Copper(II) complexes derived from substituted 2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) ligands: Synthesis, structure and catalytic activity

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Abstract
New chiral N,N-bidentate 2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) ligands have been prepared and characterised by their ¹H and ¹³C NMR spectra and/or optical rotation. The ligands prepared were then tested for their ability to form complexes with copper(II) salts. It was found that the most stable complex is formed from the 2,2′-bis-(4-isopropyl-1,4-dimethyl-4,5-dihydro-1H-imidazol-5-one) ligand and copper(II) chloride. The structure of this complex was determined by means of quantum-chemical computations at the B3LYP or UB3LYP/6-31G(d,p) level. According to the computations, the geometry of the copper atom most resembles a tetrahedral arrangement, which was also confirmed by means of X-ray structural analysis. It was found that the structure of this copper(II) complex does not allow the copper atom to coordinate to additional ligands; therefore, it is catalytically inactive in the asymmetric Henry reaction.

Graphical abstract
New chiral N,N-bidentate ligands derived from substituted 2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) have been prepared and characterised by means of ¹H and ¹³C NMR spectroscopy and optical rotation. Their Cu(II) complexes have been prepared and their structures have been studied by computational methods and by X-ray diffraction. The catalytic activity of some complexes have been studied.
Keywords: Nitrogen bidentate ligands; 4,5-Dihydro-1H-imidazol-5-ones; Copper(II) complexes; B3LYP/6-31G(d,p); Asymmetric catalysis

1. Introduction

The importance of syntheses and tests of the properties of new nitrogen-containing heterocyclic compounds and their complex compounds with metals lies in the fact that they may be suitable catalysts in many chemical processes. If, in addition to that, the complex is formed by a heterocyclic system that involves a stereogenic centre, then the substance can be applied as a homogeneous or heterogeneous catalyst in many asymmetric syntheses [1]. Among such chiral nitrogen ligands are the derivatives of 4,5-dihydro-1H-imidazol-5-ones [2]. In our previous papers we dealt with the syntheses and catalytic properties of iron(III) [3], rhodium(III) [4] and copper(II) [5] complexes prepared from substituted 2-(4-alkyl-4-methyl-4,5-dihydro-1H-imidazol-5-yl)pyridines (Fig. 1A) [4] or 2,6-bis(4-alkyl-4-methyl-4,5-dihydro-1H-imidazol-5-yl)pyridines [3] and [4] (Fig. 1B). These chiral substituted 2-(4-alkyl-4-methyl-4,5-dihydro-1H-imidazol-5-yl)pyridines represented new types of N,N-bidentate and N,N-tridentate ligands, whose complexes were applied as enantioselective catalysts of the asymmetric Henry reaction [5] or as very effective catalysts of the deallylation reaction of substituted allyl malonates [4].

Fig. 1. Previous 4,5-dihydro-1H-imidazol-5-one ligands.

In the present paper we have dealt with the synthesis and characterisation of substituted 2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-ones) (Scheme 1). The structure of these newly prepared chiral ligands is very similar to the well-known N,N-bidentate derivatives of oxazolines ("Boxes") [6]. However, in comparison with the previous N,N-bidentate 2-(4,5-dihydro-1H-imidazol-5-yl)pyridine ligands (Fig. 1A), the present compounds contain two chiral centres and their structure is characterised by C2-symmetry. Generally, complexes of ligands having this type of symmetry are very suitable for use as enantioselective catalysts, because they form a highly ordered chiral activated complex with the reactants, which results in formation of products of high optical purity. Hence, we decided to prepare copper(II) complexes of these ligands and to study their structure by means of both experimental and theoretical methods. The selected complexes were tested for enantioselective properties in the asymmetric Henry reaction.

Scheme 1. Synthesis of ligands (3a,b and 4a).
2. Results and discussion

2.1. Syntheses and characterisation of the ligands and complexes

Substituted 2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-ones) (3a,b; 4a) were prepared by the sequence of reactions given in Scheme 1. First, we acylated the racemic or optically pure 2-amino-2,3-dimethylbutanamide [7] with oxalyl chloride in the presence of triethylamine. Acylaminobutanamide 1a,b was obtained in a good yield of almost 90%. Subsequent base-catalysed ring closure of compounds 1a,b gave racemic 2a (93%) and (S,S)-2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) (2b) (85%). The reaction time of the ring closure reaction was relatively long (2 days) to achieve the maximum conversion; however, it was not optimised, because the product formed is stable in basic medium. The alkylation of the nitrogen atom at the 1-position of the 1H-imidazol-5-one cycle in compound 2a,b with methyl iodide or benzyl bromide in anhydrous dimethylformamide gave the final ligands 3–4 in the yields of 78–84%. 2,2′-Bis-(4-isopropyl-1,4-dimethyl-4,5-dihydro-1H-imidazol-5-one) (3a) was also prepared in the optically pure form of (S,S) 3b. The base used in the alkylation with methyl iodide was t-BuOK, whilst in the reaction with benzyl bromide anhydrous K₂CO₃ was adopted [5]. The ligands synthesised were characterised by means of ¹H and ¹³C NMR spectroscopy, elemental analysis, determination of melting point and their optical rotatory power.

Complexes 5a,b were prepared by the reaction of copper(II) chloride dihydrate with the corresponding ligand in methanol in yields of 84% (5a) and 81% (5b). The complexes were characterised by elemental analyses, and the structure of complex (5b) was determined by X-ray structural analysis. Complexes 5a,b were found to be readily soluble in organic solvents, particularly alcohols, chloroform and acetone; on the other hand, they are virtually insoluble in ether and alkanes. Isolation of the complex of 2,2′-bis-(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) (4a) with copper(II) chloride failed, probably due to its very low stability. The syntheses of the complexes of ligands 3a, 3b and 4 with copper(II) acetate failed too. Since ligand 4a exhibits bad chelate-forming ability, i.e. it is not suitable for the study of enantiocatalytic activity, its optically pure form was not prepared.

2.2. Quantum-chemical computations of the structure and stability of the complexes

The complex-forming abilities of the ligands and the stabilities of the complexes were studied by means of quantum-chemical computations at the B3LYP or UB3LYP/6-31G(d,p) level; for details, see Section 4.5. It was found that compound 4a assumes the most stable conformation, depicted in Fig. 2. Due to the presence of the bulky benzyl substituents, the 1H-imidazol-5-one cycles are deviated to such an extent that the molecule loses its property as an N,N-bidentate ligand. According to the potential energy surface (PES) scan there exists only one local minimum during rotation around the single bond connecting both cycles. Next there are four local energy minima during rotation of the benzyl or isopropyl groups, but none of these conformations are able to coordinate to a metal ion. The computation shows that the formation of a complex based on 4a with CuCl₂ is energetically unfavourable by 21 kJ/mol. Such a complex should not be stable. This finding agrees with the experimental results.

Fig. 2. Structure of ligand 4a at the B3LYP/6-31G(d,p) level.
Fig. 3 depicts the structure of the complex of ligand 3a with CuCl₂. This representation shows that the substituents at the chiral centres disturb the usual planar geometry of the copper atom. The structure of this complex does not allow the copper atom to coordinate to a further two ligands. The absence of free coordination sites at the copper atom explains the lack of effectiveness of this complex in the enantioselective Henry reaction [5] and [9], because this reaction requires the presence of two free coordination sites at the transition metal atom [5]. These coordination properties of ligand 3a also explain the lesser stability of the complex with Cu(OAc)₂. Stable complexes with acetates of transition metals are formed in those cases in which the anion of acetate behaves as an η²-ligand [8]. In the complex of 3a with Cu(OAc)₂ there are only two coordination sites per two acetate anions, hence the complex is less stable.

2.3. X-ray analysis of complex 5b

The molecular structure of complex 5b was determined by means of X-ray analysis (Fig. 4). The geometry of the copper atom most resembles a tetrahedral arrangement: Cl₁–Cu₁–Cl₂ 106.00(6)°, Cl₁–Cu₁–N₁ 103.69(13)°, Cl₁–Cu₁–N₂ 133.19(14)°, Cl₂–Cu₁–N₁ 131.79(14)°, Cl₂–Cu₁–N₂ 104.22(14)°, N₁–Cu₁–N₂ 80.78(18)°. However, the plane defined by atoms Cl₁, Cl₂ and Cu₁ makes an angle of 65.2(4)° with the plane defined by atoms N₁, N₂ and Cu₁. Hence, the chlorine atoms are considerably deviated from the ideal tetrahedral arrangement (90°). This deviation is probably caused by the large steric demands of the isopropyl groups of the ligand: there are van der Waals interactions between the hydrogen atoms of the carbons of the isopropyl group, C₁₅ and C₁₆, with chlorine atom Cl₁ and/or an interaction among the hydrogen atoms at carbons C₇ and C₈ with the chlorine atom Cl₂. The 1H-imidazol-5-one rings are not coplanar; their planes are mutually deviated by an angle of 12.11°. This anomaly probably follows from an interaction between the methyl groups at the 1-position of the 1H-imidazol-5-one ring (atoms C₄ and C₁₂). The experimental structure of complex 5b agrees (Fig. 5) with the structure predicted by means of quantum-chemical methods. The two structures differ only in the position of the isopropyl group. The inter-atomic distances and bond angles in the 1H-imidazol-5-one rings are similar to those published earlier for the structures of copper(II) [5] and iron(III) [3] complexes of 1H-imidazol-5-one ligands.
Cu1–N1 103.69(13), Cl1–Cu1–N2 133.19(14), Cl2–Cu1–N1 131.79(14), Cl2–Cu1–N2 104.22(14), N1–Cu1–N2 80.78(18), N1–C1–C9 113.4(5), N2–C9–C1 114.7(5), Cu1–N1–C1 115.2(4), Cu1–N2–C9 114.0(4), Cu1–N1–C3 135.1(4), Cu1–N2–C11 136.0(4).

Fig. 5. (a) Structure of complex 5b at the UB3LYP/6-31G(d,p) level, (b) overlay, and (c) X-ray analysis of complex 5b.

2.4. Study of the enantioselectivity of ligand 3b

The copper(II) complexes of ligand 3b were studied as enantioselective catalysts of the asymmetric Henry reaction [5] and [9]. This choice of model reaction is rationalised by the fact that copper(II) complexes are amongst the most effective catalysts of the Henry reaction [9]. We found out that 5 mol% of ligand 3b together with 5 mol% of copper(II) acetate catalyse the reaction of 4-nitrobenzaldehyde with nitromethane, the yield of the isolated 2-nitro-1-(4-nitrophenoxy)ethanol being 75% after 22 days at room temperature, but the enantioselectivity was virtually zero (\( \leq 3\% \) ee). This result can be explained by the fact that the reaction is only catalysed by free copper(II) acetate, no complex being formed at all between copper(II) acetate and ligand 3b. Although zero enantioselectivity was observed in both cases, it cannot be excluded that ligand 3b may form catalytic systems with other metal ions, which may be effective in other asymmetric reactions.

3. Conclusion

While the N-methyl derivatives 3a and 3b form isolatable and air-stable complexes with copper(II) chloride, the N-benzyl derivative 4a does not produce such complexes, since its structure lacks the properties of an N,N-bidentate ligand. Likewise, the isolation of complexes of ligands 3a and 3b with copper(II) acetate failed. These experimentally found complex-forming properties of the ligands were analysed by means of quantum-chemical methods. Using the B3LYP/6-31G(d,p) model we computed the structure of complex 5b, in which the geometry of the copper atom most resembles a tetrahedral arrangement. Since the copper atom does not contain any further free coordination sites, it is not able to catalyse the Henry nitroaldol reaction. The structure of complex 5b determined by the quantum-chemical computations was confirmed by X-ray structural analysis.

4. Experimental

4.1. NMR measurements

The \(^1\)H and \(^{13}\)C NMR spectra were recorded on a Bruker Avance spectrometer at 500.13 (\(^1\)H) and 125.76 MHz (\(^{13}\)C) in \(d_6\)-DMSO. The \(^1\)H and \(^{13}\)C chemical shifts were referenced to the central peaks of the solvent (\(\delta = 2.55\) and 39.60, respectively).

4.2. Optical rotatory power determination

Optical rotation was measured on a Perkin–Elmer 341 Instrument, the concentration \(c\) is given in g/100 ml.
4.3. HPLC analyses
The optical purity of 2-nitro-1-(4-nitrophenyl)ethanol was determined by means of HPLC using a Chiralcel OD–H column (85:15 hexane:propan-2-ol, 0.8 ml/min, 220 nm; (R)-isomer: tR = 21.0 min, (S)-isomer: tS = 25.9 min).

4.4. X-ray crystallography
The single crystals of 5b were grown from ca. 10% methanol/ethyl acetate solution. The relevant crystallographic parameters and procedures are as follows: The data for a colourless crystal were collected at 150(1) K on a Nonius Kappa CCD diffractometer using Mo Kα radiation (λ = 0.71073 Å), a graphite monochromator, the structure was solved by direct methods (sir92 [10]). All reflections were used in the structure refinement based on F2 by the full-matrix least-squares technique (SHELXL97 [11]). Hydrogen atoms were mostly localized on a difference Fourier map; however, to ensure uniformity of the treatment of all crystals, all hydrogen atoms were recalculated into idealised positions (riding model) and assigned temperature factors Hiso(H) = 1.2 Ueq (pivot atom) or 1.5 Ueq for a methyl moiety (C–H = 0.96 Å for CH3 and 0.98 Å for CH group hydrogen atoms). Absorption corrections were carried out using Gaussian integration from crystal shape (Coppens [12]). Empirical formula C26H30Cu2Cu2N2O3; Formula weight 440.85; Crystal system Orthorhombic; Space group P212121; Unit cell dimensions a, b, c (Å) 6.8720(7), 13.8020(19), 20.447(4); Volume (Å3) 1939.3(5); Z 4; Density (Mg/m3) (calc.) 1.510; Absorption coefficient (mm−1) 1.419; F(0 0 0) 916; Crystal size (mm) 0.27 × 0.20 × 0.06; Theta range for data collection 1.0–27.5; h range −8 → 8; k −16 → 17; l −26 → 26; Reflections collected 17153; Tmin, Tmax 0.806, 0.937; Independent/Observed reflections (I > 2σ(I)) 4351/3344; Rint (Rint = Σ|Fo| − |Fc|)|ΣFo| 0.079; Absorption correction multi-scans (SORTAV) No. of parameters 226; S all data (S = Σ(w(Fo2 − Fc2))2/(Nparams − Nreflections)) 0.0525, 0.1165; R1, wR2 (all data) 0.0872, 0.1330; Flack parameter 0.00(2); Δρmax, Δρmin (e/Å3) 0.860, −0.772.

4.5. Computational method
Quantum-chemical computations were carried out with the Gaussian03 program [13] employing the hybrid density functional B3LYP [14]. Full geometry optimisations were performed by using the 6-31G(d,p) basis set [15]. The nature of the stationary points was verified by analytical computations of harmonic vibration frequencies. Solvation effects were included using the polarizable continuum model (PCM) [16], (solvent: methanol as in Section 4.6.8). The starting structure for optimisation was obtained after energy minimisation using the software Chem3D Ultra 10.0. Full conformational analysis was performed using the potential energy surface (PES) scan method which is directly implemented in the Gaussian software. Scans for each bond where the free rotation is possible were evaluated for 12 conformations differing in dihedral angle (30° step). The CuCl2 structure with four solvent molecules was used together with the PCM model.

4.6. Synthesis of the ligands and the copper(II) complexes
4.6.1. Preparation of (t)-N,N′-bis[1-(carbamoyl)-1,2-dimethylpropyl]ethanediamide (1a)
A solution of (±)-2-amino-2,3-dimethylbutanamide (2.6 g; 20 mmol) and triethylamine (2.8 ml; 20 mmol) in 20 ml dry CH2Cl2 was stirred at room temperature and a solution of oxalyl chloride (1.27 g; 10 mmol) in 15 ml CH2Cl2 was added drop by drop. The suspension obtained was stirred at room temperature for another 10 hour, whereupon the mixture was evaporated, and the dry evaporation residue was thoroughly washed with water. Yield 2.76 g (88%) white crystalline solid melting at 196–198 °C. 1H NMR (d6-DMSO, δ ppm): 0.84 (d, 3J = 6.8 Hz, 6H, 1 × iPrCH2), 0.85 (d, 3J = 6.8 Hz, 6H, 1 × iPrCH2), 1.52 (s, 6H, CH3), 2.19 (sp, 3J = 6.8 Hz, 2H, iPrCH), 7.28 (bs, 2H, 1 × CONH2), 7.41 (bs, 2H, 1 × CONH2), 8.41 (bs, 2H, CONH). 13C NMR (d6-DMSO, δ ppm): 17.6, 17.7, 17.9, 34.6, 62.7, 158.8, 174.2. Anal. Calc. for C16H26N2O3: C, 53.47; H, 8.34; N, 17.82. Found: C, 53.31; H, 8.39; N, 17.63%.
4.6.2. Preparation of (S,S)-N,N′-bis[1-(carbamoyl)-1,2-dimethylpropyl]ethanediamide (1b)

Compound 1b was prepared in the same way as compound 1a in a yield of 89% and with a melting point of 266–267 °C; [α]D = 38.0° (c = 0.25, CH3OH). 1H NMR (δ ppm): 0.84 (d, 3J = 6.8 Hz, 6H, iPrCH3), 0.86 (d, 3J = 6.8 Hz, 6H, iPrCH3), 1.53 (s, 6H, CH3), 2.20 (sp, 3J = 6.8 Hz, 2H, iPrCH), 7.32 (bs, 2H, 1 × CONH2), 7.40 (bs, 2H, 1 × CONH2), 8.44 (bs, 2H, CONH). 13C NMR (δ ppm): 14.7, 17.5, 17.9, 34.6, 62.7, 158.9, 174.2. Anal. Calc. for C14H22N2O2: C, 53.47; H, 8.34; N, 17.82. Found: C, 53.64; H, 8.41; N, 17.60%.

4.6.3. Preparation of (±)-2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) (2a)

A mixture of substance 1a (2.51 g, 8 mmol) and 40 ml 1 M NaOH (40 mmol) was stirred at room temperature. After 2 days, the mixture was neutralised with concentrated HCl to pH ∼7 and extracted with 4 × 30 ml CH2Cl2. The combined extracts were evaporated until dry to give 2.07 g (93%) product melting at 227–230 °C. 1H NMR (δ ppm): 0.77 (d, 3J = 7.0 Hz, 6H, iPrCH3), 0.94 (d, 3J = 7.0 Hz, 6H, iPrCH3), 1.23 (s, 6H, CH3), 1.91 (sp, 3J = 7.0 Hz, 2H, iPrCH), 11.50 (s, 2H, NH). 13C NMR (δ ppm): 16.4, 16.5, 20.6, 34.1, 74.9, 152.4, 185.9. Anal. Calc. for C14H22N2O2: C, 60.23; H, 7.85; N, 19.98. Found: C, 60.21; H, 8.19; N, 19.95%.

4.6.4. Preparation of (S,S)-2,2′-bis-(4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) (2b)

Compound 2b was prepared in the same way as compound 2a in a yield of 85% and with a melting point of 219–221 °C; [α]D = −47.4° (c = 0.50, CH3OH). 1H NMR (δ ppm): 0.77 (d, 3J = 7.0 Hz, 6H, iPrCH3), 0.93 (d, 3J = 7.0 Hz, 6H, iPrCH3), 1.23 (s, 6H, CH3), 1.92 (sp, 3J = 7.0 Hz, 2H, iPrCH), 11.59 (s, 2H, NH). 13C NMR (δ ppm): 16.4, 16.4, 20.5, 34.0, 74.7, 152.4, 185.9. Anal. Calc. for C14H22N2O2: C, 60.41; H, 7.97; N, 20.13. Found: C, 60.23; H, 7.85; N, 19.98%.

4.6.5. Preparation of (±)-2,2′-bis-(4-isopropyl-1,4-dimethyl-4,5-dihydro-1H-imidazol-5-one) (3a)

Compound 2a (1.39 g, 5 mmol), kept under argon atmosphere, was treated with a solution of potassium t-butyllate (20 mmol, 2 equiv.) in t-butyl alcohol. The mixture was stirred at room temperature for 1 h, whereupon t-butyle alcohol was distilled off under reduced pressure. The evaporation residue was dissolved in 10 ml dry DMF. After 2 days, the mixture was neutralised with concentrated HCl to pH ∼7 and extracted with 4 × 30 ml CH2Cl2. The combined extracts were evaporated until dry to give 2.07 g (93%) product melting at 60–62 °C. 1H NMR (δ ppm): 0.80 (d, 3J = 6.8 Hz, 6H, iPrCH3), 1.00 (d, 3J = 6.8 Hz, 6H, iPrCH3), 1.31 (s, 6H, CH3), 2.00 (sp, 3J = 6.8 Hz, 2H, iPrCH), 3.24 (s, 6H, NCH3). 13C NMR (δ ppm): 16.7, 17.0, 20.5, 28.3, 34.1, 73.8, 152.4, 184.6. Anal. Calc. for C16H24N2O2: C, 62.64; H, 8.39; N, 18.18%.

4.6.6. Preparation of (S,S)-2,2′-bis-(4-isopropyl-1,4-dimethyl-4,5-dihydro-1H-imidazol-5-one) (3b)

Compound 3b was prepared in the same way as compound 3a in a yield of 84% and with a melting point of 63–65 °C; [α]D = −51.3° (c = 0.74, CH3OH). 1H NMR (δ ppm): 0.80 (d, 3J = 6.8 Hz, 6H, iPrCH3), 1.01 (d, 3J = 6.8 Hz, 6H, iPrCH3), 1.30 (s, 6H, CH3), 2.01 (sp, 3J = 6.8 Hz, 2H, iPrCH), 3.25 (s, 6H, NCH3). 13C NMR (δ ppm): 16.7, 17.1, 20.5, 28.3, 34.2, 73.8, 152.3, 184.6. Anal. Calc. for C16H24N2O2: C, 62.72; H, 8.55; N, 18.29. Found: C, 62.68; H, 8.35; N, 18.17%.

4.6.7. Preparation of (±)-2,2′-bis-(1-benzyl-4-isopropyl-4-methyl-4,5-dihydro-1H-imidazol-5-one) (4a)

A mixture of compound 2a (1.11 g, 4 mmol), anhydrous K2CO3 (1.66 g; 12 mmol), KI (50 mg) and benzyl bromide (2.05 g, 12 mmol) in 10 ml dry DMF was heated under an inert atmosphere at a temperature of 150 °C for a period of 2 days. After cooling, the mixture was filtered and the solid on the filter was washed with 3 × 10 ml DMF.
The combined filtrates were evaporated under reduced pressure until dry. The residue was recrystallised from methanol with charcoal to give 1.43 g (78%) product melting at 107–117 °C. $^1$H NMR ($d_6$-DMSO, δ ppm): 0.65 (d, $^3$J = 6.9 Hz, 6H, iPrCH$_3$), 0.95 (d, $^3$J = 6.9 Hz, 6H, iPrCH$_3$), 1.27 (s, 6H, CH$_3$), 2.03 (sp, $^3$J = 6.9 Hz, 2H, iPrCH), 5.09–5.22 (m, 4H, BzCH$_2$), 6.95 (m, 4H, PhH), 7.19 (m, 6H, PhHm, Hp). $^{13}$C NMR ($d_6$-DMSO, δ ppm): 16.7, 17.0, 21.1, 34.6, 44.5, 74.6, 126.8, 127.2, 128.5, 136.9, 151.3, 185.0. Anal. Calc. for C$_{28}$H$_{34}$N$_4$O$_2$: C, 73.33; H, 7.47; N, 12.22. Found: C, 73.24; H, 7.67; N, 12.09%.

4.6.8. Synthesis of copper(II) complex 5a
A solution of ligand 3a (61.3 mg; 0.2 mmol) in 10 ml dry methanol was mixed with CuCl$_2$·2H$_2$O (34.1 mg; 0.2 mmol). The mixture was refluxed with exclusion of air moisture for 1 h. After cooling, the solvent was removed at reduced pressure, and the residue was suspended in 10 ml dry ether. The solid was collected by suction and washed with 20 ml ether. Yield 74 mg (84%) orange product. Anal. Calc. for C$_{16}$H$_{26}$Cl$_2$CuN$_4$O$_2$: C, 43.59; H, 5.94; N, 12.71. Found: C, 43.85; H, 6.16; N, 12.68%.

4.6.9. Synthesis of copper(II) complex 5b
Compound 5b was prepared in the same way as compound 5a in a yield of 81%; [X]$_D^{25}$ = −35.9° (c = 0.51, CH$_3$OH). Anal. Calc. for C$_{16}$H$_{30}$Cl$_2$CuN$_4$O$_2$: C, 43.59; H, 5.94; N, 12.71. Found: C, 43.77; H, 6.12; N, 12.59%.

4.6.10. Nitroaldol (Henry) reaction of 4-nitrobenzaldehyde with nitromethane
A typical procedure of the nitroaldol (Henry) reaction of 4-nitrobenzaldehyde with nitromethane is described in Ref. [5] (Method C and Method D).

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