Photo-controlled Lewis Acidity: Chiral (ON)Ru-Salen Catalyzed Hetero Diels-Alder Reaction and Kinetic Resolution of Racemic Epoxides

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Abstract: (ON^+)(Salen)ruthenium(II) complex **1** serves as a chiral Lewis acid catalyst for asymmetric hetero Diels-Alder reaction and for kinetic resolution of racemic epoxides when the reactions were carried out under sunlight coming through windows or incandescent light.

Key words: (ON^+)(salen)ruthenium(II) complex, photo-activation, Lewis acid catalysis, hetero Diels-Alder reaction, kinetic resolution of racemic epoxides

In some metal complexes such as ruthenium bipyridine complex, it is well known that electron transfer from a central metal ion to its ligand and the subsequent ligand-dissociation is promoted by exposure of the complex to light.[1] This electron transfer process has attracted the chemist's attention and has been extensively studied.[2] On the other hand, ruthenium complexes are well known to catalyze the various types of reactions and many useful chiral ruthenium catalysts have been developed to date.[3] It is naturally expected that electron transfer process affects the catalysis of ruthenium complexes, especially, their Lewis acidity. We recently found that the metallosalen complexes bearing the salen ligands which carry binaphthyl unit as its chiral element serve as useful catalysts for various asymmetric reactions.[4] In this context, we synthesized (*R*,*S*)-(ON^+)(salen)ruthenium(II) complex [(*R*,*S*)-(ON)Ru-salen complex] **1** and found that it served as an efficient catalyst for asymmetric epoxidation when the reactions were carried out under incandescent light, as described in the preceding communication. On the other hand, Bosnich et al. have reported that an achiral (ON)Ru-salen complex serves as a catalyst for Diels-Alder reaction.[5] These results prompted us to explore the potential of chiral (ON)Ru-salen complexes as chiral Lewis acid catalysts. Thus, we examined (*R*,*S*)-(ON)Ru-salen-catalyzed hetero Diels-Alder reaction.[6] According to the Bosnich's report, cationic (*R*,*S*)-(ON)Ru-salen complex **2** was first examined as a catalyst[7] for the reaction of Danishefsky's diene and benzaldehyde but the reaction was sluggish (Table 1, entry 1). We next examined the reactions using (*R*,*S*)-(ON)Ru-salen complex **1**. Complex **1** showed modest catalytic activity and moderate enantioselectivity of 64% ee in the reaction at room temperature on the laboratory bench exposed to scattered sunlight coming through windows (entry 2). The reactions using complexes **3** and **4** as catalysts were also examined under the same conditions but the diminished enantioselectivities of 53 and 42% ee were observed, respectively (entries 3 and 4).

We next examined the reaction using **1** as the catalyst under the direct sunlight coming through windows and found that the reaction was accelerated and both the enantioselectivity and chemical yield were improved (entry 5). On the other hand, the reaction in the dark was very slow and the enantioselectivity was decreased to a considerable extent (entry 6). This suggests that photo-activation is essential for the present reaction. The reaction was also examined in various solvents and it was found that the highest enantioselectivity of 79% ee and the moderate chemical yield were achieved when *t*-butyl methyl ether (TBME) was used as a solvent (entry 10). The similar result was obtained in the reaction under incandescent light.

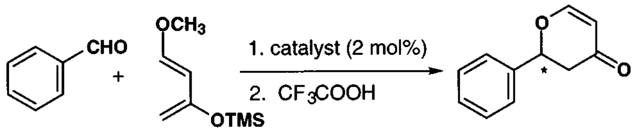


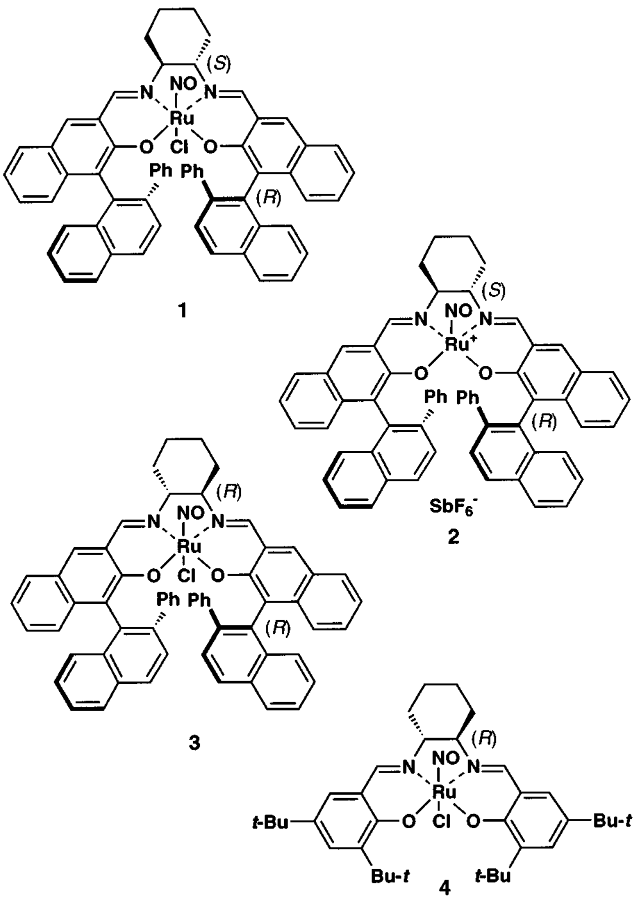
Table 1 Hetero Diels-Alder reaction using (ON)Ru-salen complexes

entry	catalyst	solvent	time (day)	%ee[a)]	yield (%)
1[b)]	**2**	C_6H_5Cl	1	4	<1
2[b)]	**1**	"	6	64	25
3[b)]	**3**	"	2	-53[c)]	45
4[b)]	**4**	"	9	-42[c)]	9
5[d)]	**1**	"	4	76	47
6[e)]	"	"	8	41	3
7[d)]	"	CH_2Cl_2	"	36	31
8[d)]	"	*i*-Pr_2O	6	68	25
9[d)]	"	ether	7	55	20
10[d)]	"	TBME	"	79	54

a) Determined by HPLC analysis using optically active column (DAICEL CHIRALCEL OD-H, hexane/2-propanol= 9/1, flow rate= 0.5 ml/min). Configuration of the major enantiomer was determined to be *S* by the comparison of the elution order with the authentic sample, unless otherwise mentioned.
b) Reaction was carried out at room temperature on the laboratory bench which was exposed to scattered sunlight coming through windows.
c) Configuration of the major enantiomer is *R*.
d) Reaction was carried out at room temperature under the direct sunlight through windows.
e) Reaction was carried out in the dark.

The reaction at 0 °C increased enantioselectivity to 83% ee (Table 2, entry 1). Under the conditions, reactions of other aldehydes also proceeded with good enantioselectivity (entries 2 and 3).

To explore the general utility of (ON)Ru-salen complexes as Lewis acid catalysts, we examined kinetic resolution of



1

2

3

4

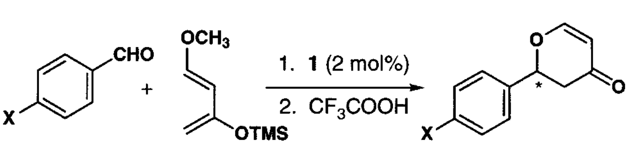


Table 2 Hetero Diels-Alder reaction using complex **1** as a catalyst[a)]

entry	X	time (days)	%ee	yield (%)
1	H	2	83[b)]	26
2	Cl	2	74[b)]	49
3	Ph	4	77[c)]	43

a) Reactions were carried out in TBME at 0 °C under incandescent light.

b) Determined by HPLC analysis using optically active column (DAICEL CHIRALCEL OD-H, hexane/2-propanol= 9/1, flow rate= 0.5 ml/min).

c) Determined by HPLC analysis using optically active column (DAICEL CHIRALPAK AD, hexane/2-propanol= 9/1, flow rate= 0.5 ml/min).

racemic epoxides.[8)] We first examined resolution of racemic 1,2-epoxy-3,4-dihydronaphthalene (Table 3). The reaction using (*R*,*S*)-(ON)Ru-salen complex **1** as the catalyst in ethyl acetate proceeded smoothly and showed excellent enantiomer differentiation of k_{rel} = 49 (entry 1). The reaction in ether also proceeded smoothly with slightly better differentiation of k_{rel} = 61 (entry 2). The reactions in acetone, acetonitrile, and dichloromethane showed the smaller relative rates. The acceleration by sunlight coming through windows was also essential for this reaction. The reaction did not occur in the dark (entry 3). On the other hand, it has been reported that an oxo (salen)manganese(V) complex shows higher Lewis acidity than the corresponding (salen)manganese(III) complex.[9)] Therefore, we examined kinetic resolution in the presence of 2,6-dichloropyridine *N*-oxide but no reaction was observed under the conditions (entry 4).[10)] Complexes **3** and **4** showed poor catalytic activity and enantiomer-differentiation (entries 5 and 6).

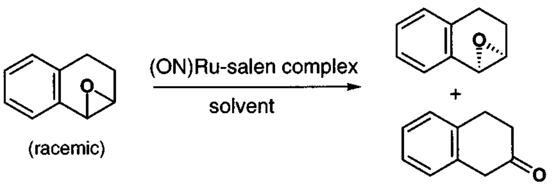


Table 3 Kinetic resolution of racemic 1,2-epoxy-3,4-dihydronaphthalene using (ON)Ru-salen complexes as catalysts[a)]

entry	catalyst	solvent	conversion (%)[b)]	%ee[c,d)]	k_{rel}
1	**1**	AcOEt	54	97.8	49
2	"	ether	54	99.0	61
3[e)]	"	"	<1	-	-
4[f)]	"	"	<1	-	-
5	**3**	AcOEt	14	9.0	4
6	**4**	"	14	1.1	1.2

a) Reaction was carried out with 2 mol% of a catalyst at room temperature on the laboratory bench exposed to scattered sunlight, unless otherwise mentioned.

b) Conversion was determined by ^{1}H NMR analysis.

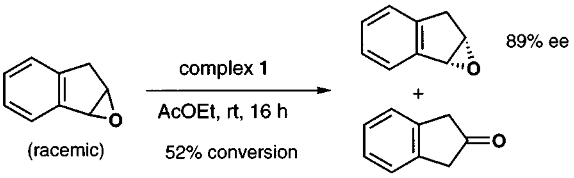
c) Percent ee of the unreacted epoxide.

d) Determined by HPLC analysis using optically active column (DAICEL CHIRALCEL OB-H, hexane/2-propanol= 50/1, flow rate= 0.5 ml/min).

e) Reaction was carried out in the dark.

f) Reaction was carried out in the presence of 2,6-dichloropyridine *N*-oxide.

Kinetic resolution of indene oxide which is the more acid sensitive proceeded smoothly in ethyl acetate with high relative ratio of 30 (Eq. 1). We also examined the rearrangement of cyclohexene oxide but no reaction occurred. This results may suggest that the substrates of the present reaction are limited to aryl or alkenyl epoxides.



Equation 1

Typical procedures of ruthenium-catalyzed hetero Diels-Alder reaction and kinetic resolution of racemic epoxides were described below. The equipments made with Pyrex glass were used through these reactions.

Hetero Diels-Alder reaction of benzaldehyde and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky´s diene): In a 5 ml round-bottomed flask were placed complex **1** (2.0 mg, 2.0 µmol) and *t*-butyl methyl ether under nitrogen atmosphere and the mixture was cooled to 0 °C. To this solution were successively added benzaldehyde (10.2 µl, 0.1 mmol) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (19.5 µl, 0.1 mmol). The mixture was stirred for 2 days at 0 °C under incandescent light (100 V, 60 W). Trifluoroacetic acid (10 µl) was added to the reaction mixture and stirred for 5 min. To this solution was added several drops of pyridine and the mixture was concentrated in vacuo. The residue was chromatographed on silica gel (hexane/ethyl acetate = 1/0 to 8/2) to give *(S)*-2-phenyl-2,3-dihydro-4H-pyran-4-one (4.6 mg, 26%). The optical purity of the product was determined to be 83% ee by HPLC analysis using optically active column (DAICEL CHIRALCEL OD-H, hexane/2-propanol = 9/1, flow rate = 0.5 ml/min).

Kinetic resolution of racemic 1,2-epoxy-3,4-dihydronaphthalene: To a solution of racemic 1,2-epoxy-3,4-dihydronaphthalene (32.2 mg, 220 µmol) in diethyl ether (2.2 ml) was added 1-bromonaphthalene (30.6 µl) as an internal standard. An aliquot (200 µl) of this solution was taken out of the flask as a zero point, concentrated and analyzed by ^{1}H NMR to determine the peak areas of the epoxide and the internal standard. To the remnant solution was added complex **1** (4.0 mg, 4.0 µmol) and the mixture was stirred for 72 h at room temperature. The mixture was passed through a pad of silica gel (pentane/diethyl ether = 1/1) to remove the complex. The eluate was concentrated on a rotary evaporator. The amounts of the unreacted epoxide (46%) and ketone (48%) were determined by ^{1}H NMR analysis. The optical purity of the unreacted epoxide was determined to be 99.0% ee by HPLC analysis using optically active column (DAICEL CHIRALCEL OB-H, hexane/2-propanol = 50/1, flow rate = 0.5 ml/min).

In conclusion, we were able to disclose an interesting Lewis acidic nature of (ON)Ru-salen complexes which is activated by sunlight or incandescent light.11) Further study is now proceeding in our laboratory.

Acknowledgement

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(7) For preparation of (ON)Ru-salen complex **1**, see the preceding communication. Cationic (ON)Ru-salen complex **2** was synthesized from (ON)Ru-salen complex **1** and $AgSbF_6$ according to the reference 5.

(8) For kinetic resolution of epoxides, see: a) Asami, M. *J. Synth. Org. Chem., Jpn.* **1996**, *54*, 188-199. b) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936-938.

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(10) As described in the preceding communication, the produced epoxide in the epoxidation of dihydronaphthalene suffered from the undesirable decomposition under the reaction conditions. This is probably attributable to that the produced epoxide is coordinated to the Lewis acidic ruthenium ion and, therefore, the epoxide is much more subject to the decomposition.

(11) The mechanism of the photo enhancement of the Lewis acidity is not clear at present but the photo-induced ligand dissociation is considered to be responsible for this phenomenon as described in *Synlett* **1999**, *1160*

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