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Supporting Information

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Isoxazole-directed Pinacol Rearrangement: Stereo-controlled Approach to Angular Quaternary Stereogenic Centers

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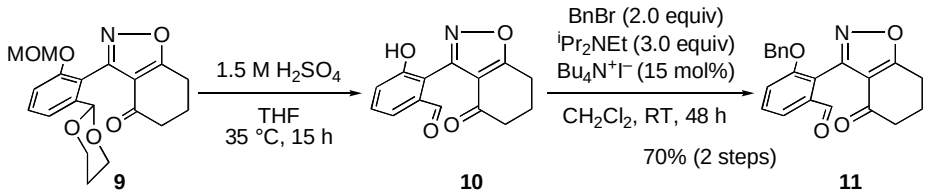
General Methods. All reactions utilizing air- or moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry Ar. CH_2Cl_2 was distilled over CaH_2. Commercially available anhydrous stabilizer-free THF (Kanto chemical No.41001) and Et_2O (Kanto chemical No. 14547-95) were used without further purification. Thin layer chromatography (TLC) was performed on Merck precoated plates (silica gel 60 F254, Art 5715, 0.25 mm) and were visualized by fluorescence quenching under UV light or by staining with phosphomolybdic acid. Silica-gel preparative thin-layer chromatography (PTLC) was performed using plates prepared from Merck Kieselgel 60 PF254 (Art 7747). Silica-gel column chromatography was performed on silica gel 60N (Spherical, neutral, 23–210 μm) from Kanto chemical. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured on a JEOL JMN Lambda-400 spectrometer. Chemical shifts are expressed in parts per million (PPM) downfield from internal tetramethylsilane ($\delta = 0$) and coupling constants are reported as Hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet. Infrared (IR) spectra were recorded on Jasco IRA-202 spectrophotometer and are reported as wavenumbers (cm^{-1}). Melting points (mp) were measured on a Yanaco MP-S3 instrument or MP-500V instrument. High performance liquid chromatography (HPLC) analyses were performed with a JASCO CO-2060 plus for column thermostat, UV-2077 plus for UV/VIS detector, PU-1580 for HPLC pump, DG-2080-53 for 3-line degasser and LG-2080-02 for gradient unit. Enantiomeric excesses were assessed by HPLC analysis on chiral stationary phases, CHIRALPAK® AD-H, CHIRALPAK® IA and CHIRALCEL® OD-H (Daicel Chemical Ind., Ltd.). Recycling Preparative HPTC was performed on LC-918 (Japan Analytical Industry Co., Ltd.) equipped with a hydrophobic size exclusion chromatography column, JAIGEL-2H, and eluted with $CHCl_3$.

Preparation of a**-ketol (*R*)-3**.



To a solution of acetal **9**[1] (10.5 g, 29.2 mmol) in THF (90 mL) was added slowly aq H_2SO_4 (1.5 M, 60 mL, 90 mmol) at 0 °C. The solution was heated to 35 °C and the stirring was continued for 15 h. After the reaction was cooled to 0 °C, sat $NaHCO_3$ was added until the solution was neutralized. The precipitate was collected by suction filtration and well-washed by H_2O and Et_2O to give phenol **10** (6.11g, ca. 79%) as a light brown solid. To a suspension of phenol **10** (3.01 g, ca. 11.7 mmol), $Bu_4N^+I^-$ (642 mg, 1.74 mmol) and $^{i}Pr_2NEt$ (4.55 g, 35.2 mmol) in CH_2Cl_2 (40 mL) was added slowly a solution of BnBr (4.05 g, 23.7 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The reaction mixuture was allowed to warm to room temperature. After stirring for 48 h at this temperature, Et_2NH (2.0 mL, 19mmol) was added and the stirring was continued for 1 h. The reaction mixture was diluted with Et_2O (30 mL) and the products were extracted with Et_2O (x2). The combined organic layer was washed with aq HCl (1 M, 50 mL), H_2O (50 mL), and brine (50 mL). The resulting extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by precipitation from EtOAc/Et_2O and the following silica-gel column chromatography (EtOAc/hexane = 60/40) to give keto-aldehyde **11** (3.59 g, 70%, 2 steps) as a colorless solid.

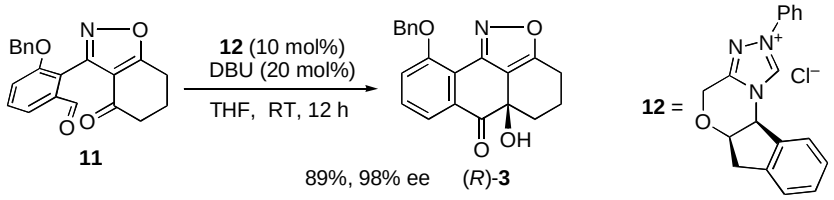
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.91 (s, 1 H), 7.66 (d, 1 H, *J* = 7.7 Hz), 7.57 (dd, 1 H, *J* = 8.0, 7.7 Hz), 7.22–7.38 (m, 6 H), 5.11 (d, 1 H, *J* = 11.4 Hz), 5.02 (d, 1 H, *J* = 11.4 Hz), 2.98–3.12 (m, 2 H), 2.00–2.54 (m, 4 H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 191.5, 190.7, 180.8, 157.5, 154.1, 136.2, 136.1, 131.3, 128.4, 128.0, 127.4, 120.9, 119.4, 117.6, 116.5, 71.0, 37.9, 23.2, 22.1;

IR (KBr) 3033, 2950, 2867, 1705, 1685, 1593, 1466, 1268, 1045, 912, 700 cm^{-1};

Anal. Calc'd for $C_{21}H_{17}NO_4$; C, 72.61; H, 4.93; N, 4.03. Found: C, 72.70; H, 5.02; N, 3.95;

mp 117.0–118.0 °C (EtOAc/hexane).



1) T. Matsuura, J. W. Bode, Y. Hachisu, K. Suzuki, *Synlett* **2003**, 1746–1748.

A mixture of keto-aldehyde **11** (1.03 g, 2.97 mmol) and triazolium salt **12** (97.4 mg, 0.299 mmol) in THF (10 mL) was degassed by three cycles of freeze-pump-thaw. To the mixture was added DBU (90 μL, 0.60 mmol) dropwise at room temperature under a nitrogen atmosphere. After stirring at this temperature for 12 h, the reaction was cooled to 0 °C, and water was added. The products were extracted with EtOAc (x3). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (EtOAc/hexane = 45/55) to give benzoin product (*R*)-**3** (919 mg, 89%, 98% ee) as a yellow solid. Recrystallization from EtOAc/hexane gave enantiomerically pure (*R*)-**3** as a colorless prism. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 20 °C: (*R*)-**3**: t_1 = 20.1 min; (*S*)-**3**: t_2 = 24.6 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (dd, 1 H, *J* = 7.7. 1.0 Hz), 7.51 (d, 2 H, *J* = 7.0 Hz), 7.41 (dd, 1 H, *J* = 8.2, 7.7 Hz), 7.36 (t, 2 H, *J* = 7.0 Hz), 7.34–7.25 (m, 1 H), 7.17 (brd, 1 H, *J* = 8.2 Hz), 5.31 (d, 1 H, *J* = 13.1 Hz), 5.26 (d, 1 H, *J* = 13.1 Hz), 2.95 (dd, 1 H, *J* = 18.4, 6.0 Hz), 2.87 (s, 1 H), 2.72–2.59 (m, 1 H), 2.43–2.27 (m, 2 H), 2.26–2.14 (m, 1 H), 1.66–1.55 (m, 1 H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.3, 171.0, 155.4, 153.3, 136.2, 133.2, 131.5, 128.6, 127.9, 126.7, 122.2, 118.4, 117.7, 113.6, 70.6, 67.4, 29.0, 22.3, 17.9;

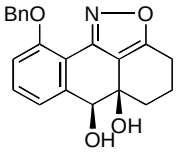
IR (KBr) 3367, 3029, 3005, 2954, 1701, 1666, 1573, 1485, 1456, 1277, 744 cm^{-1};

Anal. Calc'd for $C_{21}H_{17}NO_4$; C, 72.61; H, 4.93; N, 4.03. Found: C, 72.89; H, 4.84; N, 4.10;

Optical Rotation $[\alpha]_D^{30}$ +34 (*c* 0.90, $CHCl_3$) for >99% ee;

mp 175.5–177.0 °C.

Determination of absolute stereochemistry of α**-ketol (*R*)-3.**



13

To a suspension of $NaBH_4$ (5.8 mg, 92% assay, 0.14 mmol) in MeOH (0.5 mL) was added optically pure α-ketol (*R*)-**3** (49.4 mg, 0.142 mmol) in THF (1.5 mL) at 0 °C. After stirring for 10 min, water was added, and the products were extracted with EtOAc (x2). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane/EtOAc=20/80) to give diol **13** (48 mg, 97%) as a colorless solid.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, 2 H, *J* = 8.3 Hz), 7.46–7.34 (m, 4 H), 7.29 (d, 1 H, *J* = 7.5 Hz), 6.90 (d, 1 H, *J* = 8.2 Hz), 5.22 (d, 1 H, *J* = 12.8 Hz), 5.15 (d, 1 H, *J* = 12.8 Hz), 4.47 (d, 1 H, *J* = 10.9 Hz), 2.95–2.85 (m, 1 H), 2.77 (d, 1 H, *J* = 10.9 Hz), 2.72–2.60 (m, 1 H), 2.36–2.11 (m, 4 H), 1.49 (td, 1 H, *J* = 13.3, 3.6 Hz);

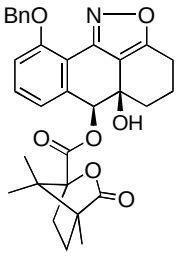
^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 155.7, 154.1, 142.3, 136.7, 131.4, 128.5, 127.6, 126.7, 119.7, 114.0, 113.4, 112.3, 75.8, 70.3, 66.1, 32.9, 22.5, 18.7;

IR (KBr) 3415, 3344, 2948, 2922, 2846, 1676, 1577, 1487, 1275, 1059, 962, 754, 739 cm^{-1};

Anal. Calc'd for $C_{21}H_{19}NO_4$; C, 72.19; H, 5.57; N, 4.01. Found: C, 72.22; H, 5.57; N, 3.95;

Optical Rotation $[\alpha]_D^{24}$ +25 (*c* 1.00, $CHCl_3$)

mp 189 °C (decomp., acetone/Et_2O).



14

To a solution of alcohol **13** (33.9 mg, 0.0970 mmol) and DMAP (18.2 mg, 0.149 mmol) in CH_2Cl_2 was added (–)-camphanic chloride (28.0 mg, 0.129 mmol) at 0 °C. After stirring for 10 min, the reaction was quenched by the addition of water. The products were extracted with Et_2O (x2), and the combined organic extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc = 20/80) to afford camphanate **14** (29.6 mg, 58%) as a colorless solid. Recrystallization from acetone/MeOH gave a single crystal of **14** for the X-ray analysis.

^{1}H NMR (DMSO-d_6, 400 MHz, 348 K) δ 7.60 (brd, 2 H, *J* = 8.0 Hz), 7.48 (bt, 1 H, *J* = 8.0 Hz), 7.40–7.36 (m, 2 H), 7.31–7.24 (m, 2 H), 6.89 (brd, 1 H, *J* = 7.1 Hz), 5.91 (s, 1 H), 5.36 (d, 1 H, *J* = 12.9 Hz), 5.27 (d, 1 H, *J* = 12.9 Hz), 5.13 (s, 1 H), 2.88–2.82 (m, 1 H), 2.72–2.60 (m, 2 H), 2.25–2.04 (m, 4 H), 1.97–1.92 (m, 1 H), 1.70–1.54 (m, 2 H), 1.18 (s, 3 H), 1.08 (s, 3 H), 1.00 (s, 3 H);

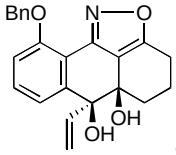
IR (KBr) 3588, 2974, 2957, 2925, 2864, 1786, 1749, 1578, 1489, 1450, 1263, 1170, 1102, 1058, 1022, 755, 740 cm^{-1};

Anal. Calc'd for $C_{31}H_{31}NO_7$; C, 70.31; H, 5.90; N, 2.64. Found: C, 70.50; H, 6.14; N, 2.66;

mp 235 °C (decomp.).

CCDC 614818 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General procedure for Addition of nucleophiles to α-ketol 3.



4a

In the flame-dried 2-necked flask was placed vinyl bromide (2.60 g, 24.3 mmol) in Et_2O (10 mL). To the solution was added ^tBuLi (1.46 M, 7.80 mL, 11.4 mmol) slowly at –78 °C. After stirring for 15 min, α-ketol (*R*)-**3** (788 mg, 2.27 mmol, 98% ee) in THF (7.6 mL) was added slowly over 5 min. The solution was warmed to 0 °C. The stirring was continued for 10 min at this temperature before quenching the reaction by adding saturated aq NH_4Cl solution. The products were extracted with EtOAc (x2). The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography (hexane/EtOAc = 70/30) to afford product **4a** (849 mg, 99%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase [CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 50:50, flow rate: 1.0 mL/min, 25 °C: t_1 = 6.5 min (major); t_2 = 13.7 min (minor)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55 (d, 2 H, *J* = 7.0 Hz), 7.45 (dd, 1 H, *J* = 7.9, 1.1 Hz), 7.42–7.33 (m, 3 H), 7.31–7.25 (m, 1 H), 6.92 (d, 1 H, *J* = 8.2 Hz), 5.50 (ddd, 1 H, *J* = 16.9, 10.6, 1.4 Hz), 5.30–5.23 (m, 2 H), 5.18 (d, 1 H, *J* = 12.6 Hz), 4.95 (dd, 1 H, *J* = 10.6, 1.4 Hz), 3.40 (d, 1 H, *J* = 1.4 Hz), 2.87 (ddd, 1 H, *J* = 17.6, 5.5, 1.7 Hz), 2.68–2.57 (m, 1 H), 2.32 (s, 1 H), 2.26–2.07 (m, 2 H), 2.01 (dt, 1 H, *J* = 13.8, 3.1 Hz), 1.68 (td, 1 H, *J* = 13.8, 3.6 Hz);

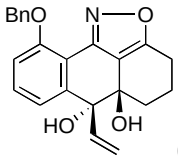
^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 155.6, 154.1, 146.1, 138.2, 136.6, 131.7, 128.5, 127.6, 126.7, 119.7, 114.2, 113.8, 113.1, 111.9, 80.2, 70.2, 68.7, 28.5, 22.5, 18.7;

IR (KBr) 3415, 2951, 2866, 1670, 1601, 1485, 1452, 1273, 1051, 985, 964, 754, 696 cm^{-1};

Anal. Calc'd for $C_{23}H_{21}NO_4$; C, 73.58; H, 5.64; N, 3.73. Found: C, 73.32; H, 5.70; N, 3.55;

Optical Rotation $[\alpha]_D^{30}$ –128 (*c* 1.00, $CHCl_3$) for 98% ee;

mp 148.0–150.0 °C (EtOAc/hexane).



6

Prepared according to the general procedure from (*R*)-**3** [a THF solution (5.5 mL), 1.12 g, 3.23 mmol, 98% ee] with vinylmagnesium bromide (1.84 M in THF, 5.26 mL, 9.68 mmol). The crude product was purified by column chromatography (hexane/acetone = 80/20), PTLC (hexane/acetone = 70/30) and

Recycling Preparative HPLC (eluent: $CHCl_3$) to afford *trans*-diol **6** (29 mg, 3%, 98% ee) as a colorless solid and *cis*-diol **4a** (1.10 g, 91%). The enantiomeric excess of *trans*-diol **6** was assessed by HPLC analysis on a chiral stationary phase [CHIRALPAK® IA, eluent: 2-propanol:hexane = 50:50, flow rate: 1.0 mL/min, 25 °C: t_1 = 11.0 min (minor); t_2 = 14.4 min (major)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50–7.44 (m, 2 H), 7.37–7.23 (m, 4 H), 7.14 (d, 1 H, *J* = 7.7 Hz), 6.86 (d, 1 H, *J* = 8.0 Hz), 6.48 (dd, 1 H, *J* = 17.4, 10.8 Hz), 5.69 (dd, 1 H, *J* = 17.4, 1.9 Hz), 5.58 (dd, 1 H, *J* = 10.8, 1.9 Hz), 5.15–5.03 (m, 2 H), 2.90–2.78 (m, 1 H), 2.71–2.58 (m, 1 H), 2.44–2.06 (m, 4 H), 1.95 (td, 1 H, *J* = 13.8, 3.9 Hz), 1.80–1.70 (m, 1 H);

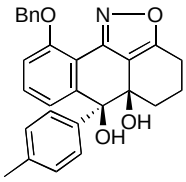
^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 156.3, 153.9, 144.1, 136.9, 136.7, 131.1, 128.6, 128.4, 127.5, 126.7, 126.6, 121.5, 117.3, 114.9, 77.9, 70.1, 69.9, 27.5, 22.4, 18.6;

IR (KBr) 3386, 3064, 3006, 2941, 1701, 1676, 1576, 1487, 1273, 1082, 985, 760 cm^{-1};

Anal. Calc'd for $C_{23}H_{21}NO_4$; C, 73.58; H, 5.64; N, 3.73. Found: C, 73.28; H, 5.68; N, 3.57;

Optical Rotation $[\alpha]_D^{29}$ –49 (*c* 2.20, $CHCl_3$) for 98% ee;

mp 95.0–97.5 °C (EtOAc/hexane).



4b

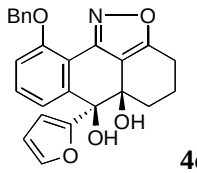
4-Methylphenyllithium was prepared by the following method. To a solution of 4-bromotoluene (167 mg, 0.976 mmol) in THF (1.0 mL) was added BuLi (1.6 M, 0.50 mL, 0.80 mmol) dropwise at –78 °C and the resulting solution was stirred at this temperature for 15 min. The obtained solution of 4-methylphenyllithium was used in the following experiment.

Diol **4b** was prepared according to the general procedure from (*R*)-**3** [a THF solution (1.6 mL), 92.7 mg, 0.267 mmol, 98% ee] with 4-methylphenyllithium (vide supra). The crude product was purified by PTLC (hexane/EtOAc = 70/30) to afford diol **4b** (98 mg, 89%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase [CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 20:80, flow rate: 1.0 mL/min, 20 °C: t_1 = 13.1 min (major); t_2 = 17.3 min (minor)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 (d, 2 H, *J* = 7.5 Hz), 7.44–7.25 (m, 5 H), 6.99 (d, 2 H, *J* = 7.7 Hz), 6.87–6.94 (m, 3 H), 5.23 (d, 1 H, *J* = 12.6 Hz), 5.14 (d, 1 H, *J* = 12.6 Hz), 4.05 (s, 1 H), 2.74 (dd, 1 H, *J* = 17.8, 5.2 Hz), 2.69 (s, 1 H), 2.44–2.32 (m, 1 H), 2.19 (s, 3 H), 2.24–2.05 (m, 1 H), 1.98–1.86 (m, 2 H), 1.08–0.94 (m, 1 H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 155.6, 155.1, 147.9, 138.3, 136.7, 136.6, 131.9, 128.6, 128.5, 127.7, 126.8, 126.1, 121.3, 113.8, 113.7, 111.8, 80.6, 70.3, 69.8, 29.0, 22.3, 20.9, 18.7;

IR (KBr) 3473, 3365, 3060, 3026, 2933, 1672, 1599, 1574, 1508, 1484, 1450, 1273, 985, 791 cm^{-1};
Anal. Calc'd for $C_{28}H_{25}NO_4$; C, 76.52; H, 5.73; N, 3.19. Found: C, 76.26; H, 5.94; N, 3.34;
Optical Rotation $[\alpha]_D^{31}$ –227 (*c* 1.00, $CHCl_3$) for 98% ee;
mp 203.0–209.0 °C (EtOAc/hexane).

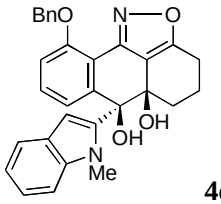


4c

2-Furyllithium was prepared by the following method. To a solution of furan (68 mg, 1.0 mmol) in THF (1.0 mL) was added BuLi (1.6 M, 0.48 mL, 0.77 mmol) dropwise at –78 °C and the resulting solution was stirred at room temperature for 25 min. The obtained solution of 2-furyllithium was used in the following experiment.

Diol **4c** was prepared according to the general procedure from (*R*)-**3** [a THF solution (1.5 mL), 86.3 mg, 0.248 mmol] with 2-furyllithium (vide supra). The crude product was purified by column chromatography (hexane/EtOAc = 60/40) and PTLC (hexane/EtOAc = 60/40) to afford diol **4c** (97 mg, 94%) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase [CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 50:50, flow rate: 1.0 mL/min, 25 °C: t_1 = 8.1 min (major); t_2 = 12.7 min (minor)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61 (d, 2 H, *J* = 7.5 Hz), 7.52 (dd, 1 H, *J* = 8.0, 1.0 Hz), 7.44–7.36 (m, 3 H), 7.34–7.28 (m, 1 H), 7.16 (dd, 1 H, *J* = 1.8, 0.7 Hz), 7.01 (d, 1 H, *J* = 8.2 Hz), 6.13 (dd, 1 H, *J* = 3.3, 1.8 Hz), 5.87 (dd, 1 H, *J* = 3.3, 0.7 Hz), 5.37 (dd, 1 H, *J* = 12.8 Hz), 5.27 (d, 1 H, *J* = 12.8 Hz), 3.81 (s, 1 H), 2.89–2.80 (m, 1 H), 2.57–2.46 (m, 1 H), 2.34 (s, 1 H), 2.24–2.00 (m, 3 H), 1.14 (m, 1 H);
^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 155.6, 154.6, 153.9, 144.6, 141.9, 136.6, 131.5, 128.5, 127.7, 126.8, 120.6, 113.8, 113.6, 112.4, 110.2, 107.7, 78.5, 70.3, 69.5, 29.4, 22.4, 18.7;
IR (KBr) 3473, 3342, 3064, 3030, 2939, 1672, 1601, 1576, 1487, 1450, 1271, 991, 785, 735 cm^{-1};
Anal. Calc'd for $C_{25}H_{21}NO_5$; C, 72.28; H, 5.10; N, 3.37. Found: C, 72.00; H, 5.30; N, 3.28;
Optical Rotation $[\alpha]_D^{30}$ –148 (*c* 0.50, $CHCl_3$) for 98% ee;
mp 142.0–145.0 °C (EtOAc/hexane).



4d

2-Indolyllithium was prepared by the following method. To a solution of *N*-methylindole (103 mg, 0.785 mmol) in THF (3.0 mL) was added BuLi (1.6 M, 0.43 mL, 0.69 mmol) dropwise at –78 °C and the resulting solution was stirred at room temperature for 30 min. The obtained solution of 2-indolyllithium was used in the following experiment.

Diol **4d** was prepared according to the general procedure from (*R*)-**3** [a THF solution (1.6 mL), 79.9 mg, 0.230 mmol, 98% ee] with 2-indolyllithium (vide supra). The crude product was purified by column chromatography (hexane/EtOAc = 60:40) to afford diol **4d** (96 mg, 87%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase [CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 70:30, flow rate: 1.0 mL/min, 20 °C: t_1 = 7.8 min (major); t_2 = 11.5 min (minor)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59 (brd, 2 H, *J* = 7.2 Hz), 7.53 (brd, 1 H, *J* = 8.0 Hz), 7.47–7.37 (m, 3 H), 7.36–7.30 (m, 1 H), 7.28–7.21 (m, 2 H), 7.13 (td, 1 H, *J* = 8.2, 1.2 Hz), 6.95 (t, 2 H, *J* = 7.0 Hz), 5.45 (s, 1 H), 5.22 (d, 1 H, *J* = 12.6 Hz), 5.10 (d, 1 H, *J* = 12.6 Hz), 4.11 (s, 3 H), 4.04 (s, 1H), 3.03 (s, 1 H), 2.71 (dd, 1 H, *J* = 18.0, 4.9 Hz), 2.45–2.32 (m, 1 H), 2.28–2.14 (m, 2 H), 2.05–1.93 (m, 1 H), 1.21 (brt, 1 H, *J* = 14.0 Hz);

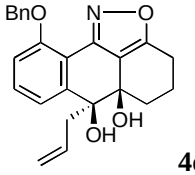
^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 155.4, 154.7, 147.4, 138.3, 137.7, 136.6, 131.8, 128.5, 127.7, 126.9, 126.7, 121.7, 121.6, 120.5, 119.3, 113.6, 113.5, 112,3, 109.2, 104.9, 80.8, 70.9, 70.4, 33.4, 29.5, 22.2, 18.8;

IR (KBr) 3442, 3057, 3033, 2945, 1664, 1576, 1468, 1315, 1236, 1045, 985 739 cm^{-1};

Anal. Calc'd for $C_{30}H_{26}N_2O_4$; C, 75.30; H, 5.48; N, 5.85. Found: C, 75.14; H, 5.70; N, 6.12;

Optical Rotation $[\alpha]_D^{31}$ –267 (*c* 1.00, $CHCl_3$) for 98% ee;

mp 219.5–223.5 °C (EtOAc/hexane).



4e

Prepared according to the general procedure from (*R*)-**3** [a THF (2.2 mL) solution, 107 mg, 0.308 mmol, 98% ee] with allylmagnesium bromide (0.23 M in THF, 4.0 mL, 0.92 mmol). The crude product was purified by column chromatography (hexane/EtOAc = 60:40) to afford diol **4e** (108 mg, 90%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase [CHIRALCEL® OD-H, eluent: 2-propanol:hexane = 70:30, flow rate: 1.0 mL/min, 20 °C: t_1 = 8.1 min

(major); t_2 = 11.5 min (minor)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (d, 2 H, *J* = 7.2 Hz), 7.42–7.33 (m, 4 H), 7.32–7.25 (m, 1 H), 6.94–6.85 (m, 1 H), 5.32–5.07 (m, 3 H), 4.80–4.68 (m, 2 H), 3.31 (s, 1 H), 2.88 (dd, 1 H, *J* = 17.7, 5.4 Hz), 2.70–2.44 (m, 2 H), 2.38 (dd, 1 H, *J* = 13.9, 6.9 Hz), 2.31–2.00 (m, 4 H), 1.81–1.70 (m, 1 H);

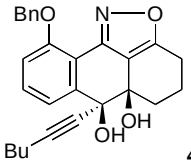
^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 155.6, 154.0, 145.6, 136.7, 132.6, 130.9, 128.5, 127.6, 126.7, 121.0, 117.8, 114.3, 113.3, 112.0, 79.0, 70.3, 69.2, 42.6, 27.9, 22.6, 18.9;

IR (neat) 3417, 3070, 3008, 2941, 1671, 1600, 1576, 1485, 1452, 1275, 1051, 764, 737, 696 cm^{-1};

Anal. Calc'd for $C_{24}H_{23}NO_4$; C, 74.02; H, 5.95; N, 3.60. Found: C, 73.99; H, 5.97; N, 3.67;

Optical Rotation $[\alpha]_D^{30}$ –34 (*c* 1.00, $CHCl_3$) for 98% ee.

mp 150.5–153.5 °C (EtOAc/hexane).



4f

1-Hexynyllithium was prepared by the following method. To a solution of 1-hexyne (100 mg, 1.22 mmol) in THF (1.5 mL) was added BuLi (1.6 M, 0.56 mL, 0.90 mmol) dropwise at –78 °C and the resulting solution was stirred at 0 °C for 10 min. The obtained solution of 1-hexynyllithium was used in the following experiment.

Diol **4f** was prepared according to the general procedure from (*R*)-**3** [a THF (1.4 mL) solution, 102 mg, 0.294 mmol, 98% ee] with 1-hexynyllithium (vide supra). The crude product was purified by column chromatography (hexane/EtOAc = 60/40) and PTLC (hexane/ EtOAc = 60/40) to afford diol **4f** (123 mg, 98%, 98% ee) as a colorless amorphous solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase [CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 1:1, flow rate: 1.0 mL/min, 25 °C: t_1 = 6.0 min (major); t_2 = 17.4 min (minor)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55–7.46 (m, 3 H), 7.43–7.32 (m, 3 H), 7.31–7.26 (m, 1 H), 6.86 (d, 1 H, *J* = 8.5 Hz), 5.12 (d, 1 H, *J* = 12.8 Hz), 5.02 (d, 1 H, *J* = 12.8 Hz), 3.27 (s, 1 H), 2.91 (s, 1 H), 2.93–2.83 (m, 1 H), 2.68–2.56 (m, 1 H), 2.32–2.04 (m, 4 H), 2.03–1.87 (m, 2 H), 1.30–1.05 (m, 4 H), 0.75 (t, 3 H, *J* = 7.2 Hz);

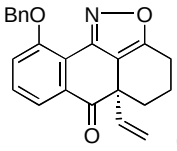
^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 155.8, 154.0, 145.1, 136.6, 131.4, 128.4, 127.6, 126.8, 119.3, 113.7, 112.7, 112.4, 87.6, 79.5, 74.5, 70.3, 69.5, 30.1, 29.3, 22.6, 21.6, 18.9, 18.2, 13.4;

IR (KBr) 3415, 3064, 3031, 2956, 2933, 2871, 2245, 1674, 1601, 1575, 1487, 1452, 1273, 910, 696 cm^{-1};

Anal. Calc'd for $C_{27}H_{27}NO_4$; C, 75.50; H, 6.34; N, 3.26. Found: C, 75.32; H, 6.52; N, 3.02;

Optical Rotation $[\alpha]_D^{30}$ –101 (*c* 1.00, $CHCl_3$) for 98% ee.

General procedure for the pinacol rearrangement.



(*S*)-**5a**

To a solution of diol **4a** (78.7 mg, 0.210 mmol) in CH_2Cl_2 (1.8 mL) was added $BF_3{\cdot}Et_2O$ (6.0 mg, 0.042 mmol) in CH_2Cl_2 (0.30 mL) at –78 °C. The solution was allowed to warm to 0 °C. After stirring for 3 h, the reaction was quenched by the addition of saturated aq $NaHCO_3$ solution. The solution was warmed to room temperature, and the mixture was extracted with EtOAc (x2). The combined organic layer was washed with brine and dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (hexane/EtOAc = 60/40) to afford product (*S*)-**5a** (72 mg, 96%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 60:40, flow rate: 1.0 mL/min, 20 °C: (*S*)-**5a**: t_1 = 7.5 min; (*R*)-**5a**: t_2 = 16.0 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64–7.52 (m, 3 H), 7.46–7.36 (m, 3 H), 7.34–7.24 (m, 2 H), 5.73 (dd, 1 H, *J* = 17.1, 10.1 Hz), 5.41 (d, 1 H, *J* = 12.8 Hz), 5.36 (d, 1 H, *J* = 12.8 Hz), 5.22 (d, 1 H, *J* = 10.1 Hz), 5.00 (d, 1 H, *J* = 17.1 Hz), 2.89 (dd, 1 H, *J* = 18.0, 5.7 Hz), 2.74–2.60 (m, 1 H), 2.29 (dt, 1 H, *J* = 13.4, 3.3 Hz), 2.18–2.05 (m, 1 H), 2.04–1.86 (m, 1 H), 1.70 (td, 1 H, *J* = 13.4, 2.9 Hz);

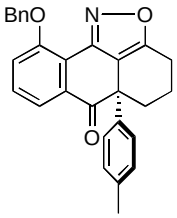
^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.2, 167.8, 155.3, 153.8, 137.9, 136.4, 133.7, 131.2, 128.6, 127.8, 126.7, 121.6, 119.9, 118.4, 118.2, 113.1, 70.8, 51.4, 28.5, 22.0, 18.2;

IR (KBr) 3066, 3032, 2966, 2856, 1701, 1668, 1572, 1446, 1275, 1240, 825, 741 cm^{-1};

Anal. Calc'd for $C_{23}H_{19}NO_3$; C, 77.29; H, 5.36; N, 3.92. Found: C, 77.20; H, 5.46; N, 4.13

Optical Rotation $[\alpha]_D^{30}$ +59 (*c* 1.00, $CHCl_3$) for 98% ee;

mp 156.5–158.0 °C (EtOAc/hexane).



5b

Prepared according to the general procedure from diol **4b** (52.3 mg, 0.119 mmol) with $BF_3{\cdot}Et_2O$ (3.4 mg, 0.024 mmol) under the conditions indicated in table 1. The detail of reaction conditions was indicated in table 1. The crude product was purified by column chromatography (hexane/EtOAc = 80/20) to afford ketone **5b** (46 mg, 92%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® OD-H, eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 20 °C: (*S*)- **5b**: t_1 = 7.6 min; (*R*)- **5b**: t_2 = 10.1 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59 (d, 2 H, *J* = 7.7 Hz), 7.48–7.30 (m, 3 H), 7.30 (t, 2 H, *J* = 7.4 Hz), 7.19–7.08 (m, 3 H), 7.03 (d, 2 H, *J* = 8.0 Hz), 5.37 (d, 1 H, *J* = 12.8 Hz), 5.33 (d, 1 H, *J* = 12.8 Hz), 2.90 (dd, 1 H, *J* = 18.1, 6.1 Hz), 2.76–2.64 (m, 1 H), 2.55 (brd, 1 H, *J* = 13.0 Hz), 2.24 (s, 3 H), 2.05–1.88 (m, 2 H), 1.70–1.54 (m, 1 H);

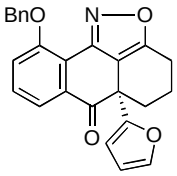
^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.5, 168.3, 155.2, 154.0, 137.5, 136.4, 135.7, 134.4, 131.2, 129.4, 128.6, 127.8, 127.4, 126.7, 121.6, 118.2, 118.0, 114.0, 70.8, 51.5, 31.7, 22.0, 20.9, 18.1;

IR (KBr) 3062, 3028, 2951, 2864, 1697, 1574, 1450, 1277, 1246, 756 cm^{-1};

Anal. Calc'd for $C_{28}H_{23}NO_3$; C, 79.79; H, 5.50; N, 3.32. Found: C, 79.82; H, 5.80; N, 3.39;

Optical Rotation $[\alpha]_D^{29}$ –96 (*c* 1.00, $CHCl_3$) for 98% ee;

mp 181.5–184.0 °C (EtOAc/hexane).



5c

Prepared according to the general procedure from diol **4c** (47.2 mg, 0.114 mmol) with $BF_3{\cdot}Et_2O$ (3.2 mg, 0.023 mmol) under the conditions indicated in table 1. The product was purified by column chromatography (hexane/EtOAc = 80/20) to afford ketone **5c** (41 mg, 90%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 20 °C: (*R*)-**5c**: t_1 = 7.6 min; (*S*)-**5c**: t_2 = 10.1 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60 (d, 2 H, *J* = 7.5 Hz), 7.53 (dd, 1 H, *J* = 7.7, 1.0 Hz), 7.44–7.28 (m, 3 H), 7.35–7.27 (m, 2 H), 7.22 (d, 1 H, *J* = 7.9 Hz), 6.19 (dd, 1 H, *J* = 3.1, 1.9 Hz), 5.99 (d, 1 H, *J* = 3.1 Hz), 5.39 (d, 1 H, *J* = 12.8 Hz), 5.35 (d, 1 H, *J* = 12.8 Hz), 2.91 (dd, 1 H, *J* = 7.9, 4.8 Hz), 2.82–2.62 (m, 2 H), 2.20–2.06 (m, 1 H), 1.84–1.75 (m, 2 H);

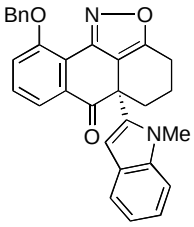
^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.1, 168.2, 155.3, 153.5, 151.4, 143.5, 136.3, 133.8, 131.3, 128.6, 127.8, 126.7, 121.7, 118.24, 118.19, 112.9, 110.6, 109.9, 70.8, 48.3, 28.0, 21.9, 18.7;

IR (KBr) 3064, 3030, 2940, 2864, 1701, 1670, 1574, 1275, 1246, 739 cm^{-1};

Anal. Calc'd for $C_{25}H_{19}NO_4$; C, 75.55; H, 4.82; N, 3.52. Found: C, 75.84; H, 4.98; N, 3.55;

Optical Rotation $[\alpha]_D^{32}$ –127 (*c* 1.00, $CHCl_3$) for 98% ee;

mp 188.0–189.5 °C (EtOAc/hexane).



5d

Prepared according to the general procedure from diol **4d** (69.1 mg, 0.144 mmol) with $BF_3{\cdot}Et_2O$ (4.1 mg, 0.029 mmol) under the conditions indicated in table 1. The crude product was purified by column chromatography (hexane/EtOAc = 60/40) to afford ketone **5d** (64 mg, 96%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® OD-H, eluent: 2-propanol:hexane = 40:60, flow rate: 1.0 mL/min, 20 °C: (*R*)-**5d**: t_1 = 7.4 min; (*S*)-**5d**: t_2 = 11.6 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 (d, 2 H, *J* = 7.7 Hz), 7.44–7.35 (m, 4 H), 7.33–7.21 (m, 3 H), 7.18 (dd, 1 H, *J* = 7.0, 1.2 Hz), 7.15 (dd, 1 H, *J* = 8.0, 1.2 Hz), 7.03 (td, 1 H, *J* = 8.0, 1.2 Hz), 6.07 (s, 1 H), 5.37 (dd, 1 H, *J* = 12.8 Hz), 5.33 (d, 1 H, *J* = 12.8 Hz), 3.83 (s, 3 H), 2.93 (dd, 1 H, *J* = 18.0, 5.9 Hz), 2.80–2.66 (m, 2 H), 2.14–2.00 (m, 2 H), 1.87–1.70 (m, 1 H);

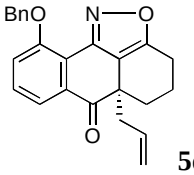
^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.3, 168.2, 155.1, 153.8, 139.4, 136.5, 136.3, 134.9, 131.4, 128.6, 127.8, 126.72, 126.66, 122.1, 121.3, 120.4, 119.8, 118.3, 117.9, 114.0, 109.1, 105.8, 70.8, 49.1, 31.0, 28.2, 21.8, 18.5;

IR (KBr) 3056, 3030, 2976, 2933, 1701, 1662, 1483, 1454, 1269, 1252, 781, 735 cm^{-1};

Anal. Calc'd for $C_{30}H_{24}N_2O_3$; C, 78.24; H, 5.25; N, 6.08. Found: C, 78.11; H, 5.39; N, 5.90;

Optical Rotation $[\alpha]_D^{31}$ –106 (*c* 1.00, $CHCl_3$) for >99% ee;

mp 214.0–216.0 °C (EtOAc/hexane).



5e

Prepared according to the general procedure from diol **4e** (51.3 mg, 0.132 mmol) with $BF_3{\cdot}Et_2O$ (4.0 mg, 0.028 mmol) under the conditions indicated in table 1. The crude product was purified by column chromatography (hexane/EtOAc = 60/40) to afford ketone **5e** (47 mg, 95%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® OD-H, eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 20 °C: (*S*)-**5e**: t_1 = 8.1 min; (*R*)-**5e**: t_2 = 11.8 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60 (d, 2 H, *J* = 7.7 Hz), 7.56 (d, 1 H, *J* = 7.7, 1.2 Hz), 7.44 (t, 1 H, *J* = 7.7 Hz), 7.39 (t, 2 H, *J* = 7.7 Hz), 7.34–7.27 (m, 1 H), 7.26 (dd, 1 H, *J* = 7.7, 1.2 Hz), 5.62–5.48 (m, 1 H), 5.42

(d, 1 H, *J* = 12.6 Hz), 5.37 (d, 1 H, *J* = 12.6 Hz), 4.99 (brd, 1 H, *J* = 9.2 Hz), 4.91 (brd, 1 H, *J* = 6.9 Hz), 2.92 (ddd, 1 H, *J* = 18.5, 6.5, 1.2 Hz), 2.72–2.60 (m, 1 H), 2.44 (d, 2 H, *J* = 7.5 Hz), 2.27 (dt, 1 H, *J* = 13.8, 3.3 Hz), 2.23–2.01 (m, 2 H), 1.57 (td, 1 H, *J* = 13.5, 4.0 Hz);

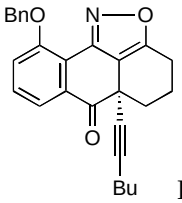
^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.5, 166.8, 155.3, 153.4, 136.4, 134.6, 131.9, 131.3, 128.6, 127.8, 126.7, 121.1, 118.9, 118.6, 118.1, 115.7, 70.7, 46.4, 41.8, 25.5, 21.7, 18.2;

IR (KBr) 3064, 2962, 2900, 1705, 1668, 1574, 1292, 1281, 1225, 739 cm^{-1};

Anal. Calc'd for $C_{24}H_{21}NO_3$; C, 77.61; H, 5.70; N, 3.77. Found: C, 77.65; H, 5.86; N, 3.72;

Optical Rotation $[\alpha]_D^{21}$ –14 (*c* 1.00, $CHCl_3$) for 98% ee;

mp 148.5–151.0 °C (EtOAc/hexane).



Ketone **19**

Prepared according to the general procedure from diol **15** (46.2 mg, 0.108 mmol) with $BF_3{\cdot}Et_2O$ (15 mg, 0.106 mmol) under the conditions indicated in table 1. The crude product was purified by column chromatography (hexane/EtOAc = 60/40) to afford ketone **19** (38 mg, 86%, 71% ee) as a colorless oil. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 20 °C: (*S*)-**19**: t_1 = 7.9 min; (*R*)-**19**: t_2 = 14.3 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (dd, 1 H, *J* = 7.7, 1.0 Hz), 7.60 (d, 2 H, *J* = 7.0 Hz), 7.46 (t, 1 H, *J* = 8.3 Hz), 7.39 (brt, 2 H, *J* = 7.4 Hz), 7.25–7.35 (m, 2 H), 5.42 (d, 1 H, *J* = 13.0 Hz), 5.38 (d, 1 H, *J* = 13.0 Hz), 2.95 (dd, 1 H, *J* = 17.9, 4.8 Hz), 2.61–2.74 (m, 1 H), 2.44 (dt, 1 H, *J* = 13.0, 3.1 Hz), 2.22–2.40 (m, 2 H), 2.02 (t, 2 H, *J* = 7.0 Hz), 1.67 (td, 1 H, *J* = 13.0, 3.4 Hz), 1.20–1.37 (m, 2 H), 1.12–1.25 (m, 2 H), 0.76 (t, 3 H, *J* = 7.2 Hz);

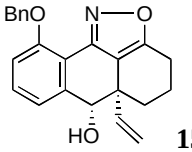
^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.4, 167.0, 155.4, 152.9, 136.4, 134.0, 131.2, 128.6, 127.8, 126.7, 121.9, 118.3, 118.2, 113.8, 85.0, 78.2, 70.7, 41.9, 30.4, 29.9, 22.0, 21.6, 19.5, 18.3, 13.4;

IR (neat) 3064, 2956, 2931, 2862, 2233, 1707, 1574, 1450, 1277, 1242, 727 cm^{-1};

Anal. Calc'd for $C_{27}H_{25}NO_3$; C, 78.81; H, 6.12; N, 3.40. Found: C, 78.56; H, 6.41; N, 3.22;

Optical Rotation $[\alpha]_D^{23}$ –33 (*c* 1.00, $CHCl_3$) for 96% ee.

Determination of absolute stereochemistry of ketone 5a.



15

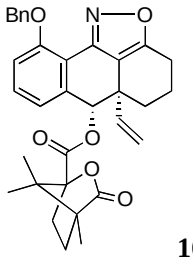
To a suspension of $NaBH_4$ (6.0 mg, 92% assay, 0.15 mmol) in MeOH (0.5 mL) was added ketone **5a** (32.7 mg, 0.0915 mmol) in THF (1.5 mL) at 0 °C. After stirring for 5 min, the reaction mixture was quenched by the addition of water. The products were extracted with EtOAc (x2), and the combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc = 50/50) to afford alcohol **15** (32.2 mg, 98%) as a colorless solid.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.57 (d, 2 H, *J* = 7.2 Hz), 7.40–7.23 (m, 5 H), 6.96 (d, 1 H, *J* = 8.2 Hz), 5.76 (dd, 1 H, *J* = 17.5, 10.5 Hz), 5.36 (d, 1 H, *J* = 12.9 Hz), 5.30 (d, 1 H, *J* = 12.9 Hz), 5.16 (brd, 1 H, *J* = 10.5 Hz), 4.86 (brd, 1 H, *J* = 17.5Hz), 4.58 (d, 1 H, *J* = 9.1 Hz), 2.84 (dd, 1 H, *J* = 17.8, 5.4 Hz), 2.71–2.60 (m, 1 H), 2.37 (dt, 1 H, *J* = 13.0, 3.1 Hz), 2.28 (d, 1 H, *J* = 9.1 Hz), 2.14–2.02 (m, 1 H), 1.95–1.81 (m, 1 H), 1.51 (td, 1 H, *J* = 13.4, 2.7 Hz);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.8, 155.5, 154.9, 142.6, 136.9, 136.0, 131.0, 128.5, 127.5, 126.7, 118.8, 118.0, 114.9, 114.2, 112.4, 77.7, 70.4, 42.4, 31.5, 22.2, 19.0;

IR (KBr) 3302, 3072, 3022, 2943, 2852, 1672, 1576, 1487, 1452, 1273, 1238, 1043, 746 cm^{-1};

Anal. Calc'd for $C_{23}H_{21}NO_3$; C, 76.86; H, 5.89; N, 3.90. Found: C, 76.68; H, 5.92; N, 3.63.



16

To a solution of alcohol **15** (28.9 mg, 0.0804 mmol) and DMAP (20.0 mg, 0.164 mmol) was added (–)-camphanic chloride (24.2 mg, 0.112 mmol) at 0 °C. After stirring for 2 h, (–)-camphanic chloride (6.4 mg, 0.030 mmol) was added and stirring was continued at room temperature for 1h. The reaction was quenched by water and the products were extracted with Et_2O (x2), and the combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc/CH_2Cl_2 = 4/3/3) to afford camphanate **16** (35.1 mg, 89%) as a colorless solid. Recrystallization from EtOAc/hexane/CH_2Cl_2 gave a single crystal of **16** for the X-ray analysis.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.56 (d, 2 H, *J* = 7.2 Hz), 7.27–7.40 (m, 4 H), 6.99 (d, 1 H, *J* = 8.5 Hz), 6.85

(brd, 1 H, *J* = 7.5 Hz), 6.06 (s, 1 H), 5.87 (dd, 1 H, *J* = 17.2, 10.4 Hz), 5.36 (d, 1 H, *J* = 12.8 Hz), 5.31 (d, 1 H, *J* = 12.8 Hz), 5.10 (dd, 1 H, *J* = 10.4, 1.2 Hz), 4.69 (dd, 1 H, *J* = 17.2, 1.2 Hz), 2.86 (dd, 1 H, *J* = 17.7, 5.3 Hz), 2.73–2.52 (m, 2 H), 2.26–2.16 (m, 1 H), 2.10–1.75 (m, 5 H), 1.67–1.60 (m, 1 H), 1.18 (s, 3 H), 1.16 (s, 3 H), 1.13 (s, 3 H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.1, 167.29, 167.26, 155.7, 154.8, 137.5, 136.8, 135.5, 131.1, 128.5, 127.6, 126.6, 119.2, 117.3, 114.5, 113.1, 113.0, 91.2, 79.4, 70.4, 54.9, 54.2, 42.2, 32.0, 31.3, 28.9, 22.0, 18.6, 17.1, 16.8, 9.7;

IR (KBr) 3056, 3030, 2976, 2933, 1701, 1662, 1483, 1454, 1269, 1252, 781, 735 cm^{-1};

Anal. Calc'd for $C_{33}H_{33}NO_6$; C, 75.45; H, 6.16; N, 2.60. Found: C, 75.68; H, 6.26; N, 2.65;

Optical rotation $[\alpha]_D^{30}$ –242 (*c* 0.72, $CHCl_3$);

mp 212.0–215.0 °C.

CCDC 606772 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Pinacol rearrangement of *trans*-diol 6 (Eq. 1).

To a solution of diol **6** (39.4 mg, 0.105 mmol) in CH_2Cl_2 (0.7 mL) was added $BF_3{\cdot}Et_2O$ (13.3 μL, 0.105 mmol) in CH_2Cl_2 (0.3 mL) at –78 °C. The solution was allowed to warm to 0 °C. After stirring for 5 h, the reaction was quenched by the addition of saturated aq $NaHCO_3$ solution. The solution was warmed to room temperature, and the mixture was extracted with EtOAc (x2). The combined organic layer was washed with brine and dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (hexane/EtOAc = 60/40) to afford product (*R*)-**5a** (72 mg, 92%, 95% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 60:40, flow rate: 1.0 mL/min, 20 °C: (*S*)-**5a**: t_1 = 7.5 min; (*R*)-**5a**: t_2 = 16.0 min).

Acid-catalyzed racemization of a**-ketol (*R*)-3 (Eq. 2).**

To a solution of (*R*)-**3** (98% ee, 56.0 mg, 0.161 mmol) in THF (1.6 mL) was added 3 M H_2SO_4 (0.3 mL) at ambient temperature. After stirring at 40 ºC for 12 h, the reaction mixture was cooled to 0 °C, and saturated aq $NaHCO_3$ was added. After products were extracted with EtOAc (x2), the combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC (EtOAc/hexane = 60/40) to re-isolate ketol **3** (53 mg, 94%, 60% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase: CHIRALPAK® AD-H (eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 25 °C: (*R*)-**3**: t_1 = 20.1 min; (*S*)-**3**: t_2 = 24.6

min).

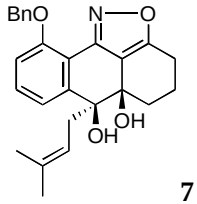
Allylation of a**-ketol (*R*)-3 (Eq. 3).**

To a solution of (*R*)-**3** (98% ee, 53.1 mg, 0.153 mmol) and allylsilane (52.4 mg, 0.459 mmol) in CH_2Cl_2 (1.5 mL) was added $BF_3{\cdot}OEt_2$ (28.0 μL, 0.224 mmol) at 0 ºC. The solution was allowed to warm to room temperature. After stirring for 0.5 h, the reaction mixture was cooled to 0 °C and saturated aq $NaHCO_3$ was added. The products were extracted with EtOAc (x2). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC (EtOAc/hexane = 1/2) to give ketone **5e** (53 mg, 94%, racemic) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® OD-H, eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 20 °C: (*S*)-**5e**: t_1 = 8.1 min; (*R*)-**5e**: t_2 = 11.8 min).

Rearrangement of $Co_2(CO)_6$-complex 4g (Table 1, entry 6).

To a CH_2Cl_2 (2.2 mL) solution of diol **4f** (96.0 mg, 0.224 mmol) was added $Co_2(CO)_8$ (153 mg, 0.447 mmol) at room temperature. After stirring for 2 h at this temperature, the solvent was evaporated under reduced pressure. The resulting residue was quickly purified by short column chromatography (hexane/EtOAc = 100/0 to 3/1) to afford the $Co_2(CO)_6$-complex **4g**. Successively, to a solution of the complex in CH_2Cl_2 was slowly added $BF_3{\cdot}OEt_2$ (28.0 μL, 0.224 mmol) at –78 ºC. The solution was allowed to warm to 0 °C. The stirring was continued for 5 h at this temperature. The reaction was quenched by the addition of saturated aq $NaHCO_3$ solution. The products were extracted with EtOAc (x2), and the combined organic layer was washed with brine, and dried over Na_2SO_4. After evaporation, the residue was dissolved in methanol and CH_3CN (2.0 mL, v/v=1/1), to which was added $Ce(NH_4)_2(NO_3)_6$ (490 mg, 0.894 mmol) at 0 ºC followed by phosphate buffer (pH 7) after 15 min. Extraction with EtOAc (x3) followed by washing with brine, drying over Na_2SO_4 and purification with PTLC (hexane/acetone = 30/70) gave ketone **5f** [75 mg, 82% (3 steps), 96% ee] as a colorless oil. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase: CHIRALPAK® AD-H (eluent: 2-propanol:hexane = 30:70, flow rate: 1.0 mL/min, 25 °C: (*S*)-**5f**: t_1 = 7.9 min; (*R*)-**5f**: t_2 = 14.3 min).

Selective installation of a prenyl group (Scheme 5).



7

Prenylbarium chloride was prepared according to the literature method.[2] To a suspension of anhydrous BaI_2 (2.03 g, 5.20 mmol) in dry THF (25 mL) was added a solution of lithium biphenylide, prepared from lithium (72.1 mg, 10.4 mmol) and biphenyl (1.67 g, 10.8 mmol) in THF (25 mL). The reaction mixture was stirred for 30 min at room temperature. To the resulting suspension of barium in THF was slowly added a THF (6 mL) solution of 1-chloro-3-methyl-2-butene (398 mg, 3.80 mmol) at –78 °C. The reaction mixture was stirred for 1 h at this temperature. The obtained solution of Prenylbarium chloride was used in the following experiment.

Diol **7** was prepared according to the general procedure from (*R*)-**3** [a THF (2.6 mL) solution, 266 mg, 0.766 mmol, 98% ee] with prenylbarium chloride (vide supra). The crude product was purified by column chromatography (hexane/EtOAc = 72/28 to 60/40) to afford diol **7** (250 mg, 78%, 98% ee) as a colorless solid. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase [CHIRALCEL® OD-H, eluent: 2-propanol:hexane = 15:85, flow rate: 1.0 mL/min, 25 °C: t_1 = 11.4 min (major); t_2 = 14.9 min (minor)].

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, 2 H, *J* = 7.5 Hz), 7.40–7.26 (m, 5 H), 6.88 (d, 1 H, *J* = 8.0 Hz), 5.24 (d, 1 H, *J* = 13.0 Hz), 5.20 (d, 1 H, *J* = 13.0 Hz), 4.66 (brt, 1 H, *J* = 7.7 Hz), 3.32 (s, 1 H), 2.80–2.95 (m, 1 H), 2.58–2.71 (m, 1 H), 2.40 (s, 1 H), 2.33 (dd, 1 H, *J* = 14.0, 7.5 Hz), 2.28–2.12 (m, 2 H), 2.11–2.00 (m, 2 H), 1.78 (td, 1 H, *J* = 13.3, 3.4 Hz), 1.45 (s, 3 H), 1.03 (s, 3 H);

^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.7, 155.4, 154.1, 146.0, 136.8, 135.2, 130.7, 128.5, 127.6, 126.7, 121.1, 117.7, 114.4, 113.7, 112.0, 79.8, 70.2, 69.3, 36.7, 28.0, 25.7, 22.6, 18.9, 17.1;

IR (neat) 3419, 2931, 1672, 1576, 1487, 1236, 760 cm^{-1};

Anal. Calc'd for $C_{26}H_{27}NO_4$; C, 74.80; H, 6.52; N, 3.35. Found: C, 74.90; H, 6.71; N, 3.26;

Optical Rotation $[\alpha]_D^{28}$ –71 (*c* 1.00, $CHCl_3$) for 98% ee;

mp 126–129 °C (EtOAc/hexane).

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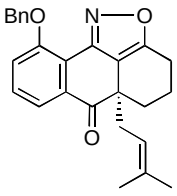
2) Yanagisawa, A.; Habaue, S.; Yasue, K.; Yamamoto, H. *J. Am. Chem. Soc*., **1994**, *116*, 6130–6141.



8

To a solution of diol **7** (86.5 mg, 0.207 mmol) in CH_2Cl_2 (1.9 mL) was added $BF_3{\cdot}Et_2O$ (6.0 mg, 0.042 mmol) in CH_2Cl_2 (0.2 mL) at –78 °C. The solution was allowed to warm to 0 °C. After stirring for 0.5 h, the reaction was quenched by the addition of saturated aq $NaHCO_3$ solution. The solution was warmed to room temperature, and the mixture was extracted with EtOAc (x2). The combined organic layer was washed with brine and dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (hexane/EtOAc = 60/40) to afford ketone **8** (78 mg, 94%, 98% ee) as a colorless oil. The enantiomeric excess was assessed by HPLC analysis on a chiral stationary phase (CHIRALPAK® AD-H, eluent: 2-propanol:hexane = 40:60, flow rate: 1.0 mL/min, 20 °C: (*S*)-**8**: t_1 = 8.0 min; (*R*)-**8**: t_2 = 11.8 min).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59 (d, 2 H, *J* = 7.5 Hz), 7.55 (d, 1 H, *J* = 7.7 Hz), 7.44–7.35 (m, 3 H), 7.33–7.27 (m, 1 H), 7.23 (d, 1 H, *J* = 7.2 Hz), 5.42 (d, 1 H, *J* = 12.8 Hz), 5.37 (d, 1 H, *J* = 12.8 Hz), 4.90 (brt, 1 H, *J* = 7.7 Hz), 2.92 (dd, 1 H, *J* = 18.0, 6.4 Hz), 2.72–2.60 (m, 1 H), 2.44 (d, 1 H, *J* = 14.7, 8.6 Hz), 2.37 (dd, 1 H, *J* = 14.7, 6.8 Hz), 2.28–2.02 (m, 3 H), 1.57 (td, 1 H, *J* = 13.5, 9.5 Hz), 1.52 (s, 3 H), 1.39 (s, 3 H);

^{13}C NMR (acetone-d_6, 100 MHz) δ 201.1, 167.6, 156.1, 154.1, 138.0, 135.8, 135.7, 132.1, 129.1, 128.3, 127.7, 121.4, 119.5, 119.3, 118.9, 116.4, 71.1, 47.7, 37.2, 26.9, 26.0, 22.3, 19.3, 18.0;

IR (neat) 2939, 1697, 1666, 1574, 1450, 1284, 1234, 756 cm^{-1};

Anal. Calc'd for $C_{26}H_{25}NO_3$; C, 78.17; H, 6.31; N, 3.51. Found: C, 78.14; H, 6.57; N, 3.39;

Optical Rotation $[\alpha]_D^{31}$ –15 (*c* 0.80, $CHCl_3$) for 98% ee.