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SUPPORTING INFORMATION

Title: Diastereoselective and Enantioselective Henry (Nitroaldol) Reaction Utilizing a Guanidine-Thiourea Bifunctional Organocatalyst

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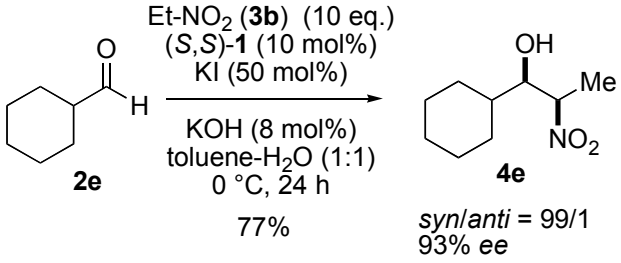
Ref. No.: O200600307

General Remarks

Flash chromatography was performed using Silica gel 60 (spherical, particle size 0.040-0.100 mm; Kanto Co., Inc., Japan). Optical rotations were measured with a JASCO DIP polarimeter 370. IR spectra were measured with JASCO VALOR-III FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-AL300 or JEOL JMN-EX400 instrument. Mass spectra were recorded on JEOL JMA-HX110 spectrometer.

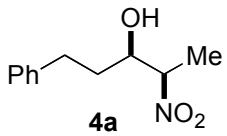
Typical procedure for enantio- and *syn*-selective Henry reaction (Table 1 and 2)



To a mixture of (*S*,*S*)-**1e** (12.9 mg, 0.0112 mmol), KI (9.3 mg, 0.0558 mmol) and nitroethane (**3b**) (80.1 μL, 1.12 mmol) in toluene (1.12 mL)/8 mM KOHaq (1.12 mL) was added cyclohexanecarboxaldehyde (**2e**) (13.4 μL, 0.112 mmol) at 0 °C. The resulting mixture was stirred vigorously at 0 °C for 24 h. Then saturated NH_4Claq was added, and the organic layer was extracted with ethyl acetate. The extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 20/1, 10/1, chloroform/methanol = 9/1) to give **4e** (16.0 mg, 77%) and **1e** was recovered (12.8 mg, 99%). Relative stereochemistry and diastereoselectivity (*syn*/*anti* = 99/1) of **4e** were determined based upon the reported ^{1}H NMR.[1] $[\alpha]_D^{26}$ = -6.7 (*c* 0.52, $CHCl_3$). IR (neat) 2925, 2852, 1552, 1450, 1391 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.72 (dq, *J* = 6.8, 6.8 Hz, 1H), 3.65 (dd, *J* = 6.8, 4.9 Hz, 1H), 2.13 (br s, 1H), 1.78-1.65 (m, 4H), 1.53 (d, *J* = 6.7 Hz,

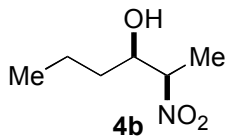
3H), 1.48-0.94 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ85.5, 77.2, 39.9, 30.0, 26.3, 26.2, 26.1, 25.9, 16.6. The enantiomeric excess of **4e** (93% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 97/3, 1.0 mL/min, Minor; 16.8 min, Major; 25.3 min).

Spectral data for 4a-d and 4f-4p



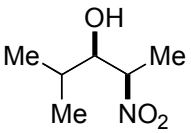
4a
syn/*anti* = 90/10
83% *ee*

Compoud **4a**.[2] $[\alpha]_D^{25}$ = +29.0 (*c* 0.96, EtOH). IR (neat) 3408, 3061, 3027, 2921, 2850, 1548, 1454, 1390, 1360 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.14 (m, 5H), 4.55 (dq, *J* = 7.0, 7.0 Hz, 1H), 3.97-3.93 (m, 1H), 2.88 (ddd, *J* = 14.2, 8.9, 5.8 Hz, 1H), 2.76 (ddd, *J* = 14.2, 9.1, 7.4 Hz, 1H), 2.27 (d, *J* = 7.1 Hz, 1H), 1.93-1.63 (m, 2H), 1.54 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8, 128.5, 128.4, 126.2, 87.7, 72.1, 34.6, 31.3, 16.1. HRMS (FAB, M+H) calcd for $C_{11}H_{16}NO_3$ 210.1130, found 210.1123. The enantiomeric excess of **4a** (83% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 90/10, 1.0 mL/min, Major; 11.1 min, Minor; 12.0 min).



4b
syn/*anti* = 87/13
84% *ee*

Compoud **4b**. $[\alpha]_D^{25}$ = +6.6 (*c* 1.05, $CHCl_3$). IR (neat) 3404, 2961, 2922, 2874, 2851, 1550, 1457, 1391, 1361 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (dq, *J* = 6.9, 6.9 Hz, 1H), 3.91 (br, 1H), 2.25 (br s, 1H), 1.55 (d, *J* = 6.9 Hz, 3H), 1.51-1.40 (m, 4H), 0.95 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 87.7, 72.6, 35.1, 18.4, 16.2, 13.8. The enantiomeric excess of **4b** (84% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 97/3, 1.0 mL/min, Major; 16.5 min, Minor; 18.3 min).

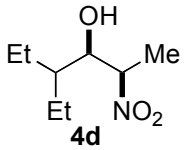


4c

syn/*anti* = 97/3

90% *ee*

Compoud **4c**.[3] $[\alpha]_D^{23}$= -2.0 (*c* 0.85, $CHCl_3$). IR (neat) 3399, 2963, 2920, 2850, 1551, 1464, 1390, 1366 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.67 (dq, *J* = 7.0, 7.0 Hz, 1H), 3.69 (m, 1H), 2.14 (br d, *J* = 7.0 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.93 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.2, 77.2, 29.9, 19.8, 16.4, 15.5. The enantiomeric excess of **4c** (90% *ee*) was determined by means of chiral HPLC analysis. (CHIRALCEL OD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99/1, 1.0 mL/min, Major; 22.6 min, Minor; 27.3 min).

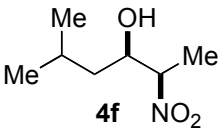


4d

syn/*anti* = 99/1

91% *ee*

Compoud **4d**. $[\alpha]_D^{24}$ = +15.2 (*c* 0.54, $CHCl_3$). IR (neat) 2962, 2921, 2877, 2850, 1555, 1462, 1391, 1358 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.73 (dq, *J* = 7.9, 6.8 Hz, 1H), 3.94 (br, 1H), 2.05 (br d, *J* = 11.7 Hz 1H), 1.53 (d, *J* = 6.8 Hz, 3H), 1.51-1.28 (m, 1H), 0.95 (q, *J* = 4.2 Hz, 3H), 0.92 (q, *J* = 3.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.5, 74.1, 42.7, 22.3, 20.25, 16.5, 11.6, 11.4. The enantiomeric excess of **4d** (91% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99/1, 1.0 mL/min, Minor; 21.7 min, Major; 28.1 min).

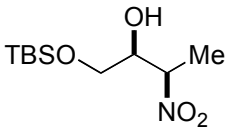


4f

syn/*anti* = 93/7

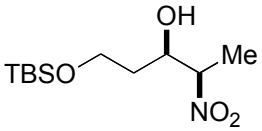
99% *ee*

Compoud **4f**. $[\alpha]_D^{24}$ = +12.5 (*c* 0.96, EtOH). IR (neat) 2958, 2924, 2871, 2850, 1551, 1465, 1391, 1359 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.51 (dq, *J* = 6.8, 6.8 Hz, 1H), 3.95 (ddd, *J* = 10.0, 6.8, 2.9 Hz, 1H), 2.19 (br s, 1H), 1.88 (m, 1H), 1.56 (d, *J* = 6.8 Hz, 3H), 1.42 (ddd, *J* = 13.9, 10.0, 4.4 Hz, 1H), 1.24 (ddd, *J* = 13.9, 9.8, 2.9 Hz, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 88.1, 71.2, 42.0, 24.3, 23.6, 21.4, 16.2. The enantiomeric excess of **4f** (99% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99/1, 1.0 mL/min, Major; 14.2 min, Minor; 15.4 min).



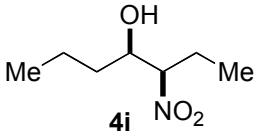
4g
syn/*anti* = 93/7
99% *ee*

Compoud **4g**. $[\alpha]_D^{26}$ = -10.8 (*c* 0.73, $CHCl_3$). IR (neat) 2953, 2928, 2857, 1553, 1471, 1389, 1361, 1255, 1109 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.69 (dq, *J* = 6.8, 6.8 Hz, 1H), 3.96 (br, 1H), 3.76 (dd, *J* = 10.6, 3.8 Hz, 1H), 3.69 (dd, *J* = 10.6, 4.1 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ85.0, 73.1, 63.1, 25.8, 18.3, 16.0, -5.4, -5.5. HRMS (FAB, M+H) calcd for $C_{10}H_{24}NO_4Si$ 250.1475, found 250.1462. The enantiomeric excess of **4g** (98% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99.6/0.4, 1.0 mL/min, Minor; 33.1 min, Major; 35.0 min).



4h
syn/*anti* = 90/10
92% *ee*

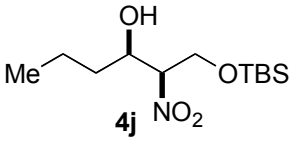
Compound **4h**. $[\alpha]_D^{24}$ = -5.3 (*c* 0.96, $CHCl_3$). IR (neat) 2955, 2929, 2857, 1554, 1463, 1389, 1361, 1255, 1085 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.60 (dq, *J* = 6.8, 6.8 Hz, 1H), 4.21 (ddd, *J* = 7.8, 7.8, 3.7 Hz), 3.95-3.84 (m, 2H), 3.77 (br s, 1H), 1.75-1.69 (m, 2H), 1.53 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ87.4, 73.1, 61.6, 33.9, 25.9, 18.2, 15.6, -5.5, -5.5. HRMS (FAB, M+H) calcd for $C_{11}H_{26}NO_4Si$ 264.1631, found 264.1654. The enantiomeric excess of **4h** (92% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 98/2, 1.0 mL/min, Major; 7.7 min, Minor; 9.2 min).



4i
syn/*anti* = 90/10
85% *ee*

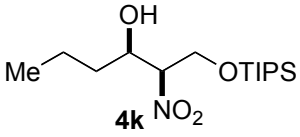
Compoud **4i**. $[\alpha]_D^{25}$ = +14.3 (*c* 1.11, $CHCl_3$). IR (neat) 3399, 2962, 2927, 2875, 1551, 1462, 1378 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.39 (m, 1H), 3.90 (br, 1H), 2.14 (br d, *J* = 7.3 Hz, 1H), 2.09-2.01 (m, 1H), 1.95-1.81 (m, 1H), 1.58-1.39 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.95 (dd, *J* = 7.7, 5.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ94.3.

71.5, 35.7, 35.7, 24.0, 18.6, 13.9, 10.3. The enantiomeric excess of **4i** (85% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99.5/0.5, 1.0 mL/min, Minor; 25.5 min, Major; 28.3 min).



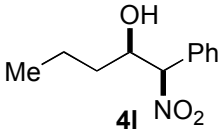
4j
syn/*anti* = 93/7
87% *ee*

Compoud **4j**. $[\alpha]_D^{25}$ = +14.5 (*c* 0.99, $CHCl_3$). IR (neat) 3434, 2958, 2930, 2883, 2858, 1555, 1465, 1390, 1362, 1258, 1120 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.56 (ddd, *J* = 7.7, 5.9, 3.9 Hz, 1H), 4.18 (dd, *J* = 11.4, 7.7 Hz, 1H), 4.04 (br, 1H), 4.02 (dd, *J* = 11.4, 3.9 Hz, 1H), 2.30 (br s, 1H), 1.62-1.43 (m, 4H), 0.95 (t, *J* = 5.7 Hz), 0.86 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 93.2, 69.5, 62.3, 35.7, 25.7, 18.6, 18.2, 13.8, -5.6, -5.6. HRMS (FAB, M+H) calcd for $C_{12}H_{28}NO_4Si$ 278.1788, found 278.1794. The enantiomeric excess of **4j** (87% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99.5/0.5, 1.0 mL/min, Minor; 25.5 min, Major; 28.3 min).



4k
syn/*anti* = 92/8
87% *ee*

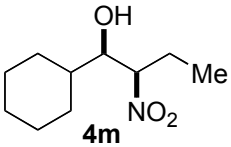
Compoud **4k**. $[\alpha]_D^{23}$ = +11.6 (*c* 0.42, $CHCl_3$). IR (neat) 2925, 2868, 1556, 1464, 1361, 1257, 1121 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (ddd, *J* = 7.6, 5.6, 3.9 Hz, 1H), 4.30 (dd, *J* = 11.0, 7.6 Hz, 1H), 4.14 (dd, *J* = 11.0, 3.9 Hz, 1H), 4.07 (br, 1H), 2.29 (d, *J* = 8.1 Hz, 1H), 1.57-1.47 (m, 4H), 1.05 (s, 18H), 1.04 (d, *J* = 5.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ93.7, 69.4, 62.8, 35.6, 29.8, 25.8, 18.6, 17.9, 17.9, 17.8, 13.8, 12.4, 11.9. HRMS (FAB, M+H) calcd for $C_{15}H_{34}NO_4Si$ 320.2257, found 320.2263. The enantiomeric excess of **4k** (87% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99.6/0.4, 1.0 mL/min, Minor; 23.4 min, Major; 27.3 min).



4l

syn/*anti* = 91/9
87% *ee*

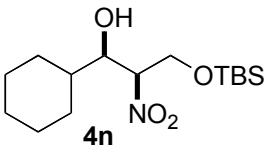
Compoud **4l**. $[\alpha]_D^{25}$ = +21.0 (*c* 1.05, $CHCl_3$). IR (neat) 3401, 2963, 2932, 2875, 2851, 1555, 1456, 1364 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.47-7.37 (m, 5H), 5.33 (d, *J* = 9.7 Hz, 1H), 4.57 (ddd, *J* = 9.7, 9.7, 2.9 Hz), 1.61 (m, 4H), 0.84 (t, *J* = 7.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.1, 130.2, 129.2, 128.0, 96.8, 72.3, 34.3, 18.2, 13.7. HRMS (FAB, M+Na) calcd for $C_{11}H_{15}NO_3Na$ 232.0950, found 232.0972. The enantiomeric excess of **4l** (87% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 98/2, 1.0 mL/min, Major; 26.7 min, Minor; 30.6 min).



4m

syn/*anti* = 99/1
95% *ee*

Compoud **4m**.[4] $[\alpha]_D^{26}$ = -1.1° (*c* 0.93, CHCl3). IR (neat) 2927, 2854, 1552, 1450, 1378, 1259 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.57 (ddd, *J* = 9.9, 6.0, 4.4 Hz), 3.62 (t, *J* = 6.0 Hz, 1H), 2.12-2.01 (m, 2H), 1.92-1.12 (m, 1H) 0.99 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 91.8, 76.0, 40.4, 29.9, 27.0, 26.2, 26.1, 26.1, 25.8, 24.1, 10.3. HRMS (FAB, M+H) calcd for $C_{10}H_{20}NO_3$ 202.1443, found 202.1412. The enantiomeric excess of **4m** (95% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 97/3, 1.0 mL/min, Minor; 21.4 min, Major; 25.7 min).

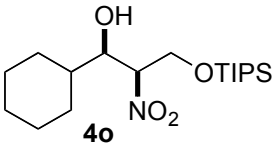


4n

syn/*anti* = 99/1
90% *ee*

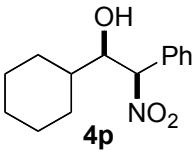
Compoud **4n**. $[\alpha]_D^{26}$ = +5.6 (*c* 1.00, $CHCl_3$). IR (neat) 2928, 2855, 1553, 1464, 1451, 1361, 1257, 1122 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.77 (ddd, *J* = 8.1, 5.3, 3.9 Hz, 1H), 4.21 (dd, *J* = 11.2, 8.1 Hz, 1H), 4.08 (dd, *J* = 11.2, 3.9 Hz, 1H), 3.69 (br, 1H), 1.86-1.62 (m, 11H), 0.87 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (75 MHz,

$CDCl_3$) δ 90.8, 74.2, 62.8, 40.6, 30.5, 29.6, 27.5, 26.1, 25.9, 25.7, 25.6, 18.1, -5.6, -5.7. HRMS (FAB, M+H) calcd for $C_{15}H_{32}NO_4Si$ 318.2101, found 318.2076. The enantiomeric excess of **4n** (90% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99.5/0.5, 1.0 mL/min, Minor; 23.1 min, Major; 33.2 min).



4o
syn/*anti* = 99/1
90% *ee*

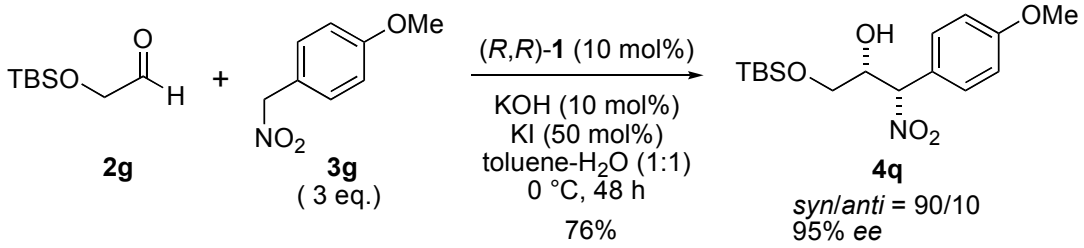
Compoud **4o**. $[\alpha]_D^{25}$ = +3.6 (*c* 1.07, $CHCl_3$). IR (neat) 2927, 2866, 1554, 1464, 1366, 1258, 1124 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 4.77 (ddd, *J* = 7.9, 5.3, 3.9 Hz, 1H), 4.31 (dd, *J* = 11.0, 7.9 Hz, 1H), 4.10 (dd, *J* = 11.0, 3.9 Hz, 1H), 3.73 (dd, *J* = 5.3, 5.3 Hz, 1H), 1.69-0.83 (m, 11H), 1.05 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 91.0, 74.0, 63.2, 40.6, 29.6, 27.4, 26.1, 25.9, 25.7, 17.8, 17.8, 17.7, 12.3, 11.8. HRMS (FAB, M+H) calcd for $C_{18}H_{38}NO_4Si$ 360.2570, found 360.2590. The enantiomeric excess of **4o** (90% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99.5/0.5, 1.0 mL/min, Minor; 18.2 min, Major; 27.3 min).



4p
syn/*anti* = 99/1
95% *ee*

Compoud **4p**. $[\alpha]_D^{25}$ = +12.4 (*c* 0.90, $CHCl_3$). IR (neat) 2927, 2853, 1554, 1451, 1368 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ7.49-7.38 (m, 5H), 5.53 (d, *J* = 9.9 Hz, 1H), 4.43 (dd, *J* = 9.9, 2.0 Hz, 1H) 1.95 (br, 1H), 1.72-0.88 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$) δ132.0, 130.2, 129.2, 128.1, 94.7, 76.2, 38.5, 30.3, 26.1, 26.0, 25.7, 24.7. HRMS (FAB, M+Na) calcd for $C_{14}H_{19}NO_3Na$ 272.1263, found 272.1299. The enantiomeric excess of **4p** (95% *ee*) was determined by means of chiral HPLC analysis. (CHIRALPAC AD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 99.5/0.5, 1.0 mL/min, Minor; 23.1 min, Major; 26.8 min).

Synthesis of (4*S*, 5*R*)-epi-cytoxazone (5)



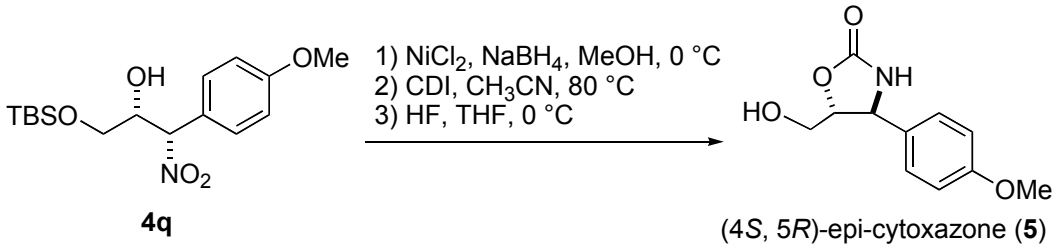
2g **3g** (3 eq.) **4q**

syn/*anti* = 90/10

95% *ee*

According to the typical procedure, the reaction of (*R*,*R*)-**1e** (55.1 mg, 0.0477 mmol), KI (39.7 mg, 0.239 mmol), (*t*-butyldimethylsiloxy)acetaldehyde (**2g**) (83.2 mg, 0.477 mmol) and **3g** [5] (239 mg, 1.43 mmol) afforded **4q** (124 mg, 76%).

$[\alpha]_D^{25}$ = +21.7 (*c* 0.82, $CHCl_3$). IR (neat) 2952, 2928, 2856, 1612, 1556, 1515, 1464, 1254 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ7.41 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 5.48 (d, *J* = 10.9 Hz, 1H), 4.53 (m, 1H) 3.82 (s, 3H), 3.60 (dd, *J* = 10.5, 3.1 Hz, 1H), 3.29 (dd, *J* = 10.5, 3.3 Hz, 1H), 0.88 (s, 9H), 0.00 (s, 3H), -0.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ161.0, 129.6, 123.7, 114.5, 93.3, 72.8, 62.5, 55.3, 25.8, 18.2, -5.6. HRMS (FAB, M+Na) calcd for $C_{16}H_{27}NO_5SiNa$ 364.1556, found 364.1547. The enantiomeric excess of **4q** (95% *ee*) was determined by means of chiral HPLC analysis. (CHIRALCEL OD-H, 0.46 cm (ϕ) × 25 cm (L), *n*-hexane/2-propanol = 97/3, 1.0 mL/min, Major; 8.5 min, Minor; 10.1 min).



4q (4*S*, 5*R*)-epi-cytoxazone (**5**)

To a mixture of **4q** (85.1 mg, 0.249 mmol), $NiCl_2$ (64.6 mg, 0.498 mmol) in MeOH (3.0 mL) was added $NaBH_4$, (94.2 mg, 2.49 mmol) at 0 °C, and the resulting mixture was stirred vigorously at 0 °C for 10 min. The resulting mixture was filterd though a

pad of Celite. The filtrates were concentrated *in vacuo*, and the residure was purified by column chromatography on silica gel (chloroform/methanol = 1:0, 9:1, 5:1) to give amine. To a solution of the amine in acetonitrile (3 mL) was added *N*, *N*'-carbonyldiimidazole (151 mg, 0.930 mmol) at room temperature, and the resulting mixture was stirred for 18 h at 80 °C. The reaction mixture was concentrated under reduced pressure and the residure was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 5/1, 2/1) to give oxazolidinone (56.2 mg, 54%, 2 steps).

$[\alpha]_D^{24}$ = -25.9 (*c* 1.30, $CHCl_3$). IR (neat) 3269, 2953, 2927, 2855, 1756, 1613, 1515, 1463, 1387, 1250, 1176, 1141, 1101, 1037 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ7.26 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 5.17 (br s, 1H), 4.80 (d, *J* = 6.1 Hz, 1H), 4.33 (m, 1H), 3.88 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.82 (s, 3H), 3.77 (dd, *J* = 11.5, 3.5 Hz, 1H), 0.91 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ159.8, 158.9, 131.9, 127.5, 114.5, 84.7, 62.4, 57.2, 55.3, 25.8, 18.2, -5.4, -5.5. HRMS (FAB, M+H) calcd for $C_{17}H_{28}NO_4Si$ 338.1788, found 338.1759.

To a solution of the oxazolidinone (37.6 mg, 0.111 mmol) in acetonitrile (3 mL) was added HF-py (0.10 mL) at 0 °C. After stirring for 3 h, saturated $NaHCO_3$aq (1 mL), $NaHCO_3$ (30 mg) and $MgSO_4$ was added. The resulting mixture was filterd though a pad of Celite. The filtrates were concentrated *in vacuo*, and the residure was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 2/1, 1/3) to give **5** (19.9 mg, 80%). [6]

$[\alpha]_D^{23}$ = -24.3 (*c* 1.20, CH_3OH). IR (KBr) 3253, 3145, 1742, 1725, 1515, 1252, 1101, 1022 cm^{-1}. ^1H NMR (400 MHz, acetone-d_6) δ7.32 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 4.77 (d, *J* = 6.4 Hz, 1H), 4.24 (ddd, *J* = 6.4, 4.4, 3.9 Hz, 1H), 3.81 (dd, *J* = 12.4, 3.9 Hz, 1H), 3.79 (s, 3H), 3.70 (dd, *J* = 12.4, 4.4 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6) δ160.4, 158.8, 133.7, 128.2, 114.9, 85.5, 62.3, 57.6, 55.5. HRMS (FAB, M+H) calcd for $C_{11}H_{14}NO_4$ 224.0923, found 224.0915.

References

(1) Denmark, S. E.; Kesler, B. S.; Moon, Y, -C. *J. Org. Chem.* **1992**, *57*, 4912.

(2) Sasai, H.; Tokunaga, T.; Watanabe, S.; Suzuki, T.; Itoh, N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388.

(3) Kisanga, P. B.; Verkade, J. G. *J. Org. Chem.* **1999**, *64*, 4298.

(4) Barrett, A. G. M.; Seefeld, M. A.; White, J. P.; Williams, D. J. *J. Org. Chem.* **1996**, *61*, 2677.

(5) Ballini, R.; Barboni, L.; Giarlo, G. *J. Org. Chem.* **2004**, 69, 6907.

(6) Sakamoto, Y.; Shiraishi, A.; Seonhee, J.; Nakata, T. *Tetrahedron Lett*. **1999**, *40*, 4203.