

1. Synthesis and Structure of the Copper(II) Complex of a Chiral Bis(dihydrooxazole) Ligand

by Jonathan Hall¹⁾, Jean-Marie Lehn^{1)*}, André DeCian²⁾, and Jean Fischer^{2)*}

Institut Le Bel, Université Louis Pasteur, 4, rue Blaise Pascal, F-67000 Strasbourg

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The bridged bis(dihydrooxazole) compound (–)-**2** and its silylated derivative (–)-**3** have been synthesised as building blocks for chiral ligands. The complex of (–)-**3** with Cu^{II} has been obtained, and its crystal structure has been determined. The Cu^{II} ion is bound to two deprotonated ligands in a twisted tetracoordinated geometry.

Introduction. – The binding of metal ions (such as Cu^I, Ag^I) displaying a tetrahedral coordination geometry to oligo(2,2'-bipyridine) (bipy) strands leads to the self-organisation of double stranded helicate complexes [1–4]. These species are obtained as racemic mixtures of left- and right-handed double helices. One may imagine several ways of inducing a given helicity in helicate formation such as: *a*) the introduction of permanent chirality in the backbone, *b*) the use of a chiral auxiliary group [5], *c*) the asymmetric delivery of the metal ion in a chiral medium or from a preformed chiral complex.

The purpose of the present work was to explore option *a*) by developing a chiral, bidentate ligand which, when included into an oligomeric species or into an oligobipyridine strand might be expected to form helicates with asymmetric induction.

The structural requirements for such a ligand are *i*) that it should have C₂ symmetry, *ii*) that it should form strong complexes with transition metals in non-planar arrangements, and *iii*) that it should have functionality close to the ligating site so that attachment of additional ligands would be possible at a later stage.

Our attention focused on the chiral dihydrooxazoles developed in recent years [6]; two identical, suitably functionalised dihydrooxazoles, connected by a bridge, appeared to be well-suited for our purpose³⁾. In addition, the ligand would be readily available by the condensation of a known bis(amide enol ether) dihydrochloride with an aminodiol from the chiral pool. Other possible chiral subunits could be bipy groups bearing an asymmetric centre [8] or chiral semicorrin-type units [9].

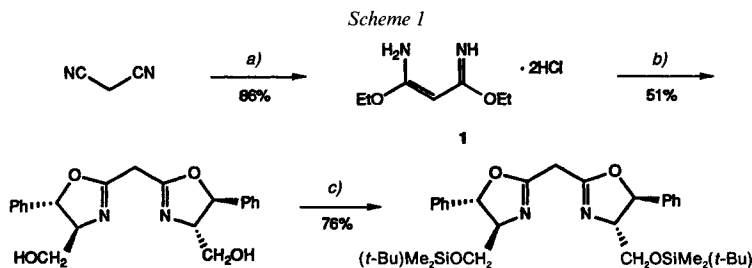
We describe here the synthesis of the chiral bridged bis(dihydrooxazole) (–)-**2** and its bis-silylated derivative (–)-**3**, containing four asymmetric centres, as well as the formation and crystal structure of the 2:1 complex of (–)-**3** with Cu^{II}.

Synthesis. – The ligands (–)-**2** and (–)-**3** were prepared as depicted in *Scheme 1*. The amide enol ether hydrochloride **1** was synthesised by the published procedure [10];

¹⁾ Laboratoire de Chimie Supramoléculaire, URA 422 of the CNRS.

²⁾ Laboratoire de Cristalochimie, URA 424 of the CNRS.

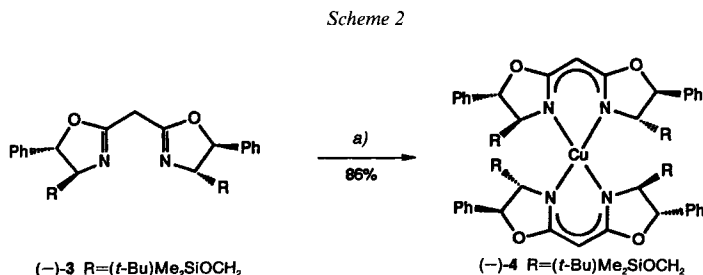
³⁾ Whilst this manuscript was in preparation, a similar example of the synthesis of chiral bis(dihydrooxazoles) appeared in the literature [7].



a) EtOH, HCl, dioxane, 18 h. b) (+)-(1*S*,2*S*)-2-Amino-1-phenylpropane-1,3-diol, DMF, 3 days. c) (*t*-Bu)Me₂SiCl, imidazole, DMF.

malonodinitrile reacted with EtOH in the presence of HCl to give the moisture-sensitive salt **1**. The enamine form agrees with the observation of a solitary methine *s* at 4.44 ppm in the ¹H-NMR spectrum. Condensation of **1** with the commercially available (+)-(1*S*,2*S*)-2-amino-1-phenylpropane-1,3-diol in DMF yielded the bis(dihydrooxazole) (–)-**2** in moderate yield⁴⁾; undesired isomers resulting from ring closure with the primary OH group were not isolated. The product was crystalline and soluble only in polar organic solvents such as MeCN, MeOH, and DMF. Silylation of the OH groups with (*t*-Bu)Me₂SiCl under standard conditions provided compound (–)-**3** as a viscous, colourless oil in good yield.

Copper(II) Complex of Compound (–)-3. – Mixing MeCN solutions of ligand (–)-**3** and Cu^IClO₄ in the presence of air led to instant purple-colour formation and precipitation, within several h, of a violet crystalline solid. This product was shown to be the Cu^{II} complex (–)-**4** by reaction of the same ligand with Cu^{II}(OAc)₂ in MeOH; in this case, the reaction was rapid and of high yield (Scheme 2). Comparison of the various physical



properties of the solids obtained in the two reactions (m.p., analysis, UV/VIS, IR, and FAB-mass spectra, magnetic moments, and optical rotations) showed them to be identical. The structure of (–)-**4** was determined by an X-ray crystallographic study (Fig.) of a suitable crystal, obtained from the Cu^I reaction.

The crystal structure of (–)-**4** shows both ligands to be deprotonated at the bridge position, and there are no external anions present. Each bidentate bis(dihydrooxazole)-

⁴⁾ Dihydrooxazoles are known to be formed with retention of configuration when imidates are condensed with optically active aminoalcohols [11].

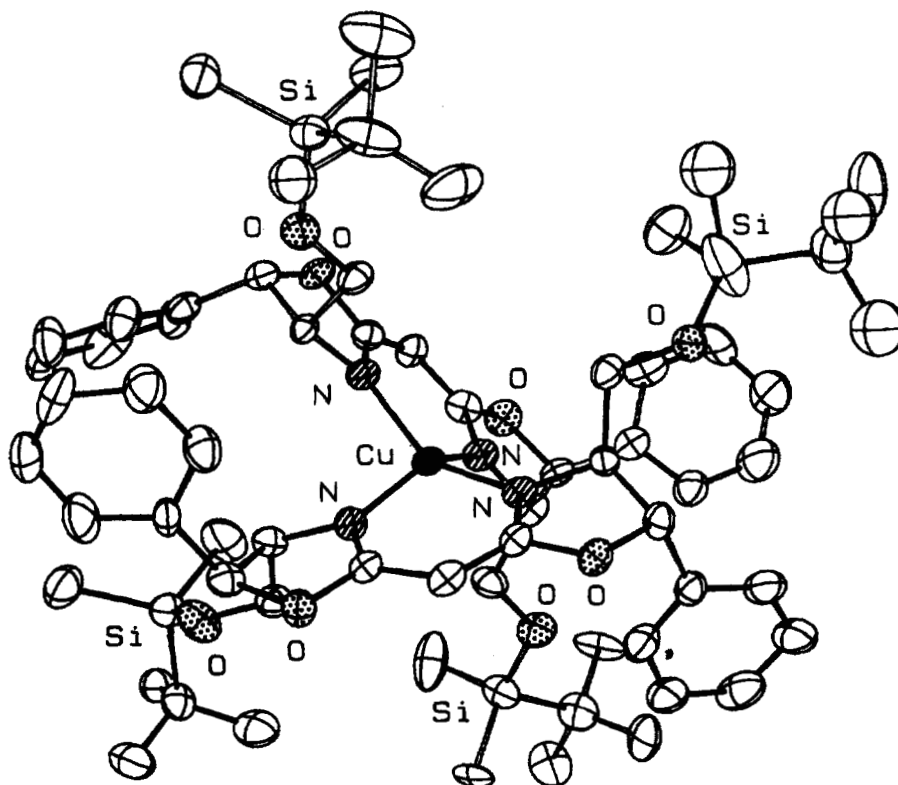


Figure. ORTEP plot of the crystal structure of complex (–)-4. Ellipsoids are scaled to enclose 50% of the electronic density. H-Atoms are omitted.

methanido ligand coordinates to the Cu^{II} ion *via* the ring N-atoms and produces a distorted tetrahedral environment about the metal atom. This is the result of increasing steric strain between the R substituents of each ligand as they approach the Cu-site [12]. The resulting deviation from planarity, measured as the dihedral angle between the two N–Cu–N planes, is 52° and is typical for such bidentate ligands. Thus, a dihedral angle of 62° has been reported for the crystal structure of a (semicorrin)copper complex [9]. Within error limits, the Cu–N bond lengths and the N–Cu–N bond angle from both ligands are equivalent (1.9 Å and 90° , resp.).

The structural features of complex (–)-4 are compatible with the use of units of type (–)-2 for helicity induction into double-stranded helicates formed from oligomeric strands of (–)-2 or from mixed strands containing both bipy and (–)-2 as subunits. Furthermore, metal complexes of (–)-2 or derivatives thereof are also suitable candidates as reagents or catalysts for asymmetric processes (see, *e.g.*, [7] [9]). Such studies are under way.

Experimental Part

General. All reactions were carried out under Ar unless otherwise stated. Solvents were dried by distillation before use: dioxane and Et₂O from Na/benzophenone, DMF and MeCN from CaH₂. EtOH, MeOH, and CH₂Cl₂ were obtained from Carlo Erba. Malonodinitrile was purified by distillation. (+)-(1*S*,2*S*)-2-Amino-1-phenylpropane-1,3-diol was purchased from Merck and used without further treatment. Cu(OAc)₂ was purchased from BLB. Flash chromatography: Merck-9385 silica gel. Magnetic moments were calculated using the Evans method from measurements of solns. of the complexes in (D₈)toluene containing 2% of dioxane; CuSO₄ · 5 H₂O, μ_{eff} (300 K) 1.88 B.M., was used as a standard. NMR spectra: Bruker-AC200 spectrometer; chemical shifts in ppm relative to CHCl₃ (¹H, 7.26 ppm; ¹³C, 77.1 ppm); coupling constants *J* in Hz; homo-decoupling and a DEPT-135 program were used when necessary to aid assignments in the ¹H- and ¹³C-NMR spectra, resp. IR spectra: Perkin-Elmer-597. UV/VIS: Perkin-Elmer Lambda 5. M.p.: uncorrected; Electrothermal IA 8100. Optical rotations: Perkin-Elmer 241MC. MS: LKB 9000S with PDP11, direct inlet onto a SE-30 capillary column (EI); ZAB-HF VG (FAB⁺); *m/z* (rel. %). Elemental analyses were performed by the Institut de Chimie, Strasbourg.

Ethyl 3-Amino-3-ethoxyprop-2-enimidate (1). HCl gas was bubbled slowly into ice-cold dioxane (50 ml) containing malonodinitrile (2.12 g, 32.09 mmol) and EtOH (3.04 g, 66.07 mmol). The soln. became yellow, and a white solid was precipitated. The ice-bath was removed and gas bubbled gently through the mixture for further 17 h. The soln. was filtered quickly in air and washed copiously with dry Et₂O. The white crystalline solid **1** (6.38 g, 86%; [10]: 95%), m.p. 120–121° ([10]: 119–120°), was dried under vacuum and used in the next step immediately. ¹H-NMR (200 MHz, (D₆)DMSO): 1.31 (*t*, *J* = 6.9, 2 CH₃); 4.21 (*q*, *J* = 6.9, 2 CH₂); 4.44 (*s*, C=CH); 7.39 (*t*, *J* = 50.8, 1 H, NH); 8.34 (br. *s*, 3 H, NH); 11.22 (br. *s*, 1 H, NH). ¹³C-NMR (50 MHz, (D₆)DMSO): 14.0 (CH₃); 63.0 (CH); 65.5 (CH₂); 168.9 (C=N).

(–)-(4*S*,4′*S*,5*S*,5′*S*)-4,4′,5,5′-Tetrahydro-2,2′-methylene-5,5′-diphenylbis[oxazole]-4,4′-di(methanol) ((–)-**2**). (+)-(1*S*,2*S*)-2-Amino-1-phenylpropane-1,3-diol (28.10 g, 168 mmol) was added to a cooled, rapidly stirred suspension of **1** (15.47 g, 67.13 mmol) in dry DMF (150 ml) under Ar. The white suspension was almost completely solubilised before a new solid began to precipitate. The ice-bath was removed immediately, and the mixture was allowed to stir for 3 days at r.t. The solid NH₄Cl was filtered off and the DMF distilled off below 50°. A small amount of the residue (6%, *v/v*) was purified by column chromatography (2–9% MeOH/CH₂Cl₂) and yielded a white crystalline solid which was recrystallised twice from hexane/AcOEt: colourless crystals of (–)-**2** (761 mg, 52%). M.p. 118.3–119.0° [α]_D²⁵ = –79.9 (*c* = 0.27, MeCN). UV/VIS (MeCN): 278 (1630), 269 (1470), 222 (3190). IR (KBr): 3450–3000, 2890, 2820, 1660, 1590, 1330, 1265, 1210, 1160, 1090, 1080, 1050, 975, 945, 920, 760, 700. ¹H-NMR (200 MHz, CD₃CN): 3.28 (br. *s*, 2 OH); 3.52 (*d*, *J* = 0.9, CH₂); 3.67 (*d*, *J* = 4.3, 2 CH₂O); 3.98 (*m*, 2 CHN); 5.42 (*d*, *J* = 6.4, 2 CHPh); 7.31–7.38 (*s*, 2 Ph). ¹³C-NMR (50 MHz, CD₃CN): 26.9 (CH₂); 63.5 (CH₂O); 76.7 (CHN); 84.4 (CHPh); 126.7 (Ph); 129.4 (Ph); 141.3 (Ph); 164.3 (C=N). EI-MS: 367 (5, [*M* + H]⁺), 366 (6), 336 (100), 261 (5), 260 (17), 192 (8), 191 (18). Anal. calc.: C 68.83, H 6.05, N 7.64; found: C 68.78, H 6.25, N 7.85.

(–)-(4*S*,4′*S*,5*S*,5′*S*)-4,4′-Bis{[*t*-(tert-butyl)dimethylsilyloxy]methyl}-4,4′,5,5′-tetrahydro-2,2′-methylene-5,5′-diphenylbis[oxazole] ((–)-**3**). A mixture of (–)-**2** (544 mg, 1.48 mmol), (*t*-Bu)Me₂SiCl (492 mg, 3.26 mmol), imidazole (534 mg, 7.84 mmol), and DMF was heated to 66° for 29 h. H₂O was added, and the products were extracted into Et₂O (3 times). The extracts were combined, washed with H₂O (once), dried (Na₂SO₄), and evaporated: yellow oil. Residual DMF was removed under vacuum at r.t. The product was chromatographed (1–3% MeOH/CH₂Cl₂): (–)-**3** as anal. pure colourless oil (665 mg, 76%). [α]_D²⁴ = –18.4 (*c* = 0.65, MeCN). UV/VIS (Et₂O): 262 (5080). IR (neat): 3050, 2930, 2920, 2840, 1650–1670, 1580, 1520, 1485, 1455, 1385, 1245, 1115, 1070, 975, 830, 770, 690, 660. ¹H-NMR (200 MHz, CDCl₃): 0.07 (*s*, 6 H, MeSi); 0.08 (*s*, 6 H, MeSi); 0.90 (*s*, 2 *t*-Bu); 3.56 (br. *s*, CH₂); 3.68 (*dd*, *J* = 10.2, 7.0, 2 CHO); 3.92 (*dd*, *J* = 10.2, 3.8, 2 CHO); 4.07–4.16 (*m*, 2 CHN); 5.45 (*d*, *J* = 6.4, 2 CHPh); 7.21–7.35 (*m*, 2 Ph). ¹³C-NMR (50 MHz, CDCl₃): –5.3 (MeSi); 18.3 (Me₃CSi); 25.9 (Me₃CSi); 28.8 (CH₂); 64.8 (CH₂O); 76.5 (CHN); 84.4 (CHPh); 125.8 (Ph); 128.0 (Ph); 128.6 (Ph); 140.9 (Ph); 162.2 (C=N). EI-MS: 594 (2, M⁺), 539 (17), 538 (45), 537 (100), 449 (17), 191 (11), 89 (37), 73 (90). Anal. calc.: C 66.62, H 8.47, N 4.71; found: C 66.83, H 8.46, N 4.82.

(–)-Bis{bis{[4*S*,5*S*]-4-[*t*-(tert-butyl)dimethylsilyloxy]methyl}-4,5-dihydro-5-phenyloxazole}methanido}-copper(II) ((–)-**4**). *a*) To a MeOH soln. (1 ml) of (–)-**3** (65 mg, 0.11 mmol) at r.t. was added Cu(OAc)₂ · H₂O (11 mg, 0.06 mmol) in MeOH (2 ml). A purple crystalline solid immediately began to precipitate. The mixture was left to stand for 3 h, and then the product was filtered from the colourless soln. and dried under vacuum: pure (–)-**4** as small purple crystals (59 mg, 86%). M.p. 179–180° (dec.). μ_{eff} (296 K) 1.8 B.M. [α]_D²⁴ = –1610 (*c* = 0.92, Et₂O). UV/VIS (Et₂O): 491 (1140), 285 (40700), 230 (16400). IR (KBr): 3030, 3010, 2980, 2920, 2880, 2860, 1600, 1530, 1450, 1255, 1215, 1150, 1110, 1050, 1010, 900, 830, 775, 735, 695, 655. FAB-MS: 1250.5 ([*M* + H]⁺), 1249.5,

1193.4, 812.4, 657.2, 595.3, 511.1; isotopic pattern as expected. Anal. calc.: C 63.34, H 7.89, N 4.48; found: C 63.40, H 7.80, N 4.33.

b) To an MeCN soln. (2 ml) of (–)-**3** (422 mg, 0.88 mmol) at r.t. was added CuClO₄ acetonitrile [13] (105 mg, 0.32 mmol) in MeCN (2 ml). The soln. quickly turned purple and deposited large purple crystals. After 2 days, the reddish soln. was filtered to give (–)-**4** as anal. pure crystals (132 mg, 33%). M.p. 179–180° (dec.). $[\alpha]_D^{24} = -1580$. μ_{eff} (296 K) 1.7 B.M. UV/VIS, IR, and FAB-MS as above. Anal. calc.: C 63.34, H 7.89, N 4.48; found: C 63.45, H 7.94, N 4.38.

Data Collection and Crystal-Structure Determination. Suitable single crystals of (–)-**4** were obtained from MeCN soln. at r.t. A systematic search in reciprocal space using a Philips PW1100/16 automatic diffractometer showed that crystals of (–)-**4** belong to the monoclinic system. Quantitative data were obtained at –100° using a local-built gas-flow device. All experimental parameters used are given in the Table. The resulting data set was transferred to a VAX computer, and for all subsequent calculations, the Enraf-Nonius SDP/VAX package [14] was used with the exception of a local data reduction program. Three standard reflections measured every h during the entire data collection period showed no significant trend. The raw step-scan data were converted to intensities using the Lehmann-Larsen method [15] and then corrected for Lorentz and polarisation factors. The structure was solved using the heavy-atom method. After refinement of the heavy atoms, a difference-Fourier map revealed maximas of residual electronic density close to the positions expected for H-atoms; they were introduced in structure-factor calculations by their computed coordinates (C–H = 0.95 Å) and isotropic temperature factors such as $B(\text{H}) = 1.3 \text{ Beqv}(\text{C}) \text{ Å}^2$ but not refined. At this stage, empirical absorption corrections

Table. X-Ray Experimental Parameters for Compound (–)-**4**

Formula	C ₆₆ H ₉₈ CuN ₄ O ₈ Si ₄	Temperature	–100°
Molecular weight	1251.44	Diffractometer	Philips PW1100/16
Color	violet	Mode	$\theta/2\theta$ flying step-scan
Crystal system	monoclinic	Scan speed [deg s ^{–1}]	0.024
<i>a</i> [Å]	11.740 (3)	Scan width [deg]	0.80 + 0.143 tg (θ)
<i>b</i> [Å]	24.698 (5)	Step width [deg]	0.05
<i>c</i> [Å]	12.545 (3)	θ limits [deg]	3/53
β [deg]	91.73 (2)	Octants	$\pm h + k + l$
<i>U</i> [Å ³]	3635.8	Number of data collected	4600
<i>Z</i>	2	Number of data with $I > 3\sigma(I)$	3869
<i>D</i> _{calc} [g cm ^{–3}]	1.145	Abs. min/max	0.48/1.15
Space group	<i>P</i> 2 ₁	<i>R</i> (<i>F</i>)	0.086
Radiation	CuK _α (graphite monochromated)	<i>R</i> _w (<i>F</i>)	0.098
Wavelength [Å]	1.5418	<i>p</i>	0.08
μ [cm ^{–1}]	14.44	<i>GOF</i>	1.96
Crystal size [mm]	0.35 · 0.30 · 0.24		

were applied using the method of Walker and Stuart [16] since face indexation was not possible under the cold gas stream. Full least-squares refinements; $s^2(F^2) = s^2_{\text{counts}} + (pI)^2$. The absolute structure was determined by comparing +*x*, +*y*, +*z* and –*x*, –*y*, –*z* refinements. A final difference map revealed no significant maxima. The scattering-factor coefficients and anomalous-dispersion coefficients were from [17a] and [17b], resp. The final *R* value was 0.086. Supplementary material was deposited with the Cambridge Crystallographic Data Centre. Table S1: temperature factors for anisotropic atoms; Table S2: H-atoms positional parameters; Table S3: complete set of bond distances; Table S4: complete set of bond angles; Table S5: observed and calculated structure-factor amplitudes ($\cdot 10$) for all observed reflections (31 pages).

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- [17] D. T. Cromer, J. T. Waber, 'International Tables for X-Ray Crystallography', The Kynoch Press, Birmingham, 1974, Vol. IV; a) Table 2.2b; b) Table 2.3.1.