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The rational design of novel chiral oxovanadium(IV) complexes for highly enantioselective oxidative coupling of 2-naphthols†

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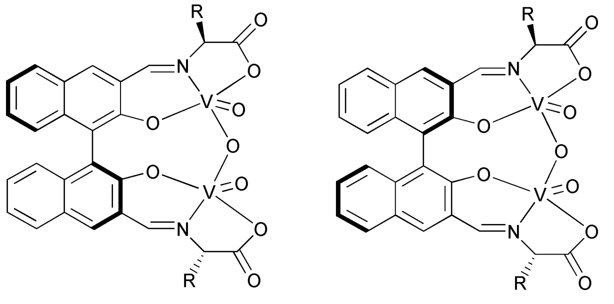
Several novel chiral oxovanadium(IV) complexes have been designed and prepared for the asymmetric catalytic oxidative coupling of 2-naphthols with high enantioselectivities of 83–98% ee.

Optically active binaphthol and its derivatives have been extensively used as chiral auxiliaries and ligands in asymmetric synthesis, and shown extremely high stereo-control property in a wide range of asymmetric transformations.[1] The importance of such molecules has fuelled the development of efficient methodologies to prepare them.[2] Resolution of racemic binaphthol has been employed for the scalemic preparation of optically pure BINOL on a large scale.[2a–f] However, a stoichiometric amount of resolving reagent has to be consumed. This drawback hinders its more practical application. Some recent studies on the asymmetric catalytic preparation of BINOLs has given several promising results by using copper complexes of chiral amines, but a high enantioselectivity has been obtained only for the coupling of 3-carboalkoxy-2-naphthols.[3] A photo-activated chiral (NO)Ru(II)–Salen complex has been evaluated for the aerobic oxidative coupling of 2-napththol derivatives with 33–71% ee.[4] Chen and Uang have independently developed similar oxovanadium(IV) complexes of chiral Schiff bases for the asymmetric catalytic coupling of 2-naphthols to result in moderate enantioselectivities up to 62% ee.[5] In this catalyst system, the stereo-discrimination depended only on the chirality in the amino acid. We envisioned that the enantioselectivity must be improved by introducing another suitable chiral centre close to the naphthoxy or phenoxy group(s) in the complex. Based on this idea, we have designed a novel oxovandium(IV) complexes **1** and **2**, as shown in Fig. 1, which contain double chiral centres (both amino acid and binaphthyl unit). In addition, these catalysts probably have helical *secondary* structures, which might be beneficial for enantioselectivity.[6]



1, R = Bn

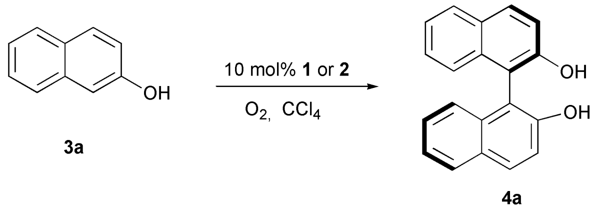
2a, R = Bn
2b, R = ^{i}Pr
2c, R = ^{i}Bu
2d, R = ^{t}Bu

Fig. 1 The catalysts designed for this study.

We prepared complexes **1** and **2** by the condensation of chiral 3,3'-diformyl-2,2'-dihydroxy-1,1'-bi-2-naphthol[6a] with (*S*)-amino acids and vanadyl sulfate, according to the literature procedure.[5b,7] Preliminary study on the characterization of the complexes by HRMS and IR confirmed their structures.

In the presence of *ca*. 10 mol% catalyst, the coupling reaction of 2-naphthol was carried out in CCl_4 by using molecular oxygen as oxidant to investigate the effects of the catalyst structure and reaction temperature on the enantioselectivity, and the results are summarised in Table 1. The first test of catalyst **1** (derived from (*S*)-3,3′-diformyl-2,2′-dihydroxy-1,1′-bi-2-naphthol and (*S*)-phenylalanine) in the oxidative coupling of 2-naphthol, gave an acceptable isolated yield, but a very poor enantioselectivity of only 6% ee with *R*-configuration (Table 1, entry 1). However, under similar conditions as used for **1**, a much higher enantioselectivity of 39% ee was induced by **2a** (from (*R*)-3,3′-diformyl-2,2′-dihydroxy-1,1′bi-2-naphthol and (*S*)-phenylalanine) (Table 1, entry 2). This result indicated that the double chirality in **2a** was suited for the oxidative coupling of 2-naphthol. Fine-tuning the structure of the chiral amino acid in a catalyst system similar to **2a** might result in a good chiral catalyst. Thus, other catalyst **2b–d** were tested for this coupling. Both oxovanadium(IV) complexes **2b** and **2c**‡ catalysed the reaction with similar moderate enantioselectivity of 57% ee under the same conditions as **2a** (Table 1, entries 5 and 8). The low reaction temperature was beneficial to the enantioselectivity, but somewhat suppressed the reactivity. For instance, lowering the reaction temperature from 20 to 10 to 0 °C led to an obvious improvement of the enantioselectivity for all of the catalysts **2a–d**, but the reactions were prolonged. At a reaction temperature of 0 °C, catalysts **2b**, **2c** and **2d** provided high

Table 1 Coupling reaction of 2-naphthol using catalysts **1** and **2a–d**[a]



Entry	Catalyst	Time/days	Temp./°C	Yield (%)[b]	Ee (%)[c]
1	**1**	5	20	70	6
2	**2a**	5	20	75	39
3	**2a**	5	10	74	42
4	**2a**	5	0	< 20	50
5	**2b**	5	20	84	57
6	**2b**	5	10	83	74
7	**2b**	8	0	70	81
8	**2c**	5	20	90	57
9	**2c**	5	10	90	77
10	**2c**	6	0	93	83
11	**2d**	5	10	86	67
12	**2d**	8	0	63	71

[a] The reaction was carried out in CCl_4. [b] Isolated yield. [c] The ee values were determined by HPLC on a Kromasil CHI-TBB column, and the absolute configuration is *R*.

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† Electronic supplementary information (ESI) available: general; representative procedure for the preparation of the complexes and coupling of 2-naphthols; HRMS spectra of **2b–d**; HPLC spectra of **4a–c**. See http://www.rsc.org/suppdata/cc/b201351g/

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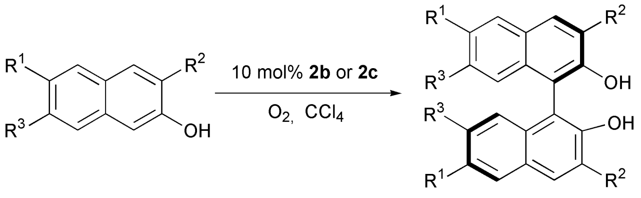
enantioselectvities of 81% (entry 7), 83% (entry 10) and 71% ee (entry 12), respectively. To the best of our knowledge, these are the best results so far reported for this oxidative coupling of 2-naphthols. Catalyst **2c** is the best reported system for the catalytic asymmetric coupling of 2-naphthol.

With comparably better chiral catalysts **2b** and **2c** in hand, we extended their applications in catalysing the oxidative coupling of other 2-naphthol derivatives **3b–d** and results are shown in Table 2. In all cases, catalyst **2c**, on average, exhibited higher enantioselectivity than **2b**. For the 2-naphthol derivatives **3b–d** tested, the corresponding coupling products **4b–d** were afforded in 86–99% yields and with 83–98% ee. The best enantioselectivity of 98% ee was obtained with 7,7′-dimethoxy-BINOL **4b** (Table 2, entry 4) and is the best result among catalytic asymmetric preparations of this type. Optically pure **4b** is very useful for the preparation of some novel chiral ligands, such as a multifunctional polymeric catalyst.[8] 3,3′-Dimethoxy-BINOL was not produced by oxidative coupling in the presence of either **2b** or **2c**. Substitution with a methoxy group at C3 suppressed the coupling reactivity.[5b]

Table 2 Coupling reaction of 2-naphthol and derivatives using catalysts **2b** and **2c**[a]



3a, $R^1 = R^2 = R^3 = H$
3b, $R^1 = H$, $R^2 = H, R^3 = OMe$
3c, $R^1 = Br$, $R^2 = H, R^3 = H$
3d, $R^1 = H$, $R^2 = OMe, R^3 = H$

4a, $R^1=R^2=R^3= H$
4b, $R^1= H$, $R^2= H,R^3=OMe$
4c, $R^1= Br$, $R^2= H,R^3=H$
4d, $R^1= H$, $R^2= OMe,R^3=H$

Entry	Catalyst	Product	Time/days	Yield (%)[b]	Ee (%)[c]
1	**2b**	**4a**	8	86	81
2	**2c**	**4a**	6	95	83
3	**2b**	**4b**	5	85	97
4	**2c**	**4b**	5	88	98
5	**2b**	**4c**	5	98	87
6	**2c**	**4c**	5	99	88
7	**2b**	**4d**	7	trace	ND
8	**2c**	**4d**	7	trace	ND

[a] The reaction was carried out at 0 °C in the presence of 10 mol% catalyst using CCl_4 as solvent. [b] Isolated yield. [c] The ee values were determined by HPLC on a Kromasil CHI-TBB column.

In summary, we have designed novel chiral oxovanadium(IV) complexes for the asymmetric catalytic oxidative coupling of 2-naphthols which results in high yields of 86–99%, and with high enantioselectivities of 83–98% ee.

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Notes and references

‡ *General procedure*: a two-neck round bottom flask (5 mL) was charged with a solution of catalyst **2c** (16 mg, 0.02 mmol) in anhydrous CCl_4 (1 mL). The solution was stirred for 10 min under an oxygen atmosphere, and then treated with a solution of 2-naphthol (29 mg, 0.2 mmol) in CCl_4 (1 mL). The reaction mixture was stirred at 0 °C until the reaction was complete (monitored by TLC). The crude mixture was concentrated under reduced pressure and the residue purified by column chromatography (ethyl acetate–light petroleum (bp 60–90 °C) (1/3)) to give the desired compound.

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