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The Chemistry of Novel C_2 Diazabiaryl Ligands : Cycloocta[2,1-*b*:3,4-*b*']dipyridine, Cycloocta[2,1-*b*:3,4-*b*']diquinoline and Their Related Compounds†1

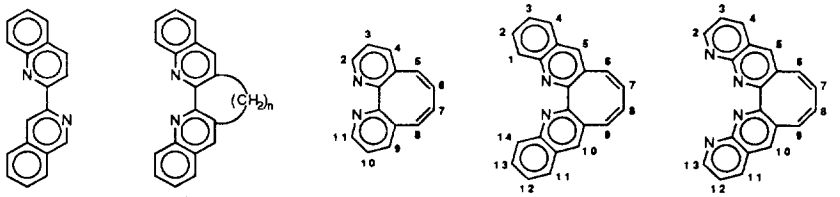
Xiu Chun Wang[2] and Henry N.C. Wong*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong.

Abstract : Three novel cyclooctadiazabiaryl ligands, namely cycloocta[2,1-*b*:3,4-*b*']dipyridine (**3**), cycloocta[2,1-*b*:3,4-*b*']diquinoline (**4**) and cycloocta[2,1-*b*:3,4-*b*']di[1,8]naphthyridine (**5**) have been synthesized and a number of metal complexes have been prepared for these novel ligands. The energy barrier to ring inversion of these compounds have also been studied.

INTRODUCTION

The chemistry of diazabiaryl compounds such as dipyridine, diquinoline, and compounds containing polypyridyl subunits and their complexes has been a matter of considerable interest in recent years,[3] because they have found application in the domains of host-guest chemistry,[4] photochemistry,[5] biochemistry[6] and organic synthesis.[7] X-ray crystallographic results reveal that 2,2'-diquinoline (**1**) exists in a *trans*-planar conformation in the solid state in order to achieve maximum conjugative interaction and minimum lone-pair repulsion.[8] Dipole moment studies show that in benzene solution **1** is still in transoid configuration, with a net interplanar angle of 20°-30°.[3a] In the metal complexes of **1**, however, the dihedral angle defined by the two heterocyclic rings becomes 0° or very close to 0°.[9]



Pioneered by the elegant study of Thummel,[10] the most significant structural feature of the diazabiaryl compounds **2** is the variation of the dihedral angle α as a function of the length of the annelating bridge at the 3,3'-positions. Consequently, the shape of the chelating envelope is thus influenced. While the trimethylene bridged diquinoline **2a** undergoes rapid conformational inversion, broadening and coalescence of the methylene ^{1}H-NMR signals of the tetramethylene bridged molecule **2b** were observed only at above 135°C,

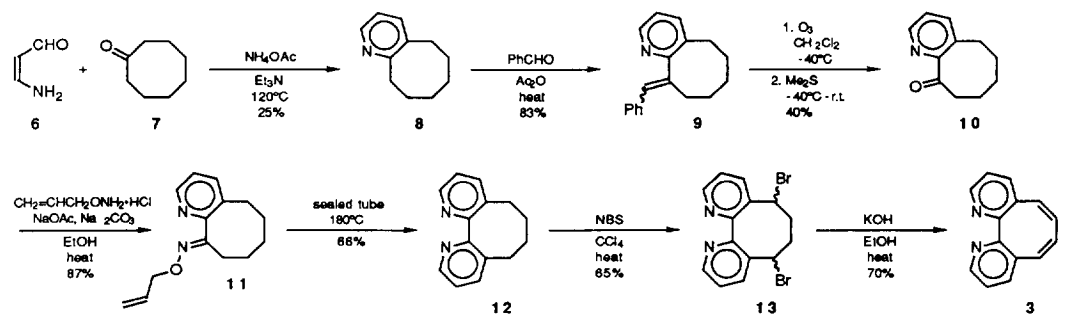
indicating that the barrier to inversion is sufficiently high that **2b** is rigid at room temperature.[11]

In light of the aforementioned points, it is thus interesting to design and to synthesize novel 2,2'-diazabiaryl ligands in order to fully comprehend their structural particulars as well as their transition metal coordination chemistry. In conjunction with our long-standing curiosity in novel planar fully-conjugated eight-membered ring compounds,[12] fusion of a cyclooctatetraene ring to 2,2'-diazabiaryl ligands is likely to result in conformationally mobile compounds, whose non-planar C_2 geometries might possibly be flattened by transition metal complexation.[12] We wish to report herein the synthesis and studies of cycloocta[2,1-*b*:3,4-*b*']dipyridine (**3**), cycloocta[2,1-*b*:3,4-*b*']diquinoline (**4**) and cycloocta[2,1-*b*:3,4-*b*']di[1,8]naphthyridine (**5**).

RESULTS AND DISCUSSION

I. Synthesis of Ligands.

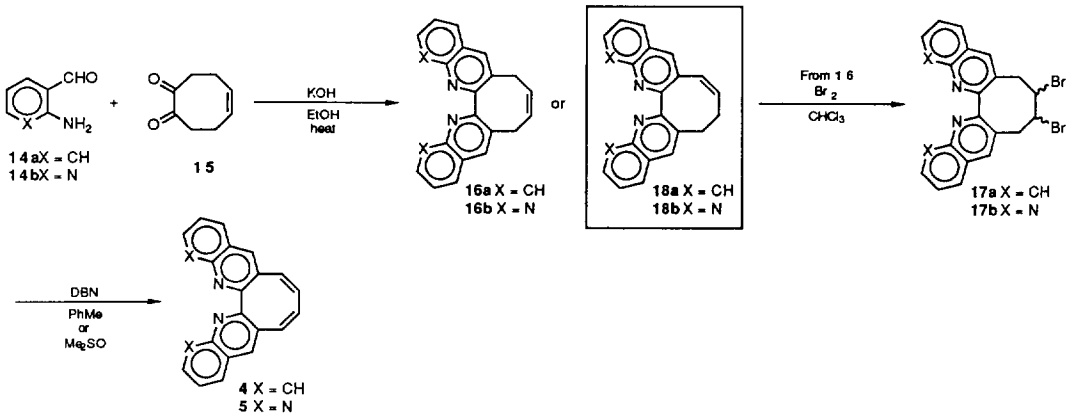
As depicted in Scheme 1, the key starting material **10** was obtained from **8**. Although the synthesis of **8** in two steps has been reported,[10b,13] we discovered independently that direct condensation of β-aminoacrolein[14] (**6**) with cyclooctanone (**7**) in the presense of a catalytic amount of ammonium acetate and triethylamine also gave **8**, albeit in only 25%. Condensation of **8** with benzaldehyde in acetic anhydride for 8 days yielded the benzylidene **9**,[10b] which was converted by ozonolysis and reduction to key compound **10**.[10b] Oxime **11** was prepared by reacting **10** with *O*-allylhydroxylamine hydrochloride.[15] The resulted **11** was heated at 180℃ in a sealed tube for 52 hours to give dipyridine **12**. Bromination of **12** with 2 equivalents of NBS provided a mixture of dibromides **13**, which was not separated and was allowed to undergo dehydrobromination with alcoholic KOH to yield **3** as colorless crystals. The four olefinic protons of **3** shows an AA'BB' pattern at δ 6.13 and 6.61 in its ^{1}H-NMR spectrum ($CDCl_3$). The aromatic region of **3** shows three doublet of doublets at δ 7.31, 7.44 and 8.68, which are typical of 2,3-disubstituted pyridine derivatives.



Scheme 1

The pivotal step for the construction of **4** and **5** is the Friedländer condensation[10,11,16] of **15**[17] with appropriate β-amino-α,β-unsaturated aldehydes **14a**[18] or **14b**[19] (Scheme 2). Thus, an ethanolic solution of **15** and **14a** was heated together with a catalytic amount of KOH to generate the condensation product **16a** in 63% yield, while 60% yield of **16b** was obtained from a similar reaction between **15** and **14b**. It is important to note that when the reactions were carried out under more basic conditions and with prolonged heating, the 6,7-dihydro isomers **18a** (60%) and **18b** (60%) resulted respectively due to the isomerization of the double bonds to the conjugated position. In their ^{1}H-NMR spectra ($CDCl_3$), the two olefinic protons on the eight-membered ring in **16a** and **16b** show only one multiplet at δ 5.97 and 5.90 respectively owing to the presence of a C_2

axis, whilst these protons in **18a** and **18b** appear as one multiplet and one doublet at δ 5.75 and 6.58 as well as at δ 5.78 and 6.60, respectively. Bromination of **16a** and **16b** yielded accordingly dibromides **17a** (92%) and **17b** (90%) as mixtures of isomers, which underwent dehydrohydromination with DBN to afford the expected molecules **4** and **5** as colorless crystals in 67% and 65% yield, respectively. Diquinoline **4** has good solubility in $CHCl_3$ and EtOH, but **5** is sparingly soluble in $CHCl_3$ as well as in water, and is moderately soluble in MeOH only on heating. The four olefinic protons show an AA'BB' pattern in their ^{1}H-NMR spectra ($CDCl_3$) at δ 6.18 and 6.83 for **4**, and δ 6.21 and 6.91 for **5**.



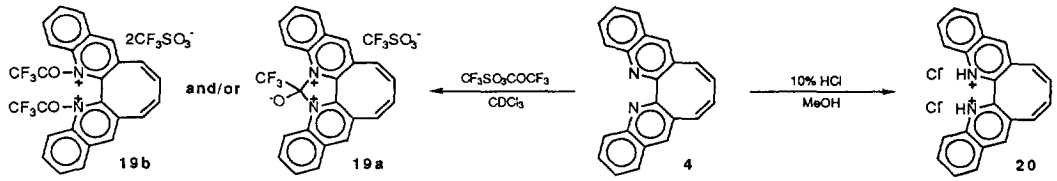
Scheme 2

II. Basicity of Cycloocta[2,1-*b*:3,4-*b*']diquinoline (4).

The coordination effectiveness of the diazabiaryl compounds is a factor of both the availability of the nitrogen lone pair electrons (basicity)[20] as well as the spatial orientation of these lone pairs with respect to one another.[10a] An approximate measurement of the σ-donor strength is the pK_a values of the conjugated acids, i.e., the equilibrium constants for complexation with a proton. It is known that the quinoline ring is significantly more basic (pK_a 4.90) than the 1,8-naphthyridine ring (pK_{a1} 2.37) but less basic than the pyridine ring (pK_a 5.18).[21] The basicity is also governed by the dihedral angle defined by the two heterocyclic rings in ligands such as **3**, **4** and **5**.[10b] Since the aromatic moieties in these molecules are of similar orientation, the basicity of which is likely in the following decreasing sequence: **3** > **4** > **5**. In light of this generalization, only the pK_{a1} value of **4** was determined by potentiometric titration. The half-neutralization potential (HNP) was found to be 329 mv and the pK_{a1} was duly computed[20] to be 3.90. When compared with pyridine and quinoline, **4** is of the lowest basicity. This result is consistent with the rules that the electronic effect of a 2-substituted-azaaryl group will generally be deactivating and that the substantially increased dihedral angle will reduce the pK_a of a diazabiaryl base.[10b] From an X-ray crystallographic analysis of **4**, its dihedral angle α has been determined to be 62.8° and the α angle of **3** and **5** is believed to be of similar values.[1a]

In order to test the reactivity of **4** as a pyridine base, it was allowed to react with a highly electrophilic trifluoroacetylating reagent, namely trifluoroacetyl triflate (TFAT),[22] and with 10% HCl, generating presumably (*N*,*N*)-trifluoroacetyl-cycloocta[2,1-*b*:3,4-*b*']diquinolinium triflate (**19a**) and dihydrochloride **20**, respectively. As can be seen in Scheme 3, the orange-red **19a** was assigned as a monotriflate and is extremely sensitive to moisture and air and the color of the solution faded immediately when the solution was exposed to air. The structure of **19a** could not be unequivocally established due to its instability. However, when a large excess of

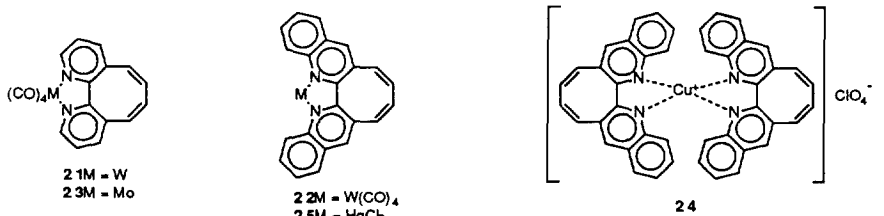
TFAT was used, (*N*,*N*)-bis(trifluoroacetyl)-cycloocta[2,1-*b*:3,4-*b*']diquinolinium ditriflate (**19b**) was presumably produced. To prevent decomposition of **19a** and **19b**, they were only examined in a sealed NMR tube. The ^{1}H-NMR spectrum of **19a** at 22℃ shows a singlet for the four olefinic protons $H_{6,7,8,9}$ at δ 6.55, which becomes a well resolved AA'BB' system (J_{AB} = 11, $J_{BB'}$ = 3 Hz, $J_{AB'}$ = -0.7 Hz) at below 11℃. Due to the diastereotopic tetrahedral carbon, monotriflate **19a** is deprived of C_2 symmetry. As such, the absorption of the four olefinic protons should not be as one singlet at 22℃ or as a symmetrical AA'BB' system at below 11℃. Our study might therefore imply that the rings of **19a** are perhaps undergoing a fast inversion and/or being flattened to a coplanar geometry. All the ^{1}H-NMR signals of **19a** are shifted to up-field, which is likely because of the paratropic contribution from a nearly planar 8π system.[12] On the other hand, **19b** displays a regular ^{1}H-NMR spectrum reminiscent of a non-planar molecule, of which relatively down-field absorptions are detected.



Scheme 3

III. Synthesis of Metal Complexes.

2,2'-Diazabiaryl ligands have been used to prepare metal complexes with most of the transition metals including the lanthanide series.[23] In order to obtain coordination compounds with different oxidation state as well as with diverse coordination geometries (tetrahedral, square planar, and octahedral), we have attempted to prepare complexes for the ligands **3**, **4** and **5** using Pd(II), Ni(II), Fe(II), Mn(IV), U(II), Ru(II), Ru(III), Cu(II), Zn(II), Hg(II), Mo(0), and W(0) as the metal nucleus. Unfortunately, only Pd(II), Zn(II), Hg(II), Mo(0), W(0) and Cu(I) complexes of **3** and **4** were suitable for further analysis. Complexes of the other metal ions were either insoluble in all the solvents tested or decomposed in solution. All the metal complexes of **5** were insoluble in organic solvents as well as in water. For this reason, the coordination chemistry of **5** was not pursued further.



(a) Tungsten (0) complexes of cycloocta[2,1-*b*:3,4-*b*']dipyridine (3) and cycloocta[2,1-*b*:3,4-*b*']diquinoline (4).[1c]

When **3** and **4** were treated with one equivalent of $W(CO)_6$ in xylenes for 3 hours at reflux, the mononuclear complexes **21** and **22** were obtained as dark red crystals in 53% and 81% yield, respectively. Their compositions were substantiated by elemental analyses. These tungsten (0) complexes are soluble in $CHCl_3$, acetone and benzene but are sparingly soluble in EtOH. While **21** and **22** are quite stable in their

crystalline forms, in solution they decomposed to give greenish-grey solid materials on standing at room temperature after a couple of days. In C_6D_6, the ^{1}H-NMR spectra of **21** and **22** displays similar AA'BB' absorptions (**21**: $H_{6,7}$ δ 5.28 and $H_{5,8}$ δ 5.60; **22**: $H_{7,8}$ δ 5.81 and $H_{6,9}$ δ 6.42) of the four cyclooctatraenyl protons. The remarkable up-field shift of the cyclooctatetraenyl absorptions in **21** as compared with those of **3** ($H_{6,7}$ δ 5.71 and $H_{5,8}$ δ 6.20) is presumably owing either to the flattening of the molecule towards a distorted 4nπ conjugated system,[12] or more correctly to the metal to ligand charge-transfer (MLCT) involving low lying π* orbitals.[24] Nonetheless, such effect is apparently not significant for **22** as compared with **4** ($H_{7,8}$ δ 5.82 and $H_{6,9}$ δ 6.47). Though the magnitude of the up-field shift for the olefinic protons in **21** and **22** cannot be quantitatively assessed due to the lack of unequivocal structural parameters, it is likely that there is a substantial MLCT effect for **21**. As a result, the shielded H_5, H_6, H_7 and H_8 exhibit absorptions at a more up-field region than those of **3**. The UV spectra of **21** and **3** are in good agreement with the above proposition, showing highest energy bands at λ_{max} 490 nm and 272 nm, respectively. It is noteworthy that the energy involving in the metal to ligand orbital-transition of **21** might be very close to the presumably planar tungsten (0) complex of 2,2'-bipyridine, whose absorption maximum is shown at 487 nm.[24e] The UV spectra of **22** and **4**, on the other hand, are very similar, showing highest energy bands both at 323 nm. The aromatic proton NMR signals of **21** and **22** also appear at higher field than those of the free ligands **3** and **4**. In contrast, the protons ($H_{1,14}$) adjacent to the coordinating tungsten in **22** show slightly down-field shift (δ 9.30) owing to metal complexation.

(b) Molybdenum (0) complex of cycloocta[2,1-*b*:3,4-*b*']dipyridine (3). [1b,1c]

Due to the difficulty encountered in the X-ray single crystal structure analysis of **21** and **22**, the molybdenum complex **23** was prepared in the hope that this molybdenum complex could be readily analyzed by X-ray crystallography. Thus, a mixture of **3** and one equivalent of $Mo(CO)_6$ in xylenes was heated to reflux to give a deep-red solution, of which a red spot for the product and a trace amount of the starting **3** were detected by thin layer chromatography. Despite that prolonged heating consumed all the ligand, a greyish-green solid material was also formed, which was believed to be an oxidation product.[25] This oxidation product was insoluble in organic solvents and water. After the reaction mixture was cooled to room temperature, pentane was added to induce crystallization of the Mo(0) complex at low temperature. The red crystals of **23** are soluble in $CHCl_3$ and benzene, but decompose gradually in solution on standing at room temperature. Expectedly, the four cyclooctatetraenyl protons again exhibit an AA'BB' signals ($H_{6,7}$ δ 5.33 and $H_{5,8}$ δ 5.59) in its ^{1}H-NMR spectrum (C_6D_6). The structure of **23** was confirmed by an X-ray crystallographic analysis,[1b] which gives a value of 51° for the torsional angle C(5)-C(6)-C(7)-C(8) as well as a value of 31° for the dihedral angle α. These angles are less than those of the similar torsional angles in **4** [C(6)-C(7)-C(8)-C(9) = 60° and α = 63°, respectively]. These results demonstrate that there is expectedly an eight-membered ring flattening effect due to metal coordination.

(c) Copper (I) complex of cycloocta[2,1-*b*:3,4-*b*']diquinoline (4). [1a,1c]

The chemistry of copper (I) and copper (II) complexes of polypyridyl derivatives has been extensively investigated.[26] The Cu(II) complexes are generally prepared using the Cu(II) salts in polar solvents,[27] while Cu(I) complexes can be obtained either by reduction of the corresponding Cu(II) complexes or from the Cu(I) salts directly.[28] In our own experiment, a solution of **4** and an excess of $Cu(ClO_4)_2 \cdot 6H_2O$ in absolute EtOH was heated to reflux. The color of the solution turned from green to deep-red during the reaction. Water was then added to the cooled reaction mixture. On evaporation of the solvent at room temperature red crystals were formed. Interestingly, the complex **24** isolated was found to be a bis-ligand Cu(I) complex. It is readily soluble

in $CHCl_3$, acetone and hot EtOH, but is insoluble in water. Another way in which **24** could be prepared was by using *in situ* generated $CuClO_4$,[28b] obtained by warming CuCl and $NaClO_4$ in CH_3CN. A dark red solution was produced when the yellow $CuClO_4$ solution was added to a CH_2Cl_2 solution of **4**. The solvents were evaporated and the residue crystallized from 50% aqueous EtOH to give **24** in 31% yield. The structure of **24** was confirmed by an X-ray crystallographic study.[1a] Again, the value of 52° for the torsional angle C(6)-C(7)-C(8)-C(9) and the value of 38° for the dihedral angle α are both smaller than those of **4** (60° and 63°, respectively).

(d) Mercury (II) and zinc (II) complexes of cycloocta[2,1-*b*:3,4-*b*']diquinoline (4).

By adding a solution of an equimolar amount of $HgCl_2$ or $ZnCl_2$ to an absolute EtOH solution of ligand **4**, the Hg(II) complex **25** and Zn(II) complex **26** were obtained in an almost quantitative yield. In both complexes, the elemental analyses are in satisfactory agreement with those calculated for 1:1 complexes. The Hg(II) complex **25** is slightly soluble in cold EtOH but is readily soluble in acetone and hot $CHCl_3$. Downfield shifts are observed for the aromatic protons in the ^{1}H-NMR spectrum ($CDCl_3$) of **25**. The Zn(II) complex **26**, on the other hand, is insoluble in all the solvents tested. When **26** was heated in d_6-DMSO, a clear solution was produced, the ^{1}H-NMR spectrum of which indicates that **26** has decomposed to regenerate the free ligand **4**. Nevertheless, the IR (KBr) spectrum of **26** shows the expected absorptions: 1448, 1450, 1416, 1360, 1299, 1200, 1140, 1031, 959, 940, 780, 749, and 735 cm^{-1}.

(e) Palladium (II) complexes of cycloocta[2,1-*b*:3,4-*b*']dipyridine (3).[1b]

The chiral palladium complex **27**[29] has been employed in the chiral recognition of 1,1'-bi-isoquinoline by Dai and his coworkers.[30] Notwithstanding the fact that 1,1'-bi-isoquinoline is able to undergo rapid rotation around the covalent single bond connecting the two isoquinoline rings, its configuration became fixed in the complexes with (*R*,*R*)-**27** or (*S*,*S*)-**27**, generating respectively two binuclear complexes. With (*S*,*S*)-**27**, the product was confirmed to be the (*S*,*S*,*S*) complex by an X-ray crystallographic study.[30] Likewise, the (*R*,*R*)-**27** and 1,1'-bi-isoquinoline afforded the (*R*,*R*,*R*) complex.[30] In our own attempted chiral resolution of **3** (Scheme 4), two equivalents of **3** were added to a suspension of one equivalent respectively of (*R*,*R*)-(-)-**27** or (*S*,*S*)-**27** in cold MeOH. The complexes formed were converted to the perchlorates by adding $NaClO_4$ to the reaction mixtures. Light yellowish crystals of two complexes were formed almost quantitatively, with the same melting range of 198-200°C. Based on the identical ^{1}H-NMR spectra[1b] of these complexes as well as on the evidence from the 2D ^{1}H-^{1}H COSY and NOESY data of (*R*,*R*,*R*)-**28** (Table 1),[1b] the structures of them were suggested to be the enantiomeric (*R*,*R*,*R*)-**28** and (*S*,*S*,*S*)-**28**.[31] As can be seen in Table 1, all the four *N*-Me groups are correlated, which is indicative that (*R*,*R*,*R*)-**28** is a pure diastereoisomer. Moreover, compelling evidence for its (*R*,*R*,*R*) stereochemistry can be obtained by observing in the 2D NOESY data a strong correlation between H_2 and Me_a. Examination of the 1D ^{1}H-NMR spectrum of **28** also reveals that Mea is eof the pyridine rings due to the (*R*) stereochemical configuration of the ligand. The integration of the ^{1}H-NMR spectra and elemental analysis results both reveal that **28** are binuclear complexes. In the ^{1}H-NMR spectra of **28**, the doubled absorptions of each pair of symmetrically related protons (H_2 and H_{11}, H_3 and H_{10}, H_4 and H_9, H_5 and H_8, etc.) were unexpected. On the pessimistic side, the complicated ^{1}H-NMR spectra of **28** (*vide infra*) can be explained as due to the absorptions of a mixture of the (*R*,*R*,*R*) and (*R*,*R*,*S*) or that of the (*S*,*S*,*S*) and (*S*,*S*,*R*) diastereoisomers. However, this appears to be unlikely because repeated crystallization of both complexes did not result in change of the melting range and the ^{1}H-NMR spectra. On the optimistic side, it is

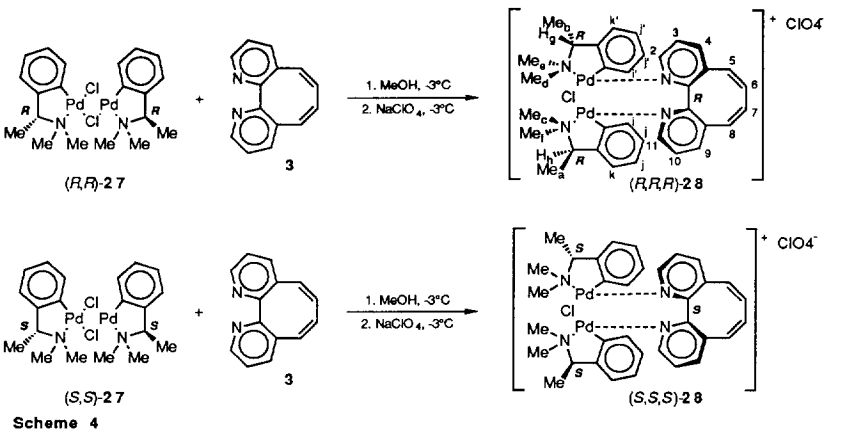
also possible that both (*R*,*R*,*R*)-**28** and (*S*,*S*,*S*)-**28** are so sterically crowded that the C_2 axis is no longer dominant. To examine the symmetry properties of the reagent **27**, the ^{1}H-NMR spectrum of (*R*,*R*)-**27** was recorded. The resonances of the four *N*-methyl groups exhibit four singlets instead of two expected for a molecule with C_2 axis, confirming the deviation of the molecule, however slightly, from C_2 symmetry. A lack of C_2 symmetry in the rigid and sterically crowded (*R*,*R*,*R*)-**28** and (*S*,*S*,*S*)-**28** is therefore likely. The change of the symmetric AA'BB' olefinic absorption in the free ligand **3** to the complicated ABCD system in **28** around δ 6.18, on the basis of decoupling experiment, might also be explained by the absence of C_2 symmetry. Indeed, computer simulation of the olefinic absorptions (H_5, H_6, H_7 and H_8) confirms that they constitute a complex four spin ABCD system (*vide infra*), which indirectly supports our argument that both (*R*,*R*,*R*)-**28** and (*S*,*S*,*S*)-**28** are pure compounds.

Table 1. 2D ^{1}H-^{1}H COSY and NOESY Correlation

Signal	*COSY*	*NOESY*
Me_a	H_h	Me_c, H_2
Me_b	H_g	Me_e
Me_c	-	Me_a, Me_d, Me_f, H_3, H_4, H_9, H_{10}
Me_d	-	Me_c, Me_e, H_g, H_2, H_3, H_4
Me_e	-	Me_b, Me_d, Me_f, H_9, H_{10}, H_{11}
Me_f	-	Me_c, Me_e, H_4, H_9, H_{10}, H_{11}
H_g	Me_b	Me_d
H_h	Me_a	-
H_i	H_j	H_j, H_{11}
$H_{i'}$	$H_{j'}$	$H_{j'}$, H_2
H_j	H_i, H_k	H_i, H_k, H_5, H_6, H_{11}
$H_{j'}$	$H_{i'}$, $H_{k'}$	$H_{i'}$, $H_{k'}$, H_2, H_7, H_8
H_k	H_j	H_j, H_9, H_{10}, H_{11}
$H_{k'}$	$H_{j'}$	$H_{j'}$, H_2, H_3, H_4
H_2	H_3, H_4	Me_a, Me_d, $H_{i'}$, $H_{j'}$, $H_{k'}$, H_7, H_8
H_3	H_2, H_4	Me_c, Me_d, $H_{k'}$, H_2, H_4
H_4	H_2, H_3	Me_c, Me_d, Me_f, $H_{k'}$, H_3, H_5
H_5	H_6, H_7	H_j, H_4, H_6, H_{11}
H_6	H_5, H_7, H_8	H_j, H_5, H_{11}
H_7	H_5, H_6, H_8	$H_{j'}$, H_2, H_8
H_8	H_6, H_7	$H_{j'}$, H_2, H_7, H_9
H_9	H_{10}, H_{11}	Me_c, Me_e, Me_f, H_k, H_8, H_{10}
H_{10}	H_9, H_{11}	Me_c, Me_e, Me_f, H_k, H_9, H_{11}
H_{11}	H_9, H_{10}	Me_e, Me_f, H_i, H_j, H_k, H_5, H_6, H_{10}

It was also anticipated that upon heating (*R*,*R*,*R*)-**28** might undergo conformational inversion to furnish a diastereomeric mixture of (*R*,*R*,*R*)-**28** and (*R*,*R*,*S*)-**28**, which are expected to display a more complicated ^{1}H-NMR spectrum. However, no change in the ^{1}H-NMR spectrum of (*R*,*R*,*R*)-**28** in $CDBr_3$ was observed after the solution had been heated to 100°C and had been subsequently cooled. Higher temperature only led to decomposition of the sample.

Despite that a great deal of effort was made, we were unable to obtain good quality single crystals of (*R*,*R*,*R*)-**28** or (*S*,*S*,*S*)-**28** for X-ray structural elucidation.

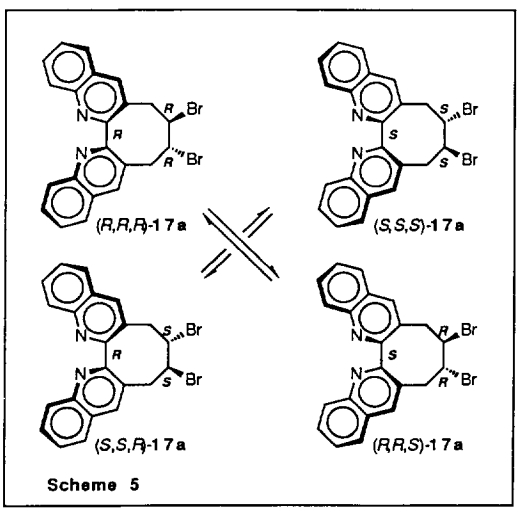


Scheme 4

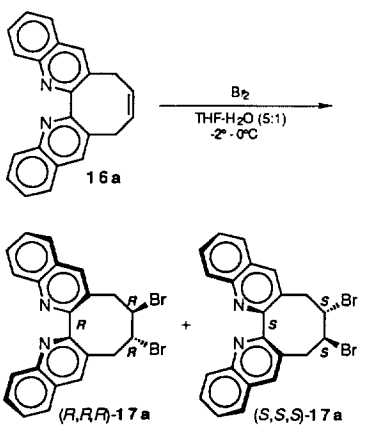
IV. Determination of Energy Barriers to Ring Inversion.

(a) Synthesis and mutarotation of (*R*,*R*,*R*/S,S,S)-7,8-dibromo-6,7,8,9-tetrahydrocycloocta[2,1-*b*:3,4-*b*']diquinoline (17a).[1c]

A 3,3'-annelated 2,2'-diazabiaryl compound is of *R* configuration if its rings are arranged in a right helical way, and is defined as *S* configuration in the case of a left helix.[31] The dibromide **17a** should have two diastereomeric forms, namely the (*R*,*R*,*R*/*S*,*S*,*S*) form and the (*S*,*S*,*R*/*R*,*R*,*S*) form. Each of these forms should contain two enantiomers as illustrated in Scheme 5. These diastereomeric forms are interconvertable at elevated temperature through a mutarotation process.[31c] In order to investigate the ring inversion in connection with mutatrotation, it is important to isolate the diastereomeric mixture of **17a** into the two corresponding pure diastereomers, namely (*R*,*R*,*R*/*S*,*S*,*S*)-**17a** and (*S*,*S*,*R*/*R*,*R*,*S*)-**17a**.



Scheme 5



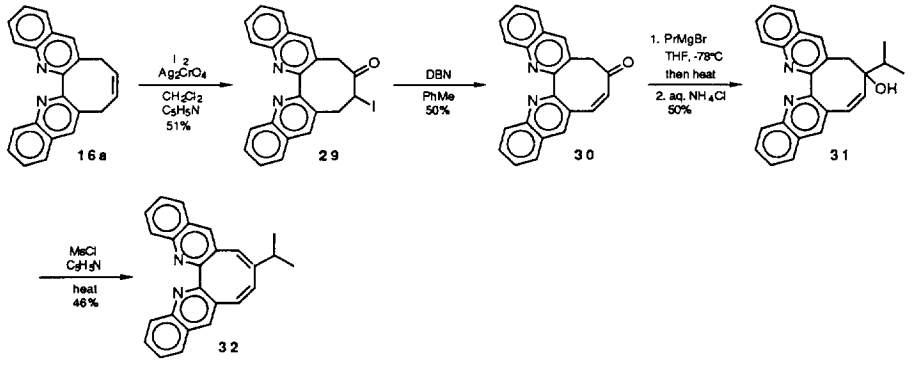
Scheme 6

The separation of the diastereomers was however accomplishd by thin layer chromatography, albeit in only very unsatisfactory yield. Another way in which (*R*,*R*,*R*/*S*,*S*,*S*)-**17a** could be obtained was by the

bromination of **16a** in THF-water at low temperature (Scheme 6). The reason for the diastereoselection is unclear at the moment, but it is believed that the sterically disfavored shielding effect of the quinoline ring might play an important role. The stereochemistry of (*R,R,R/S,S,S*)-**17a** was assigned by ^{1}H-NMR spectrometry ($CDCl_3$), which shows a doublet for the methine protons at δ 4.54 (2H). In addition to the signal at δ 4.54, the diastereomeric mixture (*R,R,R/S,S,S/S,S,R/R,R,S*)-**17a**, prepared by bromination of **16a** in $CHCl_3$ at room temperature, shows one more methine doublet at δ 5.10, which presumably is due to (*S,S,R/R,R,S*)-**17a**. Upon heating of an NMR sample of (*R,R,R/S,S,S*)-**17a** in d_6-DMSO to 140℃, a mutarotation process presumably took place. On cooling of the NMR sample to room temperature, the sample shows two absorption peaks in the ratio of approximately 1:1 at δ 4.54 and 5.10, which are due to the signals of the methine protons of the diasteromeric mixture (*R,R,R/S,S,S/S,S,R/R,R,S*)-**17a**. When a proper variable temperature ^{1}H-NMR spectral study was performed, the coalescence temperature (T_c) has been found to be 110℃ and the corresponding $\Delta G_c^{\neq}$ is therefore 93 kJ/mol.[1c,32]

(b) Synthesis and variable temperature study of 7-isopropyl-cycloocta[2,1-*b*:3,4-*b*']diquinoline (32).

It has been well established that the measurement of barrier to inversion for isopropyl-substituted molecules with a C_2 axis can frequently be accomplished by recording the dynamic ^{1}H-NMR signals of the diastereotopic methyl groups.[33] By synthesizing an isopropyl-substituted molecule **32** (Scheme 7), it is expected that the ring inversion process could be made observable through variable temperature ^{1}H-NMR spectrometry. Utilizing **16a** as the starting material, the iodo ketone **29** was obtained by employing an oxidative iodination route.[34] Ketone **29** was converted to the α,β-unsaturated ketone **30** through dehydroiodination with DBN. The isopropylation of the eight-membered ring was achieved by adding isopropylmagnesium bromide (prepared *in situ* from isopropyl bromide and magnesium metal) carefully to a THF solution of **30** at -78℃ until a pale-pink color of the solution persisted. It is important to note that excess Grignard reagent must be avoided in order to suppress side reactions. Dehydration of **31** with MsCl in pyridine yielded 7-isopropyl-cycloocta[2,1-*b*:3,4-*b*']diquinoline (**32**) as colorless crystals, whose ^{1}H-NMR spectrum manifests two doublets due to the two diastereotopic methyl groups. The absorptions of the three olefinic protons appear at δ 6.24 (d, J = 11 Hz), 6.59 (s), and 6.85 (d, J = 11 Hz).



Scheme 7

It was anticipated that the barrier to inversion of **32** could be determined by temperature dependent ^{1}H-NMR signals of the diastereotopic methyl groups. Unfortunately, no coalescence of the two methyl doublets

was observed when a $CDBr_3$ solution of **32** was heated to 135℃. From this survey, it is likely that the lower limit of the inversion barrier for **32** and **4** should be approximately 100 kJ/mol. This value is nonetheless consistent with the result of the aforementioned mutarotation study ($\Delta G_c^{\neq}$ = 93 kJ/mol, T_c = 110℃), and is also confirmed by dynamic circular dichroism spectroscopic study[35] of the enantiomers of **3** ($\Delta G_c^{\neq}$ = 105 kJ/mol),[36] **4** ($\Delta G_c^{\neq}$ = 109 kJ/mol),[37] and **5** ($\Delta G_c^{\neq}$ = 108 kJ/mol).[37]

CONCLUSION

Compounds **3** and **4** serve as ligands to form stable metal complexes in the solid state. The instability of these complexes in solution can perhaps be attributed to their weak coordination bonds in comparison with the corresponding ligands such as dipyridine. Since planar geometry is necessary for maximun coordination between the metal nucleus and the ligand nitrogen atoms, deviation of the heteroaromatic rings from a coplanar orientation may lead to weak coordination bonds in the complexes of **3** and **4**. The incorporation of a cyclooctatetraene moiety to the diazabiaryls therefore appears to greatly increase the energy requirement for the molecule to undergo ring inversion, as can be substantiated by a mutarotation study on **17a**, by an attempted variable temperature ^{1}H-NMR analysis on **32**, as well as by dynamic CD studies on the resolved enantiomers of **3**, **4** and **5**. The planarization of **3** and **4** during complex formation is thereby prevented by such structural rigidity. Despite this, a slight flattening of the eigh-membered rings as compared with their corresponding free ligands has however been confirmed for complexes **23** and **24** by X-ray crystallographic results.[1a,1b] Accordingly, the dihedral angles are generally reduced in the complexes, especially on the diazabiaryl sites of **23** and **24**, but their ligand parts remain twisted to show C_2 molecular symmetry.

EXPERIMENTAL SECTION

Solvents used were purified by standard procedures. All evaporation of organic solvents was carried out by a rotary evaporator in conjunction with a water aspirator. ^{1}H-NMR spectra were recorded on a Bruker Cryospec WM 250 (250 MHz) spectrometer or a Jeol PMX 60SI (60 MHz) spectrometer. The chemical shifts were measured with tetramethylsilane (TMS) serving as internal standard and $CDCl_3$ was used as the solvent unless stated otherwise. Mass spectra were recorded on a VG Micromass 7070F spectrometer. IR spectra were run on a Jasco A-100 Infrared spectrophotometer. UV absorption spectra were recorded on a Shimadzu 240 spectrophotometer. Basicity was determined according to the method of Markgraf and Katt[38] by potentiometric titration with a Radiometer RTS 622 recording titration system. Elemental analyses were carried out at Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, China. Merck silica gel (60 F_{254}) precoated on aluminum sheet was used for TLC studies and Merck silica gel (70-230 mesh) was used for column chromatography. Melting points were measured on a hot-stage and are uncorrected.

5,6,7,8,9,10-Hexahydro-cycloocta[*b*]pyridine (8)

A mixture of cyclooctanone (**7**) (8.9 g, 70 mmol), 3-aminoacrolein (**6**) (5 g, 70 mmol), anhyd. NH_4OAc (0.5 g, 6 mmol), and Et_3N (2 mL) was heated at 130℃ under nitrogen for 20 h. The resulting solution was cooled and dissolved in 10% HCl (100 mL). The acidic solution was washed with Et_2O (3 X 20 mL) to remove the unreacted cyclooctanone, and was then neutralized with 20% aq. NaOH (55 mL). The aq. layer was extracted with Et_2O (3 X 100 mL). The Et_2O solution was dried over anhyd. K_2CO_3, and the solvent was removed. The residue thus obtained was chromatographed on a basic alumina column (eluted with Et_2O) to afford **8** as light yellowish oil (2.8 g, 25%), bp 60-70℃ (0.5 mmHg) [lit[16] bp 95-110℃ (3 mmHg)]. MS: *m/e* 161 (M^+); ^{1}H-NMR (60 MHz): δ 1.53 (m, 8H), 2.79 (m, 4H), 6.88 (dd, 1H, H_3, J = 8, 5 Hz), 7.20 (dd, 1H, H_2, J = 8, 3 Hz), 8.20 (dd, 1H, H_4, J = 5, 3 Hz).

10-Benzylidene-5,6,7,8,9,10-hexahydro-cycloocta[*b*]pyridine (9)

A mixture of **8** (3.3 g, 20 mmol), freshly distilled benzaldehyde (4.3 g, 40 mmol) in Ac_2O (5 mL) was heated to reflux with stirring under nitrogen for 8 days. Benzaldehyde, Ac_2O, and HOAc were then removed by distillation under reduced pressure. The residue was fractionally distilled to give **9** (4.2 g, 83%), bp 160-180℃ (0.5 mmHg) [lit[10b] bp 140-160℃ (0.3 mmHg)]. MS: *m/e* 249 (M^+); ^{1}H-NMR (60 MHz): δ 1.48 (m, 6H), 2.71 (m, 4H), 6.49 (s, 1H), 7.08 (dd, 1H), 7.33 (br s, 5H), 7.42 (dd, 1H, J = 5.0 Hz), 8.46 (dd, 1H, J = 7.0, 1.8 Hz).

5,6,7,8,9,10-Hexahydro-cycloocta[*b*]pyridin-10(9*H*)-one (10)

A solution of **9** (3 g, 12 mmol) in CH_2Cl_2 (150 mL) was treated with a mixture of ozone and oxygen at -40℃ until the reaction was completed (monitored by TLC analysis). The dissolved ozone was purged with bubbling nitrogen through the solution. Me_2S (16 mL) was added, and the mixture was stirred for 0.5 h at -35℃ and then at r.t. overnight. The solution was washed with water (50 mL), 5% aq. NaOH (50 mL), dried over anhyd. K_2CO_3, and concentrated to give a yellow oil. Chromatography on silica gel (EtOAc-hexanes 1:1) yielded ketone **10** (0.84 g, 40%), bp 120-135℃ (0.5 mmHg) [lit[10b] bp 105-110℃ (0.2 mmHg)]. MS: *m/e* 175 (M^+); ^{1}H-NMR (60 MHz): δ 1.64 (br s, 6H), 2.78 (br s, 4H), 7.26 (dd, 1H, J = 8, 5 Hz), 7.55 (d, 1H, J = 8 Hz), 8.44 (d, 1H, J = 5 Hz).

5,6,7,8,9,10-Hexahydro-cycloocta[*b*]pyridin-10(9*H*)-one oxime *O*-(allyl ether) (11)

A solution of **10** (1.75 g, 10 mmol), *O*-allylhydroxylamine hydrochloride (1.1 g, 10 mmol), anhyd. NaOAc (1.2 g, 15 mmol), and anhyd. Na_2CO_3 (1.2 g, 10 mmol) in EtOH (40 mL) was refluxed for 2 h. After evaporation of the solvent, the residue was extracted with $CHCl_3$ (3 X 30 mL). The $CHCl_3$ solution was washed with water (30 mL), dried over anhyd. $MgSO_4$, concentrated and distilled to give the desired product **11** as a pink oil (2 g, 87%), bp 130-140℃ (0.3 mmHg) [lit[10b] bp 130℃ (0.2 mmHg)]. ^{1}H-NMR (60 MHz): δ 1.52 (m, 6H), 2.75 (m, 4H), 4.67 (m, 2H), 5.29 (m, 2H), 6.2-5.5 (m, 1H), 7.17 (dd, 1H, J = 8, 5 Hz), 7.46 (d, 1H, J = 8 Hz), 8.44 (d, 1H, J = 5 Hz).

5,6,7,8-Tetrahydro-cycloocta[2,1-*b*:3,4-*b*']dipyridine (12)

A pyrex glass tube (2 cm x 15 cm) containing **11** (1.0 g, 4.3 mmol) was sealed and heated at 180 ℃ for 50 h and the crude product was chromatographed on basic alumina (eluted with EtOAc) to provide **12** (0.6 g, 66%). Recrystallization from $CHCl_3$ afforded colorless crystals, mp 140-142℃ [lit[10b] mp 140-142℃]. MS: *m/e* 210 (M^+); ^{1}H-NMR (250 MHz): δ 1.53 (m, 2H), 2.11 (m, 2H), 2.21 (m, 2H), 2.73 (m, 2H), 7.29 (m, 2H, $H_{3,10}$), 7.59 (m, 2H, $H_{4,9}$), 8.62 (m, 2H, $H_{2,11}$).

5,8-dibromo-5,6,7,8-tetrahydro-cycloocta[2,1-*b*:3,4-*b*']dipyridine (13)

A mixture of **12** (500 mg, 2.4 mmol), NBS (850 mg, 4.8 mmol), and benzoyl peroxide (5 mg) in CCl_4 (40 mL) was refluxed under nitrogen for 4 h. The CCl_4 solution was cooled and washed with brine (20 mL). The brine solution was separated and extracted with $CHCl_3$ (15 mL). The $CHCl_3$ extract was combined with the CCl_4 layer. The organic solution was dried over anhyd. $MgSO_4$ and then evaporated. The residue was crystallized from a 1:1 solution of EtOH and EtOAc to provide colorless crystals of a mixture of the dibromide **13** (570 g, 65%), mp 180-181℃. MS: *m/e* 366 (M^+); Exact mass: Calcd for $C_{14}H_{12}Br_2N_2$, 365.9366, 367.9346, 369.9326; Found 365.9379, 367.9376, 369.9381; ^{1}H-NMR (250 MHz): δ 2.02 (m, 2H), 2.30 (m, 4H), 2.60 (m, 2H), 4.92 (dd, 2H, J = 11, 9 Hz), 5.36 (dd, 2H, J = 13, 5 Hz), 7.39 (dd, 2H, J = 7, 5 Hz), 7.49 (dd, 2H, J = 8, 5 Hz), 7.78 (dd, 2H, J = 8, 1.5 Hz), 8.14 (dd, 2H, J = 7, 1.5 Hz), 8.79 (m, 4H); IR (KBr): 3048, 2930, 1560, 1420, 1322, 1179, 1162, 1084, 1040, 1010, 902, 880, 839, 828, 804, 790, 764, 721 cm^{-1}; Anal.: Calcd for $C_{14}H_{12}Br_2N_2$: C 45.69, H 3.29, N 7.61; Found: C 45.33, H 3.01, N 7.56;

Cycloocta[2,1-*b*:3,4-*b*']dipyridine (3)

To a solution of **13** (100 mg, 0.27 mmol) in THF (1 mL) and absolute EtOH (10 mL) was added a solution of 10% ethanolic KOH (2 mL). The resulting mixture was refluxed for 2 h and the solution was neutralized with 10% HCl (1.2 mL). The solvent was then evaporated and the residue was extracted with $CHCl_3$ (3 X 20 mL). The $CHCl_3$ solution was washed with brine (20 mL), dried over anhyd. K_2CO_3, and concentrated to a small volume. EtOAc (3 mL) was added to induce formation of colorless crystals of **3**. The crystals were collected and further purified by recrystallization from EtOAc-hexanes (39 mg, 70%), mp 194-195℃. MS: *m/e* 206 (M^+); Exact mass: Calcd for $C_{14}H_{10}N_2$, 206.0844; Found 206.0862; ^{1}H-NMR (250 MHz): (in $CDCl_3$) δ 6.13, 6.61 (AA'BB', 4H, $H_{5,6,7,8}$, J_{AB} = 11 Hz, $J_{BB'}$ = 2.5 Hz, $J_{AB'}$ = -1.2 Hz), 7.31 (dd, 2H, $H_{3,10}$, J = 7.8, 4.6 Hz), 7.44 (dd, 2H, $H_{4,9}$, J = 7.8, 1.6 Hz), 8.68 (dd, 2H, $H_{2,11}$, J = 4.6, 1.6 Hz); (in C_6D_6) δ 5.71, 6.20 (AA'BB', 4H, $H_{5,6,7,8}$, J_{AB} = 11 Hz, $J_{BB'}$ = 2.5 Hz, $J_{AB'}$ = -1.2 Hz), 6.64 (dd, 2H, $H_{3,10}$, J = 7.8, 4.6 Hz), 6.83 (dd, 2H, $H_{4,9}$, J = 7.8, 1.6 Hz), 8.56 (dd, 2H, $H_{2,11}$, J = 4.6, 1.6 Hz); IR (KBr): 1560, 1444, 1418, 1077, 799, 779, 758, 729 cm^{-1}; UV (EtOH): λ_{max} nm (log ε): 272 (3.66); Anal.: Calcd for $C_{14}H_{10}N_2$: C 81.53, H 4.89, N 13.58; Found: C 81.81, H 4.88, N 13.31.

6,9-Dihydro-cycloocta[2,1-*b*:3,4-*b*']diquinoline (16a)

A solution of *cis*-5-cycloocten-1,2-dione (**15**) (1 g, 7.2 mmol), 2-aminobenzaldehyde (**14a**) (1.76 g, 14.5 mmol) and KOH (50 mg) in absolute EtOH (40 mL) was refluxed under nitrogen for 4 h. The solution turned to wine-red in color during the reaction. The solution was cooled, neutralized with 10% HCl (0.3 mL) and concentrated to a small volume under reduced pressure. The residue was extracted with $CHCl_3$ (3 X 40 mL) and the $CHCl_3$ solution was washed with brine (30 mL). The solution was then dried over anhyd. Na_2SO_4 and the solvent was evaporated. The crude product obtained was recrystallized from EtOH to give **16a** (1.4 g, 63%) as colorless needles, mp 257-258℃. MS: *m/e* 308 (M^+); ^{1}H-NMR (250 MHz): δ 3.10-3.50 (m, 4H, $H_{6,6',9,9'}$), 5.97 (m, 2H, $H_{7,8}$), 7.57 (m, 2H, $H_{3,12}$), 7.73 (m, 2H, $H_{2,13}$), 7.84 (d, 2H, $H_{5,11}$, J = 8.3 Hz), 8.05 (s, 2H, $H_{5,10}$), 8.27 (d, 2H, $H_{1,14}$, J = 8.3 Hz); IR (KBr): 3020, 2948, 2800, 1618, 1596, 1485, 1438, 1409, 1138, 1039, 996, 950, 880, 825, 760, 741, 704 cm^{-1}; Anal.: Calcd for $C_{22}H_{16}N_2$: C 85.69, H 5.25, N 9.08; Found: C 85.70, H 5.23, N 9.08.

(*R*,*R*,*R*/*S*,*S*,*S*/*S*,*S*,*R*/*R*,*R*,*S*)-7,8-Dibromo-6,7,8,9-tetrahydro-cycloocta[2,1-*b*:3,4-*b*']-diquinoline (17a)

To a solution of **16a** (0.31 g, 1 mmol) in $CHCl_3$ (30 mL) was added a solution of Br_2 (0.20 g, 1.25 mmol) in $CHCl_3$ (2 mL) at r.t. over a period of 10 min until a light orange color persisted. The mixture was stirred for 1 h at r.t. The solvent was removed and the residue was crystallized from EtOH to give the dibromides **17a** (two diastereomers) as colorless crystals (0.43 g, 92%) mp 208-210℃. MS: *m/e* 468 (M^+); IR (KBr): 1622, 1600, 1494, 1449, 1418, 1322, 1176, 1142, 1021, 935, 810, 755, 725 cm^{-1}; Anal.: Calcd for $C_{22}H_{16}Br_2N_2$: C 56.44, H 3.44, Br 34.13, N 5.98; Found: C 56.31, H 3.26, Br 34.06, N 6.03. The ^{1}H-NMR spectrum was rather complex, see below for spectra of individual isomers.

(*R*,*R*,*R*/*S*,*S*,*S*)-7,8-dibromo-6,7,8,9-tetrahydro-cycloocta[2,1-*b*:3,4-*b*']diquinoline (17a)

To a solution of **16a** (31mg, 0.1mmol) in THF (4 mL) was added water (1 mL) and the solution was cooled by an ice-salt bath to -5 ℃. A solution of Br_2 (1 drop from a disposable pipet) in THF and water (4:1) (1 mL) was then added slowly to this pre-cooled solution and the mixture was stirred at -5 ℃ for 0.5 h. The solvents and excess Br_2 were removed at r.t. under reduced pressure, the residue was washed with EtOH and dried. The two diastereomeric pairs of dibromides obtained in this reaction were in the ratio of 6:1 (de = 86%), with the (*R*,*R*,*R*/*S*,*S*,*S*)-**17a** being the major product on the basis of ^{1}H-NMR spectral analysis. The product was then dissolved in $CHCl_3$. Hexanes were added to the solution and the mixture was cooled to induce

crystallization. Essentially diastereomerically pure colorless crystals of the (*R*,*R*,*R*/*S*,*S*,*S*)-**17a** were collected by filtration. A small amount of spectroscopically pure samples of (*R*,*R*,*R*/*S*,*S*,*S*)-**17a** and (*S*,*S*,*R*/*R*,*R*,*S*)-**17a** could be separated by repeated chromatography on preparative silica gel plates (EtOAc-hexanes, 1:2). ^{1}H-NMR (250 MHz): (*R*,*R*,*R*/*S*,*S*,*S*)-**17a** (major product): δ 3.18 (m, 2H, $H_{6,9}$), 3.68 (d, 2H, $H_{6',9'}$, J = 15.7 Hz), 4.54 (dd, 2H, $H_{7,8}$, J = 8.0, 3.3 Hz), 7.65 (m, 2H, $H_{3,12}$), 7.76 (m, 2H, $H_{2,13}$), 7.91(d, 2H, $H_{4,11}$, J = 8.0 Hz), 8.27 (s, 2H, $H_{5,10}$), 8.30 (d, 2H, $H_{1,14}$, J = 8.0 Hz); (*S*,*S*,*R*/*R*,*R*,*S*)-**17a** (minor product) δ 3.18 (m, 2H, $H_{6,9}$), 3.24 (d, 2H, $H_{6',9'}$, J = 15.2 Hz), 5.10 (d, 2H, $H_{7,8}$, J = 6.0 Hz), 7.65 (m, 2H, $H_{2,13}$), 7.76 (m, 2H, $H_{3,12}$), 7.91 (m, 2H, $H_{4,11}$), 8.22 (s, 2H, $H_{5,10}$), 8.30 (d, 2H, $H_{1,14}$, J = 8.0 Hz).

6,7-Dihydro-cycloocta[2,1-*b*:3,4-*b*']diquinoline (18a)

To a solution of **14a** (0.9 g, 7.4 mmol) and **15** (0.5 g, 3.6 mmol) in absolute EtOH (25 mL) was added a solution of KOH (0.1 g) in absolute EtOH (2 mL). The solution was refluxed under nitrogen overnight and a brown-red solution resulted. The reaction mixture was then cooled. The precipitate thus formed was collected by filtration and recrystallized from EtOH. Diquinoline **18a** was obtained as colorless crystals (0.62 g, 60%), mp 244-245.5℃. MS: *m/e* 308 (M^+); Exact mass: Calcd for $C_{22}H_{16}N_2$: 308.1062; Found 308.1058; ^{1}H-NMR (250 MHz): δ 2.5 (m, 2H, $H_{7,7'}$), 2.9 (m, 2H, $H_{6,6'}$), 5.75 (m, 1H, H_8), 6.58 (d, 1H, H_9, J = 12 Hz), 7.58 (m, 2H, $H_{2,13}$), 7.72 (m, 2H, $H_{3,12}$), 7.83 (d, 2H, $H_{4,11}$, J = 7.2 Hz), 8.01 (s, 2H, $H_{5,10}$), 8.24 (m, 2H, $H_{1,14}$).

Cycloocta[2,1-*b*:3,4-*b*']diquinoline (4)

A suspension of dibromide **17a** (466 mg, 1 mmol) in dry toluene (10 mL) was added to a solution of DBN (0.3 mL, 2.4 mmol) in toluene (10 mL) at r.t. and a clear solution resulted on stirring of the mixture. The resulting solution was stirred overnight under a nitrogen atmosphere. The solvent was evaporated and the residue was dissolved in $CHCl_3$ (50 mL). The solution was then washed with brine (20 mL), dried over anhyd. Na_2SO_4, and evaporated. The residue was crystallized from EtOH-EtOAc to give colorless crystals which were recrystallized from EtOH to give **4** (205 mg, 67%), mp 272-273℃. MS: *m/e* 306 (M^+); ^{1}H-NMR (250 MHz): (in $CDCl_3$) δ 6.18, 6.83 (AA'BB', 4H, $H_{7,8}$, $H_{6,9}$, J_{AB} = 11 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -1.5 Hz), 7.53 (m, 2H, $H_{2,13}$), 7.70 (m, 2H, $H_{3,12}$), 7.83 (d, 2H, $H_{4,11}$, J = 8.0 Hz), 7.97 (s, 2H, $H_{5,10}$), 8.21 (d, 2H, $H_{1,14}$, J = 8.0 Hz); (in C_6D_6) δ 5.82, 6.47 (AA'BB', 4H, $H_{7,8}$, $H_{6,9}$, J_{AB} = 11 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -1.5 Hz), 7.15 (m, 2H, $H_{2,13}$), 7.33 (m, 2H, $H_{3,12}$), 7.42 (d, 2H, $H_{4,11}$, J = 8.0 Hz), 7.42 (s, 2H, $H_{5,10}$), 8.33 (d, 2H, $H_{1,14}$, J = 8.0 Hz); IR (KBr): 3010, 1620, 1600, 1580, 1558, 1490, 1411, 1140, 1021, 920, 819, 782, 761, 742 cm^{-1}; UV (EtOH): λ_{max} nm (log ε): 233 (4.42), 255 (4.20), 312 (3.52), 323 (3.49); pK_{a1} = 3.9 (HNP 329 mv); Anal.: Calcd for $C_{22}H_{14}N_2$: C 86.25, H 4.61, N 9.15; Found: C 86.36, H 4.56, N 9.12.

6,9-Dihydro-cycloocta[2,1-*b*:3,4-*b*']di[1,8]naphthyridine (16b)

cis-5-Cyclooctene-1,2-dione (**15**) (1.38 g, 10 mmol), 2-aminonicotinaldehyde (**14b**) (2.5 g, 20 mmol), and absolute EtOH (40 mL) was placed in a three-necked 100-mL flask. A solution of KOH (30 mg) in absolute EtOH (3 mL) was added and the mixture was refluxed under nitrogen for 2 h. The solution turned from light yellow to brown-red. The reaction mixture was cooled and the precipitate was collected by filtration. Recrystallization of the crude product from EtOH afforded **16b** as colorless crystals (1.86 g, 60%), mp > 300℃. MS: *m/e* 310 (M^+); Exact mass: Calcd for $C_{20}H_{14}N_4$, 310.1218; Found 310.1211; ^{1}H-NMR: δ 3.30 (m, 4H, $H_{6,6',9,9'}$), 5.90 (m, 2H, $H_{7,8}$), 7.56 (dd, 2H, $H_{3,12}$, J = 7.0, 5.2 Hz), 8.10 (s, 2H, $H_{5,10}$), 8.25 (d,, 2H, $H_{4,11}$, J = 7.0 Hz), 9.19 (d, 2H, $H_{2,13}$, J = 5.2 Hz); Anal.: Calcd for $C_{20}H_{14}N_4$: C 77.40, H 4.55, N 18.05; Found: C 77.44, H 4.56, N 18.01.

7,8-Dibromo-6,7,8,9-tetrahydro-cycloocta[2,1-*b*:3,4-*b*']di[1,8]naphthyridine (17b)

To a solution of **16b** (345 mg, 0.73 mmol) in $CHCl_3$ (40 mL) was added a solution of Br_2 (120 mg, 0.75 mmol) in $CHCl_3$ (2 mL) during a period of 5 min and a light orange solution resulted. The solution was evaporated to dryness under reduced pressure. The residue was extracted with hot MeOH (5 mL) and crystals of dibromide **17b** precipitated on cooling of the solution (470 mg, 90%), mp 245-247℃. The product was used for subsequent reaction without further purification. MS: *m/e* 470 (M^+); Exact mass: Calcd for $C_{20}H_{14}N_4Br_2$, 467.9584; Found: 467.9588. Since the diastereomeric excess of this bromination reaction was approximately 78%, ^{1}H-NMR (250 MHz) assignments could be made on the basis of integration of the major (more soluble) component of **17b**: δ 3.20 (dd, 2H, J = 15, 10 Hz), 3.30 (d, 2H, J = 15 Hz), 5.40 (d, 2H, J = 10 Hz), 7.61 (dd, 2H, J = 8, 6 Hz), 8.29 (s, 2H), 8.40 (dd, 2H, J = 8, 2 Hz), 9.25 (dd, 2H, J = 6, 2 Hz); minor (less soluble) component of **17b**: δ 3.20 (dd, 2H, J = 15, 10 Hz), 4.72 (d, 2H, J = 10 Hz), 4.58 (d, 2H, J = 10 Hz), 7.61 (dd, 2H, J = 8, 6 Hz), 8.29(s, 2H), 8.40 (dd, 2H, J = 8, 2 Hz), 9.25 (dd, 2H, J = 6, 2 Hz).

6,7-Dihydro-cycloocta[2,1-*b*:3,4-*b*']di[1,8]naphthyridine (18b)

To a solution of **15** (138 mg, 1 mmol) and **14b** (244 mg, 2 mmol) in absolute EtOH (40 mL) was added a solution of KOH (100 mg) in absolute EtOH (4 mL). The solution was then refluxed under nitrogen overnight and the precipitate formed on cooling of the reaction solution was collected by filtration. The product was recrystallized from MeOH to give colorless crystals of **18b** (186 mg, 60%), mp > 280℃. MS: *m/e* 310 (M^+); Exact mass: Calcd for $C_{20}H_{14}N_4$ 310.1218; Found 310.1221; ^{1}H-NMR (250 MHz): δ 2.52 (m, 2H, $H_{7,7'}$), 3.00 (m, 2H, $H_{6,6'}$), 5.78 (m, 2H, H_8), 6.60 (d, 1H, H_9, J = 12 Hz), 7.58 (m, 2H, $H_{3,12}$), 8.02 (s, 1H), 8.03 (s, 1H), 8.22 (d, 2H, $H_{4,11}$, J = 7 Hz), 9.16 (d, 2H, $H_{2,13}$, J = 5 Hz); Anal.: Calcd for $C_{20}H_{14}N_4$: C 77.40, H 4.55, N 18.05; Found: C 77.38, H 4.57, N 18.03.

Cycloocta[2,1-*b*:3,4-*b*']di[1,8]naphthyridine (5)

To a suspension of **17b** (470 mg, 1 mmol) in toluene (20 mL) was added a solution of DBN (250 mg, 2 mmol) in dry toluene (2 mL) and the mixture was stirred under nitrogen at r.t. overnight. A clear solution was obtained with some brown sticky material on the bottom of the flask. After the solvent was removed under reduced pressure, the residue was separated by column chromatography (basic alumina, EtOAc-MeOH 3:1). The product was then recrystallized from MeOH to give **5** as colorless crystals (200 mg, 65%), mp > 300℃. MS: *m/e* 308 (M^+); Exact mass: Calcd for $C_{20}H_{12}N_4$ 308.1062; Found 308.1058; ^{1}H-NMR (250 MHz): δ 6.21 and 6.91 (AA'BB', 4H, $H_{7,8}$ and $H_{6,9}$, $J_{AB'}$= 11 Hz, $J_{BB'}$ = 3 Hz, $J_{AB'}$ = -1 Hz), 7.52 (dd, 2H, $H_{3,12}$, J = 8, 4 Hz), 8.01 (s, 2H, $H_{5,10}$), 8.21 (dd, 2H, $H_{4,11}$, J = 8, 2 Hz), 9.12 (dd, 2H, $H_{2,13}$, J = 4, 2 Hz); IR (KBr): 1605, 1590, 1463, 1451, 1018, 921, 792, 747 cm^{-1}; UV (EtOH) λ_{max} nm (log ε): 232 (4.66), 235 (4.63), 325 (3.84); Anal.: Calcd for $C_{20}H_{12}N_4$: C 77.92, H 3.92, N 18.17; Found: C 77.80, H 3.60, N 18.60.

(*N*,*N*)-Trifluoroacetyl-cycloocta[2,1-*b*:3,4-*b*']diquinolinium triflate (19a)

To a $CDCl_3$ (1 mL, freshly distilled from P_2O_5) solution of **4** (2.1 mg, 0.01 mmol) in a flame dried NMR tube was added under nitrogen one drop of the solution of trifluoroacetyl triflate (about 5% v/v) in dry $CDCl_3$. An orange red solution resulted and the NMR tube was sealed immediately under nitrogen. ^{1}H-NMR (250 MHz): (at 22℃) δ 6.55 (s, 4H, $H_{6,7,8,9}$), 7.95 (m, 2H, $H_{3,12}$), 8.14 (m, 2H, $H_{2,13}$), 8.42 (d, 2H, $H_{4,11}$, J = 7.6 Hz), 9.01 (d, 2H, $H_{1,14}$, J = 8.8 Hz), 9.24 (s, 2H, $H_{5,10}$). The signal at δ 6.55 becomes an AA'BB' system (J_{AB} = 11 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -0.7 Hz) at 11℃ to -60℃.

(*N*,*N*)-Bis(trifluoroacetyl)-cycloocta[2,1-*b*:3,4-*b*']diquinolinium ditriflate (19b)

To a solution of **4** (2.1 mg, 0.01 mmol) in freshly distilled $CDCl_3$ (1 mL) in a dry NMR tube was added

5 drops of TFAT (about 5% v/v). A yellowish solution was afforded and the NMR tube was sealed immediately under nitrogen. ^{1}H-NMR (250 MHz): δ 6.49 (d, 2H, $H_{7,8}$, J = 10 Hz), 7.08 (d, 2H, $H_{6,9}$, J = 10 Hz), 8.07 (m, 2H), 8.23 (m, 4H), 8.51 (m, 2H), 8.56 (s, 2H, $H_{5,10}$).

Cycloocta[2,1-*b*:3,4-*b*']diquinoline dihydrochloride (20)

To a solution of **4** (6.2 mg, 0.02 mmol) in MeOH (1 mL) was added 10% HCl (0.2 mL). The dihydrochloride **20** was obtained as light yellow crystals in an almost quantitative yield, mp 254-255℃. ^{1}H-NMR (250 MHz) (CD_3OD): δ 6.48, 7.00 (AA'BB', 4H, $H_{6,7,8,9}$, J_{AB} = 11 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -1.5 Hz), 7.92 (m, 2H, $H_{2,13}$), 8.08 (m, 2H, $H_{3,12}$), 8.22 (d, 2H, $H_{4,11}$, J = 7.2 Hz), 8.28 (d, 2H, $H_{1,14}$, J = 5.2 Hz), 8.70 (s, 2H, $H_{5,10}$); UV (EtOH) λ_{max} nm (log ε): 251 (4.42), 342 (3.76); Anal.: Calcd for $C_{22}H_{16}N_2Cl_2$: C 69.70, H 4.25, N 7.39; Found: C 69.70, H 4.24, N 7.40.

Cycloocta[2,1-*b*:3,4-*b*']dipyridine tungsten (0) tetracarbonyl (21)

A mixture of **3** (10 mg, 0.05 mmol) and tungsten hexacarbonyl (17 mg, 0.05 mmol) in xylenes (137-144℃) (3 mL) was refluxed under nitrogen for 2 h and a dark red solution was obtained. Pentane (2 mL) was added to the reaction mixture and the solution was kept at a temperature below -5 ℃. Dark red crystals of **21** were obtained (13 mg, 53%), mp 253-258℃. Anal.: Calcd for $C_{18}H_{10}N_2O_4W$: C 43.06, H 2.01, N 5.58; Found: C 43.60, H 1.91, N 5.41; ^{1}H-NMR (250 MHz): (in C_6D_6) δ 5.28, 5.60 (AA'BB', 4H, $H_{6,7}$, $H_{5,8}$, J_{AB} = 11.0 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -0.2 Hz), 6.12 (dd, 2H, $H_{3,10}$, J = 7.9, 5.2 Hz), 6.45 (dd, 2H, $H_{4,9}$, J = 7.9, 1.1 Hz), 8.75 (dd, 2H, $H_{2,11}$, J = 5.2, 1.1 Hz); UV-visible (EtOH): λ_{max} nm (log ε): 255 (4.49), 302 (4.07), 395 (3.69), 490 (3.54).

Cycloocta[2,1-*b*:3,4-*b*']diquinoline tungsten (0) tetracarbonyl (22)

A mixture of **4** (10 mg, 0.03 mmol) and tungsten hexacarbonyl (9.7 mg, 0.03 mmol) in xylenes (137-144℃) (3 mL) was refluxed under nitrogen for 2 h and a dark red solution was formed. Pentane (2 mL) was added and the complex **22** was formed as dark red crystals (11 mg, 81%) on cooling of the solution, mp 198-203℃. ^{1}H-NMR (250 MHz): (in $CDCl_3$) δ 6.45, 6.57 (AA'BB', 4H, $H_{6,7,8,9}$, J_{AB} = 10 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -0.2 Hz), 7.73 (m, 2H, $H_{2,13}$), 7.88 (m, 2H, $H_{3,12}$), 7.94 (d, 2H, $H_{4,11}$, J = 8.2 Hz), 8.09 (s, 2H, $H_{5,10}$), 9.04 (d, 2H, $H_{1,14}$, J = 8.9 Hz); (in C_6D_6) δ 5.81, 6.42 (AA'BB', 4H, $H_{7,8}$, $H_{6,9}$ J_{AB} = 10 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -0.2 Hz), 7.25 (s, 2H, $H_{5,10}$), 7.38 (m, 4H, $H_{2,3,12,13}$), 8.40 (d, 2H, $H_{4,11}$, J = 8 Hz), 9.30 (d, 2H, $H_{1,14}$, J = 7 Hz); IR (KBr): 1995, 1880, 1860, 1840, 1811, 1482, 776, 742 cm^{-1}; UV (EtOH) λ_{max} nm (log ε): 236 (4.92), 250 (4.86), 310 (4.03), 323 (4.10); Anal.: Calcd for $C_{26}H_{14}N_2O_4W$: C 51.85, H 2.34, N 4.65; Found: C 50.36, H 2.25, N 4.87.

Cycloocta[2,1-*b*:3,4-*b*']dipyridine molybdenum (0) tetracarbonyl (23)

A mixture of **3** (10 mg, 0.05 mmol) and molybdenum hexacarbonyl (12.8 mg, 0.05 mmol) in xylenes (137-144℃) (3 mL) was heated at 140 ℃ under nitrogen for 2 h and the dark red solution thus formed was cooled to r.t. Pentane (2 mL) was added and the mixture was kept at temperature below -5℃. Dark red crystals of **23** were collected, mp 215℃ (dec) (15 mg, 74%). ^{1}H-NMR (250 MHz): (in $CDCl_3$) δ 6.28, 6.38 (AA'BB', 4H, $H_{5,6,7,8}$, J_{AB} = 11 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -0.2 Hz), 7.37 (dd, 2H, $H_{3,10}$, J = 7.8, 5.2 Hz), 7.55 (dd, 2H, $H_{4,9}$, J = 7.8, 1.2 Hz), 8.98 (dd, 2H, $H_{2,11}$, J = 5.2, 1.2 Hz); (in C_6D_6) δ 5.33, 5.59 (AA'BB', 4H, $H_{5,6,7,8}$, J_{AB} = 10.3 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -0.1 Hz), 6.17 (dd, 2H, $H_{3,10}$, J = 7.8, 5.2 Hz), 6.48 (dd, 2H, $H_{4,9}$, J = 7.8, 1.4 Hz), 8.63 (dd, 2H, $H_{2,11}$, J = 5.2, 1.4 Hz); IR (KBr): 2050, 1930, 1900, 1855, 1800, 1408, 800, 780, 732, 712 cm^{-1}; UV-visible (EtOH): λ_{max} nm (log ε): 256 (4.05), 280 (3.90), 391 (3.35), 480 (3.14); Anal.: Calcd for $C_{18}H_{10}N_2O_4Mo$: C 52.19, H 2.43, N 6.76; Found: C 52.31, H 2.26, N 6.63.

Cycloocta[2,1-*b*:3,4-*b*']diquinoline copper (I) perchlorate (24)

Compound **4** (31mg, 0.1 mmol) was dissolved in absolute EtOH (10 mL) with heatig and to this hot

solution was added a solution of $Cu(ClO_4)_2 \cdot 6H_2O$ (185 mg, 0.5 mmol) in absolute EtOH (3 mL). A brown solution was obtained, which turned to deep red in color after the solution was refluxed for 0.5 h under nitrogen. The reaction mixture was kept at room temperature for 2 h and the reaction mixture was evaporated under reduced pressure to a small volume (about 4 mL). Water (1 mL) was added and the solution was then allowed to evaporate slowly at r.t. and dark red fine needles of **24** were obtained (53 mg, 67%), mp 300℃. ^{1}H-NMR (250 MHz): (in $CDCl_3$) δ 6.41, 6.64 (AA'BB', 4H, $H_{6,7,8,9}$, J_{AB} = 11 Hz, $J_{BB'}$ = 3.0 Hz, $J_{AB'}$ = -1.5 Hz), 7.27 (m, 2H, $H_{3,12}$), 7.38 (d, 2H, $H_{4,11}$, J = 8.5 Hz), 7.48 (m, 2H, $H_{2,13}$), 7.81 (d, 2H, $H_{1,14}$, J = 8.0 Hz), 8.01 (s, 2H, $H_{5,10}$); (in CD_3COCD_3): δ 6.54, 6.85 (AA'BB', 4H, $H_{6,7,8,9}$, J_{AB} = 11 Hz, $J_{BB'}$ = 3Hz, $J_{AB'}$ = -1.5 Hz), 7.37 (m, 2H, $H_{3,12}$), 7.47 (d, 2H, $H_{4,11}$, J = 8.4 Hz), 7.55 (m, 2H, $H_{2,13}$), 7.97 (d, 2H, $H_{1,14}$, J = 8.0 Hz), 8.30 (s, 2H, $H_{5,10}$); IR (KBr): 3002, 1616, 1570, 1481, 1380, 1139, 1090, 921, 821, 797, 746, 725 cm^{-1}; UV (EtOH): λ_{max} nm (log ε): 236 (4.97), 240 (4.97), 262 (4.98), 337 (4.38), 520 (2.94); Anal.: Calcd for $C_{44}H_{28}N_4CuClO_4$: C 68.13, H 3.64, N 7.22; Found: C 68.75, H 3.63, N 7.10.

Cycloocta[2,1-*b*:3,4-*b*']diquinoline mercury (II) chloride (25)

Compound **4** (5 mg, 0.016 mmol) was dissolved in absolute EtOH (1 mL) with heating. To this solution was added mercury(II) chloride (9 mg, 0.03 mmol, pre-dried under vacuum) in absolute EtOH (1 mL) and the mixture was kept at r.t. for 12 h. Colorless crystals thus produced were collected and washed with absolute EtOH to remove excess mercury(II) chloride. Recrystallization of the crystals from EtOH gave colorless needles of **25** (8.5 mg, 92%), mp 225-227℃. ^{1}H-NMR: δ 6.37, 6.72 (AA'BB', 4H, $H_{6,7,8,9}$, J_{AB} = 11 Hz, $J_{BB'}$ = 3 Hz, $J_{AB'}$ = -1.5 Hz), 7.70 (m, 2H, $H_{2,13}$), 7.88 (m, 2H, $H_{3,12}$), 7.96 (d, 2H, $H_{4,11}$, J = 8.0 Hz), 8.18 (s, 2H, $H_{5,10}$), 8.33 (d, 2H, $H_{1,14}$, J = 8.0 Hz); Anal.: Calcd for $C_{22}H_{14}N_2Cl_2Hg$: C 45.73, H 2.44, N 4.85; Found: C 45.54, H 2.33, N 4.80.

Cycloocta[2,1-*b*:3,4-*b*']diquinoline zinc (II) chloride (26)

Compound **4** (5 mg, 0.016 mmol) and zinc(II) chloride (5 mg, 0.037 mmol) were dissolved in absolute EtOH (2 mL) with stirring and the solution was kept at r.t. for 24 h. Yellow granules were formed during the process. The solvent was evaporated and the excess zinc(II) chloride was washed off with acetone (2 X 1 mL). The complex **26** was obtained (6.5 mg, 90%), mp > 300℃. The complex was insoluble in common NMR solvents. IR (KBr): 1488, 1450, 1416, 1360, 1299, 1200, 1140, 1031, 959, 940, 780, 749, 735 cm^{-1}; Anal.: Calcd for $C_{22}H_{14}N_2Cl_2Zn$: C 59.70, H 3.19, N 6.33, Cl 16.02; Found: C 58.88, H 3.04, N 6.14, Cl 16.78.

(*R*,*R*,*R*)- and (*S*,*S*,*S*)-Palladium (II) perchlorate complex (28)

To a suspension of *R*,*R*-**27** (or *S*,*S*-**27**) (7 mg, 0.012 mmol) in MeOH (1 mL) in a 5-mL flask at -3℃ was added a solution of **3** (5 mg, 0.024 mmol) in MeOH (1 mL) and the mixture was stirred in an ice-bath for 2 h. To this nearly colorless solution was added $NaClO_4 \cdot H_2O$ (7 mg, 0.05 mmol) and the solution was stirred for 0.5 h. Ether (1 mL) was added to the reaction mixture after the ice-bath was removed. Light yellow crystals of **28** (almost quantitative from **3**) were obtained on cooling of the reaction mixture. The product was washed with water and was recrystallized from MeOH-Et_2O, mp 198-200℃. ^{1}H-NMR (250 MHz): δ 1.14 (d, 3H, CH_3, J = 6.6 Hz), 1.48 (d, 3H, CH_3, J = 6.5 Hz), 2.34 (s, 3H, NCH_3), 2.50 (s, 3H, NCH_3), 2.53 (s, 3H, NCH_3), 2.84 (s, 3H, NCH_3), 3.54 (q, 1H, ArCH, J = 6.5 Hz), 3.70 (q, 1H, ArCH, J = 6.5 Hz), 5.51 (d, 1H, ArH, J = 7.8 Hz), 5.63 (d, 1H, ArH, J = 7.1 Hz), 6.18 (ABCD, 4H, $H_{5,6,7,8}$, $J_{5,6}$ = 11.2 Hz, $J_{5,7}$ = -2.4 Hz, $J_{6,7}$ = 2.8 Hz, $J_{6,8}$ = -2.4 Hz, $J_{7,8}$ = 12.0 Hz), 6.69 (m, 2H, ArH), 6.78 (m, 2H, ArH), 6.96 (m, 2H, ArH), 7.80 (m, 4H, $H_{3,4,9,10}$), 9.13 (dd, 1H, H_2, J = 5.1, 1.6 Hz), 9.19 (dd, 1H, H_{11}, J = 6.9, 1.5 Hz); Anal.: Calcd for $C_{34}H_{38}N_4Cl_2O_4Pd_2$: C 48.02, H 4.50, N 6.59; Found: C 47.15, H 4.75, N 6.45.

7-Iodo-6,7,8,9-tetrahydro-cycloocta[2,1-*b*:3,4-*b*']diquinolin-8(9*H*)-one (29)

To a suspension of silver chromate (0.39 g, 1.1 mmol) and 4 Å molecular sieves (0.4 g) in dry CH_2Cl_2

(30 mL) were added iodine (380 mg,1.5 mmol) and a solution of pyridine (50 mg, 0.6 mmol) in CH_2Cl_2 (2 mL) at 0℃ (ice-bath) and the mixture was stirred for 5 min at the same temperature. A solution of **16a** (310 mg, 1 mmol) in CH_2Cl_2 (5 mL) was added dropwise during 5 min to the ice-cooled suspension and the mixture was stirred for 20 min at 0℃. The cooling bath was then removed and the reaction mixture was stirred for 3 h at r.t. The mixture was suction filtered through celite and the filtered cake was washed with CH_2Cl_2 (10 mL). The combined filtrate was washed with 5% aq. $Na_2S_2O_3$ (30 mL), brine (20 mL), and then dried over anhyd. $MgSO_4$. After the solvent was removed the residue was crystallized from $CHCl_3$-EtOAc (1:1) and the product **29** was collected as colorless crystals (0.23 g, 51%), mp 193-194℃. MS: *m/e* 450 (M^+); ^{1}H-NMR (250 MHz): δ 3.26 (d, 1H, $H_{6'}$, J = 6.0 Hz), 3.32 (d, 1H, H_6, J = 6.0 Hz), 4.10 (d, 1H, H_9, J = 12.2 Hz), 4.98 (m, 1H, H_7), 6.20 (d, 1H, $H_{9'}$, J = 12.2 Hz), 7.75 (m, 4H, $H_{2,3,12,13}$), 7.93 (d, 1H, H_4, J = 8.1 Hz), 8.03 (d, 1H, H_{11}, J = 8.1 Hz), 8.37 (s, 1H, H_5), 8.37 (m, 2H, $H_{1,14}$), 8.39 (s, 1H, H_{10}); Anal. Calcd for $C_{22}H_{15}N_2IO$: C 58.66, H 3.36, N 6.22; Found: C 58.16, H 3.05, N 6.11.

6,7-Dihydro-cycloocta[2,1-*b*:3,4-*b*']diquinolin-7(6*H*)-one (30)

A solution of **29** (0.25 g, 0.56 mmol) and DBN (70 mg, 0.56 mmol) in dry toluene (20 mL) was stirred under nitrogen overnight and the solvent was evaporated under reduced pressure. The residue was dissolved in $CHCl_3$ (50 mL). The $CHCl_3$ solution was washed with brine (20 mL) and was dried over anhyd. $MgSO_4$. The solvent was removed and the residue was recrystallized from $CHCl_3$-EtOAc (1:1) to yield colorless crystals of **30** (90 mg, 50%), mp 275-276℃. MS: *m/e* 322 (M^+); ^{1}H-NMR (250 MHz): δ 3.90 (m, 2H, $H_{6,6'}$), 5.99 (d, 1H, H_8, J = 12 Hz), 7.38 (d, 1H, H_9, J = 12 Hz), 7.65 (m, 2H, $H_{3,12}$), 7.85 (m, 2H, $H_{2,13}$), 7.88 (d, 1H, H_{11}, J = 8 Hz), 7.92 (d, 1H, H_4, J = 8 Hz), 8.12 (s, 1H, H_5), 8.28 (s, 1H, H_{10}), 8.30 (d, 1H, H_1, J = 8 Hz), 8.35 (d, 1H, H_{14}, J = 8 Hz); Anal.: Calcd for $C_{22}H_{14}N_2O$: C 81.97, H 4.38, N 8.69; Found: C 81.97, H 4.18, N 8.69.

7-Hydroxy-7-isopropyl-6,7-dihydro-cycloocta[2,1-*b*:3,4-*b*']diquinoline (31)

Magnesium turnings (30 mg, 1.25 mmol) and dry THF (2 mL) were placed in a two-necked 10-mL flask (flame dried) under nitrogen. A solution of isopropyl bromide (150 mg, 1.2 mmol) in dry THF (1 mL) was added through a dropping funnel. The mixture was heated to reflux for 0.5 h to give a clear greyish solution of isopropylmagnesium bromide.

A solution of **30** (0.32 g, 1 mmol) in dry THF (15 mL) was cooled to -72℃ and to this was added very slowly a solution of the freshly prepared isopropylmagnesium bromide solution in THF until a light pink color persisted (excess Grignard reagent should be avoided!). The temperature of the solution was allowed to rise gradually to r.t. and the resulting mixture was refluxed under nitrogen for 3 h. Sat. aq. NH_4Cl (5 mL) was added to the reaction mixture, the upper layer was separated, extracted with $CHCl_3$ and the $CHCl_3$ layer was dried over anhyd. $MgSO_4$. The solvent was removed and the residue was purified by chromatography on a silica gel column (EtOAc-hexanes, 1:2) to afford **31** (0.18 g, 50%) as colorless crystals, mp 269-270℃. MS: *m/e* 366 (M^+); Exact mass: Calcd for $C_{25}H_{22}N_2O$, 366.1732; Found: 366.1730; ^{1}H-NMR (250 MHz): δ 0.97 (d, 6H, 2-CH_3, J = 6.9 Hz), 1.98 (m, 1H, C<u>H</u>$(CH_3)_2$), 2.86 (d, 1H, H_6, J = 13.9 Hz), 3.07 (d, 1H, $H_{6'}$, J = 13.9 Hz), 5.61 (dd, 1H, H_8, J = 13.0, 1.8 Hz), 6.57 (d, 1H, H_9, J = 13.0 Hz), 7.62 (dd, 2H, $H_{2,13}$, J = 8.5, 7.8 Hz), 7.77 (dd, 2H, $H_{3,12}$, J = 8.5, 7.3 Hz), 7.87 (d, 1H, J = 7.8 Hz), 7.90 (d, 1H, J = 7.3 Hz), 8.05 (s, 1H), 8.29 (s, 1H), 8.30 (d, 1H, J = 8.5 Hz), 8.40 (d, 1H, J = 8.5 Hz).

7-Isopropyl-cycloocta[2,1-*b*:3,4-*b*']diquinoline (32)

Compound **31** (37 mg, 0.1 mmol) was dissolved in dry pyridine (3 mL) and the solution was cooled in an ice-bath. MsCl (30 mg, 0.23 mmol) was added under nitrogen and the mixture was heated at 100℃ for 2 h. The reaction solution was then cooled in an ice-bath and water (4 mL) was added. The resulting mixture was extracted with $CHCl_3$ (3 X 15 mL), and the extracts were dried over anhyd. $MgSO_4$ and evaporated. The crude

residue was chromatographed on a silica gel column (EtOAc-hexanes, 1:2) to yield **32** which was recrystallized from EtOH-EtOAc to afford colorless crystals (16 mg, 46%), mp 275-276°C. MS: *m/e* 348 (M^+); Exact mass: Calcd for $C_{25}H_{20}N_2$, 348.1626, Found 348 1629; ^{1}H-NMR (250 MHz): δ 0.97 (d, 3H, CH_3, J = 6.9 Hz), 1.02 (d, 3H, CH_3, J = 6.9 Hz), 2.51 (septet, 1H, $CH(CH_3)_2$, J = 6.9 Hz), 6.24 (d, 1H, H_8, J = 11 Hz), 6.59 (s, 1H, H_6), 6.85 (d, 1H, H_9, J = 11 Hz), 7.62 (m, 2H, $H_{2,13}$), 7.80 (m, 2H, $H_{3,12}$), 7.90 (s, 2H, $H_{5,10}$), 8.10 (m, 2H, $H_{4,11}$), 8.40 (m, 2H, $H_{1,14}$).

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