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LEWIS ACID CATALYSIS IN INTERMOLECULAR [2+2] PHOTOCYCLOADDITION OF COUMARIN-3-CARBOXAMIDE BEARING 2-OXAZOLIDINONE AUXILIARY WITH *n*-PROPYL VINYL ETHER AND VINYL PIVALATE

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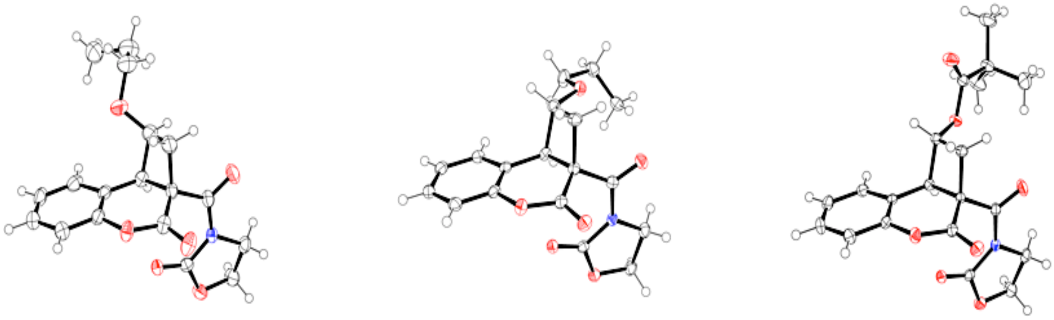
Abstract – Intermolecular [2+2] photocycloaddition reactions between 3-(2-oxo-2*H*-chromene-3-carbonyl)oxazolidin-2-one with *n*-propyl vinyl ether and vinyl pivalate were carried out to give [2+2] cycloadducts in excellent yield with perfect regioselectivity. A Lewis acid catalyst (30 mol%) was moderately effective in accelerating the reaction. Furthermore, enantioselective reactions catalyzed by chiral Lewis acid catalysts (30 mol%) were performed to give cycloadducts in excellent yields with up to 13% ee.

Coumarin derivatives are known as good photo-responsive compounds which react with several alkenes under photoirradiation to give chroman-2-one-containing cyclobutane derivatives. A number of reactions have been developed so far regardless of whether they follow an intramolecular or an intermolecular fasion.[1] Intermolecular [2+2] photocycloaddition reactions of coumarins with alkenes have been investigated in the area of a total synthesis of natural product *i.e.* linderol synthesis,[2] and asymmetric synthesis.[3] However, catalytic asymmetric intermolecular [2+2] photocycloaddition reactions of coumarins have not been well investigated. Three decades ago, Lewis and co-workers found that the

Lewis acid catalyst, BF_3•OEt_2, accelerated [2+2] photodimerization of coumarin derivatives and controlled stereoselectivity of the reaction predominantly.[4] These investigators clearly elucidated the interaction of coumarin with Lewis acid by a spectroscopic observation. Bach and co-workers also showed clearly by spectroscopic methods that the Lewis acid coordinated to the coumarin derivatives and influenced reactivity and stereoselectivity of the intermolecular and intramolecular [2+2] photocycloaddition reactions.[5] We were fascinated by Lewis's and Bach's work and we realized that Lewis acid catalysts, especially transition metal salts and lanthanide salts, had a role in promoting intermolecular [2+2] photocycloaddition of coumarin derivatives. These reactions have drawn much attention, leading to the development of the catalytic asymmetric reaction. A few examples have been published of a catalytic asymmetric intermolecular [2+2] photocycloaddition reaction of alkene catalyzed by a chiral catalyst, regardless of whether or not the coumarin backbone was used for the reaction.[6,7] In this paper, we reported the rate acceleration of intermolecular [2+2] photocycloaddition of coumarin-3-carboxamide bearing 2-oxazolidinone with *n*-propyl vinyl ether (**2**) and vinyl pivalate (**3**) in the presence of perchlorate salts of metal ion complexes and an enantioselective version of the intermolecular [2+2] photocycloaddition by the use of chiral Lewis acid catalysts (4*R*,4'*R*,5*R*,5'*R*)-BOX•metal/benzophenone possessing bifunctional properties: Lewis acid and photosensitizer.

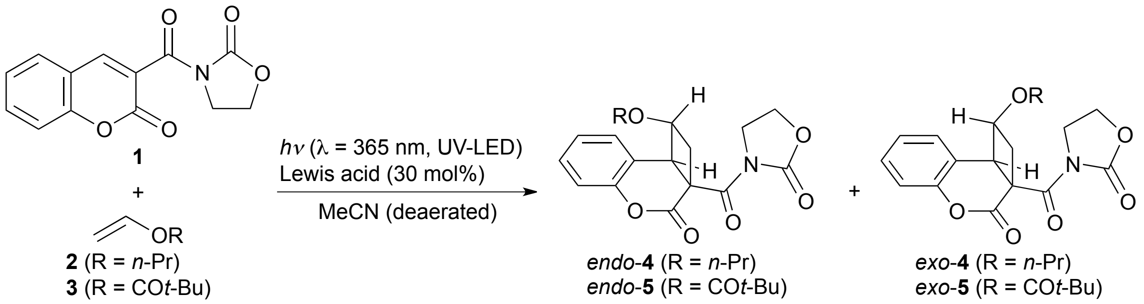
We began by evaluating Lewis acid catalysts for the intermolecular [2+2] photocycloaddition reaction of 3-(2-oxo-2*H*-chromene-3-carbonyl)oxazolidin-2-one (**1**) with **2** and **3** in acetonitrile at room temperature (Table 1). We used UV-LED light (λ = 365 nm) as an irradiation source. Initially, the reaction was conducted in the absence of a Lewis acid catalyst under an argon atmosphere. As a result, the reaction was complete in a few hours to give cyclobutane derivatives as a diastereomeric mixture with excellent regioselectivity and yield (entries 1 and 14). Desired cycloadducts *endo*- and *exo*-**4**, **5** were not observed in the presence of air. Therefore, the reaction mixture was degassed by argon bubbling for 15 min prior to irradiation. Both diastereomers were easily separable by flash silica gel chromatography. X-Ray crystallographic analyses of diastereomers were successfully achieved to reveal the structures of *endo*-**4**, *exo*-**4** and *exo*-**5** (Figure 1).[8]



endo-**4** *exo*-**4** *exo*-**5**

Figure 1. ORTEP drawing of *endo*-**4**, *exo*-**4** and *exo*-**5** cycloadducts

Table 1. Lewis acid catalysis in intermolecular [2+2] photocycloaddition reaction[a]



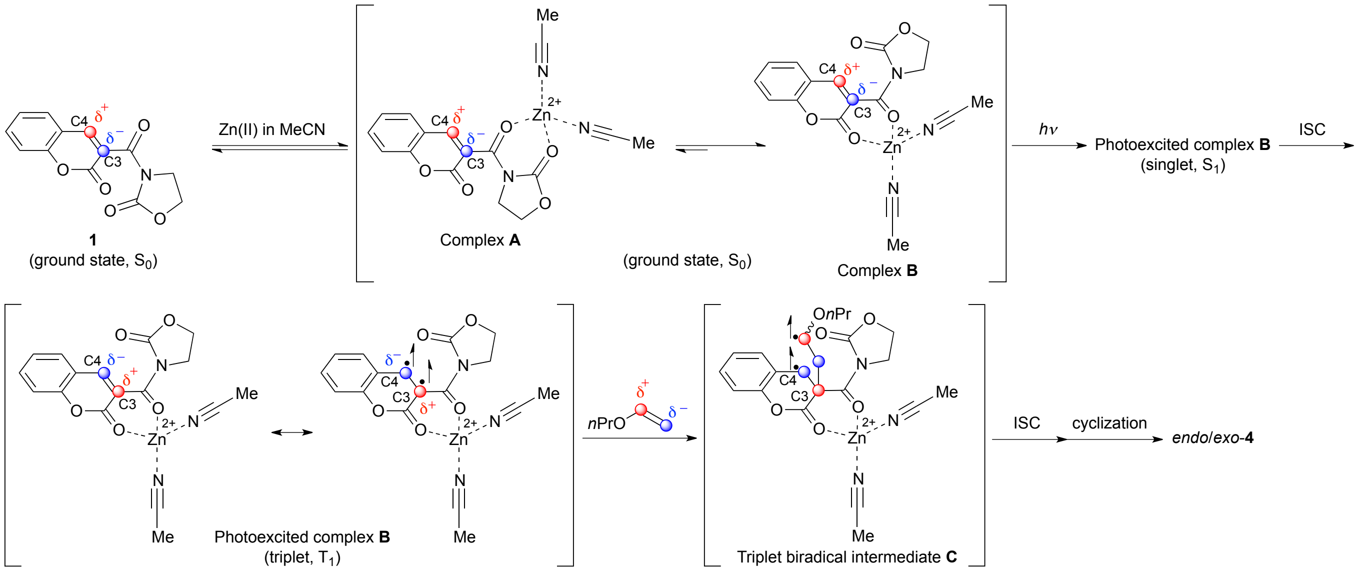
entry	vinyl ether	Lewis acid	temp./°C	time/h	yield/%[b]	*endo*:*exo*[c]
1	**2**	none	rt	5	quant.	52:48
2	**2**	$Zn(ClO_4)_2 \bullet 6H_2O$	rt	1.5	99	55:45
3	**2**	$Mg(ClO_4)_2$	rt	2	99	55:45
4	**2**	$AgClO_4$	rt	3	77	58:42
5	**2**	$Ni(ClO_4)_2 \bullet 6H_2O$	rt	4	89	63:37
6	**2**	$Co(ClO_4)_2 \bullet 6H_2O$	rt	6	94	68:32
7	**2**	$Fe(ClO_4)_2 \bullet xH_2O$	rt	8	90	67:33
8	**2**	$Cu(ClO_4)_2 \bullet 6H_2O$	rt	24	0[d]	-
9	**2**	$(MeCN)_4CuPF_6$	rt	3	97	55:45
10	**2**	$Yb(OTf)_3$	rt	24	90	55:45
11	**2**	$La(OTf)_3$	rt	24	0	-
12	**2**	$Ho(OTf)_3$	rt	24	0	-
13	**2**	$Zn(ClO_4)_2 \bullet 6H_2O$	-20	4.5	97	60:40
14	**3**	none	rt	7	94	60:40
15	**3**	$Zn(ClO_4)_2 \bullet 6H_2O$	rt	3	90	60:40

[a] The external irradiation was carried out by the use of UV-LED as the irradiation source which was directed toward the Pyrex test tube with a working distance of 1 cm. All reactions were degassed by argon bubbling for 15 min prior to irradiation. [b] Isolated yield. [c] Determined by ^{1}H NMR of crude products. [d] **1** was recovered in 95%.

Next, we evaluated several Lewis acid catalysts for the intermolecular [2+2] photocycloadditions of **1** with **2**. The use of 30 mol% of $Zn(ClO_4)_2 \bullet 6H_2O$ eventually showed good Lewis acid character for accelerating the reaction in comparison with the uncatalyzed reaction and gave cycloadducts as a diastereomeric mixture with excellent yields (entry 2). Several Lewis acids such as $Mg(ClO_4)_2$, $AgClO_4$ and $Ni(ClO_4)_2 \bullet 6H_2O$ also showed good potential to accelerate the reaction, but not as effectively as the reaction with $Zn(ClO_4)_2 \bullet 6H_2O$ (entries 3-5). In contrast, $Co(ClO_4)_2 \bullet 6H_2O$ and $Fe(ClO_4)_2 \bullet xH_2O$ retarded the reaction, but diastereoselectivities were slightly improved (entries 6 and 7). According to the Peason's hard and soft acid and bases (HSAB) theory, Fe(II), Co(II) and Zn(II) ion have been categorized into borderline Lewis acids.[9] However, the putative complex formed by the reaction of $Zn(ClO_4)_2 \bullet 6H_2O$ with

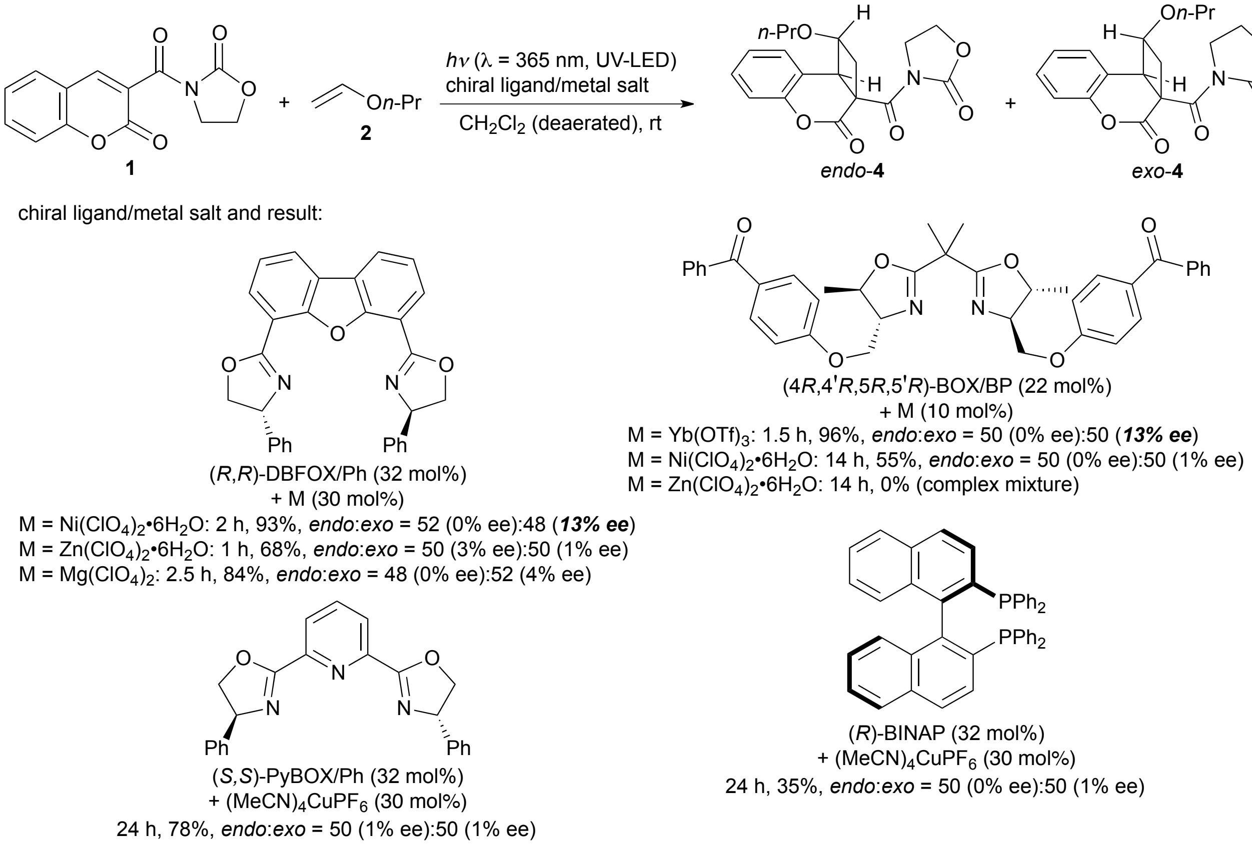
1 in the presence of MeCN having the filled *d*-orbitals of Zn(II) ion might be the tetrahedral complex and its solution was colorless. Therefore, the resulting Zn(II) complex could exclude unnecessary photophysical processes by the absorbing photon energy.[10,11] On the other hand, putative complexes formed by the reaction of $Fe(ClO_4)_2•xH_2O$ or $Co(ClO_4)_2•6H_2O$ with **1** in MeCN provided colored solutions which could have possibilities of absorbing photon energy to cause unnecessary photophysical processes and be eventually followed by losing photon energy. Furthermore, such putative complexes might be octahedral complexes having coordinating neutral ligands which were probably due to increased steric hinderance around the reaction site of complexed **1**. Hence, the rate of reaction was decreased while simultaneously improving diastereomeric ratio in the presence of $Fe(ClO_4)_2•xH_2O$ and $Co(ClO_4)_2•6H_2O$. Desired cycloadducts **4** were not obtained at all when a divalent copper salt such as $Cu(ClO_4)_2•6H_2O$ was used for the reaction and 95% of **1** was recovered (entry 8). A monovalent copper salt such as $(MeCN)_4CuPF_6$ accelerated the reaction to give **4** in excellent yield (entry 9). The color of solution in the presence of $Cu(ClO_4)_2•6H_2O$ was brownish black, which would be caused by the same reason as the case of $Fe(ClO_4)_2•xH_2O$ and $Co(ClO_4)_2•6H_2O$ being lost photon energy. As a result, the reaction would not occur. A complex mixture was obtained when $La(OTf)_3$ or $Ho(OTf)_3$ was used for the reaction (entries 11 and 12). On the other hand, $Yb(OTf)_3$, possessing a smaller ionic radius and a lower oxophilicity than $La(OTf)_3$ and $Ho(OTf)_3$, did not prevent the reaction completely to give **4** in good yield (entry 10).[12,13] Furthermore, we conducted the reaction of **1** with **2** catalyzed by 30 mol% of $Zn(ClO_4)_2•6H_2O$ at -20 ^oC, diastereoselectivity was improved as we expected (entry 13). In the case of the reaction of vinyl pivalate, the effect of rate acceleration was also observed by the use of $Zn(ClO_4)_2•6H_2O$ to give desired cycloadducts **5** as a diastereomeric mixture with excellent yields (entries 14 and 15). Based on the investigation of Lewis acid catalysts, it has been reported that $Zn(ClO_4)_2•6H_2O$ was the best catalyst for promoting the reaction.[14]

We undertook a computational study to optimize the structure for **1**, **1**/zinc(II) cationic complexes **A** and **B**, as well as photoexcited complexes **A** and **B** in acetonitrile by the use of the Gaussian16 program to perform density functional theory (DFT) calculations and time-dependent density functional theory (TD-DFT) calculations (Scheme 1).[15,16] The CAM-B3LYP hybrid functional with long range correction and a 6-311++G(d,p) basis set were adopted in this work. The solvent effect of acetonitrile was modeled via the polarizable continuum model using the integral equation formalism variant (IEF-PCM). We observed that the tetrahedral zinc(II) complex **B** was 1.3 kcal/mol more stable than that of **A** in the ground state (S_0). Therefore, the reaction would mainly proceed from complex **B**. Natural population analyses (NPA) for **1**, complexes **A** and **B** were carried out to reveal that electron density of the C4 position of the complexes was lower than that of **1** in S_0, which would lead to increasing reactivity with electron-rich alkenes such as *n*-propyl ether. Furthermore, electron density of C3 was lower than that of the C4 position in the triplet state (T_1) of photoexcited complexes **A** and **B**, which would follow a mechanistic consideration of inducing regioselectivity into the intermolecular [2+2] photocycloaddition of vinyl ethers with α,β-unsaturated carbonyl compounds.[17] Hence, the reaction would proceed predominantly via photoexcited complex **B** (S_1) followed by intersystem crossing (ISC) to generate T_1 of the photoexcited complex **B** which would then be subjected to the carbon-carbon bond forming reaction with *n*-propyl vinyl ether in a regioselective manner to generate the triplet biradical intermediate **C**. Finally, *endo*- and *exo*-**4** would be formed via triplet biradical intermediate **C** with the subsequent occurrence of ISC and cyclization.



Scheme 1. Proposed reaction mechanism

With good Lewis acid catalysts for promoting the [2+2] photocycloaddition in hand, we next attempted to develop the enantioselective reactions between **1** and **2**, as catalyzed by chiral Lewis acid catalysts (Scheme 2). Several Lewis acid catalysts, *e.g.*, (*S*,*S*)-PyBOX/Ph•metal complexes, (*R*,*R*)-DBFOX/Ph•metal complexes, and (*R*)-BINAP•$CuPF_6$ complex were used for the reaction. *Exo*-**4** was obtained in 13% ee when the aqua complex of (*R*,*R*)-DBFOX/Ph•$Ni(ClO_4)_2$, originally developed by Kanemasa and co-workers,[18] was used for the reaction. Furthermore, we successfully synthesized the benzophenone (BP)-containing chiral bis(oxazoline) ligand (4*R*,4'*R*,5*R*,5'*R*)-BOX/BP[19] and tried to prepare a novel chiral Lewis acid-photosensitizer bifunctional catalyst (4*R*,4'*R*,5*R*,5'*R*)-BOX/BP•metal complexes to utilize the asymmetric reaction, which is based on the similar concept reported by Xiao and co-workers.[20] As a result, the reaction smoothly progressed to give cycloadducts **4** in excellent yield with 13% ee by the use of the ytterbium(III) complex. On the other hand, the rate of the reaction, yield, and ee of cycloadducts were decreased by the use of a nickel(II) complex. A complex mixture was obtained when the zinc(II) complex was used for the reaction. Accordingly, high enantioselectivities were not observed for both diastereomers, which would be due to competing the racemic background reaction at room temperature and uncontrolled competitive coordination of metal ion with a number of ligands in coordinating solvent such as MeCN.



Scheme 2. Intermolecular [2+2] photocycloaddition reaction catalyzed by chiral Lewis acid

In summary, we developed an intermolecular [2+2] photocycloaddition reaction of coumarin carboxamide with *n*-propyl vinyl ether and vinyl pivalate which showed the following findings and advantages: (1) Lewis acids especially zinc perchlorate hexahydrate accelerated the intermolecular [2+2] photocycloaddition of coumarin with *n*-propyl vinyl ether and vinyl pivalate; (2) chiral bis(oxazoline)•metal complex had the ability to afford asymmetric induction (13% ee). Further studies for elucidating a mechanism of this reaction and for developing novel catalytic asymmetric [2+2] photocycloaddition reactions are ongoing.

EXPERIMENTAL

Proton NMR spectra were recorded on Bruker Biospin AV500 (500 MHz), AV300 (300 MHz) NMR spectrometer and Agilent 400 MR (400 MHz) spectrometer. Chemical shifts are reported in perts per million downfield (δ) relative to internal tetramethylsilane (TMS, δ 0.00) or with the solvent reference as the internal standard ($CDCl_3$, δ 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), integration, and assignment. Carbon NMR spectra were recorded on Bruker Biospin AV500 (125.7 MHz) and AV300 (75.4 MHz) NMR spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million downfield (δ) relative to internal TMS or/with the respective solvent reference as the internal standard ($CDCl_3$, δ 77.0). Single crystal X-ray diffraction (SCXRD) experiments were performed on a Bruker APEX II CCD detector with graphite-monochromatized Mo Kα radiation. Structure solution and refinement were performed by direct methods and the program SHELXL-97 respectively. Mass spectra were taken with a Bruker Daltonics micrOTOF II (attached to an APCI-Direct Probe or ESI ion sources). Specific rotations were recorded with JASCO P-1010 polarimeter. Infrared (IR) spectra were recorded on a JASCO FT/IR-5300 IR spectrophotometer, ν_{max} in cm^{-1}. UV-VIS spectra were recorded on a Hitachi double beam spectrophotometer U-2800. OMRON ZUV-H20MB controlled by OMRON ZUV-C20H was used as the UV-LED light source. Irradiation power was measured by USHIO UIT-250 equipped with UV sensor (UVD-S365). Melting points were recorded on Yanako MP-S3 and were not corrected. Flash chromatography was performed using Silica Gel (PSQ-60B) from Fuji Silysia Chemical, LTD. Anhydrous reaction solvents were purchased from commercial sources. Coumarin-3-carboxylic acid, *n*-propyl vinyl ether, vinyl pivalate and (*R*)-BINAP were purchased from Sigma-Aldrich Co. LLC. Oxalyl chloride was purchased from Wako Pure Chemical Industries, Ltd. *n*-Butyllithium in *n*-hexane and NaH (60% dispersion in mineral oil) were purchased from Kanto Chemical Co., Inc. 1,3-Oxazolidin-2-one and (*S*,*S*)-PyBOX/Ph were purchased from Tokyo Chemical Industry Co., Ltd. (*R*,*R*)-DBFOX/Ph was purchased from Kishida Chemical Co., Ltd. (4*R*,4'*R*,5*R*,5'*R*)-2,2'-(Propane-2,2-diyl)bis(5-methyl-4,5-dihydrooxazole-4,2-diyl)bis(methylene)dimetha-nesulfonate was prepared utilizing a previously reported procedure[21] and was used for the starting material of (4*R*,4'*R*,5*R*,5'*R*)-BOX/BP.

Typical Procedure for the Preparation of 1

To a suspension of coumarin-3-carboxylic acid (3.00 g, 15.8 mmol, 1.00 equiv.) in anhydrous CH_2Cl_2 (70.0 mL) at 0 °C under an argon atmosphere, oxalyl chloride (1.60 mL, 19.0 mmol, 1.20 equiv.) and anhydrous DMF (2 drops) were added. The resulting suspension was warmed to room temperature and stirred for 23 h. The reaction solvent and volatile compounds were evaporated and dried under high vacuum for 1 h to give coumarin-3-carboxylic acid chloride which was used for the preparation of **1** without purification. In a dried round bottom flask under argon atmosphere, 1,3-oxazolidin-2-one (1.37 g, 15.8 mmol, 1.00 equiv.) was dissolved in anhydrous THF (80.0 mL) and cooled to -78 °C, and then *n*-butyllithium (1.57 M in *n*-hexane solution) (10.6 mL, 16.6 mmol, 1.05 equiv.) was added dropwise and stirred for 30 min. The resulting suspension was warmed to 0 ^{o}C and stirred for 30 min. A solid coumarin-3-carboxylic acid chloride (3.30 g, 15.8 mmol, 1.00 equiv.) was added to the reaction mixture in one portion under an argon stream. The resulting suspension was warmed to 0 ^{o}C and stirred for 30 min. The reaction mixture was allowed to warm to room temperature and stirred for 24 h. A colorless precipitate that had formed was collected by filtration and washed with water and EtOAc. The resulting colorless powder was suspended in EtOAc and stirred for 1 h at 80 ^{o}C. A colorless powder was collected by filteration and dried under high vacuum in the presence of P_2O_5 for 6 h to give **1** (2.63 g) in 64% yield. Compound **1**: Colorless powder; mp 221-223 ^{o}C; R_f : 0.17 (1:1 hexane/EtOAc); IR (KBr) ν 3431, 3044, 2990, 2925, 1775, 1727, 1689, 1384, 1339, 1208, 1117, 758 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.14-4.23 (2H, m), 4.49-4.59 (2H, m), 7.29-7.65 (4H, m), 7.93 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 42.5, 62.8, 117.1, 118.0, 124.1, 124.9, 128.9, 133.4, 143.2, 152.9, 154.4, 157.8, 164.0; HRMS (ESI-TOF) Calcd for $C_{13}H_9NO_5$ $[M+Na]^+$: 282.0373; Found: 282.0394.

Typical Procedure for 4

In a Pyrex test tube, a solution of **1** (50.0 mg, 0.19 mmol, 1.00 equiv.), *n*-propyl vinyl ether (0.11 mL, 0.95 mmol, 5.00 equiv.) and $Zn(ClO_4)_2•6H_2O$ (21.2 mg, 0.0570 mmol, 0.30 equiv.) were dissolved in anhydrous MeCN (3.80 mL) and degassed by argon bubbling for 15 min with stirring. The Pyrex test tube was wrapped roughly with aluminum foil and the external irradiation was directed toward the tube with a working distance of 1 cm. The UV-LED light sources (OMRON ZUV-H20MB) were controlled by OMRON ZUV-C20H [irradiation power was set at maximum value at the controller; mean value and error range of irradiation power of UV-LED light sources was measured by UV meter (USHIO UIT-250) equipped with a UV sensor (UVD-S365) to be revealed as 422 mW/cm^2 and ± 3% respectively][22] for 1.5 h. MeCN and excess *n*-propyl vinyl ether were evaporated *in vacuo*. The residue was purified by flash silica gel column chromatography (FC) eluted with *n*-hexane/EtOAc = 4/1-1/1 (gradient over 30 min) to provide analytically pure cycloadducts **4** (64.9 mg) in 99% yield.

Typical Procedure for 4 in the presence of the aqueous complex of (*R*,*R*)-DBFOX/Ph•Ni(ClO$_4$)$_2$

In a Pyrex test tube, (*R*,*R*)-DBFOX/Ph (27.9 mg, 0.0608 mmol, 0.32 equiv.) and $Ni(ClO_4)_2•6H_2O$ (0.8 mg, 0.0570 mmol, 0.30 equiv.) were suspended in anhydrous CH_2Cl_2 and stirred for 3 h. To a resulting suspension of the aqueous complex of (*R*,*R*)-DBFOX/Ph•$Ni(ClO_4)_2$ and **1** (50.0 mg, 0.19 mmol, 1.00 equiv.), *n*-propyl vinyl ether (0.11 mL, 0.95 mmol, 5.00 equiv.) was added and degassed by argon bubbling for 15 min with stirring. The experimental procedure was the same as described above for the typical procedure to give **4** (61.0 mg) in 93% yield.

Photoadduct *endo*-**4**: Colorless prisms from *n*-hexane/EtOAc; mp 150-151 ^{o}C; R_f : 0.33 (1:1 *n*-hexane/EtOAc); Ee was determined by chiral HPLC analysis on a doubly-connected chiral column, Daicel Chiralpak AD-H/Daicel Chiralpak AD-3, *n*-hexane/2-propanol (9:1 v/v), 0.5 ml/min, 254 nm, t_r =

70.8 min, t_r = 74.0 min; IR (KBr) ν 2962, 1770, 1738, 1697, 1455, 1394, 1241, 1190, 1138, 759 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82 (3H, t, *J* = 7.4 Hz), 1.48 (2H, sext, *J* = 6.8, 7.4 Hz), 2.42 (1H, dd, *J* = 9.2, 11.5 Hz), 3.31-3.47 (3H, m), 3.99 (1H, dd, *J* = 4.7, 7.4 Hz), 4.07-4.24 (3H, m), 4.42-4.55 (2H, m), 7.05-7.32 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.4, 22.8, 36.6, 42.6, 45.5, 47.3, 68.9, 71.0, 71.3, 116.3, 117.4, 123.9, 128.5, 130.8, 150.8, 153.8, 163.9, 167.9. HRMS (ESI-TOF) Calcd for $C_{18}H_{19}NO_6Na$ $[M+Na]^+$: 368.1105; Found: 368.1110.

X-Ray diffraction analysis data of *endo*-**4**: monoclinic space group $P2_1/c$, a = 14.3156(19) Å, b = 10.5343(14) Å, c = 11.2428(14) Å, α 90°, β 95.387(2)°, γ 90°, V = 1688.0(4) Å^3, Z = 4, ρ = 1.359 g cm^{-3}, μ = 0.103 mm^{-1}. The structure was solved by the direct method. And the refinement was performed using the full matrix least-squares, where the final *R* and w*R* were 0.0574 and 0.1540 for 8466 reflections. CCDC-1819848.

Photoadduct *exo*-**4**: Colorless needles from *n*-hexane/EtOAc; mp 169-171 °C; R$_f$: 0.46 (1:1 *n*-hexane/EtOAc); $[\alpha]_D^{23}$ -2.40 (c 0.10, $CHCl_3$, 13% ee); Ee was determined by chiral HPLC analysis on a doubly-connected chiral column, Daicel Chiralpak AD-H/Daicel Chiralpak AD-3, *n*-hexane/2-propanol (9:1 v/v), 0.5 ml/min, 254 nm, t_r (minor) = 81.1 min, t_r (major) = 109.5 min; IR (KBr) ν 2962, 2927, 2881, 1770, 1736, 1697, 1394, 1323, 1261, 1186, 1094, 761 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (3H, t, *J* = 7.4 Hz), 1.61 (2H, sext, *J* = 6.7, 7.4 Hz), 2.75 (1H, ddd, *J* = 1.2, 6.3, 13.7 Hz), 3.32-3.45 (3H, m), 3.65 (1H, m), 3.80 (1H, dt, *J* = 1.2, 6.3 Hz), 4.07-4.22 (2H, m), 4.42-4.52 (2H, m), 7.07-7.30 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.6, 22.8, 32.9, 42.7, 48.4, 49.8, 63.0, 69.7, 79.8, 117.6, 120.5, 125.1, 127.6, 128.5, 150.6, 153.8, 165.0, 167.1; HRMS (ESI-TOF) Calcd for $C_{18}H_{19}NO_6Na$ $[M+Na]^+$: 368.1105; Found: 368.1101.

X-Ray diffraction analysis data of *exo*-**4**: orthorhombic space group P_{bca}, a = 13.9812(15) Å, b = 11.6104(13) Å, c = 19.748(2) Å, α 90°, β 90°, γ 90°, V = 3205.6(6) Å^3, Z = 8, ρ = 1.431 g cm^{-3}, μ = 0.108 mm^{-1}. The structure was solved by the direct method. And the refinement was done using the full matrix least-squares, where the final *R* and w*R* were 0.0385 and 0.0842 for 17043 reflections. CCDC-1819842.

Photoadduct *endo*-**5**: Colorless pellicles from *n*-hexane/EtOAc; mp 194-196 °C; R$_f$: 0.35 (1:1 *n*-hexane/EtOAc); IR (KBr) ν 2976, 1765, 1745, 1728, 1699, 1397, 1163, 763 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (9H, s), 2.64 (1H, ddd, *J* = 0.9, 9.2, 12.2 Hz), 3.58 (1H, ddd, *J* = 4.3, 7.8, 12.2 Hz), 4.09-4.22 (3H, m), 4.46-4.56 (2H, m), 5.24 (1H, dt, *J* = 7.8, 9.2 Hz), 6.88-6.91 (1H, m), 7.07-7.13 (2H, m), 7.27-7.31 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ26.9 (3C, overlapping signals), 34.3, 38.5, 42.6, 46.4, 47.1, 63.0, 66.0, 115.7, 117.7, 124.3, 129.0, 129.9, 150.9, 153.9, 163.4, 167.1, 177.9. HRMS (ESI-TOF) Calcd for $C_{20}H_{21}NO_7Na$ $[M+Na]^+$: 410.1210; Found: 410.1212.

Photoadduct *exo*-**5**: Colorless needles from *n*-hexane/EtOAc; mp 233-235 °C; R$_f$: 0.49 (1:1 *n*-hexane/EtOAc); IR (KBr) ν 2981, 2874, 1770, 1740, 1697, 1494, 1393, 1363, 1281, 1137, 1113, 1085, 1030, 759 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.23 (9H, s), 2.98 (1H, ddd, *J* = 1.2, 6.6, 14.1 Hz), 3.48 (1H, ddd, *J* = 1.5, 5.0, 14.1 Hz), 3.66 (1H, d, *J* = 5.0 Hz), 4.00-4.06 (1H, m), 4.18-4.23 (1H, m), 4.43-4.53 (2H, m), 4.68 (1H, dt, *J* = 1.2, 6.6 Hz), 7.09-7.10 (1H, m), 7.16-7.19 (1H, m), 7.29-7.32 (1H, m), 7.46-7.47 (1H, m); ^{13}C NMR (125 MHz, CDCl$_3$) δ 26.9 (3C, overlapping signals), 32.3, 38.6, 42.7, 48.6, 49.9, 63.0, 75.5, 117.5, 119.0, 125.3, 128.5, 129.1, 150.3, 153.8, 164.2, 166.9, 178.1. HRMS (ESI-TOF) Calcd for $C_{20}H_{21}NO_7Na$ [M+Na]$^+$: 410.1210; Found: 410.1223.

X-Ray diffraction analysis data of *exo*-**5**: monoclinic space group $P2_1/c$, a = 16.0143(17) Å, b = 10.7266(11) Å, c = 11.1665(12) Å, α 90°, β 90.938(10)°, γ 90°, V = 1917.9(4) Å^3, Z = 4, ρ = 1.342 g cm^{-3}, μ = 0.102 mm^{-1}. The structure was solved by the direct method. And the refinement was performed using the full matrix least-squares, where the final *R* and w*R* were 0.0410 and 0.1110 for 10891 reflections. CCDC-1832376.

Typical Procedure for photosensitizer-containing chiral bis(oxazoline) ligand (4*R*,4'*R*,5*R*,5'*R*)-BOX/BP

In a dried round bottom flask, 4-hydroxybenzophenone (218 mg, 1.10 mmol, 2.20 equiv.) was dissolved in anhydrous DMF (5.00 mL) followed by the addition of NaH (60% dispersion in mineral oil) (43.8 mg, 2.00 equiv.) at 0 °C and stirred for 30 min. A solution of (4*R*,4'*R*,5*R*,5'*R*)-2,2'-(propane-2,2-diyl)bis(5-methyl-4,5-dihydrooxazole-4,2-diyl)bis(methylene)dimethanesulfonate[21] (222 mg, 0.52 mmol, 1.00 equiv.) in anhydrous DMF (5.00 mL) was added dropwise to the reaction mixture at 0 °C. The resulting solution was warmed to room temperature and stirred for 18 h, and then warmed to 50 °C and stirred for 7 h. Then, the reaction mixture was warmed to 80 °C and stirred for an additional 23 h. The reaction mixture was poured into saturated aqueous ammonium chloride and extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous magnesium sulfate, and filtered. The azeotropic removal of DMF with toluene by the use of a rotary evaporator (water-bath temperature: 60 °C) gave a pale yellow oil which was purified by flash silica gel column chromatography (FC) eluted with *n*-hexane/EtOAc/MeOH = 10/10/1 to provide analytically pure (4*R*,4'*R*,5*R*,5'*R*)-BOX/BP (162 mg) in 51% yield.

(4*R*,4'*R*,5*R*,5'R)-BOX-BP: Colorless oil; R$_f$: 0.20 (1:1 hexane/EtOAc); $[\alpha]_D^{23}$ +123.2 (c 0.10, CHCl$_3$); IR (neat) ν 2978, 2932, 1651, 1599, 1254 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.39 (6H, d, *J* = 6.3 Hz), 1.55 (6H, s), 3.96 (2H, dd, *J* = 7.1, 9.3 Hz), 4.05-4.08 (2H, m), 4.24 (2H, dd, *J* = 3.9, 9.3 Hz), 4.68 (quint, *J* = 6.1 Hz), 6.96 (4H, d, *J* = 8.8 Hz), 7.46 (4H, t, *J* = 7.6 Hz), 7.56 (2H, *t*, J = 7.4 Hz), 7.74 (4H, d, *J* = 7.0 Hz), 7.81 (4H, d, *J* = 8.8 Hz); ^{13}C NMR (125 MHz, CDCl$_3$) δ 21.1, 24.5, 40.3, 70.4, 72.7, 80.9, 115.5, 129.5, 130.7, 131.6, 133.4, 133.7, 139.5, 164.2, 172.3, 197.6. HRMS (ESI-TOF) Calcd for $C_{39}H_{39}N_2O_6$ [M+H]$^+$: 631.2808; Found: 631.2795.

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concomitant with inseparable compounds (<30% yield, *endo*:*exo* = 81:29). Coincidentally, a few crystals were obtained from a mixed solution of *endo*-cycloadduct and unknown compounds in *n*-hexane/AcOEt. X-Ray crystallographic analyses of the crystals were successfully achieved to reveal the structure of *endo*-cycloadduct (CCDC-1832687). See the supporting information for details.

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