Synthesis and Properties of Cu(I) Complexes of Isoquinoline-Related Bidentates

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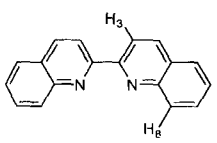
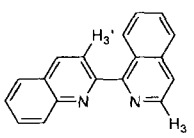
The increasing interests in the complexes of copper with 1,4-diimine type ligands stem from the interdependence of coordination geometry and redox as well as photochemical behaviors.[1] Complexes of Cu(I) adopt a tetrahedral or pseudotetrahedral geometry and are often deep red in color. In the absence of restricting steric effects, these complexes are readily oxidized to the stable Cu(II) species which is square-planar in geometry and green in color. Although most of the Cu(I) complexes exhibit this sort of instability, Cu(I) complexes of 2,2'-biquinoline (bq) and its annelated compounds were found to be somewhat redox stable.[2]

The usages of Cu(I) complexes have been extended to the catalytic electroreduction of dioxygen,[3] the energy transfer,[4] and the cleaving activity on nucleic acids.[5] Additionally, Sauvage and co-workers have extensively studied Cu(I) complexes as a template for the formation of tetrahedrally organized catenane derivatives in part of supramolecular chemistry.[6]

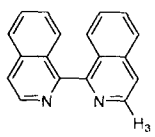
Herein we described the synthesis and the physicochemical as well as biochemical properties of Cu(I) complexes of isoquinoline-related non-coplanar bidentates, such as 1-(2'-quinolyl)isoquinoline (**2**, qisq), and 1,1'-biisoquinoline (**3**, bisq) comparing to complex of 2,2'-biquinoline (**1**, bq).



1 (bq)



2 (qisq)



3 (bisq)

Experimental Section

Melting points were determined using a Fischer-Jones melting points apparatus and are not corrected. IR spectra were obtained using a Perkin-Elmer 1330 spectrophotometer. Nuclear magnetic resonance spectra were obtained using a Bruker-300 spectrometer 300 MHz for ^{1}H NMR and 75.5 MHz for ^{13}C NMR and are reported as parts per million from the internal standard tetramethylsilane. The starting 1-acetylisoquinoline,[8] $[Cu(CH_3CN)_4]ClO_4$,[9] and $[Cu(\mathbf{1})_2]ClO_4$ were prepared by either previously reported method or modification of such a method. 2,2'-Biquinoline was obtained from Lancaster Synthesis, Inc. Chemicals and solvents were commercial reagent grade and used without further purification. Cyclic voltammographs were recorded using BAS CV-27 voltammograph and a Hitachi Model 057-1025 X-Y recorder. Elemental analyses were taken on a Hewlett-Packard Model 185B elemental analyzer. The previously reported method[5b] was employed for the evaluation of cleaving activity on DNA.

1-(2'-Quinolyl)isoquinoline (2). A mixture of 1-acetylisoquinoline (0.17 g, 1.0 mmol), and 2-aminobenzaldehyde (0.12 g, 1.0 mmol) in 15 mL of absolute EtOH was refluxed for 2 h with three drops of sat. KOH in absolute EtOH. After cooling to room temperature, the reaction mixture was concentrated to dryness and dissolved in CH_2Cl_2 (50 mL). The resulting solution was washed with H_2O, followed by brine. The organic layer was dried over anhydrous $MgSO_4$. Evaporation of the solvent gave pale yellow solid which recrystallized from EtOH afforded 0.22 g (85%) of white needles: mp 142-143 °C (lit.[10] mp 142-143 °C). Unreported spectral data are as follows: ^{1}H NMR($CDCl_3$, 500 MHz) δ 8.83 (d, J = 8.4 Hz, $H_{8'}$), 8.70 (d, J = 5.7 Hz, H_3), 8.38 (d, J = 8.4 Hz, $H_{3'}$), 8.26 (d, J = 8.4 Hz, H_8), 8.15 (d, J = 8.4 Hz, $H_{4'}$), 7.94-7.90 (overlapped d, J = 8.4 Hz, 2H, H_5 and $H_{5'}$), 7.79 (td, J = 7.2, 0.9 Hz, 1H, H_7), 7.76 (d, J = 5.7 Hz, H_4), 7.73 (td, J = 7.8, 1.2 Hz, 1H, $H_{6'}$), 7.65-7.60 (overlapped t, 2H, $H_{7'}$ and H_6).

1,1'-Biisoquinoline (3). Prepared by the previously reported method, mp 164-165 °C (lit.[11] mp 162-163 °C). Unreported spectral data are as follows: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.69 (d, J = 8.7 Hz, H_3), 7.92 (d, J = 8.4 Hz, H_8), 7.79 (d, J = 5.7 Hz, H_4), 7.72 (d, J = 8.4 Hz, H_5), 7.68 (d, J = 7 5 Hz, H_6), 7.45 (td, J = 7.2, 0.9 Hz, H_7).

$[Cu(2)_2]ClO_4$. Into a solution of 51.2 mg (0.2 mmol) of 1-(2'-quinolyl)isoquinoline in 3 mL of dry CH_3CN was degassed and kept under Ar pressure, was added 32.7 mg (0.1 mmol) of $[Cu(CH_3CN)_4]ClO_4$ in 1 mL of dry CH_3CN. The dark purple solution formed was stirred for an additional hour and removed the solvent under Schlenk-line to give red platelets. *Caution! Perchlorate salts are potentially explosive!* ^{1}H NMR (CD_3CN, 300 MHz with 6.0 mg of ascorbic acid) δ 8.80 (d, J = 8.4 Hz, 1H, $H_{3'}$), 8.62 (d, J = 8.4 Hz, 1H, $H_{4'}$), 8.44 (d, J = 5.7 Hz, 1H, H_3), 8.42 (overlapped d, J = 5.7 Hz, 1H, H_4), 8.11 (d, J = 7.8 Hz, 1H, $H_{5'}$), 8.03 (d, J = 8.1 Hz, 1H, H_5), 7.96 (d, J = 6.0 Hz, 1H, $H_{8'}$), 7.92 (d, J = 7.8 Hz, 1H, H_8), 7.84 (td, J = 8.7, 1.2 Hz, 1H, $H_{6'}$), 7.73 (d, J = 8.4 Hz, 1H, H_7), 7.58 (td, J = 7.8, 0.9 Hz, 1H, H_6), 7.45 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H, $H_{7'}$). UV (EtOH) λ_{max} (ε) 206 (131,800), 255 (64,600), 346 (16,600), 519 (3,500), 596 (2,600). Anal. Calcd. for $CuC_{36}H_{24}N_4ClO_4$: C, 64.00; H, 3.58; N, 8.29. Found: C, 63.99; H, 3.60, N, 8.31.

$[Cu(3)_2]ClO_4$. Into a solution of 51.2 mg (0.2 mmol) of 1,1'-biisoquinoline in 3 mL of dry CH_3CN was degassed and kept under Ar pressure, was added 32.7 mg (0.1 mmol) of $[Cu(CH_3CN)_4]ClO_4$ in 1 mL of dry CH_3CN. The red solution formed was stirred for an additional hour and removed the solvent under Schlenk-line to give red platelets. ^{1}H NMR (CD_3CN, 300 MHz with 6.0 mg of ascorbic acid) 8.02 (over-

lapped d, J = 8.1 Hz, 4H, $H_3/H_{3'}$ and $H_4/H_{4'}$), 7.84 (d, J = 5.1 Hz, 1H, $H_8/H_{8'}$), 7.73 (t, J = 7.5 Hz, 2H, $H_5/H_{5'}$), 7.38 (t, J = 7.5 Hz, 2H, $H_6/H_{6'}$), 7.20 (d, J = 8.4 Hz, 2H, $H_7/H_{7'}$). UV data were not obtainable due to the unstability of the compound. Anal. Calcd for $CuC_{36}H_{24}N_4ClO_4$: C, 64.00; H, 3.58; N, 8.29. Found: C, 64.02; H, 3.58, N, 8.31.

Cyclic Voltammetry. Into a cyclovoltammetry cell was added 5.12 mg (0.02 mmol) of ligand in 3 mL of dry CH_3CN with 0.1 M of TBAP (tetra-*n*-butylammonium perchlorate). The reduction potentials of ligand was measured from the above solution to afford the values shown in Table 1. To the solution was then added 3.27 mg (0.01 mmol) of $[Cu(CH_3CN)_4]ClO_4$ and the redox potentials were measured directly from the resulting colored solution to give redox potentials of the Cu(I) complex shown in Table 1.

Results and Discussion

Three quinoline and isoquinoline-related bidentates were prepared by employing previously reported methods.[10,11] The reaction of these ligands in a 2 : 1 fashion with $[Cu(CH_3CN)_4]ClO_4$ in CH_3CN provided the complex as a red crystalline salt in quantitative yields. To prevent possible air oxidation, the reaction was carried under Ar, followed by removal of solvent under Schlenk-line. Although the ligand bisq was claimed not to form metal complex with Fe(II) due to the strong interference between the H's at the 8 and the 8' position.[11] If one assumes that the bisq is planar, these two hydrogen atoms would completely overlap thus preventing the formation of complex. The reaction of bisq with $[Cu(CH_3CN)_4]ClO_4$, however, smoothly results Cu(I) complex in quantitative yield.

The computer generated geometry of the ligands bq, qisq, and bisq are somewhat distorted through the 2,2'-, 2,1'- and 1,1'-bond, respectively, thus to have 179.3°, 128,4° and 124.8° as dihedral angles.[7] From the geometric points of view, the formation of tetrahedral complex is favored by ligands qisq and bisq. However, the ^1H NMR study showed that Cu(I) complex of ligand bq was the most redox-stable one, thus affording a more clearly resolved ^1H NMR as has been reported.[2] On the other hand, the Cu(I) complexes of latter two are somewhat redox-unstable enough to undergo at least partial oxidation yielding paramagnetic Cu(II) species, thus fail to provide a good ^1H NMR spectra at either room temperature or even lower temperature (-78 °C). However, the addition of ascorbic acid as a reducing agent stabilizes Cu(I) species in ^1H NMR solvent to result a well-resolved spectrum (Figure 1).

The proton resonances of the ligands as well as the corresponding complexes were assigned by a double-quantum filtered COSY experiments (Figure 2). It is worthy to note that upon complexation with Cu(I) the H4 resonances of the quinoline moiety for bq and qisq shifted downfield by 0.66-0.99 ppm. This effect is greatest ($\Delta\delta$ 0.99 ppm) for qisq due to the depletion of charge at C4 of the quinoline nucleus and to the deshielding effect of the adjacent isoquinoline ring that occur upon coordination. Such an effect diminishes to 0.66 for bq in which the deshielding effect of the isoquinoline ring is absent. On the other hand, the H7 and H8 of bq, H3 and H8' of qisq, and H3 and H3' for bisq experience a shielding effect by the aromatic ring current of the orthogonal ligand thus shifted upfield. The H8' and H3 resonances of qisq are most sensitive to this effect ($\Delta\delta$ 0.87 and 0.25 ppm, respectively). The H3 resonance of bisq is under the similar environment thus to have $\Delta\delta$ 0.67, which are comparable to $\Delta\delta$ 0.67 for H8 of ligand bq.

The redox potentials were measured by cyclic voltammetry in dry CH_3CN, and these data are given in Table 1. The oxidation waves are quasi-reversible and show a steady decrease upon going from $[Cu(\mathbf{1})_2]ClO_4$ to $[Cu(\mathbf{3})_2]ClO_4$. The Cu(I) complex of the most distorted ligand $[Cu(\mathbf{3})_2]^+$ has

Table 1. Half-Wave Redox Potentials of the Ligands and Cu(I) Complexes

Compound	$E_{1/2}$ (oxid)	$E_{1/2}$ (red)
1		-1.02(120)
2		-1.02(120)
3		-0.87(300)
$[Cu(\mathbf{1})_2](ClO_4)$	+0.88(90)	-1.26(110)
$[Cu(\mathbf{2})_2](ClO_4)$	+0.47(90)	-1.02(120)
$[Cu(\mathbf{3})_2](ClO_4)$	+0.38(170)	-0.87(300)

[a]Potentials are in volts *vs* SCE. Solutions were 0.1 M TBAP(tetra-*n*-butylammonium perchlorate) in CH_3CN; T=25±1 °C: the sweep rate was 200 mV/sec. The number in parentheses is the difference between the anodic and cathodic waves.

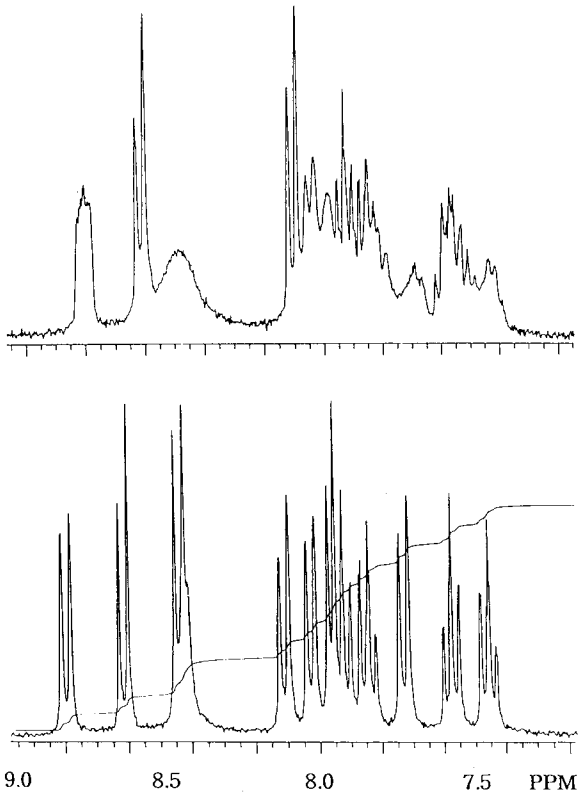


Figure 1. 300 Hz ^1H NMR spectra of $[Cu(\mathbf{2})_2](ClO_4)$ in CD_3CN in the absent (top) and in the presence (bottom) of 0.6 mg of ascorbic acid as a reducing agent.

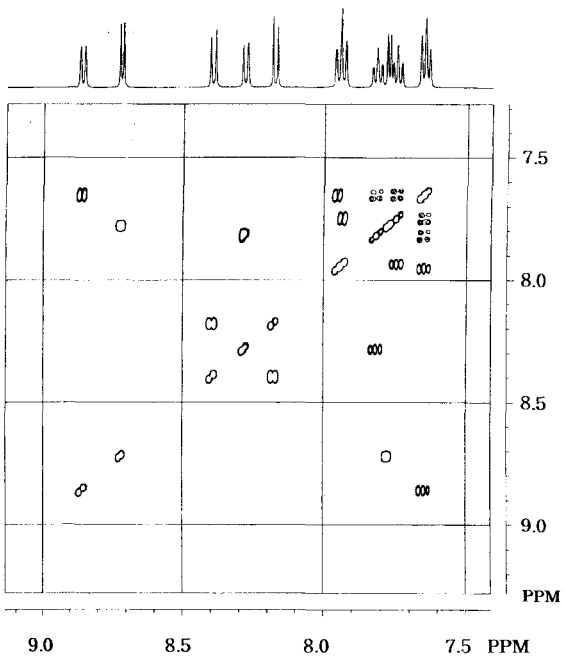


Figure 2. 500 MHz ^{1}H NMR COSY spectrum of 1-(2'-quinolyl)-isoquinoline.

smaller oxidation potential (+0.38 V *vs* SCE) over $[Cu(\mathbf{1})_2]^+$ and $[Cu(\mathbf{2})_2]^+$ by $E_{1/2}(ox)$ of 0.50 V and 0.09 V, respectively, thus showing the susceptibility in oxidation. It is well established that Cu(I) complexes are stabilized toward oxidation by ligands which will interfere the ability of the system to become planar and flexible.[6] An observation is consistent with the fact that the ligand **1** is the most planar in geometry, which is reflected to the higher oxidation potential in Cu(I) complex.

The reduction of Cu(I) complex is generally ligand based and reflects the electronegativity of the ligand, the redox properties of the ligands are thus usually observed in Cu(I) complexes.[1] Reductions of $[Cu(\mathbf{2})_2]^+$ and $[Cu(\mathbf{3})_2]^+$ occur at -1.02 V and -0.87 V *vs* SCE, respectively, which are about 0.24 V and 0.39 V less negative than the value for the complex $[Cu(\mathbf{1})_2]^+$ indicating that ligands qisq and bisq are better electron acceptors than bq. These reduction potentials are comparable to the value (-1.10 V) of $[Cu(dib\text{-}phen)_2]^+$ (dib-phen is dibenzo[*b*,*j*][1,10]phenanthroline) in which dib-phen is completely planar and the most electronegative one in the series.[2]

Interestingly, the absorption spectrum of complex $[Cu(\mathbf{3})_2]^+$ was not obtainable due to the unstability of the complex. During the irradiation of the UV light, the dark red solution was completely decolorized presumably due to the dissociation of the complex by UV radiation. Strong absorption bands of $[Cu(\mathbf{2})_2]^+$ are observed at 206 (131,800), 255 (64,600), and 346 (16,600) nm, respectively, which correspond quite closely to the ligand π-π^* absorptions.[10] Two weaker bands of $[Cu(\mathbf{2})_2]^+$ at 519 nm and 596 nm are comparable to the band at 546 nm of $[Cu(\mathbf{1})_2]^+$ and can be assigned to the metal-to-ligand charge transfer (MLCT) states.[2,12]

As far as biochemical property is concerned, Sigman *et al.* claimed that the redox stability may affect the DNA-cleaving ability.[5] Such a suggestion prompted us to test the cleaving activities of the Cu(I) complexes prepared. Any of these complexes, however, did not show any promising cleaving activity. The reason for the loss of such an effect remained to be clarified.

In conclusion, highly distorted bidentates, 1-(2'-quinolyl)-isoquinoline and 1,1'-biisoquinoline were prepared and readily converted to their Cu(I) complexes. Even though the geometries of the two distorted ligands prefer a tetrahedral Cu(I) complex, resulting complexes are too redox unstable to afford well-resolved ^{1}H NMR spectra. Such an unstability may due to the unfavorable conjugative interactions between the two aromatic rings of the distorted bidentates.

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