

Chiral bipyridine–copper(II) complex. Crystal structure and catalytic activity in asymmetric cyclopropanation

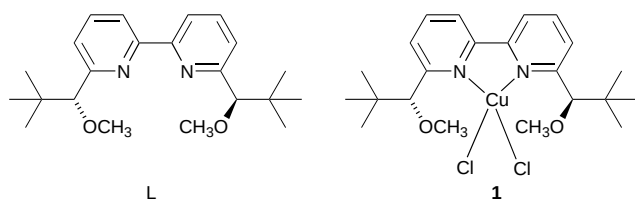
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A chiral bipyridine–copper(II) complex has been prepared and its crystal structure determined. The structure involves a CuN_2Cl_2 compressed tetrahedral stereochemistry. Chiral bipyridine complexes of copper-(I) and -(II) triflate are active catalysts for asymmetric cyclopropanation of alkenes with enantiomeric excesses up to 92%.

Despite the importance of bipyridine in catalysis, photochemistry and supramolecular chemistry, little use has been made of chiral bipyridine ligands in asymmetric catalysis, when compared with other chiral N–N bidentate ligands.¹ Cyclopropanes are useful building blocks for the construction of organic molecules. The synthesis of chiral cyclopropanes from achiral starting materials has been of considerable interest in the last few decades.² Chiral metal complexes, especially those of copper, have been widely used as catalysts for asymmetric cyclopropanation. Chiral ligands such as bis(oxazolines),³ semi-corrins⁴ and Schiff bases⁵ are the most popular for copper-catalysed cyclopropanation. Recently, Katsuki and co-workers⁶ reported the use of chiral bipyridine ligands synthesized from 2,3-cyclohexenepyrindine in asymmetric cyclopropanation.⁶ These results clearly suggested the great potential of this type of ligand. Bolm *et al.*⁷ reported the facile synthesis of the chiral bipyridine **L** and its use in diethylzinc addition to aldehydes. In order to increase the scope of this type of ligand, we report the synthesis of its copper(II) chloride complex, the crystal structure of the latter and the use of such chiral bipyridine–copper-(I), -(II) triflate (trifluoromethanesulfonate) compounds in enantioselective cyclopropanation of alkenes. The few examples of copper–chiral N–N bidentate ligand complexes characterized are either mononuclear 2:1⁸ or polymeric 1:1 ligand to copper complexes.⁹ The present compound has an unusual co-ordination environment for Cu^{II} . Unlike the previously reported chiral N–N bidentate ligands, this chiral bipyridine ligand is unique in that both copper-(II) and -(I) triflate form active catalysts for cyclopropanation.



Experimental

Chloroform was distilled under N_2 from calcium chloride. Chiral compound **L** was prepared according to the literature.⁷ *tert*-Butyl diazoacetate was prepared by modification of a literature procedure.¹⁰ All other chemicals were of reagent-grade quality used as commercially obtained. Proton and ^{13}C NMR spectra were recorded on a JEOL 270 FT spectrometer, IR spectra on a Perkin-Elmer Model FTIR-1600 spectrometer and UV spectra on a Perkin-Elmer Lambda 19 spectrometer. Elem-

ental analyses were performed by MEDAC Ltd. or on a Leco CHN-900 micro carbon hydrogen nitrogen determinator.

Preparation of the copper(II) chiral bipyridine complex **1**

Chiral compound **L** (0.14 g, 0.4 mmol) in CH_2Cl_2 (5 cm^3) was added dropwise to a solution of copper(II) chloride (0.068 g, 0.4 mmol) in absolute ethanol (5 cm^3). An intense orange-red color developed instantaneously. The solution was refluxed overnight to ensure complete complexation. Addition of diethyl ether to the cooled reaction mixture led to a deep orange microcrystalline solid. The mixture was placed in a refrigerator overnight and the microcrystalline solid then filtered off and washed with ether. It was recrystallized from CH_2Cl_2 –ether to give deep orange crystals, which were filtered off and dried *in vacuo*. The complex was characterized by X-ray crystallography, elemental analysis (C, H, N), IR and UV spectroscopy. Yield: 0.145 g (74%) (Found: 53.80; H, 6.59; N, 5.66. Calc. for $\text{C}_{22}\text{H}_{32}\text{Cl}_2\text{CuN}_2\text{O}_2$: C, 53.82; H, 6.52; N, 5.71%). IR(KBr): 3086.3w, 2967.6vs, 2946.0vs, 2830.5w, 1597.2m, 1570.2m, 1478.6s, 1458.0s, 1431.2m, 1396.0w, 1358.9m, 1225.0w, 1203.1w, 1165.6s, 1080.9vs, 1021.5m, 962.0m, 941.8w, 916.9w, 820.0m, 785.5w, 758.0w, 671.4w and 647.9w cm^{-1} . Visible spectrum (CH_2Cl_2): $\lambda_{\text{max}}(\epsilon)$ 310 (22 125), 322 (19 075), 406 (881) and 919 nm (107 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$).

X-Ray crystallography

Suitable crystals were grown by dissolving complex **1** in CH_2Cl_2 and by diffusion of diethyl ether into it. These orange crystals were air stable. Diffraction data were obtained on a Rigaku AFC7R diffractometer at ambient temperature. Crystal data and details of measurements are summarized in Table 1.

CCDC reference number 186/833.

Preparation of the copper(I)–chiral bipyridine complex

Compound **L** (0.071 g, 0.2 mmol) in CH_2Cl_2 (2.5 cm^3) was added dropwise to a solution of copper(I) chloride (0.018 g, 0.2 mmol) in CH_3CN (2.5 cm^3). An intense red colour developed instantaneously. The solution was refluxed overnight under N_2 to ensure complete complexation. Solvent was removed and the red solid obtained was washed with ether. It was then recrystallized from CH_2Cl_2 –hexane to give red crystals which were filtered off and dried *in vacuo*. The complex was characterized by elemental analysis (C, H, N), IR, UV and mass spectrometry. Yield: 0.067 g (67%) (Found: 58.25; H, 6.67; N, 6.29. Calc. for $\text{C}_{22}\text{H}_{32}\text{ClCuN}_2\text{O}_2$: C, 58.02; H, 7.08; N, 6.15%). IR(KBr): 3077.5s, 2969.8vs, 2862.1s, 2814.3s, 1593.5s, 1569.5s, 1473.8s, 1455.8s, 1431.9s, 1396.0s, 1354.1m, 1336.2m, 1258.4s, 1222.5m, 1196.6m, 1162.7s, 1090.9vs, 1043.0s, 1013.1s, 965.3s, 815.7s, 779.6s, 749.9w and 666.1m cm^{-1} . Visible spectrum (CH_2Cl_2):

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Table 1 Crystallographic data for complex **1**

Formula	C ₂₂ H ₃₂ Cl ₂ CuN ₂ O ₂
<i>M</i>	490.96
Crystal color, habit	Orange, prism
Crystal dimensions/mm	0.22 × 0.22 × 0.25
Crystal system	Monoclinic
Space group	<i>C</i> 2 (no. 5)
Lattice type	C-centered
<i>a</i> /Å	14.192(3)
<i>b</i> /Å	8.684(3)
<i>c</i> /Å	10.311(3)
β/°	105.92(2)
<i>U</i> /Å ³	1221.9(7)
<i>Z</i>	2
<i>D</i> _c /g cm ^{−3}	1.334
Radiation (λ/Å)	Mo-Kα (0.710 69)
μ(Mo-Kα)/cm ^{−1}	11.31
2θ _{max} /°	60.0
<i>F</i> (000)	514.0
No. reflections measured	total: 1959
	unique: 1889 (<i>R</i> _{int} = 0.046)
Residuals <i>R</i> , <i>R'</i>	0.045, 0.028

λ_{max}(ε) 336 (2247) and 462 nm (95) dm³ mol^{−1} cm^{−1}. Positive ion FAB mass spectrum: *m/z* 454 (*M*⁺) and 419 (*M*⁺ − Cl).

Cyclopropanations

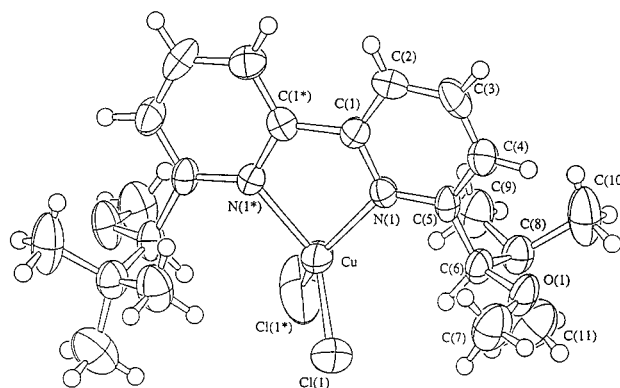
Using complex 1. To a two-neck round-bottom flask were added complex **1** (0.039 g, 0.08 mmol) and silver(I) triflate (0.041 g, 0.16 mmol) under nitrogen. Chloroform (3 cm³) was added and the solution stirred at room temperature for 2 h. The mixture was filtered through a packed filter-paper to a solution of an alkene (32 mmol) in CHCl₃ (3 cm³). A solution of ethyl diazoacetate (0.901 g, 7.9 mmol) in CHCl₃ (3 cm³) was slowly added over a period of 4 h using a syringe pump. The mixture was then stirred for 16 h at room temperature, worked up by removing the solvent and the crude product obtained purified by column chromatography (hexane–ethyl acetate). All the cyclopropanes obtained are known compounds and were characterized by ¹H, ¹³C NMR, IR spectroscopy and GC–MS. The enantiomeric excesses (e.e.s) of the cyclopropanes in entries 1–6, 9 and 11–15 in Table 3 were determined by capillary GC with a Chiraldex β-PH column (30 m × 0.25 mm) and by HPLC with a Daicel Chiralcel OJ column. For substrates in entries 7, 8, 10 and 16 the e.e.s were determined as previously.^{4a} Diastereoselectivities (*cis/trans* ratio) were measured by GC with an Ultra 2 cross-linked 5% phenyl methyl silicone column (25 m × 0.2 mm × 0.33 μm).

Using the copper(I) complex. The complex was generated by stirring copper(I) triflate and **L** for 2 h. All other steps were similar to those with complex **1**. For cyclopropane *tert*-butyl diazoacetate was used instead of ethyl diazoacetate.

Results and Discussion

Although there are large numbers of copper–bipyridine complexes in the literature,¹¹ no crystallographically characterized chiral bipyridine complex of copper of type Cu(bipy*)X₂ has been reported. The stereochemistries of Cu^{II}(bipy)_{*n*}X₂ (*n* = 1 or 2) type complexes are dominated by five- or six-co-ordinate geometries.¹¹ Four-co-ordinate copper(II) complexes only occur with two chelating bidentate ligands and non-bridging anions.¹² The chiral bipyridine **L** and copper(II) chloride form a complex in dichloromethane, which was isolated, as an orange solid in good yield.

The crystal structure, shown in Fig. 1, shows a highly distorted copper(II) ion. Table 2 summarizes the structural parameters. The complex is C₂-symmetric. The copper–nitrogen bond distances of 2.02 Å for both nitrogen atoms of the chiral

**Fig. 1** Molecular structure of complex **1****Table 2** Selected bond lengths (Å), angles (°) and torsion angles (°) for complex **1**

Cu–Cl(1)	2.186(3)	Cu–N(1)	2.017(6)
Cu–Cl(1*)	2.186(3)	Cu–N(1*)	2.017(6)
Cl(1)–Cu–Cl(1)	100.6(2)	Cl(1*)–Cu–N(1)	106.1(2)
Cl(1)–Cu–N(1)	132.8(2)	N(1)–Cu–N(1*)	83.0(3)

Torsion angles

Cl(1)–Cu–N(1)–C(1)	−130.9(5)
Cl(1*)–Cu–N(1)–C(1)	107.2(5)

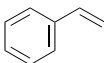
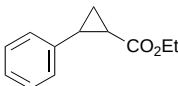
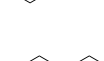
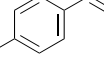
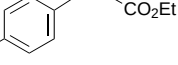
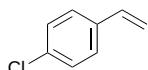
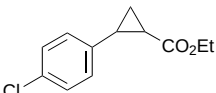
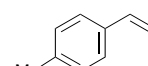
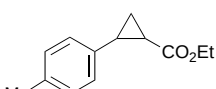
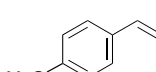
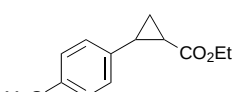
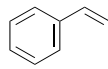
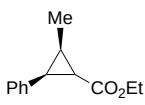
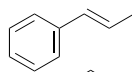
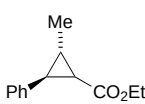
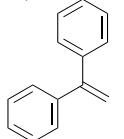
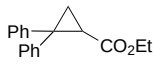
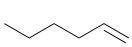
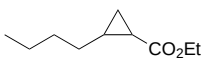
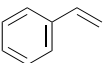
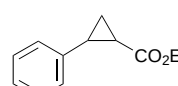
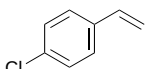
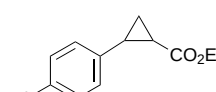
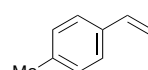
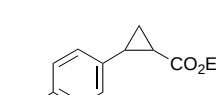
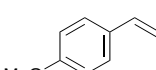
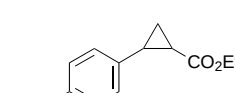
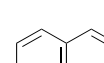
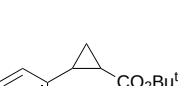
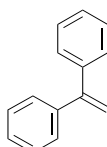
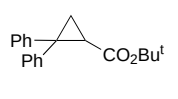
bipyridine are slightly longer than such distances for other achiral bipyridine complexes.¹³ The bite angle of 83.0° made by the chiral bipyridine and copper is considered large when compared with an average value of 77° cited in the literature.¹³ The copper–chlorine bond distances are 2.19 Å. The dihedral angles Cl(1)–Cu–N(1)–C(1) and Cl(1)–Cu–N(1*)–C(1*) of −130.9 and 107.2° clearly illustrate the distorted nature of the copper centre which can be attributed to the bulkiness of **L**. The bulkiness of this ligand is also reflected by the fact that formation of a 2:1 ligand to copper complex is not possible even with an excess of **L** and prolonged heating whereas other bipyridines form 2:1 ligand to copper complexes fairly easily.

The solution UV/VIS spectrum provided further evidence that the distorted geometry comes from the bulkiness of the ligands. Previous work has been done on relating the energies of the copper(II) d–d transition to the geometries.¹⁴ For example Cu(bipyam)Cl₂ [bipyam = bis(2-pyridyl)amine], an analogous copper(II) complex, has a typical green color and a peak in the electronic spectrum at about 700 nm. The unusual color of orange and the d–d transition of the present chiral copper(II) complex at 919 nm in CH₂Cl₂ are consistent with a pseudo-tetrahedral structure.

These results suggested that the distorted geometry observed in the solid-state structure is retained in solution. Compound **L** also forms a complex with Cu^ICl, assigned the formula Cu(bipy*)Cl, which is co-ordinatively unsaturated, based on elemental and mass spectral analyses. No complex of the form CuL₂Cl was obtained even with the use of an excess of **L** and prolonged heating.

The chloride complex **1** is not an active catalyst in cyclopropanation. However, the corresponding triflate complex, formed by treating **1** with silver triflate, was active. The potential of this copper complex as a catalyst for asymmetric cyclopropanation was illustrated by the reaction of various alkenes with diazoacetate (Table 3). The cyclopropanation of styrene by ethyl diazoacetate in the presence of 1 mol % of copper catalyst gave ethyl cyclopropanecarboxylates as the only products in 48% isolated yield. The GC analysis of the reaction mixture indicated a 80:20 *trans*:*cis* ratio and no diethyl fumarate and maleate were formed. The enantioselectivity was found to be 88% e.e. for the *trans* and 72% for the *cis* isomer. Alternatively,

Table 3 Catalytic asymmetric cyclopropanation*

Entry	Substrate	Product	<i>trans</i> : <i>cis</i>	% e.e.		Yield (%)
				<i>trans</i>	<i>cis</i>	
(a) Copper(II) complex						
1			79:21	88	72	48
2			81:19	86	69	46
3			80:20	91	82	52
4			84:16	89	84	61
5			80:20	88	83	63
6			75:25	77	63	60
7			96:4	47	32	60
8			43:57	49	42	57
9			—	83	—	56
10			73:27	76	83	42
(b) Copper(I) complex						
11			80:20	89	74	50
12			83:17	87	83	65
13			79:21	88	83	72
14			75:25	77	63	78
15			90:10	92	71	75
16			—	87	—	56

* Ethyl diazoacetate (0.2 equivalent) was used for reduction of the copper(II) catalyst before the start of cyclopropanation.

the catalyst can be generated by stirring free L with copper(II) triflate for 2 h (entry 2). However, a slight decrease in enantioselectivity was observed. Lowering the reaction temperature from room temperature to 0 °C did not hamper the reaction but increased the enantioselectivity and isolated yield (entry 3), indicating that this catalyst is highly effective. For substituted styrenes the *trans*:*cis* ratios were between 84:16 and 75:25 (entries 4–6) and the enantioselectivity between 89 and 77% e.e. for the *trans* isomer and 84 and 63% e.e. for the *cis* isomer. Styrenes with electron-withdrawing groups showed higher enantioselectivity and *trans*–*cis* selectivity than those with electron-donating groups. In the case of Katsuki's chiral bipyridine,⁶ styrene derivatives having electron-withdrawing groups showed higher enantioselectivity but lower *trans*:*cis* ratio than those with electron-donating groups. In fact, the *trans*:*cis* ratio provided by L is the highest among copper catalysts for cyclopropanation. This may come from the unusual bulkiness of L. Cyclopropanation of *cis*- β -methylstyrene showed high *trans* selectivity but the enantioselectivities for the *trans* and *cis* isomers were only moderate (entry 7). In contrast, *trans*- β -methylstyrene showed reversed *cis* selectivity and the enantiomeric excesses for both *trans* and *cis* isomers were again moderate (entry 8). The copper complex **1** was also found to be an efficient and highly enantioselective catalyst for 1,1-diphenylethene and hex-1-ene. 1,1-Diphenylethene reacted with 83% e.e. (entry 9) and hex-1-ene, which has an isolated, non-activated double bond, reacted to give a 73:27 *trans*:*cis* ratio and 76 and 83% e.e. for *trans*- and *cis*-cyclopropane respectively (entry 10).

Although the oxidation state of the copper catalyst in cyclopropanation has been the subject of some debate, it is generally believed that the copper(I) complex is the catalytically active form.⁴ In order to determine the actual catalyst involved in the present case, the copper(I)–bipyridine complex was prepared and used in cyclopropanation (Table 3, entries 11–16). The results obtained were almost identical to those with copper(II), only with better yield. Thus, we believe the active catalyst is copper(I). However, unlike the previously reported chiral N–N bidentate ligands where the copper(II) complexes were either inactive or required activation by heating, stirring of ethyl diazoacetate with this copper(II) complex at room temperature reduced the copper(II) to active copper(I) catalyst. Thus, this copper(II)–bipyridine complex, which is air stable, is a very convenient precursor to the active copper(I) catalyst.

The effect of the diazo ester structure on the *trans*–*cis* diastereoselectivity and enantioselectivity was evaluated with *tert*-butyl diazoacetate. As can be seen from entries 15 and 16 in Table 3, the *trans*:*cis* ratio for styrene increases from about 80:20 to 90:10 (entry 15). This is the best *trans*:*cis* ratio for copper-catalysed cyclopropanation using *tert*-butyl diazoacetate. The enantioselectivity for the *trans* isomer shows improvement when compared with that with ethyl diazoacetate (entry 1). This is consistent with the previously observed trends with other copper catalysts. The enantioselectivity for 1,1-diphenylethene also shows improvement with the use of *tert*-butyl diazoacetate (entry 16).

Employing L with either Cu^I or Cu^{II}, the absolute configurations of cyclopropane ester products formed from styrene were determined to be (1*R*,2*R*) and (1*R*,2*S*) for the *trans* and *cis* isomers respectively. Since L can only form a 1:1 complex with Cu^I, we believe that the catalytically active complex in the cyclopropanation is the co-ordinatively unsaturated three-coordinated Cu^IL(O₃SCF₃) complex. Although the structure of the active intermediate in the carbene transfer is still unknown, the sense of asymmetric induction observed here was the same as those for other chiral (N–N-bidentate ligand) copper catalysts reported previously. Hence, it is consistent with the model cited by Pfaltz and co-workers.^{4a}

Acknowledgements

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