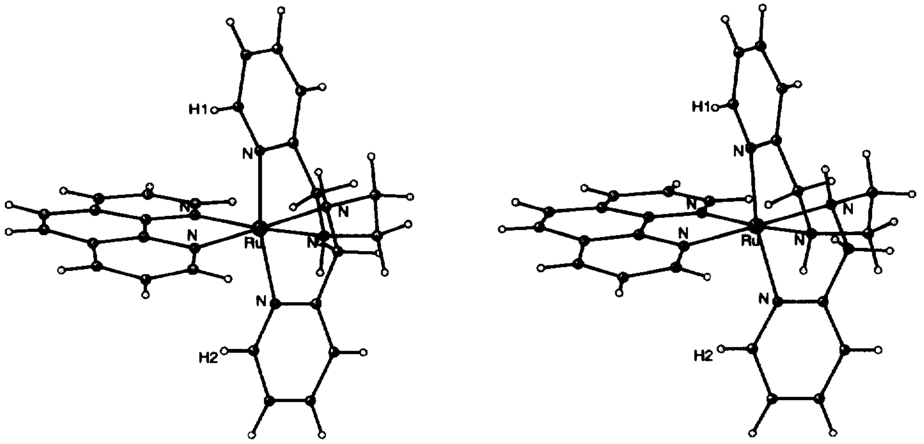


Fig. 4. A stereoview [110] of the molecular structure of the Λ enantiomer of *cis*-α-[Ru(picen)(phen)]$^{2+}$ (atomic coordinates obtained from crystallographic data [104]). The molecule has C_2 symmetry and hence the stereochemical environments above and below the phen moiety, exemplified by α-pyridyl protons H1 and H2, are equivalent. These protons would make primary steric contacts with duplex DNA for metallointercalators based on this geometry.

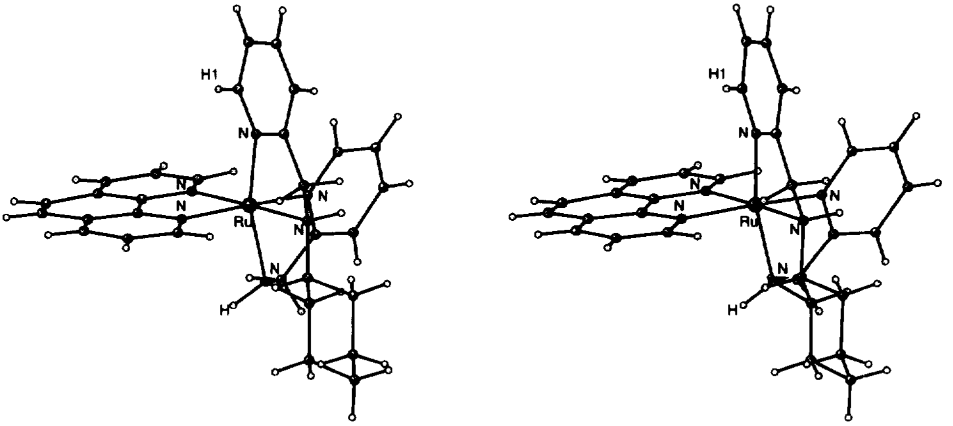


Fig. 5. A stereoview [11] of the molecular structure of the Λ-β-[Ru(*RR*-picchxn)(phen)]$^{2+}$ diastereoisomer (atomic coordinates obtained from crystallographic data [104]). Note the interchange of the positions in the coordination sphere of a pyridyl and an amine group of the tetradentate in comparison with a Λ-*cis*-α stereoisomer (Fig. 4). The lower amine group would provide the opportunity of nucleobase-sequence selectivity through H-bonding for metallointercalators based on this structure.

relative placement of the bound and unbound phen molecules clearly indicates hydrophobic bonding through a π-stacking interaction. Moreover, a bifurcated N–H···N hydrogen bonding arrangement involving the picchxnmi amine group as donor and the two unbound-phen N atoms as acceptors also is indicated by the interatomic geometries [98]. These structural features are significant factors when

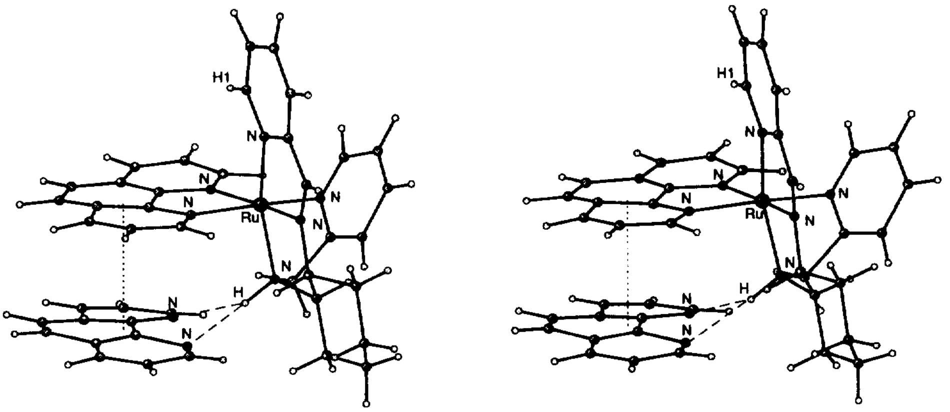
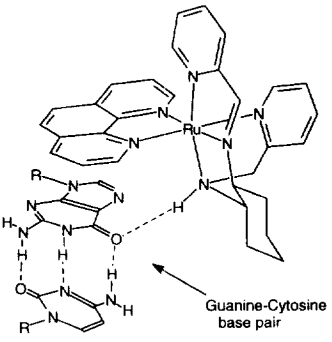


Fig. 6. A stereoview [110] of the molecular structure of the Λ-β-[Ru(*RR*-picchxnmi)(phen)]$^{2+}$·phen solvate complex obtained after photo-oxidation of the corresponding picchxn species [54,56] shown in Fig. 5. Atomic coordinates were obtained from crystallographic data [104]. Favourable intermolecular π-stacking and H-bonding interactions between the cation and the free heterocyclic base are indicated.

considering both molecular recognition potential and probe design. The π–π interaction demonstrates the propensity for cations of this type to stack with aromatic bases such as those in DNA. This is particularly so for those derived from proven intercalating bidentates such as (**V**)–(**VIII**). The indicated availability of the H-bond donor group for interaction with an acceptor on a π-bonded aromatic base also provides the potential for control of nucleobase-sequence selectivity in that interaction [84]. Molecular modelling shows this N–H group to be ideally positioned for interaction with the O6 atom of a guanine residue in the major groove of DNA, (**IX**). Analogous behaviour has been demonstrated with a set of Rh(III) ternary metallointercalators [84,105–109].



(IX)

Like H-bonding interactions are not available to the *cis*-α forms of the complexes since their amine group protons are directed away from the aromatic bidentate component (e.g. Fig. 4). Hence an important design distinction exists between the *cis*-α and *cis*-β forms when employed for DNA molecular recognition purposes. This mirrors their different intramolecular H-bonding potential when discriminating α-aminoacidates (**IV**, *vide supra*). The *cis*-α forms alone, with dyad symmetry, are structurally analogous to the tris-bidentate metallointercalators, where their molecular recognition function is thought to be determined primarily by shape selection due to steric clashes between ancillary ligands and the DNA groove surfaces [84–89]. Once again, the closest intermolecular steric contacts with the nucleic acid are likely to be those involving the two α-pyridyl protons (designated as H1 and H2 in the figures) in the *cis*-α complexes.

Unlike their Co(III) complexes, the *N,N'*-disubstituted picen* ligands are not stereospecific and commonly produce *cis*-α and *cis*-β isomeric mixtures with Ru(II), which nonetheless may be resolved by standard chemical or chromatographic means [63,74,75,102]. Ternary Ru(II) complexes of *R***R**-picchxnMe$_2$ have been isolated in both *cis*-α and *cis*-β forms [57,75,102], and the structure of the *cis*-Λ-β-[Ru(*SS*-picchxnMe$_2$)(phen)]$^{2+}$ complex cation, derived from an X-ray analysis [104], is shown in Fig. 7. A comparison of its molecular structure with that of its unsubstituted analogue (Fig. 5) allows two important distinctions to be discerned, apart from features arising from the opposite chiralities of the *R***R**-chxn fragments. The *N*-CH$_3$ substituents remove the intermolecular H-bonding potential of these probe molecules, and therefore any potential nucleobase-sequence selectivity deriving from this feature. Moreover, this methyl substituent group may be seen to protrude over the aromatic bidentate (here phen) such that it is likely to act as a source of steric hinderance to any π-stacking interactions near the metal ion centre. In contrast, the corresponding *cis*-Λ-α form would have both methyl substituents disposed well away from the aromatic bidentate moiety (cf. Fig. 3), similar to the amine protons

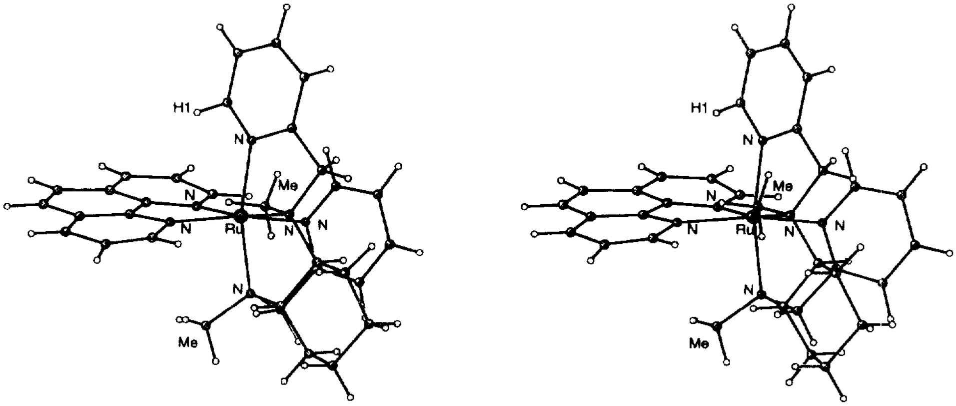


Fig. 7. A stereoview [110] of the molecular structure of the Λ-β-[Ru(*SS*-picchxnMe$_2$)(phen)]$^{2+}$ cation [75,102] derived from the crystal structure of its enantiomer [104]. A comparison with the structure of the *RR*-picchxn diastereoisomer shown in Fig. 5 illustrates topological changes resulting from *N*-methylation of the tetradentate. Primary steric contacts made with DNA by metallointercalators based on this geometry would involve the lower methyl group and the α-pyridyl proton H1.

of the unsubstituted forms (e.g. Fig. 4), and hence this steric hindrance feature would be absent. Once again the intermolecular recognition potentials of the two *cis*-α and *cis*-β forms are definably different.

Confirmation of the propensity of these molecules for π-stacking interactions is demonstrated by their solution behaviour, as measured by ^{1}H NMR experiments [57,75,82,102]. Similar to the simpler $[M(phen)_3]^{2+}$ cations [14,15], the ternary metalloprobes based on the extended bidentates phdi and dpq show evidence of significant self-association in aqueous media at higher concentrations. An analysis of proton resonance data is consistent with dimer formation through ring stacking interactions between the aromatic bidentate probe components (Fig. 8). Comparable magnetic shielding effects are apparent in NMR spectra when these complexes are allowed to interact with small synthetic oligonucleotide duplexes [57,82,102], again consistent with molecular recognition based on hydrophobic intercalative binding. These NMR studies also show these intermolecular associations to be both groove and base-sequence selective [82]. An *in vitro* bacterial DNA system also has been utilised in support of these studies. The different frameshift-detecting *S. typhimurium*

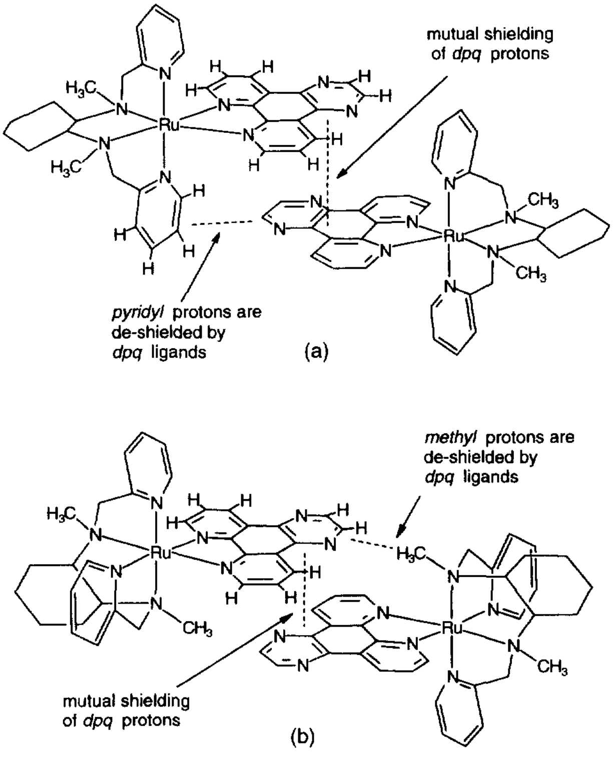


Fig. 8. Representations of possible paired structures formed through π–π interactions between aromatic bidentate components of (a) *rac-cis*-α- and (b) *rac-cis*-β-$[Ru(picchxnMe_2)(dpq)]^{2+}$ species. An interpretation of the consequent magnetic shielding effects observed in ^{1}H NMR spectra is given.

strains used indicate higher mutagenic activities for the *cis*-α diastereoisomers, and for those derived from the bidentates with higher aromatic surface areas available for intercalation [75,102,103].

As described above, the potential exists with metal complexes of this type for the determination of metalloprobe enantioselectivity through picen* chirality selection, and for control of nucleobase-sequence selectivity through intentionally designed steric bulk and H-bonding capacities. A simple example of this principle is illustrated in Fig. 9. The DNA-recognition capabilities of such complexes could be further enhanced by the synthetic incorporation of tethered secondary binding groups into the probe molecules. We are undertaking such a study. The potential exists also for the complexes to be incorporated into chimeras designed for purposes such as specific DNA sequence recognition [84] or photocontrolled repair reactions performed on the duplex [112].

5. Summary and conclusions

The significant advantages of using a picen-based tetradentate ligand rather than two bidentate ligands in octahedral metal complexes which are intended for discriminatory molecular recognition functions have been described above. An analysis in depth employing the considerable structural information accumulated on such complexes has allowed the identification of the noncovalent interactions which control their stereochemical behaviour. These discriminatory interactions may be applied at three different molecular levels, as summarised below.

5.1. *Intraligand discriminatory interactions*

The factors which determine the particular *cis* stereochemistries adopted by these tetradentates are identified as deriving primarily from intraligand torsional interactions. These are controlled by appropriate substitution on the central N–C–C–N atoms of the picen skeleton. Simple *C*-mono-substitution introduces chirality to the tetradentates but this generally results in non-discriminatory coordination behaviour. Appropriate alkyl or aryl substitution on both *vicinal* C atoms produces chiral ligands which are highly stereo- and enantioselective in their coordination behaviour. This is enhanced further by *N*-substitution, which also is a primary stereochemical determinant. The thorough understanding of these parameters has required elaborate experimental testing, but it is now clear that absolute stereospecificity, as far as can be experimentally determined, is simply a matter of choice through synthetic design for this M–picen* class of coordination complex.

5.2. *Interligand (intramolecular) discriminatory interactions*

The ability of a M–picen* moiety to act as an asymmetric template in discriminating chiral bidentate ligands in the coordination sphere of the metal ion, as exemplified by α-aminoacidates, has been studied in depth. This principle has been applied both

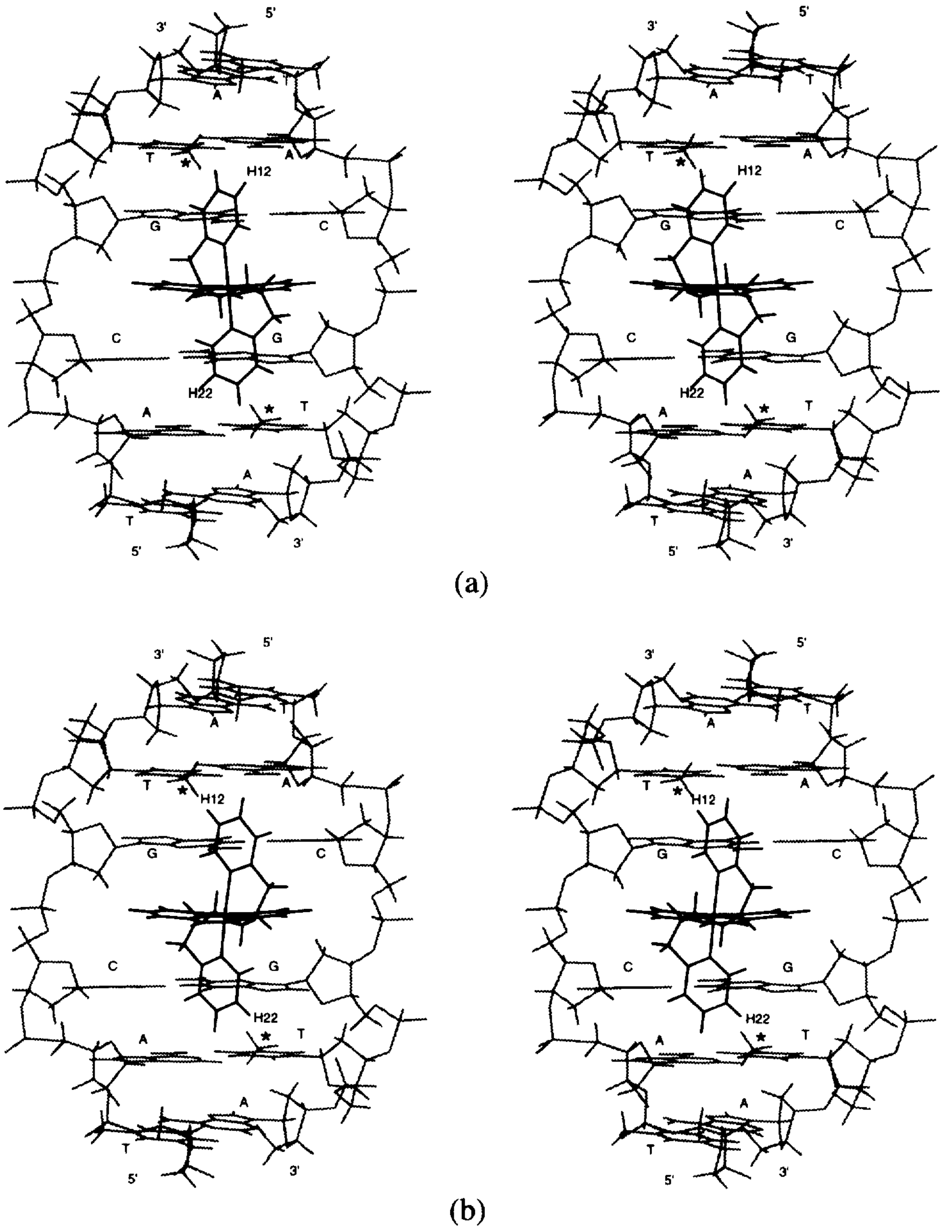


Fig. 9. Stereoscopic views of (a) the Λ-α- and (b) the Δ-α- enantiomeric forms of a *cis*-α-[Ru(picen)(bidentate)]$^{2+}$ cation positioned for intercalation into a fixed model d(TACGTA)$_2$ duplex fragment [111]. The Δ enantiomer shows a steric interaction between the pyridyl protons H12 and H22 of the picen ligand and the thymine methyl groups (indicated *) in the major groove of the duplex. Steric bulk or secondary binding components incorporated into the tetradentate in these positions should result in a major enhancement of the enantioselective and sequence recognition capabilities of metallointercalators of this type.

to enantioselective coordination or optical resolution of α-aminoacidates as well as to their asymmetric synthesis. Pronounced differences are observed for the diastereoisomeric products of these two applications, demonstrating that discriminatory behaviour cannot be predicted from intramolecular stereochemical factors alone.

At least three structural features which lead to noncovalent interligand interactions are identified as important discriminatory factors in complexes of this type. One common determinant obviously is sterically based and involves the disposition of the picen* α-pyridyl groups relative to the bidentate chelate ring. A second relates to the potential of a secondary amine group of the tetradentate to be involved in interligand hydrogen bonding in the ternary *cis*-β diastereoisomers. A third feature is the availability of the pyridyl groups for involvement in interligand hydrophobic π-stacking interactions with aromatic substituents on the bidentates. The pyridyl rings provide potential, therefore, for both unfavourable steric and favourable hydrophobic interactions. Each of these features may contribute to the subtle control of the molecular recognition functions exercised by the M–picen* template hosts on their bidentate guests.

5.3. Intermolecular discriminatory interactions

An understanding of these sources of interligand discrimination allows their application to the design of intact picen*-based complexes for selective recognition of other molecular structures. An important example lies in their use as chiral metallointercalators of nucleic acids. For this purpose we currently are investigating in detail a selection of ternary Ru(II) complexes which incorporate these tetradentates with bidentate ligands having known DNA-intercalating capabilities.

Common principles governing the control of enantioselectivity, hydrophobic or H-bonding interactions, and steric complementarity through chelate structural design apply to both intra- and intermolecular discriminatory applications. The increased synthetic flexibilty and structural diversity that this picen class of ligands allows in comparison with chelates based on simple oligopyridyl bidentates provides scope for significant enhancement of the many potential molecular recognition functions to which such compounds may be applied.

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References

[1] H. Okawa, Coord. Chem. Rev. 92 (1988) 1.
[2] P.R. Mitchell, H. Sigel, J. Am. Chem. Soc. 100 (1978) 1564.

[3] P.R. Mitchel, B. Prijs, H. Sigel, Helv. Chim. Acta 62 (1979) 1723.
[4] H. Sigel, Coord. Chem. Rev. 144 (1995) 287.
[5] D. Chen, M. Bastian, F. Gregán, A. Holý, H. Sigel, J. Chem. Soc. Dalton Trans. (1993) 1537.
[6] B.E. Fischer, H. Sigel, J. Am. Chem. Soc. 102 (1980) 2998.
[7] H. Sigel, B.E. Fischer, E. Farkas, Inorg. Chem. 22 (1983) 925.
[8] M.A. Cox, T.J. Goodwin, P. Jones, P.A. Williams, F.S. Stephens, R.S. Vagg, Inorg. Chim. Acta 127 (1987) 49.
[9] E.F. Birse, M.A. Cox, P.A. Williams, F.S. Stephens, R.S. Vagg, Inorg. Chim. Acta 148 (1988) 45.
[10] P.D. Newman, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 204 (1993) 257.
[11] P. Leverett, J. Petherick, P.A. Williams, R.S. Vagg, J. Coord. Chem. 37 (1996) 195.
[12] O. Yamauchi, A. Odani, J. Am. Chem. Soc. 107 (1985) 5938.
[13] A. Odani, S. Deguchi, O. Yamauchi, Inorg. Chem. 25 (1986) 62.
[14] P.R. Mitchell, J. Chem. Soc. Dalton Trans. (1980) 1079.
[15] Y. Masuda, H. Yamatera, Bull. Chem. Soc. Jpn. 57 (1984) 58.
[16] R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 51 (1981) 61.
[17] R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 52 (1981) 69.
[18] R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 58 (1982) 101.
[19] R.S. Vagg, P.A. Williams, Inorg. Chem. 22 (1983) 355.
[20] T.J. Goodwin, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 63 (1982) 133.
[21] T.J. Goodwin, P.A. Williams, F.S. Stephens, R.S. Vagg, Inorg. Chim. Acta 88 (1984) 165.
[22] R.S. Vagg, J. Proc. R. Soc. New South Wales 117 (1984) 99.
[23] T.J. Goodwin, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 83 (1984) 1.
[24] J.A. Chambers, R.D. Gillard, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 70 (1983) 167.
[25] J.A. Chambers, R.D. Gillard, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 72 (1983) 263.
[26] M.A. Anderson, J.P.G. Richards, A.G. Stark, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chem. 25 (1986) 4847.
[27] J. MacB. Harrowfield, S.B. Wild, in: G. Wilkinson, R.D. Gillard, J.A. McLeverty (Eds.), Comprehensive Coordination Chemistry, Pergamon, Oxford, 1987, p. 179.
[28] R.R. Fenton, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 201 (1992) 157.
[29] R.R. Fenton, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 197 (1992) 233.
[30] R.G. Asperger, C.F. Liu, Inorg. Chem. 4 (1965) 1395.
[31] R.G. Asperger, C.F. Liu, Inorg. Chem. 6 (1967) 796.
[32] R.G. Asperger, Inorg. Chem. 8 (1969) 2127.
[33] B. Bosnich, Proc. R. Soc. Ser. A 297 (1967) 88.
[34] B. Bosnich, W.R. Kneen, Inorg. Chem. 9 (1970) 2191.
[35] B. Bosnich, J. MacB. Harrowfield, J. Am. Chem. Soc. 94 (1972) 3425.
[36] J. Cragel, G.R. Brubaker, Inorg. Chem. 11 (1972) 303.
[37] G.R. Brubaker, R.A. Euler, Inorg. Chem. 11 (1972) 2357.
[38] G.R. Brubaker, J. Chem. Educ. 51 (1974) 608.
[39] J.G. Gibson, E.D. McKenzie, J. Chem. Soc. (A) (1971) 1666.
[40] H.A. Goodwin, F. Lions, J. Am. Chem. Soc. 82 (1960) 5013.
[41] J.A. Chambers, T.J. Goodwin, M.W. Mulqi, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 75 (1983) 241.
[42] K. Michelsen, K.M. Nielsen, Acta Chem. Scand., Ser. A 34 (1980) 755.
[43] Y. Yamamoto, Y. Shimura, Bull. Chem. Soc. Jpn. 53 (1980) 395.
[44] R.R. Fenton, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 231 (1995) 73.
[45] T.A. Whitney, J. Org. Chem. 45 (1980) 4214.
[46] T.J. Goodwin, R.S. Vagg, P.A. Williams, J. Proc. R. Soc. New South Wales 117 (1984) 1.
[47] R.R. Fenton, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 182 (1991) 67.
[48] R.R. Fenton, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 182 (1991) 157.
[49] P. Jones, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 126 (1987) 91.
[50] R.R. Fenton, R.S. Vagg, P. Jones, P.A. Williams, Inorg. Chim. Acta 128 (1987) 219.
[51] R.R. Fenton, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 148 (1988) 37.
[52] R.R. Fenton, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 182 (1991) 59.

[53] E.F. Birse, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 148 (1988) 57.

[54] S.E. Kidd, PhD thesis, Macquarie University, 1994.

[55] M.P. Brereton, PhD thesis, Macquarie University, 1994.

[56] S.E. Kidd, F.S. Stephens, R.S. Vagg, P.A. Williams, Proc. 29th Int. Conf. Coord. Chem., Lausanne, Switzerland, July 19–24, 1992, p. 74.

[57] R.S. Vagg, Abstr. R. Aust. Chem. Inst. 10th Natl. Conv., Adelaide, Australia, Sept. 27–Oct. 2, 1995, p. 121.

[58] J.A. Chambers, M.W. Mulqi, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 81 (1984) 55.

[59] J.A. Chambers, T.J. Goodwin, M.W. Mulqi, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 88 (1984) 193.

[60] P. Jones, P.A. Williams, F.S. Stephens, R.S. Vagg, J. Coord. Chem. 16 (1987) 25.

[61] J.A. Chambers, T.J. Goodwin, P.A. Williams, F.S. Stephens, R.S. Vagg, J. Coord. Chem. 17 (1988) 277.

[62] M.A. Anderson, E.F. Birse, M.J.E. Hewlins, J.P.G. Richards, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chem. 30 (1991) 3774.

[63] J.R. Aldrich-Wright, PhD thesis, Macquarie University, 1993.

[64] E.F. Birse, P.A. Williams, F.S. Stephens, R.S. Vagg, Inorg. Chim. Acta 148 (1988) 63.

[65] M.W. Mulqi, P.A. Williams, F.S. Stephens, R.S. Vagg, Inorg. Chim. Acta 88 (1984) 183.

[66] M.A. Cox, P.A. Williams, F.S. Stephens, R.S. Vagg, J. Coord. Chem. 41 (1997) 275.

[67] M.A. Cox, P.A. Williams, F.S. Stephens, R.S. Vagg, J. Coord. Chem. 41 (1997) 291.

[68] R.R. Fenton, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 236 (1995) 109.

[69] A.M. Sargeson, H.G. Searle, Inorg. Chem. 6 (1967) 787.

[70] A.M. Sargeson, H.G. Searle, Inorg. Chem. 12 (1973) 1014.

[71] M. Delroisse, A. Rabion, F. Chardac, D. Tétard, J.-B. Verlhac, L. Fraisse, J.-L. Séris, J. Chem. Soc. Chem. Commun. (1995) 949.

[72] P.A. Goodson, J. Glerup, D.J. Hodgson, K. Michelsen, H. Weihe, Inorg. Chem. 30 (1991) 4909.

[73] J. Glerup, P.A. Goodson, A. Hazell, R. Hazell, D.J. Hodgson, C.J. McKenzie, K. Michelsen, U. Rychlewska, H. Toftlund, Inorg. Chem. 33 (1994) 4105.

[74] J.R. Aldrich-Wright, I. Greguric, R.S. Vagg, K. Vickery, P.A. Williams, J. Chromatog. A 718 (1995) 436.

[75] K.A. Vickery, A.M. Bonin, P.H. Karuso, P.A. Williams, R.S. Vagg, Abstr. 9th Int. Symp. on Mol. Recog. and Inclusion, Lyon, France, Sept. 7–12, 1996.

[76] T.J. Goodwin, M.W. Mulqi, P.A. Williams, R.S. Vagg, Inorg. Chim. Acta 98 (1985) 141.

[77] M.A. Cox, P.D. Newman, F.S. Stephens, R.S. Vagg, P.A. Williams, Inorg. Chim. Acta 221 (1994) 191.

[78] R.C. Job, J. Am. Chem. Soc. 100 (1978) 5089, and references therein.

[79] M. Yashiro, M. Ajioka, S. Yano, K. Toriumi, T. Ito, S. Yoshikawa, Inorg. Chem. 25 (1986) 1709, and references therein.

[80] M.J. Jun, C.F. Liu, Inorg. Chim. Acta 15 (1975) 111.

[81] S. Kitagawa, T. Murakami, M. Hatano, Inorg. Chem. 14 (1975) 2347.

[82] P.H. Karuso, E.M. Proudfoot, R.S. Vagg, K.A. Vickery, P.A. Williams, unpublished results.

[83] P. Leverett, J. Petherick, R.S. Vagg, P.A. Williams, in preparation.

[84] T.W. Johann, J.K. Barton, Philos. Trans. R. Soc. Lond. A 354 (1996) 299.

[85] B. Nordén, F. Tjerneld, FEBS Lett. 67 (1976) 368.

[86] T. Härd, B. Nordén, Biopolymers 25 (1986) 1209.

[87] J.K. Barton, J.J. Dannenberg, A.L. Raphael, J. Am. Chem. Soc. 104 (1982) 4967.

[88] A. Yamagishi, J. Phys. Chem. 88 (1984) 5709.

[89] J.K. Barton, A.T. Danishefsky, J.M. Goldberg, J. Am. Chem. Soc. 106 (1984) 2172.

[90] M. Eriksson, M. Leijon, C. Hiort, B. Nordén, A. Graslund, Biochemistry 33 (1994) 5031.

[91] C. Hiort, B. Nordén, A. Rodger, J. Am. Chem. Soc. 112 (1990) 1971.

[92] S. Satyanarayana, J.C. Dabrowiak, J.B. Chaires, Biochemistry 31 (1992) 9319.

[93] S. Satyanarayana, J.C. Dabrowiak, J.B. Chaires, Biochemistry 32 (1993) 2573.

[94] T.C. Strekas, A.D. Baker, L. Zaltsman, S. Wang, J. Coord. Chem. 39 (1996) 281.

[95] C.M. Dupureur, J.K. Barton, Inorg. Chem. 36 (1997) 33.

[96] P. Lincoln, A. Broo, B. Nordén, J. Am. Chem. Soc. 118 (1996) 2644.
[97] I. Haq, P. Lincoln, D. Suh, B. Nordén, B.Z. Chowdhry, J.B. Chaires, J. Am. Chem. Soc. 117 (1995) 4788.
[98] C. B Aakeröy, K.R. Seddon, Chem. Soc. Rev. 22 (1993) 397.
[99] C.M. Dupureur, J.K. Barton, J. Am. Chem. Soc. 116 (1994) 10286.
[100] K. Naing, M. Takahashi, M. Taniguchi, A. Yamagishi, Inorg. Chem. 34 (1995) 350.
[101] A. Sitlani, J.K. Barton, Biochemistry 33 (1994) 12100.
[102] R.S. Vagg, K.A. Vickery, P.A. Williams, in: A. Coleman (Ed.), Supramolecular Chemistry, Kluwer Academic Publishers, Dordrecht, submitted for publication.
[103] K.A. Vickery, J.R. Aldrich-Wright, A.M. Bonin, P.H. Karuso, P.A. Williams, R.S. Vagg, Proc. 3rd Int. Symp. on Appl. Bioinorg. Chem., Fremantle, Australia, Dec. 11–15, 1994, p. B8.
[104] F.S. Stephens, R.S. Vagg, P.A. Williams, unpublished results.
[105] A.H. Krotz, B.P. Hudson, J.K. Barton, J. Am. Chem. Soc. 115 (1993) 12577.
[106] A.H. Krotz, L.Y. Kuo, J.K. Barton, Inorg. Chem. 32 (1993) 5963.
[107] A.H. Krotz, J.K. Barton, Inorg. Chem. 33 (1994) 1940.
[108] A.H. Krotz, L.Y. Kuo, T.P. Shields, J.K. Barton, J. Am. Chem. Soc. 115 (1993) 3877.
[109] J.G. Collins, T.P. Shields, J.K. Barton, J. Am. Chem. Soc. 116 (1994) 9840.
[110] R.S. Vagg, 3D-MOL: Integrated Microcomputer Programs for Molecular Graphics, Maquarie University, 1993.
[111] H.M. Sobell, S.C. Jain, J. Mol. Biol. 68 (1972) 21.
[112] P.J. Dandliker, R.E. Holmlin, J.K. Barton, Science 275 (1997) 1465.