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CATALYTIC AND ENANTIOSELECTIVE DIELS-ALDER REACTION OF SILYLOXYDIENE THAT INCORPORATES A PYRROLIDINE RING, AND ITS APPLICATION TO THE CONSTRUCTION OF CHIRAL TRI- AND TETRACYCLIC SKELETONS

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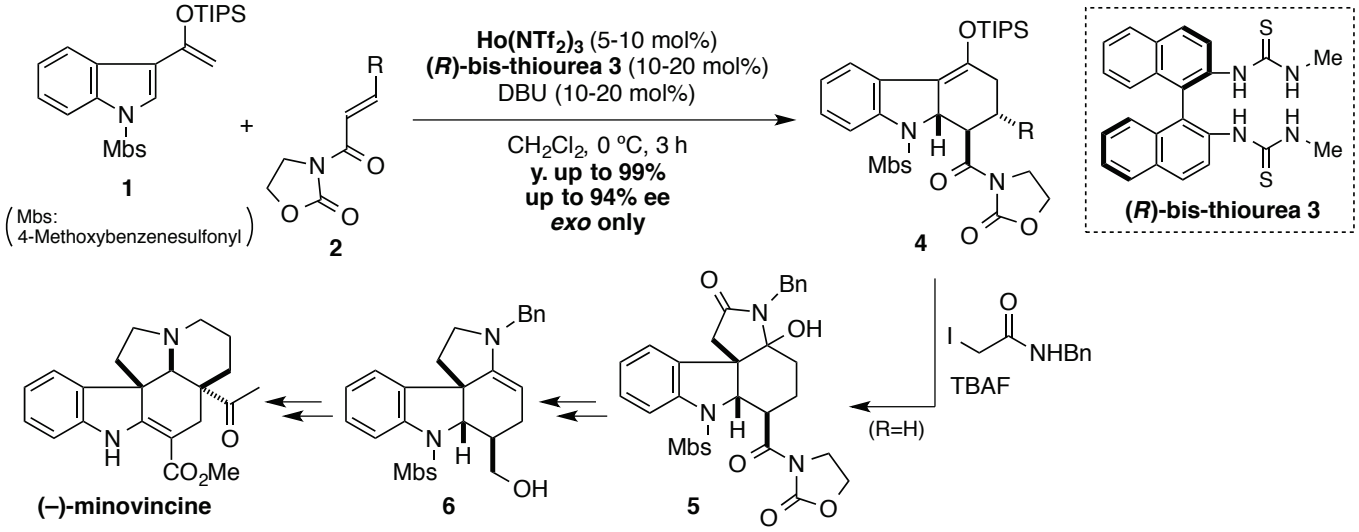
Abstract – The enantioselective Diels-Alder reaction of silyloxydiene that incorporates a pyrrolidine ring was studied. This reaction was catalyzed by a chiral holmium complex and gave multi-substituted chiral hydroindoles that contained a silyl enol ether, which is a key functional group for further transformations. We demonstrate here the synthesis of chiral pyrroloacridine, dibenzodiazocine, and pyrrolocarbazole skeletons.

INTRODUCTION

Electron-rich dienes that incorporate a heteroaromatic ring are reactive Diels-Alder substrates that can be used to realize a one-step approach to heteroaromatic ring-fused cyclohexenes.[1] Our group previously developed a chiral holmium complex-catalyzed asymmetric Diels-Alder reaction of silyloxyvinylindole **1** as a diene (**Scheme 1**).[2] This Lewis-acidic holmium catalysis promoted the Diels-Alder reaction using acid-labile silyloxydiene **1**. The product **4** was a chiral hydrocarbazole, which retained a silyl enol ether moiety that is useful for further transformations. In addition, we demonstrated that this compound could be converted to (–)-minovincine through intermediates **5** and **6**.[3]



Scheme 1. Catalytic and Enantioselective Diels-Alder Reaction of Silyloxydiene **1**, and the Total Synthesis of (–)-Minovincine

We envisioned that a more labile but useful diene that contained a heterocycle could be applied to this catalysis. Therefore, we designed a new diene **7**, which is composed of a silyloxyvinyl group and dihydropyrrole.[4] The product of the Diels-Alder reaction of **7** would be a bicyclic compound **8**, which is a chiral hydroindole with three contiguous chiral stereocenters. Here we would like to report the synthesis and properties of new diene **7**, and its application to the enantioselective Diels-Alder reaction. We also found that hydroindole **8** underwent a novel transformation, which was not observed with hydrocarbazole **4**. The further transformation of **8** to multicyclic compounds is also introduced.

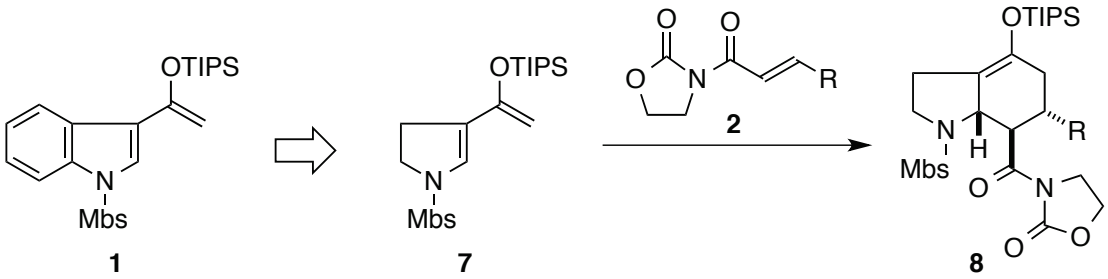


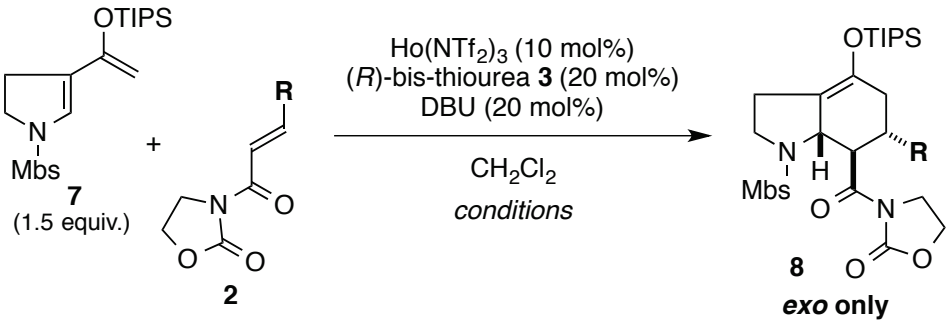
Figure 1. Silyloxyvinylindole **1** and Silyloxyvinyl-dihydropyrrole **7**

RESULTS AND DISCUSSION

Compound **7** was successfully synthesized from γ-lactam in 5 steps.[5] Consistent with our initial concerns regarding the aminodiene-like structure of **7**,[6] this silyloxydiene was less stable than indole derivative **1**. Nevertheless, compound **7** could be purified by NH-silica gel[5] column chromatography, and could be stored in a refrigerator for several months. We subjected the designed substrate **7** to the enantioselective Diels-Alder reaction.[7] A mixture of diene **7** and dienophile **2a** was treated with our chiral holmium catalyst[2a,8] (entry 1, **Table 1**). Substrate **2a** disappeared within 30 min at –20 ºC, and the product **8a** was

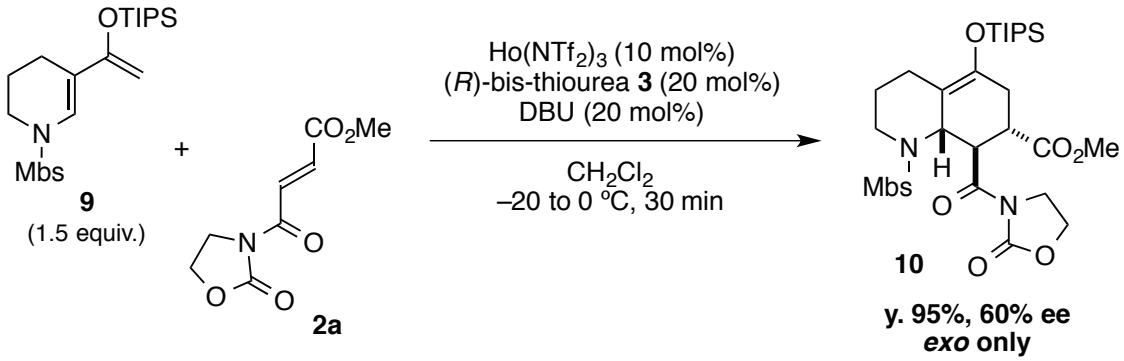
obtained in 96% yield as a single diastereomer (*exo* adduct),[9] which is the same stereoselectivity as in our previous catalytic reaction systems.[2,10] The catalytic system could be applied to substrates with a ketone (**2b**). Alkyl group-substituted dienophiles **2c** and **2d** showed relatively low reactivity. However, the enantioselectivity was good: 93% ee for **8c**, and 85% ee for **8d**. Phenyl-substituted derivative **2e** had poor compatibility with the chiral holmium catalyst, and gave **8e** in 51% ee, while the yield was 96%. No diastereoisomer of **8** was observed for any entry.

Table 1. Substrate Scope



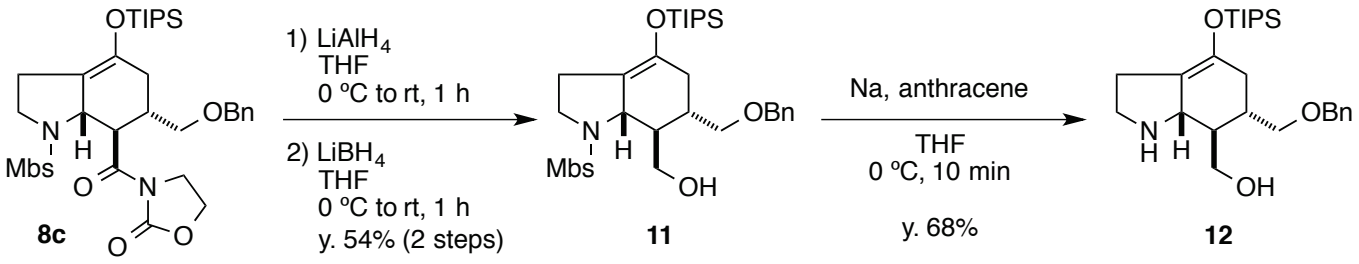
entry	**R**	*conditions*	yield (%)	% ee
1	CO_2Me (**2a**)	–20 °C, 30 min	96	95
2	COMe (**2b**)	–20 to 0 °C, 30 min	86	91
3	CH_2OCH_2Ph (**2c**)	–20 to 0 °C, 1 h	77	93
4	*n*-Pr (**2d**)	0 °C to rt, 2 h	98	85
5	Ph (**2e**)	0 °C to rt, 2 h	96	51

This catalysis could also be effective in the reaction of diene **9**, which incorporates a piperidine ring.[5] Although the enantioselectivity was moderate, hydroquinoline **10** was obtained in 95% yield (**Scheme 2**). Similar to the results in **Table 1**, we did not observe the diastereoisomer of **10**.



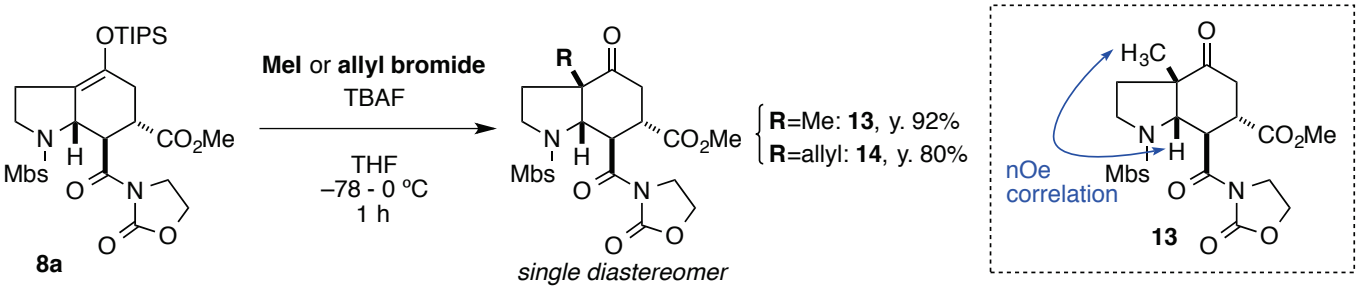
Scheme 2. Enantioselective Diels-Alder Reaction of Piperidine-Fused Diene **9**

One of the features of our lanthanide catalyst[2,10] is that the acid-labile silyl enol ether group in the substrate and the product is intact under the reaction conditions. Compounds **8** and **10** were also stable enough to be purified by silica-gel column chromatography, and could be stored in a refrigerator for several months without decomposition. To demonstrate the stability of the TIPS enol ether of **8**, we performed some transformations in the presence of TIPS enol ether (**Scheme 3**). Using **8c** as a substrate, we first examined the reduction of an acyloxazolidone unit. When we attempted direct conversion to primary alcohol **11**,[11] the reaction gave a complex mixture of byproducts derived from the partial reduction of oxazolidone. Alternatively, when **8c** was treated with lithium aluminum hydride at 0 ºC to room temperature, we obtained a mixture of products containing aldehyde. Without any purification, the residue was then treated with lithium borohydride to give **11** in 54% yield.[5] The Mbs group was successfully removed using sodium in the presence of anthracene.[12] Decomposition of the TIPS enol ether moiety was not observed during this transformation.



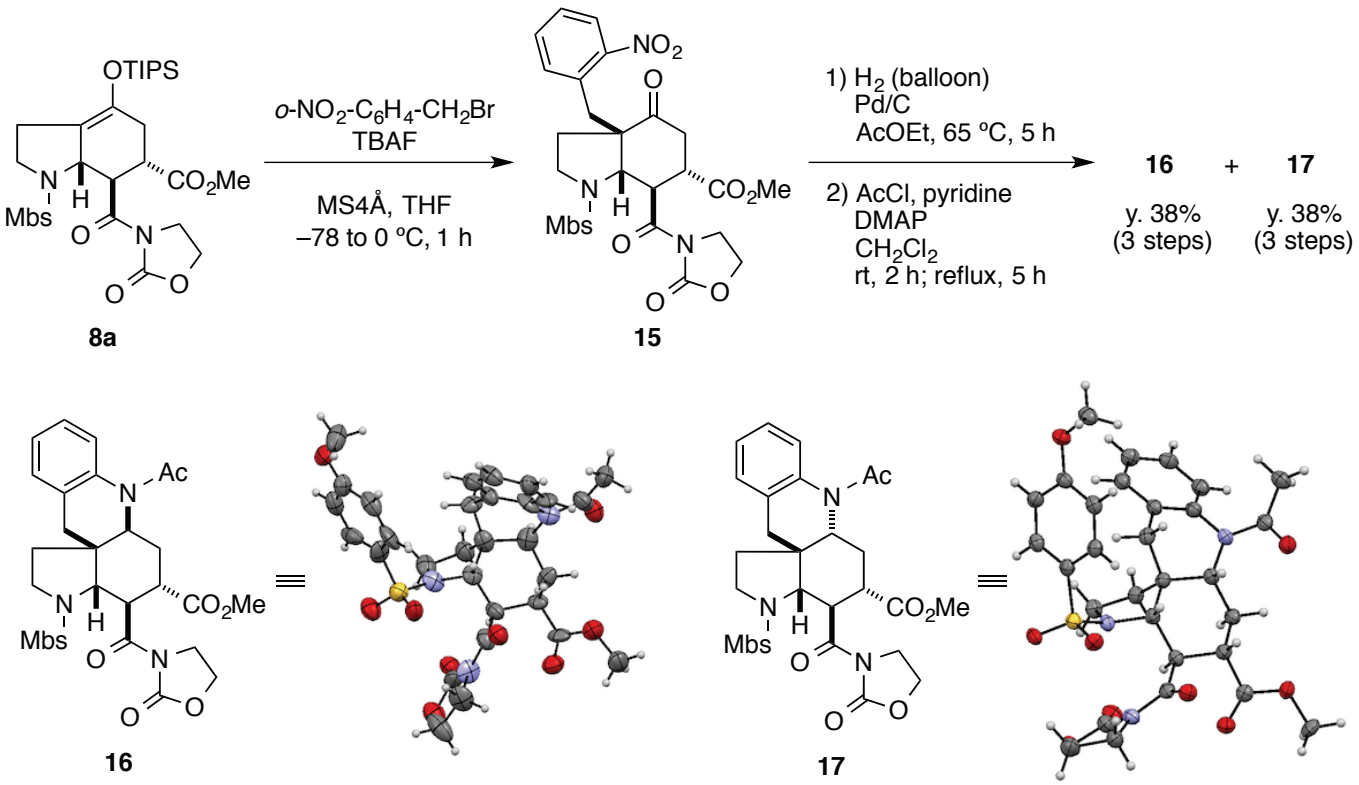
Scheme 3. Removal of Oxazolidone and Mbs

When we treated compounds that contained TIPS enol ether with tetrabutylammonium fluoride and an alkylating reagent, stereoselective alkylation proceeded smoothly to afford the product with a quaternary carbon.[2,3] Methylation gave **13** as a single diastereomer in 92% yield (**Scheme 4**). Similarly, allylation gave the desired product **14** in 80% yield. The stereochemistry of the quaternary carbon in **13** and **14** was determined by nOe experiments.



Scheme 4. Stereoselective Alkylation of **8a**, and Determination of the Relative Configuration

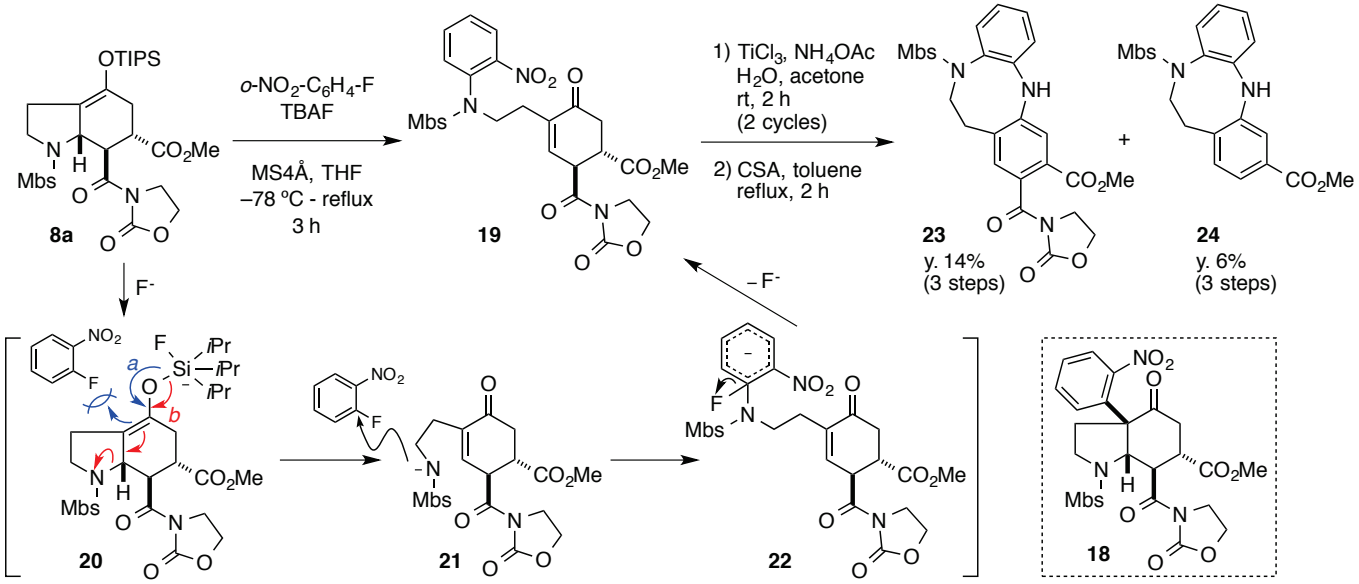
Alkylation using *ortho*-nitrobenzyl bromide proceeded smoothly to give product **15** in good yield as an inseparable mixture of byproducts (**Scheme 5**).[13] After the mixture was treated with palladium catalyst under a hydrogen atmosphere followed by acetylation, we obtained pyrroloacridines **16** and **17**. Their stereochemistry was unambiguously determined by X-ray crystallographic analysis.[14,15]



Scheme 5. Synthesis of Pyrroloacridine Skeletons

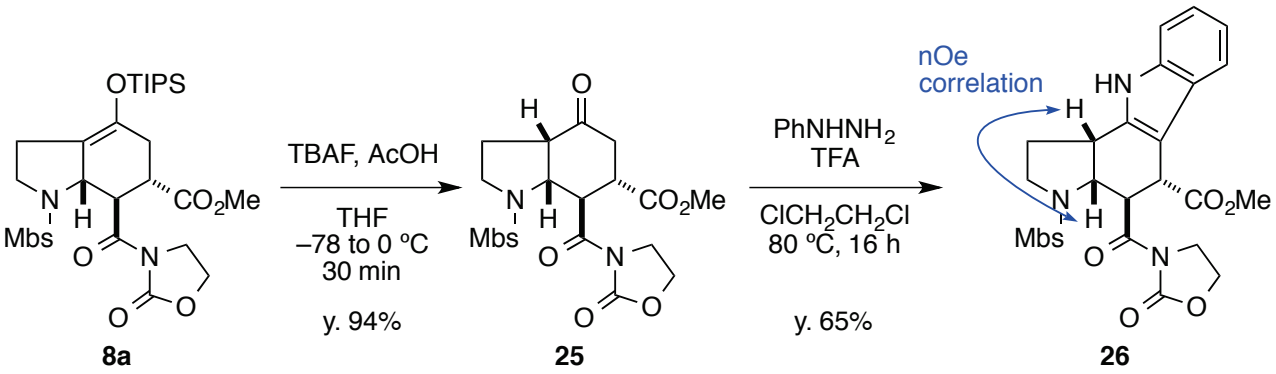
We also attempted the direct arylation of **8a** to synthesize compound **18** by a S_NAr reaction with *ortho*-nitrofluorobenzene (**Scheme 6**). However, we only obtained cyclohexenone **19**. We propose the following reaction mechanism. The fluoride-mediated activation of silyl enol ether of hydroindole **8** gives stable silicate **20**. When the reaction mixture contains a highly reactive electrophile, substitution occurs as shown in **Scheme 4** and **Scheme 5** via path *a*. On the other hand, in the presence of a less reactive electrophile, *e.g*. *ortho*-nitrofluorobenzene, substitution does not occur, and slow ring-opening of the pyrrolidine through a retro-aza-Michael reaction would proceed through path *b*. Next, *ipso*-position substitution with nitrogen would take place via Meisenheimer complex **22** to give **19**. During our previous research using hydrocarbazole **4**, we never observed this type of ring-opening. Therefore, **19** was thought to be formed due to the characteristic property of hydroindole **8**. Although all attempts to isolate the NH derivative of **21** have failed so far, the generation of **19** strongly suggests the existence of **21** as an intermediate. Under the optimized reaction conditions, **19** was finally obtained in moderate yield. Completely dehydrated reaction media and the addition of molecular sieves were essential for improving

the yield of **19**. Reduction of a nitro group of **19** with titanium(III) chloride,[16] and sequential dehydration and aromatization gave dibenzodiazocines **23** and **24**.



Scheme 6. Pyrrolidine-Opening, and Synthesis of the Dibenzodiazocine Skeleton

For synthesis of the pyrrolocarbazole skeleton, deprotected ketone **25** was treated under the conditions for Fischer indole synthesis[17] (**Scheme 7**). We obtained **26** in 68% yield, in which all stereogenic centers were retained. Pyrrolocarbazole **26** has a different skeletal composition than **5** and **6**. With silyloxydienes **1** and **7** in hand, we can access both types of chiral pyrrolocarbazoles.



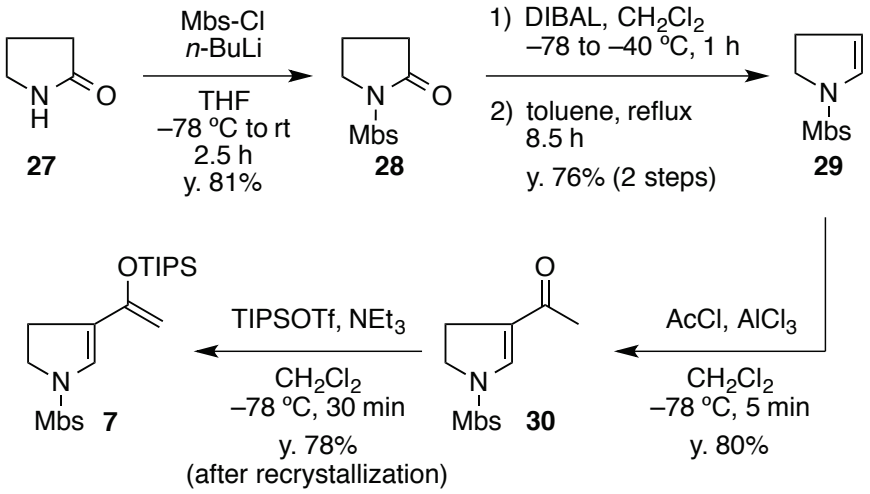
Scheme 7. Fischer Indole Synthesis Approach to Pyrrolocarbazole Skeleton

In conclusion, we have demonstrated the synthetic utility of silyloxydiene **7**. The enantioselective Diels-Alder reaction afforded chiral hydroindole **8**, which is a common intermediate for pyrroloacridines, dibenzodiazocine, and pyrrolocarbazole. During this study, we found that hydroindole **8** characteristically triggered ring-opening with tetrabutylammonium fluoride. The application of this synthesis to obtain biologically active compounds from synthesized heterocycles is now ongoing.

EXPERIMENTAL

General Information: NMR spectra were recorded at 400 MHz or 600 MHz for ^{1}H NMR, and at 100 MHz or 150 MHz for ^{13}C NMR. Chemical shifts for proton are reported in parts per million downfield from tetramethylsilane, and are referenced to residual protium in the NMR solvent ($CDCl_3$ δ: 7.26 ppm, C_6D_6 δ: 7.16 ppm). For ^{13}C NMR, chemical shifts are reported relative to the NMR solvent ($CDCl_3$ δ: 77.0 ppm, C_6D_6 δ: 128.0 ppm) as an internal reference. Infrared spectra were recorded on an ATR. Optical rotations were measured at 589 nm. Mass spectra were recorded using ESI mode with a TOF analyzer. The enantiomeric excess (ee) was determined by HPLC analysis measured at 254 nm. X-Ray crystallographic data were collected at –180 ºC using filtered Cu-Kα radiation. Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise noted. Dry CH_2Cl_2 for catalyst was purchased from Kanto Chemical Co., Inc. $Ho(NTf_2)_3$ and chiral bis-thiourea **3** were prepared according to our reported methods.[2a] Other solvents and reagents were purified by usual methods. Flash column chromatography was performed on silica gel 60 μm particle, unless otherwise noted.

Synthesis of Silyloxydiene 7:



Scheme 8. Synthesis of Silyloxydiene **7**

1-((4-Methoxyphenyl)sulfonyl)pyrrolidin-2-one (28)

n-BuLi (40.4 mL, 64.6 mmol, 1.1 equiv., 1.59 M in hexane) was added to a solution of 2-pyrolidone (**27**) (5.0 g, 58 mmol) in THF (256 mL) at –78 °C under Ar. After being stirred for 30 min at –78 °C, 4-methoxybenzenesulfonyl chloride (13.4 g, 64.6 mmol, 1.1 equiv.) was added at the same temperature. The solution was allowed to warm to room temperature and stirred for 2.5 h. The reaction was quenched with saturated aqueous NH_4Cl at 0 °C and extracted three times with CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4, and filtered through a plug of cotton. After the solvent was removed under reduced pressure, the resulting residue was purified by recrystallization from hexane/AcOEt to afford **28** (12 g, 81%) as a white powder. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.07 (tt, *J* =

8.0, 7.2 Hz, 2H), 2.43 (d, *J* = 8.0 Hz, 2H), 3.88 (s, 3H), 3.90 (t, *J* = 7.2 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.98 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 18.1, 32.2, 47.2, 55.7, 114.2, 129.5, 130.4, 164.0, 173.4; IR (neat): 2999, 1720, 1593, 1497, 1160; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}N_1Na_1O_4S_1$ $[M + Na]^+$: 278.0463, found 278.0463.

1-((4-Methoxyphenyl)sulfonyl)-2,3-dihydro-1*H*-pyrrole (29)

To a solution of **28** (6.46 g, 25.3 mmol) in CH_2Cl_2 (210 mL) was slowly added DIBAL (1.01 M in hexane, 50.1 mL, 2.0 equiv.) at –78 °C. After being stirred for 1 h at –40 °C, the reaction was quenched with the addition of MeOH and saturated aqueous potassium sodium tartrate. The organic layer was separated, and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a plug of cotton. The solvent was removed under reduced pressure. Then, a solution of crude product in toluene (210 mL) was refluxed for 8.5 h. The solvent was removed under reduced pressure, and residue was purified by silica gel column chromatography (SiO_2, hexane/AcOEt = 7/3) to afford **29** (4.60 g, 76% for 2 steps from **28**) as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42-2.56 (m, 2H), 3.47 (t, *J* = 8.8 Hz, 2H), 3.87 (s, 3H), 5.12-5.13 (m, 1H), 6.35-6.36 (m, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 29.6, 47.2, 55.6, 111.3, 114.2, 127.6, 129.8, 130.8, 163.0; IR (neat): 1595, 1498, 1345, 1260, 1156; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}N_1Na_1O_3S_1$ $[M + Na]^+$: 262.0514, found 262.0506.

1-(1-((4-Methoxyphenyl)sulfonyl)-4,5-dihydro-1*H*-pyrrol-3-yl)ethan-1-one (30)

To a solution of $AlCl_3$ (166.7 mg, 1.25 mmol, 3.0 equiv.) in CH_2Cl_2 (1.67 mL) was added AcCl (59.0 μL, 0.831 mmol, 2.0 equiv.) at 0 °C. After being stirred for 20 min at room temperature, the mixture was cooled to –78 °C. To the mixture was added **29** (100.0 mg, 0.418 mmol) in CH_2Cl_2 (10.0 mL) at –78 °C and stirred for 5 min. The reaction was quenched with the mixture of saturated aqueous $NaHCO_3$ and THF (1/1) at –78 °C and extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a plug of cotton. After the solvent was removed under reduced pressure, the resulting residue was purified by recrystallization from hexane/AcOEt to afford **30** (93.5 mg, 80%) as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.25 (s, 3H), 2.78 (td, *J* = 9.6, 1.6 Hz, 2H), 3.65 (t, *J* = 9.6 Hz, 2H), 3.89 (s, 3H), 7.02 (d, *J* = 9.2 Hz, 2H), 7.34 (t, *J* = 1.6 Hz, 1H), 7.75 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.1, 27.7, 48.2, 55.7, 114.7, 124.3, 127.5, 129.5, 141.2, 163.7, 193.5; IR (neat): 1648, 1593, 1497, 1355, 1260, 1158; HRMS (ESI): *m*/*z* calcd for $C_{13}H_{16}N_1O_4S_1$ $[M + H]^+$: 282.0800, found 282.0807.

1-((4-Methoxyphenyl)sulfonyl)-4-(1-((triisopropylsilyl)oxy)vinyl)-2,3-dihydro-1*H*-pyrrole (7)

Triethylamine (1.0 mL, 7.2 mmol, 1.4 equiv.) was added dropwise to a solution of **30** (1.5 g, 5.3 mmol) and TIPSOTf (1.9 mL, 7.1 mmol, 1.3 equiv.) in CH_2Cl_2 (10.8 mL) at –78 °C. After the mixture was stirred for 30 min at the same temperature, saturated aqueous $NaHCO_3$ was added. The aqueous layer was

extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a plug of cotton. After the solvent was removed under reduced pressure, the residue was purified by flash column chromatography (CHROMATOREX-NH, hexane/AcOEt = 10/1). Further purification by recrystallization from hexane/AcOEt afforded **7** (1.8 g, 78%) as a colorless crystal. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.10 (s, 18H), 1.15-1.30 (m, 3H), 2.57 (m, 2H), 3.57 (t, *J* = 9.2 Hz, 2H), 3.87 (s, 3H), 3.99 (d, *J* = 1.6 Hz, 1H), 4.19 (d, *J* = 1.6 Hz, 1H), 6.64 (s, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.7, 18.0, 29.3, 48.1, 55.6, 91.0, 114.2, 123.5, 127.3, 127.9, 129.7, 152.3, 163.1; IR (neat): 2943, 2865, 1594, 1497, 1354, 1259, 1159; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{36}N_1O_4S_1Si$ $[M + H]^+$: 438.2052, found 438.2052.

General Procedure for the Preparation of a Chiral Holmium Complex:

$Ho(NTf_2)_3$ (20.1 mg, 20.0 μmol, 10 mol%) and (*R*)-bis-thiourea **3** (17.2 mg, 40.0 μmol, 20 mol%) taken in a test tube with a stirring bar were heated at 115-120 °C under reduced pressure (<0.01 mmHg) for 30 min. After being allowed to cool to room temperature, the test tube was charged with dry argon. CH_2Cl_2 (0.3 mL) and DBU (6.0 μL, 40 μmol, 20 mol%) were added successively, and the resulting solution was stirred for 2 h at room temperature.

Methyl (6*S*,7*R*,7a*S*)-1-((4-methoxyphenyl)sulfonyl)-7-(2-oxooxazolidine-3-carbonyl)-4-((triisopropylsilyl)oxy)-2,3,5,6,7,7a-hexahydro-1*H*-indole-6-carboxylate (8a)

$Ho(NTf_2)_3$ (20.1 mg, 20.0 μmol, 10 mol%) and (*R*)-bis-thiourea **3** (17.2 mg, 40.0 μmol, 20 mol%) taken in a test tube with a stirring bar were heated at 115-120 °C under reduced pressure (<0.01 mmHg) for 30 min. After being allowed to cool to room temperature, the test tube was charged with dry argon. CH_2Cl_2 (0.5 mL) and DBU (6.0 μL, 40 μmol, 20 mol%) were added successively, and the resulting solution was stirred for 2 h at room temperature. To the chiral holmium complex solution, a solution of dienophile **2a** (39.8 mg, 0.200 mmol) in CH_2Cl_2 (0.1 mL + 0.1 mL to rinse) and diene **7** (131.3 mg, 0.300 mmol, 1.5 equiv.) in CH_2Cl_2 (0.2 mL + 0.1 mL to rinse) were added at –20 °C. After being stirred for 30 min at the same temperature, H_2O was added to quench the reaction. The insoluble materials were filtered through a pad of Celite®. The water layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and filtrated through a plug of cotton. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (CHROMATOREX-NH, hexane/AcOEt = 7/3 to 2/1) to give **8a** (122.1 mg, 96%) as foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.98-1.04 (m, 21H), 1.26 (ddd, *J* = 12.0, 8.4, 7.6 Hz, 1H), 2.26 (dd, *J* = 14.0, 11.2 Hz, 1H), 2.41 (ddd, *J* = 8.4, 5.6, 4.8 Hz, 1H), 2.59 (dd, *J* = 14.0, 7.6 Hz, 1H), 3.19 (ddd, *J* = 12.4, 12.0, 5.6 Hz, 1H), 3.29 (ddd, *J* = 11.2, 11.2, 7.6 Hz, 1H), 3.59 (ddd, *J* = 12.4, 7.6, 4.8 Hz, 1H), 3.70 (s, 3H), 3.86 (s, 3H), 4.00-4.15 (m, 2H), 4.27 (ddd, *J* = 10.0, 9.6, 4.8 Hz, 1H), 4.29-4.51 (m, 3H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.72 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.8, 17.8, 26.8, 32.1, 41.2, 43.2, 44.2, 48.5, 52.3, 55.6, 61.9, 62.1,

114.3, 115.8, 129.4, 129.5, 142.4, 153.9, 163.1, 173.4, 173.5; IR (neat): 2945, 2865, 1776, 1734, 1698, 1156; HRMS (ESI): *m*/*z* calcd for $C_{30}H_{44}N_2Na_1O_9S_1Si_1$ [M + Na]$^+$: 659.2429, found 659.2445; $[\alpha]_D^{21}$ +127.4 (*c* 1.00, $CHCl_3$); Daicel Chiralcel OJ-H, e: hexane/*i*PrOH = 80/20, f: 1.0 mL/min, 254 nm, 11.6 min (major), 21.3 min (minor).

3-((6*S*,7*R*,7a*S*)-6-Acetyl-1-((4-methoxyphenyl)sulfonyl)-4-((triisopropylsilyl)oxy)-2,3,5,6,7,7a-hexahydro-1*H*-indole-7-carbonyl)oxazolidin-2-one (8b)

To the chiral holmium complex solution prepared according to the general procedure, a solution of diene **7** (131.3 mg, 0.300 mmol, 1.5 equiv.) in CH_2Cl_2 (0.3 mL + 0.1 mL to rinse) and dienophile **2b** (36.6 mg, 0.200 mmol) in CH_2Cl_2 (0.2 mL + 0.1 mL to rinse) were added at –20 °C. The reaction mixture was allowed to warm to 0 °C. After being stirred for 30 min, the mixture was filtered through a pad of DIOL-silica gel (CHROMATOREX-DIOL), and washed three times with hexane/AcOEt (1/1). After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (CHROMATOREX-NH, hexane/AcOEt = 5/1, 3/1 to 2/1) to give **8b** (106.8 mg, 86%) as foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.99-1.02 (m, 21H), 1.22-1.31 (m, 1H), 2.04-2.13 (m, 1H), 2.21 (s, 3H), 2.39 (dd, *J* = 14.0, 5.6 Hz, 1H), 2.58 (ddd, *J* = 16.8, 3.6, 3.6 Hz, 1H), 3.18 (ddd, *J* = 12.8, 12.8, 5.6 Hz, 1H), 3.42 (ddd, *J* = 11.2, 11.2, 7.2 Hz, 1H), 3.58 (dd, *J* = 12.4, 8.0 Hz, 1H), 3.86 (s, 3H), 4.00 (dd, *J* = 19.6, 9.2 Hz, 1H), 4.09 (d, *J* = 9.2 Hz, 1H), 4.23 (ddd, *J* = 9.2, 9.2, 5.2 Hz, 1H), 4.37-4.50 (m, 3H), 6.97 (d, *J* = 8.8 Hz, 2H), 7.72 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.8, 17.66, 17.72, 26.8, 28.5, 31.7, 43.0, 44.0, 48.3, 48.7, 55.5, 61.9, 62.0, 114.3, 116.3, 129.4, 129.6, 142.1, 153.8, 163.1, 173.4, 207.7; IR (neat): 2947, 2867, 1779, 1698, 1386, 1157; HRMS (ESI): *m*/*z* calcd for $C_{30}H_{44}N_2Na_1O_8S_1Si_1$ [M + Na]$^+$: 643.2485, found 643.2465; $[\alpha]_D^{26}$ +119.7 (*c* 1.00, $CHCl_3$); Daicel Chiralcel OD-H, e: hexane/*i*PrOH = 70/30, f: 1.0 mL/min, 254 nm, 10.5 min (major), 16.8 min (minor).

3-((6*S*,7*R*,7a*S*)-6-((Benzyloxy)methyl)-1-((4-methoxyphenyl)sulfonyl)-4-((triisopropylsilyl)oxy)-2,3,5,6,7,7a-hexahydro-1*H*-indole-7-carbonyl)oxazolidin-2-one (8c)

To the chiral holmium complex solution prepared according to the general procedure, a solution of diene **7** (131.3 mg, 0.300 mmol, 1.5 equiv.) in CH_2Cl_2 (0.3 mL + 0.1 mL to rinse) and dienophile **2c** (52.3 mg, 0.200 mmol) in CH_2Cl_2 (0.2 mL + 0.1 mL to rinse) were added at –20 °C. The reaction mixture was allowed to warm to 0 °C. After being stirred for 1 h, the mixture was filtered through a pad of DIOL-silica gel (CHROMATOREX-DIOL), and washed three times with hexane/AcOEt (1/1). After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (CHROMATOREX-DIOL, hexane/AcOEt = 5/1, 3/1 to 2/1, then SiO_2, 3/1 to 5/2) to give **8c** (108.2 mg, 77%) as foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.00-1.16 (m, 21H), 1.32-1.40 (m, 1H), 2.08-2.15 (m, 1H), 2.28-2.34 (m, 1H), 2.47 (dd, *J* = 13.6, 2.0 Hz, 1H), 2.53-2.62 (m, 1H), 3.20 (ddd, *J* = 8.0, 8.0, 6.0 Hz, 1H), 3.48 (d, *J* = 4.8 Hz, 2H), 3.58 (dd, *J* = 12.0, 11.6 Hz, 1H), 3.62-3.69 (m, 1H), 3.86

(s, 3H), 4.11-4.18 (m, 4H), 4.31-4.40 (m, 1H), 4.43 (d, *J* = 1.6 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.27-7.35 (m, 5H), 7.74 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ: 13.2, 18.07, 18.09, 26.8, 33.2, 36.7, 43.3, 45.5, 49.3, 54.9, 61.7, 63.2, 72.3, 73.1, 114.4, 115.7, 127.7, 127.9, 128.5, 130.1, 130.7, 138.9, 144.0, 154.4, 163.1, 173.8; IR (neat): 2945, 2867, 1777, 1698, 1386, 1159; HRMS (ESI): *m*/*z* calcd for $C_{36}H_{50}N_2Na_1O_8S_1Si_1$ $[M + Na]^+$: 721.2955, found 721.2962; $[\alpha]_D^{24}$ +95.8 (*c* 1.00, $CHCl_3$), Daicel Chiralcel OD-H, e: hexane/*i*PrOH = 80/20, f: 1.0 mL/min, 254 nm, 15.5 min (major), 35.8 min (minor).

3-((6*S*,7*R*,7a*S*)-1-((4-Methoxyphenyl)sulfonyl)-6-propyl-4-((triisopropylsilyl)oxy)-2,3,5,6,7,7a-hexahydro-1*H*-indole-7-carbonyl)oxazolidin-2-one (8d)

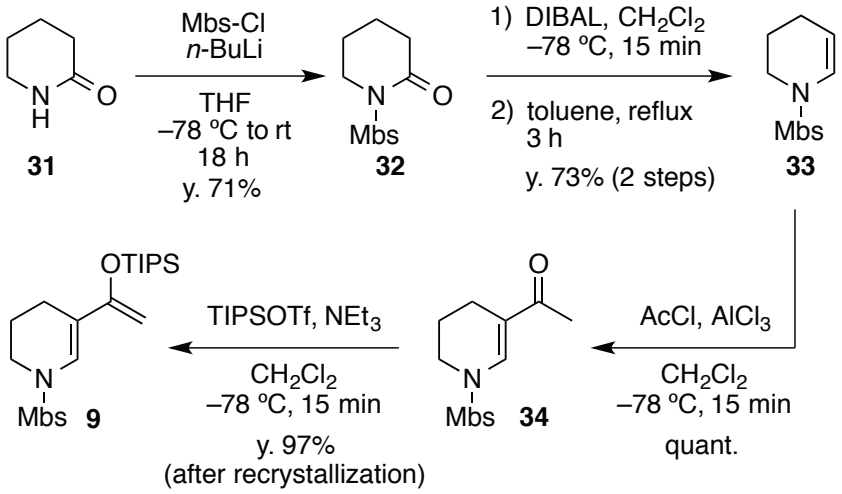
To the chiral holmium complex solution prepared according to the general procedure, a solution of diene **7** (131.3 mg, 0.300 mmol, 1.5 equiv.) in CH_2Cl_2 (0.3 mL + 0.1 mL to rinse) and dienophile **2d** (36.6 mg, 0.200 mmol) in CH_2Cl_2 (0.2 mL + 0.1 mL to rinse) were added at 0 °C. The reaction mixture was allowed to warm to room temperature. After being stirred for 2 h, the mixture was filtered through a pad of silica gel, and washed three times with hexane/AcOEt (1/1). After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (SiO_2, hexane/AcOEt = 4/1, 3/1 to 2/1) to give **8d** (121.7 mg, 98%) as foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (dd, *J* = 3.2 Hz, 3H), 1.01-1.02 (m, 21H), 1.12-1.42 (m, 5H), 1.90 (dd, *J* = 16.8, 10.4 Hz, 1H), 2.18 (br, 1H), 2.25-2.32 (m, 1H), 2.49 (dd, *J* = 12.8, 6.0 Hz, 1H), 3.20 (ddd, *J* = 12.0, 12.0, 6.0 Hz, 1H), 3.56 (dd, *J* = 12.0, 8.0 Hz, 1H), 3.86 (s, 3H), 4.01-4.11 (m, 3H), 4.29-4.50 (m, 3H), 6.97 (d, *J* = 8.8 Hz, 2H), 7.75 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.9, 14.0, 17.8, 17.9, 19.6, 26.0, 34.8, 35.4, 35.6, 43.2, 48.1, 49.0, 55.5, 62.1, 62.4, 114.2, 114.3, 129.5, 129.7, 144.0, 154.0, 163.0, 174.8; IR (neat): 2943, 2867, 1778, 1697, 1386, 1159; HRMS (ESI): *m*/*z* calcd for $C_{31}H_{48}N_2Na_1O_7S_1Si_1$ $[M + Na]^+$: 643.2849, found 643.2826; $[\alpha]_D^{25}$ +102.2 (*c* 1.00, $CHCl_3$); Daicel Chiralcel OD-H, e: hexane/*i*PrOH = 80/20, f: 1.0 mL/min, 254 nm, 7.5 min (major), 38.6 min (minor).

3-((6*S*,7*R*,7a*S*)-1-((4-Methoxyphenyl)sulfonyl)-6-phenyl-4-((triisopropylsilyl)oxy)-2,3,5,6,7,7a-hexahydro-1*H*-indole-7-carbonyl)oxazolidin-2-one (8e)

To the chiral holmium complex solution prepared according to the general procedure, a solution of diene **7** (131.3 mg, 0.300 mmol, 1.5 equiv.) and dienophile **2e** (43.4 mg, 0.200 mmol) in CH_2Cl_2 (0.5 mL + 0.2 mL to rinse) were added at 0 °C. The reaction mixture was allowed to warm to room temperature. After being stirred for 2 h, the mixture was filtered through a pad of silica gel, and washed three times with hexane/AcOEt (1/1). After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (SiO_2, hexane/AcOEt = 5/1, 4/1, 3/1 to 5/2) to give **8e** (126.5 mg, 96%) as foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.00-1.01 (m, 21H), 1.54 (dd, *J* = 13.2, 9.6, 9.6 Hz, 1H), 2.44 (d, *J* = 8.8 Hz, 2H), 2.61 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.15-3.37 (m, 2H), 3.45-3.58 (m, 2H), 3.87 (s, 3H), 3.97-4.06 (m, 2H), 4.23-4.27 (m, 2H), 4.74 (dd, *J* = 11.6, 9.2 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 2H),

7.20-7.24 (m, 1H), 7.28-7.29 (m, 4H), 7.78 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.9, 17.83, 17.85, 25.9, 37.9, 42.7, 43.8, 48.0, 49.0, 55.6, 61.76, 61.84, 114.2, 114.3, 127.0, 127.9, 128.5, 129.2, 129.8, 141.8, 144.0, 153.5, 163.0, 173.7; IR (neat): 2941, 2867, 1777, 1703, 1387, 1159; HRMS (ESI): m/z calcd for $C_{34}H_{46}N_2Na_1O_7S_1Si_1$ [M + Na]$^+$: 677.2693, found 677.2711; $[\alpha]_D^{24}$ +63.2 (c 1.00, $CHCl_3$); Daicel Chiralcel OD-H, e: hexane/iPrOH = 80/20, f: 1.0 mL/min, 254 nm, 10.6 min (major), 45.9 min (minor).

Synthesis of Silyloxydiene 9:



Scheme 9. Synthesis of Silyloxydiene **9**

1-((4-Methoxyphenyl)sulfonyl)piperidin-2-one (32)

n-BuLi (34.8 mL, 53.9 mmol, 1.1 equiv., 1.55 M in hexane) was added to a solution of 2-piperidone (**31**) (4.7 mL, 51 mmol) in THF (100 mL) at –78 °C under Ar. After being stirred for 1 h at –78 °C, 4-methoxybenzenesulfonyl chloride (11.1 g, 58.2 mmol, 1.1 equiv.) was added at the same temperature. The solution was warmed to room temperature and stirred for 18 h. The reaction was quenched with saturated aqueous NH_4Cl at 0 °C. The water layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a plug of cotton. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (SiO_2, hexane/AcOEt = 1/1) to afford **32** (9.7 g, 71%) as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.78 (tt, J = 6.4, 6.0 Hz, 2H), 1.90 (tt, J = 6.0, 6.0 Hz, 2H), 2.42 (t, J = 6.8 Hz, 2H), 3.87 (s, 3H), 3.90 (t, J = 6.0 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.4, 23.3, 34.1, 46.8, 55.6, 113.8, 130.4, 131.0, 163.7, 170.1; IR (neat): 2949, 1690, 1593, 1497, 1347, 1260, 1159; HRMS (ESI): m/z calcd for $C_{12}H_{15}N_1Na_1O_4S_1$ [M + Na]$^+$: 292.0620, found 292.0618.

1-((4-Methoxyphenyl)sulfonyl)-1,2,3,4-tetrahydropyridine (33)

To a solution of **32** (5.0 g, 19 mmol) in CH_2Cl_2 (66 mL) was slowly added DIBAL (1.0 M in hexane, 59.3

mL, 3.2 equiv.) at –78 °C. After being stirred for 15 min at –78 °C, the reaction was quenched with the addition of MeOH and saturated aqueous potassium sodium tartrate. The organic layer was separated, and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a plug of cotton. The solvent was removed under reduced pressure. Then, a solution of crude product in toluene (200 mL) was refluxed for 3 h. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (SiO_2, hexane/AcOEt = 4/1) to afford **33** (3.7 g, 73% for 2 steps from **32**) as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.66 (quin, *J* = 5.6 Hz, 2H), 1.89-1.92 (m, 2H), 3.36 (t, *J* = 5.6 Hz, 2H), 3.87 (s, 3H), 4.97 (dt, *J* = 8.0, 4.0 Hz, 1H), 6.64 (dt, *J* = 8.0, 2.0 Hz, 1H), 6.99 (d, *J* = 9.2 Hz, 2H), 7.73 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.8, 20.9, 43.7, 55.5, 108.3, 114.2, 125.0, 129.1, 129.6, 162.9; IR (neat): 1594, 1496, 1336, 1257, 1156; HRMS (ESI): *m/z* calcd for $C_{12}H_{16}N_1O_3S_1$ $[M + H]^+$: 254.0851, found 254.0844.

1-(1-((4-Methoxyphenyl)sulfonyl)-1,4,5,6-tetrahydropyridin-3-yl)ethan-1-one (34)

To a solution of $AlCl_3$ (4.5 g, 34 mmol, 3.0 equiv.) in CH_2Cl_2 (46 mL) was added AcCl (1.6 mL, 23 mmol, 2.0 equiv.) at 0 °C. After being stirred for 20 min at room temperature, the mixture was cooled to –78 °C. To the mixture were added **33** (2.8 g, 11 mmol) in CH_2Cl_2 (10 mL) at –78 °C and stirred for 15 min. The reaction was quenched with the mixture of saturated aqueous $NaHCO_3$ and THF (1/1) at –78 °C and extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtrated through a plug of cotton. After the solvent was removed under reduced pressure, the resulting residue was purified by silica gel chromatography (SiO_2, hexane/AcOEt = 3/2) to afford **34** (3.4 g, quant.) as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72 (tt, *J* = 6.0, 5.2 Hz, 2H), 2.21 (t, *J* = 6.0 Hz, 2H), 2.29 (s, 3H), 3.38 (t, *J* = 5.2 Hz, 2H), 3.89 (s, 3H), 7.02 (d, *J* = 9.2 Hz, 2H), 7.76 (d, *J* = 9.2 Hz, 2H), 7.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.4, 20.2, 24.7, 43.4, 55.7, 114.7, 119.5, 128.8, 129.3, 136.6, 163.7, 196.1; IR (neat): 1616, 1593, 1260, 1158; HRMS (ESI): *m/z* calcd for $C_{14}H_{18}N_1O_4S_1$ $[M + H]^+$: 296.0957, found 296.0946.

1-((4-Methoxyphenyl)sulfonyl)-5-(1-((triisopropylsilyl)oxy)vinyl)-1,2,3,4-tetrahydropyridine (9)

Triethylamine (0.61 mL, 4.4 mmol, 1.3 equiv.) was added dropwise to a solution of **34** (1.0 g, 3.4 mmol) and TIPSOTf (1.18 mL, 4.39 mmol, 1.3 equiv.) in CH_2Cl_2 (6.7 mL) at –78 °C. The mixture was stirred for 15 min at the same temperature. A solution of saturated aqueous $NaHCO_3$ was added. After the layers were separated, the water layer was extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a plug of cotton. After the solvent was removed under reduced pressure, the residue was purified by flash column chromatography (CHROMATOREX-NH, hexane/AcOEt = 95/5). Further purification by recrystallization from hexane/AcOEt afforded **9** (1.5 g, 97%) as a colorless crystal. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.15 (d, *J* =

7.2 Hz, 18H), 1.27 (m, 3H), 1.76 (quin, *J* = 5.2 Hz, 2H), 2.06 (t, *J* = 4.4 Hz, 2H), 3.35 (t, *J* = 5.2 Hz, 2H), 3.86 (s, 3H), 4.16 (s, 2H), 6.93 (d, *J* = 9.2 Hz, 2H), 7.32 (s, 1H), 7.69 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.8, 18.1, 20.9, 21.4, 43.3, 55.6, 88.0, 114.2, 115.6, 123.6, 129.1, 129.6, 155.4, 163.0; IR (neat): 2944, 2359, 1595, 1161; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{38}N_1O_4S_1Si_1$ $[M + H]^+$: 452.2285, found 452.2293.

Methyl (7*S*,8*R*,8a*S*)-1-((4-methoxyphenyl)sulfonyl)-8-(2-oxooxazolidine-3-carbonyl)-5-((triisopropylsilyl)oxy)-1,2,3,4,6,7,8,8a-octahydroquinoline-7-carboxylate (10)

To the chiral holmium complex solution prepared according to the general procedure, a solution of diene **9** (135.5 mg, 0.300 mmol, 1.5 equiv.) in CH_2Cl_2 (0.3 mL + 0.1 mL to rinse) and dienophile **2a** (39.8 mg, 0.200 mmol) in CH_2Cl_2 (0.2 mL + 0.1 mL to rinse) were added at –20 °C. The reaction mixture was allowed to warm to 0 °C. After being stirred for 30 min, the mixture was filtrated through a pad of silica gel (CHROMATOREX-DIOL), and washed three times with hexane/AcOEt (1/1). After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (CHROMATOREX-DIOL, hexane/AcOEt = 3/1 to 2/1) to give **10** (124.1 mg, 95%) as a foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.67 (ddd, *J* = 11.6, 10.4, 10.4 Hz, 1H), 1.00-1.07 (m, 21H), 1.24 -1.32 (m, 2H), 2.34 (dd, *J* = 15.6, 11.2 Hz, 1H), 2.45-2.55 (brs, 2H), 3.14 (ddd, *J* = 15.6, 9.6, 9.2 Hz, 1H), 3.31 (ddd, *J* = 11.2, 11.2, 6.4 Hz, 1H), 3.60-3.72 (m, 4H), 3.87 (s, 3H), 4.03 (ddd, *J* = 9.6, 9.4, 9.2 Hz, 1H), 4.22 (ddd, *J* = 9.2, 9.0, 4.4 Hz, 1H), 4.40 (ddd, *J* = 9.2, 8.4, 4.4 Hz, 1H), 4.49 (ddd, *J* = 9.4, 9.0, 8.4 Hz, 1H), 4.55-4.67 (m, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.0, 17.8, 18.5, 21.8, 32.0, 39.4, 40.2, 42.5, 43.2, 52.2, 55.5, 60.2, 62.0, 110.7, 114.1, 129.1, 132.6, 143.4, 153.9, 162.7, 173.6, 173.7; IR (neat): 2945, 2866, 1776, 1735, 1693, 1365, 1208, 1155; HRMS (ESI): *m*/*z* calcd for $C_{31}H_{47}N_2O_9S_1Si_1$ $[M + H]^+$: 651.2772, found 651.2747; $[\alpha]_D^{23}$ +57.3 (*c* 1.00, $CHCl_3$); Daicel Chiralpak IA, e: hexane/*i*PrOH = 70/30, f: 1.0 mL/min, 254 nm, 11.8 min (minor), 30.3 min (major).

((6*S*,7*R*,7a*S*)-6-((Benzyloxy)methyl)-1-((4-methoxyphenyl)sulfonyl)-4-((triisopropylsilyl)oxy)-2,3,5,6,7,7a-hexahydro-1*H*-indol-7-yl)methanol (11)

To a solution of **8c** (62.8 mg, 89.9 μmol) in THF (0.9 mL) was added lithium aluminum hydride (10.3 mg, 0.270 mmol, 3.0 equiv.) at 0 °C. The resulting solution was stirred at room temperature for 1 h under Ar. The reaction was quenched with saturated potassium sodium tartrate aqueous solution. The aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtered through a plug of cotton, and evaporated under reduced pressure. Then, the crude residue was added THF (0.9 mL) and lithium borohydride (70 μL, 0.14 mmol, 1.6 equiv., 2.0 M in THF) at 0 °C. The resulting solution was stirred at room temperature for 1 h under Ar, and quenched with 1.0 M aqueous HCl at 0 °C. The water layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4 and filtrated through a plug of cotton. After the solvent was evaporated, the crude product was

purified by flash column chromatography (SiO_2, hexane/AcOEt = 2/1 to 1/1, and then to 1/2) to give **11** (29.8 mg, 54%) as a brown oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.99-1.11 (m, 21H), 1.22-1.29 (m, 1H), 1.38 (dd, *J* = 10.8, 10.8 Hz, 1H), 2.22-2.24 (m, 1H), 2.28-2.29 (m, 2H), 2.38 (dd, *J* = 13.8, 4.8 Hz, 1H), 3.01 (ddd, *J* = 12.6, 12.6, 4.8 Hz, 1H), 3.15 (brs, 1H), 3.55 (dd, *J* = 9.0, 1.8 Hz, 1H), 3.59 (dd, *J* = 12.6, 7.2 Hz, 1H), 3.69 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.74 (dd, *J* = 9.6, 9.6 Hz, 1H), 3.86 (s, 3H), 4.12 (d, *J* = 10.8 Hz, 1H), 4.20 (d, *J* = 12.0, 1H), 4.52 (d, *J* = 2.4 Hz, 2H), 6.98 (d, *J* = 7.8 Hz, 2H), 7.26-7.34 (m, 5H), 7.78 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 12.8, 17.79, 17.83, 26.8, 33.3, 33.4, 43.8, 48.5, 55.6, 58.5, 59.9, 70.9, 73.0, 114.4, 115.6, 127.4, 128.2, 129.6, 138.5, 143.3, 163.2; IR (neat): 3555, 2944, 1708, 1596, 1497; HRMS (ESI): *m*/*z* calcd for $C_{33}H_{49}N_1Na_1O_6S_1Si_1$ $[M + Na]^+$: 638.2948, found 638.2972; $[\alpha]_D^{23}$ +76.6 (*c* 0.86, $CHCl_3$, 75% ee).

((6*S*,7*R*,7a*S*)-6-((Benzyloxy)methyl)-4-((triisopropylsilyl)oxy)-2,3,5,6,7,7a-hexahydro-1*H*-indol-7-yl)-methanol (12)

To a solution of **11** (18.2 mg, 29.6 μmol) in THF (0.3 mL) at 0 °C was slowly added sodium anthracenide in THF (0.2 mL) dropwise which was prepared by sonicating the THF (0.7 mL) solution of anthracene (52.7 mg, 0.296 mmol) and sodium (6.8 mg, 0.30 mmol) at room temperature for 2 h. After the mixture turned deep blue and was stirred at 0 °C for further 10 min, the mixture was added H_2O to quench the reaction. The aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a plug of cotton, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (CHROMATOREX-DIOL, hexane/AcOEt = 2/1, 1/1 to 0/1, and then CH_2Cl_2/MeOH = 5/1). The eluent was concentrated, and the resulting residue was dissolved in CH_2Cl_2 and added 2.0 M aqueous NaOH. The water layer was extracted three times with CH_2Cl_2. The combined organic layers were evaporated to give **12** (9.0 mg, 68%) as a brown oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.11-1.15 (m, 21H), 1.37-1.43 (m, 1H), 1.92-1.98 (m, 1H), 2.09-2.14 (m, 1H), 2.21-2.28 (m, 2H), 2.50-2.55 (m, 1H), 2.84-2.88 (m, 1H), 3.06-3.10 (m, 1H), 3.30 (d, *J* = 9.6 Hz, 1H), 3.42 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.48 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.69 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.88 (dd, *J* = 10.8, 4.2 Hz, 1H), 4.51 (d, *J* = 2.4 Hz, 2H), 7.28-7.36 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.0, 18.0, 27.7, 34.5, 36.2, 45.0, 46.1, 62.9, 64.2, 72.3, 73.3, 118.0, 127.6, 127.7, 128.4, 138.0, 141.6; IR (neat): 3329, 2924, 1713, 1463, 1194; HRMS (ESI): *m*/*z* calcd for $C_{26}H_{44}N_1O_3Si_1$ $[M + H]^+$: 446.3090, found 446.3076; $[\alpha]_D^{25}$ +12.0 (*c* 0.57, $CHCl_3$, 75% ee).

Methyl (3a*S*,6*S*,7*R*,7a*S*)-1-((4-methoxyphenyl)sulfonyl)-3a-methyl-4-oxo-7-(2-oxooxazolidine-3-carbonyl)octahydro-1*H*-indole-6-carboxylate (13)

A THF solution of tetra-*n*-butylammonium fluoride (0.12 mL, 0.12 mmol, 1.5 equiv., 1.0 M in THF) was added dropwise to **8a** (50.0 mg, 78.5 μmol) and iodomethane (9.8 μL, 0.16 mmol, 2.0 equiv.) in THF (0.52 mL) at –78 °C. Then, the solution was allowed to warm to 0 °C over 30 min. The resulting slurry

was stirred for another 30 min at 0 ºC. The reaction was quenched by the addition of saturated aqueous NH_4Cl. The water layer was extracted three times with CH_2Cl_2 (5.0 mL), and combined organic layers were washed with brine and dried over Na_2SO_4. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (SiO_2, hexane/AcOEt = 7/3) to give **13** (35.8 mg, 92%) as a foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.48 (s, 3H), 1.60 (dt, *J* = 12.8, 7.2 Hz, 1H), 2.35 (dt, *J* = 12.8, 9.6 Hz, 1H), 2.61 (dd, *J* = 16.8, 13.2 Hz, 1H), 2.78 (dd, *J* =16.8, 5.2 Hz, 1H), 3.04 (dt, *J* = 9.6, 8.0 Hz, 1H), 3.25 (ddd, *J* = 13.2, 11.2, 5.2 Hz, 1H), 3.69 (dt, *J* = 8.0, 7.2 Hz, 1H), 3.70 (s, 3H), 3.80 (d, *J* = 10.8 Hz, 1H), 3.87 (s, 3H), 4.06 (dt, *J* = 9.2, 8.8 Hz, 1H), 4.28 (dt, *J* = 9.2, 4.8 Hz, 1H), 4.44 (dt, *J* = 8.4, 4.8 Hz, 1H), 4.51 (dt, *J* = 8.8, 8.4 Hz, 1H), 4.86 (dd, *J* = 11.2, 10.8 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.5, 34.7, 38.9, 40.6, 43.2, 45.0, 45.1, 52.6, 54.5, 55.6, 62.2, 69.4, 114.2, 128.4, 129.8, 154.1, 163.3, 172.4, 172.8, 207.5; IR (neat): 2957, 1772, 1697, 1260, 1153; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{26}N_2Na_1O_9S_1$ $[M + Na]^+$: 517.1251 found 517.1255; $[\alpha]_D^{21}$ +70.2 (*c* 0.67, $CHCl_3$, 70% ee).

Methyl (3a*S*,6*S*,7*R*,7a*S*)-3a-allyl-1-((4-methoxyphenyl)sulfonyl)-4-oxo-7-(2-oxooxazolidine-3-carbonyl)octahydro-1*H*-indole-6-carboxylate (14)

A THF solution of tetra-*n*-butylammonium fluoride (70 μL, 0.070 mmol, 1.5 equiv., 1.0 M in THF) was added dropwise to **8a** (30.0 mg, 47.1 μmol) and allyl bromide (10.0 μL, 0.118 mmol, 2.5 equiv.) in THF (1.0 mL) at –78 °C. Then the solution was allowed to warm to 0 °C over 30 min. The resulting slurry was stirred for another 30 min at 0 ºC. The reaction was quenched by the addition of saturated aqueous NH_4Cl. The water layer was extracted three times with CH_2Cl_2, and combined organic layers were washed with brine and dried over Na_2SO_4. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (SiO_2, hexane/AcOEt = 1/1) to give **14** (19.1 mg, 80%) as a foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.29 (dd, *J* = 14.0, 7.2 Hz, 1H), 1.71 (dt, *J* = 12.8, 8.4 Hz, 1H), 2.01 (dd, *J* = 12.0, 7.2 Hz, 1H), 2.33 (dd, *J* = 12.8, 8.8 Hz, 1H), 2.55 (dd, *J* = 17.2, 12.4 Hz, 1H), 2.74 (dd, *J* = 17.2, 6.0 Hz, 1H), 3.03 (dt, *J* = 9.2, 8.4 Hz, 1H), 3.24 (ddd, *J* = 6.0, 11.2, 12.4 Hz, 1H), 3.60 (dt, *J* = 8.8, 9.2 Hz, 1H), 3.69 (s, 3H), 3.87 (s, 3H), 4.02-4.10 (m, 2H), 4.27 (ddd, *J* = 10.0, 4.8, 4.4 Hz, 1H), 4.41-4.54 (m, 2H), 4.69 (d, *J* = 16.8 Hz, 1H), 4.79 (dd, *J* = 11.2, 11.2 Hz, 1H), 5.01 (d, *J* = 10.0 Hz, 1H), 5.41 (ddd, *J* = 16.8, 10.0, 7.2 Hz, 1H), 6.09 (d, *J* = 8.8 Hz, 2H), 7.76 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.7, 37.0, 39.6, 40.0, 43.2, 44.8, 44.9, 52.6, 55.7, 58.7, 62.1, 66.0, 114.3, 119.8, 128.6, 129.8, 132.3, 154.1, 163.3, 172.6, 172.7, 207.4; IR (neat): 2155, 1771, 1733, 1697, 1157; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}N_2Na_1O_9S_1$ $[M + Na]^+$: 543.1413 found 543.1400; $[\alpha]_D^{21}$ +65.9 (*c* 0.72, $CHCl_3$, 70% ee).

Methyl (3a*S*,6*S*,7*R*,7a*S*)-1-((4-methoxyphenyl)sulfonyl)-3a-(2-nitrobenzyl)-4-oxo-7-(2-oxooxazolidine-3-carbonyl)octahydro-1*H*-indole-6-carboxylate (15)

To a solution of **8a** (25.4 mg, 39.9 μmol), *o*-nitrobenzyl bromide (13.0 mg, 60.2 μmol, 1.5 equiv.),

activated MS4Å (80.0 mg, powder) in THF (0.8 mL) was added tetra-*n*-butylammonium fluoride in THF (60.0 μL, 60.0 μmol, 1.5 equiv., 1.0 M in THF, dried by activated MS4Å (pellet) prior to use) at –78 °C. Then the solution was allowed to warm to 0 °C over 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The resulting mixture was filtered through a pad of Celite® and evaporated. The crude mixture was roughly purified by flash column chromatography (SiO_2, hexane/AcOEt = 1/1 to 1/2) to give **15** with some byproducts as a brown oil. We identified the structure of **15** after partially isolating the pure compound by preparative TLC. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.79 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.30 (ddd, *J* = 13.6, 9.6, 9.6 Hz, 1H), 2.46 (d, *J* = 15.6 Hz, 1H), 2.61 (dd, *J* = 17.6, 10.4 Hz, 1H), 2.82 (d, *J* = 15.6 Hz, 1H), 3.00 (dd, *J* = 17.6, 7.6 Hz, 1H), 3.23 (dd, *J* = 17.6, 9.6 Hz, 1H), 3.57-3.71 (m, 2H), 3.71 (s, 3H), 3.83 (s, 3H), 3.89-4.14 (m, 1H), 4.20 (d, *J* = 10.8 Hz, 1H), 4.85-4.31 (m, 1H), 4.43-4.55 (m, 2H), 4.77 (dd, *J* = 11.2 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.40 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.50 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 32.7, 35.9, 38.5, 39.8, 43.3, 44.8, 45.3, 52.7, 55.7, 58.5, 62.2, 67.5, 114.4, 125.8, 128.1, 128.4, 129.6, 131.3, 131.5, 133.1, 149.1, 154.1, 163.5, 172.4, 172.5, 206.8; IR (neat): 2925, 2853, 1775, 1699, 1595, 1528; HRMS (ESI) *m/z* calcd for $C_{28}H_{29}N_3Na_1O_{11}S_1$ $[M + Na]^+$: 638.1421, found 638.1414.

Methyl (3a*S*,4*R*,5*S*,6a*S*,12a*R*)-7-acetyl-3-((4-methoxyphenyl)sulfonyl)-4-(2-oxooxazolidine-3-carbonyl)-1,2,3,3a,4,5,6,6a,7,12-decahydropyrrolo[2,3-k]acridine-5-carboxylate (16)

Methyl (3a*S*,4*R*,5*S*,6a*R*,12a*R*)-7-acetyl-3-((4-methoxyphenyl)sulfonyl)-4-(2-oxooxazolidine-3-carbonyl)-1,2,3,3a,4,5,6,6a,7,12-decahydropyrrolo[2,3-k]acridine-5-carboxylate (17)

To a solution of **15** (6.0 mg, impure) in AcOEt (0.8 mL) was added Pd/C (1.8 mg, 30 w/w%). The mixture was vigorously stirred for 5 h under hydrogen gas at ambient pressure at 65 °C. The resulting mixture was filtered through a pad of Celite® and evaporated. Then, to a solution of the crude residue in CH_2Cl_2 (0.8 mL) was added 4-dimethylaminopyridine (4.9 mg, 40 μmol, 1.0 equiv.), AcCl (14.2 μL, 200 μmol, 5.0 equiv.), and pyridine (32.2 μL, 400 μmol, 10 equiv.). After the mixture was stirred for 2 h at room temperature and refluxed for 5 h, the reaction was quenched with H_2O at room temperature. The water layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and filtered through a plug of cotton. After the solvent was evaporated, the crude product was purified by flash column chromatography (SiO_2, hexane/AcOEt = 1/1 to 1/2) to give **16** (9.2 mg, 38%, 3 steps from **8a**) as foam, and **17** (9.4 mg, 38%, 3 steps from **8a**) as foam. Spectral Data of **16**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.87 (dd, *J* = 13.2, 8.4 Hz, 1H), 1.94-2.00 (m, 2H), 2.12 (s, 3H), 2.12-2.13 (m, 1H), 2.33-2.46 (m, 3H), 3.14 (d, 1H), 3.25 (d, *J* = 10.8, 1H), 3.58-3.61 (m, 1H), 3.61 (s, 3H), 3.89-3.94 (m, 1H), 3.93 (s, 3H), 3.98-4.01 (m, 1H), 4.33 (dd, *J* = 8.4, 8.4 Hz, 2H), 4.46 (dd, *J* = 10.8, 10.8 Hz, 1H), 4.66 (s, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 9.0 Hz, 2H), 7.19 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.32

(dd, *J* = 7.8, 7.8 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 23.1, 30.8, 35.2, 35.9, 40.4, 43.0, 43.7, 44.9, 49.6, 52.2, 55.8, 56.4, 61.8, 63.8, 114.2, 125.3, 126.2, 127.9, 128.8, 129.8, 130.3, 132.0, 138.6, 153.9, 163.2, 170.1, 173.6, 173.9; IR (neat): 2919, 1774, 1734, 1698, 1655, 1595, 1496, 1595, 1496; HRMS (ESI): *m*/*z* calcd for $C_{30}H_{33}N_3Na_1O_9S_1$ $[M + Na]^+$: 634.1835, found 634.1825; $[\alpha]_D^{25}$ +96.6 (*c* 0.11, $CHCl_3$, 88% ee). Spectral Data of **17**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.82 (dd, *J* = 13.2, 8.4 Hz, 1H), 1.33 (d, *J* = 15.0, 1H), 1.88 (d, *J* = 15.0 Hz, 1H), 1.97-2.05 (m, 2H), 2.08 (s, 3H), 2.93 (ddd, *J* = 13.2, 3.6, 3.6 Hz, 1H), 3.03 (dd, *J* = 12.6, 10.2 Hz, 1H), 3.15 (ddd, *J* = 12.6, 12.6, 3.6 Hz, 1H), 3.61-3.63 (m, 1H), 3.66 (s, 3H), 3.69-3.72 (m, 1H), 3.92 (s, 3H), 3.94 (dd, *J* = 12.0, 3.0 Hz, 1H), 4.06 (dd, *J* = 19.2, 9.0 Hz, 1H), 4.23 (ddd, *J* = 9.0, 9.0, 5.4 Hz, 1H), 4.41 (ddd, *J* = 9.0, 9.0, 5.4 Hz, 1H), 4.46 (dd, *J* = 18.0, 9.0 Hz, 1H), 4.72 (dd, *J* = 12.0, 10.2 Hz, 1H), 6.48 (d, *J* = 7.2 Hz, 1H), 7.02-7.07 (m, 2H), 7.07 (d, *J* = 9.0, 2H), 7.17 (dd, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 24.4, 26.9, 27.5, 37.3, 43.3, 43.6, 44.8, 44.9, 48.7, 52.3, 55.8, 61.6, 62.0, 68.8, 114.3, 125.6, 125.7, 126.8, 128.8, 129.5, 130.0, 131.3, 139.2, 154.0, 163.3, 172.2, 173.0, 174.2; IR (neat): 2925, 1776, 1732, 1697, 1594, 1496; HRMS (ESI): *m*/*z* calcd for $C_{30}H_{33}N_3Na_1O_9S_1$ $[M + Na]^+$: 634.1835, found 634.1823; $[\alpha]_D^{25}$ –67.2 (*c* 0.12, $CHCl_3$, 88% ee).

Methyl (1S,2S)-4-(2-((4-methoxy-*N*-(2-nitrophenyl)phenyl)sulfonamido)ethyl)-5-oxo-2-(2-oxooxazolidine-3-carbonyl)cyclohex-3-ene-1-carboxylate (19)

To activated MS4Å (80.0 mg, powder) in reaction vessel was added a solution of **8a** (20.0 mg, 31.4 μmol, azeotropically dried three times with toluene) in THF (0.63 mL), *o*-fluoronitrobenzene (17.0 μL, 161 μmol, 5.1 equiv.). The mixture was added tetra-*n*-butylammonium fluoride in THF (47.0 μL, 47.0 μmol, 1.5 equiv., 1.0 M in THF, dried by activated MS4Å (pellet) prior to use) at –78 °C. Then, the mixture was allowed to warm to room temperature, and refluxed for 3 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl at room temperature. The resulting mixture was filtered through a pad of Celite® and evaporated. The crude mixture was roughly purified by flash column chromatography (SiO_2, hexane/AcOEt = 2/1, 1/1 to 1/2) to give **19** with a byproduct as a brown oil. We identified the structure of **19** after isolating the pure compound by preparative HPLC. ^{1}H NMR (600 MHz, C_6D_6, 75 °C) δ: 2.29 (dd, *J* = 7.8, 7.8 Hz, 1H), 2.39-2.41 (m, 1H), 2.58-2.61 (m, 1H), 2.88 (d, *J* = 12.6 Hz, 1H), 3.16 (s, 3H), 3.27 (s, 3H), 3.25-3.30 (m, 2H), 3.39-3.42 (m, 1H), 3.42-3.53 (m, 1H), 3.54 (d, *J* = 7.2 Hz, 1H), 3.61 (brs, 2H), 5.21 (d, *J* = 8.4 Hz, 1H), 6.50 (d, *J* = 9.0 Hz, 2H), 6.67 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.85 (m, 2H), 6.98 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 9.0, 2H); ^{13}C NMR (150 MHz, C_6D_6, 75 °C) δ: 30.3, 38.7, 41.9, 42.8, 44.4, 50.1, 51.6, 55.0, 61.9, 114.4, 125.7, 128.4, 130.3, 130.4, 130.9, 132.3, 133.6, 137.0, 141.5, 149.9, 153.5, 163.6, 170.8, 172.8, 194.6; IR (neat): 2932, 2852, 1776, 1681, 1534; HRMS (ESI): *m*/*z* calcd for $C_{27}H_{27}N_3Na_1O_{11}S_1$ $[M + Na]^+$: 624.1264, found 624.1264; DAICEL CHIRALPAK IB, e:

hexane/*i*PrOH/AcOEt = 55/5/40, f: 3.0 mL/min, 254 nm, 13.6 min (minor), 15.0 min (major).

Methyl 5-((4-methoxyphenyl)sulfonyl)-9-(2-oxooxazolidine-3-carbonyl)-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4]diazocine-10-carboxylate (23)

Methyl 5-((4-methoxyphenyl)sulfonyl)-5,6,7,12-tetrahydrodibenzo[b,e][1,4]diazocine-10-carboxylate (24)

Ammonium acetate (72.6 mg, 942 μmol, 30.0 equiv.) in H_2O (0.6 mL) was added $TiCl_3$ (0.6 mL, 20% solution) at room temperature, and the mixture was stirred for 20 min. To this mixture was added acetone (0.2 mL) and a solution of **19** (12.2 mg, impure) in acetone (0.2 mL + 0.1 mL + 0.1 mL to rinse) at room temperature. After being stirred for 2 h at the same temperature, the reaction mixture was diluted with H_2O, and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4 and filtered through a plug of cotton. After the solvent was evaporated, the crude product was roughly purified by flash column chromatography (SiO_2, hexane/AcOEt = 1/1 to 1/2) to give the mixture containing trace amount of **19** (monitored by ^{1}H NMR). This mixture was treated again under the same reaction conditions and purification process *vide supra*. Then, the crude mixture (9.6 mg) was refluxed with CSA (3.6 mg, 15 μmol, 0.49 equiv.) in toluene (3.1 mL) for 2 h. After the solvent was evaporated, the residue was purified by flash column chromatography (CHROMATOREX-DIOL, hexane/AcOEt = 2/1, then SiO_2, hexane/AcOEt = 1/0, 4/1, 2/1, 1/1 to 1/2) to give **23** (2.5 mg, 14%, 3 steps from **8a**) as a yellow oil, and **24** (0.8 mg, 6%, 3 steps from **8a**) as a red oil. Spectral Data of **23**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.60 (dd, *J* = 13.8, 3.6 Hz, 1H), 2.83 (ddd, *J* = 13.8, 4.8, 4.8 Hz, 1H), 3.50 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.79 (s, 3H), 3.87 (s, 3H), 3.86-3.88 (m, 1H), 4.20-4.27 (m, 2H), 4.43-4.51 (m, 2H), 5.74 (s, 1H), 6.71 (d, *J* = 9.0 Hz, 2H), 6.83 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.91 (s, 1H), 6.92 (s, 1H), 7.00 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H), 7.23-7.26 (m, 3H), 7.40 (dd, *J* = 7.8, 1.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 31.1, 42.9, 46.9, 52.4, 55.4, 62.1, 113.8, 119.5, 120.4, 122.3, 124.1, 127.2, 128.7, 129.1, 129.9, 130.3, 130.5, 131.9, 133.7, 142.0, 142.5, 153.0, 162.4, 165.7, 168.9; IR (neat): 3362, 2925, 2851, 1785, 1716, 1685, 1594, 1497; HRMS (ESI): *m*/*z* calcd for $C_{27}H_{25}N_3Na_1O_8S_1$ $[M + Na]^+$: 574.1260, found 574.1266. Spectral Data of **24**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.62 (dd, *J* = 13.2, 3.6 Hz, 1H), 2.84 (ddd, *J* = 13.2, 5.4, 5.4 Hz, 1H), 3.50 (dd, *J* = 12.0, 3.6 Hz, 1H), 3.76-3.81 (m, 1H), 3.81(s, 3H), 3.92 (s, 3H), 5.75 (s, 1H), 6.64 (d, *J* = 8.4 Hz, 2H), 6.83 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.91 (ddd, *J* = 8.4, 8.4, 1.2 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 7.14 (d, *J* = 1.2 Hz, 1H), 7.21-7.24 (m, 3H), 7.28-7.29 (m, 1H), 7.46 (dd, *J* = 8.4, 1.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 30.9, 47.1, 52.1, 55.4, 113.6, 119.1, 120.8, 121.1, 122.7, 123.4, 129.1, 129.2, 129.7, 130.8, 131.7, 132.4, 133.0, 141.3, 142.9, 162.4, 166.7; IR (neat): 3366, 2924, 2852, 1715, 1496; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{22}N_3Na_1O_5S_1$ $[M + Na]^+$: 461.1147, found 461.1165.

Methyl (6*S*,7*R*,7a*R*)-1-((4-methoxyphenyl)sulfonyl)-4-oxo-7-(2-oxooxazolidine-3-carbonyl)-octahydro-1*H*-indole-6-carboxylate (25)

A THF solution of tetra-*n*-butylammonium fluoride (47.0 μL, 47.0 μmol, 1.5 equiv., 1.0 M in THF) was added dropwise to **8a** (20.0 mg, 31.4 μmol) and AcOH (5.4 μL, 94 μmol, 3.0 equiv.) in THF (0.6 mL) at –78 °C. Then, the solution was allowed to warm to 0 °C over 30 min. The reaction was quenched by the addition of 1.0 M aqueous HCl. The water layer was extracted three times with AcOEt, and combined organic layers were washed with brine, dried over Na_2SO_4, and filtered through a plug of cotton. After the solvent was removed under reduced pressure, the crude product was purified by flash column chromatography (SiO_2, hexane/AcOEt = 1/1 to 1/2) to give **25** (14.2 mg, 94%) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.02 (m, 1H), 2.15-2.24 (m, 2H), 2.53 (dd, *J* = 16.0, 13.6 Hz, 1H), 2.72 (dd, *J* = 16.0, 4.8 Hz, 1H), 3.08-3.15 (m, 1H), 3.25 (ddd, *J* = 13.6, 11.2, 4.8 Hz, 1H), 3.67-3.70 (m, 4H), 3.88 (s, 3H), 4.04-4.08 (m, 1H), 4.11 (ddd, *J* = 15.6, 10.8, 6.8 Hz, 1H), 4.29 (ddd, *J* = 10.8, 8.8, 4.8 Hz, 1H), 4.44-4.48 (m, 1H), 4.52 (ddd, *J* = 19.6, 8.4, 4.8 Hz, 1H), 4.83 (dd, *J* = 11.2, 11.2 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.8, 39.0, 41.1, 42.9, 43.2, 47.1, 51.3, 52.6, 55.6, 62.3, 63.4, 114.6, 128.2, 129.3, 154.0, 163.3, 172.2, 172.7, 205.8; IR (neat): 1772, 1697, 1594, 1394, 1261, 1156; HRMS (ESI): *m*/*z* calcd for $C_{21}H_{24}N_2Na_1O_9S_1$ $[M + Na]^+$: 503.1100 found 503.1105; $[\alpha]_D^{21}$ +77.2 (*c* 1.35, $CHCl_3$, 85% ee).

Methyl (3a*R*,4*R*,5*R*)-3-((4-methoxyphenyl)sulfonyl)-4-(2-oxooxazolidine-3-carbonyl)-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,2-*a*]carbazole-5-carboxylate (26)

To a solution of ketone **25** (35.8 mg, 74.5 μmol) in 1,2-dichloroethane (2.5 mL) was added phenylhydrazine (22.2 μL, 0.225 mmol, 3.0 equiv.), followed by trifluoroacetic acid (45 μL, 0.59 mmol, 7.9 equiv.). The reaction mixture was heated to 80 °C. After being stirred for 16 h, the reaction mixture was cooled to room temperature and quenched with a saturated aqueous $NaHCO_3$. The resulting mixture was diluted with CH_2Cl_2. The layers were separated, and the water layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered through a plug of cotton, and evaporated under reduced pressure. The resulting residue was purified by column chromatography (SiO_2, hexane/AcOEt = 7/1 to 2/3) to afford **26** (26.9 mg, 65%) as a foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.11-2.24 (m, 2H), 2.76 (ddd, *J* = 10.4, 7.2, 6.8 Hz, 1H), 3.14 (dd, *J* = 17.6, 10.0 Hz, 1H), 3.55-3.70 (m, 1H), 3.80 (s, 3H), 3.85 (s, 3H), 4.04 (dt, *J* = 9.6, 9.6 Hz, 1H), 4.19 (dd, *J* = 10.0, 7.2 Hz, 1H), 4.28 (dt, *J* = 9.6, 4.8 Hz, 1H), 4.40 (dt, *J* = 8.8, 4.8 Hz, 1H), 4.49 (dt, *J* = 9.6, 8.8 Hz, 1H), 4.52 (d, *J* = 10.4 Hz, 1H), 5.03 (dd, *J* = 10.4, 10.0 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.03-7.13 (m, 2H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.8, 37.9, 41.9, 43.3, 44.7, 48.8, 52.3, 55.6, 62.3, 62.4, 105.6, 110.9, 114.4, 118.8, 120.1, 122.2, 125.3, 128.2, 129.5, 132.5, 136.4, 153.9, 163.2, 172.5, 173.1; IR (neat): 3386, 2950, 1772, 1731, 1690, 1594, 1497, 1456,

1386, 1333, 1259, 1197, 1154; HRMS (ESI): *m/z* calcd for $C_{27}H_{27}N_3Na_1O_8S_1$ $[M + Na]^+$: 576.1417, found 576.1420; $[\alpha]_D^{21}$ +83.9 (*c* 0.54, $CHCl_3$, 68% ee).

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