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The Chemistry of Novel C₂ Diazabiaryl Ligands : Cycloocta[2,1-b:3,4-b']dipyridine, Cycloocta[2,1-b:3,4-b']diquinoline and Their Related Compounds^{†1}

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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 biochemistry⁶ 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 $20^{\circ}-30^{\circ}$.^{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 ¹H-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 eightmembered 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 aminoacrolein¹⁴ (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°C 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 three doublet of doublets at δ 7.31, 7.44 and 8.68, which are typical of 2,3-disubstituted pyridine derivatives.



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 6,7dihydro isomers 18a (60%) and 18b (60%) resulted respectively due to the isomerization of the double bonds to the conjugated position. In their ¹H-NMR spectra (CDCl₃), 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 CHCl₃ and EtOH, but **5** is sparingly soluble in CHCl₃ 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 ¹H-NMR spectra (CDCl₃) 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 computed²⁰ 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 ¹H-NMR spectrum of 19a at 22°C 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 $(J_{AB} = 11, J_{BB} = 3 \text{ Hz}, J_{AB'} = -0.7 \text{ Hz})$ at below 11°C. 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°C or as a symmetrical AA'BB' system at below 11°C. 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 ¹H-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 ¹H-NMR spectrum reminiscent of a non-planar molecule, of which relatively down-field absorptions are detected.



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(II), 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 CHCl₃, 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 C₆D₆, the ¹H-NMR spectra of 21 and 22 displays similar AA'BB' absorptions (21: H_{6.7} & 5.28 and H_{5.8} & 5.60; 22: H_{7.8} & 5.81 and H_{6.9} & 6.42) of the four cyclooctatraenyl protons. The remarkable up-field shift of the cyclooctatetraenyl absorptions in 21 as compared with those of 3 $(H_{6,7} \delta 5.71 \text{ and } H_{5,8} \delta 6.20)$ is presumably owing either to the flattening of the molecule towards a distorted $4n\pi$ 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 $H_{6,0}$ 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 H5, H6, H7 and H8 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 (8 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 CHCl₃ 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} & 5.33 and H_{5,8} & 5.59) in its ¹H-NMR spectrum (C₆D₆). 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) = 60° and $\alpha = 63°$, 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(ClO₄)₂•6H₂O 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 CHCl₃, acetone and hot EtOH, but is insoluble in water. Another way in which 24 could be prepared was by using *in situ* generated CuClO₄,^{28b} obtained by warming CuCl and NaClO₄ in CH₃CN. A dark red solution was produced when the yellow CuClO₄ solution was added to a CH₂Cl₂ 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 CHCl₃. Downfield shifts are observed for the aromatic protons in the ¹H-NMR spectrum (CDCl₃) 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 ¹H-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 27²⁹ 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 NaClO₄ 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 ¹H-NMR spectra^{1b} of these complexes as well as on the evidence from the 2D ¹H-¹H 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 H2 and Mea. Examination of the 1D 1H-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 ¹H-NMR spectra and elemental analysis results both reveal that 28 are binuclear complexes. In the ¹H-NMR spectra of 28, the doubled absorptions of each pair of symmetrically related protons (H₂ and H₁₁, H₃ and H₁₀, H₄ and H₉, H₅ and H₈, etc.) were unexpected. On the pessimistic side, the complicated ¹H-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 ¹H-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 ¹H-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 (H₅, H₆, H₇ and H₈) 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
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Signal	COSY	NOESY
Me _a	H _h	Me _c , H ₂
Meb	Hg	Me _e
Me	-	Me _a , Me _d , Me _f , H ₃ , H ₄ , H ₉ , H ₁₀
Med	-	$Me_{c}, Me_{e}, H_{g}, H_{2}, H_{3}, H_{4}$
Me	-	$Me_{h}, Me_{d}, Me_{f}, H_{9}, H_{10}, H_{11}$
Me _f	-	Me _c , Me _e , H ₄ , H ₉ , H ₁₀ , H ₁₁
Н,	Me _b	Me _d
H _h	Mea	-
H,	H _i	H _i , H ₁₁
H _i .	H _{i'}	H _i , H ₂
H	H _i , H _k	H_{i} , H_{k} , H_{5} , H_{6} , H_{11}
H _i .	H _{i'} , H _{k'}	H _i , H _k , H ₂ , H ₇ , H ₈
H _k	\mathbf{H}_{i}	$H_{i}, H_{9}, H_{10}, H_{11}$
H _k .	H _i .	$H_{i'}, H_2, H_3, H_4$
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	$H_{i}, H_{4}, H_{6}, H_{11}$
H ₆	H5, H7, H8	H_{i} , 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	$\mathrm{Me_{c}},\mathrm{Me_{e}},\mathrm{Me_{f}},\mathrm{H_{k}},\mathrm{H_{9}},\mathrm{H_{11}}$
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 ¹H-NMR spectrum. However, no change in the ¹H-NMR spectrum of (R,R,R)-28 in CDBr₃ 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.



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 mutarotation, 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.



The separation of the diastereomers was however accomplished 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 ¹H-NMR spectrometry (CDCl₃), which shows a doublet for the methine protons at δ 4.54 (2H). In addition to the signal at δ 4.54, the diastereometric mixture (R, R, R/S, S, S/S, S, R/R, R, S)-17a, prepared by bromination of 16a in CHCl₃ 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°C, 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 diasterometric mixture (R, R, R/S, S, S/S, S, R/R, R, S)-17a. When a proper variable temperature ¹H-NMR spectral study was performed, the coalescence temperature (T_c) has been found to be 110°C and the corresponding ΔG_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 ¹H-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 ¹H-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°C 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 ¹H-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).



It was anticipated that the barrier to inversion of 32 could be determined by temperature dependent ¹H-NMR signals of the diastereotopic methyl groups. Unfortunately, no coalescence of the two methyl doublets was observed when a CDBr₃ solution of 32 was heated to 135°C. 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, $T_c = 110$ °C), and is also confirmed by dynamic circular dichroism spectroscopic study³⁵ 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 ¹H-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. ¹H-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 CDCl₃ 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 Katt³⁸ 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. NH₄OAc (0.5 g, 6 mmol), and Et₃N (2 mL) was heated at 130°C under nitrogen for 20 h. The resulting solution was cooled and dissolved in 10% HCl (100 mL). The acidic solution was washed with Et₂O (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 Et₂O (3 X 100 mL). The Et₂O solution was dried over anhyd. K₂CO₃, and the solvent was removed. The residue thus obtained was chromatographed on a basic alumina column (eluted with Et₂O) to afford **8** as light yellowish oil (2.8 g, 25%), bp 60-70°C (0.5 mmHg) [lit¹⁶ bp 95-110°C (3 mmHg)]. MS: *m/e* 161 (M⁺); ¹H-NMR (60 MHz): δ 1.53 (m, 8H), 2.79 (m, 4H), 6.88 (dd, 1H, H₃, J = 8, 5 Hz), 7.20 (dd, 1H, H₂, J = 8, 3 Hz), 8.20 (dd, 1H, H₄, 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°C (0.5 mmHg) [lit^{10b} bp 140-160°C (0.3 mmHg)]. MS: m/e 249 (M⁺); ¹H-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(9H)-one (10)

A solution of 9 (3 g, 12 mmol) in CH₂Cl₂ (150 mL) was treated with a mixture of ozone and oxygen at -40°C until the reaction was completed (monitored by TLC analysis). The dissolved ozone was purged with bubbling nitrogen through the solution. Me₂S (16 mL) was added, and the mixture was stirred for 0.5 h at -35°C and then at r.t. overnight. The solution was washed with water (50 mL), 5% aq. NaOH (50 mL), dried over anhyd. K₂CO₃, 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°C (0.5 mmHg) [lit^{10b} bp 105-110°C (0.2 mmHg)]. MS: *m/e* 175 (M⁺); ¹H-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(9H)-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. Na₂CO₃ (1.2 g, 10 mmol) in EtOH (40 mL) was refluxed for 2 h. After evaporation of the solvent, the residue was extracted with CHCl₃ (3 X 30 mL). The CHCl₃ solution was washed with water (30 mL), dried over anhyd. MgSO₄, concentrated and distilled to give the desired product **11** as a pink oil (2 g, 87%), bp 130-140°C (0.3 mmHg) [lit^{10b} bp 130°C (0.2 mmHg)]. ¹H-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 °C for 50 h and the crude product was chromatographed on basic alumina (eluted with EtOAc) to provide **12** (0.6 g, 66%). Recrystallization from CHCl₃ afforded colorless crystals, mp 140-142°C [lit^{10b} mp 140-142°C]. MS: m/e 210 (M⁺); ¹H-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 CCl₄ (40 mL) was refluxed under nitrogen for 4 h. The CCl₄ solution was cooled and washed with brine (20 mL). The brine solution was separated and extracted with CHCl₃ (15 mL). The CHCl₃ extract was combined with the CCl₄ layer. The organic solution was dried over anhyd. MgSO₄ 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°C. MS: *m/e* 366 (M⁺); Exact mass: Calcd for C₁₄H₁₂Br₂N₂, 365.9366, 367.9346, 369.9326; Found 365.9379, 367.9376, 369.9381; ¹H-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 C₁₄H₁₂Br₂N₂: 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 CHCl₃ (3 X 20 mL). The CHCl₃ 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°C. MS: *m/e* 206 (M⁺); Exact mass: Calcd for C₁₄H₁₀N₂, 206.0844; Found 206.0862; ¹H-NMR (250 MHz): (in CDCl₃) 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 C₆D₆) 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 C₁₄H₁₀N₂: 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 CHCl₃ (3 X 40 mL) and the CHCl₃ solution was washed with brine (30 mL). The solution was then dried over anhyd. Na₂SO₄ 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°C. MS: *m/e* 308 (M⁺); ¹H-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 C₂₂H₁₆N₂: 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 CHCl₃ (30 mL) was added a solution of Br_2 (0.20 g, 1.25 mmol) in CHCl₃ (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°C. 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 C₂₂H₁₆Br₂N₂: 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 ¹H-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 °C. A solution of Br₂ (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 °C for 0.5 h. The solvents and excess Br₂ 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 ¹H-NMR spectral analysis. The product was then dissolved in CHCl₃. 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). ¹H-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 = 15.7Hz), 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°C. MS: *m/e* 308 (M⁺); Exact mass: Calcd for $C_{22}H_{16}N_2$: 308.1062; Found 308.1058; ¹H-NMR (250 MHz): δ 2.5 (m, 2H, H_{7,7}·), 2.9 (m, 2H, H_{6,6}·), 5.75 (m, 1H, H₈), 6.58 (d, 1H, H₉, *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 CHCl₃ (50 mL). The solution was then washed with brine (20 mL), dried over anhyd. Na₂SO₄, 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°C. MS: *m/e* 306 (M⁺); ¹H-NMR (250 MHz): (in CDCl₃) 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 C₆D₆) 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 C₂₂H₁₄N₂: 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°C. MS: *m/e* 310 (M⁺); Exact mass: Calcd for $C_{20}H_{14}N_4$, 310.1218; Found 310.1211; ¹H-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 CHCl₃ (40 mL) was added a solution of Br₂ (120 mg, 0.75 mmol) in CHCl₃ (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°C. The product was used for subsequent reaction without further purification. MS: m/e 470 (M⁺); Exact mass: Calcd for C₂₀H₁₄N₄Br₂, 467.9584; Found: 467.9588. Since the diastereomeric excess of this bromination reaction was approximately 78%, ¹H-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); 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°C. MS: *m/e* 310 (M⁺); Exact mass: Calcd for $C_{20}H_{14}N_4$ 310.1218; Found 310.1221; ¹H-NMR (250 MHz): δ 2.52 (m, 2H, H_{7,7}·), 3.00 (m, 2H, H_{6,6}·), 5.78 (m, 2H, H₈), 6.60 (d, 1H, H₉, *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°C. MS: m/e 308 (M⁺); Exact mass: Calcd for C₂₀H₁₂N₄ 308.1062; Found 308.1058; ¹H-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 CDCb (1 mL, freshly distilled from P₂O₅) 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 CDCl₃. An orange red solution resulted and the NMR tube was sealed immediately under nitrogen. ¹H-NMR (250 MHz): (at 22°C) 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°C to -60°C.

(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 CDCl₃ (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. ¹H-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°C. ¹H-NMR (250 MHz) (CD₃OD): 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 C₂₂H₁₆N₂Cl₂: 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°C) (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 °C. Dark red crystals of 21 were obtained (13 mg, 53%), mp 253-258°C. 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; ¹H-NMR (250 MHz): (in C₆D₆) 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°C) (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°C. ¹H-NMR (250 MHz): (in CDCl₃) 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 C₆D₆) 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 C₂₆H₁₄N₂O₄W: 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°C) (3 mL) was heated at 140 °C 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°C. Dark red crystals of **23** were collected, mp 215°C (dec) (15 mg, 74%). ¹H-NMR (250 MHz): (in CDCl₃) 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 C₆D₆) 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 C₁₈H₁₀N₂O₄Mo: 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(ClO₄)₂•6H₂O (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°C. ¹H-NMR (250 MHz): (in CDCl₃) & 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 CD₃COCCD₃): & 6.54, 6.85 (AA'BB', 4H, H_{6,7,8,9}, $J_{AB} = 11$ Hz, $J_{BB'} = 3$ Hz, $J_{AB'} = -1.5$ 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): \aleph_{max} nm (log ε): 236 (4.97), 240 (4.97), 262 (4.98), 337 (4.38), 520 (2.94); Anal.: Calcd for C₄₄H₂₈N₄CuClO₄: 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°C. ¹H-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 C₂₂H₁₄N₂Cl₂Hg: 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°C. 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°C 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 NaClO₄•H₂O (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-Et₂O, mp 198-200°C. ¹H-NMR (250 MHz): δ 1.14 (d, 3H, CH₃, J = 6.6 Hz), 1.48 (d, 3H, CH₃, J = 6.5 Hz), 2.34 (s, 3H, NCH₃), 2.50 (s, 3H, NCH₃), 2.53 (s, 3H, NCH₃), 2.84 (s, 3H, NCH₃), 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, H₂, J = 5.1, 1.6 Hz), 9.19 (dd, 1H, H₁₁, J = 6.9, 1.5 Hz); Anal.: Calcd for C₃₄H₃₈N₄Cl₂O₄Pd₂: 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(9H)-one (29)

To a suspension of silver chromate (0.39 g, 1.1 mmol) and 4 Å molecular sieves (0.4 g) in dry CH₂Cl₂

(30 mL) were added iodine (380 mg,1.5 mmol) and a solution of pyridine (50 mg, 0.6 mmol) in CH₂Cl₂ (2 mL) at 0°C (ice-bath) and the mixture was stirred for 5 min at the same temperature. A solution of **16a** (310 mg, 1 mmol) in CH₂Cl₂ (5 mL) was added dropwise during 5 min to the ice-cooled suspension and the mixture was stirred for 20 min at 0°C. 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 CH₂Cl₂ (10 mL). The combined filtrate was washed with 5% aq. Na₂S₂O₃ (30 mL), brine (20 mL), and then dried over anhyd. MgSO₄. After the solvent was removed the residue was crystallized from CHCl₃-EtOAc (1:1) and the product **29** was collected as colorless crystals (0.23 g, 51%), mp 193-194°C. MS: *m/e* 450 (M⁺); ¹H-NMR (250 MHz): δ 3.26 (d, 1H, H₆, *J* = 6.0 Hz), 3.32 (d, 1H, H₆, *J* = 6.0 Hz), 4.10 (d, 1H, H₉, *J* = 12.2 Hz), 4.98 (m, 1H, H₇), 6.20 (d, 1H, H₉, *J* = 12.2 Hz), 7.75 (m, 4H, H_{2,3,12,13}), 7.93 (d, 1H, H₄, *J* = 8.1 Hz), 8.03 (d, 1H, H₁₁, *J* = 8.1 Hz), 8.37 (s, 1H, H₅), 8.37 (m, 2H, H_{1,14}), 8.39 (s, 1H, H₁₀); Anal. Calcd for C₂₂H₁₅N₂IO: 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(6H)-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 CHCl₃ (50 mL). The CHCl₃ solution was washed with brine (20 mL) and was dried over anhyd. MgSO₄. The solvent was removed and the residue was recrystallized from CHCl₃-EtOAc (1:1) to yield colorless crystals of **30** (90 mg, 50%), mp 275-276°C. MS: *m/e* 322 (M⁺); ¹H-NMR (250 MHz): δ 3.90 (m, 2H, H_{6,6}·), 5.99 (d, 1H, H₈, *J* = 12 Hz), 7.38 (d, 1H, H₉, *J* = 12 Hz), 7.65 (m, 2H, H_{3,12}), 7.85 (m, 2H, H_{2,13}), 7.88 (d, 1H, H₁₁, *J* = 8 Hz), 7.92 (d, 1H, H₄, *J* = 8 Hz), 8.12 (s, 1H, H₅), 8.28 (s, 1H, H₁₀), 8.30 (d, 1H, H₁, *J* = 8 Hz), 8.35 (d, 1H, H₁₄, *J* = 8 Hz); Anal.: Calcd for C₂₂H₁₄N₂O: 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°C 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. NH₄Cl (5 mL) was added to the reaction mixture, the upper layer was separated, extracted with CHCl₃ and the CHCl₃ layer was dried over anhyd. MgSO₄. 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°C. MS: m/e 366 (M⁺); Exact mass: Calcd for C₂₅H₂₂N₂O, 366.1732; Found: 366.1730; ¹H-NMR (250 MHz): δ 0.97 (d, 6H, 2-CH₃, J = 6.9 Hz), 1.98 (m, 1H, CH(CH₃)₂), 2.86 (d, 1H, H₆, J = 13.9 Hz), 3.07 (d, 1H, H₆, J = 13.0, 1.8 Hz), 6.57 (d, 1H, H₉, 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°C 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 CHCl₃ (3 X 15 mL), and the extracts were dried over anhyd. MgSO₄ 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 C₂₅H₂₀N₂, 348.1626, Found 348 1629; ¹H-NMR (250 MHz): δ 0.97 (d, 3H, CH₃, J = 6.9 Hz), 1.02 (d, 3H, CH₃, J = 6.9 Hz), 2.51 (septet, 1H, CH(CH₃)₂, J = 6.9 Hz), 6.24 (d, 1H, H₈, J = 11 Hz), 6.59 (s, 1H, H₆), 6.85 (d, 1H, H₉, 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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