Cationic Aqua Complexes of the C₂-Symmetric *trans*-Chelating Ligand (*R,R*)-4,6-Dibenzofurandiyl-2,2′-bis(4-phenyloxazoline). Absolute Chiral Induction in Diels−Alder Reactions Catalyzed by Water-Tolerant Enantiopure Lewis Acids

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Homogeneous catalysts including transition metals of low oxidation levels have been used as Lewis acid catalysts. Pioneering work by Bosnich and co-workers has recently unveiled a new category of transition metal Lewis acid catalysts. Some aqua complexes of titanium[1] and ruthenium[2] salts are highly air-stable and water-tolerant. They show high catalytic activity and effective turnover numbers of catalytic cycle in the Diels−Alder reactions using α,β-unsaturated carbonyl dienophiles. This suggests that the aqua ligands can be very rapidly replaced with dienophiles even in the presence of additional water.[3] An enantiopure titanium catalyst with aqua ligands shows reasonable enantioselectivities.[1a]

In this Communication, we introduce a new class of enantiomerically pure complex catalyst formed by combining transition metal salts with our *trans*-chelating tridentate ligands.[3−5] The resulting cationic aqua complexes of C₂-symmetric *trans*-chelating ligand, (*R,R*)-4,6-dibenzofurandiyl-2,2′-bis(4-phenyloxazoline) (**1**, DBFOX/Ph),[6] are highly effective Lewis acid catalysts. Two chiral 4-phenyloxazoline rings are attached to the 4 and 6 positions of dibenzofuran so that the minimum distance

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(6) DBFOX/Ph *R,R*-**1** can be prepared by the following sequence in the total yield of 28%: lithiation of dibenzofuran with *n*-BuLi; carboxylation with dry ice; chlorination with SOCl₂ in CFCOOH and DMF; treatment with (*R*)-2-amino-2-phenylethanol; chlorination with SOCl₂; cyclization with aqueous NaOH.

(7) The authors have deposited atomic coordinates for the structures of **1** and **4** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, U.K. The coordinates are also attached as Supporting Information.
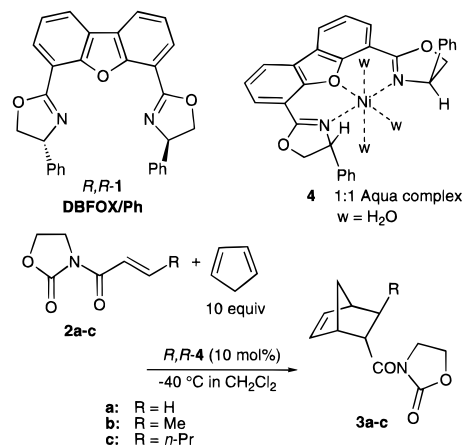
Scheme 1

Table 1.   Catalysis of DBFOX/Ph·Metal Perchlorate Complexes in the Diels−Alder Reaction of Cyclopentadiene with 3-Acryloyl-2-oxazolidinone (2a) Leading to Cycloadduct 3a[a]

entry	metal salts[b]	temp/ °C	time/ h	yield/ %[c]	*endo/ exo*[d]	% ee[e]
1	Mn(ClO₄)₂	rt	2	91	89/11	64
2	Fe(ClO₄)₂	−40	48	90	99/1	98
3	Co(ClO₄)₂·6H₂O	−40	48	97	97/3	99
4	Ni(ClO₄)₂·6H₂O	−40	14	96	97/3	>99
5	Ni(ClO₄)₂	−40	24	quant	95/5	96
6	Cu(ClO₄)₂ + 3H₂O	−40	15	99	97/3	96
7	Zn(ClO₄)₂ + 3H₂O	−40	15	99	96/4	97

[a] Catalyst: 10 mol %. [b] Catalysts were prepared in situ from DBFOX/Ph and the metal salts. Some perchlorates were prepared in situ by treatment of the corresponding halides (entry 2, FeCl₂; entry 6, NiBr₂; entry 7, CuCl₂; entry 9, ZnI₂) with AgClO₄. [c] Yield of isolated products. [d] Determined by ¹H NMR. [e] Optical purity of the *endo*-cycloadduct **2a** was determined by HPLC (Chiralcel OD).

between these two nitrogen is regulated to be 4.1 Å on the basis of X-ray diffraction analysis.[7]

A variety of metal salts, especially transition metal perchlorates, become soluble in dichloromethane on complexation with tridentate ligand **1**. The resulting complexes show high catalytic activity in the Diels−Alder reactions of cyclopentadiene with 3-acryloyl-2-oxazolidinone (**2a**) (Scheme 1 and Table 1).[8] Although the DBFOX/Ph complexes of Mg(OTf)₂ (rt, 1 h; 93%, 25% ee),[9] MgBr₂ (rt, 1 h, 99%, 41% ee), MgBr₂/I₂ (rt, 1 h, 96%, 6% ee) show only poor enantioselectivity,[10] the complex of Mg(ClO₄)₂ is a good catalyst (>90% ee). With Mg(ClO₄)₂, essentially complete chiral induction is observed in the stoichiometric reaction, indicating that DBFOX/Ph ligand **1** gives a highly effective chiral space around the metal ion. Unfortunately, this catalyst is not very reactive. Although complexes of Fe(ClO₄)₂ and Cu(ClO₄)₂ are

(8) A typical procedure: Commercially available Ni(ClO₄)₂·6H₂O (10 mol %) is treated with **1** (10 mol %) in dichloromethane (0.16 M with respect to **2a**) at room temperature for 2 h during which time the insoluble nickel salt is completely dissolved. After **2a** is introduced, the mixture is cooled down to −40 °C, and excess (10 equiv) of cyclopentadiene is allowed to react. The reaction is continued at −40 °C for 14 h. Usual hydrolytic workup with saturated aqueous ammonium chloride gives 96% yield of (1*S*,4*S*,5*S*)-(bicyclo[2.2.1]hept-2-ene-5-carbonyl)-3-(2-oxazolidinone) (**3**, *endo*:*exo* = 97:3, *endo* 100% ee).

(9) Strong coordination of triflate ligands to the magnesium ion may be a reason for the poor catalytic activity (Evans, D. A.; Murry, J. A.; von Matt, P.; Norcross, R. D.; Miller, S. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 798−800).

(10) The 5 position of the oxazoline ring is activated by the coordination of magnesium ion so that the nuceophilic counteranion attacks to cause the ring opening.

Table 2. DBFOX/Ph·Ni(ClO₄)₂·3H₂O-Catalyzed Diels−Alder Reactions of Cyclopentadiene with 3-Alkenoyl-2-oxazolidinones 2a−c Leading to Cycloadduct 3a−c

entry	2	catalyst[a]	mol %	temp/ °C	time/ h	product	yield/ %[b]	endo/ exo[c]	% ee[d]
1	2a	DBFOX/Ph	10	rt	2	3a	95	92/8	89
2	2a	DBFOX/Ph	10	−40	14	3a	96	97/3	>99
3	2a	DBFOX/Ph	2	−40	21	3a	95	98/2	96
4	2a	catalyst 4	10	−40	72	3a	98	98/2	>99
5	2a	complex C[a]	10	−40	72	3a	quant	97/3	>99
6	2a	complex C[b]	10	−40	48	3a	quant	96/4	>99
7	2a	MBOX/Ph[c]	10	−40	72	3a	97	88/12	−52
8	2b	DBFOX/Ph	10	rt	20	3b	90	92/8	93
9	2c	DBFOX/Ph	10	rt	72	3c	quant	93/7	94

[a] Complex catalyst **C** was isolated by evaporation of the solvent. [b] The catalyst **C** was allowed to expose to air for 30 days. [c] MBOX/Ph: (*R,R*)-isopropylidene-2,2′-bis(4-phenyloxazoline).

Scheme 2

Re-face **A**

1*S*,4*S*,5*S*-Enantiomer of **3a**

B

Poor reactivity and low selectivity
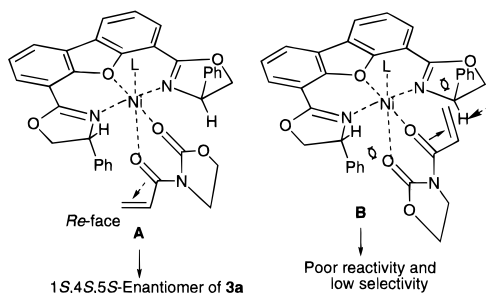
excellent, those of Fe(ClO₄)₃, Fe(ClO₄)₃·*n*H₂O (*n* = 6−9), and CuClO₄ are unselective.

Complexes of Co(ClO₄)₂·6H₂O and Ni(ClO₄)₂·6H₂O, both possessing six aqua ligands, exhibit highly effective catalysis. Diels−Alder reactions with 10 mol % of these catalysts at −40 °C give *endo*-**3a** as a single enantiomer. The results remain satisfactory with a catalytic loading of as little as 2 mol % (Table 2). The DBFOX-modified complex catalysts have two remarkable features: (1) the nickel aqua complex is more effective, both for catalytic activity and enantioselectivity, than the corresponding anhydrous complex[11] and (2) several anhydrous complexes show equally high catalytic activity and enantioselectivity in the presence of water (3 equiv).

We propose that the reacting catalyst−dienophile complex between **1**/Ni(ClO₄)₂·3H₂O and **2a** is a square bipyramidal structure containing an octahedral nickel ion. Although there is evidence for two coordination structures **A** and **B** in solution, the sterically more hindered **B** should be less reactive than **A** (Scheme 2). Therefore, we suggest that complex **A** is responsible for the highly selective reaction on the *re* face of dienophile. This analysis is consistent with the observed absolute configuration of *endo*-**3a**. Perpendicular coordination structures such as **A** and **B** are the only possible structures for metal complexation with DBFOX/Ph. This simplicity is an important advantage over the traditional *cis*-chelating bisoxazoline ligands.[12]

Since both ligand **1** and substrate **2a** are neutral chelating ligands, they should undergo competitive exchange with the nickel ion. If **2a** is a better ligand than

(11) Formation of the 1:1 diastereomeric mixture of catalyst−dienophile complexes has been directly observed in the ¹H NMR spectral study (in CD₂Cl₂) between DBFOX/Ph·Zn(ClO₄)₂ and 3-acetyl-2-oxazolidinone, the octahedral coordinated structure being assigned as a reacting complex. The DBFOX/Ph·Zn(ClO₄)₂ complex does not undergo dissociation into components even in the presence of 3-acetyl-2-oxazolidine.

(12) The Ni(ClO₄)₂·6H₂O complex of the 4-substituted isopropylidene-2,2′-bisoxazoline forms these two transition structures depending upon the steric nature of 4-substituent (unpublished results).
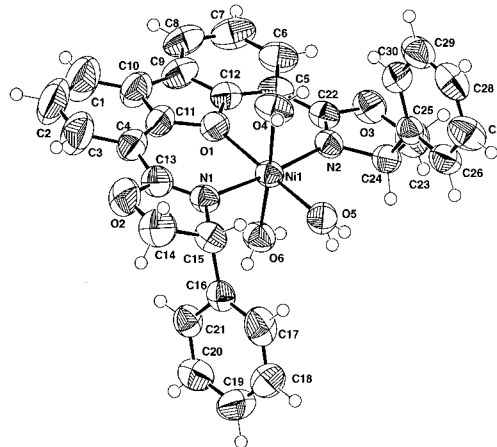

Figure 1. Stereostructure of DBFOX/Ph·Ni(ClO₄)₂·3H₂O (**4**).

1, then effective catalysis is not expected. The results then suggest that **1** is a better ligand than **2a**. The solubility of Ni(ClO₄)₂·6H₂O in dichloromethane is very low in the absence of DBFOX/Ph ligand, and only the amount of nickel ion necessary for complexation is extracted by DBFOX/Ph ligand into solution. Accordingly, excess Ni(ClO₄)₂·6H₂O can be employed in the reaction without loss of enantioselectivity. Fortunately, dienophile **2a** itself does not solubilize the nickel ion at all, and no rate acceleration is observed in the Ni(ClO₄)₂·6H₂O-catalyzed Diels−Alder reaction in the absence of **1**. Such improved solubility is no doubt due to the exceptionally high stabilization of DBFOX/Ph·Ni(II) complexation.[13] On the other hand, nickel complexes of the known *trans*-chelating pybox/Ph ligand,[2] both aqua and anhydrous complexes, show much lower selectivities (2 and 38% ee at −40 °C).

The complex catalyst shows high water tolerance against moisture in air. Thus, a pale blue solid **C** can be isolated when Ni(ClO₄)₂·6H₂O is treated with *R,R*-**1** in dichloromethane, followed by evaporation of the solvent. This solid shows a high catalytic activity and enantioselectivity (-40 °C, quant, *endo:exo* = 97:3, >99% ee) even after storage in air at room temperature for weeks.

Fine crystals of complex catalyst **4** were obtained by crystallization of the anhydrous complex DBFOX/Ph·Ni-(ClO₄)₂ from acetone−dichloromethane. The X-ray stereostructure of **4** is shown in Scheme 1 and Figure 1.[7] The complex has a molecular formula of DBFOX/Ph·Ni(ClO₄)₂·3H₂O with an octahedral structure. The two oxazoline rings are coplanar to that of dibenzofuran, and the nickel ion is bound to three water molecules and the furan oxygen atom. This crystal **4** is also an active catalyst in the Diels−Alder reaction leading to the complete chiral induction at −40 °C. Although the aforementioned complex **C** shows an almost the identical IR spectrum to that of **4**, complex **C** is a hydroxo monoperchlorate complex whose molecular formula (DBFOX/Ph·Ni(ClO₄)(OH)·2H₂O) corresponds to a product formed by elimination of a perchloric acid from **4**.

With *β*-substituted dienophiles **2b,c** which are much less reactive than the unsubstituted one **2a**, the reactions were performed at room temperature. The observed optical yields of 93 and 94% ee are satisfactory for the conditions employed.

Supporting Information Available: Experimental procedures and analytical data for important compounds and X-ray crystallographic data of **4** (8 pages).